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ABSTRACTS COLLECTION

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Acute Leukemia

P001.

Measurable Residual Disease, FLT3-ITD Mutation And Disease Status Have Independent Prognostic Influence on Post-Transplant Outcomes in NPM1-Mutated Acute Myeloid Leukemia

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Background: Nucleophosmin-1 (NPM1) mutations in acute myeloid leukemia (AML) confer a survival advantage in the absence of *FLT3*-internal tandem duplication (*FLT3*-ITD). Current data suggest that the concomitant presence of *FLT3*-ITD and NPM1, MRD positivity before or after transplant, and disease status at the time of transplant influence the risk of post-transplant relapse and thus affect outcome. Nonetheless, the respective and independent contributions of these factors remain largely unknown.

Methods: Here we investigated the main predictors of outcome after allogeneic hematopoietic stem cell transplantation (allo-HCT) in AML patients with NPM1 mutation. We identified 1572 adult (age ≥ 18 years) patients with NPM1-mutated AML in first complete remission (CR1: 78%) or second complete remission (CR2: 22%) who were transplanted from matched sibling donors (30.8%), matched unrelated donors (33.7%), mismatched unrelated donors

(7.6%) and haploidentical donors (11.8%) between 2007 and 2019 at EBMT participating centers.

Results:

	Relapse		NRM		LFS		OS	
	HR (95% CI)	*p* value	HR (95% CI)	*p* value	HR (95% CI)	*p* value	R (95% CI)	*p* value
CR2 *versus* CR1	1.36 (1.04–1.77)	0.026	1.08 (0.76–1.55)	0.66	1.26 (1.02–1.57)	0.033	1.17 (0.92–1.49)	0.20
FLT3-ITD	1.66 (1.28–2.16)	0.0001	1.28 (0.91–1.81)	0.15	1.53 (1.24–1.88)	0.00006	1.6 (1.26–2.03)	0.0001
MRD positivity	2.18 (1.76–2.71)	$<10^{-5}$	1.07 (0.8–1.45)	0.64	1.71 (1.44—2.04)	$<10^{-5}$	1.61 (1.32–1.96)	$<10^{-5}$
Age (per 10 years)	0.93 (0.84–1.02)	0.14	1.41 (1.21–1.64)	$<10^{-5}$	1.06 (0.98–1.15)	0.14	1.22 (1.1–1.34)	0.00007
UD	0.91 (0.71–1.16)	0.44	1.79 (1.22–2.63)	0.003	1.12 (0.92–1.38)	0.26	1.35 (1.07–1.71)	0.012
Haplo	0.7 (0.47–1.06)	0.089	2.63 (1.61–4.3)	0.0001	1.14 (0.84–1.54)	0.41	1.45 (1.02–2.05)	0.037
KPS≥90	0.74 (0.58–0.94)	0.012	0.65 (0.48–0.88)	0.006	0.7 (0.58–0.85)	0.0002	0.73 (0.59–0.91)	0.004

Median follow up for survivors was 23.7 months. *FLT3*-ITD was present in 69.3% of patients and 39.2% had detectable minimal/measurable residual disease (MRD) at transplant. In multivariate analysis, relapse incidence (RI) and leukemia-free survival (LFS) were negatively affected by concomitant *FLT3*-ITD mutation (HR 1.66 $p = 0.0001$, and HR 1.53 $p = 0.00006$, respectively), MRD positivity at transplant (HR 2.18 $p < 10^{-5}$ and HR 1.71 $p < 10^{-5}$, respectively), and transplant in CR2 (HR 1.36 $p = 0.026$, and HR 1.26 $p = 0.033$, respectively), but positively affected by Karnofsky performance score ≥90 (HR 0.74 $p = 0.012$, and HR 0.7 $p = 0.0002$, respectively). Overall survival was also negatively influenced by concomitant *FLT3*-ITD (HR 1.6, $p = 0.0001$), MRD positivity at transplant (HR 1.61, $p < 10^{-5}$) and older age (HR 1.22, $p = 0.0007$), but positively affected by matched sibling donor (unrelated donor: HR 1.35, $p = 0.012$; haploidentical donor: HR 1.45, $p = 0.037$) and Karnofsky performance score ≥90 (HR 0.73, $p = 0.004$). Similarly, in subgroup analysis, among patients harboring *FLT3*-ITD, MRD positivity negatively affected RI, LFS and OS (22% vs 38.7%, $p = 0.001$; 63% vs 46.9%, $p = 0.001$ and 70.3% vs 55.8%, $p = 0.001$, respectively) which was comparable to the impact of MRD positivity on RI and LFS in *FLT3*-wt NPM1-mutated AML (26.9% vs 17.7%, $p = 0.001$ and 55.3% vs 67.1%, $p = 0.003$, respectively).

Conclusions: These results highlight the independent and significant roles of *FLT3*-ITD, MRD status, and disease status on post-transplant outcomes in patients with NPM1-mutated AML allowing physicians to identify patients at risk of relapse who may benefit from post-transplant prophylactic interventions.

Disclosure: Nothing to declare.

P002.

Azacytidine And Donor Lymphocyte Infusions (DLI) as Salvage Treatment in Patients with AML And MDS Relapsed After Allogeneic Stem Cell Transplantation: A Retrospective Single Center Analysis

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Background: Patients with acute myeloid leukemia (AML) and myelodysplastic syndrome (MDS) relapsing after allogeneic hematopoietic stem cell transplantation (HSCT) have poor prognosis with 2-year survival rates of less than 20%.

Methods: A total of 27 consecutive adult AML/MDS patients were treated in a single center with Azacytidine with or without DLI for post-transplant relapse. Azacytidine was administered mainly in an out-patient setting at a dose of 100 mg/m2 from d1-5 or 75 mg/m2 from d1-7 every 28 days according to the individual decision of the treating physician. DLI were infused at escalating doses (from 1 × 106 to 1 × 108 CD3+/kg) at day 8 of every second cycle starting from the second cycle. Each case was reviewed and approved by the Hospital Commission for Off Label Use of Drugs.

Results: After a median of 257,5 (range: 59–5226) days from HSCT, morphological ($n = 26$) or molecular ($n = 1$) relapse of AML ($n = 21$) or MDS ($n = 6$) was diagnosed.

The median number of Azacytidine cycles was $n = 2$ (range 1–24), whereas the median number of DLI was $n = 2$ (range: 1–6). Of note, 15 patients did not receive DLI, mainly due to disease progression ($n = 5$) and GVHD ($n = 5$). During treatment a total of 19 adverse events were documented, including pneumonia ($n = 9$, 33%), fever of unknown origin ($n = 5$, 19%), a dental and a perianal abscess, a central venous catheter infection, a blood stream infection due to gram negative rod and a cholangitis. Interestingly, in 6 (22,2%) patients no complication emerged during therapy whereas in 10 (37%) cases complications evolved under disease progression. In the course of treatment 3 patients developed GVHD that responded to immunosuppressive treatment. Overall, after a median of 147 (range: 72–892) days, 6 patients (22,2%) achieved a complete remission and 5 patients (19%) a stable disease resulting in an overall response rate of 41,2%. Among all responding patients after a median follow up of 388 (range: 77–1180) days 2 patients are still alive and in complete remission.

Conclusions: Given its acceptable toxicity and ease of administration, the present results emphasize a role for Azacytidine and DLI as a novel treatment strategy in patients with relapsed AML/MDS after allogeneic HSCT.

Clinical Trial Registry: Not applicable.

Disclosure: Nothing to declare.

P003.

T-Cell-Deplete Allogeneic Haematopoietic Stem Cell Transplant After Reduced-Intensity Conditioning for Myeloid Malignancies in the Over-65s – A Single Centre Experience of 90 Patients

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Background: For patients with high-risk myeloid malignancies, allogeneic haematopoietic stem cell transplantation (alloSCT) brings the benefits of the graft-versus-leukemia effect, and offers the best chance of cure. However, the intensity of myeloablative conditioning regimens have historically precluded its use in older patients. More recently, the development of reduced-intensity conditioning (RIC) regimens has brought the option of alloSCT to an older population: the current increase in transplant rates is largely driven by adoption of RIC protocols in this patient group. In the absence of prospective data regarding different alloSCT approaches, current evidence is largely driven by retrospective analysis of patient outcomes. We report our experience from a large transplantation center in delivering alloSCT to older patients.

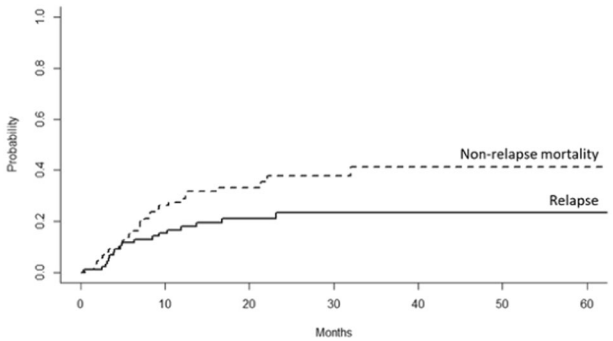
Methods: Consecutive patients aged 65 or over, who underwent RIC alloSCT, were retrospectively identified at University Hospitals Birmingham NHS Foundation Trust, a tertiary hematology unit in the UK. Key demographic, disease, transplant and outcome data were extracted from the patient records, and used to perform exploratory analyses of our experience.

Results: A total of 90 patients were identified (median age 68, range 65 to 75; 73% men), who between January 2010 and August 2020 had received alloSCT for acute myeloid leukemia (57%), myelodysplasia (33%), chronic myelomonocytic leukemia (6%), and myelofibrosis (4%). The majority (89%) had unrelated donors, although a sibling donor was available and used in 10%. Most patients (66%) underwent fludarabine/melphalan conditioning, 22% received fludarabine/busulfan; T-cell depletion was with alemtuzumab in 80% and anti-thymocyte globulin in 19%.

Grade 3–4 acute graft-versus-host disease was observed in 19% of patients, CMV reactivation occurred in 40%, and 7 deaths (8% of patients) within 100 days were attributed to transplant complications. Non-relapse mortality at 1 and 2 years post-alloSCT occurred in 28% and 38%, respectively, censoring for relapse as a competing risk. Disease relapse was demonstrated in 18% and 23% of patients at 1 and 2 years post-alloSCT, respectively, with non-relapse mortality as a competing risk (see figure). with a median follow-up of 30 months, the median overall survival in this patient cohort is 20 months (95% confidence interval (CI) 10 to 30 months). 5-year overall survival is estimated at 29% of patients (95% CI 17% to 42%).

Overall survival is imperfectly predicted by haematopoietic stem cell transplant-specific comorbidity index (hazard ratio (HR) 1.7 for patients with a score of 2 or more, $p = 0.08$) or disease risk index (HR 2.8 for intermediate- or high-risk disease, $p = 0.09$). Within this cohort, age was not associated with survival ($p = 0.56$).

Conclusions: in our large cohort of older patients undergoing alloSCT for high-risk myeloid malignancies, up to one third benefit from long-term survival. Most deaths during follow-up were due to non-relapse causes, likely reflecting the higher baseline morbidity in this patient group, and the accumulated toxicities of the induction and transplant regimens. to better serve this important population and address the significant non-relapse mortality, prospective trials are needed to establish the optimal conditioning and post-alloSCT treatment strategies. This could be aided through improving pre-treatment assessments that more accurately quantify the risk of the older patient.



Disclosure: Nothing to declare.

P004.

Allogeneic Stem Cell Transplantation in First Complete Remission is Associated with Superior Outcomes in Acute Myeloid Leukemia Independent of Recipient Age And Donor Type

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Athanasiadis[1], Marina Papageorgiou[1], Maria-Eleni Karatza[1], Dimitra Oikonomopoulou[1], Sosana Delimpasi[1], Maria Bouzani[1], Maria Pagoni[1], Themistoklis Karmiris[1], Stavros Gigantes[1], Ioannis Baltadakis[1], Dimitrios Karakasis[1]

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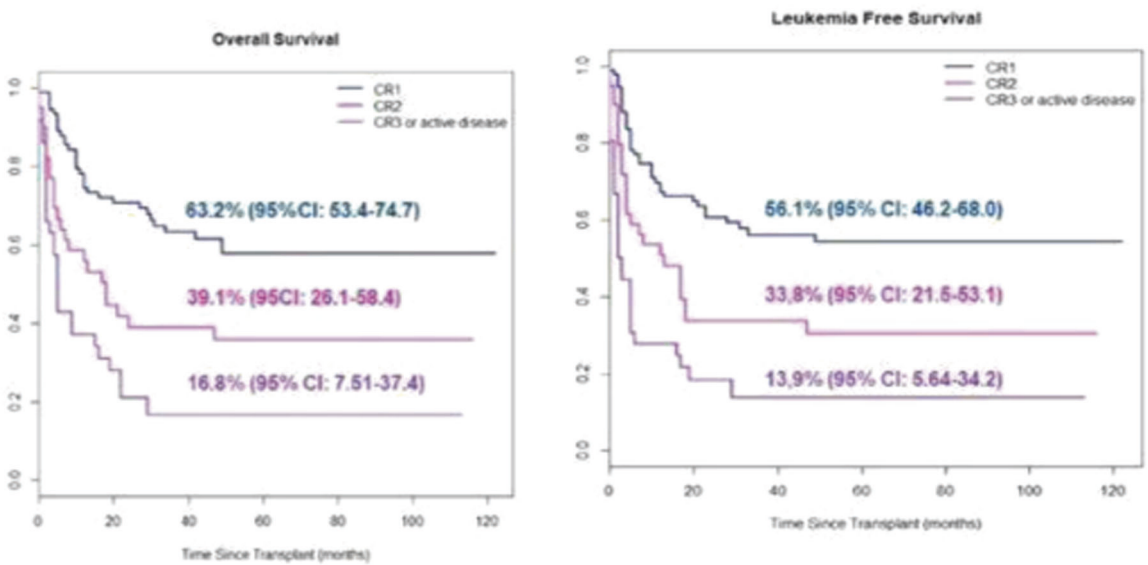
Background: Improvements in donor availability and use of alternative donors over the last decade have enabled access to allogeneic stem cell transplantation (allo-SCT) in virtually all patients with acute myeloid leukemia (AML), who comprise a significantly heterogeneous population. Aim of the study was the investigation of the outcomes of allo-SCT during a recent time period, as well as the examination of patient-, disease-, and transplant-related factors that may affect transplantation outcomes.

Methods: The study enrolled 166 consecutive patients (female: 84, male: 82), who received first allo-SCT for de novo ($n = 131$, 78.9%) or secondary ($n = 35$, 21.1%) AML over a 10-year period (from 01/2010 to 05/2020). The median age of recipients was 47.5 years (range, 17–72). The majority were transplanted in 1st ($n = 91$, 54.8%) or 2nd ($n = 39$, 23.5%) complete remission (CR), whereas 36 (21.7%) had more advanced phase of disease at transplant. Donor type was HLA identical sibling ($n = 53$, 31.9%), 8/8 matched unrelated ($n = 50$, 30.1%), 7/8 matched unrelated ($n = 29$, 17.4%), haploidentical relative ($n = 24$, 14.5%) or double umbilical cord blood ($n = 10$, 6.1%). The conditioning regimen was myeloablative in 82.5% of cases. Factors included in univariate analysis for overall (OS) and leukemia-free survival (LFS) were recipient age group (<40, 40–60, and >60 years), hematopoietic cell transplantation comorbidity index (HCT-CI), disease phase at allo-SCT, donor type, AML type (de novo vs. secondary), European Leukemia Net (ELN) risk category (2010), and Disease-Related Index (DRI). Multivariate analysis was performed by Cox regression.

Results: Engraftment of neutrophils was achieved in 95% of cases by day +28. The cumulative incidence of grade II-IV acute GVHD and moderate/severe chronic GVHD was 42.3% at 6 months and 31.6% at 12 months, respectively. The cumulative incidence of non-relapse mortality (NRM) and relapse was 28.6% and 29.6% at 3 years, respectively. OS and LFS were 47.6% and 41.8% at 3 years, respectively. In univariate analysis, factors significantly associated with OS and LFS were disease phase at transplant ($p < 0.0001$) and HCT-CI ($p < 0.05$). Recipient age was significantly correlated with OS ($p = 0.02$), but not with LFS ($p = 0.1$). By contrast, donor type did not emerge as a significant risk factor for survival. In multivariate analysis, only disease phase remained an independent risk factor for OS (Hazard ratio [HR]: 1.92, 95% Confidence Interval [CI]: 1.40–2.63, $p < 0.0001$) and OS (HR: 1.89, 95% CI: 1.41–2.53, $p < 0.0001$). In the subgroup of patients who were transplanted in 1st CR, OS and LFS at 3 years reached 63.2% (95% CI: 53.4–74.8%) and 56.1% (95% CI: 46.2–68.0%), respectively. On the other hand, OS and LFS were significantly inferior in patients transplanted in 2nd CR or more advanced disease phase (Figure).

Conclusions: Given the curative potential of allo-SCT for AML and the comparable results with matched or alternative donors, timely transplantation in 1st CR represents the single most important prognostic factor of a favorable outcome. Early referral for transplant and initiation of donor search from the time of diagnosis is therefore warranted.

Disclosure: Nothing to declare.



P005.

Gilteritinib Monotherapy in Relapsed or Refractory Acute Myeloid Leukemia Flt3+ in Adult Patients

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Background: FMS-like tyrosine kinase 3(FLT3) gene mutations occur in 20–30% of adult patients with acute myeloid leukemia(AML). FLT3-ITD mutations are most commonly observed and have prognostic significance in patients with normal karyotype. After relapse(Rel) remissions are rarely achieved with chemotherapy and are usually very short. In 2018 the FDA approved a second-generation FLT3-inhibitor gilteritinib(Gilt) for the treatment of relapsed and refractory(r/r) AML FLT3+.

Methods: The study included 32 patients (median age 56 (18–79) years) with r/rAML who received Gilt monotherapy at a dose of 120 mg/d. Median follow-up was 7(2–16) months. FLT3-ITD mutation was detected in 29(91%), FLT3-TKD mutation in 3(9%) patients. Additionally, NPM1 was detected in 4, WT1 and BAALC overexpression in 18 and 2 patients, respectively. The intermediate prognostic group ELN2017 (PG-ELN2017) included 21(66%) patients, 12 of them with normal karyotype. The unfavorable group included 11(34%) pts, 4 of them with a complex karyotype, 5 with t(6;9)(p23;q34). Eleven (34%), 16(60%) and 5(15%) pts had primary resistance(PrRes), Rel1 and Rel2, respectively. AlloHSCT was performed after Gilt therapy in 8(25%) pts, 6(19%) pts received Gilt in relapse after alloHSCT. The median duration of therapy was 4(1–12) cycles.

Results: Overall(OS) and event-free(EFS) survival were 36% (95% CI, 17–55) and 28% (95% CI, 6–50). Complete remission (CR) was achieved in 9 (28%), CR with incomplete hematological recovery (nCR) in 7 (22%) pts. An overall response rate (ORR) was 50% (16/32). All but one pts who achieved CR responded to the first cycle. Three pts achieved nCR after the first and 4 pts after the second cycle. The ORR did not depend on PG-ELN2017 and the level of blasts. The ORR was 64% (7/11) in PrRes, 50% (8/16) in Rel1 and only 20% (1/5) in Rel2. The median CR duration was 5.5 (1.5–16.3) months. OS and EFS of ORR pts were 58% (95% CI, 29–87) and 45% (95% CI, 12–78), Rel incidence was 25% (4/16), at 1, 3 and 10 months. Causes of death were AML progression ($n = 10$), infections ($n = 6$) and cerebral hemorrhage ($n = 1$). Currently 47% (15/32) of pts are alive.

Adverse events were nausea, shortness of breath, increased blood pressure, increase ALT and AST 2–3 gr 6% (2/32) each, bone and joint pains 12% (4/32), edema and skin itching 16% (5/32) each, febrile neutropenia 41% (13/32), neutropenia 3–4 gr 78% (25/32), thrombocytopenia 3–4 gr 56% (18/32), infectious complications 28% (9/32), of which 4 pneumonia, 6 sepsis. No cases of differentiation syndrome were observed. No drug withdrawal was required.

Conclusions: This study demonstrated efficacy and an acceptable toxicity profile of Gilt in adult patients with r/r AML before and after alloHSCT.

Disclosure: Nothing to declare.

P006.

Venetoclax Combined with Azacitidine or low-dose Cytarabine for Relapsed Acute Myeloid Leukemia Post Allogeneic Stem Cell Transplant

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Background: The effectiveness of Venetoclax in combination with Azacitidine (VEN/AZA) or low-dose Cytarabine (VEN/CYT) for first-line treatment of patients with AML, who are unfit for intensive chemotherapy, is well-established. Data on its role in the relapsed/refractory (R/R) setting are emerging, although there are limited data regarding its use specifically in relapse post allogeneic stem cell transplant (Allo-SCT).

Methods: A single-center retrospective analysis was carried out on 12 patients treated with VEN/AZA or VEN/CYT for relapsed disease post Allo-SCT at the Royal Marsden Hospital from 2019–2020.

Results: Patient Characteristics are shown in table 1. The median time from transplant to first relapse of AML was 1.8 years (range 0.2–5.9). Five patients (42%) had de novo AML, 1 (8%) therapy-related AML and 6 (50%) previous MDS/MPN. Ten patients (83%) had adverse cytogenetic or molecular abnormalities. Six patients received VEN/AZA and 6 VEN/CYT.

Response was assessed after 2 cycles of treatment. Eight patients (67%) achieved complete remission with

incomplete hematologic recovery (CRi), as defined by ELN criteria. Three (25%) were primary refractory and 1 (8%) died of sepsis during cycle 1. Two patients proceeded to second Allo-SCT in second remission.

Median follow up of live patients was 102 days (33–406). Median duration of response was 65 days (range 5–345): 50 days (range 5–183) for VEN/AZA and 80 days (41–345) for VEN/CYT. Median overall survival was 124 days for VEN/AZA and 110 days for VEN/CYT, $p = 0.8$. Median progression free survival was 120 days for VEN/AZA and 80 days for VEN/CYT, $p = 0.4$.

Ten patients (83%) developed grade 3/4 infections. Infection rates were comparable for VEN/AZA and VEN/CYT (5/6 patients in each). Other adverse events included DIC (1 patient). No tumor lysis syndrome was observed.

There were 5 treatment-related deaths (4-infection, 1-acute neuropathy post second-SCT). Two patients died of progressive disease.

Table 1

	Patient Characteristics	N=
Sex	Male: Female	6 (50%): 6 (50%)
Age	Median age (range)	59 (18–71)
AML subtype	De novo	5 (42%)
	Therapy-related	1 (8%)
	Previous MDS/MPD	6 (50%)
Cytogenetic/ Molecular abnormalities	Non adverse	2 (17%)
	Adverse	10 (83%)
HCT- CI	0	9 (75%)
	1–2	2 (17%)
	3 or above	1 (8%)
No. Of prior lines of treatment	0	4 (33%)
	1	3 (25%)
	2	2 (17%)
	3	3 (25%)
Donor type (of first Allo-SCT)	Sibling donor	1 (8%)
	MUD	11 (92%)
Conditioning (of first Allo-SCT)	Myeloablative	3 (25%)
	Reduced intensity	9 (75%)
Combination treatment	Venetoclax-Azacitidine	6 (50%)
	Venetoclax- low-dose Cytarabine	6 (50%)

Conclusions: VEN/AZA or VEN/CYT is a potential therapeutic option for treatment of relapsed AML post Allo-SCT. High initial response rates were seen although duration of response was short. There were very high rates of infectious complications, reflecting the heavily immunocompromised patient group and risks of profound and prolonged neutropaenia with these regimens. This treatment could be considered as a bridging strategy to second transplant, but with careful patient selection. Treatment breaks between cycles is recommended to allow neutrophil recovery, with GCSF support once CR documented. Use of these regimens for R/R AML post Allo-SCT should be assessed further in a prospective study.

Disclosure: Nothing to declare.

P007.

Long-Term Outcome of Allogeneic Stem Cell Transplantation in Patients with Acute Myeloid Leukemia – Focus on Mortality

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Background: Allogeneic hematopoietic cell transplantation (alloHCT) is a standard treatment of high risk or relapsed patients (pts) with acute myeloid leukemia (AML). The outcome of the procedure is influenced not only by relapse, but also non-relapse mortality (NRM). Herein we present a retrospective analysis of the long-term outcomes of alloHCT in pts with AML in one institution with focus on mortality.

Methods: The study group consisted of 209 de novo AML pts, median age 46 years (range, 18–69), transplanted in our institution between 2007–2017, from HLA-identical sibling (29%) or 9–10/10 matched unrelated donor (71%) in first complete remission (CR1) (58%) with intermediate to adverse genetics or beyond CR1 (42%), who were conditioned with myeloablative (42%) or reduced intensity (58%) therapy. The stem cells were collected from peripheral blood (83%) or bone marrow (17%). Graft versus host disease (GvHD) prophylaxis consisted of calcineurin inhibitor combined with methotrexate or mycophenolate mofetil, plus ATG in 152 patients (73%). Only first transplants were analyzed.

Results: in the whole cohort 136 (65%) pts were transplanted with low HCT-CI, while intermediate or high were assessed in 67 (32%) or 6 (3%), respectively. Only 25 (12%) pts were older than 60 years. Within a median follow-up of 55.5 (range 1–138) months acute GvHD was diagnosed in 66 (32%) pts, chronic in 111 (53%). Relapse of disease occurred in 71 pts, mostly within first 3 years after alloHCT (90%). Relapse incidence (RI) at 36 months was 36%.

During follow-up the median OS was 86 months, and 97 (46%) pts died. Relapse of disease was the main reason for death (54 pts), however a number of pts died because of infections (19 pts) or GvHD (12 pts). Most of fatal infections were bacterial, caused by resistant Gram negative pathogens.

The 3-year estimated overall survival (OS) was 54% and the relapse free survival (RFS) was 49%. In multivariate analysis CR1 before alloHCT was the prognostic variable for longer OS (HR 0.557; $p < 0.001$) and RFS (HR 0.584; $p < 0.001$) and adverse genetics for shorter OS (HR 1.656; $p < 0{,}001$) and RFS (HR 1.806; $p < 0.001$). For pts over 60, OS and RFS did not differ significantly ($p = 0.224$ and 0.188).

In multivariate analysis CR1 before alloHCT favorably influenced RI (HR 0.53, $p = 0.027$), but adverse genetics unfavorably (HR 3.073; $p < 0.001$).

The 1-year cumulative incidence of non-relapse mortality (NRM) was 17.2% and has increased up to 20.3% at 3 year. Age >60 did not influenced NRM significantly, but intermediate and high HCT-CI score correlated with higher NRM as an variable in multivariate analysis for all pts (HR 2.973; $p < 0.001$).

Conclusions: Long-term observations of pts with AML after alloHCT indicate that relapse is the main issue and cause of death. Most relapses occur within first 3 years after alloHSCT, after which relapses are rare and the risk of death is low. Substantial incidence of deaths are related to infectious complications. The probability of survival does not differ significantly between younger and older pts and the most important factor which influence the risk of NRM is HCT-CI.

Disclosure: Nothing to declare.

P008.

Sorafenib Maintenance After Hematopoietic Stem Cell Transplantation Improves Outcome of FLT3-ITD Positive Acute Myeloid Leukemia

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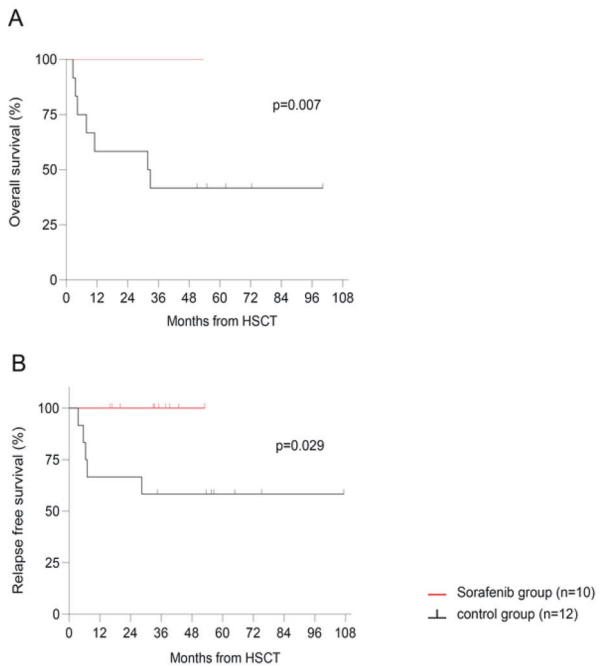
Background: Relapse of FLT3-ITD mutated acute myeloid leukemia (AML) after allogeneic hematopoietic stem cell transplantation (HSCT) has a miserable outcome with a 1-year survival below 20%. Recently, initial reports refer promising improvements in preventing relapse with single Sorafenib maintenance in post allogeneic HSCT complete remission (CR) patients.

Methods: in the present study a total of 13 patients of two Italian hematologic centers received Sorafenib in CR after allogeneic HSCT. Their outcome was confronted retrospectively with a control group of 17 patients that in CR after allogeneic HSCT did not receive Sorafenib. Only adult FLT3-ITD patients were included in both groups, FTL3-TKD patients were excluded. Each clinical case was reviewed by the Hospitals Commissions for Off Label Use of Drugs, which assessed the benefit-risk balance and licensed the treatment of each individual patient.

Results: Patients baseline and transplant characteristics, including disease stage at transplant were comparable in both groups. Sorafenib was initiated after a median of 81 (range: 29 – 232) days after allogeneic HSCT with a median daily dosage of 200 (range: 200 – 800) mg orally and lasted a median of 365 (range: 7- 853) days. Eleven patients were able to reach at least the maximum dose of 400 mg per day. Treatment was neither associated with higher incidence of graft versus host disease (GVHD) nor with enhanced toxicity compared to the control group. Adverse effects were manageable with dose adjustment/temporary discontinuation of the drug and revealed reversible in all 10/11 cases. with a median follow up of 33 (range: 3,8–43,3) months Sorafenib maintenance improved significantly overall survival (100%) and relapse-free survival (90,1%), especially in patients that went in first CR at transplant, $p = 0.007$ and $p = 0.029$, respectively.

Conclusions:

OS and RFS of the patients that in CR underwent HSCT and received Sorafenib post transplant



In conclusion, the present data indicates that Sorafenib maintenance after allogeneic HSCT is safe and may prolong overall and relapse-free survival in FLT3-ITD patients. The impact of FLT3 inhibitors is addressed in ongoing trials and will help us to understand the biology between FLT3-inhibitor maintenance therapy and allo-immunogeneity.

Clinical Trial Registry: Not applicable.

Disclosure: Nothing to declare.

P009.

Baseline Somatic Mutations Predict Disease Free Survival After Allogeneic Stem Cell Transplantation in Acute Myeloid Leukemia: A Retrospective Monocentric Report

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Background: in the last years the advent of Next Generation Sequencing (NGS) contributed to the identification of new somatic mutations involved in the leukemogenesis process, allowing a revised stratification of the biological risk for acute myeloid leukemia (AML) and providing a new tool for minimal residual disease evaluation.

Methods: We enrolled 64 patients with AML submitted to allogeneic stem cell transplantation (HSCT) in our department between November 2015 and September 2020. NGS panel performed at diagnosis included 18 genes: CBL, SF3B1, U2AF1, ZRSR2, KRAS, ASXL1, CEBPA, KIT, DNMT3A, EZH2, IDH1, IDH2, RUNX1, SRSF2, TET2, TP53, WT1, NRAS.

Results: Mutation distribution was as follows: CBL ($n = 1$), SF3B1 ($n = 1$), U2AF1 ($n = 1$), ZRSR2 ($n = 1$), KRAS ($n = 1$), ASXL1 ($n = 9$), CEBPA ($n = 9$), KIT ($n = 15$), DNMT3A ($n = 22$), EZH2 ($n = 17$), IDH1 ($n = 10$), IDH2 ($n = 10$), RUNX1 ($n = 6$), SRSF2 ($n = 2$), TET2 ($n = 30$), TP53 ($n = 3$), WT1 ($n = 6$), NRAS ($n = 4$). Median age was 55.5 years (17–73). Risk group according to European Leukemia Net was as follows: favorable ($n = 8$), intermediate ($n = 42$), adverse ($n = 14$). Thirty-nine patients achieved a first complete remission before transplant, 8 were in second remission, 14 had relapsed disease and 3 received HSCT upfront. A significant difference in terms of DFS was found accordingly to some mutations. Patients mutated for TP53 ($n = 3$) showed a 6 months DFS of 66.7% as compared to 81.4% in non mutated ($n = 61$) ($p = 0.02$). Mutated WT1 patients ($n = 6$) had a 6 months DFS of 40% as compared to 84.8% in non mutated ($n = 58$) ($p = 0.047$). Six-months DFS was of 63.5% and 83% in patients with ($n = 4$) and without ($n = 60$) NRAS mutation, respectively ($p = 0.005$). Accordingly to FLT3 mutation, 6 months DFS was of 63.5% in mutated patients ($n = 14$) as compared to 83% for non mutated ($n = 49$) ($p = 0.048$). Multivariate analysis for DFS confirmed TP53 (HR 12.96, 95% CI 4.16–39.61, $p = 0.0009$), WT1 (HR 5.03, 95% CI 1.08–23.37, $p = 0.04$), FLT3 (HR 4.63, 95% CI 1.22–17.50, $p = 0.02$) and NRAS (HR 8.17, 95% CI 4.42–39.62, $p = 0.0004$) together with absence of complete remission at the time of transplant (HR 7.89, 95% CI 2.23–27.92, $p = 0.001$) as independent factors for relapse after transplant. Moreover, we found a detrimental impact of triple mutation FLT3-+NPM1+DNMT3A on DFS. Patients with any of these mutations ($n = 30$) had 6 months DFS of 85.2% as compared to 89.8% for patients with one or two mutations ($n = 23$) and 50% in patients triple mutated ($n = 8$) ($p = 0.04$). We then evaluated if a difference might be in young (<60 years) and old patients in terms of mutations influence. TP53, WT1, FLT3 and triple mutation DNMT3A, FLT3 and NPM1 were confirmed in young whereas only NRAS was confirmed in old patients.

Conclusions: The presence of some mutations like as WT1, TP53, NRAS, FLT3 or concomitant mutated status for FLT3, NPM1 and DNMT3A worsened post transplant outcome in terms of disease free survival, independently from transplant features. Certainly, these finding need to be confirmed in a larger study population.

Disclosure: Conflict of interest. Nothing to declare.

P010.

Unmanipulated Haploidentical Hematopoietic Stem Cell Transplantation in Adult Patients with Acute Myeloid Leukemia

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Background: Acute myeloid leukemia (AML) is the most common indication for allogeneic hematopoietic stem cell transplantation(alloHSCT) in adults. However, despite the

extensive experience of using sibling (MSD) or unrelated (MUD) donors, the problem with timely availability suitable donors still remains. AlloHSCT from a haploidentical donor(haploHSCT), having clear advantages in donor availability, nevertheless is still considered as backup option due to the high risk of complications.

Arm: to estimate the main factors affecting overall survival(OS) in haploHSCT in adult patients with AML.

Methods: The study included 54 patients (pts) for the period 2013-Jun 2020, median age – 32(18–63) years. The median follow-up was 10(2–75) months. Twenty seven (50%), 13(24%) and 14(26%) pts had complete remission (CR) 1, CR2 and active disease(AD) respectively. The intermediate(Int) risk group included 31(57%) and the unfavorable(Unfav) – 11(20%) pts. AML de novo was in 41 (76%) cases, 13(24%) pts had secondary AML. Primary refractory AML had 26(48%) pts. Myeloablative conditioning FluBu10-14 mg/kg was administered in 37(69%) pts, reduced intensity conditioning in 17(31%) pts. Prophylaxis GVHD was on the basis PTCy+Tacro+MMF. The haplo donors were 26 siblings, median age 33(18–54) years; 12 children, median age 29(18–34) years; 16 parents, median age 47(30–61) years. Graft sources were BM in 40(74%) cases (CD34+ 3,0 x106/kg b.w.) and PBSC in 14(26%) cases (CD34+ 6,9 x106/kg b.w.).

Results: The OS in CR1, CR2 and AD was 57%(95% CI, 31-83), 51%(95% CI, 19-84) and 10%(95% CI, 1-29), respectively (p=.02). Relapse rate (RR) – 26%(95% CI, 1-66), 49%(95% CI, 12-79) and 52%(95% CI, 4-87) (p=.05). Non-relapse mortality (NRM) – 33%(95% CI, 15-54), 23% (95% CI, 5-48) and 25%(95% CI, 3-58) (p=.9). Eleven pts developed primary graft failure, 9 pts underwent second haploHSCT, 5 of them are alive in CR1. There was no influence of haplo donor type and graft source on engraftment. Incidence of acute GVHD(aGVHD) was 33%, including 6% of grade 3-4. The cumulative incidence of chronic GVHD(cGVHD) was 27% and extensive cGVHD 16%. A total of 25(46%) pts died (in CR1 33% (9/27), in CR2 38%(5/13) and in AD 79%(11/14)). The causes of death were AML progression (8/25), infections (8/25), primary graft failure (6/25), organ toxicity (2/25) and aGVHD (1/25).

We compared results alloHSCT in our center from MSD, MUD or haplo donors in CR1 and CR2. OS was 63%(95% CI, 47-79), 70%(95% CI, 61–79) and 55%(95% CI, 33-77), respectively ($p = 0.003$). RR were 29%(95% CI, 16–42), 22%(95% CI, 15–30) and 36%(95% CI, 7–68) ($p = 0.1$). NRM were 5%(95% CI, 1–13), 10%(95% CI, 6–15) and reached 30%(95% CI, 15–46) after haploHSCT ($p = 0.001$). RR in Int risk group were 22%(95% CI, 7–43), 17%(95% CI, 9–28), 9%(95% CI, 1–33) ($p = 0.6$). In Unfav group 58%(95% CI, 16–85), 49%(95% CI, 25–70) and 53% (95% CI, 1–91) ($p = 0.7$).

Conclusions: The OS was lower after haploHSCT in comparison with MSD or MUD alloHSCT due to the increased NRM. Thus, haploHSCT for AML in adult patients still remains an option only in a case of no available HLA-matched donor.

Disclosure: Nothing to declare.

P011.

Survival of Patients with Acute Myeloid Leukemia, Taken to Hematopoietic Stem Cell Transplantation: Experience of A Center in Colombia

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Background: Acute myeloid leukemia is a hematological neoplasm with an estimated 5-year survival of 27.3%, however use of hematopoietic progenitor cell transplantation (HSCT) in its different modalities, is the best postmission treatment to achieve a long-term survival. The aim of this study is to describe the clinical characteristics and overall survival (OS) of AML patients who underwent HSCT in a center in Colombia.

Methods: Retrospective study of adult patients with AML who underwent HSCT at the Clínica FOSCAL between January 2009 and October 2020. Treatment was based, according to the PETHEMA protocol for AML.

Results: Twenty-seven patients with a median age of 42 years (18-65 years) were included, 16 were men. 19 had de novo AML and 8 developed secondary AML (s-AML) (4 MDS, 2 CML, 1 myelofibrosis, and 1 AML secondary to therapy). Of all the patients, 25 were RC1 with negative EMR and 3 were with RC1 with EMR +, 1 RC2, one patient received a second Allo-HSCT because of early relapse. Only one patient was refractory with 12.3% blasts in the bone marrow despite 3 lines of treatment. According to the Eruopean Leukemia Net (ELN 2017) classification, 10 had intermediate risk, 10 had unfavorable risk, 4 had low risk, and in 3 their risk was not classifiable. Of the patients 24 received allo-HSCT (5 haploidentical and 1 sequential). In all patients the source of stem cells was peripheral blood. The most common conditioning regimen was TTBuFlu (16

patients), followed by BuFlu (5 patients), RIC (10 patients) and MAC (14 patients). Transplant-related mortality (TRM) at 100 days and one year was 0%. For allogenics OS at one year and at 5 years, was 91.78% (CI95% 70.85-97.89), and 75.72% (CI95% 45.01-90.77) respectively, and LFS at 1 year and 5 years was 92.31% (CI95%72.6-98.02), and 87.45% (CI95% 65.63-95.82) respectively. For the patient who underwent allo-HSCT refractory to treatment, received the sequential conditioning protocol, and presented early relapse and died. The OS at 1 and 5-year in AML de novo was 100%, and 77.8% (CI95% 36.5- 93.9) respectively. The LFS at 1 and 5-years in AML de novo was 100%, and 93.3% (CI95% 61.3-99.0) respectively. The OS for s-AML at 1 and 5 years was 90.6 (CI95% 67.3-97.6), and 81.6% (CI95% 50.2-94.1), respectively. The LFS at 1 and 5 years in s-AML was 75% (CI95% 31.5-93.1) for both of them. The 5-year OS was 100%, 80% (CI95% 20.3-96.9), and 80% (CI95%40.9-94.6) for favorable, intermediate and unfavorable risk respectively. Three patients underwent auto-HSCT, one low risk, another intermediate and the other unavailable. The unclassified patient presented post-autoHSCT relapse at 27.7 months after HSCT, refractory to treatment and death from the disease. The other two patients are alive without disease at 3 and 5 years respectively.

Conclusions: The patients of our study show a greater OS after HSCT similar to the reported in the literature, in the same way OS in S-AML are lower compared to de novo AML despite transplant. Unfortunately a weakness of our study are the few amount patients.

Disclosure: None declare.

CAR-based Cellular Therapy – Clinical

P012.

Manufacturing Commercial Axicabtagene Ciloleucel (Axi-Cel) for European Patients: A 2-Year Retrospective Analysis

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Background: Axi-cel, an autologous anti-CD19 chimeric antigen receptor (CAR) T-cell therapy, was granted marketing authorisation (MA) by the European Commission on 28 Aug 2018 for use in adults with relapsed/refractory diffuse large B-cell lymphoma and primary mediastinal large B-cell lymphoma after ≥2 prior lines of systemic therapy. The aim of this abstract is to describe 2 years of post-MA experience in manufacturing from T-Cell Factory 3 (TCF03) and supplying commercial axi-cel lots in European countries and Israel.

Methods: From apheresis material collected at a qualified treatment center, peripheral blood mononuclear cells (PBMCs) were manufactured and cryopreserved in The Netherlands and then shipped to TCF03 (El Segundo, CA, USA) to continue manufacturing. If additional apheresis was needed, the first apheresis was considered for each patient, and is subsequently referred to as that patient's lot. The finished product lot was shipped back to The Netherlands for European Qualified Person (QP) release and then sent to the hospital for administration to the patient.

Results: From first apheresis after MA, 06 Sep 2018, until 05 Sep 2020, 1074 patients were included on the Kite Konnect® website and provided apheresis material for axi-cel manufacturing. The median and mean turnaround times from apheresis to QP release were 25 days and 26.2 days, respectively. The median and mean times from apheresis to shipment were 29 days and 31.5 days, respectively. Despite the transatlantic air travel disruption due to the COVID-19 pandemic, the median turnaround time from apheresis to QP release from March 2020 to August 2020 was not affected (25 days).

For those 1074 patients for whom manufacturing was started, 1040 commercial axi-cel lots (97%) were released, and 1000 (93%) were delivered, including 19 lots (1.8%) that were out of specification (OOS). OOS commercial axi-cel lots were released exceptionally and on physician's request based on a risk/benefit assessment according to the European Union Advanced Therapy Medicinal Product guidelines.

To obtain this level of manufacturing success, a re-manufacturing step was required either from frozen PBMC bags in 19 cases (1.8%) or from new apheresis in 19 cases (1.8%). In addition, 18 patients (1.7%) had batches rejected; 7 patients (0.7%) had production terminated, and 9 patients (0.8%) had orders canceled.

In June 2020, a new facility (TCF04) in Hoofddorp, The Netherlands opened to engineer cell therapies for European patients with the objective of substantially reducing time from apheresis to QP release and to avoid transatlantic transport.

Conclusions: in conclusion, the initial 2-year experience in manufacturing commercial axi-cel for European countries shows high manufacturing success (97%), with a reliable time from apheresis to QP release (median, 25 days) and a very low percentage (1.8%) of OOS released on physician request.

Disclosure: Louis van de Wiel: employment with Kite, a Gilead Company; leadership with Kite Pharma B.V., a Gilead Company; and stock or other ownership in, speakers' bureau with, expert testimony for, and travel fees from Gilead.

P013.

Expansion Dynamics Detected by Flow Cytometry Correlates with Clinical Response After CAR-T Cell Therapy in the Real World Setting

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Background: Proliferation of chimeric antigen receptor (CAR) T-cell may be associated to outcome and durability of the response after infusion. The aims of this study were to describe CAR-T cell expansion and its correlation with cytokine release syndrome (CRS), immune effector cell-associated neurotoxicity syndrome (ICANS) and clinical response in patients undergoing CAR T-cell therapy in the commercial setting.

Methods: Consecutive patients diagnosed with lymphoma and infused with either axi-cel or tisa-cel in our center between June-19 to November-20 were reviewed. Flow cytometry technique was performed using labeled CD19 protein. CAR-T cell detection in peripheral blood was analysed on days +3, +7, +14 and +30 after infusion. In this study, response was assessed on days +30 and +90. CRS and neurotoxicity were assessed by the ASTCT consensus scale.

Results: As of 30 November 2020, 28 patients were treated, 20 (71%) with axi-cel and 8 (29%) with tisa-cel. Median age was 56 years (22-79) and 46.4% were male ($n = 13$). Eighty-nine percent ($n = 25$) patients were diagnosed with diffuse large B cell lymphoma and 9% ($n = 3$) with primary mediastinal lymphoma. All patients had evaluable samples at day +3 and +7, 27/28(97%) on day +14 and 24/28(86%) on day +30. Status prior to lymphodepletion was stable/progressive disease in 96% ($n = 27$) and partial response in 4% ($n = 1$).

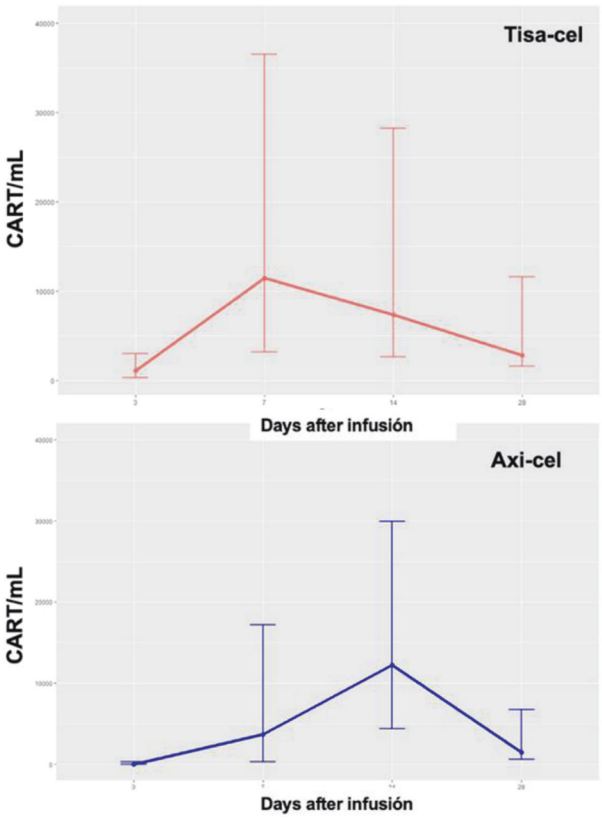
Median values of CAR-T cells on days +3, +7, +14 and +30 were: in the Tisa-cel cohort 1070/mL (day+3), 11465/mL (day+7), 7340/mL(day+14), and 2810/mL (day+30), respectively; in the Axi-cel cohort 0/mL (day+3), 3680/mL (day+7), 12223/mL (day+14), 1480/mL (day+30). Tisa-cel expanded earlier on day +3 compared to Axi-cel on day +14 (Figure 1).

CRS occurred in 85% (24) patients in a median of 2.5 days (1-10) 1 patient developed grade 3-4. ICANS was presented in 9 (32%) patients with a median of 6 days (4-35), 3 patients (11%)grade 4. There was no correlation between CAR-T expansion and toxicity on different timepoints.

Median follow-up was 194 days (27-478). At day +30, out of 25 evaluable patients, 19 (76%) patients showed overall response (OR) (11 CR, 8 PR) and 6 patients (24%) progressed. At day +90, out of 23 evaluable patients, 13 (56%) showed OR (9 CR,4 PR), 6(44%) progressed.

When looking at the correlation between CAR-T expansion and response, CAR-T quantification on peak-value days (+7 for tisa-cel and +14 for axi-cel) was related to response at day +30. In the Axi-cel cohort, detection of > 6042 CAR-T cells/mL at day +14 showed a 86% sensitivity and 80% specificity for OR at day +30. This was confirmed by logistic regression ($p = 0.015$). However, this effect was lost on day +90. In the tisa-cel cohort, detection at day +7 with >4095 CAR-T cells/mL had a sensitivity of 80% and specificity 100% ($p = 0.06$) for OR at day +30.

Figure 1: CAR T-cell expansion(median, IQR range).



Conclusions: Flow cytometry monitoring was feasible for both approved CD19 CAR-T products in patients with

lymphoma. In our experience, peak of expansion was significantly associated with response on day +30. These findings should be confirmed with further studies including higher number of patients.

Disclosure: No conflict of interest.

P014.

Cost-Effectiveness of KTE-X19 Car T Therapy Following Bruton Tyrosine Kinase Inhibitor Treatment for Relapsed/Refractory Mantle Cell Lymphoma in England

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Background: Mantle cell lymphoma (MCL) is an aggressive B-cell non-Hodgkin lymphoma, with an incidence of 0.86 per 100,000 in the United Kingdom. MCL typically relapses and becomes increasingly challenging to manage, with a median survival of three to five years at diagnosis and as low as 4 months for patients relapsing after receiving Bruton tyrosine kinase (BTK) inhibitors. KTE-X19 is a highly effective chimeric antigen receptor T-cell (CAR T) therapy, administered as a one-off treatment after conditioning chemotherapy. The objective of this study was to estimate the cost-effectiveness of KTE-X19 versus standard of care (SoC) in the treatment of relapsed/refractory (R/R) MCL patients in England from an NHS and personal and social services perspective.

Methods: A three-state partitioned-survival model (pre-progression, progression and death) with a cycle length of one month was used to extrapolate progression-free survival and OS over a lifetime horizon. Due to the long tail of the OS curve, OS was modeled applying a mixture-cure methodology, using the assumption that patients whose disease had not progressed after five years experienced long-term remission. These patients switched to age- and sex-matched background mortality at five years and were assumed to incur costs and utilities equal to those of the general population. Population inputs, as well as efficacy and safety of KTE-X19, were derived from the ZUMA-2 trial (N=68, 12-month data cut). The efficacy and safety of SoC, comprising cytotoxic chemotherapy, proteasome inhibitors, immunomodulatory drugs, Bcl-2 protein inhibitors and BTK inhibitors, was estimated based on a meta-analysis, conducted with published SoC data. Costs and resource use inputs were derived from the published literature and publicly available data sources. Costs were expressed in 2019 British pounds (GBP). Health state utilities and adverse event disutilities were derived from the published literature. Costs and health outcomes were discounted at 3.5% per year. The model estimated total expected life years, quality-adjusted life years (QALYs) and costs for KTE-X19 and SoC, including the incremental difference. Based on this, the incremental cost per life-year and cost per QALY were derived. Deterministic and probabilistic sensitivity analyses (PSA) were performed.

Results: Median survival was 14.13 years for KTE-X19 and 0.79 years for SoC. Discounted life years were higher for KTE-X19 than SoC, at 9.75 versus 1.62, respectively. Similarly, total discounted QALYs were 7.06 and 1.21 for KTE-X19 versus SoC, respectively. Conversely, discounted costs were higher for KTE-X19 (£399,160) than SoC (£46,485). These values translated to a cost per life-year gained of £43,359 for KTE-X19 versus SoC, and a cost per QALY gained of £60,314. Sensitivity analyses demonstrate that these model outcomes were relatively stable to changes in inputs with the PSA yielding a cost per QALY gained of £61,309.

Conclusions: From an NHS and personal and social services perspective, the cost-effectiveness of KTE-X19 in the treatment of R/R MCL patients in England appears to be associated with substantial incremental gains in survival in comparison to SoC. Thereby, KTE-X19 presents a promising alternative to SoC for R/R MCL patients, with the potential to significantly extend survival after relapse.

Clinical Trial Registry: NCT02601313.

Disclosure: GAM, employee of Kite, a Gilead Company, and previously employed by BMS, has received research funding from Kite, a Gilead company and BMS, a speaker's honorarium from BMS and is a stockholder of Gilead, BMS and Amgen. CLS, SP and CB are employees of Pharmerit - an OPEN Health Company and are consultants for Kite, a Gilead Company. MW has consulted for Pharmacyclics, Celgene, Janssen, AstraZeneca, MoreHealth, Pulse Biosciences, Nobel Insights, Guidepoint Global, Kite Pharma, Juno, Loxo Oncology, InnoCare, Oncternal, VelosBio, has received research funding from Janssen, AstraZeneca, Acerta Pharma, Pharmacyclics, Juno Therapeutics, Celgene, Kite Pharma, Loxo Oncology, VelosBio, Verastem, Molecular Templates, BioInvent, Oncternal, honoraria from Pharmacyclics, Janssen, AstraZeneca, OMI, Targeted Oncology, OncLive, Dava Oncology, Beijing Medical Award Foundation, Lu Daopei Medical Group, Genentech,

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P015.

Characterization of Infections After Chimeric Antigen Receptor T-Cell Therapy in Patients With Large B-Cell Lymphoma

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Background: Anti-CD19 chimeric antigen receptor (CAR) T-cell therapy has shown promising efficacy in patients with relapsed/refractory large B-cell lymphoma (LBCL). Infectious complications can occur after CAR T-cell therapy. However, incidence, type of infections, timings and risk factors are not well characterized. to that end, we conducted a retrospective single-center study focused on the infectious complications after CAR T-cell therapy in patients with LBCL.

Methods: We retrospectively reviewed the clinical records of LBCL patients treated with CAR T-cells from July 2018 to September 2020 at our institution, and identified all infectious episodes occurring between infusion and progression disease, death or last follow-up visit within the first 100 days after infusion. All febrile neutropenia episodes without microbiological isolation occurring within the first 2 weeks after CAR T-cell infusion were considered related to cytokine-release syndrome. Febrile events with evident primary focus of infection occurring beyond 2 weeks were considered an infectious event even if no microbiological isolation could be made.

Results: Overall, 76 patients met the inclusion criteria. Median age was 61 (range 23-77) years and 52 (68%) were men. Median number of previous therapies before CAR T-cells was 3 (range 1-9) and 25 (33%) had previously received autologous HCT.

All patients received primary prophylaxis with acyclovir and cotrimoxazole, and 26 (36%) also received anti-mold prophylaxis, following the local guidelines (Los-Arcos et al. Infection 2020). Hypogammaglobulinemia was observed in 42 (64%) and 29 (64%) patients during days 1-30 and 30-100 after infusion. However, immunoglobulin replacement was not prescribed in any patient. Forty-seven infection episodes were observed in 31 patients; 11 (15%) had two, 1 had three and 1 had four infectious episodes. The most frequent isolates and location were bacteria and respiratory tract (Table 1). There were 31 (66%) events during hospitalization for CAR T-cell infusion; and 16 (34%) after hospital discharge, only 5 of them needed inpatient management; ICU admission due to infection was not required. Cytomegalovirus reactivation was diagnosed in 23 (35%) patients but only 2 received treatment and none of them developed disease. Regarding fungal infection, there were 1 episode of catheter-related bloodstream infection and 2 oral candidiasis; none of these patients were on antifungal prophylaxis. There were no infection mortality-related events.

Table 1. Characterization of infections during the study period.

	Study Period ($n = 47$)	Day 1-30 ($n = 35$)	Day 30-100 ($n = 12$)
MIcrobiological isolate			
Bacteria	27 (57%)	21 (60%)	6 (50%)
Virus / Fungus	9 (19%) / 3 (7%)	6 (17%) / 3 (9%)	3 (25%) / 0 (0%)
No microbiological diagnosis	8 (17%)	5 (14%)	3 (25%)
Location			
Bloodstream	11 (23%)	9 (26%)	2 (17%)
Respiratory tract	16 (34%)	10 (29%)	6 (50%)
Urinary tract	14 (30%)	11 (31%)	3 (25%)
Other location	6 (13%)	5 (14%)	1 (8%)

Conclusions: Infections are frequent but not severe in the first 100 days after CAR T-cell therapy in patients with LBCL. Not proceeding with systematic immunoglobulin supplementation seems a safety approach for these patients.

Disclosure: Dr. Barba has received honoraria from Novartis, Gilead, BMS, Amgen and Pfizer.

Dr. Ruiz-Camps has received honoraria from Gilead, Pfizer, Janssen, MSD and Astellas.

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P016.

Clinical Application of Haploidentical Donor-Derived CD19 CAR-T Cells Manufactured From Memory T Cell (CD45RA-Depleted) Fraction

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Background: Autologous chimeric antigen receptor (CAR) T cells have changed the therapeutic landscape in B-lineage hematological malignancies. The use of allogeneic donors-derived CAR T cells has many potential advantages over autologous approaches; however, allogeneic CAR T cells may cause life-threatening graft-versus-host disease and may be rapidly eliminated by the host immune system. A potential solution for these limitations is the use of donor-derived memory (CD45RA-depleted) T cells as a starting population for CAR-T manufacturing and infusion of haploidentical memory CAR-T cells as part of haplo HSCT.

Methods: A total of 4 pts with relapsed/refractory BCP-ALL (1 female, 3 male, median age 10 y) were enrolled. All patients had relapsed BCP-ALL after haploidentical HSCT and after autologous CD19 CAR-T cell therapy and had CD19 positive blast cells in bone marrow ($n = 2$ MRD+, $n = 2$ >20% blasts in BM). Peripheral blood mononuclear cells used to produce CAR T cells were derived from the patient's transplant donor.

The CliniMACS Prodigy T cell transduction (TCT) process was used to produce CD19 CAR-T cells. Automatic production included consecutive steps of CD45RA depletion, CD4/CD8 selection, CD3/CD28 stimulation with MACS GMP T Cell TransAct, transduction with lentiviral (second generation CD19.4-1BB zeta) vector (Lentigen, Miltenyi Biotec company) and expansion over 7-10 days in the presence of serum-free TexMACS GMP Medium supplemented with MACS GMP IL-7/IL-15 combination.

Final product was administered without cryopreservation. Two patients received allogeneic CD19 CAR CD45RO T cell simultaneously with haploidentical αβ T cell-depleted graft after myeloablative preparative regimen, one patient received allogeneic CD19 CAT CD45RO T cell on day +45 after haplo αβ T cell-depleted HSCT without lymphodepletion and one patient received CD19 CAR-CD45RO T cell after fludarabine/cyclophosphamide preconditioning.

Results: The cell products were administered at a dose of 0,1*106/kg of CAR-T cells in all pts. Cytokine release syndrome occurred in 3 patients (75%), and all were grade ≤3. No neurologic events or GVHD were observed. The median time of CAR-T cell persistence was 14 days (7-28). All patients achieved CR (MRD negative) at day +28 after CAR-T cell therapy and are alive with median follow up 355 days (193-493). Two patients relapsed (one had testicular relapse after 1.5 years, one had BM relapse 6 months after second HSCT). Two patients, who received CAR-T cell concurrently with allograft are alive in CR with median follow up 242 days.

Conclusions: Allogeneic donor-derived memory T cell-derived anti-CD19 CAR T-cell therapy constitute a potential safe approach to individualized allo CAR-T therapy. Persistence of the memory CAR-T product might be shortened due to biological properties of the starting population.

Disclosure: Nothing to declare.

P017.

Abstract already published

P018.

ICU Resource Utilization in Pediatric And Adolescent Young Adult Patients Post CAR-T Therapy

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Background: Chimeric antigen receptor T cell (CAR-T) therapy has been associated with remarkable clinical benefit in patients with relapsed or refractory B-cell acute lymphoblastic leukemia (ALL). However, it may be associated with unique and potentially life threatening toxicities, leading to the need for intensive care unit (ICU) admission in up to 45% of these patients, with significant resource utilization.

Methods: We conducted a single center, retrospective study to compare outcomes and resource utilization among admitted pediatric, adolescent and young adult (AYA) (≤25 years) patients with ALL who did and did not receive tisagenlecleucel and subsequently required admission to our pediatric ICU between November 2017 and December 2019. Patients who were admitted to the pediatric ICU (post tisagenlecleucel) for routine observation and who never met standard ICU admission criteria were excluded from the ICU cohort.

Results: During the study period, 213 eligible patients with ALL were identified with 15 patients receiving tisagenlecleucel. Two patients, who were admitted to the ICU (post tisagenlecleucel) for routine observation and never met standard ICU admission criteria, were excluded. The overall incidence of ICU admission was 20.6% ($n = 44$). The incidence of ICU admission was higher amongst patients

receiving tisagenlecleucel (9/13, 69%) compared to those who did not (35/198, 17.7%) (p value<0.01). Despite the higher incidence of ICU admission amongst patients receiving tisagenlecleucel vs those who did not, the median ICU length of stay was comparable at 10 days (2-108 days) vs 5 days (1-64days) (p value 0.07) respectively. ICU survival to discharge among patients who received tisagenlecleucel was 88.9% and 68.6% among those who did not (p value 0.4).

There were no significant differences in age, gender or sequential organ failure assessment (SOFA) scores between the two groups of patients. Patients who received tisagenlecleucel were primarily admitted for cytokine release syndrome (CRS) 66.7% ($n = 6$), 22.2% ($n = 2$) for immune effector cell-associated neurotoxicity syndrome (ICANS) and 11.1% ($n = 1$) admitted for renal replacement therapy. In the non-CAR-T therapy group, patients were most commonly admitted for respiratory failure and shock; 45.7% (n= 16) and 28.6% ($n = 10$) respectively. For the duration of their ICU admission, there were no significant differences between the patients who received tisagenlecleucel and those who did not in the use of vasopressors, inotropes, sedatives and paralytic medications. Likewise, the frequency of imaging and procedures including mechanical ventilation, intubation, chest radiographs, electrocardiogram, echocardiography, electroencephalogram, computerized tomography and magnetic resonance imaging of the brain, lumbar puncture, bronchoscopy and paracentesis were comparable between the two groups.

Conclusions: Despite a higher incidence of ICU admission in patients receiving CAR-T therapy for ALL versus those who did not, clinical outcomes and overall resource utilization once admitted to the ICU may be similar in both groups of patients. Multi-center cohort studies may confirm our findings.

Disclosure: Nothing to declare.

CAR-based Cellular Therapy – Preclinical

P019.

Non-Viral Sleeping Beauty Transposon Engineered CD19-CAR-NK Cells With High Antileukemic Efficiency

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Background: Natural Killer (NK) cells are known for their high intrinsic cytotoxic capacity. Recently, we showed that virally transduced NK cells equipped with a synthetic chimeric antigen receptor (CAR) targeting CD19 induced enhanced killing of acute lymphoblastic leukemia (ALL) cells. Furthermore, we established a new optimized protocol for non-viral NK cell modification using the *Sleeping Beauty* (SB) transposon/transposase system for stable genetic expression of CD19-specific CAR in primary NK cells.

Methods: Primary NK cells were isolated from peripheral blood mononuclear cells and genetically engineered to express CD19-CAR using viral or non-viral vectors. For non-viral gene delivery, SB transposons vectorized as minicircles (MC) that express either a Venus fluorescent protein or a CD19-CAR were introduced in combination with the hyperactive SB100X transposase in the form of mRNA into NK cells via electroporation. Stable gene delivery was monitored by flow cytometry and the cytotoxicity of viral and non-viral CD19-CAR NK cells was addressed in a CD19 positive ALL cell line. Furthermore, genomic integration pattern after viral modification was compared with the non-viral transposon integration profile.

Results: Herein, we present an optimized protocol for the electroporation of primary NK cells and stable SB-mediated generation of highly cytotoxic SB.MC-CD19-CAR NK cells.

In initial screening assays with different electroporation pulses (EP) using a pmaxGFP vector, we could show highest viability (60%) and highest transient pmaxGFP expression (40%) measured at 48h after EP. After testing different viable (such as time of EP after NK enrichment, EP programs, plasmid ratios) for optimal SB-mediated genetic transposition using a minicircle transposon vector that expresses Venus fluorescent protein and SB100X mRNA, Venus expression resulted in a significantly higher long-lasting Venus expression (up to 50%) over time of up to four weeks (end of experiment) under 25-fold expansion of the genetically modified NK cells.

Based on these newly established methods, SB transposon-engineered primary MC.CD19-CAR-NK cells showed increasing high viability, similar to non-treated (NT) NK cells and to Venus-modified NK cells. CD19-specific CAR-NK cells generated with the SB platform demonstrated an high cytotoxicity measured by tumor cell lyses against the CD19 positive pediatric ALL cell line Sup-B15, as compared to control NT-NK cells (72% vs. 15% for E:T 10:1 and 36% vs 5% for E:T 1:1). Remarkably, even under long-term ex vivo culturing using IL-15 and feeder-cell-free conditions, the non-virally modified MC.CD19-CAR-NK cells remained highly functional. These results are comparable with our

previously reported protocol for lenti- and alpharetrovirally engineered primary CD19-CAR NK cells.

Conclusions: The SB transposon system is a highly promising new and innovative gene therapeutic approach for the non-viral engineering of highly functional CAR-NK cells not only for ALL therapy but also for a broad range of other applications in cancer therapy.

Disclosure: Zoltan Ivics is an inventor on patents related to Sleeping Beauty and MC DNA system. Michael Hudecek is an inventor on patents related to MC DNA. Winfried S. Wels is an inventor on a patent describing chimeric antigen receptors with an optimized hinge region. The remaining authors have nothing to disclose.

Cellular Therapies other than CARs

P020.

Prolonged Repeatedly Administered Low Dose Donor Lymphocyte Infusion for Prevention of Relapse After Allogeneic Stem Cell Transplantation for Patients With High Risk Acute Leukemia

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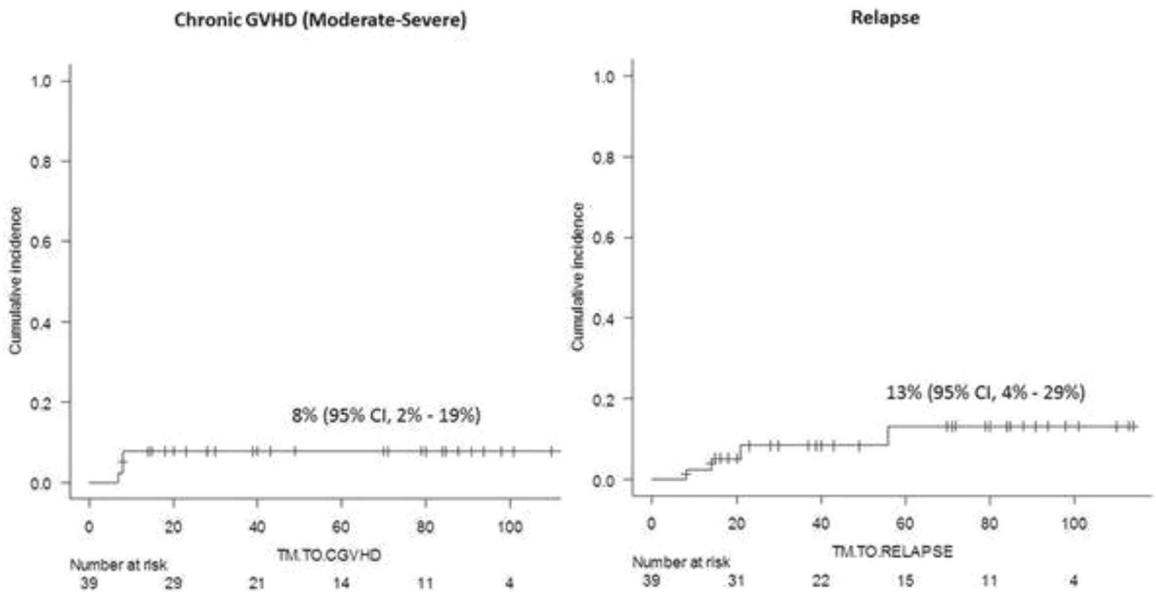
Background: in an effort to reduce the relapse rate of patients with high risk acute myeloid (AML) and lymphoblastic leukemia (ALL), various therapeutic methods have been implemented into clinical practice. Our group tested the safety and efficacy of a novel method of prophylactic-DLI based on repeated administration of low lymphocyte doses.

Methods: in our department, prophylactic-DLI is administered to all pts with high risk AML or ALL. High risk leukemia is defined as follows: (1) AML/ALL with unfavorable-cytogenetics in CR1, (2) AML/ALL with intermediate-cytogenetics in CR2, (3) pts with refractory disease or measurable residual disease. DLI was administered between days +150 and +180. Pts with previous acute-GVHD (grade 3-4), active chronic-GVHD, and not in CR were excluded. DLI was administered at a dose of 2X106/kg CD3-positive cells. DLI at the same dose was repeated every two months until 36 months, or until relapse, or development of GVHD, whichever occurred first.

Thirty-nine consecutive patients who underwent allo-SCT between 2011 and 2019 were included. Twenty-nine AML and 10 high-risk ALL pts received PBSC either from a matched related (36 pts) or a matched-unrelated donor (3 pts). Twelve pts with unfavorable genetics in CR1, 15 pts in CR2, and 12 pts had active disease at the time of transplant. Disease risk index (DRI) was high and intermediate in 20 and 19 pts respectively. Low-dose alemtuzumab plus cyclosporine was administered for GVHD-prophylaxis.

Results: Thirty-two pts completed treatment and received a median of 8 DLI-doses, (range, 1-15). Fifteen pts received all planned doses until month-36. DLI was discontinued in 3 pts because of relapse, in 6 because of donor unavailability, in 7 because of GVHD development, and in 1 pt because of development of secondary malignancy (lung cancer). Seven pts are still on treatment and until today have received a median of 4 doses, (range, and 2-11).



With a median follow up of 8 months, (range, 8-114) the overall survival (OS) is 76%, (95% CI, 55%-88%), while the cumulative incidence of non-relapse mortality (NRM) and relapse was 14%, and 13%, respectively.

The cumulative incidence of acute-GVHD grade II-IV after DLI administration was 20% (95% CI, 7% - 32%). Acute-GVHD was transient and successfully managed in all cases with short course steroids. None of the pts developed acute GVHD grade III-IV.

The cumulative incidence of moderate-severe chronic-GVHD after DLI administration was 8% (95% CI, 2% - 19%). Two out of 3 pts who developed chronic GVHD are free of active chronic GVHD and off immunosuppression. (Figure).

The cumulative incidence of relapse in patients with intermediate and high DRI was 7% and 17%, respectively.

Conclusions: in our study we observed that prolonged (up to 3y) low dose prophylactic-DLI administered every 2 months is safe and effective in reducing the relapse rate of pts with high risk acute leukemias. It seems that the low dose strategy reduce the risk of severe GVHD, while the prolonged repeated administration helps in preventing relapse possibly by keeping the immunological pressure on the leukemic cells. This novel strategy deserves testing in larger cohort of leukemic pts.

Disclosure: Authors have nothing to disclose.

P021.

Clinimacs Plus® Selection as a Reliable And Safe Alternative Procedure For Clinimacs Prodigy® TCRAB And CD19 Depletion

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Background: TCRα/β+ T cells are responsible for developing Graft Versus Host Diseases (GvHD), TCRγ/δ+ T cells and NK cells are responsible for Graft versus Leukemia effect. Selective depletion of TCRα/β T cells in haploidentical stem cell transplantation can help prevent GvHD. Miltenyi Biotec CliniMACS Prodigy® TCRαβ depletion system is a functionally closed automated system.

Methods: Having an unexpected clumping problem during the first washing step using CliniMACS Prodigy® System, Hot Line recommended to continue with the CliniMACS Plus® instrument. Two vials of each; CliniMACS® TCRα/β-Biotin, CliniMACS® Anti-Biotin and CliniMACS® CD19 reagent were used as they had been opened for Prodigy selection. The result was excellent. This modified "rescue" CliniMACS Plus® protocol was repeated in the following period if CliniMACS Prodigy® was "busy" and the procedure was urgent. We compared 12 automated (Prodigy) and 6 manual (CliniMACS Plus®) TCRαβ depletion processes in 2020. Statistical analyses were performed using unpaired two-tailed Student's t-test. $P<0.05$ was considered to indicate statistically significant differences.

Results: The results of the automated and manual process were comparable, there were no significant difference neither in CD34 recovery (mean: 79.53% vs 88.17%) nor in depletion rate (CD3: 1.73 log vs 1.81 log, TCRαβ: 4.05 log vs 3.84 log, CD20: 2.99 log vs 3.04 log). The recovery of TCRγδ (56.89% vs 76.32%) and NK cells (71.00% vs 86.33%) were also comparable. The target cell viability was significantly better after manual processing (95.42% vs 97.32%). Processing time from starting the selection until the end of the procedure was also significantly shorter in manual processing (0.3 vs. 1.0). There was no microbial contamination after either automated or manual processes.

	CliniMACS Prodigy®	CliniMACS Plus®	P
Number of procedures	12	6	
CD34+ recovery (%)	79.53 (±13.20)	88.17 (±11.42)	0.19
Target viability (%)	95.42 (±1.93)	97.32 (±1.39)	0.048
TCRγδ recovery (%)	56.89 (±15.95)	76.32 (±20.34)	0.07
NK cell recovery (%)	71.00 (±28.03)	86.33 (±10.29)	0.11
CD3 depletion (log)	1.73 (±0.33)	1.81 (±0.43)	0.68
TCRαβ depletion (log)	4.05 (±0.60)	3.84 (±0.64)	0.50
CD20 depletion (log)	2.99 (±0.28)	3.04 (±0.54)	0.78
Processing time (day)	1.01 (±0.10)	0.30 (±0.03)	2.96x10E-9

Conclusions: The CliniMACS Plus® depletion is a safe, reliable alternative of CliniMACS Prodigy® TCRαβ depletion system with similar results. The recovery of CD34+, NK cells and TCRγδ+ T cells and the depletion of TCRαβ+ T cells and CD20+ B cells were at least comparable or even non-significantly better after CliniMACS Plus® depletion. The target cell viability and processing time were significantly better in CliniMACS Plus® procedures. In case of products with high granulocyte and/or platelet contamination and total nucleated cell count nearing the upper limit

(80x10E9) or lacking immediate availability of fully automated technique, the CliniMACS Plus® depletion may be an excellent alternative option.

Disclosure: Nothing to declare.

P022.

Impact of Cryopreserved Photopheresis in Graft Versus Host Disease for Non-Malignant Disorders After Allogeneic Hematopoietic Stem Cell Transplantation in Pediatric Patients

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Background: The development of GvHD limits the success of allogeneic Hematopoietic stem cell transplantation (HSCT) and remains a major cause of treatment-related morbidity and mortality. Extracorporeal photochemotherapy (ECP) is an effective treatment in managing patients with graft versus host disease (GvHD) after allogeneic HSCT. However, some serious concerns limit the widespread use of ECP in children, such as the risk of pediatric apheresis and the need for intravenous access at each session. Usage of cryopreserved cells offers several advantages that make ECP an acceptable therapeutic option, especially in pediatric setting.

Methods: Nine patients whom were resistant to steroid or second line of treatment for GvHD, enrolled in this study (7 patients with Primary immune deficiency disorder, 2 cases of Major Thalassemia). We scheduled ECP for acute GvHD (aGvHD), two sessions per week for 12 times, and in chronic GvHD (cGvHD), weekly 6-8 times, then biweekly for two months, and then monthly until improvement of symptoms. ECP was started in two patients with aGvHD, including one with stage IV of skin and one with stage IV of GI & Skin, and seven patients with cGvHD (three with limited and four with Extensive cGvHD). At each session of apheresis, collected cells divide into 6–8 equal bags (30-50 ml) depending on patients' body weight. One bag was treated and infused into the patient, and the rest were frozen and used for other sessions.

Results: We performed a total of 79 sessions of ECP in our patients (2-18 sessions). with the start of the ECP protocol in aGvHD cases, both of them have complete response in skin but GI symptoms did not respond. In cGvHD cases, ECP was stopped for one patient with limited cGvHD after the second session because of an anaphylactic reaction to psoralen. Five Patients with cGvHD (two limited and three extensive), respond to ECP, (improvement in range of motion and movement capabilities with decrease in lichenoid rashes and sclerodermatous lesions), and usage of immunosuppressive drugs was decreased and they continue ECP to complete sessions. In one patient with extensive liver cGvHD, despite a 50% decrease in total bilirubin during ECP sessions, GvHD flared up because of CMV infection.

Conclusions: Our results suggest that ECP with cryopreserved cells can rescue GvHD-patients and could be a new modality of treatment in GvHD in pediatric patients because of cost effectiveness and difficulty in venous access in this setting.

Disclosure: Nothing to declare.

P023.

Donor Lymphocyte Infusion After Allogeneic Stem Cell Transplantation: A Retrospective Analysis

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Background: Donor lymphocyte infusion (DLI), alone or in combination with chemotherapy, is a salvage method commonly used both in post-transplant relapse and in case of mixed chimerism and risk of graft failure. Our objective is to report the experience of our center using DLI in various hematologic malignancies.

Methods: Retrospective, descriptive and single center analysis of 40 patients with various hematologic malignancies who received post-transplant DLIs between January/2005 and October/2020. Demographic characteristics are shown in Table 1.

Statistical analysis was performed using SPSS v 25.0; values defined as statistically significant were $p < 0.05$. Survival analysis were assessed using the Kaplan- Meier method.

Table 1. Demographic characteristics

	N (%)
N	40
Age: median (range)	27 (8- 67)
Adult / Child	29 (72.5) / 11 (27.5)
Gender (male / female)	17 (42.5) / 23 (57.5)
Base pathology	
Acute myeloblastic leukemia	15 (37.5)
Acute lymphoblastic leukemia Phi +	4 (10)
Acute lymphoblastic leukemia Phi −	6 (15)
Myelodysplastic syndrome	4 (10)

Table (continued)

	N (%)
Biphenotypic leukemia	3 (7.5)
Multiple myeloma	2 (5)
Hodgkin lymphoma	2 (5)
Non- Hodgkin's lymphoma	1 (2.5)
Other	3 (7.5)
Conditioning	
Myeloablative	28 (70)
Non- myeloablative	12 (30)
Source	
Peripheral blood	32 (80)
Bone marrow	7 (17.5)
CBU	1 (2.5)
Donor	
Related	26 (65)
Unrelated	14 (35)
Pretransplant disease status	
1st CR with negative MRD	16 (40)
1st CR with positive MRD	5 (12.5)
> 1st CR with negative MRD	1 (2.5)
> 1st CR with positive MRD	4 (10)
Partial response	4 (10)
Stable disease	3 (7.5)
Progression	3 (7.5)

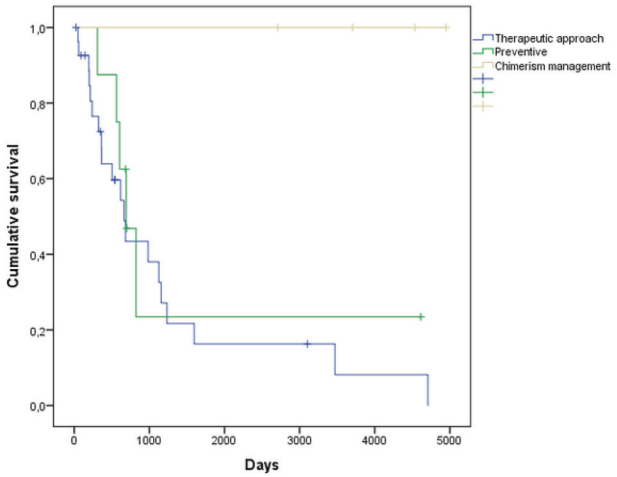
Results: A total of 40 patients received DLIs. The main indication was disease relapse (28/40, 70%), followed by positive minimal residual disease (8/40, 20%) and mixed chimerism (4/40, 10 %).

A total of 98 DLIs were administered, with a median of 2 infusions per patient (range 1-7). The median starting dose was 1x10e6/kg and the median final dose received was 1x10e7/kg. The median time from transplantation to the first DLI was 388 days (range: 87-1680).

Nineteen out of 40 (47.5%) patients achieved complete remission (CR) with negative minimal residual disease (MRD), 3/40 (7.5%) obtained CR with positive MRD, 5/40 (12.5%) did not respond, and 13/40 (32.5%) progressed after treatment.

Graft-versus-host-disease (GVHD) was observed in 18 /40 (45%). Thirteen out of 40 (32.5%) patients developed acute GVHD (grade III-IV: 7/13) and 6/40 (15%) chronic GVHD (moderate/severe forms: 3/6).

A total of 25/40 (62.5%) patients died. The main causes were: progression (16), GVHD (1), infection (4), toxicity (1) and others (3). with a median follow-up of 610 days (24-4947) after the first DLI, 1-, 3-, and 5- year overall survival (OS) of the whole group from start of DLI treatment was 70, 47, and 25%, respectively. Significant differences were found in terms of survival between those patients who received DLIs for mixed chimerism with respect to those in morphologic or molecular relapse ($p = 0.012$) (Figure 1). Better survival was also observed among those patients who obtained CR with negative MRD ($p = 0.009$).



Conclusions: DLIs are a safe procedure, GVHD being the main complication but with low incidence of severe forms. It could be an effective strategy in patients in relapse in combination with other systemic therapies. Differences in terms of survival were found based on treatment indication and response achieved after DLI treatment.

Disclosure: Nothing to declare.

P024.

Donor Lymphocyte Infusion (DLI). A Strategy to Prevent or Treat Relapse Following Allogenic Stem Cell Tranplantation. One Single Center Experience

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Background: Despite improvements in stem cell transplantation in patients with acute leukemia, relapse is still one of the main cause of mortality, especially in those patients with early relapse. DLI is one of the strategies used in high risk patients, allowing us to rescue 30-55% of relapses and reduces risk 2.3 times when it used as a pre-emptive strategy of relapse.

Methods: A retrospective cohort study was performed among adults recipients of allogeneic HSCT between 2016 and 2019 who subsequently underwent DLI as a prophylaxis, preemptive or treatment strategy for relapse.

Results: 10 patients were included, 7 women (70%) and 3 men (30%), with a median age of 52 (24-69). Underlying disease were: 7 acute myeloid leukemia (70%), 2 acute lymphoid leukemia (20%) and 1 myelodisplastic syndrom (10%). Patients received ASCT from related HLA indentical (10%), haploidentical (80%) and unrelated donor (10%). Related to disease status previous HSCT, 2 patients had disease persistence (20%), 7 complete response (CR), 4 of them with negative minimal residual disease (MRD) and the other 3 with positive MRD (molecular, cytogenetics or inmunophenotypic markers) and 1 patient with MDS with no previous treatment. After HSCT, in day +30, 90% presented CR, 4 of them with complete chimerism (CC) and the other 6 with mixed chimerism (MC). Patient with MDS presented persistence disease. One of the patient underwent a 2º HSCT and received DLI after both transplants.

The median time for inmunesuppressive treatment interruption was 91 days (45-147) and the median time to DLI indication was 137 days (114-475).

DLI indications were: 4 (36.4%) as treatment (3 relapse disease and 1 refractory), 4 (34.4%) prophylaxis because of high risk disease and 3 (27.2%) preemptive because of positive MRD or CC. The median dosis of ILD was 3 (1-4).

In the treatment indication group, 75% received DLI in combination with Azacitidine (1 one them as well in combination with Sorafenib), 1 in monotherapy. In the prophylaxis group, 50% received it in combination with azacitine+sorafenib or sorafenib only and the other 50% in monotherapy. In preemptive group, 67% received it in combination with Azacitidine, 33% in monotherapy.

Related to response after DLI, in the treatment group: 75% were refractory, 25% achieved CR with positive MRD and MC. In prophylaxis group, 75% CR, negative MDR and CC, 25% CR and MC. In preemptive group: 67% CR, negative MRD and CC, 33% MRD and MC.

Therefore, 45.4% of all patients achieved CR with negative MDR and CC and the other 27.3% present refractoriness.

GVHD rate was 50%. After a median time of follow-up of 4 years (1-4), 40% still are in remission. 4 patients died, 2 of them due to relapse (20%) and the other two because of infections.

Conclusions: DLI represents a useful and safe strategy in patients with high risk of relapse, especially in combination with systemic therapies as Azacitidine. In our cohort, we achieved remission in 30-40%, similar to other studies. In treatment indication, there was a limited response being necessary the use of intensive therapies with an important decreased survival.

Disclosure: No conflict of interest.

P025.

New, LN_2-Free Solution for Cryogenic Transport of Cell Therapies

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Background: Administration of cell therapies, in clinical trials or as commercial products, involves complex logistics between sometimes numerous partners and sites. Timings are critical and cryopreservation affords extra time and flexibility, but also brings its own challenges. Cryogenic transportation of starting material or finished product is currently carried out in dry shippers, maintained cold for a period of time by liquid nitrogen (LN_2). If it appears difficult to predict with great confidence the cryogenic standby time offered by such devices, their fast warm-up profile and the requirement of dedicated infrastructure for their re-charge makes it difficult to manage unforeseen events and delays during transit. Alternative cryogenic shipping devices, more predictable and easier to re-charge during transit, hence LN_2-free, appear necessary to develop. For that, a better understanding of the boundaries not to be crossed in terms of transit time and temperature, to maintain cell integrity post-thaw, is needed, and studied here. We also present the post-thaw cellular outcome following shipping of a cell therapy in such an LN_2-free device, the VIA Capsule™ (Cytiva).

Methods: to define the transit time and temperature boundaries to maintain cell integrity of cryopreserved samples, we evaluated the impact of storage periods of 5 and 10 days at -60, -80 and -100°C, and compared this to -120°C, the glass transition temperature (Tg') of DMSO-containing cell suspensions ($n = 5$) under which indefinite storage is theoretically possible. A range of cell lines was used for these tests, including an immortalised T cell line to emulate the behavior of some cell therapies. After thawing, samples were re-cultured and viable cell numbers and metabolic activity were measured after 24, 48 and 72h, to also evaluate cell proliferation ability post-thaw.

The real-life LN_2-free cryogenic shipping test in the VIA Capsule™ involved the ORBCEL cell therapy product,

embarked on an 8-leg journey across 2 manufacturing sites and 3 clinical sites in Great Britain via air and road. Transportation was managed by World Courier as our privileged specialist courier partner and specifically trained personnel. Cell viability post-thaw was measured on un-transported versus transported samples ($n = 2$).

Results: A 5-day transit at -100°C did not significant impair cell parameters post-thaw compared to a 10-day period at -120°C. However, longer transit periods (10 days) at this temperature or at higher temperatures appeared detrimental, and the extent of the impact increased as the temperature gap to Tg' became more important.

Cryogenic shipping of the ORBCEL products in the VIA Capsule™ did not lead to significantly different cell viabilities post-thaw compared to un-transported products.

Conclusions: Molecular mobility is greatly slowed down in frozen samples, but still exists above Tg', which may lead to cellular damages over time, observable post-thaw. The extent of these damages depend on the time and temperature gap to Tg'. The VIA Capsule™ is a safe and predictable LN_2-free, cryogenic shipping solution which ensures a 5-day fully passive shipping window below -120°C. Moreover, it is extremely easy to handle and re-charge anywhere using electricity, to mitigate any unforeseen event or delay in transit.

Disclosure: Authors received funding from the Midlands & Wales Advanced Therapy Treatment Center (MW-ATTC) programme, Innovate UK Project Number: 104232. Julie Meneghel, Peter Kilbride, Stuart Milne and William Shingleton are employees of Cytiva, which manufactures the VIA Capsule™ devices used in this work. Stephen Elliman is an employee of Orbsen Therapeutics.

Conditioning Regimens

P026.

Outcomes of Allogeneic Hematopoietic Cell Transplantation in Elderly Patients: is Age The Limit?

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Background: Although a cut-off has not been established for allogeneic hematopoietic cell transplantation (allo-HCT), increasing age is associated with higher mortality especially with myeloablative conditioning regimens. Therefore, an adequate patient selection and the modulation of the allo-HCT strategy based on individual patients' characteristics (malignancy, comorbidities, functional status and age) may improve the outcomes.

The main objective of our study is to describe outcomes of allo-HCT in patients ≥60 years-old, and to investigate possible prognostic factors.

Methods: We retrospectively analysed 97 patients ≥60 years-old who underwent allo-HCT in our institution between 2011 and 2019. They were stratified by age: 60-64 ($n = 37$), 65-69 ($n = 45$) and ≥70 ($n = 15$) years-old.

The conditioning regimen was selected based on pre-transplant disease status and patients' comorbidities. Myeloablative regimens were preferred when higher risk of relapse. Immunosuppression was adjusted based on stem cell source and HLA-matching.

Results: Median age of patients was 66 (range, 60-79) and 67% of them were male. Table 1 shows patients' characteristics. Patients ≥65 were more frequently in complete remission at the allo-HCT. Differences between age groups did not reach statistical significance for other variables. The median follow-up was 33.9 (range, 7.9-111.5) months.

	All patients ($n = 98$)	60-64 years ($n = 37$)	65-69 years ($n = 45$)	>70 years ($n = 15$)	*p value*
Diagnoses, n (%)					0.111
- Acute leukemia	49 (50.5)	15 (40.5)	26 (57.8)	8 (53.3)	
- Chronic leukemia	9 (9.3)	7 (18.9)	2 (4.4)	0	
- MDS/MPD	23 (23.7)	6 (16.2)	13 (28.9)	4 (26.7)	
- Lymphoma/MM	13 (13.4)	8 (21.6)	3 (6.7)	2 (13.3)	
- Bone marrow aplasia	3 (3.1)	1 (2.7)	1 (2.2)	1 (6.7)	
Disease status, n (%)					0.013
- Complete remission	55 (56.7)	15 (40.5)	32 (71.1)	8 (53.3)	
- Partial remission	23 (23.7)	15 (40.5)	7 (15.6)	1 (6.7)	
- Stable disease	11 (11.3)	3 (8.1)	4 (8.9)	4 (26.7)	
- Progression disease	8 (8.2)	4 (10.8)	2 (4.4)	2 (13.3)	
Prior autologous-HCT, n (%)	13 (13.4)	7 (18.9)	4 (8.9)	2 (13.3)	0.415
HCT-CI score, n (%)					0.359
- <3	52 (53.6)	21 (56.8)	21 (46.7)	10 (66.7)	
-≥3	45 (46.4)	16 (43.2)	24 (53.3)	5 (33.3)	
DRI, n (%)					0.290
- Low	12 (12.8)	8 (22.2)	3 (6.8)	1 (7.1)	
- Standard	65 (69.1)	22 (61.1)	32 (72.7)	11 (78.6)	
- High	17 (18.1)	6 (16.7)	9 (20.5)	2 (14.3)	
Donor, n (%)					0.103
- HLA-matched sibling	24 (24.7)	6 (16.2)	13 (28.9)	5 (33.3)	

Table (continued)

	All patients ($n = 98$)	60-64 years ($n = 37$)	65-69 years ($n = 45$)	>70 years ($n = 15$)	*p value*
- HLA-haploidentical sibling	26 (26.8)	6 (16.2)	15 (33.3)	5 (33.3)	
- HLA-matched unrelated	37 (38.1)	18 (48.6)	15 (33.3)	4 (26.7)	
- HLA-mismatched unrelated	10 (10.3)	7 (18.9)	2 (4.4)	1 (6.7)	
Stem cell source, n (%)					0.926
- Peripheral blood	43 (44.3)	17 (45.9)	19 (42.2)	7 (46.7)	
- Bone marrow	54 (55.7)	20 (54.1)	26 (57.8)	8 (53.3)	
Myeloablative conditioning, n (%)	57 (58.8)	22 (59.5)	28 (62.2)	7 (46.7)	0.567
GvHD prophylaxis, n (%)					0.368
- Calcineurin inhibitor + MMF/MTX	67 (69.1)	28 (75.7)	29 (65.4)	10 (66.7)	
- FK + MMF + Cy post	26 (26.8)	6 (16.2)	15 (33.3)	5 (33.3)	
- Cy post	2 (2.1)	2 (5.4)	0	0	
- Other	2 (2.1)	1 (2.7)	1 (2.2)	0	
- ATG	36 (37.1)	15 (40.5)	17 (37.8)	4 (26.7)	0.639

At day +100 post-HCT, cumulative incidence (CI) of grades III-IV acute graft-versus-host disease (GvHD) was 14%. The CI of moderate/severe chronic GvHD at 1 and 2-years were both 35%. At 3-years post-HCT, CI of non-relapse mortality (NRM) was 32% and relapse rate (RR) was 22%. Three-years overall (OS) and progression-free survivals (PFS) were 50% and 46%, respectively.

Stratifying by age (groups 60-64, 65-69 and ≥70 years-old), CI of grades III-IV acute GvHD by 100-days trends to be lower in older patients (22% vs. 13% vs. 0%, $p = 0.140$). CI of moderate/severe chronic GvHD at 1-year was similar in all groups (40% vs. 31% vs. 33%, $p = 0.760$). Likewise, at 3-years post-HCT there were no differences in NRM (34% vs. 27% vs. 41%, $p = 0.658$), RR (27% vs. 24% vs. 7%, $p = 0.357$), OS (39% vs. 58% vs. 52%, $p = 0.415$) and PFS (39% vs. 49% vs. 52%, $p = 0.691$).

In multivariate analysis, complete remission pre-transplant (HR 0.49, CI95%0.27-0.88; $p = 0.018$), low/moderate DRI (HR 0.25, CI95%0.13-0.49; $p = 0.000$) and peripheral blood as stem cell source (HR 0.51, CI95%0.28-0.93; $p = 0.028$) were independently associated with higher OS. Patient age, sex, number of preceding chemotherapy regimens, prior autologous-HCT, pre-HCT Karnofsky, HCT-CI score, donor and conditioning regimen did not have significant impact on OS.

Conclusions: A careful patient selection with individualized approach allows safer performance of allo-HCT in elderly patients, even with myeloablative conditioning. In our experience, pre-transplant disease status and peripheral blood as stem cell source were associated with better OS.

Disclosure: Nothing to declare.

P027.

The Impact of Melphalan De-Escalation on Efficacy And Safety in Patients With Multiple Myeloma Undergoing Autologous Stem Cell Transplantation: A Single-Center Experience

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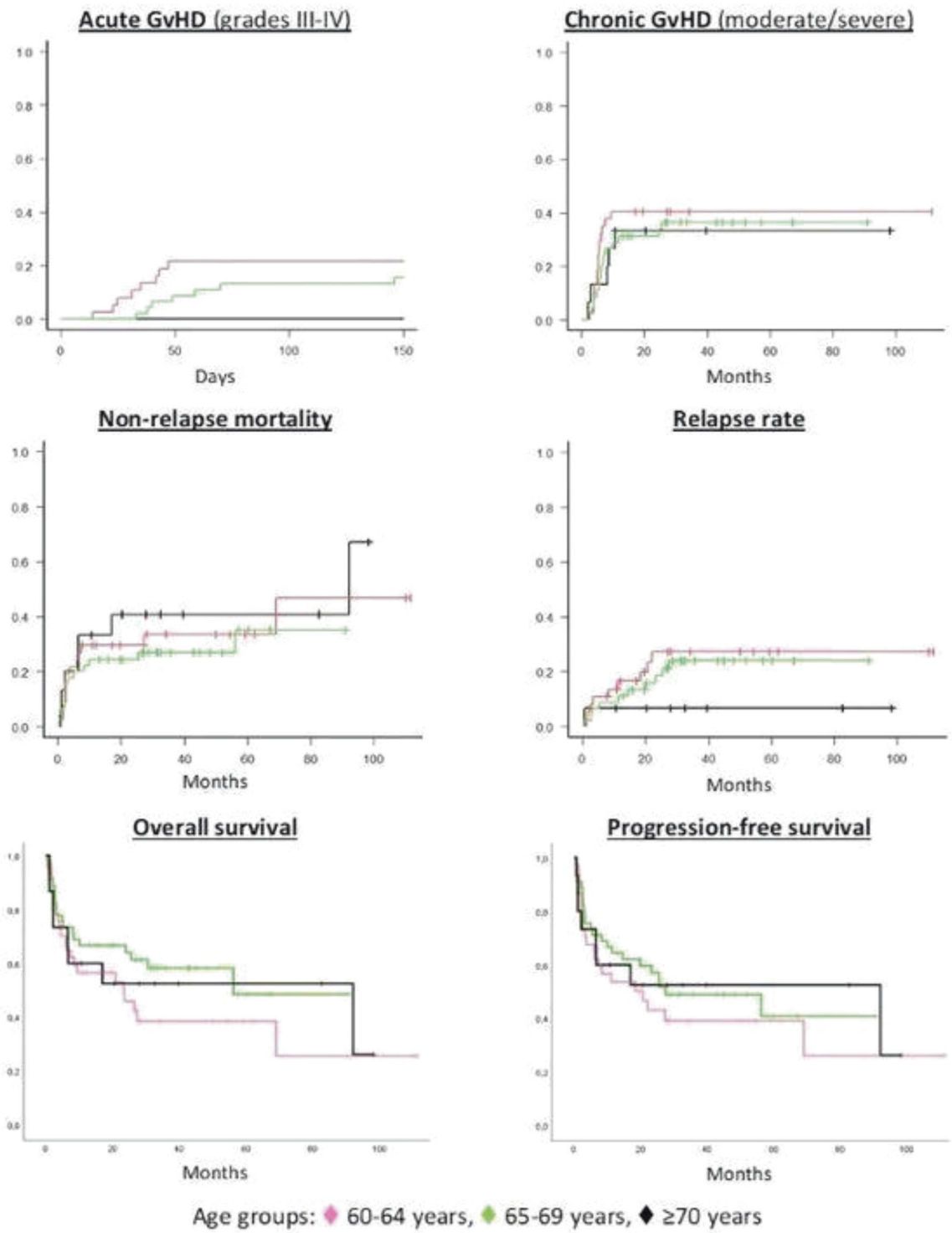
Background: Melphalan (MEL) at a dose 200 mg/m^2 (MEL200) is a standard conditioning before autologous hematopoietic stem cell transplantation (ASCT) in patients with multiple myeloma (MM). We assessed the effect of dose de-escalation to 140 mg/m^2 (MEL140) on short- and long-term toxicity using CTACE scale and the outcome of the treatment as well as algorithm for choosing the right dose.

Methods: We performed a retrospective analysis of 307 patients (pts) with MM who underwent ASCT as consolidation of the first line treatment at Department of Hematology and Bone Marrow Transplantation at Poznan University of Medical Sciences in years 2006–2019. Pts were studied in 2 subgroups according to the dose of MEL: MEL200 and MEL140. Age above 65, Karnofsky <90 and HCT-CI>2 were the criteria determining the lower dose of MEL (two of them had to be met).

Results: Out of 307 pts with MM who undergone ASCT 194 received MEL200 (104 men, 90 women), median age 55 (29-67). In the subgroup of MEL140 ($n = 113$) there were 70 men and 43 women with median age of 64 years (44-75). All patients engrafted. The reconstitution of granulopoiesis defined as absolute neutrophil count ≥0.5 G/L (MEL200: median 11 (8-32) days, MEL140: median 11 (8-16) days) was not significantly different between the groups (the Mann Whitney U test; $p = 0.31$). In pts with MEL200, we found a statistically significant increased risk of complications (both infectious and non-infectious) in the post-transplant period 126/194 (65%) vs 57/113 (55.4%) in MEL140 subgroup - OR 1.82 (95% CI: 1.135, 2.919; $p = 0.012$). However, patients treated with MEL140 had a significantly increased risk of serious complications (G3 and G4 according to the CTCAE) 9/57 (16%) vs 6/126 (4.8%) – OR 3.72 (95% CI: 1.255, 11.019; $p = 0.019$). In MEL140, infectious complications with septic shocks predominated (5/9 - 56%). At the median follow-up of 34 (3-161) months, relapse occurred in 93/170 (55%) pts in MEL200 group, with 6/93 (6.4%) at 3 months and 53/93 (54%) at 24 months and in 58/101 (57%) of MEL140



group, with 4/58 (6.9%) at 3 months and 35/58 (60.3%) at 24 months. The deaths during observation were reported in 44% (86/197) in MEL200 (including 1 death while transplant procedure) and 26% (29/113) in MEL140. Cause of death was mainly due to progression of MM – 72.1% vs 74%. In the analysis, there was a statistically significant PFS advantage for MEL200 subgroup with a HR of 0.54 (95% CI: 0.33, 0.90; $p = 0.017$). The median PFS was 43 months in MEL200 and 29 months in MEL140. However, no differences in OS were seen.

Conclusions: MEL200 remains the standard conditioning prior ASCT with superior progression free survival in patients with MM, however the dose reduction to MEL140 allows the eligibility to ASCT, patients with high transplantation risk. MM patients who received MEL140 had similar long-term outcomes to MEL200 patients but more often severe complications which were associated with causes of reduction of dose.

Disclosure: Nothing to declare.

P028.

Conditioning With High Dose Total Body Irradiation And Post Transplantation Cyclophosphamide in Early Relapsed Multiple Myeloma Patients Receiving Allogeneic Stem Cell Transplantation

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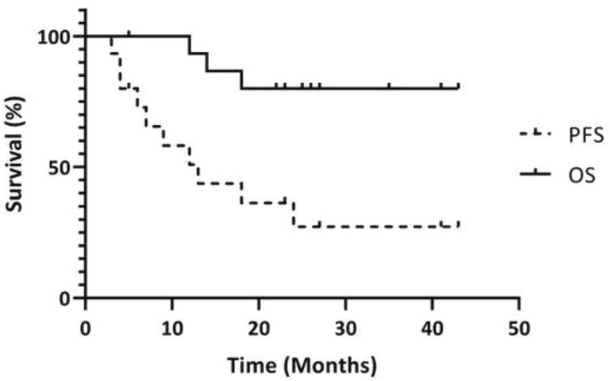
Background: Despite the introduction of novel therapies the prognosis of multiple myeloma patients with early relapsed disease after autologous hematopoietic cell transplantation (autoHCT) remains poor.

Methods: We retrospectively analysed all patients transplanted between January 2017 and September 2020 with early relapsed multiple myeloma who subsequently received an allogeneic hematopoietic cell transplantation (alloHCT) with a conditioning regimen consisting of high dose TBI (8 or 12 Gy in fractions of 4 Gy), and cyclophosphamide (PTCy) and tacrolimus as post transplantation immunosuppression (tapered from day 56-128 or earlier in case of signs of disease activity). Patients were eligible for alloHCT if they had relapsed disease within 24 months after autoHCT (either first or second). All patients had at least a partial response after re-induction therapy and were fit to receive 8 to 12 Gy TBI.

Results: Fifteen patients received an alloHCT (7 male, 8 female). Mean age was 57 years (range [45-69]), 75% had high risk cytogenetics, 40% was lenalidomide refractory and 40% was previous treated with daratumumab. Median number of previous therapies was 3 (range [2-5]). Seven patients had an early relapse after 1 autoHCT, and 8 after 2 autoHCTs. Progression free survival (PFS) since autoHCT was 13,7 months (range [2-20]). Ten patients (75%) achieved a complete remission, of the 13 evaluable patients 8 (62%) were MRD negative. with a median follow up of 25 months (range [5-43]) the 12 and 24 months PFS was 51% and 27%. The overall survival (OS) was 93% and 79% at 12 and 24 months (figure 1). Of the patients who were MRD negative after transplantation the PFS at 12 and 24 months was 71% and 54%. to date, two of the patients died due to progression, another died due to a pneumonia. Seven patients experienced a grade 1-2 aGVHD; all were steroid responsive. One patient had a grade 4 aGVHD of the intestine that did not responded to 2 mg/kg prednisolone but resolved completely with the addition of ruxolitinib. We observed only grade 2 chronic GVHD in two patients, with one patient needing low dose of immunosuppressive treatment. The overall treatment related mortality was 6,7%.



Conclusions: The role of alloHCT has to been challenged for patients with relapsed multiple myeloma, with the availability of novel treatment modalities. In this study we show that alloHCT with high dose TBI, PTCy, and early tapering of tacrolimus is a safe and feasible option for patients with early relapsed multiple myeloma after autoHCT. The remarkable OS in this poor risk patient group merits further exploration.

Clinical Trial Registry: Not applicable.

Disclosure: Nothing to declare.

P029.

Preventing Aki in Transplant for Pediatric All With TBI And Etoposide Conditioning

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Background: Relapsed leukemia is the most common indication for hematopoietic stem cell transplant (HSCT).

Conditioning regimens for relapsed acute lymphoblastic leukemia (rALL), usually consist of total body irradiation (TBI) and a single chemotherapy agent. In Royal Manchester Children's Hospital, Leeds Children's Hospital and Sheffield Children's Hospital the preferred conditioning regimen for rALL consists of TBI-12Gy and etoposide 60mg/kg, delivered as etoposide phosphate, based on outcomes from the FORUM study.

Acute Kidney Injury (AKI) is graded using the pRIFLE (Pediatric Risk, Injury, Failure, Loss, End Stage Renal Disease) criteria. Studies show AKI is an independent predictor of length of hospital stay, increased pediatric intensive care stay, and increased mortality.

We review the incidence of AKI in this patient group in all 3 units and consider the impact of improving management with hyperhydration.

Methods: A retrospective review of all pediatric transplants for rALL using 12Gy TBI and etoposide (60 mg/kg delivered as etoposide phosphate) at three stem cell transplant units between 2015-July 2020 was undertaken. Collection of the data was from computerised results, observations and clinical notes. Inclusion criteria were defined as: pediatric patients (≤16 years), rALL going to transplant, conditioning with TBI & etoposide (delivered as etoposide phosphate). Exclusion criteria defined as: recent acute AKI - pRIFLE >stage 2 within 3 months preceding transplant and pre-existing chronic kidney disease stage ≥2.

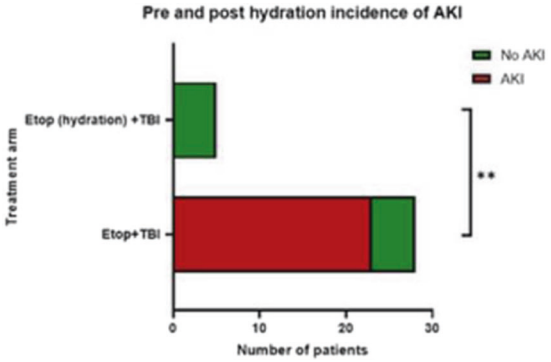
From July 2020 conditioning with TBI and etoposide was modified to include 2 hours pre- and 24 hours post-hydration at 125ml/m2/hr and 4 hours of hydration with the etoposide phosphate: ensuring a minimum time of 24 hours between etoposide and commencing immunosuppression with ciclosporin/tacrolimus.

Baseline eGFR (modified Schwartz equation – 41.3xheight(cm)/creatinine(umol/L)) was calculated for each patient and the greatest fall in eGFR within 72 hours of receiving etoposide was used to identify if AKI occurred. A pRIFLE of grade 1 or more was considered an AKI. The incidence of AKI in the patients that received hyperhydration was compared to those who had not.

Both groups received standard prophylaxis agents including nephrotoxic medications such as aciclovir, immunosuppression with ciclosporin/tacrolimus and at a standard time as per local protocol.

Statistical analysis using a Fischer's exact, two-tailed test was performed to assess for difference between the two groups.

Results: The retrospective group included 23 patients, age 3-16 years, weight 7 kg– 66 kg and height 97 cm–162 cm. Baseline eGFR ranged from 140-247 mL/min/1.73 m^2. Regarding AKI, 82% (19/23) of all patients had a stage 1 renal injury. Of these, 63% (12/19) were stage 2 AKI. The hyperhydration group included 5 patients age 5-13 years, weight 20 kg–55 kg and height 116 cm-169 cm. Baseline eGFR ranged from 150-233 mL/min/1.73 m^2. There was no recorded AKI stage 1 or 2 in this group (Figure 1) which was a significant change compared to the group not treated with pre- and post-hydration, $p = 0.0011$.



Conclusions: This quality improvement project demonstrates a significant decrease in AKI in those treated with etoposide phosphate when receiving pre- and post-hydration. Fluid status, loading of other nephrotoxic medications and pre and post-hydration should be considered when using etoposide phosphate in conditioning.

Clinical Trial Registry: NA.

Disclosure: Nothing to declare.

P030.

Long-Term Safety And Efficacy of a Myeloablative Conditioning Regimen of Reduced Toxicity in Allogeneic Hematopoietic Cell Transplantation

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Background: We have previously shown an advantage of a myeloablative conditioning regimen with reduced toxicity (Fludarabine 150 mg/m^2, Treosulfan 42 g/m^2, FluTreo) compared to a reduced intensity regimen. However, the long-term safety and efficacy of this regimen remain unknown.

Methods: We retrospectively studied consecutive patients that received FluTreo in our center (2014-2019). FluTreo has been introduced FluTreo for patients with a suitable donor that would have been previously eligible only for reduced intensity conditioning/RIC due to age and/or

comorbidities. The following factors were studied: age, type of disease/donor/graft, phase at transplant, HCT-CI score, CD34 cells infused, infections, cumulative incidence/CI of graft-versus-host disease (GVHD), and treatment-related mortality (TRM), overall (OS) and disease-free survival (DFS).

Results: We studied 68 FluTreo recipients, with a median age of 58.5 (25-70) years, transplanted for de novo acute myeloid leukemia/AML (31 patients), secondary AML (20), myelodysplastic syndrome/MDS (14), myeloproliferative neoplasms (2). The majority was transplanted in first complete remission/CR (45/68), while 18 in second CR, and 5 in refractory/relapsed disease. Grafts were peripheral blood stem cells from unrelated (33 matched and 10 mis-matched) and sibling (25) donors. Median HCT-CI was 3 (0-7), and previous lines of treatment 3 (1-6). Full donor chimerism was achieved in all patients at median 30 (12-90) post-transplant days.We calculated acceptable rates of CI in acute (gr 2-4) and extensive chronic GVHD (29.9% and 30.9%, respectively). Chronic GHVD was associated only with age ($p < 0.001$), and mis-matched donors ($p = 0.042$). Interestingly, 3-year CI of TRM was only 19.1%. TRM was associated only with acute GVHD ($p < 0.001$). Disease relapse was observed in 16/68 patients. with a median follow-up of 27.3 (range 5.7-84.5) months in surviving patients, 3-year OS was 56.6% and DFS 54.9%. Median survival has not been reached yet. Among pre-transplant and transplant factors, only HCT-CI was associated with DFS and OS ($p = 0.022$ and $p = 0.043$, respectively). Patients with HCT-CI<3 had significantly higher OS (71.2% versus 45.1%, $p = 0.019$), and DFS (70.3% versus 40.8%, $p = 0.006$) at 3 years.

It should be also noted that diagnosis of secondary AML did not impact transplant outcomes. Among post-transplant factors, acute GVHD ($p = 0.045$) and relapse ($p < 0.001$) were associated with OS. In the multivariate model, relapse ($p = 0.002$) was the only independent predictive factor of OS.

Conclusions: Our real-world study confirms that alloHCT with FluTreo expands the transplant population with outcomes comparable to other myeloablative conditionings, even in secondary AML. The choice of alloHCT in patients of a rather older age and comorbidity index needs to be revisited.

Disclosure: E.G. is supported by the ASH Global Research Award. The remaining authors have nothing to declare.

P031.

Enhanced Immunosuppression in T-Cell Replete Haploidentical Transplantation With Post-Transplant Cyclophosphamide is Associated With Favorable Outcomes

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Background: Haploidentical transplantation with post-transplant cyclophosphamide (PTCy) is being increasingly used with encouraging outcomes, in patients lacking fully-matched donors. We here aimed to study transplant-related outcomes in patients post T-cell replete haploidentical transplantation with the use of PTCy.

Methods: We analyzed the outcomes of 33 haploidentical transplants with post-transplant cyclophosphamide-based graft-versus-host disease (GVHD) prophylaxis that were performed in our JACIE-accredited unit, between 2013 and 2020. In low/intermediate risk for relapse patients, enhanced anti-GVHD prophylaxis with low (2.5 mg/Kg) dose of rabbit ATG was used in addition to standard Cy (5 mg/kg/d, days+3,+4), cyclosporin (3 mg/kg, starting day +5) and mycophenolate mofetil (30-45 mg/kg, day +5 to +35) scheme. The conditioning regimens used were either TBI- (low or high dose) or chemotherapy-based and myeloablative (Thiotepa/Bu/Flu:$n = 16$, TBI/Thiotepa/Flu: $n = 6$), reduced intensity (Thiotepa/Flu/Mel: $n = 4$, TBI/Fl: $n = 1$) or reduced toxicity (Flu/Treo/TBI: $n = 6$).

Results: A total of 33 patients (23 male/10 female) with median age 45 (20-64) years underwent haplo-transplant for myeloid (21) or lymphoid (12) malignancies with 48.4% of them at an advanced disease stage (CR2, primary refractory, active disease). Donors (median age 35) were siblings (17), parents (5) or children (11) and no patient had donor-specific antibodies. Bone marrow was the main graft source (28/33 pts); median number of CD34+ and CD3+ cells infused was 4.25×10^6/kg ($1.68\text{-}8.75 \times 10^6$) and 0.78×10^8/kg ($0.33\text{-}4.47 \times 10^8$) respectively. Median time to engraftment was 16 (9-23) and 20 (9-35) days for neutrophils and platelets, respectively. No case of primary graft failure occurred, although three patients developed secondary graft failure from whom two were rescued with a second T-cell depleted transplantation using PBSC-mobilized grafts from the same donor. The cumulative incidence (CI) of all grade acute GVHD was 48.5% and of grIII-IV 12.1%; while the overall and severe chronic GVHD CI was 45.5% and 12.2%. Viral reactivations were the most common cause of morbidity (CMV 15, EBV 16, BKV 13, HHV-6 8 pts). The majority of patients (24/33, 72.7%)

developed at least one viral reactivation requiring treatment; CMV reactivation/disease occurred in 45.5%, EBV reactivation/disease in 48.4% and BK viruria/hemorrhagic cystitis in 39.3% of patients. In 6 virus-reactivating patients trivirus-specific T-cells (against CMV, EBV and BKV) were administered to control infections and provide long-term immune protection. There have been 5 cases of TMA and none of hepatic veno-occlussive disease. Reduced intensity conditioning was significantly associated with cGVHD in multivariate analysis ($p = 0.017$). Relapse incidence was 15.1%. Probability of overall (OS) and disease-free survival (DFS), were 56% and 51%, respectively and cumulative incidence of treatment-related mortality (TRM) 31%, in 5 years. In multivariate analysis, high comorbidity index (HCT-CI) was independently associated with TRM ($p = 0.015$) while the addition of ATG favored both OS and DFS ($p = 0.048$ and $p = 0.035$, respectively).

Conclusions: Our study shows that enhanced immunosuppression with incorporation of ATG during conditioning, significantly improves both OS and DFS in haploidentical transplants with PTCy, thus challenging the current practice of leaving Cy unhindered to selectively.

Disclosure: nothing to declare.

P032.

Treosulfan vs. Busulfan-Based Regimens in Pediatric Patients: A 7-Year Retrospective Study

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Background: Treosulfan-based conditioning is increasingly employed in pediatric HSCT due to its potent immunosuppressive and cytotoxic effects combined with a favorable toxicity profile. This study describes and compares the key characteristics and outcomes of patients who received treosulfan-based vs. busulfan-based conditioning.

Methods: We performed a retrospective review of allogenic HSCT with treosulfan and busulfan-based conditioning regimens of all consecutive pediatric patients (2012–2019) in a single-center setting. Cases were identified from the EBMT registry. We included HSCTs performed for both nonmalignant ($n = 41$) and malignant diseases ($n = 57$). Epidemiological and clinical data were recorded from the medical history. Data were analyzed with the SPSS 26.0 program.

Results: A total of 94 patients with 98 HSCT were included: 65 (66.3%) with busulfan and 33 (33.7%) with treosulfan-based conditionings.

In the case of malignant diseases, busulfan-based conditioning was more commonly employed than treosulfan: 86% vs 14% ($p < 0.0001$). However, the use of treosulfan for malignant conditions has increased in recent years: 6.5% of HSCT in 2012–2015 vs. 23.1% of HSCT in 2015–2019 ($p = 0.07$).

The median time to neutrophil engraftment (ANC>0.5x109/L) was 16 days (range 11–104) in the treosulfan group and 17 days (range 8–70) for the busulfan group. Regarding the incidence of graft failure, there was no significant difference between the groups (12.7% with busulfan vs. 9.1% with treosulfan, $p = 0.7$).

There were more cases of veno-occlusive disease in the busulfan group compared with the treosulfan group, but this difference was not significant (21.9% vs. 9.1%, $p = 0.1$).

Acute GVHD was more frequent when busulfan based-conditioning was employed (57.8% vs. 36.4%, $p = 0.045$). This difference was also significant in the subgroup of malignant diseases (72.9% vs. 37.5%, $p = 0.047$). No difference was observed in overall survival.

Table 1. Key characteristics, complications and outcomes in the conditioning regimen groups.

	Malignant disease			Nonmalignant disease		
	Busulfan ($n = 49$)	Treosulfan ($n = 8$)	p	Busulfan ($n = 16$)	Treosulfan ($n = 25$)	p
Type of HSCT	MRD:22.5%	MRD:12.5%	0.9	MRD:6.3%	MRD:20%	0.5
	MMRD:12.0%	MMRD:12.5%		MMRD:25.0%	MMRD:16.0%	
	MUD:38.8%	MUD:50.0 %		MUD:31.3%	MUD:40.0%	
	MMUD:26.5%	MMUD:25.0 %		MMUD:37.5%	MMUD:24.0%	
Primary or secondary graft failure	8.5% (4/47)	0% (0/8)	0.4	25.0% (4/16)	12.0% (3/25)	0.3
VOD	25% (12/48)	12.5%(1/8)	0.4	12.5%(2/16)	8.0% (2/25)	0.6
aGVHD	71.9% (35/48)	37.5% (3/8)	0.047	12.5% (2/16)	36.0% (9/25)	0.098
cGVHD	16.7% (8/48)	25.0% (2/8)	0.6	6.2% (1/16)	16.0% (4/25)	0.6
Relapse	18.3% (9/49)	0% (0/8)	0.2	-	-	
Alive	55.1% (27/49)	62.5% (5/8)	0.7	75.0% (12/16)	80.0% (20/25)	0.7
5-year OS, SE	55 (7.4)	62.5 (17.1)	0.8	75 (10.8)	79 (8.4)	0.8

Conclusions: in our institution, busulfan-based conditionings are more frequently used for children undergoing allogenic HSCT, but treosulfan-based conditioning is gaining acceptance.

Treosulfan-based conditionings also showed a significantly lower frequency of aGVHD in malignant diseases.

Disclosure: Nothing to declare.

P033.

Immune Reconstitution After Sequential Conditioning in Elderly, High-Risk AML And MDS Patients: A Matched-Pair Analysis Among Different Donor Types

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Background: Sequential conditioning regimens have been successfully used for high-risk (HR) AML/MDS in matched related (MRD) and unrelated donor (MUD) HSCT and have found their way into the HLA-haploidentical donor (HaploD) HSCT setting when PTCY for GvHD prophylaxis is used. However, little is known about immune reconstitution in elderly, HR AML/MDS patients undergoing sequential reduced intensity conditioning (RIC) in different transplantation settings.

Methods: Here we report on a comparison of immune reconstitution in patients with advanced myeloid disease, aged >50 years, undergoing sequential conditioning, transplanted between January 2009 and June 2017 at our institution from either an HaploD (PTCY-based), a MRD (ATG-based) or a MUD (ATG-based). We aimed to explore the clinical impact of lymphocyte subset counts on outcome among the different donor types and transplantation platforms.

Seventeen patients undergoing PTCY HaploD HSCT were pair-matched with an equal number of patients undergoing MRD and MUD HSCT according to (1) disease activity: $p = 1.0$; (2) disease status: $p = 1.0$; (3) modified DRI: p= 0.9; (4) HCT-CI score: p= 0.92, (5) age: ($p =$ 0.95). Immune reconstitution was measured in fresh peripheral blood samples collected at predefined time points after allo-HSCT quantifying total number of CD45, CD3, CD4, CD8, NK and B-cells, measured by flow cytometry.

Results: Median age of the entire cohort was 51 years (50-70). Lymphocyte subset counts did not differ between the groups at start of sequential conditioning. MRD and MUD HSCT was uniformly performed using FLAMSA-RIC and PBSCs as stem cell source, whereas in HaploD HSCT 4/17 patients received clofarabine-RIC and 9/17 patients a bone marrow graft.

Standard values for ALC were reached earlier in MRD compared to MUD and HaploD cohort. CD3+ cells were lower throughout the first three months in PTCY treated patients as compared to ATG (day +30: 115/μl vs. 275/μl, $p = 0.04$). Differences in CD3+ T-cell counts were more pronounced at three months after HSCT (MRD: 750/μl vs. MUD 260/μl vs. HaploD 130/μl, $p = 0.01$). Higher CD3+ cell counts at day +30 were significantly associated with lower NRM ($p = 0.01$). No significant difference in CD4+ cells could be detected, however patients with higher CD4+ count (> 35/μl vs. <35/μl) at day +30 were more likely to suffer from aGvHD ($p = 0.04$). CD8+ T cells showed significantly lower levels at day +100 in HaploD compared to MRD transplantation (85/μl vs. 490/μl, $p = 0.02$). NK cells in PTCY treated patients showed a delayed recovery compared to the ATG cohort (day 30: 30/μl vs. 160/μl, p 0.03) but it was followed by a robust proliferation of NK cells. HaploD patients were more likely to reach higher NK cell levels. Higher NK cell count at day 365 showed a significant impact in CI relapse (1y: 50% vs. 0%, 5y: 50% vs. 0%; p 0.03) and as such on OS and DFS.

Conclusions: Our data suggest a delayed immune reconstitution after sequential RIC irrespective of donor type. Overall no difference in survival was seen. Subgroup analysis showed lower CI aGvDH in patients with higher CD4 counts at day +30. Higher NK cells reflected on better disease control and higher OS/DFS.

Disclosure: Nothing to declare.

P034.

Post-Transplant Cyclophosphamide (PTCY) as GVHD Prophylaxis for Hematopoietic Stem Cell Transplantation From Matched-Related Sibling Donors

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Background: Post-Transplant Cyclophosphamide (PTCY) has revolutionized the field of Hematopoietic Stem Cell Transplantation (HSCT) allowing safe procedures even across the HLA barrier. Nevertheless, Graft Versus Host Disease (GVHD) remains the most feared complication of HSCT, even in the setting of transplantation from HLA-related sibling donors.

Methods: We have investigated a PTCY-based prophylaxis in a cohort of 14 consecutive patients undergoing HSCT from sibling donors (Cohort 1), comparing them with two distinct cohorts of patients who have received either a HLA-matched HSCT from sibling donors using a standard non-PTCY GVHD prophylaxis ($n = 47$; Cohort 2), or an haploidentical HSCT using PTCY+cyclosporine+micophenolate mofetil ($n = 54$; Cohort 3). Non-PTCY GVHD prophylaxis was based on standard cyclosporine±methotrexate±anti-thymocyte globulin, with this latter exploited in all patients receiving peripheral blood stem cells. All patients were transplanted between 2011 and 2020 at the transplant centers of Avellino ($n = 14$, PTCY for siblings), Naples and Salerno ($n = 71$ and $n = 30$, respectively). The outcomes of the study were

non-relapse mortality (NRM), acute and chronic GVHD, relapse and overall survival (OS).

Results: Median age was 52.5 (range 20-62), 52 (range 18.4-64) and 47.6 (range 19-71) in Cohorts 1, 2 and 3, respectively. Patients transplanted for acute leukemias were 91.5%, 100% and 81.5% in the three cohorts, whereas myeloablative conditioning regimens were given to 71.4%, 91.5% and 96.3% of patients in the three cohorts. The stem cell source was bone marrow in 64.3%, 31.9% and 83.3% in Cohort 1, 2 and 3, respectively. Single-agent PTCY was well tolerated in HSCT from sibling donors, without recurrent, clinically meaningful treatment-emerging adverse event. The day-100 NRM rate was 14% in Cohort 1, which was not statistically different from those observed in Cohort 2 (21%; p>0.05) and Cohort 3 (20%; p>0.05). The rate of grade II-IV and III-IV acute GVHD were 42.9% and 14% in Cohort 1, which were not statistically different, as compared to those observed in Cohort 2 (29.8% and 8.5%; p>0.05) and Cohort 3 (31.5% and 13%; p>0.05). The rate of chronic GVHD was 15.4% in Cohort 1, which was significantly reduced as compared to those observed in Cohort 2 (68.4%; $p = 0.01$) and Cohort 3 (57.5%; $p = 0.011$). The rate of relapse was 21.4% in Cohort 1, which was overlapping to that of Cohort 3 (3) (15.2%; $p = 0.685$), and slightly lower, albeit not statistically different, to that of Cohort 2 (36.6%; $p = 0.301$). The OS at 36 months was 43% in Cohort 1, which was not statistically different from those observed in Cohort 2 (45%; p>0.05) and Cohort 3 (54%; p>0.05). The leading cause of death was relapse, which accounted for 50%, 63% and 40% of events in Cohort 1, 2 and 3, respectively.

Conclusions: PTCY was safe and effective as single agent GvHD prophylaxis in HSCT recipients from sibling donors, resulting in excellent NRM and survival with reduction of chronic GvHD. Because PTCY alone was unable to reduce acute GvHD rate as compared with standard Csa+MTX±ATG regimens, we are now investigating in a prospective trial a PTCY-CsA double-agent immunosuppressive regimen for HSCT recipients from HLA-matched sibling donors.

Disclosure: Nothing to declare.

Experimental Stem Cell Transplantation

P035.

Synergistic Effect of ATG Plus PTCY for Dual T Cell Modulation in Haploidentical Stem Cell Transplantation for Poor Prognosis Acute Leukemia

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Background: in evolution of Haploidentical Transplantation (Haplo-SCT), implementation of two different GvHD prophylaxis regimens, including G-CSF/ATG-based and high-dose post-transplant cyclophosphamide (PTCy) had a great impact in improving the outcomes. We hypothesized that concomitant use of PTCy and ATG with proper sequence and timing has synergistic effect on immune tolerance.

Methods: This historical cohort study was conducted on 119 patients with poor prognosis acute Myeloid/Lymphoid leukemia (AML/ALL) including; first remission of high/intermediate- risk acute leukemia, recurrent disease (beyond CR1) and primary refractory AML/ALL, underwent Haplo-SCT with a same protocol including "myeloablative conditioning regimen (MAC), unmanipulated peripheral blood graft (PBSC) and intensified immunosuppression" in our center from 2010-2019.

Results: Outcome of 100 patients who received combination of ATG (2.5 mg/kg/d for 3 days) plus modified PTCy (40 mg/kg/days +3, +4) was compared with 19 patients who received ATG-based regimen. The median follow up was 35.8 months.

Both arms shared similar characteristics except for the donor median age, the distribution of relationship and median time between diagnosis and transplantation.

Cumulative incidence of acute GvHD (II–IV) was significantly lower in the ATG-PTCy group ($p < 0.0001$), although the incidence of 30-day neutrophil engraftment was better in the ATG group ($p = 0.036$). Survival and relapse rate were comparable between two arms.

Subgroup analyses stratified by disease status separately for AML and ALL that was shown in Table 1, indicated 3-year outcomes such as leukemia-free survival (LFS) and relapse incidence (72% and 5.1%) of patients with high/intermediate- risk AML undergoing Haplo-SCT in first CR were interestingly better than other subgroups of present study and also similar population of other studies.

After adjustment in Multivariate model, receiving Haplo-SCT in recurrent and refractory disease status compared to first remission of high/intermediate- risk AML (HR: 3.42; $p = 0.022$ & HR: 4.48; $p = 0.042$ respectively), and Major ABO-mismatched compared to ABO-matched (HR: 2.82; $p = 0.050$) were the hazard factors associated with worse LFS in patients with AML.

Table:1		OS (95% CI)	LFS (95% CI)	RI (95% CI)	NRM (95% CI)	A GvHD (95% CI)
AML	CR1	70 (45.5_86)	72 (48_86.4)	5.1 (0_21.7)	23.2 (7.9_43)	50 (28.4_68)
	Relapsed	33.6 (19_48.8)	34.5 (20 _49)	10.5 (3_23)	52.6 (36_67)	59 (42.8_72)
	Refractory	46.7 (12.5_76)	47 (12.5_75)	25 (2.7_58.6)	25 (2.8_58)	62.5 (17.4_88)
	P.value	0.056	0.065	0.27	0.07	0.77

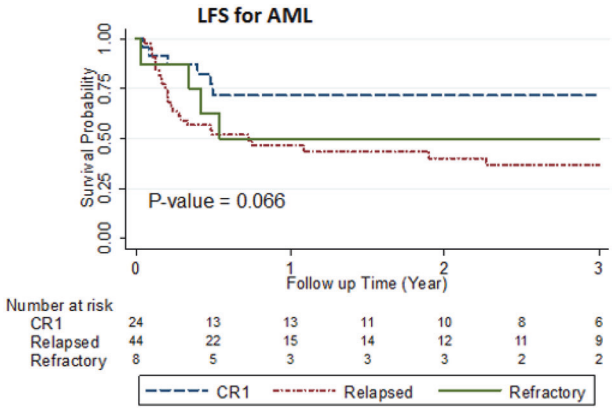
Table (continued)

Table:1		OS (95% CI)	LFS (95% CI)	RI (95% CI)	NRM (95% CI)	A GvHD (95% CI)
ALL	CR1	24.2 (6.75_47)	24.6 (7_47.8)	25 (6.9_48.7)	52.9 (21_77)	64.7 (36_83)
	Relapsed	34.6 (11_59.8)	34.57 (11_60)	22.6 (4.7_49)	41.5 (15_67)	47 (22_68.8)
	Refractory	33.3 (7.8_62)	33.3 (7.8_62)	33 (6_65)	33.3 (6.6_64)	55.5 (16_82.7)
	P.value	0.87	0.86	0.81	0.86	0.55

Abbreviations: OS overall survival; LFS leukemia-free survival; RI Relapse Incidence; NRM Non-relapse Mortality; A.GvHD acute graft-versus-host disease.

Conclusions: Our experience indicates, the combination of ATG + PTCy, could be safety administered to patients with poor prognosis acute leukemia undergoing Haplo-SCT, associated with lower incidence of acute GvHD compared to ATG-based regimen.

It also concluded that our protocol for Haplo-SCT containing MAC, PBSC and concomitant use of PTCy and ATG, has been most effective in improving outcome of patients with high/intermediate- risk AML receiving Haplo-SCT in first remission, while in other subgroups, some modifications can be useful. (Figure).



Disclosure: Nothing to declare.

P036.

Day 0 Easix Score Might Predict Overall Survival And Transplant Related Mortality After Allogeneic Stem Cell Transplantation: Single Center Experience

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Background: Recently, Endothelial Activation and Stress Index (EASIX), calculated at the onset of acute GvHD, was reported as reliable predictor of survival in patients receiving reduced intensity conditioning at transplant. We wondered if an early evaluation of the EASIX score might be able to predict survival regardless of GvHD development.

Methods: We enrolled 179 patients consecutively submitted to allogeneic stem cell transplantation (HSCT) in our center from January 2017 to November 2019. The most frequent diagnosis was leukemia ($n = 104$), followed by myeloproliferative disease ($n = 32$), myelodysplastic syndrome ($n = 19$), lymphoma ($n = 22$) and SAA ($n = 2$). Median age was of 53 years (range, 14-72). Twenty patients received a mismatched donor, 72 a haploidentical donor and 87 a matched donor. Donor was unrelated in 60 patients and a relative in the others. Stem cell source was cord blood in 7 patients, bone marrow in 76 patients and peripheral blood in the other 96. Seventy-nine patients received a myeloablative conditioning and 100 a reduced intensity conditioning. EASIX score (lactate dehydrogenase U/L × creatinine mg/dl / platelets × 109/L) was calculated at day 0 before stem cell infusion (EASIX-0). No log transformation was applied.

Results: Median level of EASIX-0 was of 1.67 (95% CI 1.39-1.96) for surviving patients and 4.64 (95% CI 2.36-8.59) for patients dying after HSCT ($p < 0.0001$). Multivariate analysis for survival confirmed EASIX-0 (HR 1.01, 95% CI 1.00-1.02, $p = 0.01$) as predictive factor for mortality together with relapse occurrence (HR 2.92, 95% CI 1.3-4.92, $p = 0.0001$). One-year overall survival (OS) according to EASIX-0 was as follows: <25th quartile ($n =$ 31) 86.9% (95% CI 74.9-98.9), 25th-50th quartile ($n = 90$) 80.9% (95% CI 72.8-89.1), 50th-75th quartile ($n = 25$) 56% (95% CI 36.2-75.5) and >75th quartile ($n = 33$) 48.5% (95% CI 31.4-65.5) ($p < 0.0001$). Moreover, EASIX-0 was significantly associated to the cumulative incidence of transplant related mortality (TRM): HR 1.01 (95% CI 1.00-1.02) ($p = 0.004$). Multivariate analysis confirmed EASIX-0 (HR 1.06, 95% CI 1.01-1.12, $p = 0.01$) as predictive factor for TRM together with grade 2-4 acute GvHD occurrence (HR 8.05, 95% CI 1.92-33.80, $p = 0.004$). One-years cumulative incidence of TRM was as follows: <25th quartile 0%, 25th-50th quartile 13.6% (95% CI 7.9-23.6), 50th-75th quartile 26.3% (95% CI 12.4-55.8) and >75th quartile 50% (95% CI 35-71.5) ($p < 0.0001$). No association was found for relapse incidence.

Conclusions: Early EASIX score, calculated at day 0 of transplant, appeared to be a reliable prognostic score of survival after allogeneic stem cell transplantation. We plan to enlarge the study cohort to confirm our data.

Disclosure: Conflict of interest. Nothing to declare.

Experimental Transplantation

P037.

Influence of Polymorphisms Related to Drug Metabolism in Allogeneic Bone Marrow Transplantation

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Background: in hematopoietic stem cell transplantation (allo-HSCT), the study of pharmacogenetics can provide markers that predict individual variability and tolerability to treatments and possible complications of various drugs.

Methods: 54 transplant patients between 2017-2018 in our center were selected. DNA samples were genotyped in triplicate using mass spectrometry in the MassARRAY equipment (Agena Bioscience, San Diego, CA, USA), following the SNPs panel "VIP Basic" designed and registered by our center´s Pharmacogenetics Platform. This panel is aimed at SNPs whose alterations could be related to drugs used in solid organ transplantation.

Cystitis/Graft *vs* host disease (GvHD) and blood recovery were evaluated using logistic and linear regression models respectively penalized with elastic net. To assess overall survival (OS), Cox regression model penalized with elastic net was performed.

Results: Patients median age was 46 years. 33% of the patients were women and 67% men. Median HCT-CI score was 2. We will describe the SNPs that were arbitrarily considered to be most relevant after performing the statistical analysis: those that presented an Odds Ratio (OR) <0.9 and> 1,1 and were related to drugs used regularly in allo-HSCT.

GG genotype in SNP Rs1799931 (NAT2 gene) presented an increased risk of GvHD, with an OR 1,176. In our series, 47 patients presented this SNP. Twenty-four of them had at least one NAT2*6 allele (slow acetylator). AC and CC genotypes in SNP Rs2032582 (ABCB1 gene) were related to GvHD in the opposite way. AC genotype presented an OR 0.72, while CC genotype presented an OR 1.23. CG genotype in SNP 1800462 (TPMT gene) corresponds to TPMT*1/*2 haplotype of this gene. Patients with at least one *2 allele were more likely to have myelosuppression. TT genotype in SNP rs3740066 (ABCC2 gene) was associated with a decreased risk of hemorrhagic cystitis, with an OR 0.42. AC genotype in SNP rs11212617 (ATM gene) was associated with an increased risk of hemorrhagic cystitis, with an OR 1.89. GT genotype in SNP rs3745274 (CYP2B6 gene) was associated with greater OS than GG or TT genotypes, with an OR 0.73. CC genotype in SNP rs2032582 (ABCB1 gene) was associated with lower OS compared to AA and AC genotypes, with an OR 0.9.

Conclusions: The current study presents a series of limitations, among them: small cohort, SNPs panel not specific for allo-HSCT, and the large number of drugs involved in the bone marrow transplantation. Because of this, it requires a cautious interpretation of the results. However, this study makes it possible to propose a series of hypotheses that should be studied more in depth in future works. Pharmacogenetics is part of future medicine, oriented towards individualized pharmacological treatments. Its implementation within allo-HSCT will be of great importance given its potential to improve patients´ life quality and prognosis by avoiding toxicities and drug failure.

Disclosure: Nothing to declare.

P038.

Reduced-Intensity Unmanipulated Haploidentical Stem Cell Transplantation for Relapsed High-Risk Neuroblastoma After Autologous Stem Cell Transplantation

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Background: Neuroblastoma (NB) is one of the most common indications for autologous stem cell transplantation (auto-SCT) in pediatrics, however, the main cause of treatment failure after auto-SCT is relapse/progression, rather than treatment-related mortality.[i] This unsatisfactory results in patients with relapsed NB, together with the growing insights in the mechanisms of graft-versus-solid tumor effects has inspired clinicians to undertake trials investigating the effect of allogenic SCT (allo-SCT).[ii] Here, we report the outcomes of haploidentical allo-SCT in two patients with NB who relapsed after auto-SCT.

[i] Yi ES, Son MH, Hyun JK, Cho HW, Ju HY, Lee JW, Yoo KH, Sung KW, Koo HH. Predictors of survival in patients with high-risk neuroblastoma who failed tandem high-dose chemotherapy and autologous stem cell

transplantation. Pediatric Blood & Cancer. 2020 Feb;67(2): e28066.

[ii] Willems L, Waer M, Billiau AD. The graft-versus-neuroblastoma effect of allogeneic hematopoietic stem cell transplantation, a review of clinical and experimental evidence and a perspective on mechanisms. Pediatric blood & cancer. 2014 Dec;61(12):2151-7.

Hirayama et al., 2006; Inoue et al, 2003; Lang et al., 2006; Marabelle et al., 2007; Toporski et al., 2009.

Methods: The first patient was a 20-year-old male with progression of high risk NB, 4 years after high dose chemotherapy with autologous peripheral blood stem cell rescue (HDCT/ASCT), referred with multiple Iodine 131-metaiodobenzylguanidine (MIBG) avid metastatic lesions. Before allo-SCT, he underwent salvage chemotherapy and one week after that, imaging revealed no MIBG-avid tumoral lesion throught the body. He received MIBG-therapy together with allogeneic peripheral blood stem cell transplant from his HLA-haploidentical father.

The second patient was a 14-year-old boy with high risk NB who had failed HDCT/ASCT, presneted with multiple MIBG-avid tumoral masses. Five courses of salvage chemotherapy were relatively effective and he was referred for allo-SCT. MIBG scan before transplant demonstrated MIBG-avid tumoral lesion in the posterior arch of the left 12th rib. He received MIBG-therapy together with allogeneic peripheral blood stem cell transplant from his HLA-haploidentical father.

Results: Complete donor lymphocyte chimerism was achieved on day 15 post SCT in both patients. No acute and chronic graft versus host disease (GVHD) occurred in neither of patients. Disease response was evaluated on days +100, +180, +365 post transplant, with MIBG scan which revealed no tumoral lesion through the body in the first patient and a stable lesion on the left 12th rib in the second patient.

Conclusions: Early studies of allo-SCT in children with high-risk NB suggest that this is a feasible approach that may improve the outcome in this deadly disease.

Disclosure: Non declared.

Gene Therapy

P039.

Betibeglogene Autotemcel (Beti-Cel; Lentiglobin for B-Thalassemia) Gene Therapy Treatment of A Greek Patient with Transfusion-Dependent B-Thalassemia (TDT)

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Background: Gene therapy with betibeglogene autotemcel (beti-cel; LentiGlobin for β-thalassemia) is being evaluated in patients with transfusion-dependent β-thalassemia (TDT) in two Phase 3 studies, Northstar-2 (NCT02906202) and Northstar-3 (NCT03207009). We present a case report of the first Greek patient treated with gene therapy for β-thalassemia; a 33-year-old male with a β0/β+ (IVS-I-110) genotype.

Methods: Following hematopoietic stem cell collection via G-CSF plus plerixafor mobilization and apheresis, CD34+ cells were transduced with the BB305 lentiviral vector (LVV) encoding a functional βT87Q-globin gene. The patient was under a hypertransfusion scheme before mobilization and conditioning, maintaining a pre-transfusion hemoglobin (Hb) of ≥11g/dL. After receiving pharmacokinetic-adjusted, single-agent busulfan myeloablation, beti-cel was infused intravenously.

Results: The patient's annualized pRBC transfusions (number [volume]) 2 years prior to enrollment were 39.5 (175.5 mL/kg/year). During myeloablation, the estimated average daily busulfan area under the curve was 5,350 μM*min. The patient was infused with 7.6x106 CD34+ cells/kg. The percentage of LVV+ cells in the drug product was 78% and the vector copy number per diploid genome transduced cells was 4.3 in the drug product and ranged from 1.01–1.31 in peripheral blood, after infusion throughout follow-up. Neutrophil and platelet engraftment occurred after 26 and 58 days, respectively.

After beti-cel infusion, the patient received 8 RBC transfusions until Day 39 and has since not received transfusions for 15.3 months. Total Hb values were 12.1, 13.1, and 12.7 g/dL at Months 6, 9, and 12, respectively, and were predominantly driven by the gene therapy-derived HbAT87Q, which was 9.9, 11.3, and 11.1 g/dL at the same time points. The patient achieved and maintained transfusion independence (TI) (defined as weighted average Hb ≥9 g/dL without RBC transfusions for ≥12 months), for an ongoing duration of TI of 12.9 months. Weighted average Hb during TI was 12.7 g/dL.

Serum ferritin increased from 1,203 ng/mL at baseline to 1,571 ng/mL at Month 6, due to the myeloablative procedure with preceding hypertransfusion and the suspension of chelation, and decreased back to 1,227 ng/mL at Month 12. The patient started phlebotomy for iron reduction at Day 238 post-infusion. Soluble transferrin receptor levels

were 78.8 nmol/L at baseline and decreased to 68.2 nmol/L at Month 12.

The patient experienced grade 2 abdominal pain/discomfort during infusion, considered as possibly related to treatment. Grade ≥3 adverse events post-infusion were all considered to be related to myeloablative conditioning, including anemia, neutropenia, febrile neutropenia, thrombocytopenia, and stomatitis. All samples showed polyclonal vector integration, with no evidence of clonal dominance post-treatment and no single integration site contributing to more than 5% of all integration sites at any time.

Conclusions: Following treatment with beti-cel, a heavily transfused 33-year-old patient with TDT and a β0/β+ (IVS-I-110) genotype reached gene therapy-derived HbAT87Q levels above 11 g/dL by Month 9, enabling the patient to become and remain transfusion independent for an ongoing period of more than one year. Total Hb value was 12.7 g/dL at Month 12. The treatment regimen had a tolerability profile consistent with that of busulfan myeloablation.

Clinical Trial Registry: Northstar-3 (NCT03207009). LTF303 (NCT02633943).

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DM nothing to disclose.

Graft-versus-host Disease – Clinical

P040.

Effect of Extracorporeal Photopheresis On Enrichment, Survival And Cytokine Production Capacity of Monocytes From Chronic Graft Versus Host Disease Patients

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Background: Extracorporeal photopheresis (ECP) is a second line therapy for steroid refractory, dependent or intolerant chronic GVHD (cGVHD) where patients undergo cycles of infusion with high numbers of apheresed autologous leukocytes primed to die by apoptosis. Monocytes are precursors of macrophages, which produce factors that contribute to the formation of GVHD fibrotic lesions, and have been found to infiltrate cGVHD skin. Indeed new strategies for cGVHD therapy involve blocking macrophage trafficking and profibrotic functions. Where previous data have demonstrated that monocytes are as highly susceptible to ECP-induced apoptosis as lymphocytes (1), more recent data have suggested that ECP-treated monocytes have selective survival and maintain ability to secrete pro-inflammatory cytokines such as IL-1B (2,3). Given these conflicting data and their implications for ECP, we have investigated the degree to which clinical ECP delivered by a closed inline system concentrates peripheral blood monocytes of cGVHD patients, whether it induces monocyte apoptosis and impact on monocyte cytokine production capacity.

Methods: Pre-treatment peripheral blood and matched ECP leukapheresis bag samples were collected from a cohort of 25 cGVHD patients (17male /8 female; age range: 30-66) treated with the Therakos Cellex system. Patients had GVHD affecting skin (25/25), mucosal membranes (11/25), liver (6/25), joints (5/25), gut (8/25), eye (10/25), genital (7/25) and subsets were enumerated using an Advia hematology analyser. Monocytes were positively selected from paired blood and ECP bag samples and apoptosis was assessed after 18h culture, in the presence or absence of pro-survival M-CSF, by flow cytometry using annexin-v and propidium iodide staining. Monocyte cytokine production was stimulated with LPS; either immediately (d0) or 1 day after isolation (d1), and supernatants collected 18h later. Secreted cytokines were assessed using Cytometric Bead Analysis assays. Statistical analysis was 2-way ANOVA with repeat measures and appropriate post-hoc tests for multiple comparisons using GraphPad Prism 6. A p value <0.05 was considered significant.

Results: Absolute monocyte counts in post-ECP leukapheresis samples were highly variable (range: 0.5 – 40 × 109/l) though substantially enriched (median: 2.3 × 109/l and IQR:1.1 – 4 × 109/l) compared to pre-ECP blood (median 0.4 × 109/l and IQR: 0.3 – 0.55 × 109/l; $n = 25$). ECP consistently induced high levels of monocyte apoptosis after overnight culture compared to pre-ECP controls (79% +/- 10% vs 15%% +/- 6.3% apoptotic, respectively; $n = 9$; $P < 0.0001$), which could not be rescued by M-CSF. ECP treatment significantly inhibited LPS-induced monocyte IL-1B, IL-6 and IL-10 production stimulated at d0 compared to pre-ECP controls ($P < 0.01$, $P<0.001$ and $P < 0.0001$, respectively) and additionally the capacity to produce IL23p40 and TNFa after delayed LPS stimulation on d1 ($P < 0.001$ and $P < 0.05$, respectively).

Conclusions: Clinical ECP of cGVHD patient leukocytes enriches monocytes for infusion, induces massive levels of monocyte apoptosis and causes rapid and profound suppression of LPS-induced monocyte cytokine production including IL-1B. These depleting effects on potentially pro-inflammatory monocytes may contribute to the therapeutic immunomodulatory impact of ECP in cGVHD.

Disclosure: NCM,AA have received research grant from Mallincrodt Ltd.

P041.

Acute And Chronic Graft-Versus-Host-Disease Impair B-Cell Reconstitution in Allogeneic-Transplanted Patients at Different Maturation Stages

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Background: Allogeneic stem cell transplantation is a curative treatment for hematological neoplasms but associated with Graft-versus-Host Disease (GvHD). GvHD is induced by co-transplanted T cells and affects a variety of organs and tissues including host marrow stroma cells. Patients with acute GvHD suffer from delayed recovery of the B cell compartment. While murine models indicate a medullary maturation arrest at the level of the common lymphoid progenitors (CLP), the pathophysiology in humans has been much less elucidated.

Methods: We investigated the effects of acute and chronic GvHD on the reconstitution of the medullary and peripheral B cell compartment in 76 allogeneic-transplanted recipients treated at the University Hospital Regensburg (funding: SFB Transregio 221, DFG). For assessment of GvHD the MAGIC (aGvHD) and NIH 2015 criteria (cGvHD) were applied and patients were retrospectively divided into 4 groups: no GvHD ($n = 23$), aGvHD °II-IV ($n = 18$), de novo cGvHD ($n = 17$) and quiescent cGvHD ($n = 13$). Patients with aGvHD °I without systemic treatment ($n = 5$) were excluded. On days +28, +90 and +180 bone marrow and peripheral blood samples were collected and cytometrically analyzed with respect to the composition of B cell subpopulations. We defined hematopoietic stem cells (HSCs) and CLPs as CD45+CD22-CD19-CD34+ (HSCs CD7-CD45RA-, CLPs CD7+CD45RA+), Pro-/Pre-B cells as CD45+CD22+CD19+CD10+ (Pro-B cells CD34+, Pre-B cells CD34-), medullary immature B cells as CD45+CD22+CD19+CD10+IgM+ and mature naïve B cells as CD19+CD21+CD27-.

Results: at d90 we observed a 1.5- to 16.5-fold increase in bone marrow precursor and peripheral mature subpopulations in the no GvHD control group as compared to d30. Until d180 the proportion of HSCs (0.02%) and CLPs (0.01%) slightly decreased, while Pro- (0.17%), Pre- (1.15%), medullary immature (0.15%) and mature naive B cells (2.01%) reached a plateau. The occurrence of aGvHD °II-IV and quiescent cGvHD had no impact on HSCs (0.01%) or CLPs (0.01%) at d180, whereas an almost complete and protracted maturation arrest occurred in almost all subsequent B cell development stages. In contrast, de novo cGvHD patients reconstituted the B cell compartment like patients without GvHD. In GvHD-free patients that later developed cGvHD the proportion of immature B cells was distinctly (though not significantly) reduced already before disease onset at d90 in the bone marrow (0.03 vs 0.18%) and in the peripheral blood at d180 (0.01 vs 0.26%).

Conclusions: These results demonstrate a maturation arrest of the B cell compartment at the CLP level in acute GvHD °II-IV, while de novo cGvHD does not affect the regeneration of B cell precursors, but potentially affects the development of immature B cells.

Clinical Trial Registry: The study was approved by the local ethics committee (number 17-624-101).

Disclosure: M Fante has received grants from Neovii and Novartis. D Wolff has received honoraria from Mallinckrodt, Novartis, Takeda, MACO and Neovii. All other authors declare no conflicts of interest.

P042.

Prolonged Suppression of Butyrate Producing Bacteria Indicates Dysbiosis And is Associated with Acute Gastrointestinal Graft-Versus-Host Disease And Transplant Related Mortality After Allogeneic Stem Cell Transplantation

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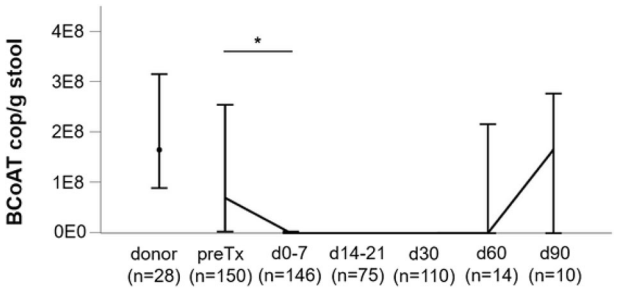
Background: Butyrogenic bacteria play an important role in gut microbiome homeostasis and intestinal epithelial integrity. Previous studies have demonstrated an association

between administration of short chain fatty acids like butyrate and protection from acute graft-versus-host disease (aGvHD) after allogeneic stem cell transplantation (ASCT).

Methods: Here we examined the abundance and butyrogenic capacity of butyrate producing bacteria in 28 healthy donors and 201 patients after ASCT. We prospectively collected serial stool samples and performed PCR analysis of butyryl-CoA:acetate CoA-transferase (BCoAT) in fecal nucleic acid extracts.

Results:



Our data demonstrate a strong and prolonged suppression of butyrate producing bacteria early in ASCT ($p < 0.001$). In a multivariable analysis, early use of broad-spectrum antibiotics before d 0 (day of transplantation) was identified as independent factor associated with low BCoAT copies at d 0-7 post tx (odds ratio 0.370 (0.175-0.783), $p = 0.009$). Diminished butyrogens correlated with other biomarkers of microbial diversity such as low 3-indoxyl sulfate (3-IS) levels, reduced abundance of Clostridiales and low Simpson and Shannon indices ($p < 0.001$, respectively). Low BCoAT copies at GvHD-onset correlated with GI-GvHD severity ($p = 0.003$) and were associated with significantly higher GvHD associated mortality ($p = 0.043$). Furthermore, low BCoAT copies at d 30 in both GvHD and non-GVHD patients were associated with significantly higher transplant related mortality ($p = 0.025$).

Conclusions: Our data affirm the hypothesis that microbiome alterations may play an important role in GvHD pathogenesis and that microbial parameters such as BCoAT might serve as potential biomarkers to identify patients at high risk for developing lethal GI-GvHD. Further studies are needed to truly understand how microbes may contribute to GvHD.

Disclosure: Nothing to declare.

P043.

Reduced Gvhd with Triple Ptcy Based Gvhd Prophylaxis, As Compared to Triple Atg Based Prophylaxis, in Hla Matched Transplants

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Background: Post transplant high dose cyclophosphamide (PTCY) has been the greatest change in GvHD prophylaxis of the past two decades, pioneered by the Baltimore group. This has been true for transplants from HLA haploidentical donors, though several Centers are now considering the use of PTCY in HLA matched grafts. The question is, how does a PTCY based GvHD prophylaxis compare with an ATG based prophylaxis.

Methods: We are now reporting a retrospective comparison of HLA matched transplants ($n = 159$), from 2015 to 2020, receiving a triple PTCY based ($n = 72$) versus a triple ATG based ($n = 87$) prophylaxis.

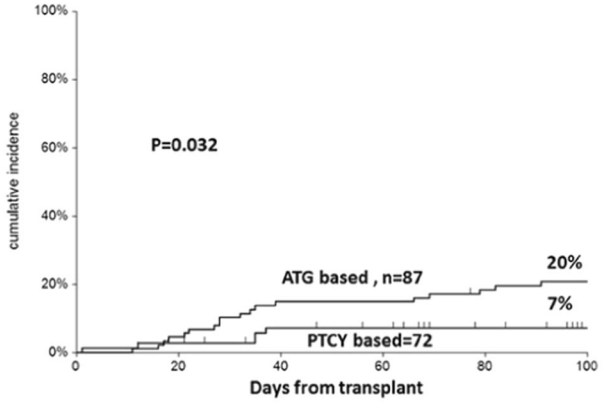
Patients selected for this analysis received HLA matched grafts from HLA identical siblings ($n = 77$) or unrelated donors ($n = 82$). Triple PTCY prophylaxis consisted of PTCY 50 mg/kg day for two days post-HSCT, plus cyclosporine (CSA) and michophenolic acid (MMF). Triple ATG prophylaxis consisted of ATG 2.5 mg/kg (siblings) or 5 mg/kg (unrelated donors) plus CSA and methotrexate (MTX). The stem cell source was G-SCF mobilized peripheral blood for all patients. Clinical characteristics in the ATG and PTCY group were as follows: median age 51 vs 48 years; diagnosis of NHL 6 vs 5, HL 0 vs 4, SAA 5 vs 0, acute leukemia 47 vs 39, MDS 10 vs 4, MPD 14 vs 15 and non-malignant disease 5 vs 5; conditioning including ablative TBI 4 vs 12, reduced intensity 19 vs 1, thiotepa-busulphan-fludarabine (TBF) 53 vs. 49 and Baltimore regimen 11 vs. 10.

Results: The cumulative incidence of acute GvHD grade II-IV was of 20% in the ATG group as compared to 7% in the PTCY group ($p = 0.032$, Figure 1). Multivariate analysis confirmed that PTCY based prophylaxis reduced grade II-IV acute GvHD as compared to ATG based prophylaxis (HR 0.26, 95% CI 0.09-0.73, $p = 0.01$), while a trend for a greater risk was seen for unrelated as compared to related donors (HR 2.3, 95% CI 0.88-6.35, $p = 0.09$). Another trend was seen for an increased risk of relapse at two-years for the PTCY group (1%) as compared to the ATG group (19%) ($p = 0.07$), whereas the two-year transplant-related mortality (TRM) was comparable in the two groups (16% vs. 4% respectively, $p = 0.2$), as well as for disease free survival.

Conclusions: Triple PTCY based GvHD prophylaxis, reduces the risk of aGvHD II-IV in HLA matched

transplants, as compared to an ATG based prophylaxis. This does not translate, to date, in a significant reduction of TRM, and may be associated with an increased risk of relapse.

Figure 1. Acute GvHD II-IV in HLA matched transplants: the effect of the GvHD prophylaxis.



Disclosure: Conflict of interest. Nothing to declare.

P044.

The Same for Less: 2.5 mg/kg vs. 4.5 mg/kg Rabbit Anti-Thymocyte Globulin in Patients Undergoing Matched Unrelated Donor Allogeneic Stem Cell Transplantation for Hematological Malignancies

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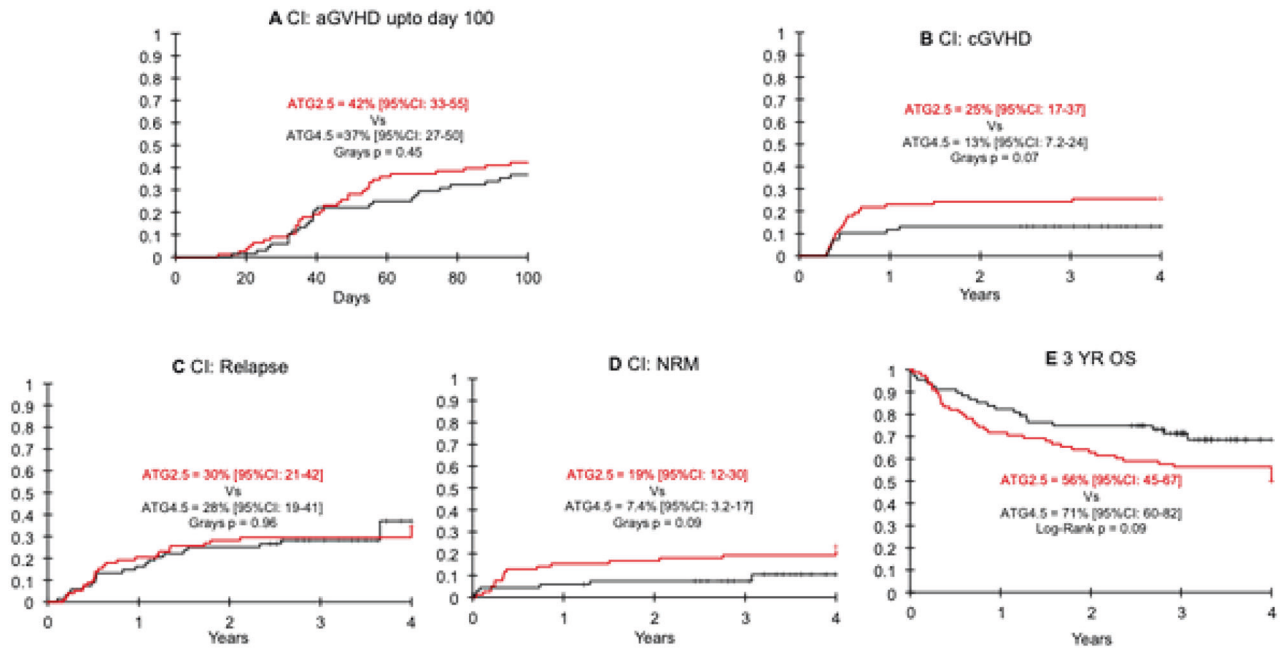
Background: Anti-thymocyte globulin (ATG) prior to matched unrelated donor (MUD) alloSCT reduces the incidence and severity of graft-versus-host disease (GVHD), in some studies. Higher doses have been associated with adverse outcomes of infection and relapse that may offset the beneficial effect on GVHD. We hypothesized that ATG2.5 would result in similar incidence of GVHD and survival with less toxicity than ATG4.5.

Methods: Retrospective review of two cohorts of patients from The Ottawa Hospital BMT Program who underwent MUD AlloSCT for hematological malignancies and received rabbit ATG thymoglobulin (rATG) 2.5 mg/kg (ATG2.5) from 2010-2014 or 4.5 mg/kg (ATG4.5) from 2016-2017 along with short course methotrexate and calcineurin inhibitor for GVHD prophylaxis. rATG was administered at a dose of 0.5 mg/kg on day -2, and 2 mg/kg on day -1 (ATG2.5) or 0.5 mg/kg on day -3 and 2 mg/kg/day on days -2 and -1 (ATG4.5).

Results: ATG2.5 ($n = 78$) and ATG4.5 ($n = 68$) groups, were balanced for median age (48yrs vs 54yrs p= 0.59),%



female (38 vs 32 p = 0.44),% KPS ≥80 (91vs 86, p = 0.41), % CMV -/- (43 vs 35, p = 0.3),% HCT-CI ≥ 3 (9 vs 16, p = 0.18), and%DRI High/very-high (18 vs 28, p= 0.15). The ATG2.5 had more% MAC (73 vs 50, $p < 0.01$) and fewer% PB graft (85 vs 100, $p < 0.01$). On univariate analysis, there was no difference between ATG2.5 and ATG4.5 in days to engraftment of neutrophils (median 16 vs 17, $p = 0.31$), platelets (median 18 vs 18, $p = 0.67$), and length of stay (median 30.5 vs 30 $p = 0.18$).

In ATG2.5 vs ATG4.5 groups, on univariate analysis, there was no difference in aGVHD requiring systemic steroid by day 100 (42% vs 37%, $p = 0.45$), 3-yr cumulative incidence of cGVHD (25% vs 13% $p = 0.07$), relapse (30% vs 28% p= 0.96), non-relapse mortality (19% vs 7.4% $p = 0.09$) or 1 yr and 3 yr OS: 71% (95%CI 60-80) vs 82% (95%CI 73-91); and 56% (95%CI 45-67%) vs 71% (95%CI 60-82%) respectively, $p = 0.09$.

On univariate analysis,% GRFS at 1 and 3-yr favored ATG4.5 vs. ATG2.5: 51 (95%CI 40-63) and 45 (95%CI 33-57) vs 33 (95%CI 22-43) and 24 (95% CI 14-33), $p = 0.01$. In multivariate analysis (adjusted for Age, ATG dose, DRI, HCT-CI, KPS, CMV status, and conditioning intensity), only RIC was associated with improved GRFS; HR 0.54 (95%CI 0.34-0.86, $p = 0.007$).

Conclusions: in this single-center retrospective analysis, ATG2.5 and ATG4.5 were not different with regard to major clinical outcomes of interest. with MVA, only conditioning regimen intensity was associated with GRFS. In the absence of an RCT, these results support our standard practice of using ATG2.5 in combo with MTX and FK506 as GVHD prophylaxis in MUD alloSCT.

Disclosure: Nothing to declare.

P045.

Comparison of Post-Transplantation Cyclophosphamide Versus Anti-T-Lymphocyte Globulin As Gvhd Prophylaxis in Adult Patients with Acute Lymphoblastic Leukemia Undergoing Allogeneic Hematopoietic Stem Cell Transplantation in CR1

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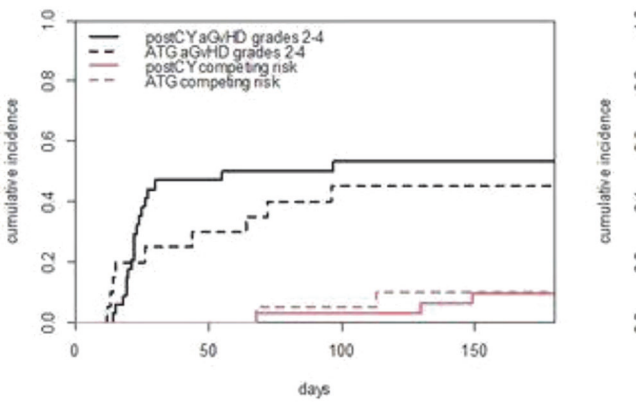
Background: High risk acute lymphoblastic leukemia (ALL) in first complete hematologic remission (CR1) is best treated by allogeneic stem cell transplantation (alloSCT). Standard myeloablative conditioning combines total body irradiation (TBI) with cyclophosphamide, and sometimes anti T-lymphocyte globulin (ATG). Overall survival (OS) after 2 years is 60%-76%. Novel approaches to induce a more potent graft-versus-leukemia effect are warranted.

Methods: 54 adult patients with ALL in CR1 were transplanted after conditioning with TBI 12Gy, cyclophosphamide 120 mg/kg BW, ATG 30-90 mg/kg BW (20 patients), and TBI 8-12Gy, fludarabine 120 mg/m², cyclophosphamide 100 mg/kg BW post transplantation (days +3, +4, 34 patients).

Results: Patients in the postCY cohort were considerably older. The cumulative incidence of acute graft-versus-host-disease (GvHD) grades 2-4 did not differ between the groups (ATG: 45%, standard error (SE) 11.5%, versus postCY: 53.4%, SE 8.8%, p=.522, Figure 1A). Neither did chronic GvHD (all grades, ATG: 45%, SE 11.6%, versus postCY: 58.6%, SE 10%, p=.469; NIH grade 2 and 3, ATG: 26.7%, SE 10.7%, versus post CY: 43.4, SE 10.4%, p=.336, Figure 1B). Two-year-OS was 80% (95% confidence interval 64.3%-99.6%, ATG) versus 70.4% (54.7%-90.6%, postCY, p=.57), disease free survival (DFS) at 2 years 80% (64.3%-99.6%) versus 67.9% (52.4%-87.9%, p=.42). In a competing risk model, incidences of non-relapse-mortality and relapse did not differ.



Conclusions: Prophylaxis of GvHD with post transplant cyclophosphamide leads to an incidence of both aGvHD and cGvHD comparable with that achieved when using ATG. AGvHD seems to occur at an earlier time. Consequently, similar results of OS and DFS are seen. Larger trials are warranted to corroborate these findings.

Disclosure: Nothing to declare.

P046.

Triple PTCY Based GVHD Prophylaxis: HLA Matched Versus HLA Haploidentical Transplants

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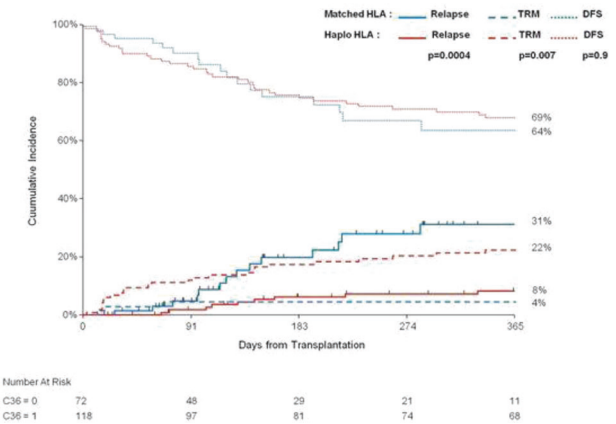
Background: Post-transplantation cyclophosphamide (PTCy) is a widely used strategy for Graft versus host disease (GVHD) prophylaxis. Despite traditional platforms still consider PTCy purely for HLA-haploidentical donors, there is growing interest in PTCy usage in HLA-matched donors setting.

Methods: We report a retrospective analysis of 190 patients who underwent an allogeneic stem cell transplant (HSCT) at our Institution from 2016. All patients received the same triple GVHD prophylaxis, namely PTCy, cyclosporine and mycophenolate mofetile. We compared HLA matched transplants (matched-HLA), including siblings (31 patients,16%) and matched unrelated donors (41 patients,22%), versus HLA haploidentical related transplants (haplo-HLA) (118 patients,62%). Patients receiving SCT from cord blood units and mismatched unrelated donors were excluded.

Results:



The stem cell source was GCSF-primed peripheral blood for matched-HLA donors, and unmanipulated bone marrow for haplo-HLA donors. Patients in matched-HLA group were younger (median age 48.5 vs 57), and were transplanted more recently (median year of SCT 2020 vs 2018); no other significant difference was found among the two groups. The diagnosis was acute leukemia(58%), myelofibrosis(20%), lymphoma(11%) or myelodisplastic syndrome(9%), with no significant difference between groups ($p = 0.16$). Conditioning regimen was myeloablative in 78% and 73% of the two groups, respectively ($p = 0.45$).Overall, 36(19%) patients developed acute GVHD grade II-IV: 7% and 26% in the matched and haplo-HLA group, respectively ($p = 0.001$). Also moderate to severe chronic GVHD was more frequent in the haplo-HLA group (6% vs 22%, $p = 0.002$). In pre-letermovir era, cytomegalovirus (CMV) reactivation (>1,000 viral copies/ml) was more incident in haplo-HLA (13% vs 45%, $p < 0.001$), with similar median onset (42 vs 40 days) and duration (7 vs 8 days) among the two groups.

The Cumulative Incidence (CI) of transplant related mortality (TRM) at 1 year for matched-HLA vs haplo-HLA was 4% vs 22% ($p = 0.007$) in a Cox multivariate analysis haplo-HLA transplants remained a significant predictor of TRM (HR 3.3, $p = 0.04$) when compared to matched-HLA patients, together with age over 60 years (HR 3.7, $p = 0.04$).

The Cumulative incidence (CI) of relapse at 1 year for matched-HLA vs haplo-HLA was 31% vs 8% ($p = 0.0004$). In a Cox multivariate analysis matched-HLA remained a significant predictor of relapse (HT 3.1, $p = 0.01$) when compared to haplo-HLA, together with advanced disease (HR 3.2, $p = 0.02$). When selecting patients in CR1/CR2 there was only a trend ($p = 0.07$) for more relapse in the matched HLA patients (6% vs 21%). In patients with advanced disease the difference was more pronounced (10% vs 39%, $p = 0.002$).

Disease free survival (DFS) at 1 year was 64% and 69% in matched and haplo HLA group, respectively ($p = 0.9$). Predictive variables for DFS were older age (over 60 years) (HR 2.8, $p = 0.03$), and advanced disease (HR 1.9, $p = 0.04$).

Conclusions: in conclusion: GVHD is reduced in HLA-matched transplants when receiving PTCy+CSA+MMF, as compared to haploidentical grafts, with 7% grade -IV acute GVHD and 6% moderate-severe chronic GVHD in the HLA-matched group. This translates in significantly reduced TRM. However, relapse appears to be increased, particularly in advanced diseases, leading to identical disease free survival. One may therefore consider tailored GVHD prophylaxis strategies according to disease burden and patients characteristics.

Disclosure: Nothing to declare.

P047.

A Phase 2/3, Multicenter, Randomized, Double-blind, Placebo-Controlled Study of ALPHA-1 Antitrypsin for The Prevention of Acute Graft Versus Host Disease Following Hematopoietic Cell Transplant

John Magenau[1], Scott Adler[2], John Mallee[2], Christine Voigt[2], H. Joachim Deeg[3]

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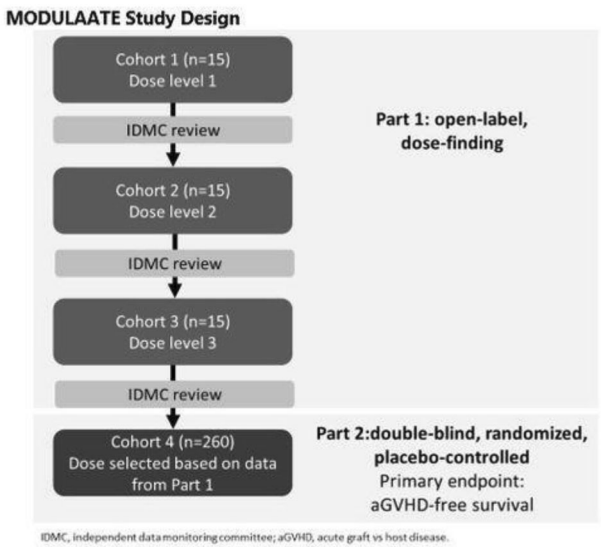
Background: Approximately 40–60% of patients will develop acute graft versus host disease (aGVHD) following allogeneic hematopoietic cell transplantation (HCT), resulting in very high morbidity and mortality (1-year overall survival is 10–30% for Grades III–IV aGVHD). Current prophylaxis for GVHD is typically based on calcineurin inhibitors (CNI) combined with methotrexate (MTX) or other agents including mycophenolate mofetil, antithymocyte globulin, post-transplant cyclophosphamide or sirolimus. Despite multiple approaches, no regimen has demonstrated consistent clinical benefit over CNI +MTX-based prophylaxis for the prevention of GVHD, reflecting an urgent unmet clinical need for improving outcomes after allogenic HCT.

Alpha-1 antitrypsin (AAT) is a plasma protein produced by the liver; it inactivates several serine proteases and it has immunomodulatory properties. AAT is currently approved to treat patients with AAT deficiency and related emphysema (Zemaira®/Respreeza®, CSL Behring). Preclinical data have shown that administration of AAT is associated with the induction of anti-inflammatory and reduction of pro-inflammatory cytokine secretion, induction of regulatory T cells and interference of dendritic cell maturation, which are associated with improved GVHD-free survival in mice. Two open-label clinical studies of AAT treatment in patients with steroid-refractory aGVHD have demonstrated few GVHD manifestations and promising response rates with a manageable tolerability profile.

Methods:



This is a 2-part study: a dose-finding part in 3 cohorts will determine the dose of AAT to be evaluated for efficacy in the randomized double-blind, placebo-controlled part (Figure 1). The modified Harris acute GVHD criteria will be used to assess aGVHD through 180 days, with the primary endpoint of aGVHD-free survival, measured as time to aGVHD (Grades II–IV) or death. Secondary outcome measures include ranges and individual grades of GVHD post-allogenic HCT through 100 and 180 days, time to all-cause mortality, and rate of systemic infections. Secondary and exploratory objectives are to further evaluate the safety of AAT, steady-state pharmacokinetics of AAT, biomarkers of aGVHD and the effect of AAT on quality of life measures.

Results: Recruitment is ongoing across international sites in North America, Europe and Australia.

Conclusions: The current phase 2/3 study will evaluate the safety and efficacy of AAT for the prevention of aGVHD in patients aged ≥12 years undergoing T-cell replete allogenic HCT for hematological malignancies with a planned high intensity (myeloablative) conditioning regimen.

Clinical Trial Registry: Clinicaltrials.gov – NCT03805789.

Disclosure: John M. Magenau: Merck - Collaborator, Research Funding; OncoImmune - Collaborator, Research Funding.

Scott Adler: CSL-Behring - Clinical TA Head, Ownership Interest and Salary.

John Mallee: CSL-Behring - Employee, Ownership Interest and Salary.

Christine Voight: CSL-Behring - Employee.

H. Joachim Deeg: Nothing to declare.

P048.

Chronic And Late Acute Gvhd in Children Using The NIH 2014 Consensus Criteria

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Background: The diagnostic criteria for chronic graft versus host disease (cGVHD) were developed primarily from adult data. The clinical applicability of the National Institutes of Health 2014 Consensus Criteria (NIH 2014-CC) still remains unknown and very little is known about late acute GVHD (L-aGVHD) in children.

Methods: Between January 2014–December 2019, 405 children who underwent the first HSCT in Medicalpark Göztepe Hospital Pediatric Bone Marrow Transplantation Unit were evaluated retrospectively.

Results: This study involved 405 children (female $n =$ 194, male $n = 211$); the median age of the patients was 79 months (1-263 months), and the primary disease was malign in 120 patients and non-malign in 285 patients. According to donor type, 204 transplants were performed

from matched unrelated donor (MUD) (10/10 MUD $n =$ 112, 9/10 MUD $n = 92$), 123 from matched sibling donor (MSD), 57 from matched family donor (MFD), and 21 from haploidentical donors. The leading stem cell source was bone marrow (BM) for 227 transplants, followed by peripheral blood stem cells (PBSC) for 154, combined BM+PBSC for 13 (in only haplo-procedures), cord blood (CB) for 7, and combined BM+CB for 4 (from MSDs) transplants. Myeloablative and non-myeloablative conditioning were preferred for 357 patients, and 41 patients, respectively, and 7 transplants were performed without conditioning. Total body irradiation was used only in 20 patients with malign disorders. Anti-thymocyte globulin (ATG) was used for serotherapy in 255 transplants (malign $n = 35$, non-malign$n = 220$) with total doses of 30-45 mg/kg on 3 consecutive days. Twenty-nine patients (7.2%) developed cGvHD at a median day +240 (range day 85-1747) according to NIH-2014 Consensus Criteria. Twenty patients (5%) developed L-aGvHD, the majority ($n = 12$) experienced persistent late acute, 5 patients had recurrent L-aGvHD and only 3 of them developed true de novo L-aGvHD. The remaining 356 patients (87.8%) had no evidence of L-aGvHD or cGvHD.The most frequent organ systems involved with diagnostic or distinctive cGVHD manifestations in children, included the skin ($n = 23$),mouth ($n = 13$),eyes ($n = 11$), nails ($n = 9$), lungs ($n = 7$), hair ($n = 4$) and musculoskeletal system ($n = 4$). At initial diagnosis children with confirmed NIH 2014-CC, cGVHD were assessed at maximal severity as having mild cGVHD (6/29;20.6%), moderate cGVHD (17/29;58.8%), or severe cGVHD (6/29;20.6%); the median number of organs involved was 3 (range,1-6).The univariable analysis revealed a significant increase in the risk of cGVHD with malignant disease (p = .007), recipient age ≥5 years at the time of transplant (p = .027), and a history of classical aGVHD grade 2-4 (p = .000). Such risk was significantly reduced when using ATG as serotherapy in conditioning (p< .01). The 5-year overall survival for all patients, cGvHD, and L-aGvHD were 80,2% 80,3%, and 84,5% respectively. And 2-year relapse-free survival for all patients, cGvHD, and L-aGvHD were 80,0% 85,4% and 90,9%, respectively. Both survival analyzes are found statistically insignificant.

Conclusions: Although the rate of cGvHD (7.2%) is low compared to literature, still it is a matter of debate on the classification of L-aGvHD (5%). Usage of ATG, age of the recipient, and history of aGvHD are impacting factors for cGvHD. Administration of ATG and age of the recipient affect the development of L-aGVHD.

Disclosure: Nothing to declare.

P049.

Abstract already published

P050.

Ibrutinib for Steroid Refractory Chronic Graft Versus Host Disease: Data And Clinical Experience From A Single Center

Panayotis Kaloyannidis[1], Ahmed Ayyad[1], Zakarya Bahaliwah[1], Zahra Alshammasi[1], Wael Alanazi[1], Hamdi Soudi[1], Ibrahim Ibrahim[1], Hani Al Hashmi[1]

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Background: Steroid refractory chronic graft vs. host disease (SR-cGvHD) remains a leading cause for late non-relapse mortality post allogeneic stem cell transplantation, it also adversely affects the quality of life of the long-term survived allografted patients and so far, no standard therapy exists. Recently, the bruton tyrosine kinase inhibitor (Ibrutinib®), has been approved by the US Food and Drug administration for the treatment of SR-cGvHD, showing remarkable efficacy and acceptable toxicity in a phase 1b/2 study, however, the real-world data from its clinical use are still limited.

Methods: We retrospectively evaluated 11 patients aged of 28,6 (17-62) years who received Ibrutinib® as ≥2 line of treatment for severe SR-cGvHD (as per NIH criteria). All had received peripheral blood stem cells from full matched sibling donors after myeloablative ($n = 8$) or reduced intensity conditioning regimen ($n = 3$). Acute GvHD was preceded in 6 (de-novo=2, induced=4) patients. The involved organs were skin ($n = 11$), oral mucosal ($n = 9$), liver ($n = 6$), lungs ($n = 5$), gastrointestinal tract ($n = 2$), musculoskeletal system ($n = 2$). Five patients had 3 organs involvement, four had 4 organs, one had 5 organs and one had 2 organs involvement. Nine patients received Ibrutinib® as 3rd line while 2 as 2nd line of treatment with a starting dose of 140 or 280mg daily and if it was well tolerated, the dose was escalated to the maximum of 420mg daily. All patients received the recommended prophylaxis against bacteria, viruses, fungi and pneumocystis Carinii.

Results: Within a median of 6,5 (3- 16) months of Ibrutinib® treatment, the overall response rate (ORR) was 82% (9/11 patients). Two patients achieved complete remission and currently are out of any immunosuppressive treatment (IST), three are off steroids and receive only ibrutinib® at low doses (140-280 mg/day), while in three was feasible steroids dose reduction by 35-75%. One patient failed to respond after 4 months of treatment, while one

patient who initially responded, eventually experienced cGvHD progression while on Ibrutinib®. Two patients experienced primary disease progression during the treatment. Infections were the commonest observed adverse event (5/11 patients, 45%) and interestingly in 4 patients (35%) it was related to possible invasive fungal infection (IFI). Currently, after a median follow up of 14 (8-23) months after Ibrutinib® initiation, 7 patients (63%) are alive; 2 out of IST for more than 8 months, 3 out of steroids, one is on low dose of steroids, while one patient who progressed during Ibrutinib® treatment continues with another 4th line IST. Four patients died. Two due to disease relapse and 2 (both responders to ibrutinib®) died because of possible IFI with CNS involvement.

Conclusions: in agreement with previous reports, in our small series of heavily pretreated patients with SR-GvHD, Ibrutinib® showed high rates of efficacy, offering ORR of approximately 80%. However, the observed high rates of fungal infections (approximately 50%) cannot be explained only from the previous heavy immunosuppression. Definitely, it merits of further investigation the role of Ibrutinib® in SR-GvHD and more effective approaches in terms of antifungal prophylaxis for patients treated with Ibrutinib® are needed.

Clinical Trial Registry: No clinical trial.

Disclosure: Nothing to declare.

P051.

Routine Use of The Amicus Blue™ Online ECP System in Patients with Chronic And Acute Graft Versus Host Disease

Angelo Ostuni[1], Maria Colonna[1], Angela Tullo[1], Maria Luigia Iaculli[1], Claudia Citarella[1], Anna Mestice[1], Cosima Battista[1]

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Background: A new system for extracorporeal photopheresis, the Amicus Blue™ ECP System (Fresenius Kabi, Germany), is now CE marked and commercially available in Europe. ECP is a new protocol on the Amicus Separator® which we have used since 7 years for MNC collection for DLI and offline ECP. The system incorporates a photoactivation device (Phelix), a functionally closed disposable kit, and 8-MOP (20 μg/mL, SALF) to perform ECP therapy in an online, closed system. We evaluated the system in routine use for the treatment of patients with chronic and acute GVHD.

Methods: Between March and October 2020, we performed 110 procedures in 14 patients (9 male, 5 female). Ten patients were under treatment for cGVHD ($n = 92$) and 4 for aGVHD ($n = 16$). All adult patients prescribed ECP and eligible for our standard offline procedure had treatment with Amicus Blue incorporated into their existing regimen. All patients had previous offline ECP treatment. Amicus v6.0, Phelix v2.0 and double-needle disposable kits were used. A 12:1 whole blood (WB) to ACD-A anticoagulant ratio was used, 1.24 mg/kg/min citrate infusion rate and maximum WB draw rate 80 ml/min. Most procedures targeted 2000ml WB processed ($n = 85$), while 3000ml was targeted for patients with low lymphocyte counts ($n = 25$). Hematology counts were performed on the patient WB and the treated MNCs, and lymphocyte apoptosis was measured at 72 hours.

Results: No adverse events were reported. Three patients had mild citrate reactions resolved with calcium gluconate. Median (range) WB flow rate was 40 (20 - 68) mL/min and total procedure time including collection, photoactivation and reinfusion was 97 (65 – 231) minutes. Collected cell yields are presented in the table. MNC purity was 96% (47-99), and median collection efficiency (CE2) was 54%. Lymphocyte apoptosis was as expected. In 15 instances of consecutive procedures ($n = 30$), there were no statistically significant differences in patient counts, treated cell counts/yields/CE between Day 1 and Day 2 procedures.

	2000 mL n.85	3000 mL n.23	cGVHD n.92	aGVHD n.16	Combined n.108
WBC ($x10^9$)	1.8 (0.5 – 4.9)	1.9 (0.6 – 7.5)	1.9 (0.5 – 7.5)	1.4 (0.6 – 3.8)	1.9 (0.5 – 7.5)
Lym ($x10^9$)	1.0 (0.1 – 4.3)	0.9 (0.1 – 3.3)	1.0 (0.2 – 4.3)	0.3 (0.1 – 1.2)	1.0 (0.1 – 4.3)
Mon ($x10^9$)	0.6 (0.0 – 1.8)	1.0 (0.3 – 4.4)	0.7 (0.0 – 4.4)	0.5 (0.3 – 2.9)	0.6 (0.0 – 4.4)
MNC ($x10^9$)	1.7 (0.4 – 4.6)	1.8 (0.5 – 7.2)	1.8 (0.4 – 7.2)	1.1 (0.5 – 3.3)	1.7 (0.4 – 7.2)
Hct (%)	2.3 (0.5 – 4.1)	2.3 (1.7 – 6.3)	2.4 (0.5-6.3)	2.2 (1.7 – 6.3)	2.3 (0.5 – 6.3)
PLT ($x10^{11}$)	0.2 (0.0 – 1.3)	0.2 (0.0 – 0.7)	0.2 (0.0 – 1.3)	0.1 (0.0 – 0.5)	0.2 (0.0 – 1.3)

Conclusions: Results for cell yields and apoptosis are comparable to published literature for online and offline systems. Our patients and staff prefer the Amicus Blue ECP System for its shorter, predictable procedure time. We observed no differences in clinical response compared to previous offline treatment. We continue to use the system and have expanded our program to more patients due to the increased operational efficiencies compared to multi-step offline ECP.

Disclosure: Nothing to declare.

P052.

Ruxolitinib Off-Label Use in Steroid-Refractory Chronic Graft Versus Host Disease: A Single Center Experience in 36 Patients

Elisabetta Xue[1], Francesca Lorentino[1], Carlo Messina[1], Sarah Marktel[1], Francesca Farina[1], Francesca Pavesi[1], Stefania Girlanda[1], Francesca Lunghi[1], Andrea

Assanelli[1], Jacopo Peccatori[1], Consuelo Corti[1], Fabio Ciceri[1], Maria Teresa Lupo Stanghellini[1]

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Background: Chronic Graft-versus-Host-Disease (cGvHD) is a serious complication of allogeneic transplant that severely impacts quality of life and long-term survival. About 50-to-60% of patients require a multiple treatment lines due to lack of sustained response to steroid. Ruxolitinib, a Janus kinase 1/2 inhibitor, has recently been approved as a second-line treatment of acute GvHD; aim of this study was to evaluate its feasibility and efficacy in the setting of steroid refractory cGvHD.

Methods: We retrospectively evaluated ruxolitinib use as a salvage treatment for moderate (28%) to severe (72%) steroid refractory cGvHD in our Institution. Ruxolitinib was given off-label after provision of an informed signed consent and in the absence of valid alternative therapeutic options. CGvHD was graded according to NIH criteria; at diagnosis, immune reconstitution (IR) parameters were collected to stratify according to IR score. We collected data regarding new onset cytopenia, renal and liver disfunction, dyslipidaemia, and infections after ruxolitinib start. CGvHD responses were evaluated by comparing pairwise parameters at baseline, after three and six months and at last on-treatment follow-up. Friedman's analysis of variance by ranks was used. Data on IR parameters before and after ruxolitinib were collected. Survival outcomes including overall survival, transplant-related mortality and relapse rate were analysed as well as the impact of IR score on cGvHD responses.

Results: Thirty-six patients received ruxolitinib for a median of 8.6 months (r 1-51.6), after a median of three previous lines (range, r 1-11). Cutaneous GvHD was the most frequent presentation (86% of cases, almost all of which had sclerotic features); no patients had hepatic cGvHD. Overall response rate was 61% (CR 10%, PR 51%) at three months, 61% (CR 15%, PR 46%) at six months, and 75% (CR 25%, PR 75%), at the last on-treatment evaluation. Skin, eyes, mouth, gastroenteric and genital tracts had significant responses; joints and pulmonary cGvHD did not show major changes, although decreased oxygen requirement was reported. Performance status and patient-reported Lee scores also improved. Forty-two percent of patients were off steroid 12 months after ruxolitinib start. Two patients discontinued the treatment due to leukemia recurrence; no other permanent discontinuations due to adverse events were documented. Ruxolitinib determined a reduction in B-cell counts but had no effects on T and NK subsets. Six percent experienced grade 3-4 neutropenia, whereas 8% and 6% experienced grade 3-4 bacterial and viral infections, respectively; two patients died for infections while still on treatment. All other adverse events were graded as 1-2. Survival outcomes were in line with historical data from our institution; we observed no statistical differences in overall survival between responders and non-responders, as well as through the three IR risk groups. High IR score at diagnosis did not correlate with a reduced probability of response.

Conclusions: Ruxolitinib appears to be a safe and effective option as salvage treatment for cGvHD at advanced stages. Prospective analyses on larger multicenter clinical-trial cohorts are ongoing and preliminary analysis are confirming this result. Furthermore, evaluation of response durability after ruxolitinib discontinuation will be object of study.

Disclosure: Nothing to declare.

P053.

Pharmacokinetic Modeling to Guide Dose Selection of ALPHA-1 Antitrypsin in A Study of Graft Versus Host Disease Prevention in Patients Receiving Allogenic Hematopoietic Cell Transplant

Henry Hu[1], H. Joachim Deeg[2], John Magenau[3], Gautam Baheti[1], Scott Adler[1], John Mallee[1], Christine Voigt[1], John Roberts[1]

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Background: There are no approved therapies to prevent graft versus host disease (GVHD) after allogenic HCT: prevention is attempted with immunosuppressive drugs to suppress donor T-cell function. This requires a difficult balance of risk/benefit, highlighting an unmet clinical need for targeted immunomodulatory options to prevent GVHD without causing broad immunosuppression.

Alpha-1 antitrypsin (AAT) is a plasma protein produced by the liver. Through its main function as a serine protease inhibitor, it has recently been shown to have immunomodulatory properties. In preclinical models of allogenic HCT, AAT appeared to induce anti-inflammatory cytokines, reduce secretion of pro-inflammatory cytokines, interfere with maturation of dendritic cells, and suppress development of GVHD in mice.

Patients treated for AAT deficiency show a dose-dependent increase in serum AAT antigen concentration. However, in the GVHD setting, AAT is being explored for its potential immunomodulatory effects and not only as replacement therapy. Stool losses of AAT have been shown to occur during allogenic HCT conditioning and have been associated with the occurrence of GVHD. In GVHD, it is thought that higher doses of AAT may be required versus replacement given that serum AAT antigen concentrations

vary considerably in patients during the inflammatory stages of GVHD, and with gastrointestinal GVHD and associated losses. To date, an understanding of serum AAT kinetics in the allogenic HCT setting is lacking.

Methods: A pharmacokinetic (PK) model was developed to characterize the PK of AAT antigen concentration and to identify sources of variability in AAT antigen concentration in subjects who receive AAT for prevention of GVHD. Model outputs will inform dose selection in the second part of a phase 2/3 study (NCT03805789) investigating the safety and efficacy of AAT for the prevention of GVHD following allogenic HCT in patients who plan to undergo a myeloablative conditioning regimen.

Blood samples for PK analysis were collected from up to 45 patients for whom selected demographic and clinical data were available or could be reliably imputed. Modeling will be performed using first order conditional estimation with interaction, in NONMEM version 7.3 or later. One- and two-compartmental models will be explored. Model covariates will be selected using forward addition and backward deletion until all covariates remaining in the model are significant at $p < 0.001$. Tested covariates will be presented and the final model will be evaluated based on visual predictive checks.

Results: The structure of the final model and population PK estimates, along with covariates and their effect on the PK of AAT in subjects undergoing allogenic HCT, will be presented.

Conclusions: This is the first population PK analysis of AAT for prophylaxis of GvHD in subjects undergoing allogenic HCT. Initial PK analyses inform dosing and may support recruitment to the ongoing randomized, double-blind part of a phase 2/3 study (NCT03805789).

Clinical Trial Registry: Clinicaltrials.gov – NCT03805789.

Disclosure: Henry Hu: CSL Behring - Employee.

H. Joachim Deeg: Nothing to declare.

John M. Magenau: Merck - Collaborator, Research Funding; OncImmune - Collaborator, Research Funding.

Gautam Baheti: CSL Behring - Director, Clinical Pharmacology, Salary.

Scott Adler: CSL Behring - Clinical TA Head, Ownership Interest and Salary.

John Mallee: CSL Behring - Employee, Ownership Interest and Salary.

Christine Voigt: CSL Behring - Employee.

John Roberts: CSL Behring - Management, Ownership Interest and Salary.

P054.

Basiliximab for The Treatment of Patients with Steroid Refractory Acute Graft Versus Host Disease: Literature Review And Pooled Analysis

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Background: Acute graft versus host disease (aGVHD) is one of the major problem after allogeneic hematopoietic stem cell transplantation. Corticosteroids is the standard first-line therapy for the treatment of aGVHD, and about 50% patients showed resistance. IL-2 receptor antibodies (IL-2RA) is one of the treatment option for steroids refractory aGVHD (SR-aGVHD). The objective of this study was to assess the efficacy of basiliximab, one of a IL-2RA, in patients with SR-aGVHD by pooled analysis of published literatures.

Methods: We conducted a literature review in EMBASE, Cochrane, MEDLINE and MEDLINE in process, which included Phase II/III randomized controlled trials (RCTs) and observational studies about basiliximab in adult patients (≥18 years) with SR-aGVHD. The outcomes of interest were objective response rate (ORR), complete response (CR), partial response (PR) and survival rate (SR). Efficacy data was extracted at different time points and pooled analysis were performed for two scenarios: (1) at study endpoint and (2) at either endpoint/28 days.

Results: A total of six single-arm observational studies were identified through literature search, with the sample number ranging from 13 to 230. The most common stem cell source were peripheral blood stem cells (82% to 92.8%) and bone marrow (5% to 96.5%). The type of the donor sources included HLA-matched sibling and HLA-matched unrelated. All studies reported the response rates with endpoint time undescribed or 28-day. Literatures reported ORR with basiliximab was >70% and CR ranged from 6% to 53%, and PR from 13% to 65%. Our pooled analysis showed ORR, CR, and PR were 70.49%, 25.09% and 37.66% respectively at trial endpoint, and were 66.64%, 23.85%, and 29.29% respectively at 28-day.

Conclusions: Pooled analysis results suggests that the response rate of basiliximab in SR-aGVHD is consistent with previous conducted studies. Therefore, basiliximab might be considered as a potential treatment for SR-aGVHD. A key limitation of our findings is that it is based on observational studies due to data scarcity and need larger sample size RCTs to verify these findings.

Disclosure: Shan Li and Yuxian Zhu are employees of Beijing Novartis Pharma Ltd. Xiaodong Mo is working as an associate chief physician with Peking University People's Hospital.

P055.

First Line Single-Agent Ruxolitinib for Grade II-III Acute Graft-Versus-Host Disease in Patients with Severe Infectious Complications: Case Series

Ivan Moiseev[1], Evgeniya Borzenkova[1], Irina Golubovskaya[1], Olga Kudyasheva[1], Anna Smirnova[1], Elena Morozova[1], Alexandr Kulagin[1]

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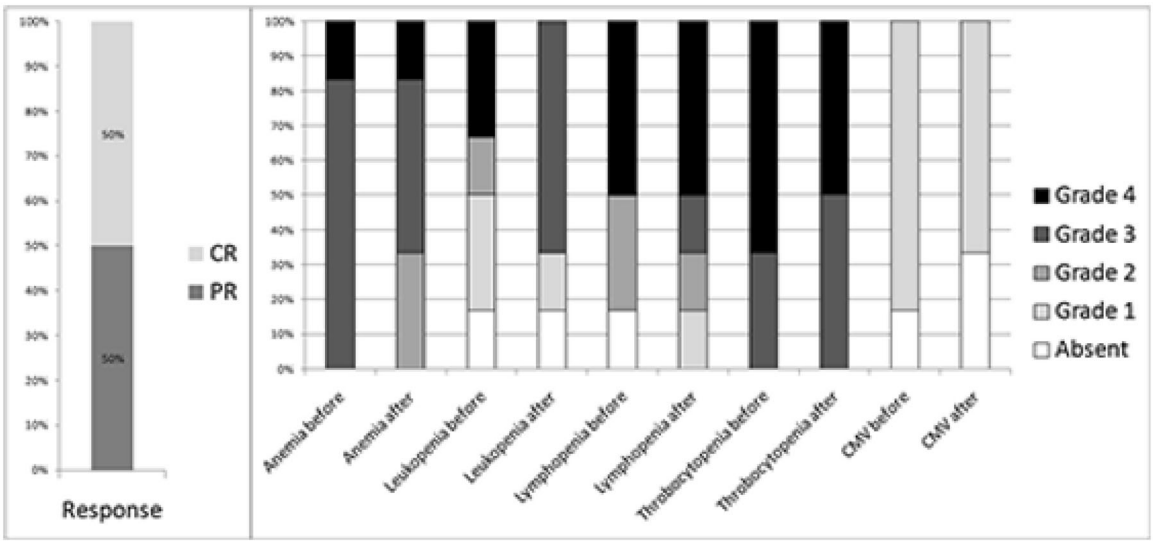
Background: Systemic corticosteroids is the standard of care for acute graft-versus-host disease (aGVHD) since 1980s, but the infection-related mortality is common with this type of treatment. Also second line therapy is required in half of the patients. Recent randomized trial demonstrated that ruxolitinib had higher response rate compared to the best available therapy in the second line. In that study also there was an improvement in survival probably due to lower incidence of infections. We hypothesized that in patients with severe bacterial or fungal infections ruxolitinib will not exacerbate the existing anti-infectious control and will control GVHD without concurrent steroids.

Methods: This case series included 6 patients with poorly controlled severe bacterial or fungal infections who developed grade II-IV acute GVHD with indications for systemic therapy. 5/6 had infections related to multi-drug resistant (MDR) gram-negative bacteria, including severe sepsis in 3, necrotizing laryngitis in one and persistent febrile neutropenia in 2. One patient had third consecutive allograft and persistent febrile neutropenia without MDR bacteria identification. Four patients had grade II aGVHD and 2 grade III. Median starting dose of ruxolitinib was 10 mg (range 5-15 mg). At the time of ruxolitinib initiation all patients had fever and CRP>50 mg/l or procalcitonin> 1 ug/l despite adequate anti-infectious therapy, or localized infection with poor local control.

Results: Median follow up was 9 months range (1-25). All six patients had a response, three - complete response and three - partial response. Median time to partial response was 16 days. Median time to complete response was 29 days. After discontinuation of ruxolitinib two patients had GVHD flair and were treated with steroids and ECP. Two patients required additional treatment while on ruxolitinib (steroids and etanercept). Two patients did not require additional treatments. At last follow two patients completely discontinued immunosuppressive therapy, two patients died from severe poor graft function (pre-existed before ruxolitinib) and infectious complications. In two patients immunosuppressive therapy is ongoing. 2-year overall survival was 56%. Overlap syndrome and subsequent development of chronic GVHD was observed in all patients with grade III aGVHD. Toxicity was moderate and majority of patients had improvement in the grade of cytopenia (Figure 1). Subsequent episodes of infections complications requiring systemic antibiotics were observed in 4 patients, one patient required systemic antifungal therapy. Recurrence of MDR sepsis was observed in 2 patients, which was the cause of mortality.

Conclusions: Ruxolitinib monotherapy is an option in patients with severe infectious complications and debut of aGVHD. The survival is comparable to the published data on the fit patients treated with steroids. However this preliminary data creates the rationale for prolonged administration of ruxolitinib beyond day+100 given the observed flairs of GVHD and overlap syndrome after early discontinuation of ruxolitinib.



Disclosure: I Moiseev has has received honoraria from MSD, Novartis, Pfizer, Celgene, Takeda, BMS and Celgene, grants from Novartis and BMS.

P056.

A Phase 2 Open-label, Single-arm, Multicenter Study of Ruxolitinib Added to Corticosteroids in Pediatric Subjects with Moderate/Severe Chronic Gvhd After Allogeneic Stem Cell Transplantation (REACH5)

Donna Wall[1], Katsuyoshi Koh[2], Sunil Bhat[3], Yoshiyuki Takahashi[4], Angela Zhang[5], Christine Rosko[6], Yvonne Smith[7], Tommaso Stefanelli[5], Cristina Diaz-de-Heredia[8], Franco Locatelli[9,10]

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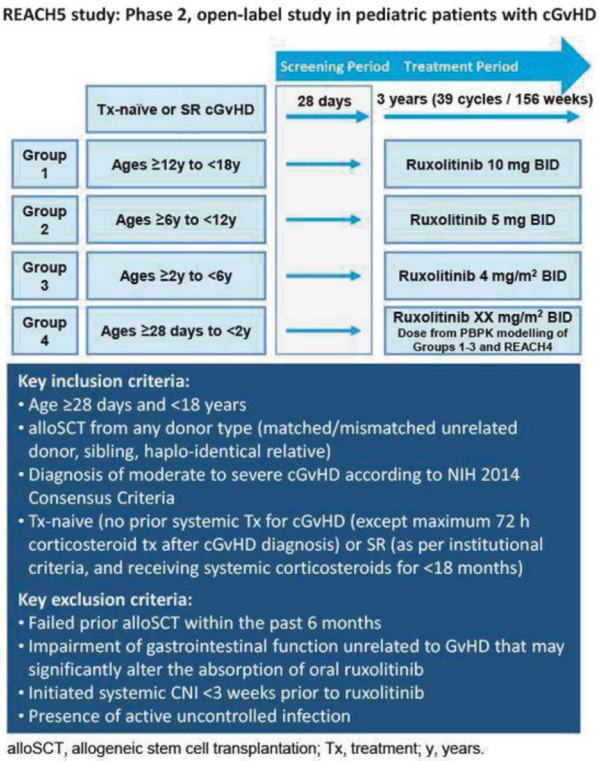
Background: Graft-vs-host disease (GvHD) may significantly impair the success rate of allogeneic stem cell transplantation. In pediatric patients, cGvHD can lead to considerable morbidity, impaired quality of life and transplant-related mortality (Inagaki 2015). Although systemic corticosteroids are the standard of care in initial stages of moderate to severe cGvHD, there is little controlled trial evidence to indicate the best initial or second-line treatment strategy. In recently reported data from the phase 3 REACH3 study, ruxolitinib improved overall response rate (ORR) versus best available therapy in adults and adolescents (≥12 years of age) with steroid-refractory (SR) or steroid-dependent cGvHD (Zeiser ASH 2020 [abstract 77]; NCT03112603). Furthermore, ruxolitinib has demonstrated encouraging activity in SR cGvHD pediatric patients in case series and a single center study (González Vicent 2019, Moiseev 2020). These data, combined with knowledge of the role played by janus kinase-signal transducer and activator of transcription (JAK-STAT) signaling in cGvHD pathophysiology, support the investigation of ruxolitinib in the pediatric cGvHD patients. The REACH5 study will assess the safety, efficacy, and pharmacokinetics (PK) of ruxolitinib in pediatric patients with moderate to severe treatment-naive or SR cGvHD.

Methods: REACH5 is a Phase 2 open-label, single-arm, multicenter study of pediatric patients aged ≥28 days to <18 years divided into four age groups (see Figure for details). Patients are eligible for inclusion if diagnosed with moderate to severe cGvHD (National Institutes of Health [NIH] 2014 Consensus Criteria) and are either treatment-naïve or SR (as per institutional criteria and still receiving systemic corticosteroids). Patients will be treated for up to approximately 3 years (39 cycles/Week 156). The primary objective is to evaluate the activity of ruxolitinib twice daily (BID) added to corticosteroids +/- calcineurin inhibitor (CNI) measured by ORR at Cycle 7 Day 1. Secondary endpoints include ruxolitinib safety, PK in treatment-naive and SR cGVHD, percentage of participants with ≥50% reduction from baseline in daily corticosteroid dose at Cycle 7 Day 1, duration of response, best overall response and failure-free survival. The study will enroll a minimum of 5 evaluable patients in Groups 1, 2 and 3, no minimum number of evaluable subjects in Group 4, and no cap to enrollment in any group. Group 1 patients will be treated at 10 mg BID, which is already considered the recommended phase 2 dose for this age group. Based on a review of PK data in the same aged group of patients treated in the pediatric acute GvHD study REACH4 [NCT03491215], the Group 2 dose has been confirmed at 5mg BID and Group 3 dose is pending. Enrollment initiation into Group 4 will be subject to the availability of data in this age group from REACH4, as well as a review of available PK, safety, and activity data generated from Groups 1 to 3 in the current study.

Results:



alloSCT, allogeneic stem cell transplantation; Tx, treatment; y, years.

Conclusions: Fourteen patients have been enrolled as of November 2020. Enrollment is ongoing for Groups 1 and 2, with Group 3 opening in 2021 (ClinicalTrials.gov: NCT03774082).

Clinical Trial Registry: NCT03774082. https://clinicaltrials.gov/ct2/show/NCT03774082.

Disclosure: Donna Wall has nothing to declare.
Katsuyoshi Koh has nothing to declare.
Sunil Bhat has nothing to declare.
Yoshiyuki Takahashi has nothing to declare.
Angela Zhang is employed by Novartis.
Christine Rosko is employed by Novartis.
Yvonne Smith is employed by Novartis.
Tommaso Stefanelli is employed by Novartis.
Cristina Diaz-de-Heredia has participated in speaker bureau for Jazz Pharmaceuticals, Novartis, Sobi, and an advisory committee for MSD. Franco Locatelli has participated in speaker bureau for Amgen, Jazz Pharmaceuticals, Medac, Miltenyi, Novartis, and Takeda, and has been a member of board of directors or advisory committee for Amgen, Bellicum Pharmaceuticals, Neovii, and Novartis.

P057.

Pre-Transplantation Plasma Vitamin D Levels And Acute Graft-Versus-Host Disease After Myeloablative Allogeneic Hematopoietic Cell Transplantation

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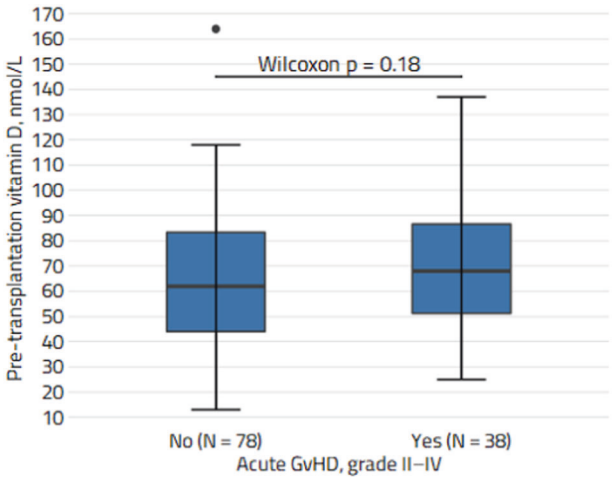
Background: The association between vitamin D and acute graft-versus-host disease (GvHD) remains controversial, especially within the subgroup of myeloablative conditioned patients.

Methods: We measured plasma vitamin D levels in 116 adult patients who underwent a myeloablative allogeneic transplantation at Rigshospitalet, Copenhagen between July 2015 and August 2018. Vitamin D (25-hydroxyvitamin D_3+D_2) was measured in stored plasma samples obtained at day –23 (±15 days) by competitive electrochemiluminescence. Spearman's ρ was used to evaluate correlations between vitamin D and clinical characteristics and other biomarkers. Odds ratios (OR) with 95% confidence intervals (CI) were estimated using logistic regression.

Results: The 116 patients had a median (Q1, Q3) age of 50 (36, 58) years, 34% and 29% were transplanted for AML and MDS, respectively, and 72% received an allograft from an HLA-matched unrelated donor. The most common conditioning regimens were cyclophosphamide and 12 Gy total-body irradiation (34%) and fludarabine and treosulfan (51%). Anti-thymocyte globulin was used in 27% of patients. The median (Q1, Q3) pre-transplantation plasma vitamin D level was 64 (47, 85) nmol/L. Insufficient levels (<50 nmol/L) and moderate deficiency (<25 nmol/L) were found in 29% and 8% of patients, respectively; no patients had a severe deficiency (<12 nmol/L). Pre-transplantation vitamin D was uncorrelated with age, sex, body mass index, Karnofsky score, diagnosis of acute leukemia, albumin and C-reactive protein (all $p > 0.30$). Grade II–IV acute GvHD occurred in 38 (33%) patients at a median (Q1, Q2) of 32 (26, 41) days after stem cell infusion. Pre-transplantation vitamin D levels did not differ according to later development of grade II–IV acute GvHD (Figure). An increase in the pre-transplantation vitamin D level from 47 to 85 nmol/L (Q1 to Q3) was associated with a crude OR of grade II–IV acute GvHD of 1.48 (95% CI: 0.87, 2.52, $p = 0.15$) and an adjusted OR of 1.39 (95% CI: 0.77, 2.53, $p = 0.27$, adjusting for age, sex, Karnofsky score, acute leukemia, donor age, stem cell source, donor match, anti-thymocyte globulin and 12 Gy total-body irradiation). For vitamin D insufficiency (vs. sufficiency at the 50 nmol/L level), the crude and adjusted OR of grade II–IV acute GvHD was 0.66 (95% CI: 0.27, 1.60, $p = 0.35$) and 0.68 (95% CI: 0.25, 1.85, $p = 0.45$), respectively.



Conclusions: We found no support for an association between pre-transplantation vitamin D levels or vitamin D insufficiency and acute GvHD in patients receiving myeloablative conditioning. Our findings suggest that peri-transplantation vitamin D supplementation is unlikely to reduce the incidence of acute GvHD after myeloablative allogeneic transplantation in adults.

Disclosure: Nothing to declare.

P058.

Elevated REG3α predicts refractory aGVHD in Patients Who Received Steroids- Ruxolitinib as the First Line Therapy

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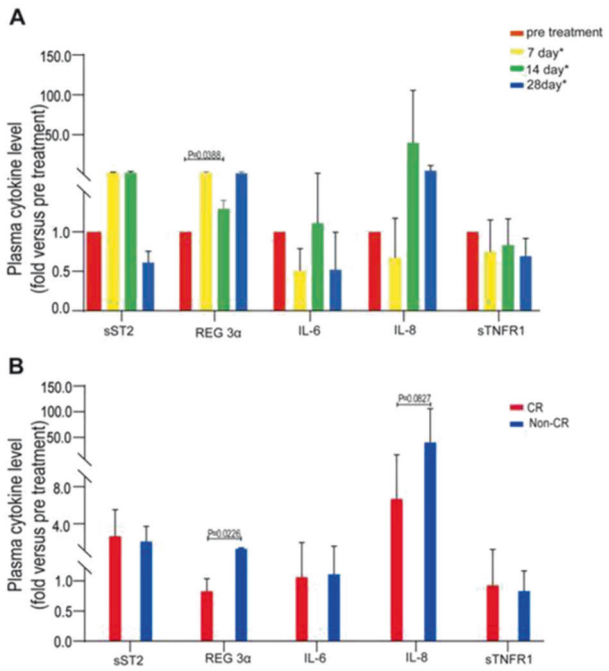
Background: Acute graft versus host disease (aGVHD) is a main reason for treatment failure and delayed immune reconstitution after allogeneic hematopoietic stem cell transplantation. Its response rate to the first line therapy of corticosteroids was around 40%. Biomarkers associated with the clinical outcomes of aGVHD have been investigated. Ruxolitinib has been shown to be a promising agent for steroids-resistant aGVHD. We started a single-arm, phase II, open label, prospective clinical trial using steroids-ruxolitinib as the first line therapy for aGVHD (NCT04061876). Here, we report the association of biomarker panel (sST2, sTNFR1, IL-6, IL-8 and REG3α) with responses to GVHD therapy along with the ongoing of the trial. The kinetics of the biomarkers were prospectively detected in patients enrolled in this trial.

Methods: The candidates were patients newly diagnosed as moderate to severe risk aGVHD, which were stratified according to high Minnesota acute GVHD Risk Score and MAGIC 2/3 biomarker risk. The novel first line therapy consisted of 1mg/kg predinisone and 5mg/d ruxolitinib. Serum concentrations of the biomarkers panel were prospectively detected at four established time-points (aGVHD onset and pretreatment, Day 7, Day 14, Day 28 after enrollment). Thirty-nine patients with newly diagnosed acute GVHD were enrolled.

Results: A total of 2,886 from the JSHCT/JDCHCT registry and 804 patients from the Eurocord/ALWP-EBMT registry were included. The median ages of the Japanese and European cohorts were 50 and 38 years, respectively. Three or more HLA mismatches in HLA-A, -B, and -DRB1 loci were more frequently observed in the JSHCT/JDCHCT cohort (23% vs. 3%). Median TNC counts were 2.58 and 3.51 × 107/kg in the JSHCT/JDCHCT and Eurocord/ALWP-EBMT cohorts, respectively. ATG was used in only 2% of the Japanese cohort compared with 66% of the European cohort. A multivariate analysis of OS revealed a positive impact of grade II acute GVHD compared with grade 0-I GVHD, in the Japanese cohort (HR, 0.81; $P = 0.001$), and an adverse impact in the European cohort (HR, 1.37; $P = 0.007$) (Figure 1). A negative impact of grade III-IV acute GVHD on OS was observed in both registries. In the analysis of relapse, a positive impact of grade II acute GVHD compared with grade 0-I GVHD was observed only in the Japanese cohort, regardless of disease risk. A multivariate analysis of NRM showed that an adverse impact of grade III-IV acute GVHD compared with grade 0-I GVHD was consistently observed in the Japanese cohort (HR, 2.97; P<0.001) and in the European cohort (HR, 3.91; P<0.001). A positive impact of limited chronic GVHD on OS and LFS was observed in the Japanese cohort (OS; HR, 0.51; P < 0.001, LFS; HR, 0.59; P < 0.001) only. An adverse impact of extensive chronic GVHD was observed in the European, but not in the Japanese cohort.

Figure 1 Impact of acute GVHD on overall survival and leukemia-free survival.



Of the 39 patients, 11 patients (28.21%) developed aGVHD Grade I, 25 patients (64.10%) Grade II, and 3 patients (7.69%) Grade III. At day 28 after the first line therapy, the complete response rate was 82.05%. The 1-year probability of OS, DFS and FFS after transplantation were 75.58%, 69.25% and 57.52%, respectively.

In patients who achieved complete remission (CR) after the first line GVHD therapy, the concentrations of REG3α (p14=0.01; p 28=0.10) and sTNFR1 (p 14=0.42; p 28=0.04) declined at day 14 and day 28. In patients who were refractory to therapy (no remission or steroid

dependence), the concentration of REG3α at Day 7, Day 14 and Day 28 after treatment were higher than those pre-treatment ($p = 0.04$, Figure A). There were no significant differences in the concentrations of sST2, sTNFR1 and IL-6 between CR and refractory patients at Day 7, Day 14 and Day 28 after treatment. No difference in MAGIC scores were noted in CR and refractory patients either. REG3α ($P=0.02$) was elevated in the refractory patients compared with the patients achieving CR at Day 14 after the treatment (Figure B).

Conclusions: The response rate of the novel first line therapy, steroids-ruxolitinib, for aGVHD was promising in patients with intermediate and high "Minnesota and MAGIC" risk. The kinetics of the concentration of REG3α was associated with the response of treatment. Elevated REG3α level may predict poor response and refractory aGVHD.

Clinical Trial Registry: Clinical Trials.gov Identifier: NCT04061876.

Disclosure: This work was partially supported by grants from the Beijing Nova Program (2011114), the National Natural Science Foundation of China (Nos. 82070178), the Beijing Natural Science Foundation of China (No. 7172200, and 7132217), the Capital's Funds for Health Improvement and Research (No. 2016-1-4082), the Fund Sponsorship of the Capital Public Health Project for DH Liu, National Key Clinical Specialized Military Construction Project for DH Liu (Clinical Medicine), the Hainan Provincial Natural Science Foundation of China (818MS157), the Military Translational Medicine Fund of Chinese PLA General Hospital (ZH19003) and the Medical big data and artificial intelligence development fund of Chinese PLA General Hospital (2019MBD-016).

Conflict of interest statement: The authors have no conflict of interest.

Graft-versus-host Disease – Preclinical and Animal Models

P059.

The Magnitude of Intestinal T Cell Infiltration Determines Epithelial Regeneration During Immune-Mediated Tissue Injury

Sascha Göttert[1], Julius Fischer[1], Gabriel Eisenkolb[1], Thomas Engleitner[1], Erik Thiele Orberg[1], Simon Heidegger[1], Hendrik Poeck[1,2,3]

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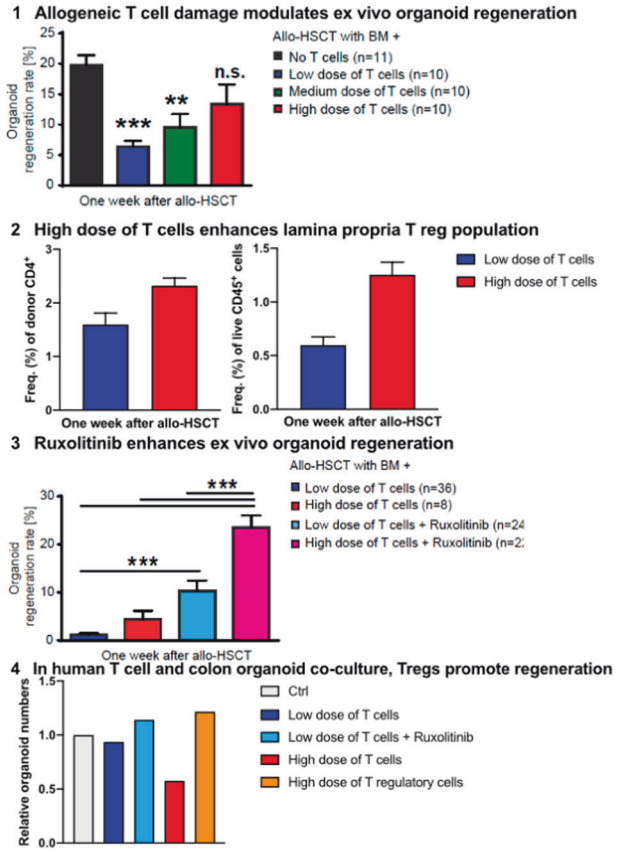
Background: Damage to the intestinal barrier can augment the development of inflammatory diseases such as graft versus house disease (GVHD) after allogeneic hematopoietic stem cell transplantation (allo-HSCT). Intestinal stem cells (ISC) are essential for the regeneration of damaged intestinal epithelium and the maintenance of intestinal integrity, but are themselves a primary target of donor-derived allo-reactive T cells. Yet, little is known about.

(i) whether and how T cells contribute to intestinal regeneration and.

(ii) the ISC compartment adapts to varying degrees of T cell infiltration and damage.

Methods: in mouse models of major mismatch acute GVHD, we administered increasing numbers of donor T cells (low, medium and high doses) and measured the impact on the ISC compartment via clinical scoring, histology and organoid regeneration. We then profiled the populations of donor T cells infiltrating the intestinal epithelium via flow cytometry. We performed unbiased RNA sequencing of bulk intestinal tissue of allo-HSCT recipients. For mechanistic studies, we generated murine and human intestinal crypt-derived organoids and co-cultured them with increasing numbers of purified T cell populations ($CD4^+CD25^-$ and $CD4^+CD25^+$).

Results: We observed that mice co-transplanted with high numbers of allogeneic T cells developed more severe GVHD but also showed better clinical recovery early after allo-HSCT. RNAseq revealed that co-transfer of escalating doses of alloreactive T cells lead to the upregulation of signaling pathways associated with (i) allogeneic T cell activation as well as (ii) protection from GVHD and epithelial regeneration. We transplanted mice with escalating T cell doses resulting in fulminant GVHD. However, we observed that the regenerative capacity of ISCs was dependent on the magnitude of epithelial T cell infiltration, with higher infiltration resulting in improved organoid regeneration (Figure 1). FACS analysis of intraepithelial and lamina propria lymphocytes revealed higher abundance of regulatory T cells in mice that received a high dose of T cells (Figure 2). We then treated allo-HSCT recipients with Ruxolitinib, a known T cell modulator, and found that it enhanced ex vivo organoid regeneration independent of transplanted T cell dose (Figure 3). Co-cultures of human organoids with donor T cell subpopulations showed a growth stimulating effect of T regs (Figure 4). Treatment with Ruxolitinib enhanced organoid growth in the presence of $CD4^+CD25^-$ T cells, but not when administered to organoids alone.



Conclusions: Despite the well-characterised role of donor T cells in immune-mediated damage to the intestinal epithelium, we show that they also contribute directly to the level of intestinal regeneration. We propose that the degree of intestinal T cell infiltration determines both ISC damage and T reg dependent epithelial regeneration during immune-mediated tissue injury, leading to a sensitive equilibrium that harbors potential for therapeutic intervention.

Disclosure: Nothing to declare.

P060.

Itacitinib Attenuates Xenogeneic GVHD in Humanized Mice

Justine Courtois[1], Caroline Ritacco[1], Sophie Dubois[1], Lorenzo Canti[1], Benoît Vandenhove[1], Sophie Servais[1], Yves Beguin[1], Grégory Ehx[1], Frederic Baron[1]

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Background: We assessed the impact of the Januse Kinase (JAK) 1 inhibitor itacitinib on xenogeneic graft-versus-host disease (xGVHD).

Methods: XGVHD was induced by i.v. injection 20x106 human peripheral blood mononuclear cells (hPBMC) in NSG mice on day 0. Itacitinib (3 mg, ≈ 120 mg/kg) or methylcellulose was administered by force-feeding twice a day from day 3 to day 28. Mice were followed for xGVHD score and survival. In addition, human T-cell engraftment and as well as human T-cell subtypes were monitored in NSG blood on days 14, 21 & 28.

Results: The impact of itacitinib on xGVHD was assessed in 3 independent experiments using hPBMC from 3 different donors. Combining data from the 3 experiments, itacitinib-treated mice had significantly longer survival than control mice (median 44 versus 33 days; P=0.0003). Itacitinib-treated mice had lower peripheral blood absolute numbers of CD4+ T cells on days 21 and 28 after transplantation as well as of CD8+ T cells on days 14, 21 and 28 after transplantation. In addition, itacitinib-treated mice had higher frequencies of regulatory T cells (Treg) on days 21 and 28 after transplantation.

Conclusions: in summary, our data indicates that itacitinib decreased human T-cell engraftment, increased Treg frequencies and attenuated xGVHD in NSG mice transplanted with hPBMC.

Clinical Trial Registry: NA.

Disclosure: Itacitinib was provided by Incyte Biosciences.

Haematopoietic Stem Cells

P061.

Letermovir Prophylaxis Reduces The Risk for Cmv Infection After Stem Cell Transplantation

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[1]*Technical University of Munich, Munich, Germany*

Background: Cytomegalovirus (CMV) infection is one of the most frequent clinically significant complication in allogeneic stem cell recipients and associated with high mortality. Although ganciclovir and valganciclovir are well known prophylaxis for CMV reactivation in solid-organ transplantation, the use of these drugs induces unacceptable side effects like myelosuppression in allogeneic stem cell recipients. Letermovir, an antiviral drug that inhibits the CMV-terminase complex, is now a new available and approved drug for CMV prophylaxis.

Methods: in a retrospective single center analysis, we investigated the benefit of letermovir as CMV prophylaxis in allogeneic stem cell recipients. For this purpose, we included 48 CMV-seropositive transplant recipients from

January 2017 to August 2020 who underwent an allogeneic stem cell transplantation at the Department of Internal Medicine III, Hematology/Oncology, Klinikum rechts der Isar and compared the rate of CMV infections in patients who received letermovir as prophylaxis from day 0 after the allogeneic stem cell transplantation with a control group which did not receive letermovir as prophylaxis. Letermovir was applied at a dose of 480 mg once a day or 240 mg once a day if ciclosporin was used as initial immunosuppressive drug. The primary end point was the clinically significant CMV infection up to day + 100 after the allogeneic stem cell transplantation. CMV-Infection was defined as an increase of CMV copies over 1250 UI/ml in the peripheral blood. Secondary endpoints were overall survival up to day + 150 after stem cell transplantation and the time to engraftment after allogeneic stem cell transplantation.

Results: Both groups were well balanced with regard to the baseline characteristics. 27 patients (56%) were male and the median age was 55 years (54 years in the letermovir group versus 52 years in the control group). 21 patients were included in the control group and 27 patients in the letermovir group. 85.7% (18 of 21 patients) of the patients in the control group suffered a CMV infection whereas only 3.7% (1 of 27 patients) of the patients in the letermovir group had a significant CMV infection up to day + 100 after allogeneic stem cell transplantation ($p < 0.001$). There was no significant difference regarding leucocyte engraftment (19 days in the letermovir group (95% CI, 17 to 20) versus 20 days in the control group (95% CI, 18 to 23), p 0.140) and platelet engraftment (25 days in the letermovir group (95% CI, 16 to 35) versus 27 days in the control group (95% CI, 22 to 23), p = 0.171) between both groups. All-cause mortality at day + 150 after allogeneic stem cell transplantation was 4.8% among letermovir recipients and 19% among control group recipients ($p = 0.07$).

Conclusions: The use of letermovir prophylaxis is associated with a significant lower risk of CMV infections after allogeneic stem cell transplantation. Furthermore, we did not see any toxicity in terms of leucocyte and platelet engraftment as well as overall survival.

Disclosure: Nothing to declare.

P062.

Kir B Haplotypes in Unrelated Hematopoietic Stem Cell Transplantation, Revisited

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[1]Institute of Hematology and Transfusion Medicine, Warsaw, Poland, [2]Poltransplant - Organization and Coordination Center for Transplantation, Warsaw, Poland

Background: Killer cell immunoglobulin-like receptors (KIRs) are regulatory components of antitumor immunity via natural killer (NK) cells. KIR genes are organized in type A and B haplotypes and centromeric and/or telomeric parts of haplotypes are implicated in cancer and infection outcome. In the recent study, it was shown the favorable role of donor KIR B haplotype and centromeric KIR BB genotype in reducing acute myeloid leukemia (AML) relapse and improvement of survival in the bone marrow transplant recipients.

Methods: in our study, we have replicated the KIR haplotype study using the previously proposed methods, however with different results. In N=419 recipients with AML, ALL or other hematological malignancy and their donors we performed KIR genotyping and assigned for A and B haplotype within centromeric and telomeric fragments.

Results: The disease-free survival (DFS) and time dependent relapse incidence (RI) were not statistically different in AML patients with high (>=2) and low (0 or 1) B fragment content. (DFS/AML: 49% vs. 59%, $p = 0.16$, HR = 1.11; RI/AML: 15% vs. 19%, $p = 0.67$, HR = 0.95). Neutral, better and best KIR B content shown reciprocal trend in our AML cohort than previously shown (DFS/AML: 59%, 53% and 41%, $p = 0.11$, HR = 1.16, respectively) or was not statistically different (RI/AML: 19%, 9% and 32%, $p = 0.94$, HR = 1.01, respectively). Unlike previous study, homozygous CenBB genotype in donor have shown adverse influence in AML patients (DFS/AML: 41% vs. 64%, $p = 0.049$, HR = 1.92; RI/AML: 32% vs. 14%, $p = 0.047$, HR = 2.75). In the multivariate analysis in DFS and RI all the KIR B content variables were eliminated from the model. Notably, in multivariate analysis changed number of inhibitory KIR: HLA pairs remained an independent prognostic factor for DFS (DFS/AML: $p = 0.0047$, HR = 0.43, 95%CI 0,24-0,77). For the total cohort (AML, ALL, other malignancies) the KIR B content has no significant effect on relapse incidence (see, Table 1) and DFS.

Table 1. Relapse incidence (RI) in malignant patients (AML, ALL, other malignancies) transplanted from donors with KIR haplotypes (N=390).

KIR haplotypes in donor	N	Relapse+/ Hp + (%)	Relapse+/ Hp (-) (%)	p	HR	CI ±95%
KIR BB vs. KIR AB or AA (d)	390	1/2 (50)	69/388 (18)	0.41	2.30	0.32-16.64
KIR AB vs. KIR homozyg. (d)	387	54/276 (20)	16/111 (14)	0.10	1.60	0.91-2.80

Table (continued)

KIR haplotypes in donor	N	Relapse+/ Hp + (%)	Relapse+/ Hp (-) (%)	p	HR	CI ±95%
KIR AA vs. KIR AB or BB (d)	387	15/109 (14)	55/278 (20)	0.073	0.59	0.33-1.05
KIR TelBB vs. Tel A (d)	390	4/27 (15)	66/363 (18)	0.91	0.95	0.34-2.60
KIR TelAB vs. Tel homozyg. (d)	390	26/153 (17)	44/237 (19)	0.86	0.96	0.59-1.56
KIR TelAA vs. Tel B (d)	390	40/210 (19)	30/180 (17)	0.82	1.06	0.66-1.70
KIR CenBB vs. Cen A (d)	390	9/36 (25)	61/354 (17)	0.20	1.57	0.78-3.17
KIR CenAB vs. Cen homozyg. (d)	387	32/183 (17)	38/204 (19)	0.83	1.05	0.66-1.68
Cen B vs. CenAA (d)	387	41/219 (19)	29/168 (17)	0.36	1.25	0.78-2.01

Conclusions: It seems likely that HLA binding provides strong functionality for KIR bearing NK cells. The composition of KIR haplotypes can shape the function of NK cells depending on additional factors, such as HLA ligation.

Clinical Trial Registry: Retrospective model.

Disclosure: Nothing to declare.

P063.

Results of Second Allogeneic Hematopoietic Stem Cell Transplantation in Patients with Hematological Diseases: Retrospective Analysis of Our Hospital

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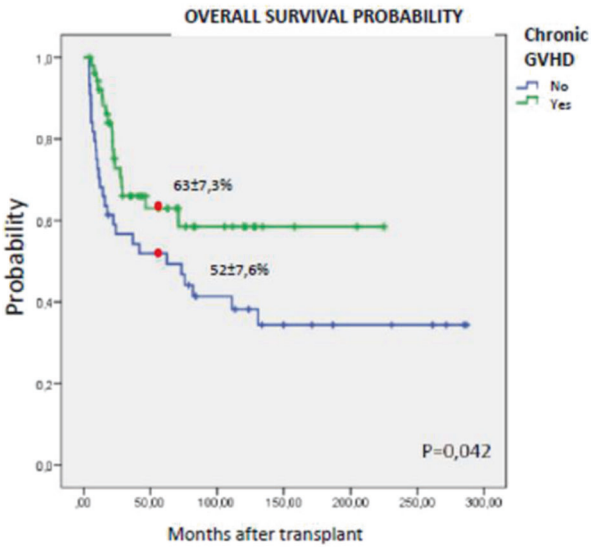
Background: Performing a 2nd Hematopoietic Stem Cell Transplantation (HSCT) after the relapse of the underlying disease is one of the therapeutic strategies in patients who achieve a response after relapse. The aim of our study is to analyze the results and prognostic factors in patients who underwent a 2nd allogeneic HSCT.

Methods:

Table (continued)

	Autologous-allogenic ($n = 94$)	Allogenic-allogenic ($n = 32$)
Sex (M/F)	67 (71%)/27 (29%)	23 (72%)/9(28%)
Age at 2nd transplant (median-range)	47 (5-66)	21 (1-59)
Hematological disease		
•Acute leukemia	25 (27%)	21 (66%)
•Lymphoma	39 (41%)	0
•Multiple mieloma	27 (29%)	0
•Others	3 (3%)	11 (34%)
Criteria for performing 2nd transplant		
•Relapse	84 (99%)	28 (88%)
•Graft failure	1 (1%)	4 (12%)
•Tandem	9 (10%)	0
2nd transplant type		
•Sibling HLA identical	41 (44%)	13 (41%)
•Matched unrelated donor	31 (33%)	9 (28%)
•Haploidentical	17 (18%)	10 (31%)
•Umbilical cord blood	5 (5%)	0
Pre-transplant disease status		
•Complete remission	43 (46%)	13 (40%)
•Not complete remission	50 (53%)	15 (47%)
•Graft failure	1 (1%)	4 (13%)

We studied 126 patients who received a 2nd allogeneic HSCT in our center between 1995-2019, the 1st HSCT being autologous or allogeneic. Two groups were established: 1st: 1st autologous-2nd allogeneic / 2nd: 1st allogeneic-2nd allogeneic. Patient's characteristics are shown in Table 1.



Results: with a median follow-up of 77 months (range: 4-287), the probabilities of overall survival (OS), progression-free survival (PFS), and probability of relapse (RP) at 5 years are 46 ± 5%, 39.7± 5% and 42 ± 6% in the 1st group and 37±9.9%, 33± 9.5 and 57±11% in the 2nd group, respectively. Transplant-related mortality in the first 100 days (TRM100) and global TRM are 23.4% and 39.4% in the 1st group and 12.5% and 18.8% in the 2nd group, respectively. There are no differences in the TRM100 or global TRM according to the intensity of the 2nd HSCT conditioning. PFS is higher in patients transplanted in complete response: 45 ± 7% vs 30±6% ($p = 0.17$). This advantage in PFS reached statistical

significance in the 1st group: 47.6 ± 8% vs 28.7 ± 6%, p = 0.05.

The presence of acute GVHD did not influence significantly OS, PFS or PR in any of the groups. However, the presence of chronic GVHD decresases RP and increases PFS and OS, being statistically significant in the case of OS in the total sample: 63±7% vs 52± 8% (p = 0.04). (Figure 1).

We did not observe differences in OS, PFS or PR depending on whether the same or different donor was used in the 2nd HSTC, or whether the relapse was early or late.

Conclusions: Carrying out a 2nd HSCT in patients who relapse after a 1st HSCT is a feasible treatment option that offers a survival of 45 ± 4.6% at 5 years, being the main influencing factors the disease status at the 2nd HSCT and the presence of chronic GVHD.

Disclosure: Nothing to declare.

P064.

The Impact of Age On Hematologic Recovery After Allogeneic Transplantation

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Background: Hematologic recovery is not satisfactory in every patient undergoing an allogeneic HSCT. A significant proportion have been reported to have low platelet counts, despite full donor chimerism. This condition can be related to several factors including: number of CD34+ cells infused, stem cell source, underlying disease, conditioning regimen, GvHD and CMV infection. Recently transplant platforms have changed, including the use of haploidentical transplants and modified GvHD prophylaxis.

Methods: The aim of the study is to investigate factors associated with hematological recovery in current transplant years. We included 1311 patients with hematological disease undergoing to HSCT from 2000 to 2020 in two transplant center: Genova and Roma, as shown in Table 1, in patients stratified according to age </> 60 years. Platelet counts were taken as a surrogate marker of hematologic recovery.

Results: We first ran a multiple regression analysis on factors influencing platelet counts between 50 and 100 days post-transplant. These were patients age >60 years, GvHD grade II-IV, non sibling donor and a diagnosis of myelofibrosis.

Platelet recovery at different time points, up to over 4 years post-transplant, is shown in Figure 1a in patients stratified according to an age cut off of 60 years. Patients younger than 60 years showed significantly improved platelet recovery, at each time point, when compared to patients younger than 60 years ; the difference persisted beyond 4 years. There was no difference in platelet recovery in patients aged 18-40 and 41-60. Donor age and year of transplant had no effect on platelet recovery. We then asked whether low platelet counts predicted TRM. Patients with a platelets count higher than 20 and 50x10^9 on days 50-100 post-HSCT, showed a reduced TRM as compared to patients with a lower platelet count (13%vs 39%: $p < 0.000001$; 11% vs31%, $p < 0.000001$).

Conclusions: Platelet recovery post-HSCT seems to be strongly influenced by patient's age, together with GvHD, diagnosis of myelofibrosis and donor type. Slow recovery in older patients remains statistically significant beyond 4 years after HSCT. Recovery after HSCT has not improved over the past 2 decades. Low platelet counts are a strong risk factor for mortality after allogeneic HSCT. Clinical trials with TPO agonists post HSCT are warranted to assess whether hematologic recovery can be improved, and whether this will translate in reduced mortality.

Table 1: Patients' charactheristics according to age.

Age cut off	<60	>60	p value
Number of patients	1108	203	
Age (median value)	40	64	$p < 0.0001$
Age Range (years)	1-60	61-74	
Gender (male/female)	634/474	130/73	$p = 0.01$
Donor age			
Median value (range) years	37 (15-72)	37 (17-73)	P=0.01
Diagnosis n° (%)			
Acute leukemia	605 (90)	85 (10)	$p < 0.0001$
Chronic myeloid leukemia	80 (96)	3 (4)	
Lymphoproliferative disease	147 (94)	10 (6)	
Myeloproliferative neoplasm (MFI)	110 (70)	47 (30)	
Multiple Myeloma	48 (85)	9 (15)	
Myelodisplatic syndrome	94 (70)	42 (30)	
other	24 (77)	7 (23)	
Conditioning regimen			
Total body irradiation	444	2	$p < 0.0001$
Thiotepa-Busulfan-fludarabine	345	136	
Busulfane+fludarabine or cyclophosphamide	102	13	
Baltimore scheme	25	11	
other	192	41	

Disclosure: Conflicts of interest: Nothing to declare. No disclosure.

P065.

Hematopoietic Stem Cell Transplantation in Pediatric Acute Myeloid Leukemia with Aberrant CD7 Antigen Expression

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Background: The association of aberrant expression of lymphoid marker CD7 in acute myeloid leukemia (AML) with poor outcome was made in adults, but has not yet been established in children. We retrospectively analyzed pediatric patients diagnosed with AML expressing CD7 and report their outcome.

Methods: We reviewed data of 55 pediatric patients with newly diagnosed AML since 2010, followed in our Department. Patients were enrolled into AEIOP AML 2002/01 and AML 2013/01 protocols. They were risk stratified and treated with chemotherapy according to their respective protocol. Patients with acceptable donors and intermediate and high risk disease, according to Measurable Residual Disease (MRD), underwent Allogenic Hematopoietic Stem Cell Transplantation (allo-HSCT).

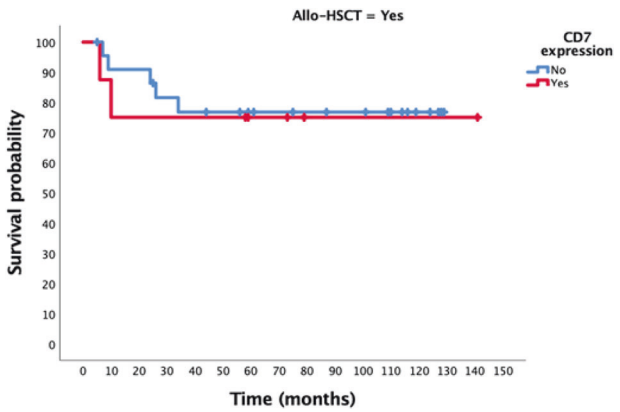
Patients with concomitant Down syndrome underwent specific chemotherapy without allo-HSCT, if they achieved a complete remission.

Results: Patients, disease and transplant characteristics are summarized in Table1.

Twenty (36%) patients had AML that expressed CD7, and thirty-five (64%) were CD7-. Eight (40%) and 23 (66%) children underwent HSCT and achieved an undetectable MRD before transplant in 5 and 17 cases (62% and 74% among transplanted patients) in CD7+ and CD7- AML, respectively. Relapse occurred in one (5%) and three (9%) patients while non-relapse mortality rates were 15% and 27%, in CD7+ and CD7- groups. Median overall survival (OS) could not be estimated for either group, while 2- and 5-year survival were 85% vs 79% and 79% vs 72% in CD7+ vs CD7- AML ($p = 0.571$). Estimated median DFS was not reached (NR) in both groups and 2- and 5-years DFS were 100% vs 89% and 93% vs 89% in CD7+ vs CD7- AML ($p = 0.52$).

The patients with intermediate- and high-risk AML undergoing allo-HSCT had a median OS NR, a 2-years OS of 75% vs 86% and 5-year OS of 75% vs 77% ($p = 0.83$) and a median DFS NR, 2-year and 5-year DFS of 100% vs 91% ($p = 0.4$) in CD7+ and CD7- AML.

Characteristics	CD7+ AML	CD7- AML
Total patient, n	20	35
Median age, years (range)	7 (1-17)	8 (0-17)
Sex, n (%)		
Male	11 (55)	17 (49)
Female	9 (45)	18 (51)
Cytogenetic risk, n (%)		
Standard	2 (10)	9 (26)
Intermediate	11 (55)	14 (40)
High	2 (10)	12 (34)
Allo-HSCT n (%)	8 (40)	23 (66)
MRD undetectable before allo-HSCT, n (%)	5 (62)	17 (74)
Donor type, n (%)		
HLA-identical	3 (38)	12 (52)
MUD	4 (50)	11 (48)
Haplo-identical	1 (12)	0
Stem cell source, n (%)		
Bone marrow	3 (38)	13 (57)
Cord blood	2 (24)	4 (17)
Peripheral blood	3 (38)	6 (26)



Conclusions: The meaning of CD7 expression is controversial in adult patients, where it is predictive of a dismal prognosis according to most studies. We observed that the expression of CD7 in pediatric AML did not associate with poor prognosis.

In our population, the patients with standard-risk, who did not undergo allo-HSCT, and with intermediate- and high-risk CD7+ AML, who underwent allo-HSCT both with low (MRD-) and high disease burden (MRD+), did not show a higher risk of relapse or death compared to children with CD7- AML. Our results need to be validated in wider prospective clinical trials.

Disclosure: Nothing to declare.

P066.

Outcome of Second Allogenic Stem Cell Transplantation in Children with Primary Immune Deficiencies

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Background: Second stem cell transplantation (SCT) is usually associated with high morbidity and mortality and data on its outcome in children with primary immune deficiencies (PID) are scarce.

Methods: The data were collected using an in-house database at the Great North Children's Hospital, Newcastle over 20 years (2000-2019).

Results: We present 26 children with PID who underwent second SCT at our institution for mainly graft failure (GF) or graft versus host disease (GVHD) after their first SCT. The underlying diseases were severe combined immune deficiency (SCID) in 38% and chronic granulomatous disease (CGD) in 19%.

Median ages at first and second SCT were 19 months (range 1 month- 15years) and 6 years (range 10 months-19 years), respectively. Median interval between the first and second SCT was 1 year (range 3 months- 12 years). The indication for second SCT was secondary GF in 20 (77%), primary GF in 2 (7.7%), GVHD in 3 (11.5%) and severe immune dysregulation in one patient. Five (19%) patients received an unconditioned top-up before second SCT. Patients were conditioned with fludarabine (22) with treosulfan and thiotepa (11), melphalan (5), treosulfan (5) or busulfan (1). Cyclophosphamide was given with busulfan in 3 and with treosulfan in one patient. They all received serotherapy except 3 patients. Donors were matched or mismatched unrelated (MUD, MMUD) in 11, haploidentical in 9 (including TCR ab/CD19 depletion in 7), matched or mismatched sibling (MSD, MMSD) in 5 and matched family (MFD) in one case. Stem cell source was peripheral blood (PB) in 16 (61%) and bone marrow (BM) in 10 (38%). Neutrophil engraftment occurred at a median of 15 days (range 10-26). Acute skin GVHD grade I-II was seen in 6/26 (23%) and one patient developed mild chronic skin GVHD. One patient required a further top up infusion and another underwent a third conditioned SCT due to graft loss. Donor engraftment of CD15 and T cells > 90% was seen in 77% of surviving patients. 85% had CD4+ >500 cells/μl and were off immunoglobulin replacement therapy with normal vaccine responses at last follow up. 10 year overall (OS) and event fee survival (EFS) were 81% and 78%, respectively. OS in patients who had their second SCT in 2010-2019 was higher at 93% compared to 67% in 2000-2009 ($p = 0.12$). Patients age at second SCT had no significant effect on OS (OS in patients ≥5 years was 84% compared to 78% in patients <5 years, p= 0.9). OS was 100% in haploidentical TCR ab depletion (including 3 patients with previous GVHD GIII-IV), 88% in MUD, 75% in MFD and 60% in MMUD (p=<0.001). The main cause of death was infection.

Conclusions: 10 year OS of second SCT in our institution is comparable with results of first SCT in other studies (Dvorack et al 2008, Gennery et al 2010). OS has improved in the last decade (93%) due to using advanced methods. Haploidentical TCR ab/CD19 depletion is an advanced cost-benefit rescue therapy which can be used if no matched donor is available.

Disclosure: There is no conflict of interest.

P067.

Outcome of Allogenic Stem Cell Transplantation in Elderly Patients: A Single Center Study

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Background: Recent advances and improvement of supportive care allowed allogeneic stem cell transplantation (HCT) to be offered to selected older patients. However, data regarding outcome and factors affecting the outcomes are limited.

Methods: We retrospective analyzed the outcome in 332 patients, median age 65 years (60-76), who underwent HLA-matched related ($n = 85$), matched unrelated ($n = 205$) and haploidentical donor ($n = 42$) HCT, between January 2014 till December 2019. Of these 60% were male. Diagnosis was leukemia: 193, MDS: 76, MF: 46 and others: 17. Graft source was PBSC in 98%. Reduce-intensity conditioning regimen in 95%, and in vivo T-cell depleted was given in 89% of patients. We categorized them to 3 age-groups (G): G1 60-65y, ($n =$ 175), G2 >65-70y ($n = 127$), and G3 >70y ($n = 30$).Outcomes examined included overall survival (OS), non-relapse mortality(NRM), event free-survival (EFS), length of hospitalization

for HCT, GVHD and reasons of re-hospitalization during the first year.

Results:

Multiple Cox regression results	HR (95% CI)	P
OS		
Age		0.16
60-65 vs >70	0.55 (0.30-1.02)	0.05
>65-70 vs >70	0.64 (0.34-1.20)	0.16
Re-admission in the 1st 6-month post HCT	1.14 (1.40-3.27)	0.0005
Acute-GVHD		
III-IV vs II-IV	2.53 (1.64 – 3.92)	<0.0001
Chronic-GVHD		
Moderate-severe vs mild	0.48 (0.28 – 0.80)	0.005
NRM		
Age		0.05
60-65 vs >70	0.47(0.22-0.99)	0.05
>65-70 vs >70	0.61 (0.29-1.3)	0.20
HCT-CI		
2-3 vs 0-1		0.01
>3 vs 0-1	1 (0.55-1.83)	0.99
	2.18 (1.24-3.3)	0.007
Re-admission in the 1st 6-month post HCT	3.25 (1.7-6.22)	0.0004
Acute-GVHD		
III-IV vs II-IV	4.18 (2.49-7.02)	<0.0001
EFS		
Age		0.05
60-65 vs >70	0.46 (0.25-0.86)	0.01
>65-70 vs >70	0.57 (0.31-1.05)	0.07
Re-admission in the 1st 6-month post HCT	1.93 (1.27-2.93)	0.002
Acute-GVHD		
III-IV vs II-IV	2.34 (1.52-3.61)	0.0001
Chronic-GVHD		
Moderate-severe vs mild	0.44 (0.26-0.74)	0.002

The median follow up was 14 months (1-123). Median days of hospitalization during HCT period were 30-days (20-132), not statistically different when stratified by age group ($p = 0.049$). HCT-CI scores were 0-1 (143), 2-3 (107) and >3 (70). The cumulative incidences of grade II-IV acute-GVHD was 38.3% and 16.3% for grades III-IV. Moderate-severe chronic-GVHD was 23.7%. Increasing age was not associated with increases in acute GVHD ($p = 0.86$) or chronic-GVHD (p= 0.6). Overall, 187 (56%) patients were re-hospitalized within the first 6-month of HCT, while 61 (18%) in the second 6-month. The 2-year OS rate were 56% in G1, 53% in G2 and 34% in G3 ($p = 0.14$). The 2-year EFS rate were 54% for G1, 49% for G2, and 31% for G3 (P=0.05). Cumulative incidence of NRM at 2-year were 25% in G1, 36% in G2 and 52% in G3 ($p = 0.008$). Risk factors such as age, KPS, HCT-CI, donor-type, readmission and GVHD were analyzed for their associations with outcomes using univariate analyses, those with significant results entered in multivariate-analysis (table 1).

Conclusions: Age was not a significant factor for OS and NRM, but was significant for EFS. HCT-CI, acute and chronic-GVHD and readmission in first 6-month post-HCT were significant risk factors. Selecting patients based on HCT-CI, and good management of GVHD and post-HCT complications may improve clinical outcomes.

Disclosure: Nothing to declare.

P068.

Allogeneic Hematopoietic Stem Cell Transplantation for Patients 60 Years Or Older. A Single-Institution Experience

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Background: Nowadays, Allogeneic stem cell transplantation (Allo-HSCT) is the only potentially curative option for hematologic malignancies. Improvements in reduced intensity conditioning (RIC) regimens, supportive care and management of transplant-related complications, have contributed to the increase in HSCT activity in elderly patients. However, outcome data in those who are 60 years or older are limited. The main aim of this study is measure overall and relapse-free survival (OS and RFS) in among elderly hematological patients (≥60 years) who underwent Allo-HSCT. Secondary outcomes were transplant-related mortality (TRM) and time to engraftment.

Methods: We retrospectively evaluated two cohorts of patients (A:<60 years; B: 60 years or older), identifying 56 patients who underwent allo-HSCT between 2015 and 2019 at the 12 de Octubre University Hospital in Spain. Statistical analyses were performed using STATA 14.0. RFS was calculated as the time from the date of transplant to the date of relapse or death from any cause. Length of stay (LOS) was compared among study groups using Wilcoxon Test.

Results: The median age at the time of Allo-HSCT was 50 years (46-54). The underlying disease among younger

patients was mostly AML (27%) and MDS (33.3%) for older patients (Table 1).

Regarding the analysis of comorbidities, there were no significant differences in the distribution of patients according to the Disease risk index and HCT-CI score. The conditioning regimen was selected according to perfomance status and risk of relapse. The median follow-up was 19.51 months.

Table 1. Characteristics of patients

	<60 years ($n = 41$)	≥60 years ($n = 15$)	p-value
Sex, n (%)			
Female	18 (44%)	6 (40%)	0,739
Male	23 (56%)	9 (60%)	
Pathology, n (%)			0,246
Myelofibrosis	1 (2,4%)	2 (13,5%)	
MDS/CMML	8 (19,5%)	5 (33,3%)	
AML	11 (27%)	4 (26,7%)	
ALL	2 (5%)	1 (6,7%)	
AA	3 (7,3%)	0	
HL	10 (24,2%)	0	
NHL	6 (14,6%)	3 (20%)	
DRI, n (%)			0,874
Low risk	13 (31,7%)	3 (20%)	
Intermediate risk	17 (41,5%)	8 (53,3%)	
High risk	11 (26,8%)	4 (26,7%)	
Disease status at transplant, n (%)			0,901
Complete remission	30 (73%)	11 (73,3%)	
Partial response	4 (10%)	1 (6,7%)	
Stable/progressive disease	7 (17%)	3 (20%)	
HCT-CI score, n (%)			0,263
<3 pts	35 (85%)	11 (73%)	
≥3 pts	6 (15%)	4 (27%)	
Donor type, n (%)			0,803
Match related donor	25 (61%)	9 (60%)	
HLA-Haploidentical donor	15 (36,5%)	6 (40%)	
Match-unrelated donor	1 (2,5%)	0	
Graft type, n (%)			0,550
PBSC	38 (92,5%)	15 (100%)	
BM	3 (7,5%)	0	
GVHD prophylaxis, n (%)			0,261
MTX+CYA/Tac	23 (56%)	5(33,3%)	
CYA+MMF+PT-CY	15 (37%)	10 (66,6%)	
ATG	3 (7%)	0	

We reported prolonged overall survival (OS) at 3-year: 61% for <60 years (95% CI, 41% to 70%) and 41% for elderly (95% CI, 16%-52%), (HR 2,71; 95%CI 1,16-6,56, $p = 0.02$) (Figure 1). There were no significant difference in RFS when comparing age groups, younger and older, respectively (83.8% vs. 83.3%, $p = 0{,}921$).

Engraftment was prompt, with median time to neutrophil engraftment of 17 days ($p = 0{,}282$). In the multivariate analysis, ICU admission (HR 7.11, 95%CI 1.12-29.3, $p = 0{,}034$) and primary graft failure (HR 4.72, 95%CI 1.55-40, $p = 0{,}048$) were associated with poorer survival.

Conclusions: HSCT is being increasingly performed in elderly patients. Although in our study elderly was associated with poorer overall survival, allo-HSCT was well tolerated in older patients with good performance status and age ≥60 had no impact on time to engraftment, relapse rate, LOS, RFS and TRM. The success of hematopoietic stem cell transplantation is determined by multiple factors and it could be a safe and effective option for carefully selected patients aged 60 or older.

Disclosure: Conflicts of interest: None.

P069.

Allogeneic Hematopoietic Stem Cell Transplantation in Patients Older Than 65 Years with AML And MDS: Risk Factors for Overall Survival And Disease Free Survival

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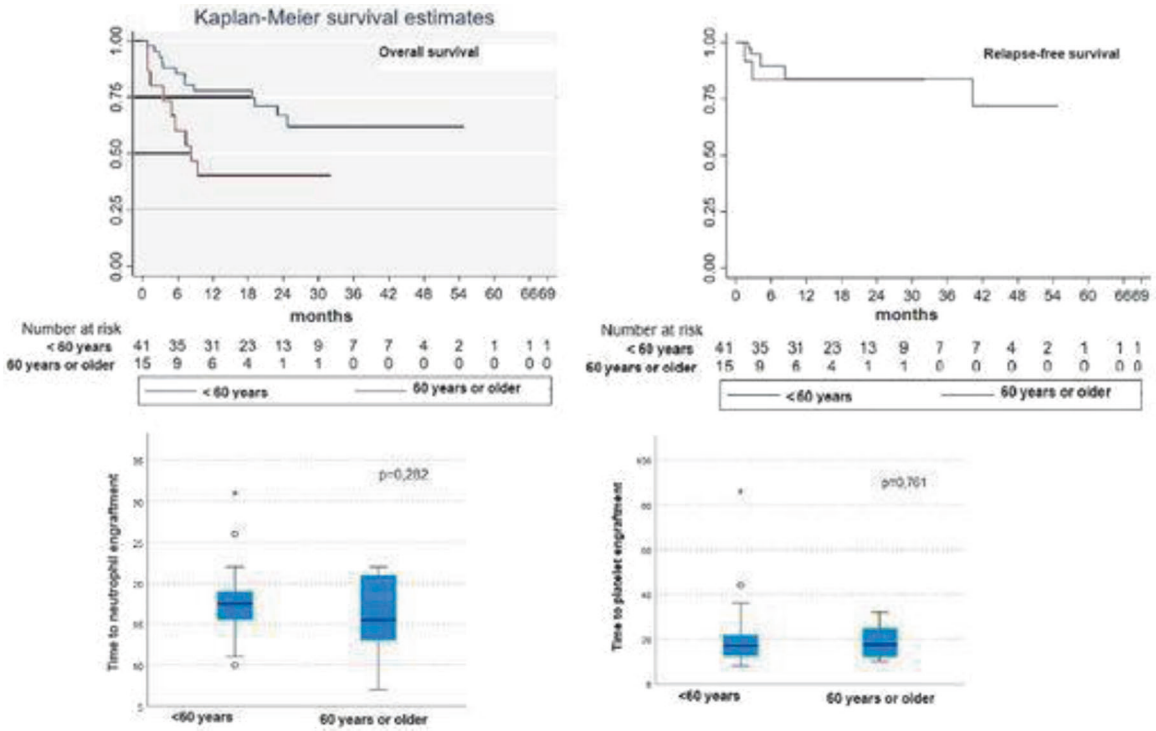
Background: Median age of occurrence of acute myeloid leukemias (AML) and myelodisplastc syndromes (MDS) is 65 years and older. Nevertheless, the use of allogeneic stem cell transplant (allo-HCT) has been historically limited to younger population, namely due to excess in non-relapse-mortality (NRM) in olders. Here we report our 15-year experience in allo-HCT in patient older than 65 years diagnosed with AML or MDS.

Methods: All consecutive patients aged more than 65 years and receiving an allo-HCT (as first transplant) for AML or MDS at our center from January 2005 to December 2019 were included in this analysis.

Results: Ninety patients fulfilled the inclusions criteria (71, 81% AML and 19, 19%, MDS). Median age at transplant was 68.29 years (65.02-76.54), with 29% being older than 70 years. Donors were HLA-matched related in 13pts (14%), matched unrelated (10/10) in 20pts (22%), mismatched unrelated (9/10) in 13pts (14%) and haploidentical in 44pts (50%). In 78pts (87%) conditioning was treosulfan-based. Fourty-six (51%) patients received a myeloablative conditioning regimen. Eighty-five (94%)



pts received in-vivo T-cell depletion: in 54 (63%) with anti thymocyte globulin (ATG) and in 31 (37%) with post-transplant cyclophosphamide (PTCy). Fourty-four (49%) pts had a HCT-CI of 0, 31 (34%) pts of 1 or 2 and 15 (17%) pts ≥ 3. Disease Index Risk was low for 1 (1%) pt, intermediate for 39 (44%) pts, high for 42 (48%) pts and very high for 7 (8%) pts (not available in 1 pt). Forty-one pts died: 14 (36%) from disease relapse, 16 (42%) from infection, 7 (18%) from GvHD, 1 (2%) from cardiac toxicity, 1 (2%) from multi organ failure, 2 unknown. Median duration of hospitalization was 48 days (24-198).

Median follow-up among survivors was 35.08 (2.82-104) months. The 3-year overall survival (OS) was 53+/-6%, and disease free survival (DFS) was 45+/-6%. Day-100 NRM was 17+/-2%, while at 3 years was 29+/-2%. The 3-year CI of relapse was 22+/-2%. Day-100 CI of acute GvHD grade II-IV was 21+/-2%, being 13+/-1% for grade III-IV. CI of cGvHD at 3-year was 35+/-3%, extensive 20 +/-2%. Outcomes were not different for patients younger or older than 70 years. In multivariate analysis (MVA), factors independently associated with both higher OS and DFS were diagnosis of MDS ($p = 0.011$, HR: 0.277, CI: 0.103-0.742; $p = 0.034$; HR: 0.383, CI: 0.157-0.932) and use of matched donors (both related or unrelated) with PTCy ($p =$ 0.037, HR: 0.234, CI: 0.060-0.918; $p = 0.027$, HR: 0.306, CI: 0.107-0.877). Donor age > 38 years was associated with lower DFS in MVA ($p = 0.019$, HR: 2.146, CI: 1.132-4.067). In MVA NRM was lower in transplants receiving a matched donor ($p = 0.040$, HR: 0.375, CI: 0.147-0-958) while higher for patients with a HCI-CI ≥ 3 ($p = 0.015$, HR: 3.058, CI: 1.243-7.520).

Conclusions: Our results confirm that age alone should not limit allo-HCT eligibility of patients diagnosed with AML and MDS. HCT-CI is an important tool to help in selecting those patients more likely to benefit from allo-HCT. HLA matched donor (sibling and unrelated) with PTCy as GvHD prophylaxis improved both OS and DFS compared to ATG.

Disclosure: Nothing to declare.

P070.

Impact of Human Leukocyte Antigen Allele Polymorphisms On The Outcomes of Transplantation From HLA-Matched Unrelated Donors

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Background: Among many factors that affect the outcomes of allogeneic hematopoietic stem cell transplantation (allo-HSCT) polymorphism of the classical human leukocyte antigen (HLA) genes represents a significant interest. Some

studies demonstrated that single mismatch for HLA-A, -B, -C, or -DRB1 are associated with increased risk of post-transplant complications. However, there is still limited data on the influence of HLA polymorphism on the success of transplantation from HLA-matched unrelated donors (10/10).

The aim of the present study was to investigate an association between HLA alleles and the results of allo-HSCT in Russian population of patients.

Methods: The study included 535 patients transplanted from HLA-matched unrelated donors between 2002 and 2019 at the RM Gorbacheva Research Institute, Pavlov University. Median age was 30 years (1-70). Most frequent diagnosis in transplanted patients was acute leukemia (68%, $n = 368$). Median follow-up was 15 months (0,5-132 mo).

We executed a machine learning algorithm for association between HLA-alleles and allo-HSCT outcomes of transplantation in 2 cohorts of patients. The first cohort (group A, $n = 103$) included patients who died within 6 months after transplantation due to relapse or transplant associated mortality. The second cohort (group B, $n = 146$) included patients with a favorable prognosis who survived for 3 years or more without relapse of the disease. HLA-A, -B, -C, -DRB1, and -DQB1 high resolution typing results were analyzed. For each of the HLA-alleles we formed a contingency table, calculated an odds ratio (OR) and determined a p-value. The between-group HLA-alleles difference analysis was performed using the Fisher's exact test, with $P<0.05$ considered to indicate a statistical significance. The impact of selected alleles was evaluated in the whole group of patients.

Results: Among all of the alleles, only DRB1 11:01 ($p =0.007$), DRB1 11:04 ($p= 0.04$) and DRB1 16:01 ($p= 0.04$) showed significant variance of frequencies between the considered groups.

The results showed that the gene frequency HLA-DRB1 11:01 was significantly higher in group A (16/103 pts) compared with group B (7/146 pts) with a statistically significant difference (OR = 0,27). In contrast, survival probability at 3 years without relapse was significantly higher for patients that expressed HLA-DRB1 11:04 (17/146 pts, OR = 3,25) and HLA-DRB1 16:01 (14/146 pts, OR = 3,52). Moreover, we detected a significant decrease cumulative incidence of NRM for patients with HLA-DRB1 11:04 (25% vs 13%, $p = 0,05$).

We also analyzed an association between HLA-allele polymorphisms and graft failure. In the whole group graft failure was detected in 20 patients and was significantly more frequent in patients with HLA-A 68:01 ($p = 0,038$, 3/20 pts, OR = 0,2), HLA-B 05:01 ($p = 0,037$, 1/20 pts, OR = 0), HLA-B 07:10 ($p = 0,037$, 1/20 pts, OR = 0), HLA-B 17:02 ($p = 0,037$, 1/20 pts, OR = 0), HLA-B 38:01 ($p = 0,041$, 4/20 pts, OR = 0,27), HLA-C 14:54 ($p = 0,037$, 1/20 pts, OR = 0), HLA-DQB 03:05 ($p = 0,037$, 1/20 pts, OR = 0), HLA-DQB 06:03 ($p = 0,01$, 8/20 pts OR = 0,28), HLA-DRB 13:01 ($p = 0,009$, 8/20 pts, OR = 0,17).

Conclusions: in this study, we found that several HLA alleles are noted as correlates of early mortality and graft failure. At the same time, the carriers of HLA-DRB1 11:04 and HLA-DRB1 16:01 alleles have a more favorable outcome after allo-HSCT.

Disclosure: Nothing to declare.

P071.

Efficacy of Modified FC/ATG Pretreatment in Haploid And Allogeneic Hematopoietic Stem Cell Transplantation for Severe Aplastic Anemia

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Background: Severe aplastic anemia (SAA) is a disease of young people, in which allogeneic hematopoietic transplantation (HCT) provides curative therapy. We evaluated outcomes of haplo-HSCT in patients with SAA.

Methods: To evaluate the efficacy and safety of improved FC/ATG Flu 30mg/m2/d, -5~-2d, CTX 50mg/kg/d,-5~-2d, ATG: 2.5mg/kg/d, -5~-2d pretreatment in the treatment of severe aplastic anemia (SAA). Clinical data of 65 patients with severe aplastic anemia who received allogeneic hematopoietic stem cell transplantation in our hospital from June 2012 to June 2020 were retrospectively analyzed, 29 cases were MSD-HSCT and 35 cases were Haplo-HSCT.

Results:

Table: Comparison of aGVHD, EB virus, CMV virus and related serious complications between MSD-HSCT group and Haplo-HSCT group.

	I–II° aGVHD	III–IV° aGVHD	EB virus	CMV virus	related serious complications	Preconditioning death	The total survival
MSD-HSCT group ($n = 29$)	7	1	5	6	0	0	29
Haplo-HSCT group ($n = 35$)	15	5	15	20	4	1	30
$\chi 2$	2.463	1.102	4.844	8.737	1.854	60.099	2.729
P	0.117	0.294	0.028	0.003	0.173	0.000	0.099

Note: Severe complications include severe pneumonia, hepatic venular occlusion, hemorrhagic cystitis, TMA, etc.

Results: 1 patient died of intracerebral hemorrhage before transplantation, and all the other 63 patients were completely implanted. The median follow-up time was 14.5 (1-95) months, and the total survival (OS) rate was 92.2%.The OS rates of the Haplo-HSCT group and the

MSD-HSCT group were 100% and 85.7% (P=0.099), respectively, and the difference in survival analysis between the two groups was not statistically significant. Haplo-HSCT group I ~ II ° aGVHD, III ~ IV ° aGVHD, EBV, CMV disease incidence, associated severe complication rates were 42.9%, 14.3%, 42.9%, 57.1% and 8.6%, were higher than in MSD-HSCT group24.1%, 3.4%, 17.2%, 20.7% and 0, (P = 0.117, 0.294, 0.028, 0.003, 0.173), The infection rates of EB and CMV virus in haplo-HSCT group were significantly higher than those in MSD-HSCT group, and the difference between the two groups was statistically significant (P<0.05).I ~ II ° aGVHD, III ~ IV ° aGVHD, relevant incidence of serious complications, the total survival had no statistical significance.

Conclusions: The efficacy of modified FC/ATG pretreatment for SAA was similar to that of other pretreatments at home and abroad, but with fewer toxic and side effects and higher OS rate.The infection rates of EB and CMV virus in haplo-HSCT group were significantly higher than those in MSD-HSCT group, but there was no statistically significant difference between the two groups in survival analysis.The efficacy of Haplo-HSCT group was similar to MSD-HSCT group, It can be selected as a replacement donor for SAA patients who lack a total congruent donor.

Clinical Trial Registry: No Clinic Trial.

Disclosure: Nothing to declare.

P072.

Long-Term Results of Hematopoietic Stem Cell Transplantation for Hodgkin's And Non-hodgkin's Lymphoma: Experience of A Single Center in Colombian Northeast

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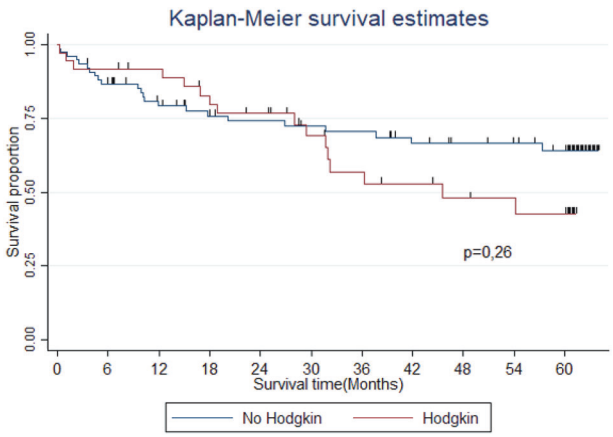
Background: Patients with Hodgkin's lymphoma (HL) and non- Hodgkin's lymphoma (NHL) are cured with initial radiation therapy, chemotherapy, or a combination thereof. However, patients with refractory or relapsed lymphoma presents poor outcome from conventional salvage treatment regimens, instead, hematopoietic stem cell transplantation (HSCT) has been frequently used to treat this group of patients, with often good prognosis. The aim of this study was to evaluate the overall survival (OS) of a group of patients diagnosed with Lymphoma and treated with HSCT in a Colombian population.

Methods: An analytical and observational retrospective cohort was conducted, eligible patients were diagnosed with Hodgkin's or non- Hodgkin's lymphoma and treated from 2011 to 2020 at a university medical center in Colombia. We collected demographic variables, clinical features and survival patterns. Graft-versus-host disease prophylaxis were applied in all allogeneic patients. The Kaplan-Meier method was used to estimate OS, using time of relapse after HSCT as the starting point.

Results: A total of 113 patients with NHL and HL were included for analysis. We identified 76 patients diagnosed with NHL, being B cells the most common type (86.4%), and 37 patients diagnosed with HL. The median age at HSCT was 47 years (14-73), and 73.8% were man. All patients were treated with 1 to 5 lines of treatment. Average time between diagnosis and HSCT was 1,7 years (0-8). Autologous-HSCT was performed in 105 patients, while only 8 allogeneic-HSCT were done, from which 6 were performed as a second HSCT after relapse or disease progression. At the time of transplantation, 70.8% patients were at complete response, while the other 29.2% were at partial response. Most common complication after transplantation was infection (55.2%), followed by gastrointestinal toxicity (28.9%). Sixty-five patients (57%) are still in remission after HSCT, from which sixty-two (95.4%) are autologous and three (4.6%) are allogeneic. OS was 66% (95%CI 55.39-74.65) at one year, and 57.26% (95%CI 45.91-67.07) at five years. By response at HSCT when comparing complete response with partial response, HR = 2.7 (95%CI 1.07-6.81, $p = 0.035$) at first year, HR = 1.5 (95%CI 0.74-3.07, $p = 0.255$) at third year, and HR = 1.3 (95%CI 0.69-2.62, $p = 0.378$) at fifth year. Progression or relapse after HSCT was the cause of death in 57.1%, others causes were undetermined or non-related to transplantation causes.



Conclusions: Early intervention with HSCT improves outcomes in patients with refractory o relapsed lymphoma. Allogeneic-HSCT should be considered as salvage treatment after autologous-HSCT relapse and maintenance approaches should be considered for improved therapies after transplantation. Also, further studies integrating minimal residual disease and risk factors may be better identified for early progression.

Disclosure: Nothing to declare.

P073.

Indications And Survival of Allogeneic Transplant in Patients Over 65 Years Old

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Background: The incidence of allogeneic transplant (HSCT) is increasing among patients over 65 years old, but it is still an infrequent treatment because of high toxicity. The aim of this study is to compare the survival after HSCT of patients aged 60 to 65 years versus patients over 65.

Methods: We performed an unicentric retrospective analysis of 70 patients over 60 years old transplanted with an allogeneic peripheral blood stem cells transplant between 2013 and September 2020.

Results: 52/70 patients were included in the 60-65 years group, with a median age of 62 years; and 18/70 in the >65years group, with a median age of 67 (62-69). Baseline characteristics of entire cohort are reflected in Table1. Most of the patients were transplanted with diagnosis of AML or MDS with no differences between the groups regarding the predictive models (EBMT score, HTIC score and allogeneic disease index) or persistence of disease prior to transplantation. 77% of the patients >65 received an haploidentic transplant whereas in 60-65 the donor type was equally distributed in haploidentic, MSD and MUD.The median follow-up of the entire cohort was 8 months. No significant differences were found between the two groups in progression free survival (PFS), with a median PFS of 7 months in 60-65 versus 34 months in >65; Hazard Ratio (HR) 0.54 (95% IC: 0.25-1.16). The Overall Survival (OS), was 8 months versus 51 months respectively; HR 0.51 (95% IC: 0.23-1.16) (Figure1). Survival was also similar depending on donor type ($p > 0.05$).

We also analyzed in the global cohort the impact in terms of OS of the pre-HSCT predictive models. According to HTIC score, median OS was 9, 14 and 18 months for low, intermediate and high risk respectively (HR 0.81, 95% IC: 0.53-1.24); according to EBMT score, with 8, 9 and 32 months (HR 0.94, 95% IC: 0.61-1.46); and finally to allogenic disease index, with 7, 10 and 10 months (HR 0.78, 95% IC: 0.45-1.34).

	60-65 ($n = 52$)	>65 ($n = 18$)	p
GENDER, male n (%)			
DIAGNOSIS n (%)			
AML	35 (71.2%)	14 (77.8%)	>0.05
MDS	26 (30.8%)	7 (38.9%)	>0.05
NHL	6 (11.5%)	1(5.6%)	
Others	6 (11.5%)	3 (16.7%)	
EBMT score n (%)			
0-3 pts	19 (38.8%)	5 (33.3%)	>0.05
4-5 pts	22 (44.9%)	5 (33.3%)	
>6 pts	22 (44.9%)	5 (33.3%)	
HTIC score n (%)			
Low (0 pts)	17 (34.7%)	5 (29.4%)	>0.05
Intermediate (1-2 pts)	16 (32.7%)	9 (52.9%)	
High (>3pts)	16 (32.7%)	3 (17.6%)	
ALLOGENEIC DISEASE INDEX n (%)			
Low	4 (8.3%)	1 (5.9%)	>0.05
Intermediate	26 (54.2%)	11 (64.7%)	
High / Very high	18 (37.5%)	5 (29.4%)	
DONOR TYPE n (%)			
MSD	14 (27.5%)	2 (11.1%)	<0.05
Haploidentic	22 (43.1%)	14 (77.8%)	
MUD	15 (29.4%)	2 (11.1%)	
CONDITIONING			
Reduced-intensity	45 (93.8%)	18 (100%)	>0.05
Mieloablative	3 (6.2%)	-	
NEUTROPHILS, Grafting time median (range)	18 (9-31)	20 (11-28)	>0.05

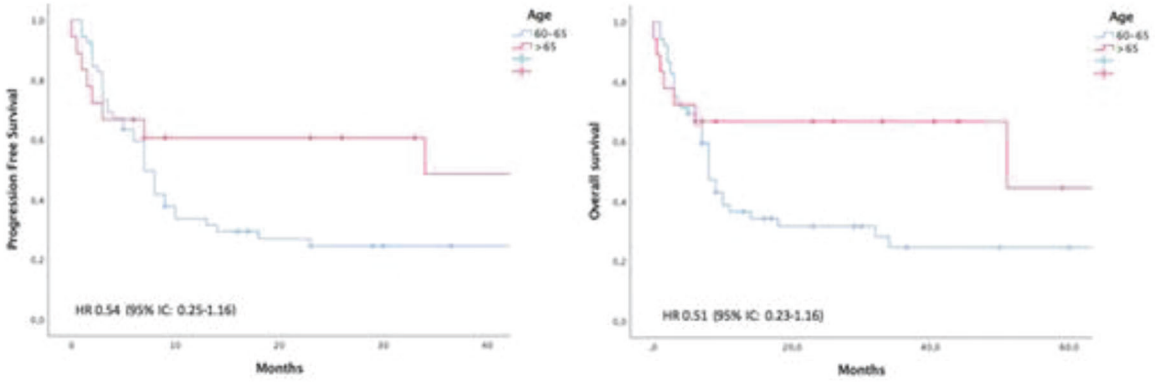
Table 1: basal characteristics of patients. Abbreviations: AML, Acute Myeloid Leukemia; MDS, myelodisplasic syndrome; NHL, non-Hodgin lymphoma; MSD, matched sibling donor; MUD, matched unrelated donor.

Conclusions: in our population, we found similar outcomes in the group of >65 comparing to 60-65 years patients undergoing HSCT in terms of OS and PFS; therefore, HSCT should be considered in elderly and fit patients when indicated avoiding limitations regarding just age. PreHSCT score models should probably be supplemented with functional evaluation or scores in elderly patients to predict post HSCT survival and transplant indication.

Disclosure: Nothing to declare.

P074.

Unmanipulated Haploidentical Stem Cell Transplantation for Pediatric Patients with Acute Leukemia: An Experience From The Largest Children'S Hospital in Iran



Rashin Mohseni[1], Mahta Mardani[1], Maryam Behfar[1], Parisa Naji[1], Fereshteh Jafari[1], Zeynab Nikfetrat[1], Leila Hejazipour[1], Dima Barhoom[1], Poorya Salajegheh[2], Amir Ali Hamidieh[1]

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Background: Nowadays, the application of Haploidentical hematopoietic stem cell transplantation (Haplo- HSCT) is a curative option in pediatric patients with ALL and AML. Development of the efficient techniques for in vitro T-cell depletion and in vivo pharmacological prophylaxis of graft versus host disease (GvHD) enabled us to use the Haplo-HSCT for patients who have no access to an HLA-matched donor. In most lower-income countries, the administration of conditioning drugs is more common.

Methods: Since November 2016, 25 pediatric patients with high-risk acute leukemia (6 AML, 18 ALL, and 1 mixed linage) with ages ranged from 4 to 17 years (median: 9 y) have received Haplo-HSCT in Children's Medical Center, Tehran, Iran. The donors were Father, Mother, and Sibling in 12, 4, and 6 patients in order. The myeloablative conditioning protocol included Busulfan, Cyclophosphamide, and Antithymocyte Globulin (ATG) for all patients. Graft versus host disease prophylaxis consisted of cyclosporine A, Methotrexate, and post-transplant Cyclophosphamide. Based on a protocol approved by the Institutional Review Board, nine patients who didn't have any symptoms of acute GvHD on day 30 received a donor lymphocyte infusion (DLI).

Results: Overall 23/25 patients (92%) engrafted. Stage 1-2 aGVHD occurred in 8 patients and stage 3-4 aGvHD was seen in 12 patients. The incidence of aGVHD in patients based on the donor type was 3/4 for mother, 5/12 for father, and 5/6 of sibling Haplo-HSCT recipients. Chronic GvHD occurred in 10/23 patients. The incidence of cGVHD for Haplo-HSCT recipients from mother, father, and sibling was 1/4, 5/12, and 2/6 respectively. Relapse occurred in one AML and 6 ALL patients. The rate of relapse based on the donor type was 3/12 in the father and 2/6 in sibling Haplo-HSCT recipients. The probability of 4 years' event-free survival (EFS) was 4/5 in the AML and 9/19 in the ALL patients and the 4-year overall survival (OS) for patients transplanted was 5/5 in the AML and 12/19 in the ALL patients.

Conclusions: We had experienced favorable results for our Haplo-HSCT recipients as same as most parts of the world with pharmacological prophylaxis. Longer EFS and OS was achieved in AML transplanted patients. However, the type of available donor should not play a significant role in the decision to offer Haplo-HSCT to an AML or ALL pediatric patient.

Disclosure: Nothing to declare.

P075.

Is Haploidentical Haematopoietic Stem Cell Transplantation (Haplo Sct) Using Post-Transplantation Cyclophosphamide (PTCY) Feasible in Sub-Saharan Africa?

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Background: Background: Identifying a suitable unrelated donor (UD) in South Africa is challenging due to the highly diverse ethnic groups and mixed-race populations in this region, making Haplo SCT an attractive procedure for patients with high risk hematological malignancies.

Methods: To assess our experience with haplo SCT in South Africa, we retrospectively analyzed the outcome of 134 patients with hematological malignancies who received unmanipulated haplo SCT with PTCY at the two highest volume public and private SCT centers between 2014 and 2019. We determined patient characteristics, overall survival (OS), disease free survival (DFS), relapse incidence (RI), non-relapse mortality rate (NRM) and incidence of acute graft-versus-host-disease (aGVHD) at day +100.

Results: Median recipient and donor age was 44 years (range, 15-73 years) and 36 years (range, 9-68 years) respectively. Acute myeloid leukemia or myelodysplastic syndrome (AML/MDS) and acute lymphoblastic leukemia (ALL) were the most common indications for haplo SCT (61,2%). The EBMT risk score was > 5 in 44 patients (32,8%). Seventy seven patients (57,4%) received myeloablative conditioning regimens. The majority of patients (57,4%) received sex matched transplants and peripheral blood stem cells (PBSC) (70,9%) as cell source. Sixteen patients (11,9%) had an incongruent CMV serostatus at transplant. Median follow up was 10,8 months (range 0,36-70,8 months).

OS at 1 and 3 years were 56% (95% CI 47-64) and 37% (95% CI 28-47) respectively. The 1 and 3-year DFS were 47% (95% CI 38-55) and 32% (95% CI 24-41) respectively. The 100-day and 3-year Cumulative Incidence of NRM were 18% (95% CI 11-25) and 41% (95% CI 32-50) respectively, whereas the 1 and 3-year Cumulative RI were 16% (95% CI 11-24%) and 21% (95% CI 14-29) respectively. The 1-year OS for AML/MDS was 55% (95% CI 41-67) vs. 41% (95% CI 21-60) for ALL. Forty-one patients (39,8%) developed aGVHD at day 100, of these, 80,5% had Grades I & II disease whereas 19,5% had grades III & IV disease.

In univariate analysis, no risk factors were associated with OS; risk for lower DFS increased for older donor age (46-68y vs. 9-25y) (RR 1.9; 95% CI 1.02-3.5; $p = 0.43$). Risk for RI increased for "other" diagnoses (predominantly lymphoma) vs. AML/MDS (RR = 2.52; 95% CI 1,1-5,8; $p = 0.029$), decreased for PBSC vs. bone marrow (RR = 0.45; 95% CI 0,21-0,94;$p = 0.034$), decreased for child vs. parent donors (RR = 0,32; 95% CI 0,13-0,79;$p = 0.013$) and increased for >1 transplant vs first transplant (RR = 2,37; 95% CI 1,15-4,88; $p = 0.019$). Risk for NRM increased for older recipients (> 57 years) (RR = 2,24; 95% CI 1,01-4,99; $p = 0.049$).

In multivariable analysis, older donor age remained an independent risk factor for lower DFS. RI was higher for "other" diagnoses (RR = 2,62; 95% CI 1,12-6,15; $p = 0.027$), decreased for PBSC vs BM (RR = 0,43; 95% CI 0,19-0,95; $p = 0.038$) and decreased for child donors (RR = 0,25; 95% CI 0,09-0,67; $p = 0.006$).

Conclusions: These data support the feasibility of haplo SCT and suggest that unmanipulated haplo SCT utilizing a younger parent or child donor are valid options for adults with acute leukemia and MDS lacking a suitable UD in sub-Saharan Africa.

Disclosure: Nothing to disclose.

P076.

Impact of Covid 19 Pandemic On HSCT Activities: Report From A Single Center

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Background: The current COVID-19 pandemic, caused by SARS-CoV-2, is responsible of a severe acute respiratory syndrome. This pandemic poses unprecedented stress on the health care system including HSCT. Several international organization such as EBMT, WBMT, CIBMTR, produced guidelines for the management of different aspects of HSCT.

Methods: Aim of the study is to assess how COVID-19 pandemic has modified internal management of different steps of HSCT, during pandemic. We compared HSCT activity between 2019 and 2020, taking into account the same six months period from March to September.

Results: During pandemic Covid19, our transplant center has modified his procedures and activities according to the EBMT guidelines. Non-urgent transplants were deferred as much as possible, especially for non-malignant disorders. The decision was made based on individual considerations. All patients were tested for SARS-CoV-2 before start of the conditioning and all donors too before start of donation. We started to cryopreserve all stem cell product before start of conditioning.

Comparing HSCT activity between 2019 and 2020, we performed the same numbers of HSCT. In both periods, patients submitted to HSCT were predominantly with acute leukemia, so we respected the urgency criteria. Sibling donors and cord blood unit remained the same, but we increased MUD donors, in particular from European registry and we reduced the haploidentical ones. This change is due to mandatory cryopreservation for all apheresis products. We have avoided to cryopreserve bone marrow products due to the higher risk to drastically reduce CD34+ cell count during the process. For urgent patients with only haploidentical donors, we decide to use PBSC after G-CSF stimulation and so we modified GVHD prophylaxis. We used PTCY on day+3 +5, cyclosporine,

tapering dose from day+100 and mycophenolic acid until day+90 post HSCT. So use of bone marrow as stem cell source was drastically reduced.

Despite this changes, outcome post transplant were not affected: graft failure, sepsis and acute GVHD did not differ between the two time period. (Table 1).

We stopped Car-T infusion after the beginning of lockdown on March 2020, due to logistic difficulties and we started again on September 2020. For the outpatient follow up, we increased telehealth method, using telephone and/or televideo conferences for patients over six months after transplant, without serious complications.

Conclusions: According to the international guidelines, we were able to continue HSCT activities in the order to ensure a lifesaving treatment for patients for whom this procedure cannot be postponed.

Table 1: Patients' characteristic

	2019	2020
Allogeneic HSCT n°	34	33
Underlying disease		
Acute leukemia	22	23
Myelodisplatic syndrome	3	1
Myeloproliferative neoplasms (MFI)	4	5
Lymphoproliferative disease	3	4
Multiple myeloma	0	0
others	2	0
Donor type		
Mud	10	14
Sibling donor	11	12
Haploidentical donors	10	4
CBU	3	3
Stem cell source		
PBSC	17	28
BM	14	2
CBU	3	3
Conditioning regimen		
Myeloablative	29	26
Reduced intensity regimen	5	7
Gvhd prophylaxis		
PTCY	31	32
none	3	1
Graft failure n°(%)	2/34 (6%)	2/33 (6%)
Sepsis n°(%)	18/33 (54%)	19/34 (56%)
Relapse n°(%)	8/33 (24%)	10/34 (29%)
Overall Survival n°(%)	27/33 (82%)	27/34 (79%)

Disclosure: Conflicts of interest: Nothing to declare. No disclosures.

P077.

Defibrotide as Treatment for Transplant-Associated Microangiopathy (TA-TAM) in Pediatric Patients: A Single Center Experience

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Background: Transplant-Associated Microangiopathy (TA-TAM) is a rare complication of allogeneic hematopoietic stem cell transplantation (allo-HSCT), characterized by generalized endothelial dysfunction, microangiopathic hemolytic anemia, platelet activation, thrombotic events and organ failure. Defibrotide, is currently approved for the treatment of Sinusoidal Obstructive Syndrome (SOS), another complication involving endothelium and microangiopathy. We report our single institution experience of patients who developed TA-TAM, including patients treated with defibrotide.

Methods: We retrospectively reviewed our pediatric patients who underwent HSCT at our institution since 2007 and developed TA-TAM. TA-TAM diagnosis was determined according to Jodele criteria and resolution was marked by normalization of lactate dehydrogenase (LDH), lack of schistocytes and independence from transfusion for the microangiopathic process.

Results: We identified 14 patients who met Jodele criteria for TA-TAM following HSCT and are summarized in Table1. These children underwent HSCT for malignant (7) and non-malignant (7) diseases. Conditioning regimen consisted of TBI plus chemo ($n = 4$) or chemo-based ($n = 10$). All patients received a calcineurin inhibitor (cyclosporine n= 13; tacrolimus $n = 1$) with/without methotrexate ($n = 8$); 10 pts received anti-thymocyte globulin (ATG).

Acute GVHD, bacteremia, viremia and fungal infection preceded the TA-TAM diagnosis in 11, 2, 6 and 1 patients, respectively. Three patients experienced other endothelial complications (1 SOS-VOD and 2 PRES).

Two patients did not receive any treatment for TA-TAM; CNI was discontinued in 7 patients; 12/14 children received defibrotide as first- (6/14) or second-line treatment 3/14. The median time from start of defibrotide was one day (0-15) and the median duration of defibrotide therapy was 30 days (3-126). Resolution of TA-TAM was observed in 10/14 patients, 80% of whom (8/10) were treated with defibrotide ($p = 0.095$). We observed a trend for resolution of TA-TAM associated with defibrotide treatment in a logistic regression model (OR: 12; CI: 0.773-186; $p = 0.076$). Statistical significance may be limited due to the very small population size.

PATIENTS, n (%)	14 (100)
MALE	10 (71)
MEDIAN AGE, years (range)	10 (1-18)
DONOR	
Matched Sibling	9 (64)
MUD (8/8)	3 (21)
MUD (7/8)	2 (15)
GVHD PROPHYLAXIS	
CSA	5 (36)
CSA + Methotrexate	8 (57)
Tacrolimus	1 (7)
OTHER ENDOTHELIAL COMPLICATIONS	
PRES	2 (14)
VOD	1 (7)
TA-TAM ORGAN INVOLMENT	
Central Nervous System	3 (21)
Kidney	8 (57)
Polyserositis	2 (14)
CALCINEURIN INHIBITOR DISCONTINUATION	
Yes	7 (50)
No	5 (36)
Before TA-TAM diagnosis	2 (14)
FIRST-LINE TREATMENT	
No treatment	2 (14)
Fresh Frozen Plasma Transfusion	6 (43)
Defibrotide	6 (43)
SECOND-LINE TREATMENT	
Plasma exchange	2 (14)
Defibrotide	3 (21)

Conclusions: TA-TAM is a multifactorial condition that can be life threatening if severe, where endothelial dysfunction is key to pathogenesis. This is similar to SOS-VOD where endothelial activation is the main event that causes the chain reaction leading to liver failure. Defibrotide is effective in treating severe SOS-VOD if started early after onset. Due to similarities between TA-TAM and SOS-VOD, we used defibrotide in pediatric cases of TA-TAM and observed a trend for resolution of TA-TAM associated with defibrotide.

Our data suggest defibrotide therapy might be a safe and effective treatment in management of TA-TAM. Further prospective studies are needed to confirm our observation.

Disclosure: Nothing to declare.

P078.

The Impact of Cryopreservation On Haematopoietic Stem Cell Grafts During The COVID-19 Pandemic at The Royal Marsden Hospital

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Background: Cryopreservation of donor haematopoietic stem cells (HPCs) during the COVID-19 pandemic was recommended to ensure a stem cell source was present prior to starting recipient conditioning in case of donor unavailability or unsuitability and to pre-empt transport issues. Whilst loss of viability has been documented with cryopreserved HPCs, we aimed to also evaluate effects on time to engraftment, T-cell chimerism and early relapses compared to allografts using fresh HPCs.

Methods: We retrospectively analysed 15 consecutive allografts using cryopreserved HPCs during the pandemic (April to August 2020). We recorded the stem cell dose infused measured by CD34/kg, post thaw 7AAD viability, time to engraftment and T-cell chimerism at 28 days and 100 days and response assessment at 100 days. We compared this data to a cohort of 15 allografts using fresh HPCs during 2019-2020, with equal numbers of the same donor source and intensity.

Results: Table 1: Comparison between cryopreserved and fresh cohorts

	Cryopreserved ($n = 15$)	Fresh ($n = 15$)
Donor source:		
Sibling	3 (reduced intensity-RIC) (20%)	3 RIC (20%)
Haplo-identical	3 (RIC) (20%)	3 RIC (20%)
Unrelated (UD)	9 (7 RIC 2 full intensity, FI) (60%)	9 (7 RIC, 2 FI) (60%)
T cell depletion with Campath	11/15 (73.3%)	11/15 (73.3%)
None	4/15 (3 haplo-identical, 1 UD) (26.7%)	4/15 (3 haplo-identical, 1 sibling) (26.7%)
Mean stem cell dose infused CD34/kg (range):	5.00 (3.56 to 7.2)	5.37 (2.69- 72)
Mean post-thaw viability (range)%	95.59 (87.99 to 99.57)	n/a
Average time to engraftment (days):		
Mean	20.86	17.6
Median	20	17
Non full T-cell chimerism at day 28:		
Failed T-cell chimerism	10/15 = 66.7%	11/15 = 73.3%
Mixed T-cell chimerism (<95%)	2/15 = 13.3%	1/15 = 6.67%
Full donor T-cell chimerism at day 28 (> = 95%)	3/15 = 20%	3/15 = 20%
Non full T-cell chimerism at day 100		
Failed T-cell chimerism at day 100	5/15 = 33.3%	3/14 = 21.4%
Mixed T cell chimerism (<95%)	5/15 = 33.3%	4/14 = 28.5%
	5/15 = 33.3%	7/14 = 50%

Table (continued)

	Cryopreserved ($n = 15$)	Fresh ($n = 15$)
Full donor T-cell chimerism at/by day 100		
Relapse at day 100	1/15 overt relapse = 6.67%	1/14 relapse = 7.14%
	1/15 MRD positivity=6.67%	1/14 MRD positive = 7.14%

As per table 1, the mean stem cell dose was comparable between the 2 cohorts. The mean post thaw viability in the cryopreserved group was >95%. Average time to engraftment was numerically higher in the cryopreserved group but not statistically significant (20 vs 17 days median p= 0.204) with 2 patients in the cryopreserved group needing more than 28 days to engraft. However all did so spontaneously. The number of failed T-cell chimerisms at day 28 was high in both cohorts likely due to low lymphocyte counts through frequent use of T-cell depletion. However by day 100, it appears more patients in the fresh cells cohort had achieved full donor chimerism but this was not statistically significant (p= 0.38). Early relapses were equal.

Conclusions: The average post thaw 7AAD viability for cryopreserved cells at our center is excellent (>=95%). Median time to engraftment in recipients of cryopreserved cells was numerically higher although the numbers are too small to detect statistical significance. However, these early data do raise a concern that engraftment might be slower following cryopreservation of cells but this needs to be assessed in larger registry studies. Early relapses and the number of failed T-chimerisms at day 28 were similar in both groups.

Disclosure: Nothing to declare.

P079.

Impact of Cytogenetic And Molecular Risk at Diagnosis On Transplantation Results in Patients with Secondary Acute Myeloid Leukemia

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Background: Patients with secondary acute myeloid leukemia (s-AML) are a high-risk group, with dismal outcomes despite intensive chemotherapy. Consolidation with allogeneic transplant is the only curative option nowadays, but we still need to improve survival in these patients. We want to analyze the post-transplantation survival and the influence of cytogenetic and molecular risk in this group compare to de novo leukemia patients.

Methods: Single-center retrospective analysis of 113 patients with AML transplanted between 2011 and 2019. We divided our cohort into two groups: Group 1 n= 52 patients with de novo leukemia and Group 2 $n = 61$ patients with s-AML (including AML-MRC, t-AML and blastic phase of MPN Ph negative). The survival analysis was performed through Kaplan-Meier method and the risk was calculated with Cox regression. The Overall Survival (OS) was defined as the period from transplantation to death and the Event-Free Survival (EFS) as the period from transplantation to either relapse or death.

Results:

Variable	De novo leukemia $n = 52$	Secondary leukemia $n = 61$
Sex, male n (%)	31 (59.6%)	37 (60.7%)
Median age at HSCT, years (range)	49 (21-68)	56.5 (20-69)
ELN classification		
Favorable risk	15 (28.8%)	3 (4.9%)
Intermediate risk	21 (40.4%)	31 (50.8%)
Adverse risk	16 (30.8%)	27 (44.3%)
Complete remission after induction (1 or 2 cycles), n (%)	45 (90%)	45 (73.8%)
State disease prior to HSCT, n (%)		
CR with MRD- by flow cytometry	33 (67.3%)	30 (51.7%)
CR with MRD+ by flow cytometry	11 (22.4%)	13 (22.4%)
Active disease	5 (10.2%)	15 (25.9%)
Patients transplanted in first CR, n (%)	36 (69.2%)	44 (72.1%)
Conditioning intensity, n (%)		
Myeloablative	35 (67.3%)	26 (42.6%)
Reduce intensity	13 (25%)	28 (45.9%)
Sequential reduced intensity	4 (7.7%)	7 (11.5%)

The baselines characteristics of both groups are reflected in Table 1. Patients with s-AML were significantly older. We found a higher percentage of intermediate and adverse risk patients by the ELN risk classification, and a higher percentage of patients with refractoriness after induction or transplanted with active disease in the group of s-AML. The median follow-up of the global cohort was 12 months (0-77). In entire population, the 2-year EFS (2y-EFS) was 39% and the 2-year OS (2y-OS) was 48%. Comparing Group 1 with Group 2 we found a 2y-EFS 58% in patients with de novo leukemia vs 24% in s-AML patients, with a Hazard Ratio (HR) of 2.4 [95% CI (1.4-4.1)]. The 2y-OS was 68% vs 37% respectively [HR 2.6, 95% CI (1.4-4.6)]. We stratified both groups according to ELN risk classification at diagnosis. Among patients with de novo leukemia, the 2y-EFS was 86% in patients with Favorable Risk (FR) vs 44% in both Intermediate Risk (IR) and Adverse Risk [HR 1.8, 95% CI (1.03-3.2)]. The 2y-OS was 86% in FR vs 65% in IR and 54% in AR [HR 1.7, 95% CI (0.9-3.3)]. In patients

with s-AML the 2y-EFS was 34% vs 26% vs 21% for Favorable, Intermediate and Adverse risk patients [HR 0.97, 95% CI (0.5-1.6)] and the 2y-OS was 34% vs 34% and 41% respectively[HR 0.8, 95% CI (0.4-1.3)].

Conclusions: s-AML are a high-risk subgroup that shows more chemo-refractoriness and worse survival rates despite consolidation with HSCT than de novo leukemia patients. Unlike in de novo AML patients, transplant results were not influenced by ELN risk classification at leukemia diagnosis.

Clinical Trial Registry: No applicable.

Disclosure: Nothing to declare.

P080.

Burnout Syndrome in Oncology Practice: Experience of A Large HSCT Center

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Background: The problem of emotional burnout occupies a key position in the deterioration of mental and physical health of medical staff. However, it becomes more important in oncology practice: professionals have to deal with situations of high vital risk and fatal outcomes daily, more than that they have to take the function of reporting bad news and providing psychological support to patients and their relatives at this stage. Not everyone has stress management skills to support themself in high-stress situations, so it may cause depletion of emotional and mental resources of the specialist, it will manifest like burnout syndrome later.

Methods: in a prospective single-center study in August - October 2020, at the Department of Rehabilitation Medicine, we conducted a study in 78 persons from the medical staff. There were 3 groups of the respondents: 1. oncology physicians ($n = 28$), 2. oncology nurses ($n = 35$), 3. non-oncology specialists ($n = 15$) including laboratory staff ($n = 3$), clinical psychologists ($n = 6$) and teachers and tutors ($n = 6$). Respondents had different gender and work experience, 61% of them were 26-45 y.o. We used two methods in the study: Boyko V.V. Express Diagnostics (modified by Ilyin E.) as a screening method and Maslach Burnout Inventory (in adaptation N. Vodopyanova) as a more in-depth assessment method.

Results: According to Boyko V.V. Express Diagnostic 4 (5.13%) and 14 (17.95%) respondents had formed burnout syndrome and signs of starting burnout, respectively. The vast majority of them were physicians and nurses (83.3%). Maslach Burnout Inventory allowed us to determine the severity of burnout, and the data were: symptoms of extremely severe, severe and medium severe burnout syndrome were observed in 78.2% ($n = 61$) of employees from all three groups studied. The largest percentage of them were physicians (42.62%, $n = 26$) and nurses (47.54%, $n = 29$). Within each group of specialists, non-oncology specialists showed the highest percentage of no burnout syndrome (60%, $n = 9$), most of them were clinical psychologists (44,45%).

Groups		Number of respondents	Extremely High	High	Medium	Low
Oncology physicians		28	9	8	9	2
Oncology nurses		35	6	12	11	6
Non-oncology specialists	teachers and tutors	6	1	1	1	3
	clinical psychologists	6	-	1	1	4
	laboratory staff	3	1	-	-	2
Total:		78	17	22	22	17

Conclusions: The combined results of the research allowed us to conclude that the issue of emotional burnout affects all of 3 medical staff groups. Doctors and nurses are under risk more than others. Presumably, this is due to a higher level of responsibility, longer interaction with patients and relatives during the day, and a lack of stress management skills. From the group of non-oncological specialists, psychologists are most at risk, but their knowledge of stress management skills allows them to demonstrate high resilience. These data suggest the need of stress management skills training for all groups of medical staff to reduce the severity of existing symptoms and prevent burnout syndrome in future.

Disclosure: All authors – nothing to disclose.

P081.

Factors Affecting Outcomes in Children with Acute Leukemia Post Hematopoietic Stem Cell Transplantation – A Retrospective Study From A Tertiary Referral Center in India

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Background: Pre-transplant measurable residual disease (MRD) status and post-transplant graft versus Leukemia (GVL) effect are the most important determinants of a successful outcome following hematopoietic stem cell transplantation (HSCT) in children with acute

leukemia. In this study, we analyzed the impact of graft versus host disease (GVHD) on relapse free survival in our cohort.

Methods: We performed a retrospective analysis of the children with acute leukemia who underwent HSCT in our blood and marrow transplantation unit between November 2002 and November 2018. The data analysed included the pre transplant MRD status, the conditioning regimen, graft source, the incidence of GVHD and relapse free survival.

Results: A total of 135 children between 6 months to 18 years of age with leukemia underwent HSCT. HSCT was performed in first complete remission (CR1) in 65 children (48%) and following a relapse in 70 children (52%). The indications in CR1 included Acute Lymphoblastic Leukemia ($n = 35$)[54%], Acute Myeloid Leukemia ($n = 18$)[28%], Mixed Phenotypic Acute Leukemia ($n = 9$)[14%] and Chronic Myeloid Leukemia in blast crisis ($n = 3$) [4%]. HSCT was performed after a relapse in 70 children with 45 for relapsed ALL (64%) and 25 for relapsed AML(36%). We performed measurable residual disease in all children prior to HSCT from 2009 by flow cytometry and data is available for 96/135. Only 3 of the 96 children had molecular disease at the time of HSCT as it was our policy to transplant children at MRD negative status.

A myeloablative conditioning regimen was used in children with ALL with 12Gy total body radiotherapy and a busulfan or melphalan based regimen in children with AML. Peripheral blood stem cells was the predominant source of stem cells in 112 children (83%), followed by cord in 15(11%) and bone marrow in 8(6%) children. Engraftment occurred in 132 children. We documented GVHD in 106 (79%) children. In children with no evidence of GVHD, pre-emptive strategies were employed to achieve a GVL effect including early withdrawal of immunosuppression, pre-emptive donor lymphocyte infusion (DLI) [$n = 12$], with additional lenalidomide ($n = 7$) to induce natural killer cell activity. 13/19 children developed GVHD and this translated into relapse free survival in 11 (58%) children. The mortality in the entire cohort was 61 (45%) with relapse of the disease being the commonest cause in 26 (41%), followed by sepsis in 17(29%), severe GVHD in 14(23%) and regimen related toxicity in 4 (7%) children. After a median follow up of 32 months the relapse free survival was 55%. The children who underwent HSCT for acute leukemia in CR1 had better survival at 63% compared to HSCT after relapse 47%. GVHD of any grade was significantly associated with a lower risk of relapse ($p = 0.008$).

Conclusions: Our study reinforces the importance of GVHD or strategies aimed at inducing GVL effect in reducing the incidence of relapse in children undergoing HSCT for acute leukemia. Even in resource constrained settings, GVHD can be induced using early withdrawal of immunosuppression, pre-emptive whole blood donor lymphocyte infusions in graded aliquots with the addition of oral lenalidomide to help prevent a relapse.

Disclosure: Nothing to declare.

P082.

EBV Colitis Post Hematopoietic Stem Cell Transplantation in Patient with Aplastic Anemia

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Background: EBV-positive mucocutaneous ulcer (EBV-MCU) is a newly recognized clinical-pathological entity characterized by ulcerated lesions affecting cutaneous and/or mucosal sites tipically in immunodepressed patients. Only two cases of EBV-MCU have been described following Hematopoietic stem cell transplantation (HSCT), and they occurred after 4 months and 60 days from transplant, respectively. Here we describe a case of EBV-MCU that developed acutely 22 days after HSCT with massive intestinal bleeding.

Methods: A 46-year-old male affected by Severe Aplastic Anemia (SAA) was treated with immunosoppressive combination therapy with horse Antithymocyte Globulin (hATG) and Cyclosporine-A (CyA).

Lacking response to first line treatment, he subsequently underwent Matched Unrelated Donor (MUD) allogenic HSCT after Myeloablative Conditioning (MAC) with Thiotepa, Busulfan, Fludarabine. The donor and the patient were IgG positive and IgM negative for EBV viral capsid antigen (VCA) before transplantation. Hematologic recovery was reached rapidly after engrafment. During aplasia the patient experienced Hepatic Veno-occlusive Disease, that required treatment with Defibrotide from day 12 to day 22 post HSCT. Treatment was stopped due to almost complete resolution of VOD and developing of melena and rectal bleeding.

Results: CT angiography of the abdomen showed multiple jejunal bleeding sites, compatible with severe erosion of the intestinal mucosa. EGDS, Colonscopy and Capsule Endoscopy confirmed multiple ulcers of the duodenum and jejunum, with spotting bleeding.

The patient was massively supported with transfusion and he underwent superselective embolization of visceral vessels without any improvement. Even if in absence of

abdominal pain and diarrohea, patient was empirically treated with steroids for supposed acute intestinal GvHD and then Ganciclovir, with no response. PCR for EBV-DNA and CMV-DNA were negative until the end of the course, when EBV-DNA became highly positive.

After many attempts to stop the bleeding with embolization and medical therapy, because of worsening clinical conditions the patient was candidate to laparotomy with double ileostomy to then remove the bleeding intestinal tract. Before admission to Surgery Room, the patient became septic with high fever, worsening tachycardia and hypotension, he had a cardiac arrest and he finally died.

The istologic evaluation performed during endoscopic exam showed regenerative epitelial hyperplasia resembling ulcerative's margines, with apoptosis signs and an inflammatory mononuclear infiltrate. Immunochemistry was positive for EBV-ISH, while CMV, HSV1/2, fungal ad parasitic infections were excluded. These characteristics were suitable with an EBV positive apoptotic duodenitis, that could be considered a form of EBV-MCU, on GvHD.

Conclusions: Massive intestinal bleeding is a rare major complication after HSCT. The differential diagnosis is between massive mucositis, aGvHD and CMV infections, but also EBV-related lesions should be considered, expecially in patient previously treated with intense immunosuppressive therapies. Endoscopic evaluation with byoptic samples should be performed in order to recognize pathological entity. Even if EBV-MCU is known to have an indolent course here we described an aggressive course, maybe related to intense immunosuppression and GvHD, and previous treatment with defibrotide. Indeed inflammatory background is a risk factor for developing of EBV-MCU. This kind of patient should be carefully evaluated in case of GI symptoms.

Disclosure: Nothing to declare.

P083.

Morbidity And Mortality of T- Cell Lymphomas Undergoing Autologous Stem Cell Transplantation (ASCT)

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Background: Non-Hodgkin´s lymphoma is a heterogeneous group of lymphoproliferative disorders. They are originated in B lymphocytes, T lymphocytes, or natural killer cells. T-cell lymphoma is infrequent, and It has the worst prognosis among lymphomas, they had unique characteristics and require individualized diagnostic and therapeutic strategies. Hematopoietic stem cell transplantation (HSCT) after the first remission improve prognosis, OS 59% vs 48% and DFS 46% vs 33% respectively HSCT as consolidation vs only chemotherapy.

Methods: A retrospective cross-sectional study, we analyzed patients diagnosed with T-cell lymphomas and undergoing Hematopoietic stem cell transplantation between 1997- April 2020, at Instituto Nacional de Cancerología, México. Demographic and clinical information was collected from patients' medical records. Data were analyzed in SPSS v23.

Results: Thirty-three patients were enrolled with a median age of 37 years (18-65), 68% were male, 39% had at least one comorbidity (hypertension was the most frequent), 70% had low socioeconomic status.

Extranodal T/NK cell lymphoma, nasal type was more frequent followed by Anaplastic large cell lymphoma ALK negative (see table 1). Seventy-six had advance disease (III-IV), 30% has extra nodal involvement, 40% of them were gastrointestinal. Forty-nine percent had low-IPI and 42% low-intermediate IPI.

Forty-five percent received two lines of treatment before transplant, 30% were in first response. Sixty-seven percent received radiation therapy to the affected site during treatment. At the time of transplant 94% of patients had ECOG 0-1. The complete response were at 91% of patients, 9% in partial response. All patients receive autologous HSCT, 55% had PEAM as conditioning regiment (cisplatin, etoposide, doxorubicin and melphalan) and 45% BEAM (carmustine, etoposide, doxorubicin and melphalan). During treatment 94% had neutropenic fever and 36% mucositis GI-II. Twenty-seven percent had relapsed, 36% patients died. Overall survival at 5-year was 60% and DFS 66%, 23-year follow- up.

We analyze the relations between gender, age, socioeconomic status, specific T-cell lymphoma, conditioning regimen, comorbidities, extra nodal involvement, radiotherapy treatment, response before transplantation, and acute and chronic complications with relapse and mortality. Low socioeconomic status, BEAM conditioning regimen, and complete response before HSCT were associated with relapse and mortality ($p < 0.05$). The subtype T-cell lymphoma with worst prognosis were T/NK nasal type and anaplasic type (table 1). The multivariate analysis identified Low socioeconomic status, BEAM conditioning regimen, complete response before ASCT for relapse and mortality (HR, 7.0; 95% CI, 1.17-41.75), ($p = 0.033$).

Table 1. Outcome by subtype of T-cell lymphoma

Subtype of T- cell lymphoma	TOTAL $n = 33$ n (%)	RELAPSE $n = 9$ n (%)	DEATH $n = 12$ n (%)
Anaplastic large cell lymphoma ALK(+)	4 (12.1)	1 (11.1)	2 (16.7)
Angioinmunoblastic T-cell lymphoma	3 (9.1)	1 (11.1)	1 (8.3)
Anaplastic large cell lymphoma ALK(-)	7 (21.2)	3 (33.3)	3 (25)
Cutaneous T-cell lymphoma	2 (6.1)	1 (11.1)	1 (8.3)
Extranodal T/NK cell lymphoma, nasal type	15 (45.5)	3 (33.3)	5 (41.7)
Peripheral T-cell lymphomas, NOS	2 (6.1)	0 (0)	0 (0)

Abbreviations: ALK anaplastic lymphoma kinase, NOS not otherwise specified.

Conclusions: in our population, a higher OS and DFS are reported compared to other series. It may be because the transplant was performed at earlier stage; fewer lines of treatments, low ECOG and IPI and complete response before ASCT.

Disclosure: Nada que decir.

P084.

Brentuximab Vedotin Strategies for Relapsed Or Refractory Hodgkin's Lymphoma And Hematopoietic Stem Cell Transplantation

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Background: Patients with Hodgkin's Lymphoma relapse to first line of treatment benefit from an autologous bone marrow transplant (BMT), in refractory disease, clinical option is an allogeneic BMT.

As for high-risk patients, when adding brentuximab as post-transplant maintenance, the progression-free survival (PFS) in the AETHERA study was 59% (5 years) vs placebo. Brentuximab has also been used as a bridge for allogeneic transplantation, with which the PFS (2 years) is 48%. In both cases, combination with brentuximab vedotin can improve OS and DFS.

Our objective is to identify response, OS and DFS for relapsed or refractory Hodgkin's Lymphoma in combination with brentuximab vedotin and bone marrow transplant.

Methods: Retrospective cross-sectional study. We included relapsed or refractory disease patients with Hodgkin's Lymphoma who underwent Hematopoietic stem cell transplantation from January 2015 to December 2019, at Instituto Nacional de Cancerologia, México. Information was collected from electronic medical records of patients, who were treated with brentuximab vedotin as salvage therapy before BMT (B-BMT), maintenance after BMT (A-BMT) or before and after BMT (BA-BMT). Data analysis was performed using the SPSS v23.

Results: We included 15 patients with Hodgkin's Lymphoma. Male predominance was 2:1, median age 30 years (21 to 62). Fifty-three were Nodular sclerosis, 40% Mixed-cellularity and 7% Lymphocyte-rich. All classic Hodgkin's Lymphoma. Sixty percent of cases at diagnosis presented as advanced stages (stage II 40%, stage III 33.3% and stage IV 26.7%). Two patient (13%) had bone marrow infiltration at diagnosis, 14 patients (93%) nodal involvement, only one patient (7%) extranodal involvement.

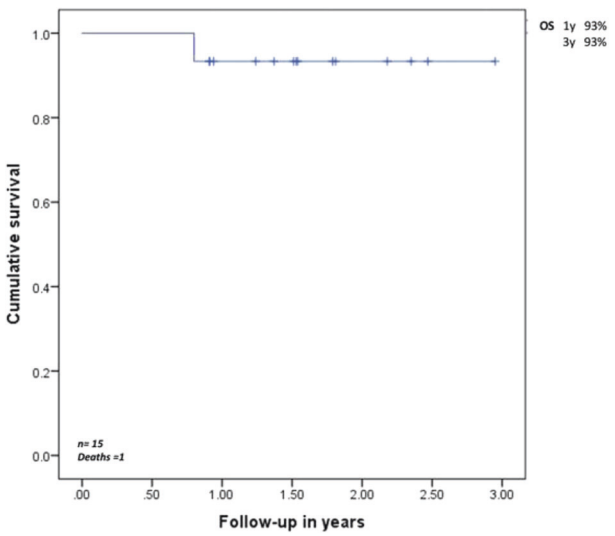
The most frequent chemotherapy regimen in first line were ABVD (86.6%), in second line of treatment were ICE and IGEV with 33% each. Forty percent received two lines of treatment and 33% three lines of treatment previous BMT.

Twelve patients were autologous BMT, 92% had relapse disease, all of them received PEAM as conditioning regimen, 58% received brentuximab as A-BMT, 25% as B-BMT and 17% like BA-BMT.

Three patients receive allogeneic BMT, all of them had refractory disease and received B-BMT combination, conditioning regimen were FLUBU 67% and BUCY 33%.

We found a complete response in 86.6%, no patient relapse after BMT, two patients had progression at 4.5 and 5.4 months, only one patient with progression died four months after relapse.

Follow-up time was 36 months after BMT. 3-years OS and DFS was 93% and 82% respectively (Figure 1).



Conclusions: in our results all the patients benefit from the combination of BMT and brentuximab vedotin. The type of combination of BMT and brentuximab (B-BMT, A-BMT, BA-BMT) and the number of lines of treatment previous BMT had no impact on OS or DFS. Even though our study has a small number of patients, we note that our DFS is more than 80% at 3 years in compared to other studies that demonstrated DFS 60%, maybe response (CR vs PR) previous BMT could impact in this outcome. We need more patients with brentuximab vedotin treatment and BMT to define the best combination in which the patient could obtain the greatest benefit.

Disclosure: Nothing to declare.

P085.

Staff Experiences And Learning From Working On A Hematological Stem Cell Transplant Ward During COVID-19

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Background: Evidence suggests that the COVID-19 pandemic has placed staff under significant additional pressure. It is important that we make space for staff to reflect on and learn from their experiences to try to tailor the support for both patients and staff. This knowledge will facilitate greater awareness of staff's needs within senior management. This will help guide service development to ensure staff can access emotional support and signposting to information and resources.

Methods: Two reflective practice sessions were held for nurses working on a hematological stem cell transplant ward to elicit their experiences and views during COVID-19. The aim was also to understand the impact on their emotional wellbeing in order to support continuing development of the psychology service. Thirty five nurses working on the stem cell transplant ward attended the reflective practice sessions. Qualitative data from focus groups were collected and analysed using thematic analysis.

Results: Staff reflected a number of different themes during COVID-19 that represented both positive and more challenging experiences. Overarching themes that staff reflected on included living with uncertainty and experiencing fear and a lack of safety, which reflected concerns about their own families and their own health and wellbeing. This was experienced alongside a sense of constantly changing 'goalposts' across the system at different levels. Importantly, staff also highlighted a sense of personal growth in their own identity and recognising the importance of team relationships.

Conclusions: These findings demonstrated the value of making space for staff to share their experiences during COVID-19 and understand their support needs. Themes that were reflected in the data represented a balance between factors relating to an external locus of control, as well as individual factors and a strong sense of personal growth in adversity. This knowledge will help establish staff wellbeing higher on the organisation's agenda. It demonstrates that this way of addressing staff wellbeing in a major incident or global pandemic needs to 'reach in' to staff and need not be expensive or complex. We might anticipate that regular sessions like this would embed staff wellbeing as a priority in the culture of the unit/organisation. Limitations include the need to consider all other members of the broader multidisciplinary team as well as only capturing views at one time point rather than across the whole pandemic.

Clinical Trial Registry: N/A.

Disclosure: Nothing to declare.

P086.

Ehealth As A Tool in Hematopoietic Stem Cell Transplantation: A Narrative Review

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Background: Patients undergoing hematopoietic stem cell transplantation (HSCT) are at greater risk of intensive care unit admission, need for mechanical ventilation, or death compared to immunocompetent patients. eHealth is one of the multidisciplinary components that can have the greatest impact on quality of life, accessibility, and quality of service due to its potential to improve efficiency and productivity in health service system processes.The objective of this study is to determine the scientific evidence on eHealth strategies, the level of implementation and their role in HSCT.

Methods: The search strategy used was: (Hematopoietic Stem Cell Transplantation OR Stem Cell Transplantation,

Hematopoietic OR Transplantation, Hematopoietic Stem Cell) AND (Telemedicine OR Mobile Health OR mHealth OR Telehealth OR eHealth OR Health, Mobile). In the bibliographic search, 98 articles were obtained from PubMED and Scopus sources. By means of evaluating pairs a first selection was made by title and abstract, in the discrepancies consensus was sought by means of discussion between pairs. Of the articles chosen for full reading, those that reported results of eHealth-based interventions were included. Articles not performing a transplant and eHealth application were excluded.

Results: A total of 46 articles were selected for full reading and 26 were finally included in this review. We identified that the majority of the studies were conducted in the USA ($n = 10$), the publication concentrates mostly on the year 2020, and a first study in 2007. The purpose of the interventions included the follow-up and management of risk factors related to cardiovascular disease, accompaniment for symptom detection and improvement of the quality of life of patients, remote monitoring of patients with telemetry, and training of patients (eLearning). The objectives of these interventions included: medication adherence, physical activity monitoring, infection prevention, patient participation in content creation, symptom tracking and management, follow-up with self-reporting of data, mainly in patients with complications associated with post-HSCT treatment, and pain management in adults. The population involved in the interventions included: patients with allogeneic and autologous transplants, adolescents, caregivers, parents of transplanted children, among others. It should be noted that the projects where patient follow-up was sought managed to improve the patient's quality of life. Remote monitoring with adequate teaching is useful for the rapid detection of complications and in adolescents it can take advantage due to their affinity with mobiles, it also had an impact for patients who lived far from the transplant centers by reducing complications and cost. The most frequent type of intervention was the use of mobile applications for data collection, monitoring and monitoring of symptoms. The interventions with the greatest impact on patients were applications due to their accessibility, feasibility, benefits, and acceptance by patients.

Conclusions: The scientific evidence on eHealth for HSCT shows products such as applications, mobile health and telemedicine, with the greatest publication of works in the last year. A multidisciplinary commitment is necessary in planning for development, costs, times and execution of projects with information technology, as well as the need for a focus on User Experience, important and necesary after the experience of COVID-19.

Disclosure: None declare.

Haemoglobinopathy

P087.

The Value of Routine Pre-TRANSPLANT Radiological Screening in Pediatric Sickle Cell Disease Patients: A Single Center Experience

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Background: Pre-transplant radiological screening such as abdominal ultrasound (US) and computed tomography (CT) scan of chest/sinuses is routinely ordered to search for possible infections such as invasive fungal infections (IFI). The value of this approach in sickle cell disease (SCD) patients is not clear.

Methods: We reviewed results of pre-transplant abdominal US and CT chest/sinuses scans in all pediatric patients with SCD who underwent HSCT at our center.

Results: A total of 61 children with SCD underwent allogeneic HSCT. The table summarizes the results of radiological findings. Abdominal US was normal or showed unremarkable findings in 52 (85%) patients. Gallstones was detected in 9 (15%) patients. One patient developed cholecystitis during HSCT. Thus, we subsequently performed elective cholecystectomy in the presence of gallstones prior to proceeding to transplant. CT scan of the sinuses was normal in 49 (80%) of patients and 11 (18%) patients had features of sinusitis in the absence of symptoms and was managed with antibiotics. CT chest was normal or showed non-specific findings in 56 (92%) patients. Two patients had lobar consolidation that was not identified in routine chest x-ray and was managed with antibiotics. Enlarged heart was observed in 3 (5%) patients which was also detected by echocardiogram. None of our patients had evidence of IFI.

Imaging/findings	Patients (%)
US abdomen	
Normal	25 (41)
Gallstones	9 (15)
Mild hepatomegaly/splenomegaly	17 (28)
Grade I-II hydronephrosis	7 (11)
Enlarged or ectopic kidney	3 (5)
CT sinuses	
Normal	49 (80)

Table (continued)

Imaging/findings	Patients (%)
Sinusitis	11 (18)
Adenoid hypertrophy	1 (2)
CT chest	
Normal	44 (72)
Mild atelectasis	9 (15)
Lobar consolidation	2 (3)
Enlarged heart/prominent pulmonary vessels	3 (5)
Bilateral air trapping/small airway disease	3 (5)

Conclusions: Routine early Pre-Transplant abdominal ultrasound screening in the outpatient setting is recommended in patients with sickle cell anemia to identify patients for elective cholecystectomy. This will serve better planning for patients and HSCT team. CT chest is rarely positive for a significant finding in our study. However, it is very difficult to replace it with regular chest X-ray without larger studies.

Disclosure: Nothing to declare.

P088.

How to Facilitate Decision-Making for Hematopoietic Stem Cell Transplantation in Patients with Hemoglobinopathies - The Perspectives of Health Care Professionals

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Background: Decision-making in hematopoietic stem cell transplantation (HSCT) for hemoglobinopathy patients is a complex process and despite (inter)national criteria for HSCT, it remains difficult for health care professionals (HCPs) to decide whether and when HSCT should be offered. Gaining insight into HCPs considerations is required to understand and to optimise the decision-making process for HSCT.

Methods: A qualitative study using semi-structured interviews with HCPs. Data were thematically analyzed.

Results: Eighteen HCPs involved in the HSCT decision-making process of hemoglobinopathy patients participated, including ten (pediatric) hematologists from referring centers, five transplantation specialists from HSCT centers, and three (pediatric) nurse specialists from referring centers. Three out of five transplantation specialists were hematologists specialized in the care for pediatric or adult patients with hemoglobinopathies. Two out of ten referring hematologists were also HSCT specialists. Two main themes emerged from the HCP's considerations: (1) *Experiencing the influence of a frame of reference* and (2) *Feeling responsible for a guided decision-makings* (table 1). The frame of reference, meaning the knowledge and experiences of HCPs regarding HSCT, appeared to be an overarching theme and influenced the way of guiding patients throughout the decision-making process. Subsequently, three subthemes evolved from this guided decision-making process: (a) weighing up disease severity against possible complications, (b) making the effort to inform and (c) support the best fitting decision for the individual patient.

Table 1 Illustrative quotations.

Theme	Situation	Illustrative quotations*
Experiencing the influence of a frame of reference	A referring hematologist talking about their need for knowledge sharing by HSCT centers regarding results in hemoglobinopathy patients and remembering previous patients.	"I have already seen several patients in the past with quite serious HSCT complications such as needing liver transplantation and more of such troubles. I don't know if I want to expose my patients to these risks, I struggle with that."
Feeling responsible for a guided decision-making.	A HSCT physician speaking about the HSCT decision-making process.	"I like it that parents have the feeling of shared. I would prefer them to say we decide because we are very well informed and we know what we are deciding about. I think that's the best answer and it it supports me thinking we did a very good job."

*The quotations are somewhat edited for legibility and anonymity

Conclusions: Our study shows the influence of the HCPs frame of reference on how they guide their hemoglobinopathy patients in the HSCT decision-making process. This demands reflection from HCPs on this phenomenon by exchange of knowledge and experiences in a two-way direction. First, the HSCT team have a responsibility of keeping the frame of reference of their referring colleagues up to date. Second, referring HCPs should share their feelings regarding HSCT and discuss their patients with HSCT centers. The HSCT decision-making process will benefit from such an open collaboration between centers. HCPs can refine the decision-making process by guiding patients in eliciting their preferences and including these in the decision.

Acknowledgements: We thank all the professionals who contributed to this study.

This study was performed in collaboration with The SCORE consortium.

Disclosure: Nothing to declare.

P089.

Endocrine Sequelae in Pediatric Hematopoietic Stem Cell Transplant Recipients with Sickle Cell Disease: A Retrospective Cohort Analysis

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Background: Myeloablative conditioning for hematopoietic stem cell transplantation (HSCT) for patients with sickle cell disease (SCD) is standard for eligible pediatric patients in many institutions. Concerns regarding potential infertility make some patients with SCD reluctant to undergo HSCT. A novel, non-myeloablative regimen using alemtuzumab, 300cGY total body irradiation, and sirolimus for graft-versus-host disease (GVHD) prophylaxis has been successfully implemented at our institutions for pediatric patients with SCD undergoing a matched sibling donor (MSD) HSCT in an effort to prevent late HSCT complications. This retrospective cohort analysis was performed to assess the prevalence of endocrine complications in pediatric SCD patients who underwent HSCT with this approach.

Methods: The medical records of SCD patients who underwent MSD HSCT with this regimen between June 2013 and June 2020 were retrospectively reviewed. Subjects were included if they were 18 years or younger at the time of HSCT and were followed at either Alberta Children's Hospital (Calgary, Alberta) or Stollery Children's Hospital (Edmonton, Alberta) post-HSCT. Individuals with known endocrine system dysfunction prior to HSCT were included. Defined time points for data collection included baseline, 1-year, 2-year, 3-year and 5-year post-HSCT evaluations. Clinical, laboratory and radiographic variables relating to anthropometrics, pubertal status, thyroid status, gonadal function, glucose status, and bone health were collected. Descriptive data analysis was utilized, with prevalence reported as a percentage.

Results: 17 subjects were enrolled. Age at transplantation ranged from 3.0 years to 18.0 years with 12 females (70.6%) and 5 males (29.4%). Event free survival (EFS) of this cohort was 100%, and no subjects developed acute or chronic GVHD. All were eligible for sirolimus weaning. All subjects (100%) had 1-year and 2-year follow-up, 13 subjects (76.5%) had 3-year follow-up, and 7 subjects (41.2%) had 5-year follow-up. Endocrine issues identified at baseline included short stature in 1 subject (5.9%) and elevated follicle stimulating hormone (FSH) levels in 1 (male) of 5 subjects (20%). FSH elevation post-HSCT occurred in 7/17 subjects (41.2%); 5 females (66.7%) and 2 males (33.3%). All females with elevated FSH had subsequent normalization of their values with longer follow-up. The elevated FSH levels of the 2 males did not normalize, though luteinizing hormone and testosterone values were normal for age. Post-HSCT secondary amenorrhea or oligomenorrhea was described in 4 females, with improvement or resolution documented in all at later follow-up. One female subject with normal gonadotrophin levels post-HSCT had a successful pregnancy and live birth. Vitamin D deficiency was present in 4/5 subjects (80%) pre-HSCT and 5/5 post-HSCT (100%). No subjects had autoimmune thyroid disease post-HSCT, despite alemtuzumab exposure.

Conclusions: A notable endocrine issue post-HSCT described in this cohort is FSH elevation. The elevation was transient in females and we identified one successful pregnancy, suggesting that non-myeloablative conditioning may convey improved fertility outcomes compared to myeloablative conditioning without compromising EFS or graft failure and excellent quality of life. Not all patients had baseline endocrine evaluations or consistent post-HSCT endocrine testing. We recommend standardizing pre- and post-HSCT endocrinology assessments for this population.

Disclosure: Nothing to declare.

P090.

Decision-Making for Hematopoietic Stem Cell Transplantation in Pediatric, Adolescent And Young Adult Patients with A Hemoglobinopathy – Shared Or Not?

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Background: Decision-making in hematopoietic stem cell transplantation (HSCT) for hemoglobinopathy patients is a complex process and shared decision-making (SDM) could be a fitting approach in case of such preference-sensitive decisions. In this study we investigated what level of SDM is used in conversations with hemoglobinopathy patients and/or their caregivers considering HSCT as a curative treatment option.

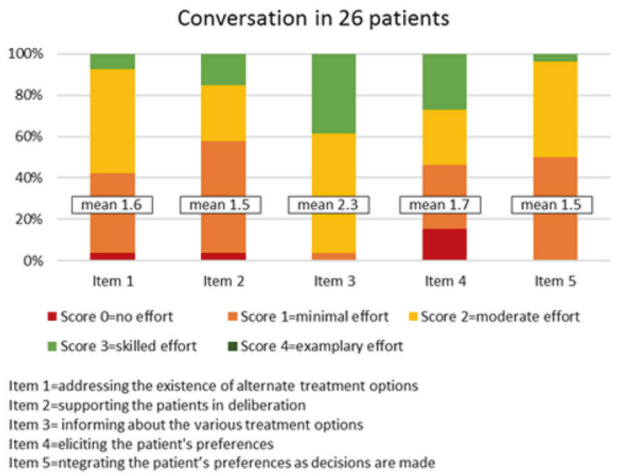
Methods: Longitudinal, descriptive study using the OPTION5-scale to determine the level of SDM in conversations with 26 hemoglobinopathy patients and/or their caregivers. Each recorded conversation was graded on five items with a 5-point-Likert scale from 0-4 (Figure. 1).

Results: in total, 40 recorded conversations with 26 patients were included (Table 1). The total mean OPTION5-score was 44% (range 20-60%), which is a moderate SDM approach. There was no difference between the mean scores of the conversations with thalassemia patients (44%) and

SCD patients, range (43%). Conversations needing an interpreter scored worse (35.5%, range 20-50) than regular conversations (38.7%, range 10-60). The best scoring OPTION5-item was item-3: 'informing about the various treatment options' (mean score 2.3 on scale 0-4), Figure 1. For OPTION5-item 4: 'eliciting patients' preferences' a more skilled effort was measured for SCD patients compared to thalassemia patients. Similar, for this OPTION5-item 4 a more skilled effort was measured for regular conversations compared to translated conversations.

Table 1 Characteristics

Characteristics	Total number of included patients ($n = 26$)	Number of sickle cell disease patients ($N = 18$)	Number of thalassemia patients ($N = 8$)
Sex patient			
Female	16	12	4
Male	10	6	4
Age patient			
<12 y	14	8	6
12-16 y	6	5	1
>16 y	6	5	1
Transplanted			
Yes	18	12	6
No	8	6	2
Conversations ($N = 40$)			
With hematologist	6	6	0
With HSCT specialist	34	21	13
Including interpreter	10	2	8



Conclusions: The mean OPTION5 score of 'moderate' was achieved mainly by giving information on available options, which is primarily a one-way communication. The SDM-process can be improved by actively inviting patients to deliberate about options and including their elicited preferences in decision-making.

Acknowledgements: This study was performed in collaboration with The SCORE consortium.

Disclosure: Nothing to declare.

Immunodeficiency Diseases and Macrophages

P091.

Clinical Manifestation And Mechanisms of Graft Failure in Primary Immunodeficiency Patients After Hematopoietic Stem Cell Transplantation

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Background: Graft failure (GF) is a cause of morbidity and mortality after allogeneic hematopoietic stem cell transplantation (HSCT). Patients with some primary immunodeficiencies (PID) have relatively high risks of GF. Secondary hemophagocytic lymphohistiocytosis (HLH) (or hemophagocytic syndrome (HS)) is a rare complication of HSCT.

Methods: From 2012 to October 2020, 310 patients with various PID (Table 1) underwent 1stallogeneic HSCT in our center. TCRab+/CD19+ graft depletion was applied in 275 patients.Matched unrelated donors were used in 150 patients, mismatched related in 128, matched related in 32. Conditioning regimen included fludarabine 150mg/m2in combination with treosulfan 36-42 g/m2alone or with melphalan or thiotepa. Patients with Nijmegen breakage syndrome additionally to fludarabine received busulfan 4 mg/kg or treosulfan 21-30g/m2with cyclophosphamide 20-40mg/kg. for serotherapy in 251 patients was used thymoglobulin 5-10 mg/kg, in 21 ATGAM 50-100 mg/kg, in 14 campath 1 mg/kg. In 24 patients no serotherapy was used. 200 patients received various regimens of post-transplant immunosuppressive therapy (IST),and 110 no IST. To define HS,next characteristics were used: fever, splenomegaly, hyperferritinemia (>500 ng/ml), hypertriglyceridemia (>2 mmol/l), hypofibrinogenemia (<1.5 g/l), hepatitis (elevated AST, ALT, LDH), cytopenia (>2 lines) and hemophagocytosis in the bone marrow. Non-engraftment was determined as primary GF and graft rejection following engraftment as secondary GF.

Results: Median follow up in survivors was 51 months (range 2 - 101). 49 out of 310 (15.8%) patients developed

GF: 11 primary and 38 secondary. All patients were divided into 2 groups: "early GF" developed within 100 days after HSCT ($n = 32$) and "late GF" developed after day 100 post-HSCT ($n = 17$). The median time to GF in early GF group was 32 days(16 – 98). Before GF, 27 patients had predominantly recipient chimerism of CD3+ cells. Interestingly, 16 patients with early GF at GF time fulfilled >5 out of 7 criteria of HS. The median time to late GF was 278 days(124-1238). Before GF, 22 patients had predominantly recipient chimerism of CD15+ cells. None of 17 patients with late GF had signs of HS except progressing cytopenia. 44/49 patients received second and 7/44 third HSCT. Two patients died of secondary malignancies after first GF,10 of transplant-related complications after second HSCT, and 2 after third HSCT. Three patients are currently awaiting second HSCT.

Table 1. GF incidence in PID groups.

Diagnosis	Patients number	Graft failure			HS
		Early		Late	
		Primary GF	Secondary GF		
Wiskott-Aldrich syndrome	62	0	3	5	0
Severe combined immunodeficiency	51	0	3	3	0
Chronic granulomatous disease	35	0	1	3	0
Familial HLH	26	1	3	0	4
Severe congenital neutropenia	21	5	2	0	3
X-linked lymphoproliferative disease type 1 and 2	18	1	2	0	3
Other PID	97	4	7	6	6

Conclusions: GF remains a significant problem of HSCT among PID patients. Chimerism analysis (increasing recipient T cells vs recipient myeloid cells) suggests that early and late GF may have different mechanisms. Early GF is often associated with HS.

Disclosure: Nothing to disclose.

P092.

Outcomes of Haematopoietic Stem Cell Transplantation in Children with Zeta Chain Associated Protein Kinase 70Kda Deficiency

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Background: Zeta chain Associated Protein Kinase 70kDa (Zap70) is an Syk family tyrosine kinase present in T cell cytoplasm. It associates with the T cell receptor zeta chain upon antigenic stimulation and phosphorylates downstream signaling proteins, including linker for activation of T cells (LAT) and Src homology 2 domain containing leucocyte phosphoprotein 76 dKA (SLP76). Deficiency results in impaired T cell differentiation, proliferation and cytokine production. ZAP70 deficiency produces a combined immunodeficiency syndrome that frequently presents with respiratory infections, dermatitis and diarrhea. Haematopoietic stem cell transplant (HCT) is the only curative treatment.

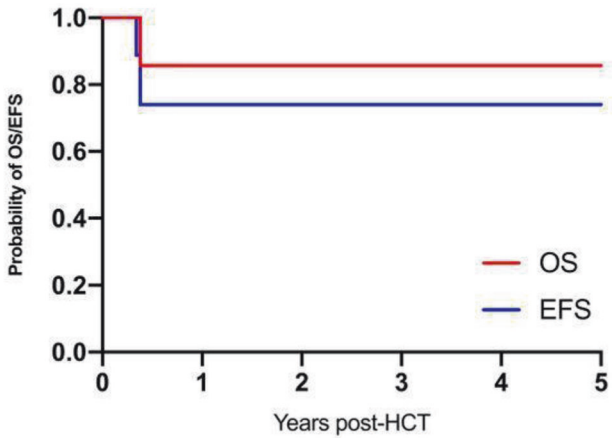
Methods: A retrospective case note review was conducted of all patients who were transplanted for ZAP70 kinase deficiency in our unit between January 1994 – December 2020. Outcomes included overall survival (OS) and event free survival (EFS; event was defined as death or graft failure), graft-versus-host disease (GvHD) and long-term disease outcomes.

Results: Nine patients with ZAP 70 deficiency were encountered during the study period. All patients presented with infection, and none had pre-transplant autoimmunity. Median age at diagnosis was 9.4 months (at birth – 24.1) and median age at HCT was 12.6 months (1.8 – 15.2) with a median interval of 3.1 months (1.3-4.9) between diagnosis and HCT. Donors were matched family donor (MFD, $n = 4$), matched unrelated donor (MUD, $n = 4$) and haploidentical parental donor ($n = 1$). Stem cell sources were marrow ($n = 4$) and PBSC ($n = 5$); 3 had ex vivo T cell depletion (1 campath-1M, 1 CD34 selection and 1 TCR ab/CD19 depletion). Conditioning was busulfan-cyclosphosphamide ±alemtuzumab ($n = 3$), fludarabine-melphalan+alemtuzumab ($n = 1$), fludarabine-treosulfan+alemtuzumab ($n = 4$) fludarabine-treosulfan-thioterapa-ATG-rituximab ($n = 1$, TCRab/CD19 depleted parental graft).

Median time to neutrophil engraftment was 14 days (8 – 28) and median time to platelet engraftment was 24 days (4 - 44). None had veno-occlusive disease. Two patients had grade I-II GVHD. None had grade III-IV GVHD or chronic GVHD.

Median duration of follow-up for surviving patients was 7.7 years (0.35-16.0). 5-year OS and EFS was 87% (95% CI, 36-98%) and 73% (29-93%) respectively (Figure 1). One patient died of bacterial sepsis at day +137 post-HCT. One patient required unconditioned stem cell boost for slipping chimerism. One had post-transplant autoimmune cytopenia requiring steroid, high dose immunoglobulin (Ig), rituximab, MMF and sirolimus. At last review, autoimmune cytopenia was in remission with low dose steroid and sirolimus.

For 8 transplant survivors, median CD15 chimerism was 100% (15 – 100%) and the median T cell chimerism was 100% (87 – 100%). Of 4 patients who were > 1 year post-transplant, 3 were off Ig replacement and one who had autoimmune cytopenia remained on Ig replacement.



Conclusions: in our center, transplant outcomes for ZAP70 deficiency are excellent.

Disclosure: Nothing to declare.

P093.

Allogeneic Hematopoietic Stem Cell Transplantation in A Patient with Clericuzio Syndrome (Poikiloderma with Neutropenia)

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Background: Clericuzio syndrome or poikiloderma with neutropenia is a rare inherited autosomal recessive disorder within a primary immune deficiencies group. It is characterized by poikiloderma, pachyonychia and neutropenia with recurrent sinopulmonary infections and high risk of myelodysplastic syndrome. A wide variety of phenotypes and rare occurrence lead to lack of clinical experience. An allogeneic HSCT can be a good treatment option for the patients with severe hematological manifestations of Clericuzio syndrome although a customized conditioning regimen needs to be developed. No cases of performed HSCT for the patients with Clericuzio syndrome were reported so far.

Methods: A patient, a 6-year-old boy, have had poikiloderma and a history of infectious diseases (bronchitises, otitis with sensorineural hearing impairment, pneumonias, stomatitises and others). From 2 months he developed a lymphoproliferative syndrome and from 3 months low level of neutrophils was noted and granulocyte-colony stimulating factor (G-CSF) was administered. In 2017 autoimmune thyroiditis, secondary hyperparathyroidism, calcinosis cutis and nephrocalcinosis were diagnosed. Based on genetic examination a Clericuzio syndrome was detected with a mutation in USB1 gene (c.395_406delACTGGATCCTCC.p. His132_Leu135del) in homozygous state. A myelodysplastic syndrome was reported in 2019 together with progression of pancytopenia and hepatosplenomegaly. An administration of G-CSF, romiplostim, sirolimus and methylprednisolone pulse therapy had no effect. The patient became transfusion dependent. He was admitted to BMT unit of Russian Children's hospital to undergo an allo-HSCT from HLA-identical sibling donor. The conditioning regimen consisted of threosulfan (36 mg/m^2), fludarabine (150 mg/m^2), melphalan (100 mg/m^2). For GVHD prevention rituximab, tocilizumab, abatocept on day before the transplantation, methotrexate on days +1, +3 and +6, and cyclosporine A from the day -1. The graft had the count CD34+ - 5.7x10^6 per kg and CD3 - 0.26x10^6 per kg.

Results: The full leukocyte recovery was achieved on +35 day and full platelet recovery – on +30 day. Complete donor chimerism both general and CD3+ was detected from +30 day. After the transplantation several complications occurred: threosulfan-associated toxicoderma of grade II and neutropenic enterocolitis of grade II. An acute GVHD of grade I developed in both intestinal (grade I-II) and skin (grade I) forms. Systemic inflammatory response syndrome was reported starting from day +15 to day +20 days. So far there are no evidence of chronic GVHD. We observed that manifestations of poikiloderma have decreased after the HSCT. The follow up time to date was 14 months. So far the patient haven't shown any signs of hematological deficiencies.

Conclusions: Our experience has shown the satisfactory efficacy of allo-HSCT for treatment of hematological manifestations of the Clericuzio syndrome. Also we observed signs of improving of skin conditions of the patient. with use of reduced intensity combined threosulfan-fludarabine-melphalan conditioning regimen the patient achieved complete donor chimerism early after the HSCT. The post HSCT complications were successfully controlled by standard therapy.

Clinical Trial Registry: Not applicable.

Disclosure: Nothing to declare.

Inborn Errors

P094.

Allogeneic Stem Cell Transplantation in Patients with Mucopolysaccharidosis Type I (Hurler) with Treosulfan-Based Conditioning

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Background: Children with mucopolysaccharidosis type IH (Hurler syndrome) suffer from an inborn deficiency of the lysosomal enzyme α-iduronidase leading to progressive organ damage, loss of neurocognitive skills and if untreated eventually death in the second decade of life. The transplantation of hematopoietic stem cells is an established therapy for patients with MPS IH. Busulfan is widely used in preparative regimens before HSCT, but is associated with potentially life threatening complications, e. g. sinusoidal obstruction syndrome (SOS) or pulmonary fibrosis. The toxicity profile of treosulfan in these children seems advantageous and might reduce the risk of transplantation related complications.

Methods: 19 patients with genetically confirmed MPS IH underwent allogeneic stem cell transplantation between March 2012 and June 2020. All patients received a conditioning regimen consisting of treosulfan, fludarabine, thiotepa and serotherapy with either ATG (Grafalon®) or thymoglobuline. GvHD prophylaxis was conducted with either cyclosporine A (CSA) and methotrexate or CSA and mycophenolate mofetil (MMF). Donors were 10/10 HLA matched unrelated (MUD), 9/10 HLA mismachted unrelated (MMUD) or haploidentical parents in 10, 5 and 4 patients, respectively. Graft source was bone marrow in 12 patients and CD34-selected peripheral blood stem cells with T-cell add-back in 7 patients. Mean age at HSCT was 1.7 years (0.4 – 2.4 years).

Results: Conditioning with treosulfan was generally well tolerated. Major complications of conditioning were oral mucositis, thiotepa associated dermatitis and nausea with need for parenteral nutrition. There was no case of SOS. Leukocyte engraftment occured at a mean of 14 days after HSCT (11 - 18 days) in patients transplanted from MUD or MMUD donors. After transplantation from haploidentical parents, 3 of 4 patients experienced acute graft rejection, but successfully underwent a second haploidentical transplantation from the other parent.

Acute GvHD grade II-IV occurred in 7 patients (3 MUD, 4 MMUD), with 2 patients suffering vom acute GvHD grade III-IV (10.5%). All cases of acute GvHD ≥ grade II were steroid-resistant and required second line treatments. GvHD symptoms eventually resolved in all affected patients and at last follow-up there was no case of chronic GvHD.

At a mean follow-up of 31 months (4 – 100 months) all patients are alive. At last-follow up 15 patients (79%) showed a donor chimerism > 90% and 2 patients have a donor chimerism ≤ 20%. The activity of α-iduronidase is below the expected lower limit of normal in 3 patients with mixed donor chimerism of 20% - 54%.

Conclusions: Treosulfan based conditioning caused low toxicity in patients with MPS IH, in particular for lung and liver, with excellent overall survival after transplantation. Donor chimerism is stable in the vast majority of patients, but the high rate of acute graft rejections in the context of haploidentical transplantion demands further improvements of pre-HSCT treatment. Longer follow-up is required for neurophysiological outcome.

Disclosure: Nothing to declare.

P095.

Outcome of Haematopoietic Cell Transplantation in Children with Lysosomal Acid Lipase Deficiency: A Study On Behalf of The Ebmt Inborn Errors Working Party

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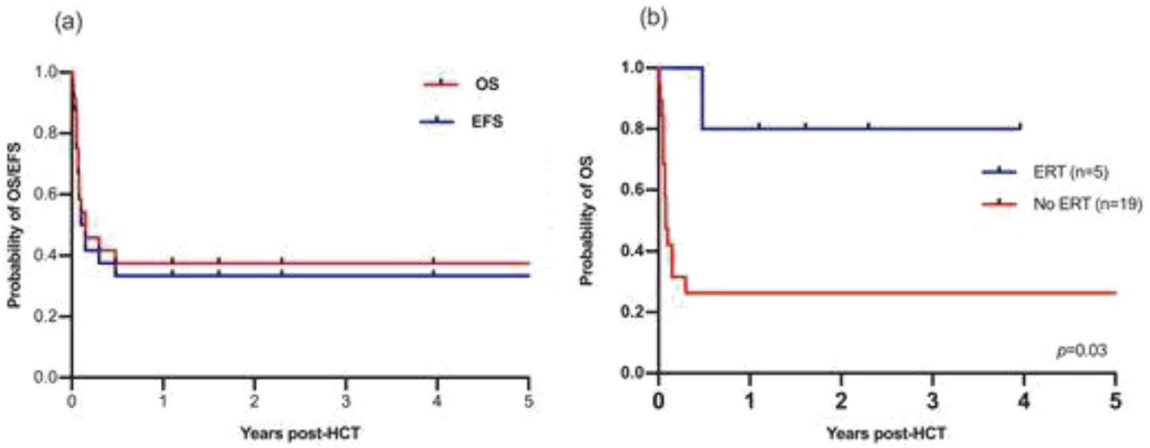
Background: Infantile onset lysosomal acid lipase deficiency (LALD), historically called Wolman disease, is a devastating lysosomal storage disease caused by a complete



absence of functional LAL. LAL is a critical enzyme for degradation of triglycerides and esterified cholesterol (CE) in the lysosomes to generate free fatty acids and cholesterol. LALD results in lysosomal lipid accumulation, leading to cellular and multi-organ dysfunctions. Death typically occurs in the first 6 months of life without therapy and the key contributors to early mortality is marked growth failure and rapidly progressive hepatic disease. Secondary haemophagocytic lymphohistiocytosis (HLH) has been reported in infants with LALD. Haematopoietic cell transplantation (HCT) has demonstrated clinical efficacy in long-term survivors of infantile onset LALD.

Methods: The Inborn Errors Working Party (IEWP) of the EBMT performed a retrospective registry study on the largest cohort of 24 children with LALD undergoing HCT between 1999 and 2019. Outcomes included overall survival (OS), event-free survival (EFS; event was defined as death and graft failure) Log-rank test was used to analyse predictors of OS. Variables included for predictor analysis were pre-transplant enzyme replacement therapy (ERT), age at transplant, donor, stem cell source and conditioning (myeloablative versus reduced toxicity conditioning).

Results: Median age at diagnosis was 1.6 months (range: 0 to 27.2) and median age at HCT was 3.5 months (1.0 to 48.0). Seven (29%) had features of HLH (none in 9 and missing data in 9) prior to transplant. Five (21%) received pre-transplant ERT. Donors were matched family donors (MFD) in 8 (33%), matched unrelated donors (MUD) in 6 (25%), mismatched unrelated donors (MMUD) in 4 (17%) and haploidentical donors in 4 (17%). Stem cell sources were marrow (8, 33%), PBSC (2, 8%), ex vivo T-depleted PBSC (4, 17%) and cord blood (CB, 9, 38%). Myeloablative conditioning was used in 11 (46%) and reduced toxicity/intensity used in 13 (54%). Two experienced grade I-II acute GvHD and none grade III-IV acute GvHD. One had chronic extensive GvHD.

Median duration of follow-up for surviving patients was 5.1 years (1.10 – 10.0). The 5-year OS and EFS for the entire cohort were 38% (95% CI, 19-56%) and 33% (16-52%) (Figure 1a). Analysis by pre-transplant ERT revealed a 5-year OS of 80% (20-97%) for children who received ERT and 21% (7-41%) for the children who did not receive ERT ($p = 0.03$) (Figure 1b). All ERT recipient were conditioned with fludarabine-treosulfan-thiotepa-ATG/Alemtuzumab. Age at transplant ($p = 0.09$), conditioning ($p = 0.27$), donor type ($p = 0.72$) and stem cell source ($p = 0.93$) had no significant impact on OS. Six (25%) had graft failure: 4 primary graft failure (2 MFD marrow, 2 unrelated CB) and 2 secondary graft failure (1 ex-vivo T-cell depleted haploidentical PBSC, 1 unknown). Three underwent second HCT but all six died. Of 16 total deaths in the entire cohort, 10 were due to transplant-related complications, 4 were due to disease-related complications, and 2 were unknown.

Conclusions: This study confirms that HCT is an effective treatment for children with LALD and pre-HCT ERT significantly improves outcome.

Clinical Trial Registry: None.

Disclosure: Robert Wynn: Research trial funding from Orchard Therapeutics (MPSIIIA).

Infectious Complications

P096.

Comparison Between Primary Prophylaxis And Pre-Emptive Therapy For Citomegalovirus After Hematopoietic Stem-Cell Transplantation

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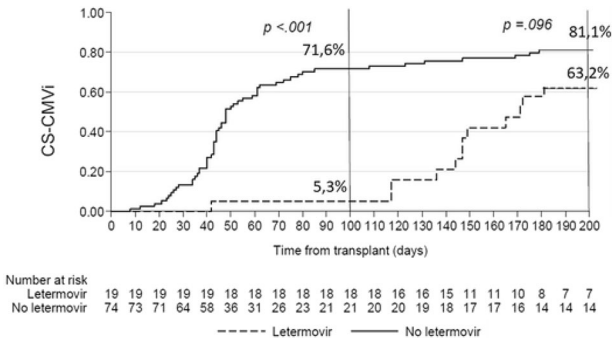
Background: Cytomegalovirus (CMV) infection is one of the most common complication after allogeneic hematopoietic stem-cell transplantation (HSCT) and remains associated with significant morbidity. Letermovir is an antiviral drug approved for prevention of CMV infection in seropositive HSCT recipients (R+), inhibiting the CMV-terminase complex and thus acting in a different way than other standard approved antiviral drugs. In Italy, Letermovir has been available since 2019.

Methods: We conducted a single-center cohort observational retrospective study, analysing 107 patients at highest risk of CMV infection according to recipient positive/donor negative (R+/D-) CMV serostatus, transplanted between January 2015 and April 2020 at our Center. Patients unable to take oral therapy at day +7 from HSCT or assuming drugs for concomitant clinical conditions bringing about major pharmacokinetic interaction were excluded. Nineteen of them received primary Letermovir prophylaxis (starting within day +28, up to day +100), whereas 74 patients did not (historical control group). In both groups, patients underwent pre-emptive therapy (PET) strategy according to twice weekly monitoring of blood CMV-DNA levels through PCR analysis. We compared cumulative incidence of clinically significant CMV infection (CS-CMVi), defined as CMV reactivation (CMV-DNAemia leading to PET) or CMV tissue invasive disease at day +100 and day +200. Patients who discontinued drug assumption before day +100 or had missing endpoint data at day +100 were imputed as having a primary endpoint event, according to the drug registration trial. Survival functions were estimated by the Kaplan-Meier method and compared using log-rank test.

Results: Letermovir prophylaxis started at a median of 11 days (range, 5-27) after HSCT. The median duration of Letermovir administration was 89 days (range, 40-113). The only early stop was due to patient death, not related to CMV or drug toxicity. None of the 19 patients in Letermovir group experienced CMV reactivation at day +100, compared to 51 in the historical group. Of note, 83% of patients receiving prophylaxes developed graft-versus-host disease (GVHD) before CS-CMVi. Overall, at day +100 CS-CMVi occurred in 5.3% and 71.6% of patients in Letermovir group and historical control group, respectively (p <.001). A trend toward lower CS-CMVi was also observed in the Letermovir group at day +200 (63,2% vs 81,1%, p=.0956). Median time to CS-CMVi was +147 and +44 days after HSCT in Letermovir group and historical control group, respectively. One patient in Letermovir group and 4 in the historical one developed CMV tissue invasive disease. No difference in mortality was observed between the two groups, even if a longer follow-up period is needed.



Conclusions: Our experience demonstrated the efficacy of Letermovir in a real-world setting for CMV prevention in the first 14 weeks after HSCT. Further studies are needed to establish the cost-effectiveness of Letermovir primary prophylaxis compared to PET approach, and the role of extension of Letermovir beyond day +100 in high-risk subgroup.

Disclosure: Nothing to declare.

P097.

Incidence of Hemorrhagic Cystitis Following Hematopoietic Stem Cell Transplantation in Pediatric Patients Based On The Underlying Disease

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Background: Although hematopoietic stem cell transplantation (HSCT) has provided treatment opportunities for many malignant and non-malignant diseases in children, the concerns about its complication remains over the years. Hemorrhagic cystitis (HC) is one of the potentially fatal complications observed after HSCT, with incidence ranges from 3.6% to 25% in pediatrics. The aim of this study is to investigate the prevalence of HC based on the underlying disease.

Methods: A total of 380 pediatric patients (230 male and 150 female) with a different type of disease who underwent HSCT (342 allogenic and 38 autologous) at Children's Medical Center between October 2016 and October 2020 enrolled in this study. Most frequent indication for HSCT were acute leukemia ($n = 109$), primary immunodeficiency disease ($n = 95$), Thalassemia major ($n = 53$), Metabolic

disorders ($n = 38$), and Fanconi anemia ($n = 23$). All patients were conditioned according to their primary disease. The patients' records were reviewed for cystitis based on clinical symptoms and laboratory data. Finally, its diagnosis has been confirmed by a pediatric urologist.

Results: Out of 380 patients, 37 cases (21 male and 16 female) with HC were diagnosed, all in allogeneic transplantation. The median age at transplant was 9 years (range: 2-17). Donors included sibling ($n = 14$, 37.8%), or other related donors ($n = 12$, 32.4%) and unrelated ($n = 11$, 29.8%). Of 37 patients with HC, the underlying disease was Fanconi anemia in 7 (30.4% in disease), acute leukemia in 21 (19.3% in disease), and other diseases in 10. Regarding primary disease, the incidence of HC was significantly higher in Fanconi anemia and lower in primary immunodeficiency disease (p-value: 0.000). Furthermore, patients with HC were received transplant from matched donor ($n = 22$, 7.9%in matching type), One-locus mismatch ($n = 6$, 17.1% in matching type) or haploidentical ($n = 9$, 27.3%in matching type). Based on HLA-matching, The HC was significantly higher in haploidentical donors (p-value: 0.002).

Conclusions: The results of our study showed the impact of the underlying disease and degree of HLA-matching in the incidence of HC after HSCT in children. Due to the fact that the current protocols used for prevention in transplant centers are not responsive to some pediatric diseases, appropriate changes should be made in the prevention protocols. Accordingly, appropriate methods of prevention based on the underlying disease and adaptation of HLA should be considered to reduce the rate of transplantation and mortality due to this complication.

Disclosure: Nothing to declare.

P098.

Epidemiology of Resistant And Refractory Cytomegalovirus Infection Following Solid Organ Or Haematopoietic Stem Cell Transplant: A Systematic Review

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Background: Cytomegalovirus (CMV) infection is known to affect solid organ transplant (SOT) and allogeneic haematopoietic stem cell transplant (HSCT) recipients, increasing the likelihood of graft complications and mortality. Current CMV management post-transplant includes prophylaxis for the highest-risk patients and pre-emptive treatment with ganciclovir and valganciclovir in patients who develop CMV infection/disease. Some patients develop resistant or refractory CMV infection, which can reduce antiviral treatment effectiveness and ultimately lead to viral syndrome or end-organ disease. Treatment algorithms for patients with resistant or refractory CMV infection include foscarnet and cidovofir. However, effectiveness of these agents is limited by toxicities and tolerability. To understand the proportion of patients who develop resistant or refractory CMV infection post-transplant, a systematic review was conducted; USA and European data were of specific interest.

Methods: A systematic review of observational (non-interventional) studies was conducted using literature searches (MEDLINE; Embase), pragmatic searches (Google, Google Scholar and conference proceedings) and snowballing (search period: 1 Jan. 2015 to 6 Aug. 2020). Case reports, case series, non-clinical and phase I–III studies were excluded. Parameters of interest were incidence estimates of refractory and resistant CMV infection following SOT or HSCT.

Results: Overall, 23 eligible studies were included in the review: 23 reported estimates of incidence of resistant CMV infection and 4 of refractory CMV infection. Among SOT recipients, incidence rates of resistant CMV infection were 0.6–13.8% (min–max), with similar estimates in Europe ($n = 4$ studies, 0.7–8.4%) and the USA ($n = 9$ studies, 0.6–13.8%). No estimates of incidence of refractory CMV infection among SOT recipients were found for Europe. Only two estimates, which were highly heterogeneous, were found in the USA: 0.66% in foscarnet-treated patients and 19.0% in patients with confirmed ganciclovir-resistant CMV infection. Among HSCT recipients, reported incidence rates of resistant CMV infection were 1.8–4.1% (min–max) in the USA ($n = 4$ studies). In Europe, only one study was found; it reported an estimate of 1.8% (in 55 pre-emptively treated patients who underwent their first allogeneic HSCT in a single center). Three studies reported on refractory CMV infection in HSCT recipients (1 in Europe; 2 in the USA); all studies were conducted prior to the marketing authorization of letermovir. In Spain, a single-center retrospective cohort study reported an incidence estimate of refractory CMV infection of 25.5% in HSCT recipients receiving pre-emptive therapy. Estimates were highly heterogeneous between the two US studies as specific subpopulations of HSCT recipients were examined: 0.74% in foscarnet-treated patients and 81.0% in patients who underwent genotypic testing for resistant CMV infection.

Conclusions: This systematic review found several recent publications reporting on the incidence of resistant CMV infection in transplant recipients. However, estimates in SOT recipients in Europe and the USA were heterogeneous; for

HSCT recipients, there was a lack of observational data from Europe. While there is limited recent data on refractory CMV infection in transplant recipients in both Europe and the USA, this review may provide insights in quantifying the potential number of patients eligible for emerging therapies for resistant or refractory CMV infection.

Disclosure: The study was funded by Shire Human Genetic Therapies, Inc, a Takeda Company.

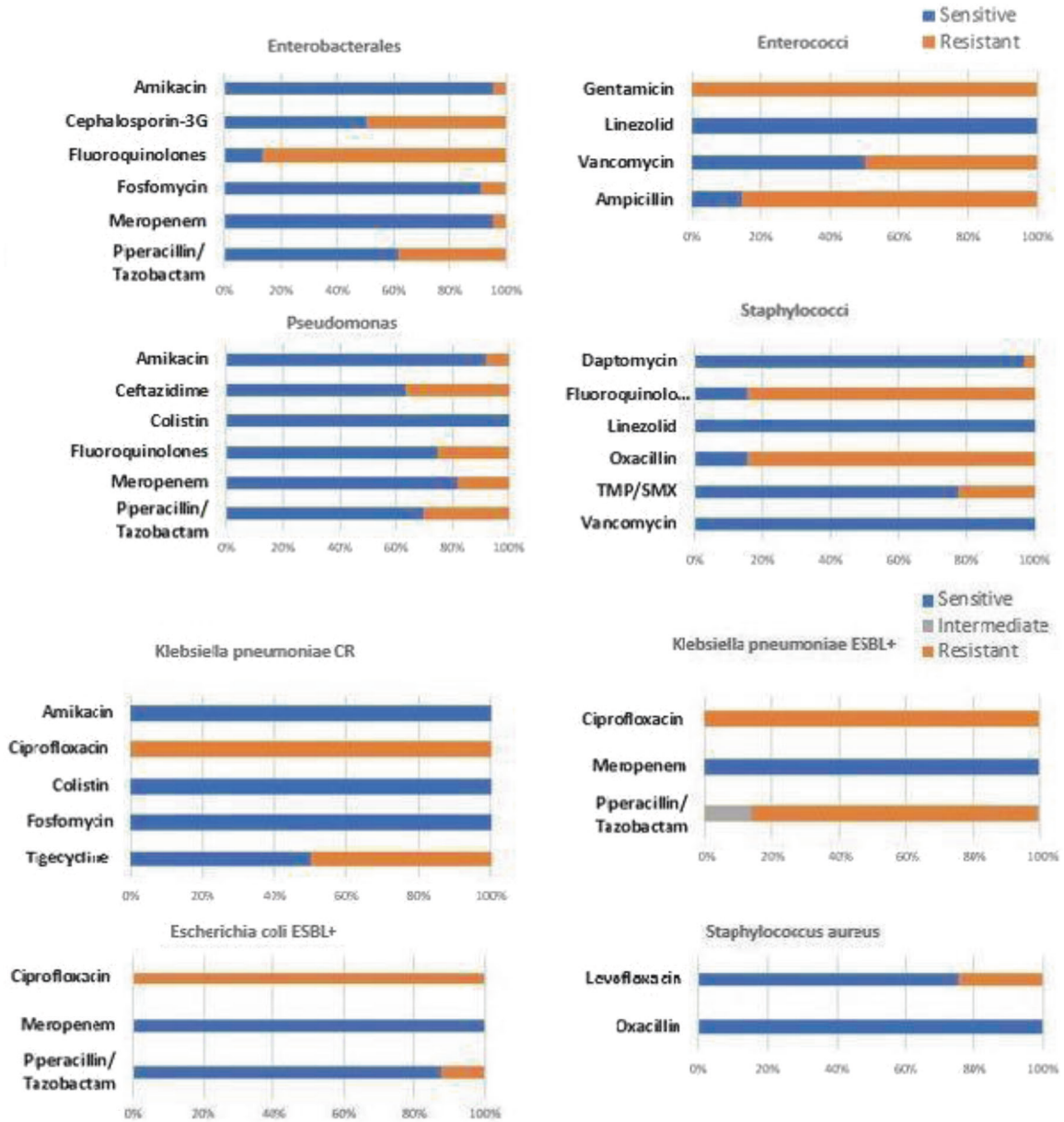
Aurore Bergamasco, Camille Goyer, Teigna Arredondo-Bisono, Yola Moride: employees: YOLARX Consultants; YOLARX Consultants received funding from Shire Human Genetic Therapies, Inc., a Takeda company, for contracted research.

Rohini Sen: employee: Millennium Pharmaceuticals Inc., a Takeda company; stock/stock options: Takeda.

Ishan Hirji: employee: Shire Human Genetic Therapies, Inc., a Takeda company; stock/stock options: Takeda.

P099.

Antibacterial Prophylaxis in Patients Undergoing Hematopoietic Stem Cell Transplantation And Development of Infections by Antibiotic-Resistant Bacteria



Filippo Maraz[1], Maria Goldaniga[1], Alessandra Bandera[1], Giorgio Bozzi[1], Andrea Lombardi[1], Riccardo Ungaro[1], Anna Grancini[1], Francesca Cavallaro[1], Giulia Galassi[1], Federica Irene Grifoni[1], Giorgia Saporiti[1], Luca Baldini[1], Francesco Onida[1]

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Background: Bacterial infections represent frequent complications of hematopoietic stem cell transplantation (HSCT). Even though antibiotic prophylaxis (AP) is widely used as a measure to prevent them, its usefulness remains a matter of debate with lack of consensus across different guidelines.

Main AP-associated concerns include possible promotion of infections by antibiotic-resistant bacteria, particularly in highly endemic countries, with consequent increased mortality. In this study, we aimed at evaluating the incidence of infections by antibiotic-resistant bacterial strains and their resistance profile in patients undergoing HSCT while on AP.

Methods: This is a monocentric retrospective study performed at the Bone Marrow Transplant Center of a tertiary University Hospital in Milan, Italy. All adult patients who consecutively underwent HSCT between 01/12/2014 and 31/12/2019 were included. Data on AP administered and bacterial infections developing within day 100 after transplantation were collected from electronic medical records. For each isolate, the antimicrobial resistance profile was recorded. <Bacteria were defined as multidrug-resistant (MDR) when presenting an acquired non-susceptibility to at least one agent in three or more antimicrobial categories.

Results: 277 HSCTs were included in the database: 173 (62.5%) autologous and 104 (37.5%) allogeneic.Regarding AP, according to internal protocol, all patients without contraindications received fluoroquinolones, with levofloxacin or ciprofloxacin administered in 97.5% of cases. Overall, 124 bacterial infections with known etiology were identified, exactly partitioned between Gram-positive and Gram-negative bacteria (62 each). MDR resistant isolates were 37 (308%), including 24 ESBL+ Enterobacterales, 2 Carbapenem-Resistant (CR) K. pneumoniae, 4 P. aeruginosa (2 of them Carbapenem-Resistant), 2 Vancomycin-Resistant Enterococci (VRE), 5 Methicillin-Resistant S. epidermidis (MRSE) [Fig. 1].

At least one bacteraemia occurred in 50 cases out of the 277 transplants (18.1%) with a total of 56 events and 62 isolates.

MDR isolates from blood culture were 18/62 (29%): 4 MRSE, 10 ESBL+ Enterobacterales, 1 Carbapenem-Resistant K. pneumoniae and 3 P. aeruginosa (2 of them Carbapenem-Resistant).

Regarding antibiograms, resistance for fluoroquinolones was observed in Enterobacterales in 38/44 cases (86.4%) and in Staphylococci in 27/32 cases (84.4%). Worth highlighting, 100% (24/24) of ESBL+ Enterobacterales were also resistant to ciprofloxacin.

Overall mortality at day +100 was 0.6% and 6.7% for autologous-HSCT and allogenic-HSCT, respectively.

Conclusions: in comparison to Italian data on surveillance of MDR bacteria, we found a higher prevalence of bacteraemia due to MDR P. aeruginosa and MDR Enterobacterales and lower prevalence of KPC K.pneumonia and CR P.aeruginosa. Overall mortality in our cohort was slightly lower than proportions reported in the literature.

Furthermore, a strikingly high frequency of resistance to fluoroquinolones was observed. Even though hampered by the lack of a control group, our results suggest that the AP with fluoroquinolones may exert a selective pressure on patients' microbiota, leading to a high incidence of infections due to MDR bacteria. Following the completion of this analysis we decided to modify our internal AP policy and definitely dismissed fluoroquinolones administration. A prospective evaluation on the impact of invasive bacterial infections was started.

Disclosure: Nothing to declare.

P100.

Epidemiology of Infectious Complications in Patients with Chronic Graft-Versus-Host Disease

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Background: Patients with chronic graft-versus-host disease (cGVHD) after allogeneic hematopoietic stem cell transplantation (HSCT) are at increased risk of developing infectious complications (IC).

Methods: Single center retrospective study included 105 adult patients with cGVHD after allo-HSCT from 2014 to 2018, predominantly with post-transplant cyclophosphamide based GVHD prophylaxis (91%). For a 5-year period 705 adult allo-HSCT had been done in CIC725, the incidence of cGVHD decreased from 22,6% in 2014 to 11,7% in 2018. The median time of cGVHD onset was

160 days (74 - 546) after allo-HSCT. The analysis of IC was carried out from the onset of cGVHD to the follow-up date. The median follow-up time was 21 months (8 days - 62.1 months). Microbiologically documented infections were included into analysis. We excluded from the analysis 15 patients with the relapse of the underlying disease after the development of cGVHD. An analysis was conducted using the Kaplan-Meier method, single factor log-rank test, landmark analysis with landmark point of 60 days, and univariate cox model.

Results: IC developed in 29 (32.2%) patients with cGVHD. Single etiology infections were registered in 65% of patients, 35% had multiple infection episodes of different etiology, more often viral infections (VI) and bacterial infections (BI); one patient had mixed infection at the same time. The incidence of BI was 22.2% ($n = 20$), VI – 21.1% ($n = 19$), and invasive fungal disease (IFD) – 5.6% ($n = 5$). The main pathogens of BI were Klebsiella pneumoniae (30%), Pseudomonas aeruginosa (15%), Escherichia coli (15%), Acinetobacter baumanii (10%), Proteus mirabilis (5%); gram-positive bacteria were documented in 25% of patients. Multiple recurring cases of BI were observed in 8 (40%) patients. Most common localizations of BI were pneumonia (60%), sinusitis (35%), colitis (20%) and bloodstream infections (5%). Risk factors for developing BI were: treatment with glucocorticosteroids (GCS) as a first line therapy for cGVHD ($p = 0.007$), the severe cGVHD ($p = 0.039$). The etiology of VI, including 21% ($n = 4$) cases of mixed VI, was represented by CMV (68.4%), EBV (26.3%), BK / JC (15.8%), HHV type 6 (10.5%), HSV type 1-2 (5.2%), RSV (5.2%). The only viral reactivation in the blood was detected in 58% of patients, viral disease was observed in 42% of patients with lungs (21%), GI (15.7%) and bladder (5,3%) affecting. The main risk factors for the development of VI were: the use of GCS as the first line of therapy for cGVHD ($p = 0.002$), and the severe cGVHD ($p = 0.012$). IFD in cGVHD were presented by the only pulmonary aspergillosis. The main risk factor for the development of IFD was the severe cGVHD ($p = 0.001$). The development of IC significantly decreasing the 2-year OS in patients with cGVHD with 60-day landmark ($p = 0.0001$). Post-landmark OS was 96% in patients without infections, and 63% in patients with IC HR = 9.55 (95% CI: 2.54 – 35.9), ($p = 0.001$).

Conclusions: The incidence of IC in patients with cGVHD was 32.2% with the prevalence of bacterial and viral etiology. The main risk factors were the use of GCS at the first line of therapy and the severe cGVHD. The infectious complications significantly decreased OS in patients with cGVHD.

Disclosure: Nothing to declare.

P101.

Clinical And Microbiological Impact of Discontinuation of Fluoroquinolone Prophylaxis in Patients Undergoing Hematopoietic Stem Cell Transplantation: A Single-Center Experience

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Background: Clinical benefit of fluoroquinolone (FQ) prophylaxis remains controversial. Reports on rising antimicrobial resistance rates and risk of inducing/selecting multi-drug resistant (MDR) strains by prolonged/repeated FQ exposure present important concerns. The utility of FQ prophylaxis is further questioned as data show an association of decreased intestinal microbial diversity with a significant increase in transplant-related mortality, acute graft-versus-host disease (aGVHD) related mortality and decrease in overall survival.

Methods: FQ prophylaxis was abandoned in November 2011 after a successful discontinuation trial. Charts of patients admitted for allogeneic haematopoietic stem cell transplantation (HSCT) from November 2011 until October 2020 were reviewed for occurrence of febrile neutropenia, bacteraemia, severe sepsis, septic shock, aGVHD, infection-related and overall mortality. Data from blood cultures and their resistance patterns were reviewed.

Results: A total of 252 consecutive allogeneic HSCT admissions were included. Median age was 57 years (range 17-74) and 61.5% (155/252) were male. The majority of HSCT were performed for AML (46%; 116/252), followed by MDS (16.3%; 41/252) and ALL (10.3%; 26/252). Donor type was most frequently MUD (52%; 131/252), followed by sibling (36.9%; 93/252), haplo-identical (8.7%; 22/252) and mismatched MUD (2.4%; 6/252). Mean duration of hospitalisation and profound neutropenia was 30.1 days and 14.8 days respectively.

Febrile neutropenia occurred in 81.0% (204/252). Of the 322 recorded fever episodes, 74 (22.3%) were classified as microbiologically documented infections, 55 (16.6%) as clinically documented infections and 203 (61.1%) as fever of unknown origin (FUO). ATG infusion was associated with 38.4% (78/203) of FUO episodes. Bacteraemia occurred in 26.6% (67/252) of admissions, severe sepsis in 5.2% (13/252) and septic shock in 2.4% (6/252).

Out of 67 bacteraemia episodes, 36 (53.7%) were caused by gram-negatives versus 31 (46.3%) by gram-positives. The majority of gram-negative bacteraemia were attributed to Escherichia coli (23/36; 63.9%), followed by Klebsiella

species (4/36; 11.1%) and Pseudomonas aeruginosa (2/36; 5.6%). Of the 36 isolated gram-negatives, 1 (2.8%) was FQ-resistant and 2 (5.6%) MDR. The most frequently occurring cause of gram-positive bacteraemia were coagulase-negative staphylococci (10/31; 32.3%), followed by S. viridans (6/31; 19.4%), Staphylococcus aureus (6/31; 19.4%) & Enterococcus faecium (5/31; 16.1%). Of the 31 isolated gram-positives, 11 (35.5%) were FQ-resistant.

Cumulative incidence of aGvHD at day 100 was 41.8% (105/251), including 47.6% (50/105) grade III/IV of which 30% (15/50) with fatal outcome. Day 30 and day 100 overall mortality rates were 3.7% (9/252) and 17.3% (43/248) respectively. Infection was cause of death in 27.9% (12/43) of events and aGVHD in 34.9% (15/43). Comparison to our older patient cohort was not relevant as transplant strategies and supportive care have changed substantially over the years. However, our reported outcomes do not seem to differ from those reported by other authors.

Conclusions: Our data confirm that FQ prophylaxis was abandoned without clinically relevant drawbacks. However, the prevalent local distribution of pathogens and their antimicrobial susceptibilities should be taken into account when guiding strategies on antimicrobial prophylaxis. High background FQ-resistance of Escherichia coli in our area as well as low prevalence of Pseudomonas aeruginosa at our hospital explain the limited benefit of FQ prophylaxis.

Disclosure: Nothing to declare.

P102.

Iron Chelation with Deferasirox Suppresses The Appearance of LPI During Conditioning Chemotherapy Prior to Allogeneic Stem Cell Transplantation

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Background: Iron release during conditioning therapy prior to allogeneic hematopoietic stem cell transplantation (HSCT) is believed to contribute to treatment related toxicity and to favor infectious complications. Labile plasma iron (LPI), which appears at high levels of transferrin saturation (TfS), represents the chelatable, redox-active fraction of non-transferrin-bound iron and therefore is a marker of acute iron overload. In this study, we investigated the influence of iron chelation therapy with deferasirox during conditioning therapy on the appearance of LPI and the incidence of infection and toxicities.

Methods: Between November 2018 and August 2020, 25 patients with documented iron overload (serum ferritin >1000 µg/l) and planned HSCT after myeloablative, busulfan-based, TDM-guided conditioning chemotherapy at the University of Hamburg were enrolled in the study. They received 14 mg/kg/d deferasirox (coated tablet) from the start of conditioning until d3 after transplantation. Iron parameters, including LPI, were obtained at chelator's trough level daily during conditioning until d0 and on d4, d7 and d14 after transplantation. LPI was measured using the FeRos™ LPI kit (Afferix, Telaviv/Israel) if TfS exceeded 70%. All patients received anti-infective prophylaxis with acyclovir (3x400 mg/d p.o. or 3x500 mg/d i.v.), ciprofloxacin (2x500 mg/d p.o. or 2x400 mg/d i.v.), trimethoprim/sulfamethoxazole (2x800/160 mg/d twice weekly) from start of conditioning and micafungin (1x100 mg/d) from d0 or start of neutropenia (WBC $<1.0 \times 10^6$/ml). Infection was defined as bacteriaemia (BSI) or invasive fungal disease (IFD) according to MSG-/EORTC-criteria. Toxicity was defined and graded according to CTCAE version 5.0. Follow-up ended on d28 after HSCT.

Results: Minor increment of ferritin was observed under conditioning therapy, whereas TfS dramatically increased. TfS levels exceeded 70% in median in 63.6% (36.4 – 90.9%) of the measured samples ($n = 252$). In eleven patients no LPI could be detected despite high TfS at all measured time points. LPI appeared in some patients either before the first dose of deferasirox had been taken ($n = 3$) and/or after medication with deferasirox had been stopped ($n = 11$). Only six patients (24%) presented also with mildly increased LPI values (≤0.5 units) during the days of chelation therapy. Deferasirox was well tolerated and no patient had to stop study medication due to adverse events. No grade IV toxicities were observed. All patients engrafted and neutropenia lasted for a median of 9 days (5 – 19 days). In five patients (20%) infections were detected (BSI = 3, probable IFD = 2), with a median onset of 15 days (7 – 19 days) after HSCT. This group of five comprised also three out of the six patients with elevated LPI values despite intake of deferasirox.

Conclusions: We demonstrate in this study that the appearance of LPI during conditioning chemotherapy prior to HCT can be suppressed safely by deferasirox in patients with iron overload. The co-occurrence of infection and elevated LPI values suggests that chelation therapy could a be an approach to lower infectious complications, but further studies are needed to evaluate its full impact on transplant-associated complications.

Clinical Trial Registry: The trial was registered with the German Clinical Trials Register, number DRKS00015498, on October 10th, 2018.

Disclosure: FA received honoraria from Novartis. All other authors declare that they have no conflict of interest.

P103.

SARS-COV-2 Infection in A Hematopoietic Stem Cell Transplant Center: A Single Center Experience in Mexico

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Background: Patients treated with hematopoietic stem cell transplantation (HSCT), are highly susceptible to opportunistic infections.[1].

The ASH developed a Research Collaborative COVID-19 Registry, with the aim to study outcomes of patients with hematologic malignancies and this infection. Mortality reported was 28%. Patients with a bad prognosis due to underlying hematologic disease had a higher proportion of severe SARS-CoV-2 infection and death.[2] Other study reports higher mortality of 40%.[3].

In the context of HSCT, the current COVID-19 pandemic had an impact on donor and candidate patient selection and the availability of blood products.[4] There have been delays in transplantation because this procedure must be deferred until the patient is asymptomatic and has two negative PCR results.[5].

This study aimed to describe the clinical characteristics and outcomes of HSCT candidates and post-HSCT patients diagnosed with COVID-19 in the HSCT center at Instituto Nacional de Cancerología, México.

Methods: All patients are tested with RT-PCR assay of a nasopharyngeal swab specimen before harvesting and transplant.

For this descriptive analysis, we included all adult patients registered in the HSCT Clinic with a confirmed SARS-CoV-2 infection. We included candidate patients and post-HSCT patients. Then, we describe their clinical characteristics and outcomes of COVID-19 infection.

Results: SARS-CoV-2 infection was diagnosed in 10 patients, 50% in HSCT candidate patients and 50% in post-HSCT period. Of those in the latter group, 60% received an autologous stem cell transplant, and 40% underwent allogeneic stem cell transplantation.

The median of after-HSCT days when the infection was confirmed was 888.8 days (range 93 – 2796 days).

Male patients represented 70% of population, with a median age at diagnosis of COVID-19 of 40.4 years (range 18 – 65).

The underlying neoplastic diagnosis was as follows: Acute lymphoblastic leukemia (30%), Non Hodgkin lymphoma (30%), Multiple Myeloma (20%), Acute Myeloid Leukemia (10%) and Hodgkin lymphoma (10%).

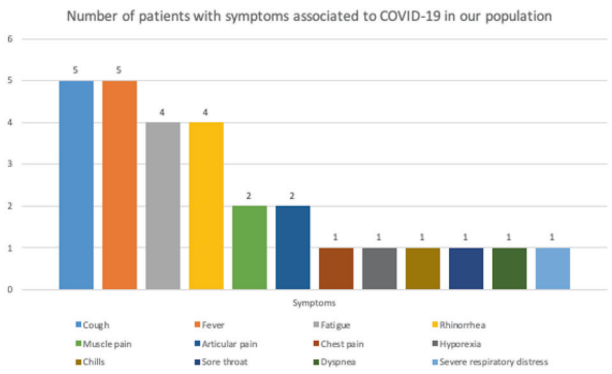
The 80% of confirmed patients had symptoms associated with COVID-19. Median duration of symptoms before confirmation was 5.87 days. The frequency of symptoms at diagnosis are presented in Graph 1.

Most common comorbidities were obesity, hypertension and chronic graft versus host disease, each one found in two patients.

Decreased lymphocyte count was common, with 60% of patients having lymphopenia at diagnosis. Ferritin was determined in 5 patients, with a median value of 2759. Blood gas analysis was performed in 5 patients, with only 2 patients (20%) with hypoxemia at diagnosis.

In this series, 90% of patients were alive at the time of data collection. There was only one death attributed to COVID-19 in a geriatric patient with Multiple Myeloma. The overall mortality of infected patients at our clinic was 10%.

Conclusions: Patients with hematologic malignancies appear to be prone to the SARS-COV-2 infection. Despite this fact, we diagnosed only 10 cases of COVID-19 in the patients registered at our clinic, with one fatality. We attribute this, in part, to the fact that our patients and their families are committed to their self-care. We cannot discard a lack of diagnosis of patients with absent or mild symptoms.



Disclosure: Nothing to declare.

P104.

Antibiotic Prophylaxis And The Rate of Bacteremia And Clostridium Difficile Infection in Pediatric Stem Cell Transplantation: A Single Center Retrospective Study

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Background: The use of prophylactic antibiotics in the pre-engraftment period to minimize the risk of bacteremia is debatable given concerns of Clostridium difficile (C. diff), antibiotics resistance, and disruption of gut microbiota.

Methods: We retrospectively reviewed the rate and characteristics of bacteremia and C.diff infection within the first 100 days post HSCT in all pediatric patients who received prophylactic antibiotics during the period 2015-2018. Patients on active anti-microbial treatment prior to HSCT and those with primary immunodeficiency were excluded. Our institutional guidelines recommend the initiation of single prophylactic anti-bacterial medication when absolute neutrophil count is below 1000/ul and until neutrophil engraftment. C.diff infection was defined by the presence of three or more unformed stools in 24-hours and positive stool test for C. diff or its toxins.

Results: 135 (100 allogeneic and 35 autologous) transplants were performed in 123 patients during the study period. Median age at transplant was 7.1 (range, 0.2-13.7), 67 (55%) were females, and diagnosis was malignant condition in 68 patients. Median time to neutrophil engraftment was 18 days (13-23). Piperacillin-tazobactam prophylaxis was used initially in 28 (21%) of patients then switched to cefepime in 105 (78%) of patients based on our institutional antibiogram. Infectious complications are shown in the table. Only 5 (3%) patients had bacteremia during the pre-engraftment period while on antibiotic prophylaxis and 13 (11%) patients developed bacteremia post engraftment. Septic shock was present in only one patient pre-engraftment and was due to gram negative bacteria. All patients who developed bacteremia received myeloablative conditioning. Thirteen patients (10%) of the total cohort developed diarrhea and fulfilled C. diff infection definition and there was no difference in the rate of C. diff with the use of piperacillin-tazobactam vs cefepime. There was no mortality related to bacterial infections among our patients.

Characteristics	Patients (%)
Bacteremia	18 (14)
Pre-engraftment	5 (3)
Post-engraftment	13 (11)
Gram positive	3 (17)
Gram negative	15 (83)
Presence of septic shock in bacteremia	4 (22)
Pre-engraftment/Post-engraftment	1/3
Gram positive/Gram negative	0/4
Positive C. diff infection	13 (10)
Piperacillin/tazobactam	2/28 (7)
Cefepime	11/105 (10)

Conclusions: The use of antibiotic prophylaxis was associated with low rate of bacteremia (3%) in the pre-engraftment period and a 10% risk of C.diff infections. Randomized control trial is needed to better evaluate the efficacy of antibiotic prophylaxis.

Disclosure: Nothing to declare.

P105.

Human Polyoma BK Virus as a Cause of Hemorrhagic Cystitis: Retrospective Cohort Study

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Background: BK virus (BKV) is a common human polyoma virus which frequently causes hemorrhagic cystitis in hematopoietic stem cell transplantation (HSCT) patients. BK viruria occurs in 50-60% of HSCT patients. The main goal of our study is to assess the prevalence of BK viremia and viruria in patients who underwent allogenic HSCT, as well as to determine the factors which contribute to the development of hemorrhagic cystitis.

Methods: A total of 59 patients who underwent allogenic HSCT were included in this study. HSCT was performed in Clinical Center of Serbia between December 2017 and October 2020. Data obtained from medical records of the patients were retrospectively collected and analyzed using the methods of descriptive and analytical statistics. BKV reactivation was recorded in blood and urine samples which were taken during the regular check-ups using PCR assays. Polyspecific intravenous immunoglobulin (IVIg) were used

prophylactically on days 1, 3, 7,14,21,28, 56, 72, and 84 after HSCT.

Results: The examined group comprised 25 women (42.4%), and 34 men (57.6%). Median age at the time of HSCT was 38 (IQR 30-47) years. BKV was detected in the serum samples of 96.6% ($n = 57$) patients and in 100% of patients' urine samples. Hemorrhagic cystitis of various degree was observed in 27 patients (45.8%). Grade III hemorrhagic cystitis, defined as macroscopic hematuria with clots was detected in 19 symptomatic patients (70.4%). Hemorrhagic cystitis was significantly more common in patients with later platelet and leucocyte engraftment ($p = 0.014$ and $p = 0.020$, respectively). However, no significant relationship between conditioning regiment intensity (myeloablative or reduced intensity) and donor type (matched related or unrelated donor) and hemorrhagic cystitis was found. Median overall survival (OS) in our group of patients was 19.5 months (IQR 13.75-35.5). No significant difference was found in OS between those who developed cystitis and asymptomatic patients ($p = 0.093$).

Conclusions: BKV reactivation was detected in every patient of our study group, while hemorrhagic cystitis was observed in almost half of the subjects, and more commonly occured in those with later leucocyte and platelet engraftment. However, further studies are needed to determine contributing factors in hemorrhagic cystitis pathogenesis.

Disclosure: Nothing to declare.

P106.

Tocilizumab in Post Hematopoietic Stem Cell Transplant COVID-19: A Pediatric Case Report

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Background: Hematopoietic stem cell transplant (HSCT) recipients are severely immunocompromised and are at higher risk of a complicated course during severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection. While cytokine storm develops in a minority of patients with coronavirus disease 2019 (COVID-19), Tocilizumab, as an interleukin-6 receptor antagonist, has been utilized in a number of patients with severe COVID-19. Here, we report a child with Mucopolysaccharidosis who dealt with SARS-CoV-2 after HSCT.

Methods: A 3-year-old boy with Mucopolysaccharidosis type VI underwent allogeneic HSCT from a full matched, unrelated donor. During the posttransplant period (19 days after HSCT), while dealing with acute GVHD, he was diagnosed with SARS-CoV-2 and was treated with remdesivir and tocilizumab.

Results: The patient's condition improved significantly within two days, he became afebrile and his tachypnea diminished. Interleukin-6 level decreased to 24 pg/ml and he gradually reached normal blood oxygen levels on room air. On his chest CT scan performed +40 days post HSCT, parenchymal opacities were reduced compared to the previous study.

Conclusions: Well-timed treatment with tocilizumab might reduce the risk of invasive mechanical ventilation requirement or death in patients with severe COVID-19 pneumonia in early post HSCT period.

Disclosure: Non declared.

P107.

Pandemic Lessons of COVID 19 in Northeast of Brazil

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Background: The emergence of COVID-19 pandemic led us to adapt the routine, since March, 2020. We are a Bone Marrow Transplantation Center in a public university hospital, located in Fortaleza/ Ceará, Northeast of Brazil and adopted the Guidelines of EBMT. We described our experience with COVID 19 in patients before and during the bone marrow transplantation.

Methods: We described the results of the PCR multiplex SARS-CoV-2 in recipients from April to November, the infections occurred into the hospitalization and also in the transplantations after COVID-19 infection.

Results: 90 RT-PCR for SARS CoV2 were collected, 5 (5,5%) were positive, all of them were asymptomatic. The hospitalizations were canceled and the patients were admitted after the negative result. Two patients are waiting the admission.

Three patients had negative PCR SARS CoV2 before hospitalization and positive tests in the hospital. Two of them were asymptomatic and collected the test (in the

second day of conditioning and the other in the infusion day) because they had contact in the hospital with a COVID-19 patient. The other one had mild symptoms, six days after the infusion and the PCR was positive. All of them had good evolution, without pulmonary disease or later graft.

Two patients had COVID-19 symptomatic and realized the BMT after. The first one had a severe pulmonary disease and needed non-invasive ventilation. We decided to postpone the haploidentical transplantation 3 months, because the patient had severe symptoms and the disease was in remission. The second patient moderate symptoms, without oxigens needs. He had transplantation match related donor in November. Both patients had hospitalization without occurrence related to COVID-19, pulmonary changes or graft failure.

Table 1. Description of patients with SARSCoV2 positive in the public university hospital, localized in Fortaleza/Ceara, Northeast of Brazil (Column 1: patient, Column 2: disease, Column 3: age, Column 4: type of BMT, Column 5: symptoms of COVID-19, Column 6: PCR SARSCoV-2 positive and Column 7: Date of BMT).

1	ALL Ph+	31	Allogeneic MRD	No	June, 16	July, 28
2	AAG	24	Allogeneic MRD	No	June, 30	July, 21
3	B cell non Hodgkin Lymphoma	68	Autologus	no	June, 16	August, 03
4	Myeloma	51	Autologus	no	August, 18	Not yet
5	AML	31	Allogeneic MRD	no	November, 17	Not yet
6	Hodgkin disease	38	Autologus	Mild	October, 07	October, 01
7	AML	39	Allogeneic MRD	no	June, 12	June, 19
8	APL	59	autologus	no	June, 12	June, 12
9	ALL PH	24	Haploidentical	50-75% of impairment pulmonary	May, 11	September, 18
10	CMML	52	Allogeneic MRD	25% of impairment pulmonary	September, 09	November, 06

Conclusions: The COVID 19 is a big challenge in the Bone Marrow transplantation units, especially in a developing country's public health. Although the costs, the PCR SARS CoV2 pre admission is necessary, because we have had asymptomatic patients (5,55%) in our experience. The occurrence of transmission in the BMT unit is possible, regardless of the strategies of prevention. Think in COVID 19 is necessary. The COVID 19 severe with pulmonary impairment is not contraindication to BMT.

Clinical Trial Registry: The COVID 19 is a big challenge in the Bone Marrow transplantation units, especially in a developing country's public health. Although the costs, the PCR SARS CoV2 pre admission is necessary, because we have had asymptomatic patients (5,55%) in our experience. The occurrence of transmission in the BMT unit is possible, regardless of the strategies of prevention. Think in COVID 19 is necessary. The COVID 19 severe with pulmonary impairment is not contraindication to BMT.

Disclosure: Nothing to declare.

P108.

Clinical Characteristics And Outcome of Polymicrobial Bloodstream Infections in ALLO-SCT Patients: A Monocentric 5 Years Survey

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Background: Very limited informations are still available on Polymicrobial Bloodstream infections (pBSI) occurring after allogeneic hematopoietic stem cell transplant (Allo-SCT).

Methods: We analyzed clinical characteristics and outcome of pBSI that occurred after Allo-SCT procedure in our Center from January 2015 to December 2020. pBSI was defined as the isolation of 2 or more bacteria from blood culture specimens obtained within 72h from the same patient.

Results: During last 5 years 142 out of 321 Allo-SCT recipients experienced at least one bloodstream infection (BSI) and, of these, 13/142 (9%) had a pBSI (7 MUD, 5 Haplo, 1 HLA-id). Median age at transplant was 54 years and the principal underlying disease was acute leukemia. Most frequent conditioning regimen was Treosulfan-Busulfan-Fludarabine (7/13). In 10/13 (77%) cases pBSI occurred within 20 days after Allo-SCT. Most common bacterial association was Gram-negative plus Gram-positive (54%). Gram-negative bacteria was involved in 9/13 (69%) pBSI and the most frequent isolates were: *S. epidermidis* (11/13), *E. coli* (4/13) and *P. aeruginosa* (2/13, of which 1 Multi Drug Resistant-MDR). All cases had a Central Venous Catheter (CVC) and in 2/13 (15%) cases a concomitant lung infection was present. During their hospitalization 7/13 (54%) patients developed further episodes of BSI but only once involved one of the isolates of pBSI. In this study we also compared the characteristics and outcome of 13/142 Allo-SCT with pBSI with 129/142 Allo-SCT with monomicrobial mBSI. All patients with pBSI were alive at 7 and 30 days after the infection onset and only one case of septic shock occurred.

Conclusions: This retrospective analysis confirms that pBSI is a very rare complication of Allo-SCT procedure. The outcome is favorable in this survey probably due to a

prevalence of Gram-positive isolates and a low incidence of MDR. However a multicenter study, with a larger number of cases, is necessary to draw definitive conclusions.

Disclosure: no one.

P109.

SARS-COOV-2 Infection in An Adolescent Patient After Haploidentical Stem Cell Transplantation

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Background: Patients that undergo Hematopoietic Stem Cell Transplantation (HSCT) are easily susceptible to respiratory viral infections (RVIs), most of which possibly fatal. Indeed, the current spread of the COVID-19 pandemic, which has already infected almost 69 million and killed more than 1.5 million people worldwide, is a concerning topic for the hematologists. The positivity to SARS-CoV2 (usually checked by nasopharyngeal swabs), even as an incidental finding before the HSCT in the patient or in the donor inevitably leads to postpone the procedure, with all the easily imaginable risks implicated. To date, there are very few reports on the clinical course and outcome of the coronavirus disease after HSCT, even less in pediatric patients. The role of the immune system in SARS-CoV-2 infection is partially unclear, especially the connection between virus replication, inflammatory response and tissue damage.

Methods: The case we report is that of a 14 y/o patient, affected by T acute lymphoblastic leukemia with extramedullary (optical neuritis) and medullary relapse, who contracted SARS-CoV2 at day +110 from maternal haploidentical NK-alloreactive HSCT with regulatory and conventional T-cell adoptive immunotherapy, and successfully recovered without severe acute respiratory syndrome and/or apparent sequelae. The neutrophil engraftment was observed at day +11 from HSCT, the platelet engraftment at day +20. Chimerism was 100% donor, and CD3+/CD4 + lymphocyte count was 137 per mmc, CD3+/CD8+ 1644 per mmc, CD3-/CD56+ 521 per mmc at day +30. At day +15 from HSCT, the patient developed grade 1 cutaneous and gastrointestinal acute GvHD, treated with hydrocortisone 100 mg/day (for one week) and extracorporeal photopheresis as first-line therapy, then beclomethasone dipropionate 10 mg/day and Ruxolitinib 5 mg bid. At day +110 from HSCT the RT-PCR on nasopharyngeal swab showed positivity for SARS-CoV2.

Results: The patient, admitted in the Infectious Disease Department, was treated with Remdesivir and intravenous immunoglobulins; he also received 3 hyperimmune plasma infusions. The immunosuppressive therapy was interrupted to stimulate the immune response and facilitate the virus clearance, since the SARS-CoV2 swabs were persistently positive with high viral load, without the production of specific antibodies. Except for a bacterial sepsis, the hospital stay was substantially uneventful: the patient was apyretic, without any need of oxygen support (arterial blood gas analysis was normal) and no relevant sign or symptom. Given these clinical features, after 40 days of hospital stay, he was discharged, in spite of the persistent SARS-CoV2 positivity and the low title of antibodies (20.1 AU/mL). After 72 days, the patient finally tested negative for SARS-CoV-2 by PCR on nasopharyngeal swab, with an elevated title of SARS-Cov-2 antibodies (78.6 AU/mL).

Conclusions: SARS-CoV-2 appears to differ from other respiratory viruses, since the role of the immune response, rather than protective, can be harmful. Our report suggests that in this patient, the immunocompromised condition may have acted as a protective factor against the COVID-19, which would corroborate the hypothesis of the major role played by the immune response in the development of the severity and mortality of the disease.

Disclosure: Nothing to declare.

P110.

Cmv Reactivation After Allogenic Hematopoietic Stem Cell Transplantation - Single Center Experience

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Background: Cytomegalovirus (CMV) infection remains one of the major morbidity and mortality factors following hematopoietic stem cell transplantation (HSCT). The goals of this study are to assess the relationship between the CMV reactivation frequency and number of CMV copies, on the one hand, and platelets and leucocytes day of engraftment, intensity of conditioning regiment (myeloablative or reduced intensity), donor type (matched related or unrelated) on the other. Moreover, the aim of this study is to

examine whether the CMV reactivation has an impact on overall survival of HSCT patients.

Methods: Medical records of 59 consecutive adult patients (25 females (42.4%); median age at HSCT 38 (IQR 30-47)), in which allogenic HSCT was performed, were retrospectively analyzed. HSCT was conducted in Clinical Center of Serbia between December 2017 and October 2020. CMV reactivation was assessed using quantitative Real Time-PCR assays in blood samples, and subsequently genotyped positive samples on the basis of the UL55 gene coding for the glycoprotein B (gB). Real Time-PCR was performed once weekly during the first 100 days after HSCT, and than twice monthly afterwards. Methods of descriptive and analytical statistics were used.

Results: CMV reactivation was noted in 40 (67.8%) patients. In 28 of those patients both recipient and donor were seropositive, while in 12 cases of reactivation donor was seronegative. Median of CMV copies in mL of serum was 4256.5 (IQR 1407.5-12508.5). Genotypes of CMV were determined in 12 patients. The most prevalent genotype was gB4 (8/12, 66.7%), followed by gB5 (5/12, 41.7%). The gB2 and gB3 were detected in 3 (25%) and 2 (16.7%) subjects. The presence of gB1 was not demonstrated. Mixed infections, those simultaneously involving more than one CMV genotype, were detected in 5 patients. An alteration in genotypic profile was noted in two subjects during follow-up. Namely, in one patient who had recurrent CMV reactivation and graft failure with subsequent second transplant (cell boost from the same donor), the prevailing genotype changed from gB4 to gB5, while in the other a hitherto undetected gB4 appeared along with the then dominant gB5. The genotype manifesting the largest number of CMV DNA copies/mL was gB4, while the smallest viremia was noted in a patient with gB5. Reactivation occured with the median time of 32 days after HSCT (IQR 27-53.75). In 6 cases (10.2%) reactivation was recorded after more than 100 days post-HSCT. No significant relationship was found between CMV reactivation and platelets and leucocytes counts on the day of engraftment, intensity of conditioning regiment and donor type. In patients with CMV reactivation secondary graft failure was registered much frequently in subjects with higher viral load ($p = 0.028$). Median overall survival was 19.5 months (IQR 13.75-35.5). No significant difference in overall survival between two groups (reactivation/no reactivation) was not recorded was found ($p = 0.522$).

Conclusions: Given the proven influence of CMV on the occurrence of graft function, it is necessary to meticulously monitor the status of CMV in blood and urine, with prophylactic, preemptive and targeted therapy, which could be designed by CMV genotyping.

Disclosure: Nothing to declare.

Lymphoma and Chronic Lymphocytic Leukemia

P111.

18Fluoromethylcholine PET/CT to Predict Outcomes of Patients Pre And Post Autologous Stem Cell Transplantation(ASCT) For CNS Lymphoma – A New Cns Lymphoma Imaging Tool

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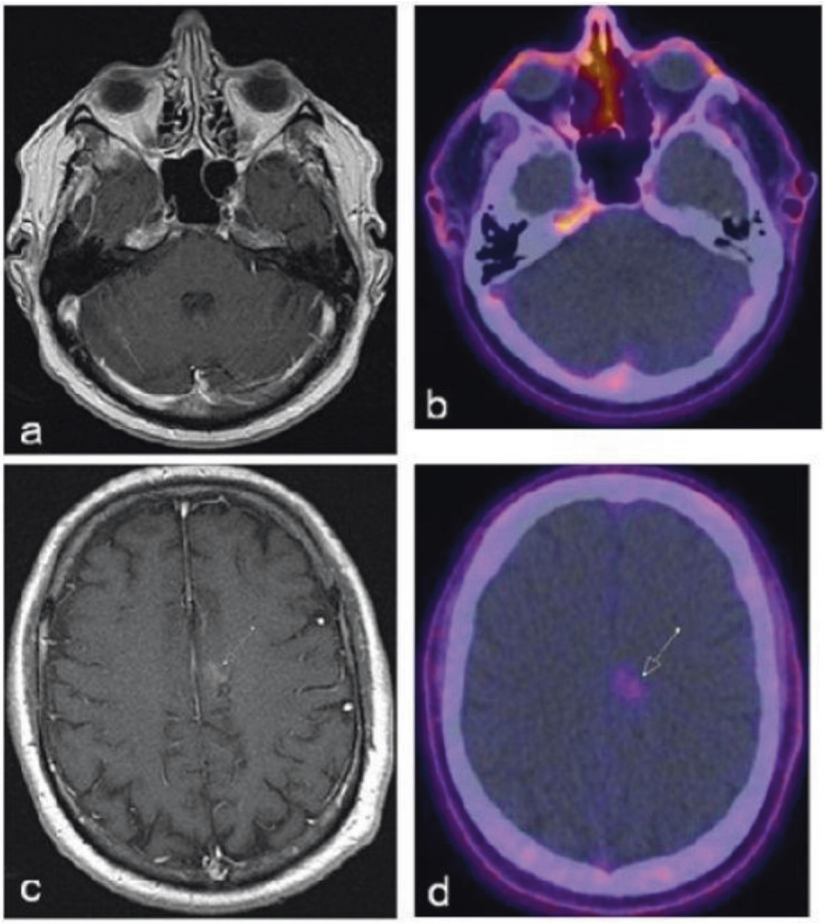
Background: ASCT is standard consolidation treatment for transplant eligible patients with central nervous system (CNS) lymphoma achieving at least stable disease following high-dose methotrexate-based chemotherapy. Contrast-enhanced MRI cranium is the neuroimaging modality of choice to evaluate response. We perform assessment pre-ASCT, 3 months(3/12) and 1-year post-ASCT. MRI interpretation is difficult with persistent abnormality or scarring. 2-deoxy-2-[18F]fluoro-D-glucose(FDG) PET/CT is not accurate given high physiological glucose-uptake by brain parenchyma. We use a novel 18F-fluoromethylcholine (FCH) radiotracer, in addition to MRI, for disease status pre-and post-ASCT.

Methods: We performed a retrospective review of medical records of 17 patients who underwent ASCT between 2016 and 2019 for CNS lymphoma.

Results: 17 patients received Busulphan/Thiotepa conditioned-ASCT. 3 had no baseline FCH-PET/CT excluding analysis. Table 1 describes patient characteristics. Median ASCT age=48 years(range 19-69).

8/14(57%) patients had concordant baseline MRI and FCH-PET/CT: 6/8 had negative MRI and FCH-PET/CT pre-transplant, remaining in complete remission(CR) on MRI at 3/12 and 1 year post-ASCT. 1 patient was negative by both techniques pre-ASCT but relapsed at 3/12. 1 patient was in partial remission(PR) by both pre-ASCT and at 3/12 but subsequently relapsed. Both died of disease progression.

6 patients(43%) had discordant baseline imaging(Figure 1): 3 had stable disease/residual enhancement on baseline MRI but negative FCH-PET/CT and were in CR by MRI +/- FCH-PET/CT at 3/12 and 1 year. 2 had PR on baseline MRI and 3/12 with negative FCH-PET/CT and have no signs of disease progression. 1 patient had negative baseline MRI but uptake of uncertain significance on FCH-PET/CT, being negative by both at 3/12 and 1 year.



There were no treatment related deaths. Median follow u$p = 1.95$ years. Overall Survival(OS) at 2 years=93% (95%CI 59-99). Progression Free Survival(PFS) at 2 years=86%(95% CI 54-96). There was no significant difference in OS($p = 0.38$) and PFS($p = 0.2$) for patients with discordant versus concordant baseline imaging.

Gender	$n = 5$	35.7%
Female	$n = 9$	64.3%
Male		
Diagnosis	$n = 9$	64.3%
PCNSL	$n = 3$	21.4%
Systemic DLBCL with CNS involvement	$n = 1$	7%
Anaplastic large cell lymphoma with CNS relapse	$n = 1$	7%
Mediastinal B cell lymphoma with CNS relapse		
Chemotherapy	$n = 7$	50%
MATRix	$n = 3$	21.4%
Rituximab/MTX/Cytarabine	$n = 3$	21.4%
TIER	$n = 1$	7%
MATRix and R-ICE		

Conclusions: We used FCH-PET/CT imaging plus MRI to assess disease status in patients undergoing ASCT for CNS lymphoma. Dysregulated choline metabolism is synonymous with oncogenesis and cancer progression. 5 patients who had PR or residual enhancement on MRI but negative FCH-PET/CT pre-ASCT have remained in CR long term. This early data suggests the utility of FCH-PET/CT in CNS lymphoma response-assessment, particularly in those with equivocal MRI findings. This is the first published study for use of FCH-PET/CT pre-and post-ASCT in CNS lymphoma, further analyses evaluating potential indications for FCH-PET/CT in staging, response-assessment and prognostication are warranted.

Disclosure: No conflicts of interest declared.

P112.

Results with Allogeneic Stem Cell Transplantation in Patients with Relapsed/Refractory Hodgkin Lymphoma Treated with ANTI-PD1: A Multicenter Retrospective Cohort Study

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Background: The efficacy of anti-PD-1 treatment followed by allogeneic stem cell transplantation (Allo-SCT) in patients with relapsed/refractory Hodgkin Lymphoma (r/r HL) has been reported. However, concerns about the risk of severe acute and chronic graft vs host disease (GVHD) has emerged.

Methods: Multicenter, retrospective cohort study between January 2010 and December 2019, with the participation of six centers in Argentina affiliated to Grupo Argentino de Trasplante de Médula Ósea y Terapia Celular (GATMO-TC). A time-to-event analysis considering competitive risks was performed to estimate incidence of GVHD, non-relapse mortality (NRM) and relapse. Kaplan-Meier estimates and log-rank test were used for survival.

Results: The study included 23 patients. Median age at time of Allo-SCT was 28 years (IQR 23-32); 12 patients (52.2%) were women. All HL subtypes were nodular sclerosis. As regards the clinical characteristics at diagnosis: 13 (56.5%) were stage III or IV, 13 patients (56.5%) were primary refractory, and 7 (36.8%) had early relapse. In 19 (82.6%) patients an history of autologous-SCT was registered. Before Allo-SCT, 18 patients (78.3%) received nivolumab, and 5 (21.7%) pembrolizumab (median cycles were 8; IQR 7-12). Only 2 (8.7%) had pre Allo-SCT autoimmune complications. Pre-transplant status by PET-CT was: complete remission $n = 18$, partial remission $n = 3$, and undetermined $n = 2$. Median time from diagnosis to transplant was 1738 days (IQR 1250.5-2224.50).

Haploidentical related donor was the most frequent type ($n = 15$; 65.2%), followed by histoidentical sibling ($n = 6$; 26.1%). The conditioning regimen was non-myeloablative (NMA; fludarabine/TBI-based) in 15 patients (65.2%), and reduced intensity conditioning (RIC; melphalan or busulfan-based) in 8 (34.7%) patients. Seventeen patients (73.9%) received post-transplant cyclophosphamide.

Median follow-up time in the surviving cohort was 471 days (IQR 273-755). Cumulative incidence of acute grade 3-4 GVHD was 30.7% (95%CI 13.3-50.2): a trend to lower incidence was observed in the NMA group (20%; 95%CI 4.5-43) vs. the RIC group (50%; 95%CI 12.5-79.4); $p = 0.220$. One-year progression-free survival at 12 months was 74.4% (95%CI 48.7-88.5) while one-year overall survival was 80.1% (95%CI 55.2-92.1). Overall survival was 100% (95%CI 9.5%-47.3) in patients without acute GVHD vs 58.3% (95%CI 22.9-82.1) in patients developing acute GVHD ($p = 0.009$); and 91.7% (95%CI 53.9-98.9) and 60% (95%CI 19.5-85.2) in patients undergoing NMA and RIC Allo-SCT, respectively ($p = 0.087$). NRM was 4.8% (95%CI 0.03-20.2) at 3 months and 19.9% (95%CI 5.9-39.8) at 12 months. Patients with acute grade 3-4 GVHD had a higher NRM (41.7% vs 0%; $p = 0.023$). Chronic GVHD only reached grade 1 in 6 patients (26.1%). One-year relapse incidence was 5.7% (95%CI 0.3-23.8). One-year GVHD and relapse-free survival was 59% (95%CI 35.6-76.3), with a tendency to better result in patients undergoing NMA vs RIC (60% vs 37.5%; $p = 0.145$).

Conclusions: Our cohort confirmed the overall survival in r/r HL and a low relapse incidence following anti PD-1 therapy and Allo-SCT. There was also an association between acute GVHD and overall survival, as previously described. The greater number of patients with RIC conditioning compared with NMA who developed GVHD may suggest that increasing the intensity of conditioning could also increase morbidity and mortality in this setting.

Disclosure: Nothing to declare.

P113.

The Outcomes of Allogeneic Stem Cells Transplantation For Relapsed/Refractory Chronic Lymphocytic Leukemia in The Era of Targeted Therapy: Single Center Experience

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Background: Chronic lymphocytic leukemia (CLL) presents a significant burden to healthcare due to high prevalence in a population. Introduction of the novel agents in the treatment of CLL revolutionized the prognosis of high-risk CLL. However, the allogeneic hematopoietic stem cell transplantation (allo-HSCT) is the only proven curative therapy for CLL. Optimizing allo-HSCT patient selection,

timing, and preparative regimen in the new landscape is an actual problem.

Methods: This retrospective analysis included 29 patients (22 male and 7 female) who were diagnosed with CLL and underwent allo-HSCT in the Pavlov University (CIC 725) between 2006 and 2020. Median age at allo-HSCT was 48 (33-66) years. The cytogenetics abnormalities presented in patient population were: del17p - 34% ($n = 10$), del11q – 24% ($n = 7$), del13q – 31% ($n = 9$), trisomy 12 – 14% ($n = 4$). IGHV mutation status was assessed in 6 patients, 5 patients had unmutated IGHV. One patient had Richter syndrome. One patient developed fludarabine-induced bone marrow aplasia prior to HSCT. Median number of therapy lines was 3 (1-8). Prior to transplant 6 (21%) patients were in complete response (CR), 11 (38%) had partial response (PR), 2 (7%) had stable disease (SD), 10 (34%) had disease progression (PD). Among 5 patients with CR, 4 patients were MRD-positive before allo-HSCT. Novel agents were used as a bridge-therapy in 13 patients (venetoclax - 2, ibrutinib - 11). Fourteen (48%) patients had resistance to chemoimmunotherapy and 4 (14%) patients were resistant to ibrutinib. Median time to transplant from diagnosis to allo-HSCT was 52 months.

Results: Fully matched related donor HSCT was performed in 10 (34%) patients, while 19 (66%) patients received allo-HSCT from matched ($n = 14$) or mismatched ($n = 5$) unrelated donor. Most patients had fludarabine and bendamustine-based conditioning ($n = 20$, 69%) with ($n = 8$) or without ($n = 12$) rituximab. Posttransplant cyclophosphamide-based graft-versus-host disease (GVHD) prophylaxis regimen was used in 19 (66%) patients. Acute GVHD was observed in 20 (69%) patients. Of these, 5 patients had grade 3-4 acute GVHD (Keystone Consensus), which was significant predictor of overall survival (OS) ($p < 0.001$).

Median follow-up was 19 (1-162) months and median follow-up of surviving patients was 31 months (1-162). Two-year OS and progression-free survival was 67% and 59%, respectively. Non-relapse mortality was 17%. MRD-negativity was achieved in the bone marrow of 13 out of 15 (87%) patients available for analysis and in the peripheral blood of 15/17 (88%) patients available for analysis. Three patients had reappearance of MRD after allo-HSCT. Other factors significantly associated with OS in univariate analysis were response prior to allo-HSCT ($p = 0.0035$), best response to allo-HSCT ($p < 0.001$), cyclophosphamide-based GVHD prophylaxis ($p = 0.02$), resistance to chemoimmunotherapy prior to allo-HSCT ($p = 0.049$), use of new agents (ibrutinib/venetoclax) prior to allo-HSCT ($p = 0.016$).

Conclusions: The results of our study demonstrate the potential of allo-HSCT in patients with relapsed/refractory CLL. Lack of response prior to transplant is an important negative predictive factor that can be addressed by novel agents.

Disclosure: Nothing to declare.

P114.

Nivolumab 40 Mg Therapy in Relapsed And Refractory Classical Hodgkin Lymphoma: Results of A Single Center Matched Case-Control Study

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Background: The efficacy of nivolumab (Nivo) 40 mg previously was demonstrated in patients with relapsed and refractory classical Hodgkin lymphoma after ASCT and in ASCT-naïve patients (Lepik KV, 2020). However, no direct comparison has been made between the efficacy of Nivo 3 mg/kg and 40 mg. In the absence of head-to-head randomized controlled trial data, indirect approaches provide an alternative method for comparing doses of Nivo.

Methods: The study group (group 1) included 34 patients with r/r cHL who were treated with Nivo 40 mg every 2 weeks. The data on 34 patients with r/r cHL who were treated with Nivo 3 mg/kg (group 2) were also collected to compare the efficacy and safety of the treatment (1:1). The patients were matched for sex, age at the moment of Nivo, history of ASCT, treatment with brentuximab vedotin prior to Nivo and the number of prior therapy lines.

After matching, overall response rate (ORR1,2), progression-free survival (PFS1,2), overall survival (OS1,2) and adverse events (AE) differences for each group were assessed. The ORR determined by PET/CT using LYRIC criteria every 3 months. Adverse events were evaluated according to CTCAE 4.03.

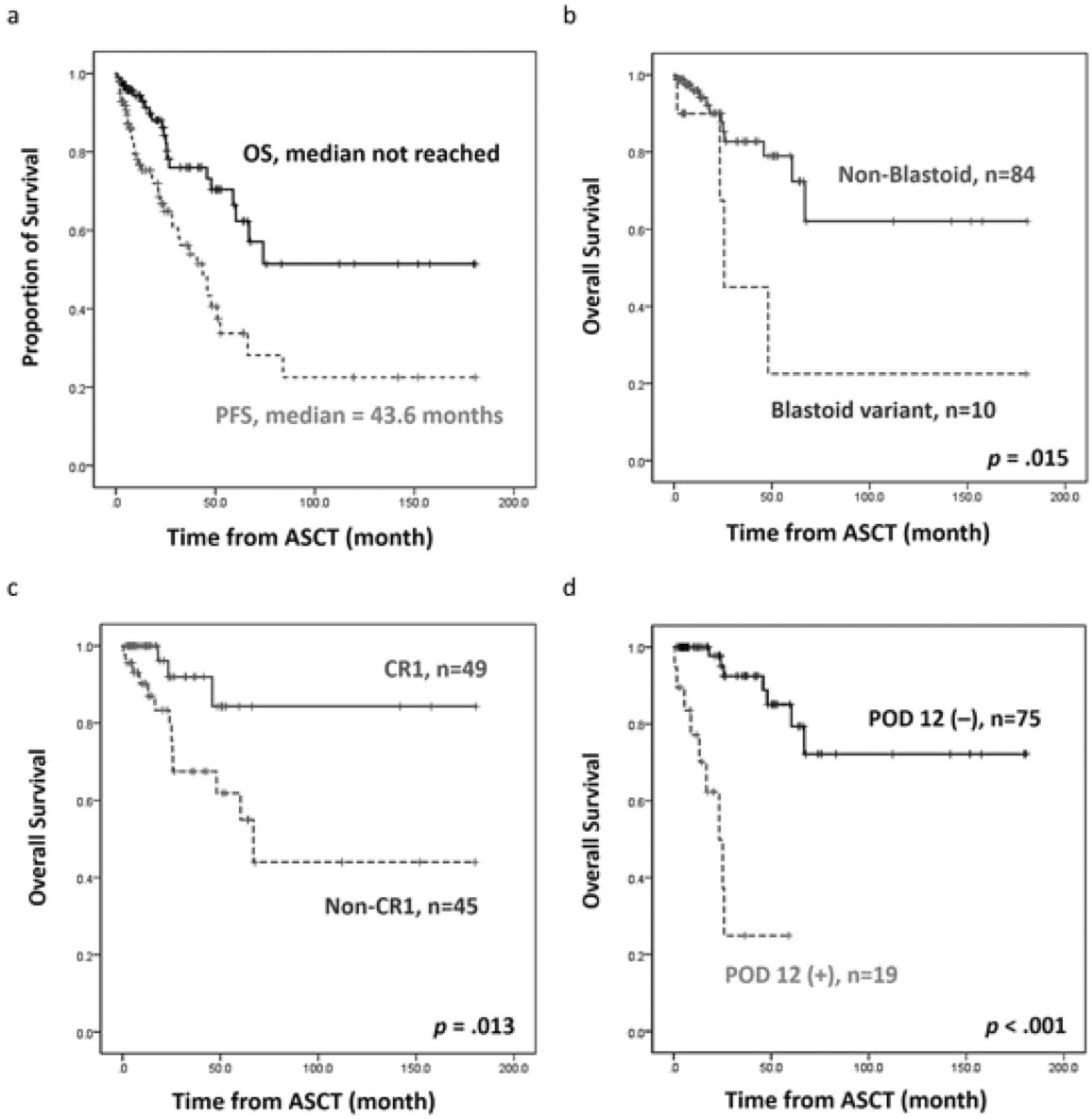
Results: Both groups were comparable for clinical characteristics and presented in the table. Median follow-up was 29 (11-37) months in group 1 and 38 (13-54) months in group 2. The median number of Nivo cycles was 24 (1-41) in group 1 and 20 (5-28) in group 2.

The ORR1 was 65% and the ORR2 was 68% with CR in 35% and 38%, respectively. Two-year PFS1 was 33% and 2-year PFS2 was 35% ($p = 0{,}846$) with median PFS 19,1 mo (95% CI, 14-24) and 20,3 mo (95% CI, 15-25), respectively. Two-year OS1 was 97% and OS2 was 94% ($p = 0.56$) with median OS1,2 not reached in each groups. Allo-HSCT after Nivo therapy was performed in 2 (6%) pts in each group.

Adverse events of any grade were observed in 25 (74%) pts in group 1 and 29 (85%) in group 2. Grade 3-4 AEs were present in 4 (12%) and 5 (15%) pts, respectively.

Patient's characteristics	Group 1 N (%)	Group 2 N (%)	P values
Median age, range	36 (22-51)	33 (22-61)	0,21
Sex male/female (%)	11/23 (32/68)	11/23 (32/68)	1,0
Prior ASCT (%)	8 (24)	8 (24)	1,0
Prior brentuximab vedotin (%)	10 (29)	10 (29)	1,0
Median number of previous lines of therapy, range	4 (2-7)	4 (2-7)	0,89
B-symptoms at Nivo initiation (%)	20 (59)	23 (68)	0,54
Bulky disease at Nivo initiation (%)	3 (9)	4 (12)	0,96
Disease stage at Nivo initiation (%)			
II	5 (15)	5 (15)	0,89
III	2 (6)	3 (9)	
IV	27 (79)	26 (76)	
Status at Nivo initiation (%)			
Partial response (PR)	3 (9)	5 (15)	0.25
Stable disease (SD)	0	2 (6)	
Progressive disease (PD)	31 (91)	27 (79)	

Conclusions: Our analysis demonstrated the comparable efficacy and safety of Nivo 40 mg and 3 mg/kg in r/r cHL.



These results create a basis for further direct comparative study of nivolumab efficacy in different doses.

Disclosure: Nothing to declare.

P115.

Stem Cell Transplantation in Mantle Cell Lymphoma: Post-Transplant Outcomes of Taiwan Blood And Marrow Transplantation Registry

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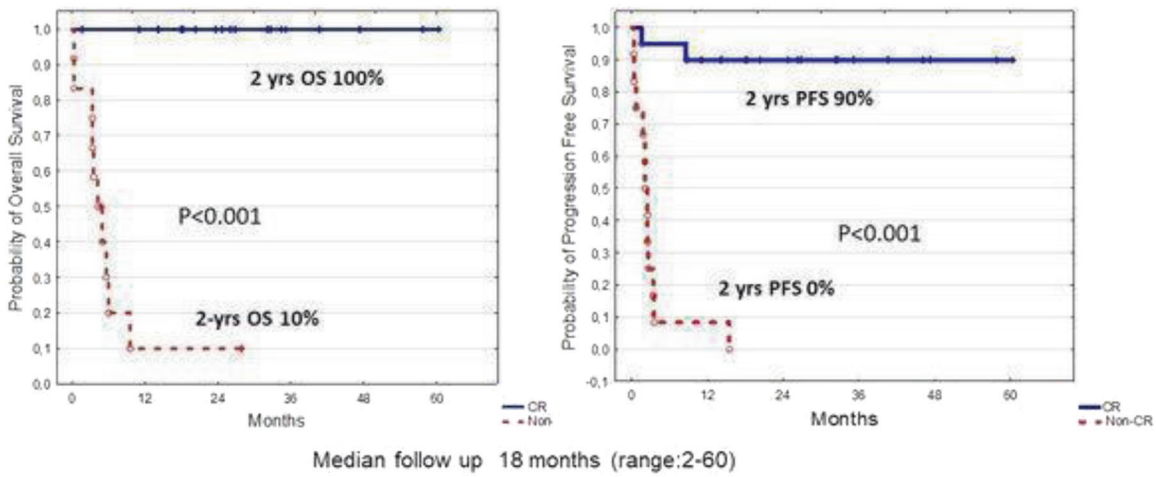
Background: Early consolidative autologous stem cell transplant (auto-SCT) has become the standard of care for mantle cell lymphoma (MCL) patients if eligible, while allogeneic SCT (allo-SCT) is usually reserved as second-line therapy. Since data describing the implementation of transplants in the Asian population are limited, we aimed to report 99 MCL patients in Taiwan and analyze their outcome.

Methods: Patient information was derived from the Taiwan Bone Marrow Transplant Registry database, including auto- and allo-SCT for MCL patients.

Results: From 1999 to 2020, 82 male patients and 17 female MCL patients were enrolled. The median age was 55 years. At diagnosis, the Ann Arbor staging was mostly stage 4 (79.8%), and 74 patients (74.7%) had bone marrow involvement. Regarding morphology subtypes, 86 patients (87%) had a classic type, 11 (11%) had blastoid variant, and pleomorphic variant, 2 (2%). Patients were stratified as low- (41.7%), intermediate- (37.5%), and high- (20.8%) risk according to Mantle Cell Lymphoma International Prognostic Index (MIPI) classification. In total, 94 patients received an auto-SCT, while 13 patients received allo-SCT. Before auto-SCT, 49 patients (52.1%) patients were in their first complete remission (CR1), 16 in second CR, and 29 were in partial remission (PR). Overall, thirty-seven patients (39.4%) had a recurrence of disease after auto-SCT. The median time to post-auto-SCT relapse was 13.1 months (range: 0.7-84). Among thirteen patients receiving allo-SCT, 8 experienced relapses after prior auto-SCT. Five patients received frontline allo-SCT because of insufficient response to prior therapies. Only two (15.4%) patients had a recurrence of MCL after allo-SCT. However, three patients died of infection after allo-SCT. Amidst those receiving allo-SCT, one had disease progression before scheduled auto-SCT; he received ibrutinib as bridging therapy to allo-SCT. Another patient who had a primary refractory disease received ibrutinib with bendamustine and rituximab and was bridged to allo-SCT. Another patient with a blastoid variant relapsed eight months after auto-SCT. She attained PR with venetoclax and underwent allo-SCT.

The median progression-free survival (PFS) and overall survival (OS) post-auto-SCT were 43.6 months and not reached (NR), respectively (Figure 1a). Conceivably, patients with blastoid variant had significantly shorter PFS and OS (25.5 months vs. NR, p=0.015, Figure 1b) than those without. Furthermore, patients who underwent auto-SCT in their first CR had more prolonged survival than those in second CR or PR (NR vs. 66.8 months, p=0.013, Figure 1c). After auto-SCT, patients who had a progression of disease within 12 months post-auto-SCT (POD12) had a significantly inferior OS than those who did not (23.3 months vs. NR, p=0.002, Figure 1d). In multivariable analysis, the presence of blastoid variant,



transplant not in first CR, and POD12 independently predicted worse post-auto-SCT survival.

Figure 1.

Conclusions: This study demonstrated the good PFS and OS conferred by early consolidative auto-SCT and also the prognostic impact of blastoid variant and POD12 in Asia patients, corroborating with the treatment landscape for MCL in western countries. Meanwhile, novel agents may play a role in bridging high-risk patients to subsequent allo-SCT, which was also demonstrated feasible in the frontline setting for selected patients.

Disclosure: Nothing to declare.

P116.

Autologous Hematopoietic Cell Transplantation For High Grade B-Cell Lymphoma with Myc And Bcl2 and/or BCL6 Rearrangements. A Single Institution Experience

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Background: High grade B-cell lymphoma (HGBL) with MYC and BCL2 and/or BCL6 rearrangements is defined in 2016 WHO Classification as a new entity distinct from DLBCL, with poor prognosis. Outcome data for HGBL patients who receive high dose therapy and autologous hematopoietic cell transplantation (auto-HCT) are limited and debatable.

Methods: Here, we evaluated outcome of 32 patients with HGBL who received auto-HCT after first or subsequent line therapy in Department of Lymphoid Malignancies Maria Sklodowska-Curie National Research Institute of Oncology between 2015-2019. Median age (range) was 48 (23-67), high risk International Prognostic Index (IPI) score was present in 66% of patients. R-CHOP, DA-EPOCH-R or CODOX M/IVAC regimens were used for remission induction treatment in 8(25%), 17(53%), and 7(22%) cases, respectively.

Results: Eighteen patients achieved complete remission (CR) after initial treatment and 20 patients were in CR before transplantation. In total, 23 patients had transplantation after first-line treatment, and 9 patients - after second or third-line treatment. At a median follow-up of 18 months (range: 2-60 months), 2-year progression free survival (PFS) and overall survival (OS) post-HCT was 56% (95%CI: 41; 71%) and 69% (95%CI: 55; 84%) for the whole group. Relapse/progression after transplantation occurred in 14 patients with a median time to relapse/progression (range) of 2 (1-15) months. Factors adversely related to PFS and OS were non-CR before transplant and R-CHOP regimen used in induction treatment: 2-year PFS and 2-year OS was 90% vs 0% ($p < 0.001$) and 100% vs 10% ($p < 0.001$) for CR vs non-CR, respectively; 2-year PFS and 2-year OS was 39% vs 64% vs 66% ($p = 0.001$) and 45% vs 80% vs 78% ($p = 0.005$) for R-CHOP vs DA-EPOCH-R, CODOX -M, respectively. Number of treatment lines before HCT had no influence on PFS or OS: 2-year PFS and 2-year OS 62% vs 48% and 78% vs 58% (for both: p=NS) for first line vs subsequent lines.

Conclusions: in conclusion, regardless of previous number of therapy lines, patients with HGBL in CR before HCT have a good outcome, if initially treated with a regimen more intensive than R-CHOP.

Disclosure: Nothing to declare.

P117.

Autologous Stem Cell Transplant in Non Hodgkin Lymphoma at Aiims: Trends in Tolerability And Long Term Outcomes

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Background: Autologous stem cell transplant (ASCT) is the standard treatment in relapsed/ refractory non-Hodgkin lymphoma (NHL). Data from Indian subcontinent is sparse in the literature.

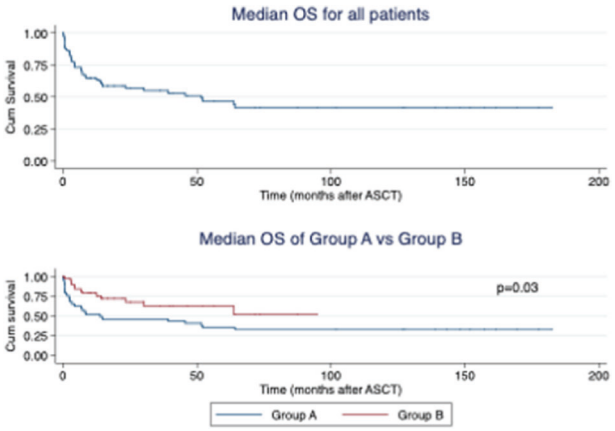
Methods: Adult NHL patients who received ASCT from 2002 to 31st March 2020 at our institute were retrospectively analysed. Toxicities, complications and long-term outcomes were compared between the patients undergoing transplant during 2002-2012 (Group A, $n = 37$) and 2013 – 2020 (Group B, $n = 37$).

Results: All 74 patients received GCSF mobilised stem cells from peripheral blood after high dose chemotherapy, most commonly BEAM- BCNU, Etoposide, cytosine Arabinoside and Melphalan ($n = 59$). At a median follow

up of 39.9 months, median event free survival (EFS) did not reach for whole cohort and was not different in two groups (p= 0.21; HR = 0.60, 95%CI 0.27-1.32). Median overall survival (OS) for all patients was 51.6% (figure 1); being superior in group B ($p = 0.03$; HR = 0.47, 95% CI 0.24-0.94). In multivariate analysis, higher International prognostic index (IPI) at diagnosis ($p = 0.006$; HR = 3.0, 95%CI 1.37-6.77) and pre-transplant hypoalbuminemia (P=0.02; HR = 2.8, 95%CI 1.13-6.99) were predictive of poor outcomes.

Patient characteristics are compared in table 1. Patients in group B received higher stem cell dose due to increased use of plerixafor, had lower median time to platelet (14 vs 19 days, $p < 0.001$) or neutrophil (11 vs 15 days $p < 0.001$) engraftment and experienced significantly reduced early (day 30) transplant related mortality (2.7% vs 21.6%, $p = 0.028$). Patients in group B also required less supportive care in terms of median antibiotic days (11 vs 16, $p = 0.020$), antibiotic number (4 vs 5, $p = 0.006$), number of PRBCs (3 vs 2 units, $p = 0.030$) or single donor platelets (5 vs 3 units, $p = 0.002$), days of GCSF injections (17.5 vs 12, $p < 0.001$) and had shorter hospital stay (19 vs 25 days, $p = 0.025$). Incidence of grade 3/ 4 mucositis decreased (63.9% vs 80%, $p = 0.006$) after 2012 while other organ related toxicities (pneumonia, sepsis, shock, renal dysfunction) were similar in two groups. Two (2.7%) patients developed secondary malignancy (both head and neck cancers) and there was no difference in long term toxicities among patient groups.

Variable	Group A	Group B	Overall cohort	P value
Age at transplant, median (IQR)	36(22-56)	30(25-60)	37.5(22-60)	0.691
Gender, n				
Female/Male	8/29	8/29	16/58	1.000
Diagnosis, n(%)				
B cell/T cell	25/12	30/7	55/19	0.183
Baseline Stage, n (%)				
1/2	11(31.4)	14(37.8)	25(34.7)	0.568
3/4	24(68.5)	23(62.1)	47(65.2)	
IPI category, n (%)				
0-2	19(76.0)	23(69.7)	42(72.4)	0.595
3-5	6(24.0)	10(30.3)	16(27.5)	
Pre-transplant disease status, n (%)				
CR/PR/PD	27(73)/5 (13.5)/5 (13.5)	23(62.2)/12 (32.4)/2(5.4)	50(67.6)/17 (23)/ 7(9.4)	0.095
Pre transplant albumin, n (%)				
Normal (> 3.5mg/dl)	31(83.8)	32(86.5)	63(85.1)	0.500
Low (<3.5mg/dl)	6(16.2)	5(13.5)	11(14.9)	
Conditioning regimen, n				
BEAM/LEAM/Other	26/9/2	33/0/4	59/9/6	0.002
Stem cell dose, median (IQR), million cells/kg	2.1(0.9-5.2)	2.5(1.8-5.4)	2.3(0.9-8.3)	0.015



Conclusions: ASCT improves survival in relapsed/ refractory NHL. IPI at diagnosis and pre-transplant serum albumin level predict survival. Better supportive care and refined expertise of transplant physician contributed to improved outcomes in group B.

Disclosure: Nothing to declare.

P118.

POLA-BR After CAR-T Cell Therapy Failure in R/R Diffuse Large B-CELL Lymphoma

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Background: Anti-CD19 CAR-T cell therapy is a promising method of immunotherapy for patients with relapsed or refractory Diffuse large B-cell lymphoma (r/r DLBCL). However, up to 60% of patients have progression or relapse of the disease after CAR-T cell therapy. The outcomes for this patient population still remain dismal and therapeutic options are limited. CD79b is a B-cell receptor component and expressed in DLBCL. The antibody-drug conjugate polatuzumab vedotin is an anti-CD79b antibody linked to microtubule-disrupting monomethylauristatin E. Polatuzumab vedotin in combination with bendamustine and rituximab (Pola-BR) demonstrated efficacy in patients with r/r DLBCL. This case series describes efficacy of Pola-BR treatment after failure of CAR-T cell therapy.

Methods: We analyzed the data of $n = 4$ patients with r/r DLBCL who had progression after anti-CD19 CAR-T cell therapy received Pola-BR treatment: bendamustine 90 mg/m2 on days 1 and 2, rituximab 375 mg/m2 on day 1 and polatuzumab vedotin 1,8 mg/kg on day 1 of each 21-day

cycle. The PET-CT scan was performed before treatment initiation and after 2, 4, 6 cycles of Pola-BR. The responses were evaluated using Lugano 2014 criteria.

Results: We describe four patients with histologically confirmed DLBCL (de novo DLBCL $n = 3$, DLBCL, transformed from follicular lymphoma (t-DLBCL) $n = 1$) with median age 50 (range 33-60) years. Two patients had primary chemoresistant disease, the median lines of previous therapy was 6 (range 5-10) lines and $n = 1$ patient received autologous stem cell transplantation. All patients had disease progression after anti-CD19 CAR-T cells therapy. Median number of Pola-BR cycles was 4 (range 2-6) cycle. After Pola-BR treatment complete response (CR) was achieved in 2 patients, and 2 patients had disease progression. CR was registered in 54 y.o. male with t-DLBCL and 60 y.o. woman with de novo DLBCL after 2 and 4 cycle of Pola-BR, respectively, this patients are alive in CR for 7 months. Disease progression was registered in 33 y.o. male with de novo DLBCL (bulky disease) and 45 y.o. male with de novo DLBCL after 1 and 2 cycle, respectively, and died 2-4 month after start of Pola-BR treatment.

Conclusions: Patient with r/r DLBCL progressing after CAR-T cell therapy have a poor prognosis. Pola-BR is one of the therapeutic options for this group of patients.

Disclosure: Nothing to declare.

P119.

Nodal peripheral T-Cell Lymphoma – The Role of Consolidative Autologous Stem Cell Transplantation in Complete Or Partial First Remission: A 10-Year Lesson From Singapore General Hospital

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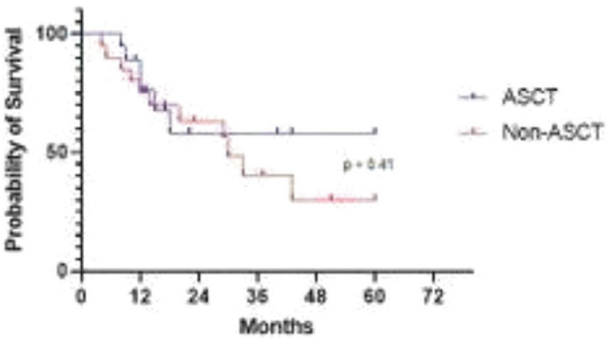
Background: Autologous stem cell transplantation (ASCT) as consolidation therapy in patients with nodal peripheral T-cell lymphoma (PTCL) who attain complete or partial first remission (CR1 or PR1) following induction chemotherapy is not a universally accepted standard of care.

Methods: This is a retrospective study from the lymphoma registry of the Department of Hematology, Singapore General Hospital. Patients with histologically confirmed nodal PTCL (excluding ALK-positive anaplastic large cell lymphoma) treated with curative intent chemotherapy between 2010 and 2020, for whom there was complete long-term follow-up data were selected. Only those achieving CR1 or PR1 (as defined by CIBMTR criteria) were included for analysis. Response to induction therapy and whether they were treated with ASCT as consolidation was recorded. The decision for ASCT was at physician and patient discretion. Follow-up data was recorded up until August 2020.

Results: A total of 39 patients with nodal PTCL achieving CR1 or PR1 were identified. Of these, 19 underwent consolidation ASCT (ASCT group) and 20 did not (non-ASCT group). 79% in the ASCT group and 80% in the non-ASCT group achieved CR1 following induction treatment; the remainder were in PR1. The two groups did not differ significantly in age, gender proportion, stage at diagnosis or ECOG performance status. CHOP-based induction chemotherapy was used in 85% of patients in both groups. Of those undergoing ASCT, 95% received carmustine, etoposide, cytosine arabinoside and melphalan (BEAM) conditioning therapy.

Kaplan-Meier survival analysis was used to compare event free survival (EFS) and overall survival (OS) between the ASCT and non-ASCT groups (Figures 1 and 2). EFS was defined as PTCL relapse or all-cause mortality. Median follow-up in surviving patients was 19.5 months (ASCT group) and 34 months (non-ASCT group). At the end of follow-up, 16 (84%) and 12 (60%) patients remained alive in the ASCT and non-ASCT groups, respectively.

There was no significant difference (by logrank test) between the two survival curves in both EFS ($p = 0.41$) and OS ($p = 0.42$). Median EFS was 30 months (non-ASCT) and not reached in the ASCT group. Median OS was not reached in either group. 2-year EFS was 65% (ASCT) and 63% (non-ASCT). 2-year OS was 83% (ASCT) and 78% (non-ASCT). 3 patients (15%) in the non-ASCT group subsequently received ASCT following disease relapse after attaining CR2 (2 patients) and CR3 (1 patient).



Conclusions: Patients undergoing consolidative ASCT show some benefit in terms of EFS and OS. This was not, however, statistically significant, likely due to small patient numbers and limited follow-up. This study is also biased by its retrospective methodology. Importantly, patients in the ASCT and non-ASCT groups did not differ significantly in terms of age or performance status, indicating that this did not impact on the decision for ASCT. However, the ASCT group had a larger proportion of patients requiring more than 1 line of induction therapy, suggesting that this was a higher risk group which may benefit from ASCT. This observed trend towards the benefit of consolidative ASCT needs to be followed up with larger-scale prospective studies.

Disclosure: No conflict of interest.

P120.

Successful Treatment of Hepatosplenic T-Cell Lymphoma with Intensified Myeloablative Conditioning Regimens Followed by Unmanipulated Haploidentical Hematopoietic Stem Cell Transplantation

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Background: Hepatosplenic T-cell lymphoma (HSTCL) is an uncommon and aggressive form of peripheral T-cell lymphoma with a median survival of approximately 10 months.

Methods: We reported the clinical outcomes of 3 patients (age at 2.5, 21 and 29) diagnosed with HSTCL who underwent haploidentical hematopoietic stem cell transplantation (haplo-HSCT). Bone marrow biopsy and aspiration were performed and analyzed with morphologic, immunologic, cytogenetic and molecular classification technique (MICM) in all 3 patients. Biopsy of the spleen was performed if possible to confirm the diagnosis. Intensified myeloablative conditioning (MAC) regimens were administered as follows: the adult patients were given CLAG (G-CSF 300ug/d×6, cladribine 5mg/m2/d×5, cytarabine 2g/m2/d×5) or VP-16 (15mg/kg) plus TBI (2Gy×6), cyclophosphamide plus anti-thymocyte globulin (ATG). The pediatric patient was treated with CLAG plus busulfan (1.2mg/kg×16), cyclophosphamide plus ATG. Cyclosporine, short-term methotrexate, and mycophenolate mofetil were used for graft-versus-host disease (GVHD) prophylaxis.

Results:

case	age (yrs)	gender	T cell type	chromosome abnormities	disease course before Tx	disease status before Tx	conditioning regimes	events after Tx	status after Tx
1	2.5	male	γδ	r(7),add(2)	8 mo	NR	CLAG +BuCy	IV aGVHD, cGVHD	DFS at 3 mo
2	21	female	γδ	complex with +8	6o	MRD +CR	VP16 +TBICy	VOD, cGVHD	DFS at 7 mo
3	29	female	αβ	-X, i(7), +8	3mo	MRD +CR	CLAG +TBICy	cGVHD	DFS at 9 mo

Two cases were γδ type and one was αβ type. Chromosomal abnormities of i(7)/r(7) were identified in 2 cases and +8 in 2 cases. STAT5B was detected in 2 patients. All 3 cases had BM involvement and 1 had central nervous system involvement. Hemophagocytic lymphohistiocystosis (HLH) was documented in one patient and was controlled with HLH94 regimen plus ruxolitinib before haplo-HSCT. Two adult patients showed significant splenic retraction and achieved complete remission (CR) of their BM, but both were minimal residual disease (MRD) positive by multicolor flow cytometry. The pediatric patient was refractory after 5 cycles of chemotherapy and had hepatomegaly after splenectomy. The disease courses for the 3 patients before transplant were 2, 6 and 8 months, respectively. No graft failure was observed after transplant. Grade IV GVHD involving skin and gastrointestinal tract was identified on Day 19 post-transplant in the pediatric patient which was successfully controlled. Veno-occlusive disease was documented on Day 57 in the adult with HLH pre-transplant and was successfully managed. To the date of December 12, 2020, with follow-up time at 3, 7 and 9 months after transplant, all 3 patients responded well with only limited chronic GVHD. All the patients were disease-free after transplant and achieved full chimerism of donor.

Conclusions: Considering the high risk and poor prognosis of HSTCL, our encouraging clinical results here showed that intensified MAC followed by haplo-HSCT can be considered as a safe and effective therapy for HSTCL.

Disclosure: Nothing to declare.

Minimal Residual Disease, Tolerance, Chimerism and Immune Reconstitution

P121.

Empiric Granulocyte-Colony Stimulating Factor (G-CSF) Adversely Impacts Survival After Allogeneic Stem Cell Transplantation (HCT) Performed with Thymoglobulin: A Cibmtr Analysis

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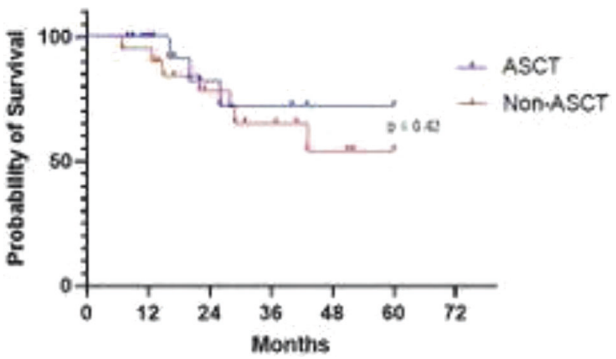
Background: The in vivo depletion of recipient and donor T-lymphocytes using anti-thymocyte globulin (ATG) is a widely adopted approach to reduce both graft rejection and graft-versus-host disease (GVHD) in allogeneic HCT. However excess toxicity to incoming donor lymphocytes may delay immune reconstitution – compromising graft versus tumor effects, and increasing infections and viral reactivations. In vitro data suggests that G-CSF administered early after HCT might increase the neutrophil-mediated phagocytosis of ATG-coated lymphocytes, adversely affecting immune reconstitution (de Koning, Blood Adv 2018). We were interested in the effect of G-CSF on HCT outcomes after ATG.

Methods: From the Center for International Blood and Marrow Transplant Research (CIBMTR) registry, we studied adult patients with myeloid disease who underwent peripheral blood HCT using ATG between 2010 and 2018 from a matched sibling/unrelated or 1-locus mismatched unrelated donor. We examined for an effect of planned G-CSF administered through day +12 post-HCT on outcomes. Those who received G-CSF after day +12 as empiric/interventional therapy were excluded. Our main outcome of interest was relapse. Other endpoints were overall survival (OS), disease-free survival (DFS), treatment-related mortality (TRM) and GVHD. Analyses were adjusted for patient, disease and treatment-related factors.

Results: in a cohort of 874 patients, 459 patients (53%) received planned G-CSF. The majority of HCTs were from matched unrelated donors (77% with G-CSF/80% without G-CSF). All received calcineurin inhibitor and MTX/MMF as GVHD prophylaxis. Groups were well-matched for all variables. All patients received thymoglobulin (median dose 4.5 mg/kg for both groups). Median time to neutrophil recovery was 12 days with G-CSF and 15 days without. Neutrophil recovery at day +28 was 98% in both groups. Planned G-CSF had no effect on relapse at 1 year (HR 1.19, $p = 0.17$) but significantly increased TRM (HR 2.03, $p < 0.0001$) with a consequent negative effect on DFS (HR 1.42, $p = 0.0006$) and OS (HR 1.52, $p = 0.0005$). There was no difference in acute or chronic GVHD between groups. The incidence of viral infections by 6 months was higher in G-CSF recipients (56% vs. 47%, $p = 0.007$), with a particular increase in EBV infections (34% vs. 26%).

Table: Adjusted probabilities of GVHD, relapse, TRM, DFS and OS

	HCT with G-CSF	HCT without G-CSF	p-value
D100 2-4 Acute GVHD	39% (95% CI 34-43)	38% (95% CI 33-42)	0.74
D100 3-4 Acute GVHD	14% (95% CI 11-17)	12% (95% CI 9-15)	0.47
1yr Chronic GVHD	33% (95% CI 29-37)	37% (95% CI 33-42)	0.21
1yr Relapse	31% (95% CI 27-35)	30% (95% CI 26-35)	0.77
1yr TRM	21% (95% CI 18-25)	12% (95% CI 9-15)	0.0001
1yr DFS	47% (95% CI 43-52)	58% (95% CI 53-63)	0.0010
1yr OS	61% (95% CI 56-65)	72% (95% CI 68-76)	0.0004



Conclusions: in conclusion, planned G-CSF administered early after allogeneic HCT performed with thymoglobulin has a significant negative effect on survival due to a twofold increase in TRM and increased viral infections.

Disclosure: Claudio Brunstein has received research funding from Astex, Fate Therapeutics, Gamida, Magenta Therapeutics and Nant, and consulting fees for Allovir.

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The remaining authors have no disclosures.

P122.

Predictive Meaning of Mrd Conversion On Days +30 And +100 in Patients with Aml After ALLO-SCT

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Background: Though several studies already reported on a role of post-transplant MRD monitoring regarding the post-transplant outcomes, the meaning of post-transplant MRD conversion and its' timing remains controversial. In this study we analysed prognostic relevance of MRD conversion (positive > negative) on days +30 and +100 in pre-transplant MRD+ patients.

Methods: A total of 96 patients (males, $n = 53$) with median age of 58 years (21-80) were included. Most of them had de novo AML (75%), were in 1 CR (81%), had intermediate ELN risk (54%), and received allografts from unrelated donors (68%) after myeloablative conditioning (79%). The MRD data on days +30 and +100 were available in 47 (converted, $n = 24$, 52%) and 50 patients (converted, $n = 29$, 60%), respectively. MRD was assessed with multicolored flow cytometry according to "different from normal" strategy on bone marrow samples. The sensitivity was 10-4 to 10-5.

The patients who developed MRD conversion on day +30 showed a trend to have rather ATG than post-transplant cyclophosphamide as immunosuppression (20/22, 91% vs 15/22, 68%, $p = 0.066$). However, we did not observe this difference regarding the day +100. Patients who achieved MRD conversion on day +100 tended to receive chemotherapy in combination with tyrosine kinase inhibitors (midostaurin or sunitinib) prior to allo-SCT (8/29, 28% vs 0%, $p = 0.057$) compared with patients with MRD persistence.

Results: The 5-year OS and LFS ($n = 96$) were 55% (95% CI 43-66%) and 36% (95% CI 23-52%), respectively. The relapses and NRM at 5 years were 52% (95% CI 38-66%) and 13% (95% CI 7-23%), respectively. Patients without day +100 MRD conversion had worse outcomes (5-year OS: 44%, 95% CI 23-68% vs 83%, 95% CI 63-93%, $p = 0.032$) due to higher relapses (63%, 95% CI 38-83% vs 27%, 95% CI 12-51%, $p = 0.046$) compared with converted patients. Regarding the other factors, we observed higher 5-year OS for female patients (69%, 95% CI 52-82% vs 44%, 95% CI 30-60%, $p = 0.044$) compared with males with a trend to low relapses in the female group (42%, 95% CI 25-61% vs 57%, 95% CI 38-74%, $p = 0.09$). Older (>58 years) patients experienced higher NRM (28%, 95% CI 15-45% vs 0%, $p < 0.001$) resulting into lower OS (40%, 95% CI 26-56% vs 68%, 95% CI 51-81%, $p = 0.003$) compared with younger (≤58 years). Further, we provide a multivariate models including patients' age, patients' sex, cytogenetics at diagnosis, ELN risk, conditioning and MRD conversion on days +30 or +100. Regarding the day +30, we did not found any significant impact of MRD conversion on outcomes. Regarding the day +100, we found significant impact of MRD conversion on relapses (3.2, 95% CI 1.2-8.4, $p = 0.02$), OS (3.6, 95% CI 1.1-11.8, $p = 0.033$) and LFS (3.5, 95% CI 1.4-8.6, $p = 0.008$).

Conclusions: The MRD conversion on day +100 but not on day +30 is associated with improved survival outcomes due to low relapses for pre-transplant MRD+ patients with AML.

Disclosure: Nothing to declare.

P123.

MRD vs Chimerism: Are Their Effectiveness Comparable to Predict Aml Relapse?

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Background: Acute Myeloid Leukemia (AML) presents a high level of relapse in the first 18 months after Hematopoietic stem cells transplantation. Effectiveness of relapse diagnosis is a crucial point for patient management and survival.

Methods: We retrospectively evaluated a French cohort of 178 patients transplanted for AML between 2009 and 2018 in Lyon hospital. Among 178 patients, 58 relapsed (32.6%) and 29 occurred during the first 15 months (10.6%).

MRD analysis was performed on bone marrow or whole blood by Immuno-Phenotyping or Molecular Biology method. Chimerism analysis was performed by real time PCR on bone marrow, whole blood, CD33 and CD34 sorted cells. All patients were tested at predefined time-points after transplantation and positive thresholds were defined for each technique.

Complete data were available for 22/29 patients. We compared for both techniques, their ability to detect recurrence of molecular recipient markers before clinical relapse. After engraftment, the relapse was evaluated by the day difference between each technique to give a positive result.

The 22 patients were 6 males and 16 females, median age was 55 years old, conditioning regimen was FLAMSA for 72% of cases, myeloablative for 9% of cases and reduced for 19%.

Results: The analysis reveals no significant differences between both techniques to detect molecular relapse. They are equally effective and become positive again in the same

delay post transplantation predicting the apparition of a relapse, confirmed by clinical data.

The evaluation of chimerism in cellular subsets such as CD33 or CD34 was limited due to the low number of available data. But no significant difference was outlined in comparison with whole blood.

Conclusions: The study of 22 LAM transplanted patients with early relapse revealed an unexpected comparable effectiveness of chimerism or MRD to detect a relapse. This shows that both techniques could be used equally after transplantation. Chimerism provides reliable results with sensitive method such as quantitative real time PCR, and could be a surrogate marker in the absence of a suitable specific MRD marker. Interestingly, it allows to follow the response after relapse treatment and to give an orientation for the therapeutic strategy.

Clinical Trial Registry: NA.

Disclosure: No conflict of interest.

P124.

Cellular Chimerism – Do Repeated Marrow Biopsies Open A Window For Relapse Intervention?

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Background: Chimerism monitoring is often used to guide therapy after reduced intensity *stem cell transplantation* (RIC-SCT) with the intent of reducing relapse risk, however there is no consensus on the frequency of monitoring or use of lineage specific chimerism. The University Hospital of Wales (UHW) uses consecutive marrow biopsies assessing *Bone Marrow Mononuclear Cells* (BMo) and *Myeloid Cells* (BMy) with *Blood T Cells* (PBT) at 1, 2, 3, 6, 12, 18 and 24 months post SCT. When available, molecular markers are also tested. We set out to evaluate whether serial chimerism monitoring could predict disease relapse and if so whether there was opportunity to intervene.

Chimerism status is defined as "full", "mixed" or "falling" if the fraction of donor cells is >95%, stable within 10% or dropping by >10% compared to last examination respectively. Relapse is defined as hematological or *Minimal Residual Disease* (MRD) if molecular.

Methods: Patients with acute leukemia (Acute Myeloid Leukemia (AML) or Acute Lymphoblastic Leukemia (ALL)), Myelodysplastic Syndrome (MDS), Chronic Myelomonocytic Leukemia (CMML), Myeloproliferative Neoplasms (MPN) or Chronic Myeloid Leukemia (CML) who received first RIC-SCT between 2008-2017 were included. Demographics are summarised in Table 1.

Table 1: Demographics.

Parameter		Relapse (N=67, MRD=7/67)	Non-Relapse (N=153)
Sex	- Male	43(64,2%)	75(49,0%)
	- Female	24(35,8%)	78(51,0%)
Median Age (Range) in years		59(27-72)	59(34-74)
Disease	- AML	40(59,7%)	92(60,1%)
	- MDS	10(14,9%)	23(15,0%)
	- Others	17(25,4%)	38(24,9%)
Transplant Type	- MUD	51(76,1%)	114(74,5%)
	- SIB	16(23,9%)	38(24,8%)
	- HAPLO		1(0,7%)

The majority of patients, 210/220(95,5%) received *FMC* (Fludarabine, melphalan, campath), *FLAMSA-Bu-ATG* (Fludarabine, amsacrine, cytarabine, busulfan, ATG) or *FB-ATG* (Fludarabine, busulfan, ATG) conditioning.

Results: Twenty two patients were excluded from analysis either due to early death or missing chimerism data. On analysis of all patients with falling chimerism (FaCC), 38/86(44,2%) relapsed whereas only 17/91(18,7%) relapsed in the full chimerism cohort. Most relapses, 54/67 (80,6%) occurred in the first 2 years post SCT, at a median of 317 (40-3060) days with only 15/67(22,4%) patients alive at last follow-up.

In all cases with FaCC, 58/86(67,4%) patients observed a fall in PBT lineage, whereas in 37/86(43,0%) a fall in BMo lineage was detected. This trend was also observed for patients who subsequently relapsed. On analysis of the 38 relapse patients with FaCC, 21/38(55,3%) had an interval from falling chimerism to relapse of a median of 187 (7-2675) days whereas in 17/38(44,7%) had no warning signal and chimerism fell at the same time as relapse.

In the non-relapse cohort we found 48/153(31,4%) with FaCC, 31 of which received Donor Lymphocyte Infusions (DLI) with 20/31(64,5%) alive at last follow up. Of note 22/31 (71%) patients attained full donor chimerism following DLI.

Conclusions: Serial chimerism monitoring can offer a signal for potential relapse and offers a potential window of opportunity to intervene with donor lymphocytes or withdrawal of immunosuppression. PBT chimerism monitoring alone fails to offer sufficient sensitivity whilst the addition of serial marrow chimerism identifies additional patients at risk of relapse. Larger studies of lineage specific chimerism

to standardise care and improve methods of MRD-monitoring are urgently needed.

Disclosure: Nothing to declare.

Multiple Myeloma

P125.

High-Dose Melphalan And Autologous Stem Cell Transplantation in Elderly Patients ≥ 70 Years is Safe And Effective – A Retrospective Analysis

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Background: Despite the increase of novel therapeutic options, high-dose melphalan is still a standard consolidation strategy in patients with newly diagnosed multiple myeloma (NDMM) responding to first-line induction and eligible for transplantation (TE). Median progression-free survival (PFS) is 2-3 years in patients without maintenance treatment and 3-5 years in patients receiving lenalidomide maintenance. Most clinical trial protocols exclude elderly patients aged 70 years or older. We performed a retrospective single-center study to analyse the safety and efficacy of high-dose melphalan in this age-group.

Methods: We reviewed 59 patients with NDMM aged ≥70 years who underwent high-dose melphalan treatment and autologous stem cell transplantation at our department from 2008 to 2019. We retrospectively analysed patient characteristics, leukapheresis data and outcome parameters.

Results: Median age of the cohort was 71 years (range 70-74 years). Induction treatment consisted of PAD, VCD, VMP or VD. All patients received chemo-mobilisation with CAD. A median of 3,64x106 (range 2-9,9 x106) CD34+ stem cells/ kg bw was collected in a median of one apheresis session (range 1-3). State of remission prior to high-dose treatment was CR in 10 (17%), VGPR in 37 (63%) and PR in 12 (20%) patients. The median HCT-CI score was one (range 0-6).

There was no non-relapse mortality. One patient (1,7%) died before day +100 and in total five (8,5%) patients died before day +365. All early fatal outcomes were related to disease progression. with a median follow-up of 1976 days (185-3387 days) the median PFS was 28 months (95% CI 18 – 38 months). Median time to next treatment was 30 months (95% CI 20 – 40 months). Fifteen of 59 patients (25%) had received a lenalidomide maintenance after transplant. The median overall survival (OS) was 86 months (95% CI 59-112 months).

Conclusions: We conclude that high-dose melphalan is a safe and efficacious option for selected TE patients aged ≥70 years leading to clinically relevant PFS and TTNT even without maintenance strategy. While new antibody-based treatment options are available for patients over 70 years, these involve continuous therapy until progression. Our results suggest that the combination of induction therapy and high-dose therapy without maintenance could provide a valid alternative with a treatment duration of only about 6 months and a median time to next treatment of 30 months. Prospective studies are warranted.

Disclosure: The authors have nothing to disclose regarding this retrospective study.

P126.

Pegylated G-CSF Versus G-CSF Following HD-CTX For PBSC Mobilization And Hematopoietic Reconstitution After ASCT in Newly Diagnosed Multiple Myeloma Patients

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Background: The aim of this prospective single center study is to compare Pegylated G-CSF (PEG-G-CSF) versus granulocyte colony-stimulating (G-CSF) following high dose cyclophosphamide for peripheral blood stem cell (PBSC) mobilization and hematopoietic reconstitution after auto-stem cell transplantation (ASCT) in newly diagnosed multiple myeloma(MM) patients.

Methods: A total of 110 patients were randomly divided into Pegylated G-CSF ($n = 48$) or G-CSF group ($n = 62$) which were all followed HD-CTX. We conducted a randomided trial comparing the outcomes of pegylated G-CSF 6mg on day 2 and G-CSF 5ug/kg daily from day 2 onwards in cyclophosphamide PBSC mobilization.Peripheral white cell was checked everyday. The comparison was made between peripheral blood stem cell yields, nember of apheresis, and the time to neutrophil and platelet engraftment after ASCT.

Results: The median number of collected PB CD34+ cells was 7.00×106/kg in PEG-G-CSF group and 7.15×106/kg in G-CSF group($p = 0.608$).The median number of apheresis was 2.46 in PEG-G-CSF group and 2.58 in G-CSF group ($p = 0.504$). The rate of mobilization was 91.89% in PEG-G-CSF group and 93.48% in G-CSF group ($p = 0.436$). The number of transfusion platelet was 0.271

in PEG-G-CSF group and 0.356 in G-CSF group ($p = 0.031$).The days and the cost in hospital of PEG-G-CSF group is shorter and cheaper than G-CSF group during mobilization. The number of subcutaneous was 1 time in PEG-G-CSF group and 12.17 times in G-CSF group ($p = 0.000$). The day of neutrophil engraftment post transplantation was 9.78 in PEG-G-CSF group and 10.72 in G-CSF group ($p = 0.047$), and also the day of platelet engraftment was 10.11 in PEG-G-CSF group and 11.27 in G-CSF group ($p = 0.016$).

Conclusions: We can conclude that Pegylated G-CSF following HD-CTX is at least equally successful as G-CSF following HD-CTX, but the toxic and side effect is less. Pegylated G-CSF can reduce the day of neutrophil and platelet engraftment post transplantation.

Disclosure: No conflict of interests.

P127.

Recombinant Human Thrombopoietin Improved Platelet Engraftment After Autologous Hematopoietic Stem Cell Transplantation in Patients with Newly Diagnosed Multiple Myeloma

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Background: To evaluate the efficacy and safety of recombinant human thrombopoietin (rhTPO) for hematopoietic reconstitution after autologous stem cell transplant (ASCT) in patients with newly diagnosed multiple myeloma (NDMM).

Methods: 35 cases with NDMM had been enrolled into a prospective clinical trial from Mar 2014. The hematopoietic reconstitution was compared between the above 35 cases (rhTPO group) and 98 historic cases not receiving rhTPO (control group) after stem cell reinfusion.

Results: 35 (100%) cases receiving rhTPO achieved both neutrophil and platelet engraftment within 30 days post-transplant. The median time to neutrophil and platelet engraftment were the 10th and 11th day after stem cell reinfusion. Multivariate analysis showed that rhTPO administration was an independent factor for accelerating platelet engraftment (HR 1.789, 95% CI 1.157-2.770, $p = 0.009$). Subgroup analysis showed that rhTPO improved platelet engraftment and alleviated platelet transfusion needs in patients with low re-infused CD34+ cell counts of < 2*109/L. All 35 patients tolerated rhTPO well. Survival analysis showed no decrease on TTP or OS by rhTPO application.

Conclusions: rhTPO accelerated the platelet engraftment after ASCT in patients with NDMM with good tolerability and long-term safety, especially for those patients with poor re-infused CD34+ cell counts. rhTPO might be recommended to be used early after ASCT for patients with NDMM.

Clinical Trial Registry: Chinese Clinical Trial Registry (ChiCTR1800017025).
http://www.chictr.org.cn/showprojen.aspx?proj=28871.

Disclosure: The authors declare no conflict of interest in relation to the work described.

P128.

Autologous Stem Cell Transplantation For Elderly Multiple Myeloma Patients – A Safety Option

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Background: High-dose therapy with melphalan followed by autologous stem cell transplant (HDT/ASCT) is the standard of care for fit patients with multiple myeloma (MM). Although being recommended in patients with up to 70 years old, safety and outcome data of ASCT for patients older than 65 years is still unclear and controversial.

Methods: Retrospective analysis of clinical records of patients with 60 or more than 60 years with newly diagnosed MM who underwent the first ASCT between January 2008 and November 2020, in a single institution. Patients were divided into two age groups: 60-65 and > 65 years. Toxicity was evaluated according to CATAE v4 and efficacy following IMWG criteria. The primary outcome was overall survival (OS) and secondary outcomes included toxicity and response at day +100 after ASCT (CR - complete response or VGPR - very good partial response). Statistical analysis was performed using SPSS v26.

Results: One hundred and fifty-four ($n = 154$) patients were included: 57.1% ($n = 88$) were female and the median age at diagnosis was 64 years [50-70]. The most frequent subtype was IgG (53.7%, $n = 84$) and the median of previous lines before ASCT was 1 [1-3]. The 60-65 and >65 years groups included 83 and 71 patients, respectively. Groups' homogeneity was verified, with no significant differences regarding gender, MM International Staging System (ISS) score and response rates after induction

therapy. HDT with melphalan 140 mg/m2 was more frequent in group of >65 years (10 vs 3 patients; $p = 0.017$) and melphalan 200 mg/m2 was administered to 85.5% of >65 years patients ($n = 59$). Comparing toxicities (60-65 vs >65 years), we haven't found differences in the mean duration of neutropenia <0.5 G/L (6.6 vs 7.6 days; $p = 0.330$), thrombocytopenia <20 G/L (5.7 vs 5.1 days; $p = 0.439$), platelets/erythrocytes transfusion needs ($p = 0.548$/$p = 0.267$) or oral/gastrointestinal mucositis severity ($p = 0.430$/$p = 0.858$). Median time to engraftment was longer in >65 years patients (12.6 vs 13.4 days; $p = 0.056$). We found no statistically significant differences between both groups in the response at day +100 after ASCT ($p = 0.982$) and regarding median overall survival (NR vs. 92 months; $p = 0.446$).

Conclusions: in our cohort, elderly MM patients have neither more toxicity nor poorer outcomes, showing that it is possible to achieve therapeutic efficacy without greater toxicity in this patient's population. These results are similar to those found in recent literature indicating ASCT as a feasible option for selected patients >65 years without increased mortality.

Disclosure: CG received honoraria from lectures and participation on Advisory Boards from Celgene, BMS, Janssen, Amgen, Takeda, Sanofi and Gilead.

P129.

Clinical Implications of ΓΔ T Cell Reconstitution After Autologous Hematopoietic Stem Cell Transplantation in Patients with Multiple Myeloma

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Background: Gamma delta (γδ) T cells are a minor T cell population with antimicrobial and antitumor properties. In peripheral blood (PB), most γδ T cells express Vδ2, usually paired with Vγ9, the remainder being mostly Vδ1.

Reconstitution of γδ T cell repertoire diversity after allogeneic hematopoietic stem cell transplantation (HSCT) has been correlated with a reduced incidence of infections, as well as with a greater event-free survival (EFS) in the first year after HSCT. However, data on the role of γδ T cell reconstitution after autologous HSCT (ASCT) are scarce.

Methods: We retrospectively analyzed 32 patients diagnosed with multiple myeloma treated in a single institution with high-dose therapy and ASCT between December 2016 and October 2017; Vδ1, Vδ2 and Vγ9 T cell counts in PB were assessed by flow cytometry at days 30 (D30), 60 (D60) and 100 (D100) after ASCT.

Results: The patients' median age was 63 years old, and 59% were male. A minority of patients (24%) had received more than one previous line of therapy, and among these, 43% (3/7) had undergone one previous ASCT. The median number of infused CD34+ cells was $3{,}105 \times 10^6$/kg. Grade 1-2 oral and gastrointestinal (GI) mucositis (according to Common Terminology Criteria for Adverse Effects, CTCAE, v5.0) were common, occurring in 96% and 74% of patients, respectively; only a minority developed grade ≥ 3 mucositis. Febrile neutropenia occurred in 79%. The median time to engraftment was 13 days. At D100 post-ASCT, 56% of patients had a Very Good Partial Response (VGPR) or better (according to the International Myeloma Working Group criteria). The median EFS of the cohort was 36 months.

A higher proportion of Vγ9 T cells at D60 was associated with a longer time to engraftment ($p = 0.037$; HR 0.007); no significant association was found between the proportion of other γδ T cell subsets and time to engraftment. Gender, number of previous lines of therapy and previous ASCT did not influence the proportion of Vδ1, Vδ2 and Vγ9 T cells in any of the 3 time points. We did not find statistically significant differences in the proportion of these γδ T subsets according to grade of oral and GI mucositis and occurrence of febrile neutropenia. EFS was also not influenced by γδ T cell count.

Conclusions: in our cohort, a higher proportion of Vγ9 T cell subset was associated with a prolonged time to engraftment, suggesting that γδ T cell reconstitution negatively affects blood cell count recovery after ASCT. However, further studies evaluating larger numbers of patients will be needed to determine a correlation between γδ T cell reconstitution and response to ASCT.

Disclosure: Nothing to declare.

P130.

Induction Response Seems to Be A Prognostic Factor For Progression-Free Survival After Autologous Stem Cell Transplantation in Patients with Mutiple Myeloma

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Background: High-dose chemotherapy followed by autologous hematopoietic stem cell transplantation (ASCT) has

been the standard consolidation treatment for multiple myeloma (MM) in patients younger than 70 years. Nevertheless new treatment lines have brought significant modifications in the reduction of MM tumor burden both in induction and relapse. It has been shown that these regimens can improve the quality of the response prior to ASCT, which would justify the use of several lines of treatment to achieve an optimal response prior to ASCT and obtain a longer progression-free and overall survival (PFS and OS).

Methods: Our aim is to analyze wether pretransplant response has an impact on the PFS and OS in patients with a view to the use of various lines of treatment that improve the survival of these patients. The 46 MCT of patients with MM performed in our center between February 2010 and July 2017 were included in the analysis. We evaluated transplant survival up to December 2019 in patients who had not received the new anti-myeloma regimens.

The median age was 56 years (range: 33-71). 27 patients were men and 19 women.

The type of monoclonal component was: IgG (65%), light chains (24%), IgA (9%) and IgD (2%). One induction treatment line was used in 56.5%, two treatment lines in 28.3%, three treatment lines in 13% and four previous lines in 2.2%. The regimens used only used conventional chemotherapy or a proteasome inhibitor or an immunomodulator interchangeably. The disease status in the ASCT was: stable disease (SD) 17.3%, very good partial response (VGPR) 19.6%, complete response (CR) 13% and 16% partial response (PR). The conditioning regimen was Melphalan 200 mg / m2 in 39 (84.8%) and Melphalan 140 mg / m2 in 7 (15.2%).

Results: Mortality during transplantation and the first 100 days was 0%. 28% died of disease progression and infectious complications. 7.7% of those transplanted in RC, 44.4% in VGPR, 31.3% in RP, and 42.9% of those transplanted in ED have died. There is no relevant association between disease status and death ($p = 2.03$). All transplant patients in ED or PR have relapsed. Only 55.6% in VGPR and 40.6% in CR relapsed. There is a statistically significant association between disease status and relapse ($p = 0.001$). Progression-free survival in our series was 14 months (range 9.2-18.9) and overall survival 86.3 months (range 73.3-99.3).

Conclusions: Our study shows that there is better progression-free survival for patients who achieve CR or VGPR on induction. For this reason, the availability of new treatment strategies that allow optimizing the pre-transplant response will mean a better PFS and probably OS in patients with MM who are candidates for ASCT, which we will be able to evaluate in the coming years.

Disclosure: Nothing to declare.

Myelodysplastic Syndromes

P131.

The Role of Age in Outcomes of Bone Marrow Transplantation in Patients From The Latin American Registry

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Background: Even though hematopoietic stem cell transplantation (HSCT) is the only curative strategy for patients

with myelodysplastic syndromes (MDS) many factors can make this procedure unviable like the age of patients and donors. For years, aging was a limitant factor for HSCT. However changes in conditioning regimen and other tools in the management of older patients is modifying this scenario.

Methods: We analyzed data from 283 patients with MDS from the transplant registry of 17 centers in Latin America from 1989 to 2020. Subjects were stratified according to the age in two groups: < 60 years (1) and ≥ 60 years (2). Statistics were performed using SPSSv.23.1 program considering a significant $p < 0.05$.

Results: Most patients were < 60 years (90%). In both groups, there was a predominance of males. Regarding to the Prognosis Scoring System (IPSS-R), the majority of patients were high/very high risk (group 1: $n = 65$; 25.5%); (group 2: $n = 12$; 42.8%). Myeloablative conditioning was performed in 217 patients (85%) of group 1 and in 4 patients (14.3%) of group 2. The drugs used in this regimen were bulsulfan/fludarabine (43.43%), bulsulfan/cyclophosphamide (34.5%) and regimes with total body irradiation (8.9%). Reduced intensity/non-myeloablative regimen (RIC) was the main regimen perfomed in group 2 ($n = 24$; 85.7%); in group 1 it represented 15% of cases ($n = 38$). The drugs in RIC were bulsulfan/fludarabine (45.5%), fludarabine/melphalan (45.5%) and regimens based on total body irradiation (7.2%). The main cell source in group 1 was peripheral blood (PB) (54.5%) and in group 2 was bone marrow (BM) (57.2%). The main post-HSCT complications were acute disease of the graft versus host (GVHD) in both groups. There was no significant difference between groups for risk of death (OR:0.995; 95%CI: 0.452-2.190; $p = 0.991$). Patients ≥60 years of age were 74.6% less likely to have acute GVHD than patients <60 years of age (OR:0.254; 95%CI: 0.086-0.754; $p = 0.014$). Patients aged ≥ 60 years were also 83.5% less likely to acquire chronic GVHD than those aged <60 years (OR:0.165; 95%CI: 0.038-0.713; $p = 0.016$). Regarding overall survival, there was no significant difference in the 5-year follow-up with medians of 49.5% and 1 year vs 49.1% and 3.15 years, respectively ($p = 0.356$). Data not published of the group shows an increase in overall survival of patients > 55 and >65 years when comparing the transplantation in last 20 years and 5 last years.

Conclusions: The use of reduced intense conditioning regimen probably has improved outcomes of patients. As we could see in the better overall survival in the last five years in patients with more than 55 and 65 when we changed the type of conditional regimen. Moreover, individual's fitness for undergoing HSCT has been evaluated no only by chronological age but through Comprehensive Geriatrics Assesments (CGA). Finally, age did not directly influence the mortality of the studied population, but it significantly influenced the development of acute GVHD and chronic GVHD after HSCT.

Disclosure: Nothing to declare.

P132.

Pre-Transplant Ferritin Predicts Non-Relapse Mortality in Patients with Myelodysplastic Syndromes Undergoing Hematopoietic Stem Cell Transplantation

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Background: Elevated serum ferritin (SF) prior to hematopoietic stem cell transplant has been associated with poor clinical outcomes (Armand et al Blood 2007, Malki BBMT 2020). The impact of SF in MDS patient population is not fully investigated, as previous studies either had low numbers of MDS patients, or grouped MDS with AML cohort. We present results investigating the effect of SF on post-HSCT outcomes in patients with myelodysplastic syndromes (MDS).

Methods: We conducted a retrospective analysis of 100 patients with MDS who underwent allo-HSCT between 2008-2018. Patient characteristics, including ferritin level 2-8 weeks prior to transplant, were abstracted. ROC analysis identified ferritin ≥860ng/ml as the cutoff which correlated with poor survival. OS was assessed using Kaplan-Meier curves. Cumulative incidence curves were used to assess incidence of non-relapse mortality (NRM), with relapse (RI) as competing risk. The Fine-Gray test was used to complete univariate and multivariate analysis. Statistics completed using EZR (Version1.53) and JMP (Version14.1.0).

Results: Compared to low serum ferritin (LF) patients, high serum ferritin (HF) patients were more likely to be transfusion dependent ($p < 0.0001$). Other patient characteristics did not differ between the two groups (Table 1).

After a median follow up of 26.5 (0-141) months, there was a trend towards better median OS in LF patients of 87 months, compared to 42 months in HF patients, which was not significant ($p = 0.121$).

HF patients had a higher cumulative incidence of NRM at 1 year, 28% [95% CI=16-42%] vs. 13% [95%CI=6-24%] $p = 0.026$, and at 3 years, 33% [95%CI=20-47%] vs. 20% [95%CI=10-32%] $p = 0.026$. There was no difference in RI between groups ($p = 0.29$).

In univariate analysis, only pre-transplant SF predicted NRM ($p = 0.014$). SF retained its significance in predicting NRM after adjusting for age, KPS, HCT CI, conditioning intensity, and graft source (HR 2.4 [95%CI=1.2-4.7] $p = 0.017$).

HF patients had increased rates of infection as a cause of death compared to LF patients (81% vs. 36%, $p = 0.01$). There was no significant difference between the two groups in incidence of aGVHD grades II-IV (46% vs. 49%, $p = 0.73$), aGVHD grades III-IV (20% vs. 19%, $p = 0.93$), or cGVHD (50% vs. 59%, $p = 0.35$). GVHD as a cause of death was not different among the two groups. ($p = 0.73$).

Table 1: Demographics.

All patients (N=100)	Low ferritin patients (Ferritin <860) N=54	High ferritin patients (Ferritin ≥860) N=46	P-value
Median age at transplant (range)	60 (30-74)	59 (20-75)	0.84
Age at transplant ≥ 65	78% (42/54)	72% (33/46)	0.50
HCT-CI ≥3	61% (33/54)	57% (26/46)	0.69
Karnofsky Performance Score ≤80	61% (33/54)	59% (27/46)	0.84
MDS Sub-Diagnosis			0.26
MDS, RAEB	57% (31/54)	59% (27/46)	
MDS, refractory cytopenia	23% (12/54)	11% (5/46)	
MDS, unclassified	20% (11/54)	30% (14/46)	
Pre-transplant Ferritin			
Median ferritin (ng/ml) (range)	405 (5-834)	1797 (862-6437)	<0.0001
Transfusion Dependent	26% (14/54)	71% (33/46)	
Graft Source			0.83
Peripheral blood	86% (46/54)	87% (40/46)	
Cord blood	7% (4/54)	9% (4/46)	
Bone marrow	7% (4/54)	4% (2/46)	
Transplant Type			0.601
Matched Related Donor	39% (21/54)	46% (21/46)	
Matched Unrelated Donor	54% (29/54)	43% (20/46)	
Other (haplo-identical or cord)	7% (4/54)	11% (5/46)	
ABO Mismatch			0.412
Matched	63% (33/53)	49% (22/45)	
Minor mismatch	24% (13/53)	31% (14/45)	
Bidirectional/Major mismatch	13% (7/53)	20% (9/45)	
CMV status (D/R)			0.87
-/-	32% (17/53)	30% (13/44)	
+/+	40% (21/53)	36% (16/44)	
-/+ or +/-	28% (15/53)	34% (15/44)	
Conditioning Intensity			0.54
Myeloablative	43% (23/54)	35% (16/46)	
Reduced intensity	57% (31/54)	65% (30/46)	
Engraftment			
Median time to ANC engraftment	17	17	0.98
Median time to platelet engraftment	19	19	0.98
Graft Failure	2% (1/54)	4% (2/46)	0.59

Conclusions: in this cohort of MDS patients, pre-transplant SF≥860 ng/mL was the only independent factor predicting higher risk of NRM. Infection appears to be a significant contributor to NRM in HF patients.

Disclosure: Nothing to declare.

P133.

Secondary And Treatment-Related Acute Myeloid Leukemia: Allogeneic Hematopoietic Cell Transplantation Remains The Best Available Option

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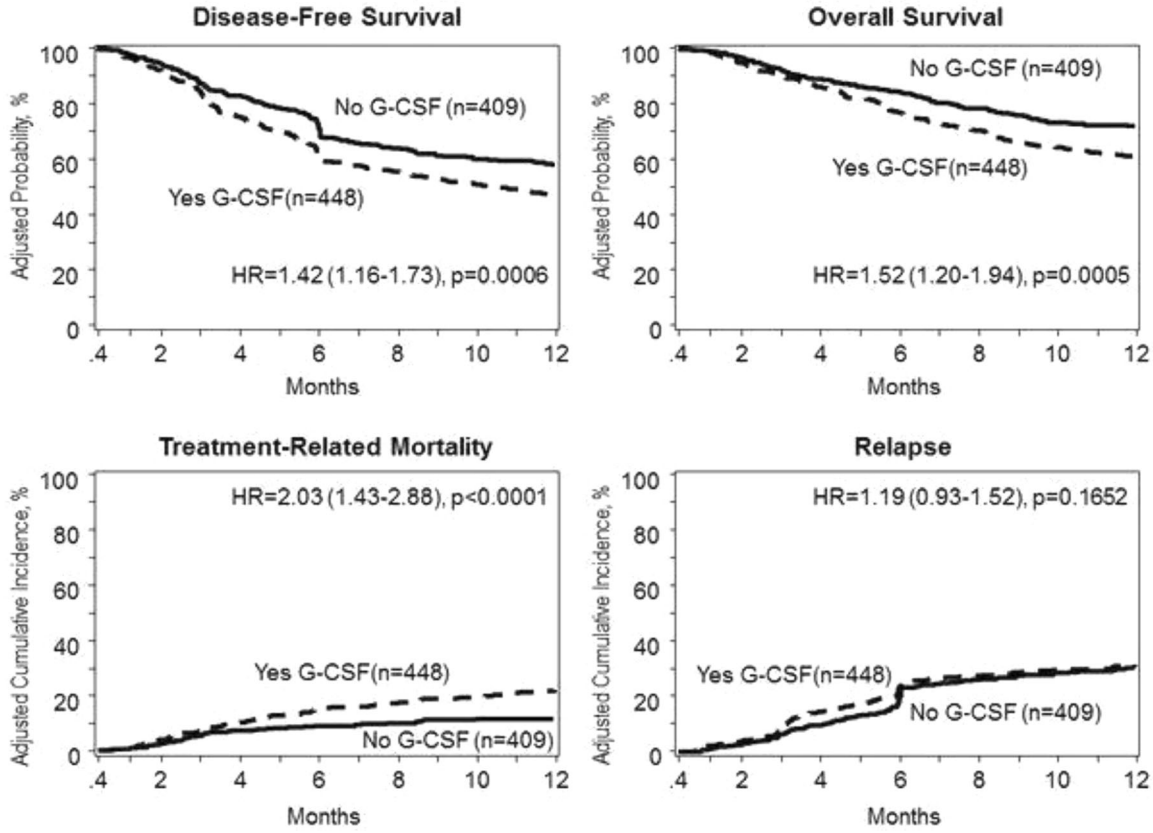
Background: Secondary acute myeloid leukemia (sAML) is associated with poor outcomes compared to de novo AML. Secondary AML with a prior diagnosis of myelodysplastic syndrome (MDS) or myeloproliferative neoplasm (MPN), also called AML with myelodysplasia-related changes (AML-MRC), has been recently linked with better outcomes compared to treatment-related AML (tAML).

Methods: We studied consecutive AML patients treated with intensive chemotherapy over the last 2 decades in our JACIE-accredited center. Detailed chart review was performed for patients with secondary AML.

Results: Among 494 AML patients, 137 (28%) suffered from secondary AML. In 94 of them (sAML or AML-MRC), disease progressed from previous MDS ($n = 78$) or MPN ($n = 15$). In 43, disease was related to previous chemotherapy and/or radiation therapy or immunosuppression due to solid tumor ($n = 11$), autoimmune disease ($n = 3$), aplastic anemia ($n = 3$), hematologic malignancy (Hodgkin lymphoma: 7, non-Hodgkin lymphoma: 7, multiple myeloma: 4, histiocytosis: 1). Favorable cytogenetics was observed only in 3 patients, all with tAML. The most common cytogenetic abnormality was Trisomy 8 (10 patients). Poor cytogenetics were detected in 56 patients (31 complex, 13 monosomal). Complete remission (CR) was achieved in 51/137 (37%) patients; while 8 succumbed to treatment-related mortality (6%). Refractory disease was observed in 78/137 (57%) and relapse after remission in 37/51 patients (72.5%). The only significant difference between sAML and tAML (Table) was age ($p = 0.001$).



There was also no significant difference in survival outcomes. Two-year overall survival was 16% and 15% in the total population for sAML and tAML respectively. In the 43% that achieved remission, two-year disease-free survival (DFS) was 16% and 32.7%, respectively. Allogeneic hematopoietic cell transplantation (alloHCT) was performed in 12 patients in first CR, and 25 in advanced disease phase. In the multivariate analysis, age, performance status, and cytogenetic risk were independent predictors of DFS. Similarly, performance status, cytogenetic risk, lactate dehydrogenase (LDH) and alloHCT independently predicted OS.

Patient characteristics		sAML ($n = 94$)	tAML ($n = 43$)
Gender, male/female		56 / 38	22 / 21
Median age (range), years		60 (22-75)	52 (15-75)
Median performance status (range)		2 (1-3)	2 (1-3)
FLT3+ mutations, %		14	27
Cytogenetics, %	Favorable	0	7
	Intermediate, *normal*	64, *43*	35, *23*
	Poor, *complex*	36, *19*	58, 30
Complete remission, %		36	40
Relapse		71	59

Conclusions: In our large real-world cohort, outcomes in secondary AML remain adverse, with increased rates of refractory disease and relapse and without significant differences between sAML and tAML. Novel targeted treatments are warranted in these patients. Until then, efforts should focus on referring patients to alloHCT.

Disclosure: E.G. is supported by the ASH Global Research Award. The remaining authors have nothing to declare.

P134.

Survival Analysis in Allogenic Hematopoietic Stem Cell Transplantation in Myelodysplastic Syndrome And Chronic Myelomonocytic Leukemia. Importance of The Previous Situation

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Background: Myelodysplastic syndromes (MDS) and

chronic myelomonocytic leukemia (CMML) are a heterogeneous group of diseases whose only curative treatment is allogeneic haematopoietic stem cell transplantation (HSCT). According to international guidelines, cytoreduction prior to HSCT should be considered when there is a high tumor burden (greater than 10% blasts), although there is no consensus on what the limit is or the best treatment strategy for this (intensive chemotherapy or hypomethylating agents). The objective of this study is to compare whether a greater or lesser burden of disease influences the results.

Methods: Retrospective observational single-center study in which 33 patients with a diagnosis of MDS or CMML who underwent HSCT between January 2012 and October 2020 were collected. Two groups were defined: the first with patients who presented less than 5% of blasts by cytology in the bone marrow aspirate prior to HSCT and the second group those with more than 5% of blasts. The characteristics of the patients are summarized in Table 1 (no significant differences were found between the two groups). The classification of SMD and CMML according to the criteria of the World Health Organization of 2016.

	< 5% blasts	> 5% blasts
Age, median (min-max)	59.5 (42-67)	59.3 (39.1-69.4)
Sex Male/Female	13/6	9/5
Excess blasts 1, n (%)	1 (5.3 %)	5 (35.8%)
Excess blasts 2, n (%)	11 (57.9 %)	8 (57.1%)
Isolated 5q, n (%)	1 (5.3%)	0 (0%)
Ring sideroblasts, n (%)	1 (5.3%)	0 (0%)
CMML type 1, n (%)	1 (5.3%)	0 (0%)
CMML type 2, n (%)	1 (5.3%)	1 (7.1%)
Multilineage dysplasia, n(%)	3 (15.6%)	0 (0%)

Results: The median follow-up was 21.8 months. Overall survival (OS) of the entire cohort at 24 months was 71% and disease-free survival (DFS) 92%.

The DFS at 24 months of the patients with less than 5% blasts was 84% and that of the of the second group with more than 5% was 80% with a Hazard Ratio (HR) = 1.6 and 95% CI of 0.4-6.6; p = 0.5 (Figure 1). The OS at 24 months of follow-up in the first group was 50% and in the second, 74% with a HR = 0.9 and 95% CI between 0.2 and 5.1 and p = 0.977 (Figure 1). Of the first group, 3 patients did not receive any treatment, 7 hypomethylating and 9 intensive; of the second, 0 did not receive any treatment, 8 were hypomethylating and 3 intensive; prior to HSCT.

Conclusions: Unlike other diseases in which reaching HSCT with the lowest possible burden of disease is associated with better outcomes, in MDS / CMML, although they share (and are equated with) certain similarities with acute myeloblastic leukemia, it may have less impact. According to our results, a lower number of blasts is not related to a better OS / DFS, so other factors could be determining factors (cytogenetics / molecular biology).

Disclosure: The authors declares that there is no conflict of interest.

New Drugs- and Cell-based Immune Therapies

P135.

Injection-Site Reactions in The Randomized Phase 3 Pegasus Trial of Pegcetacoplan Compared with Eculizumab For Individuals with Paroxysmal Nocturnal Hemoglobinuria

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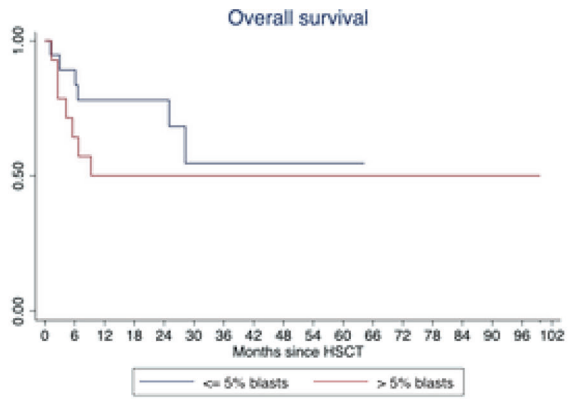

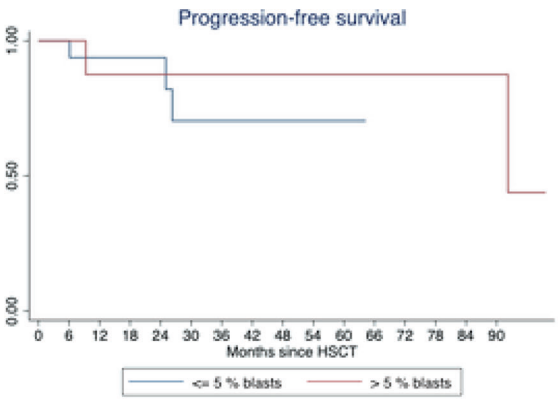

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Background: Pegcetacoplan is the first targeted C3 inhibitor being investigated for the treatment of paroxysmal nocturnal hemoglobinuria (PNH). The PEGASUS study (N=80) was a phase 3, randomized 1:1, open-label, head-to-head, 16-week study of pegcetacoplan vs eculizumab in eculizumab-treated PNH patients with a Hb level <10.5 g/dL. Pegcetacoplan is self-administered via a 20 mL subcutaneous infusion, which may lead to injection-site reactions (ISRs) relating to the injection volume, frequency, or viscosity. We report detailed ISR safety outcomes from the PEGASUS trial along with an analysis of ISRs and management strategies reported with treatments administered similarly to pegcetacoplan.

Methods: The PEGASUS trial was an open-label, head-to-head trial of pegcetacoplan compared with eculizumab in adults with PNH. All participants received twice-weekly subcutaneous infusions of 1080 mg pegcetacoplan plus their current eculizumab dose in an initial 4-week run-in period, followed by a 16-week randomized controlled period. Participants were randomized 1:1 to receive pegcetacoplan or eculizumab intravenous monotherapy. The primary endpoint was the mean change from baseline in hemoglobin levels at week 16. Safety was a secondary endpoint and included ISR and adverse event (AE) monitoring. To evaluate pegcetacoplan-associated ISRs in the context of similar treatments, a situation analysis was performed to identify therapies comparable to pegcetacoplan. Inclusion criteria were subcutaneously administered drugs with similar injection volumes (>10 mL) or PEGylation (with ≥0.5-mL injections). ISR rates and management strategies reported with identified drugs were evaluated from the prescribing information and published literature.

Results: 80 participants were enrolled and randomized to receive pegcetacoplan ($n = 41$) or eculizumab ($n = 39$). Treatment-emergent AEs (TEAEs) were reported in 69 participants (86.3%) during the run-in period and in 36 and 34 participants (87.8% and 87.2%) in the pegcetacoplan and eculizumab arms, respectively, during the randomized controlled period. Most ISRs occurred during treatment initiation, as generally higher rates of ISRs were observed in the initial run-in period compared with the randomized controlled period. During the randomized controlled period, participants in the pegcetacoplan arm experienced more ISRs compared with those in the eculizumab arm. No ISR TEAEs were serious, severe, or led to study drug discontinuation. Five drugs with comparable delivery to pegcetacoplan were identified and evaluated for ISR data: immunoglobulin with hyaluronidase, deferoxamine, daratumumab and hyaluronidase, certolizumab pegol, and pegfilgrastim. Reported ISR rates varied between evaluated drugs from ~2% to >50% of participants but were generally mild, resolved quickly, and decreased following the initial treatment. Prevention or management strategies for ISRs included ice packs, injection-site rotation, and empowering patients to gain comfort in self-administration through training and other initiatives.

Conclusions: In the PEGASUS trial, ISRs observed with pegcetacoplan treatment were highest in the initial treatment period and reduced after 4 weeks, suggesting ISRs decreased over time, as the patients became more comfortable with self-injection. ISRs were often mild or manageable, indicating these events are likely not a barrier to treatment. Comparable trends for reported ISRs have been observed with drugs delivered similarly to pegcetacoplan; management strategies for ISRs with these drugs may potentially be useful for reactions observed with pegcetacoplan.

Clinical Trial Registry: NCT03500549.

Disclosure: Ilene Weitz reports consultancy and honoraria from Alexion and Apellis Pharmaceuticals, Inc., and speakers bureau from Alexion. Kristen Drago, BSN, Crystal Chen, and Allison Bachelor, MSN, BSN, are current employees and equity holders of Apellis Pharmaceuticals, Inc.

P136.

Clinical Burden of Illness Survey Results For U.S. Patients with Paroxysmal Nocturnal Hemoglobinuria Receiving C5 Inhibitors

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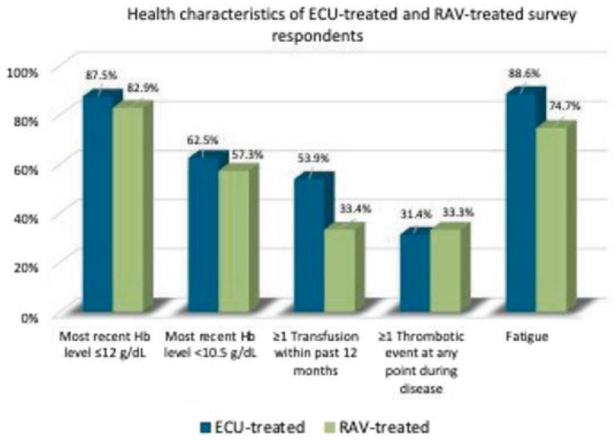
Background: Paroxysmal nocturnal hemoglobinuria (PNH) is a rare, acquired, life-threatening hematological disease associated with a significant burden of illness

(BOI) due to complement-mediated hemolysis and a subsequent need for blood transfusions that often persists despite standard treatment with the C5 inhibitors eculizumab (ECU) or ravulizumab (RAV).

Methods: Adult US patients (≥18 years) with a self-reported diagnosis of PNH were recruited via a patient advocacy group for a cross-sectional burden of illness (BOI) survey (July-October 2020). Inclusion criteria for the secure online survey included current treatment with C5 inhibitors (ECU or RAV), agreement to report adverse events, and informed consent. The impact of PNH on hematological and clinical measures was assessed using several variables including patient hemoglobin (Hb) levels, blood transfusion history, incidence of thrombotic events, fatigue level, dosage requirements, and treatment patterns. Descriptive statistics are reported as means and standard deviations, or medians and interquartile (IQR) ranges for continuous variables, and counts and frequencies for categorical variables.

Results: Survey data from 122 US PNH patients receiving treatment with C5 inhibitors were included in the study (median age: 46 years [range 18-88]; 73% female). Of these patients, 29% were taking ECU and 71% were taking RAV; most patients received treatment for at least 3 months prior to the study (ECU: 95% versus RAV: 100%). Overall, 84% of patients reported Hb values ≤12.0 g/dL (ECU: 88% versus RAV: 83%). Median (IQR) last known Hb level for ECU-treated versus RAV-treated respondents was 8.9 g/dL (7.8-11.2) and 10.1 g/dL (9.1-11.4), respectively. Within the previous 12 months, among patients who had ever experienced a transfusion and were on treatment for ≥12 months, 52% of ECU-treated and 23% of RAV-treated patients reported ≥1 transfusion, and 26% of ECU-treated and 19% of RAV-treated patients reported ≥4 transfusions; approximately 9% and 16%, respectively, were unsure of their transfusion status. Among patients on treatment for ≥12 months, 30% reported ≥1 thrombotic event at any point during their life, with 19% of those reporting any thrombotic events within the previous 12 months. Fatigue was reported by a greater proportion of ECU-treated versus RAV-treated patients (ECU: 89% versus RAV: 75%). ECU-treated patients reported a last dosage for their medication ranging from 600 mg to 1,200 mg, with 900 mg being the most common last dose reported by patients (57%). RAV-treated patients reported a last dosage of their medication ranging from 2,400 mg to 3,600 mg, with 3,300 mg being the most common last dose reported (28%). Approximately 83% of ECU-treated and 82% of RAV-treated patients reported no change in their dosage requirement, besides the planned transition to the maintenance dose, while 26% of ECU-treated and 16% of RAV-treated patients reported changes in dose or frequency of administration.



Conclusions: Findings from this BOI survey demonstrate that there is a significant unmet medical need among PNH patients, with a majority of PNH patients remaining anemic and reporting fatigue, and a notable number of PNH patients requiring blood transfusions, despite treatment with C5 inhibitors for at least 3 months.

Disclosure: David Dingli, MD, PhD is a consultant/advisory board member for Apellis Pharmaceuticals, Inc., Alexion, Janssen, Milleneum/Takeda, Novartis, R-Pharm, Rigel, and Sanofi, and recipient of research grants from Juno, and Karyopharm. Joana E. Matos, PhD and Kerri Lehrhaupt, BSc are current employees at Kantar. Sangeeta Krishnan, PharmD, MS, Michael Yeh, MD, MBA, MPH, Jesse Fishman, PharmD, MSc, Sujata P. Sarda, PhD, and Scott B. Baver, PhD are current employees and equity holders of Apellis Pharmaceuticals, Inc.

P137.

In Acute HSCT/BMT-TMA The Activation of The Lectin Pathway Induces C5B-9 Formation On Endothelial Cells And Favors Microvascular Thrombosis

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Background: Thrombotic microangiopathy (TMA) associated with hematopoietic stem cell transplantation (HSCT) or bone marrow transplantation (BMT) is a severe complication that may present in 20-40% of recipients. There is

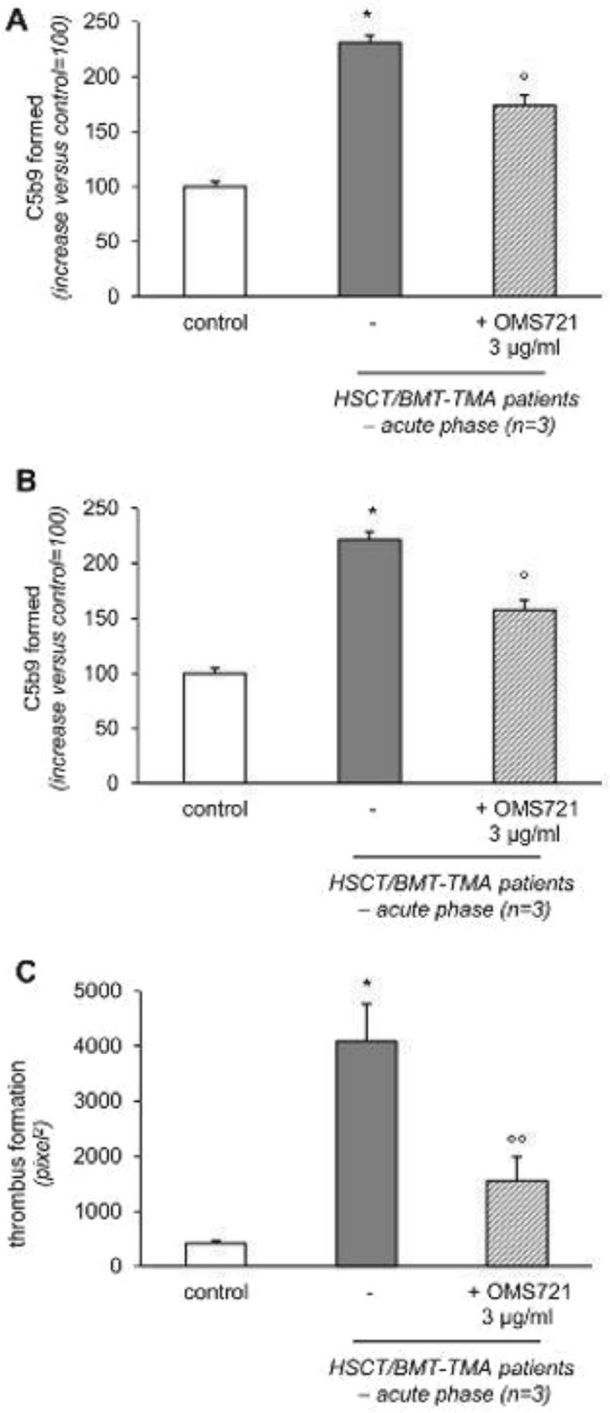
increasing evidence that complement is involved in the pathophysiology of HSCT/BMT-TMA based on elevated plasma levels of sC5b-9, C5a, and C5b-9 staining on tissue microvasculature.

In patients with atypical hemolytic uremic syndrome (aHUS), a complement-mediated TMA, we previously documented by ex vivo assays that complement is hyperactivated on endothelial cell surface and causes loss of endothelial thromboresistance (Galbusera M, et al. AJKD. 2019;74:56–72). In this study, we aimed to investigate whether the same abnormalities occur in the acute phase of HSCT/BMT-TMA.

Emerging evidence suggests that the complement lectin pathway may play a role in HSCT/BMT-TMA. Increased MASP-2 levels were found in the circulation of HSCT-TMA patients (Elhadad S, et al. Clin Exp Immunol. 2020;0:1–9). In addition, a pivotal clinical trial of the fully human MASP2 antibody narsoplimab (OMS721) in 28 HSCT-TMA patients showed a 61-74% complete response rate. Based on these collective clinical data, a further aim of this study was to assess whether OMS721 prevented complement activation and thrombus formation on endothelial cells ex-vivo in patients with HSCT/BMT–TMA.

Methods: Three patients, one with acute HSCT-TMA and 2 with BMT-TMA, were studied. We used ex vivo assays in which a monolayer of human microvascular endothelial cells (HMEC-1, unstimulated or pre-activated with ADP) was exposed to patient serum or to a pool of 10 normal sera (control). Serum-induced formation of C5b-9 ($n = 3$ patient sera versus control serum) was evaluated by confocal microscopy. The pro-thrombotic effect was then tested by flowing normal blood over ADP-activated HMEC-1 pre-exposed to patient (n-3) or control serum followed by quantification of the cell surface area covered by thrombi. The experiments were done in the absence or presence of OMS721, which was added to patients' serum (3 µg/mL f.c., corresponding to trough levels measured in narsoplimab trials).

Results: Serum from patients with acute HSCT/BMT-TMA caused a significantly higher C5b-9 formation both on unstimulated and ADP-activated HMEC-1 vs. control serum (P<0.0001; Figure 1, panels A-B). Addition of OMS721 significantly reduced C5b-9 deposits both on unstimulated and ADP-activated HMEC-1 (P<0.0001 vs. HSCT/BMT-TMA alone; Figure 1, panels A-B). Pre-exposure to serum from patients with acute HSCT/BMT-TMA resulted in massive thrombus formation on the surface of HMEC-1 after perfusion with normal human blood (P<0.0001 vs. control serum, Figure 1, panel C). The addition of OMS721 to patients' serum significantly prevented thrombus formation (P<0.001 vs. HSCT/BMT-TMA alone, Figure 1, panel C).



Conclusions: We documented that in acute HSCT/BMT-TMA, as in aHUS, activation of the complement cascade occurs on the endothelial cell surface and progresses until the formation of the terminal complex C5b-9. In addition, complement activation in acute HSCT/BMT-TMA induced loss of endothelial thromboresistance. Administration of OMS721 to patients' serum significantly inhibited formation of C5b-9 and platelet thrombi on HMEC-1, highlighting the lectin pathway's role in mediating

microvascular thrombosis in patients with acute HSCT/BMT-TMA.

Clinical Trial Registry: NA.

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P138.

Post-Hematopoietic Stem Cell Transplant Maintenance TKI's in Philadelphia Positive All: King Hussein Cancer Centre Experience

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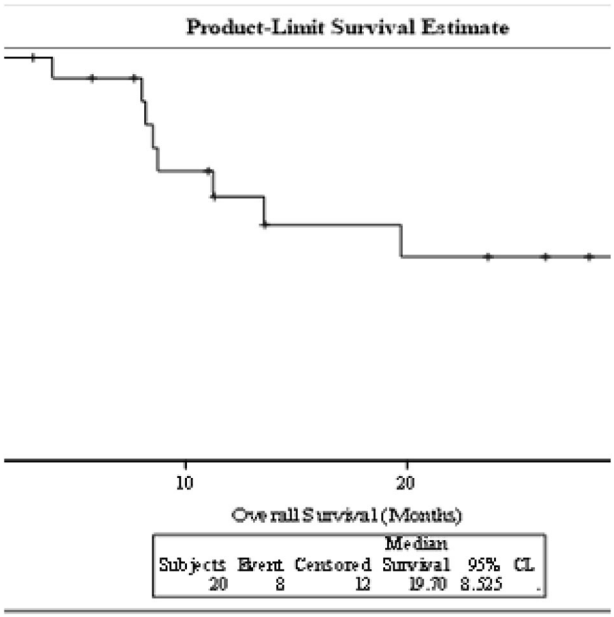
Background: Relapse after allotransplant is the most common reason of treatment failure in patients with ALL. To decrease the risk of relapse, post-transplant tyrosine kinase inhibitors (TKIs) has been used. In this retrospective study at KHCC, we aimed to evaluate the outcomes of patients, who underwent first allo-HCT and received post-transplant (TKI's).

Methods: Twenty consecutive patients with Phil+ ALL between JAN 2014-Dec 2019. Patients- and transplant-related characteristics are detailed in Table-1. 20 were in CR, 15 (75%) in CMR and negative MRD at transplant. Median age of 24.5 year (range, 6-47y), 12 adults and 8 pediatrics. The majority received matched related (80%),16 PBSC and 19 (95%) received post-HCT TKI's.

Results: All, but 2 patients in MCR and negative MRD by day+30, 2 with positive MRD on day+100 (1 relapsed). WBC engrafted at a median of 14d (range, 10-20d) and PLT at 18d (range, 13-43d). 80% achieved full donor chimerism by day+30 and all off immunosuppression at a median of 4.7mo (range, 2.1-29.8mo). After a median follow up from diagnosis (N=12) of 38.03 mo (range, 15.1-98.1mo), and from HCT of 7mo (range, 4-20mo), cumulative incidence of relapse(CIR), grade II-IV aGvHD and cGvHD were 35%, 66.6% and 50% respectively. All relapses occurred at a median of 4.7mo (range, 2.1-29.8mo),4 (57%) were MRD positive and detectable BCR-ABL pre-transplant.3-year EFS and OS for the entire group 38% (95%CI: 0.1569-0.6456) and 49% (95% CI: 0.2480-0.7383) respectively with a median of 11.25months and 19.7months respectively, Figure-1. Younger age (≤35 year) showed improved EFS (HR: 3.828, 95%CI,1.014-14.459, P=0.0477) in univariate, and OS (HR:3.042,P=0.1301),in univariate and multivariate analysis (HR:25.562,P=0.021). cGvHD showed a trend toward imp better OS (HR: 0.248, P=0.0908), but not the EFS(HR:0.500,P=0.292).100-day posttransplant Land-mark analysis (N-12) revealed an estimated 3-year CIR 27% and 5-year OS 80%. The median duration of TKI maintenance 13 mo (range 0.23 – 74 mo) with the median duration between stopping TK'sI and last follow-up 4.56 mo (range 0.16-6.23 mo). 9 continued TKI's for ≥ 2 years, had a lower risk of relapse compared to patients, who stopped before 2 years but with no significant P value (P=0.3214). Disease relapse was the most common reason for TKI's discontinuation (35%), and 6% stopped due to toxicity.



Age, range, y	24.5 y(range, 6-47y)
Follow-up, d (median, range)	38.2mo(range,15-98mo).
sex	
M	12(60.0%)
F	8(40.0%)
WBC at presentation	
> 30X10E9	> 30X10E9
<30x10E9	<30x10E9

Table (continued)

Time from diagnosis to HCT	
≤30months	10(50.0%)
>30months	10(50.0%)
Disease status at HCT, N (%)	
CR1	13(65%)
≥CR 2	7(35%)
Graft source	
BM	16(80%)
PBSC	3(15%)
Cord	1(5%)
Conditioning regimen intensity, N (%)	
MAC	18(90.0%)
RIC	2(10.0%)
Post-HCT TKI	15(75.0%)
New generation TKI Imatinib	1(5.0%)
Median FU from HCT (range),mo	7mo (range, 4-20mo)

Conclusions: Posttransplant TKI's are beneficial on reduction of hematological relapse in phil+ positive ALL and in 100-day landmark analysis. The exact impact of TKI maintenance posttransplant deserves further studies.

Disclosure: I have nothing to disclose.

P139.

Memory-Like NK Cells As Treatment For Pediatric Sarcoma

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Background: Sarcomas are heterogeneous and clinically challenging cancers. Although they account for only about 1% of all cancers in the general population, they represent 12-15% of pediatric tumors. Current treatments are based on chemotherapy, surgery, and radiotherapy combinations. This has resulted in 5-year event-free survival rates of 60-70%. Despite the great efforts of researchers and physicians to implement and continuously optimize multimodal therapies, around one-third of sarcoma patients still die because of the disease.

The spectacular success of CAR-T in patients with hematological malignancies has raised considerable interest in using other immune cells as anti-cancer living drugs. Natural killer (NK) cells have demonstrated innate anti-tumor activity and previous reports evidenced that allogeneic NK cell adoptive transfer is safe and induces remissions in leukemia patients. Nevertheless, limited persistence, expansion, and activity of NK cells in vivo make a need for biology-driven approaches to improve NK cell anti-tumor functionality before adoptive transfer.

Although it was believed that NK cells can only exert innate immune responses, increasing evidence has shown that they can acquire memory-like functional features, generating specific and stronger recall responses against acute myeloid leukemia (AML) cell lines, samples, and a small group of patients.

The goal of this work was to characterize in-depth cytokine-induced memory-like (CIML) NK cells and to explore their potential cytotoxic activity against sarcoma cells.

Methods: Highly purified NK cells were obtained from buffy coats from human healthy donors using RosetteSep Human NK-Cell Enrichment Cocktail. To generate CIML and control cells, purified NK cells were pre-activated for 16h with rhIL-12 (10 ng/mL), plus rhIL-18 (50 ng/mL) and rhIL-15 (50 ng/mL) or control conditions (rhIL-15 1ng/mL). After pre-activation, cells were maintained at least 6 days for differentiation and their functional behavior was assessed. Cytotoxicity of CIML-NK cells against sarcoma cell lines and primary cells was in vitro evaluated by conventional-4 hours Europium-TDA assays. To analyze NK degranulation and cytokine production against sarcoma cells, GolgiStop was added after 1 hour of co-culture and, 3 hours later, cells were stained for surface NK markers, CD107a, and intracellular IFNγ. Differential expression of CIML-NK surface receptors was characterized by flow cytometry.

Results: Pre-activation with cytokine cocktail allowed us to obtain a particular population of NK cells, with "memory-like properties", similar to previously described. These CIML-NK cells exhibited a phenotype characterized by low CD16 expression and high CD25, CD57, NKG2D, and DNAM-1 among other markers. When co-cultured with sarcoma cells, CIML-NK showed significantly higher cytotoxic abilities as compared to control-NK cells. Further, we observed an increased IFNγ production by CIML-NK cells, not only in basal conditions but also against sarcoma cells. Otherwise, we did not detect significant differences in degranulation of CIML- compared to control-NK cells, measured as CD107a exposure.

Conclusions: Our results strongly suggest that NK cells acquire more potent anti-tumor capabilities against sarcoma cells after pre-activation with cytokine cocktail. Enhanced

IFNγ production is responsible, at least in part, for increased killing potency of CIML-NK cells. Together, these findings raise CIML-NK cells as a promising step forward in sarcoma treatment.

Disclosure: The authors have no conflict of interest to declare.

P140.

Phase 3 Multicenter, Double-Blind, Placebo-Controlled Trial of VIRALYM-M (ALVR105) For The Treatment of Virus-Associated Hemorrhagic Cystitis After Allogeneic Haematopoietic Cell Transplant (HCT) (study Design)

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Background: Virus-associated hemorrhagic cystitis (HC) is associated with significant morbidity and mortality in allogeneic HCT recipients and is most commonly caused by BK virus (BKV). There are no approved or proven effective antiviral therapies for BKV infections. ALVR105 is an allogeneic, off-the-shelf multivirus-specific T cell therapy that targets six viruses: BKV, cytomegalovirus (CMV), adenovirus (AdV), Epstein-Barr virus (EBV), human herpesvirus 6 (HHV-6), and JC virus (JCV).

Methods: This phase 3 multicenter, double-blind, placebo-controlled trial (NCT04390113) compares the efficacy and safety of ALVR105 with placebo as treatment for severe virus-associated HC after allogeneic HCT. Patients will be randomly assigned to receive two intravenous infusions of ALVR105 or placebo (at a 3:2 ratio) 14 (±3) days apart. Patients will be followed for 6 months. To be included, patients must be >1 year of age; have had an allogeneic HCT performed at least 21 days and not more than 1 year earlier; have experienced myeloid engraftment and have a platelet count >10,000/mm^3; and be diagnosed with HC based on meeting all 3 of the following criteria: (1) clinical signs and symptoms of cystitis, (2) Grade ≥3 hematuria, defined as macroscopic hematuria with visible blood clots, and (3) viruria of >5 log_{10} copies/mL of BKV, AdV, CMV, EBV, HHV-6, or JCV. Key exclusion criteria include ongoing therapy with high-dose systemic corticosteroids; anti-T cell antibodies within 28 days prior to randomization; active Grade >2 acute graft versus host disease; uncontrolled or progressive bacterial or fungal infections, viral infections not targeted by ALVR105, or EBV-associated post-transplant lymphoproliferative disorder; or receipt of another investigational antiviral within 28 days prior to randomization and throughout the study. The study objective is to evaluate the time to clearance of macroscopic hematuria in patients receiving ALVR105 versus placebo. Key secondary objectives include time to resolution of bladder pain and number of days in the hospital.

Results: Planned enrollment is 125 patients in the United States, Europe, and Asia Pacific. The study is due to start in December 2020 and to be completed in June 2022.

Conclusions: This Phase 3 trial will provide data on the efficacy and safety of ALVR105 compared with placebo for the treatment of virus-associated HC in allogeneic HCT recipients.

Clinical Trial Registry: Clinicaltrials.gov NCT04390113. https://clinicaltrials.gov/ct2/show/NCT04390113.

Disclosure: This study is funded by AlloVir, Inc. Gérard Socié is the National Coordinating Investigator (NCI) for the study in France. Per Ljungman is the NCI for the study in Sweden.

P141.

Work Productivity Loss And Quality of Life in Paroxysmal Nocturnal Hemoglobinuria Among Patients Receiving C5 Inhibitors in The United States

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Background: Paroxysmal nocturnal hemoglobinuria (PNH) is a rare, acquired, hematologic disease characterized by chronic complement-mediated hemolysis. While treatment with the C5 inhibitors, eculizumab (ECU) or ravulizumab (RAV), reduces intravascular hemolysis, patients continue experiencing impairment in overall quality-of-life (QoL) relative to normative reference scores for the general adult population and loss of productivity.

Methods: This study investigated clinical, humanistic, and economic outcomes associated with PNH burden of illness. Productivity impairment and QoL were assessed in patients on ECU or RAV. A cross-sectional online survey (July-October 2020) was administered to US patients (≥18 years). Patients with a self-reported PNH diagnosis were recruited via patient advocacy group. Inclusion criteria included current treatment with ECU or RAV and agreement to provide informed consent and report adverse

events. The Work Productivity and Activity Impairment (WPAI)–General Health questionnaire, Functional Assessment of Chronic Illness Therapy 1(FACIT)-Fatigue scale (total score range: 0-52), and European Organization for Research and Treatment of Cancer QoL Questionnaire (EORTC-QLQ-C30; total score range: 0-100) were used, with descriptive statistics reported.

Results: Adult patients ($n = 122$) were a median age of 46 (range 18-88) and 73% female. Overall, 29% of patients were on ECU and 71% on RAV. Most patients received treatment for ≥3 months (95% ECU, 100% RAV). In total, 53 (43%) patients reported gainful employment. From those employed, 47% reported missing work hours in the prior 7 days due to health problems (61% ECU, 40% RAV), and 79% reported that their illness affected overall work productivity (83% ECU, 77% RAV). Employed patients reported an average of 11% absenteeism (proportion of work time lost due to being absent) and 32% presenteeism (productivity impairment while working). Total work productivity impairment averaged 36%. Most patients (88%) reported some impairment in normal daily activities (89% ECU, 87% RAV) regardless of employment status. On average, patients reported 39% impairment in activities in the prior 7 days. The mean FACIT-Fatigue total score (32 ±13) was lower than the general US population mean (~44). The PNH patient mean EORTC-QLQ-C30 global health status score (66±20) was also below that of the general population (~76). Furthermore, the EORTC-QLC-C30 physical functioning score mean (77±19) averaged lower than the general population mean (~90).

	Total Mean (SD)	ECU Mean (SD)	RAV Mean (SD)
Absenteeism, %	11(17)	19(24)	7(11)
Presenteeism, %	32(27)	42(32)	26(23)
Work Productivity Impairment, %	36(29)	48(34)	30(25)
Daily Activity Impairment, %	39(27)	43(27)	38(26)
FACIT-Fatigue, score	32(13)	29(14)	33(13)
EORTC-QLQ-C30, score			
Global health status	66(20)	62(21)	67(19)
Physical functioning	77(19)	76(18)	77(20)

Conclusions: The results demonstrate that QoL and work productivity and activity impairment are associated with PNH burden of illness. PNH patients treated with C5 inhibitors show substantial work productivity loss, greatly diminished ability to work, and limitations in usual activities. Patients also reported impaired overall QoL regardless of ECU or RAV treatment.

Disclosure: David Dingli, MD, PhD is a consultant/advisory board member for Apellis Pharmaceuticals, Inc., Alexion, Janssen, Milleneum/Takeda, Novartis, R-Pharm, Rigel, and Sanofi, and recipient of research grants from Juno, and Karyopharm. Joana E. Matos, PhD and Kerri Lehrhaupt, BSc are current employees at Kantar. Sangeeta Krishnan, PharmD, MS, Michael Yeh, MD, MBA, MPH, Jesse Fishman, PharmD, MSc, Sujata P. Sarda, PhD, and Scott B. Baver, PhD are current employees and equity holders of Apellis Pharmaceuticals, Inc.

P142.

Clinical Pharmacology And Population Pharmacokinetic/Pharmacodynamic Modeling of Lectin Pathway Inhibition by Narsoplimab (OMS721)

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Background: Hematopoietic stem cell transplant-associated thrombotic microangiopathy (HSCT-TMA) is a life-threatening complication that results from endothelial injury associated with HSCT. Endothelial injury specifically activates the lectin pathway of complement. IgA nephropathy (IgAN) is a glomerular disease in which immune complex deposition on the surface of mesangial cells activates the lectin pathway. Narsoplimab, a specific inhibitor of mannan-binding lectin-associated serine protease-2 (MASP-2), the effector enzyme of the lectin pathway and an activator of the coagulation cascade, is being studied in clinical trials for the treatment of both HSCT-TMA and IgAN. Here we present the pharmacokinetics (PK) and pharmacodynamic (PD) effect of narsoplimab on lectin pathway activation in patients and healthy volunteers.

Methods: Lectin pathway activation PD effect was measured by inhibition of ex vivo C4d deposition in 4 clinical studies: an open-label pivotal trial in TMAs (NCT02222545), a Phase 2 clinical trial in IgAN (NCT02682407), and 2 Phase 1 healthy volunteer studies. Sparse PK sampling was performed in the TMA and IgAN studies, while intense PK sample was performed in healthy populations. A population PK/PD (2-compartment) model was built on the subset of single and multiple narsoplimab IV dose regimens used in these clinical studies. Exposure-response relationships between serum concentrations of narsoplimab and C4d inhibition for the HSCT-TMA treatment responder and non-responder populations was also explored.

Results: The final population PK model with covariates comprised linear 2-compartment distribution and elimination, together with a non-linear elimination component described by a Michaelis–Menten term. Critical parameters (V1) were consistent with monoclonal antibodies, indicating that narsoplimab is distributed in the blood and

hydrophilic extravascular space. Total clearance (CL) of narsoplimab was concentration-dependent, with K_m values estimated to be ~5.7 μg/mL. The estimated CL for patients ranged from 0.1146 to 0.1286 L/h. The estimated terminal half-life ($T_{1/2}$) in healthy volunteers was 198 hours after 6 weekly IV doses of 4 mg/kg.

The population covariates affecting the disposition of narsoplimab were albumin level, patient status, body weight, dose, and the presence of anti-drug antibodies (ADA). ADA-positive status was associated with a higher maximum elimination velocity (V_{max}). However, the overall exposure was only slightly lower in subjects with ADA. Body weight was a significant covariate: CL increased with increased body weight, supporting the use of body weight dosing. The impacts of age, race, and sex on the disposition of narsoplimab were not found to be significant. Consequently, dose adjustment based on patient characteristics other than weight is not warranted.

A direct-link mixed-effects E_{max} model best described the exposure-response relationship. EC_{50} and EC_{90} values showed that concentrations of narsoplimab were maintained at levels greater than EC_{50} throughout the dosing interval. Narsoplimab concentration levels achieved in HSCT-TMA patients generated pharmacologically relevant exposures resulting in meaningful C4d inhibition, with concordant improved clinical response rate. Modeling indicated that by 6 weeks after the last dose of narsoplimab, there was unlikely to be any residual pharmacodynamic effect on C4d production.

Conclusions: PK/PD analysis and modeling of narsoplimab support weight-based dosing in the HSCT-TMA population, which results in favorable exposure-response relationships.

Clinical Trial Registry: ClinicalTrials.gov: NCT02222545; NCT02682407.

Disclosure:

- William Pullman: Omeros Corporation (Consultant).
- Axel Facius: Omeros Corporation (Consultant).
- Gezim Lahu: Omeros Corporation (Consultant).
- Brendan Smyth: Omeros Corporation (Employment).

Non-infectious Early Complications

P143.

Post Hematopoietic Progenitors Transplant Lymphoma (PTLD) And Replication of Epstein-Barr Virus (EBV): A Center's Experience

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Background: EBV replication and the consequent development of PTLD are two of the most severe complications associated to hematopoietic stem cell transplantation (HSCT). There have been described several risk factors to predict them, including: T-cell depletion, reduced intensity conditioning and unrelated donor HSCT. Historically, the mortality described in literature due to PTLD has been very high but, thanks to introduction of new treatments such as rituximab and anti-EBV cytotoxic T lymphocytes (CTL) in recent decades, it has improved the prognosis of these patients.

Methods: Retrospective study with collection of patients subjected to allogeneic HSCT between January 2009 and December 2018 at the University Hospital Puerta de Hierro-Majadahonda: characteristics of HSCT, EBV replication, preventive treatment and development of PTLD.

Results: EBV replication without PTLD development was documented in 78 (32.9%) of 237 allogeneic HSCT performed in that period.

Preventive therapy with Rituximab was administered to a 18.9% of EBV replicating patients, with a median administration of 4 cycles. Remaining patients (81.1%) experienced temporary replications with spontaneous negativization. None of them developed PTLD and they also showed good tolerance to treatment without relevant complications. Preventive treatment was administered with a median of EBV copies of 7640 (778-841000).

Four patients developed PTLD 1.7% of all HSCT and 5.1% of all patients with EBV replication. Most of them presented as cervical lymphadenopathy and fever. Diffuse large B cell lymphoma was the most frequent histology. EBV replication has been correlated in all patients with hybridization of the DNA's virus in the adenopathy biopsy. IPI-score was intermediate-high in all patients. Two of them had bone marrow infiltration.

When it comes to treatments, rituximab in monotherapy was the most widely used, with 50% complete responses and 50% progressions. One patient was given R-CHOP. The median survival was 6.8 months.

Other risk factors for PTLD not included in the images were: treatment with antithymocyte globulin (ATG) in 100%, graft versus host disease (GVHD) of at least grade 2 in 50%. None of them presented serological discrepancy for EBV, nor were T-cell depleted products used.

Conclusions: PTLD is a severe complication of HSCT with poor prognosis and shortened survival. However, the incorporation of new therapeutic strategies such as rituximab as well as EBV monitoring criteria have allowed the improvement of this entity prognosis. In fact, of the total number of EBV reactivation patients, only a small percentage of around 5% developed PTLD, including in our series 18.9% of EBV replication patients who were controlled with rituximab treatment.

Nevertheless, we still need to standardize EBV viral load detection methods, predictive models of PTLD risk based on risk factors, robust criteria for preventive treatment with rituximab and the incorporation of new treatment strategies as anti-EBV CTLs.

Disclosure: Nothing to declare.

P144.

Analysis of The Gut Microbiome in Pediatric Patients Undergoing Allogeneic Hematopoietic Stem Cell Transplantation (HSCT) Presenting Veno-Occlusive Disease (VOD/SOS) Reveals An Impaired Microbial Ecosystem

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Background: Veno-occlusive disease/sinusoidal obstruction syndrome (VOD/SOS) is a potentially life-threatening complication of hematopoietic stem cell transplantation (HSCT). Endothelial dysfunction seems to be a key factor in the development of this early complication after HSCT. Pediatric patients present a higher risk of developing VOD/SOS than adults, with an incidence of approximately 20% to 30%. Mounting evidence has suggested a pivotal role of the gut microbiome (GM) in major HSCT clinical outcomes, and some preclinical studies suggest that microbial products, translocated across impaired mucosal barrier, may participate in the pathogenesis of endothelial damage. However, no clinical data have been published so far on the relationship between VOD/SOS and GM.

Methods: We performed a retrospective single-institution case-control study at the pediatric HSCT Unit of the University of Bologna, from 01/01/2015 to 31/12/2019. Study inclusion criteria were the availability of a pre-HSCT fecal sample and at least two samples collected after HSCT. For each patient, we analyzed the taxonomic profile of GM by 16S rRNA gene sequencing, using the Illumina MiSeq platform.

Results: Eighteen allo-HSCT pediatric recipients were enrolled. Nine patients developed severe or very severe VOD/SOS according to the new EBMT criteria in the period of the study, for a cumulative incidence of VOD/SOS in our center of 15.38%. Nine patients in the control group were selected by matching for age, sex, source of stem cells, type of disease, conditioning regimen, antibiotic prophylaxis and type of nutrition. A total of 74 fecal samples were available, collected before HSCT and up to 72 days after HSCT. Patients developing VOD/SOS had lower GM α-diversity before transplant than controls, and the two groups significantly separated in a weighted UniFrac-based PCoA plot ($p = 0.005$). Taxonomic analysis revealed that VOD/SOS samples had a lower relative abundance of *Bacteroides*, *Ruminococcus*, *Ruminococcaceae* and *Clostridiales*. Early after transplant, samples from VOD/SOS patients and controls were similar in GM α-diversity, probably due to HSCT-related perturbation. After 30 days from HSCT α-diversity was again significantly lower in VOD/SOS-diagnosed patients than in controls ($p \leq 0.02$), with levels comparable to those before transplant.

Conclusions: This pilot study reports for the first time a possible association between GM and the onset of VOD/SOS. In particular, a rich and diverse GM before HSCT might be associated with a decreased probability of developing VOD/SOS. The protective signatures identified, i.e., *Clostridiales*, *Ruminococcaceae* and *Bacteroides*, show some similarity to the protective configuration observed in studies regarding aGvHD. The positive effect exerted by this peculiar pre-HSCT GM composition towards VOD/SOS and aGvHD could be related to the common endothelial damage that characterizes both diseases. Microbial products, as for example LPS, could reach the liver sinusoid through the portal vein and participate in endothelial damage. Studies on larger cohorts are needed to further confirm this association and to better define the GM signature associated with VOD/SOS.

Disclosure: Nothing to declare.

P145.

Clinical Outcome of Patients with Immune-Mediated Platelet Refractoriness Undergoing Hematopoietic Stem Cell Transplantation. Single Center Experience

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Vicuña Andrés[1], Raquel Alenda Asensi[2], Jose Luis Vicario Moreno[2], Beatriz Aguado Bueno[1]

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Background: Platelet refractoriness is a clinically significant problem, affecting up to 14% of hematological patients receiving platelet transfusions[1,2], displaying higher incidence and potential lethality in patients undergoing hematopoietic stem cell transplantation (HSCT)[2]. Immune causes, which account for a minority of cases, are the ones with greater potential for prevention and management[3,4]. However, they are directly associated with poor clinical outcome and increased medical costs[5]. The aim of this study was to analyze the outcome of HSCT patients with allo-immune platelet refractoriness in our center.

Methods: We retrospectively reviewed 1.154 HSCT recipients at our center between January 2000 and November 2020. We analysed antibody types, hemorrhagic complications and clinical outcome of transplantation.

Results: Patient and transplant characteristics described in *Table 1*.

We found 32 (3%) patients with a positive allo-immune platelet refractoriness test result. 17 (53%) of 32 patients were refractory prior to transplantation, 9 (28%) were diagnosed during transplantation and 6 (19%) subsequently. Most of them [29 (91%)] had IgG anti HLA-I antibodies; only 1 (3%) IgM and 2 (6%) had both. 28 patients (88%) had a history of previous polytransfusion. 3 patients (9%) had red blood cell allo-antibodies (2 anti-D, 1 anti-E). The median length of stay for transplant procedure was 48 days (31-104).

All patients were scheduled for HLA-matched platelet transfusions, receiving a median amount of 8 (1-45) transfusions during transplantation. The median platelet engraftment was on day +22 (12-85); 5 patients discharged pre-engraftment. 4 patients (13%) received platelet refractoriness therapy, 2 with IGIV + corticosteroids and 2 with thrombopoietin analogs.

Hemorrhagic complications were diagnosed in 13 patients (41%) during transplantation: 4 (21%) involving CNS, 2 (11%) pulmonary, 3 (16%) gastrointestinal, 8 (42%) genitourinary and 2 (11%) mucosa. During post-transplant follow-up we registered 12 bleedings in 7 patients (22%): 3 (25%) involving CNS, 1 (8%) pulmonary, 2 (17%) gastrointestinal, 5 (42%) genitourinary and 1 (8%) mucosa. 3 patients (9%) experienced thrombotic complications, all associated with central venous catheter (2 had <50 × 109/L platelets and one >50 × 109/L).

First year survival rate was 75% (24/32). Bleeding was the cause of decease in 3 (9%) patients, 1 during transplantation and 2 in the following 2 years.

Table 1.

Sex	Male 8 (25%)			Female 24 (75%)			
Age at HSCT	Median 53.25 years [36-70]						
Underlying disease	AML	MDS	HL	MM	Aplastic anemia	CML	ALL
	6 (50%)	9 (28%)	2 (6%)	2 (6%)	1 (3%)	1 (3%)	1 (3%)
HSCT type	Autologous			Allogeneic			
	5 (18%)			27 (84%)			
Median hospital length of stay	48 days [31-104]						
Bleeding complications	CNS	Pulmonary	GI	Genitourinary	Mucosa		
during HSCT (19 in 13 patients)	4 (21%)	2 (11%)	3 (16%)	8 (42%)	2 (11%)		
Bleeding complications	CNS	Pulmonary	GI	Genitourinary	Mucosa		
after HSCT (12 in 7 patients)	3 (24%)	1 (8%)	2 (17%)	5 (42%)	1 (8%)		
1-year survival rate	24/32 (75%)						

Conclusions: Allo-immune platelet refractoriness is a rare but significant clinical complication in patients undergoing HSCT, requiring careful coordination with transfusion community centers to schedule targeted donations. This remarkably increases length of stay, costs and worsens patient prognosis increasing morbidity of the procedure with major bleeding complications, despite a low associated mortality rate.

Disclosure: The authors have disclosed no conflicts of interest.

P146.

Hemorrhagic Cystitis During Allogeneic Stem Cell Trasplantation: A Possible Role For Prostatic Hyperplasi

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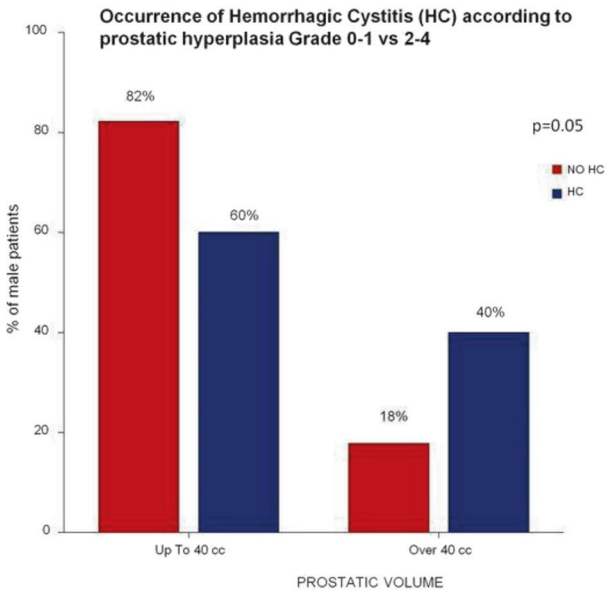
Background: Hemorrhagic cystitis (HC) is a frequent complication of allogeneic stem cell transplantation (HSCT), complicating 12-50% of all procedures. Despite several risk factors have been associated with higher risk for developing HC, its etiology remains debated. Major causes of HC have been described to be age, viral infections, HLA-mismatch and chemotherapy used for conditioning regimens or for graft versus host disease (GVH) prophylaxis. Prostatic hyperplasia has never been investigated as risk factor for HC in ASCT population.

Methods: in this report we retrospectively analyzed 198 consecutive patients of both genders who underwent ASCT

in our institution between December 2017 and August 2020. We aimed to focus on possible association between HC of grade >1 (macroscopic hematuria) and major transplant-related risk factors, namely conditioning regimen, HLA matching, genders matching and GVH prophylaxis, or patient-related risk factors, as age, gender, comorbidity index (HCT-CI) and diagnosis. We then particularly concentrated on the role of prostatic hyperplasia in the 109 male patients.

Results:



The diagnosis in the majority of patients was acute leukemia (45% AML, 15% ALL), followed by myelofibrosis (21%) and myelodysplastic syndrome (13%). The median age was 55 years and the median HCT-CI was 3. Most patients received a myeloablative conditioning regimen (90%), and 76% received triple GVH prophylaxis with post-transplant cyclophosphamide (PTCY). Prostatic diameters were measured by an expert urologist. Prostatic hyperplasia was considered significant when of grade 2 or more (volume greater than 40 cm^3): this was found in 21% of male patients at radiologic assessment at the time of ASCT.

Overall 13% of patients experienced macroscopic HC which was associated to longer post infusion hospitalization (median 41 vs 26 for non HC patients). HC occurred in 9% of female patients and 17% of male patients ($p = 0.12$). In univariate analysis, we found that recipients older age, mismatched HLA donor and PTCY based GVH prophylaxis were associated to HC ($p = 0.05$, $p = 0.03$ and $p = 0.46$ respectively); moreover, a slight trend of association with HCT-CI risk was observed ($p = 0.08$). In multivariate analysis, only HLA matching remained an independent risk factor. Treatment for HC consisted in adequate hydratation and platelets transfusions for all patients; some patients required more intensive treatments consisting in continuous bladder irrigation (60% of HC), specific antiviral therapy (7%), endoscopic diathermocoagulation (7%) or intravesical instillations with Platelet-Rich Plasma (3%) or hyaluronic acid (3%).

Among 109 male patients, 18(16%) experienced HC. Prostatic hypertrophy was found in 40% of all cases of HC. Patients with prostatic volume greater than 40 cm^3 developed HC in 30% of cases, compared to an incidence of 12% in patients with smaller prostate ($p = 0.05$). In males group, we found that older age was an other risk factor associated with HC ($p = 0.05$). These factors were not independent in multivariate analysis.

Conclusions: in conclusion: an HLA mismatched donor is major risk factor for HC. In the male population, prostatic hyperplasia and age may be additional risk factors. As this frequent complication is often associated with prolonged hospitalization, the choice of more intensive strategies for HC prophylaxis could be considered in high-risk subsets when administering PTCY.

Disclosure: Nothing to declare.

P147.

Thrombotic Events in Hematopoietic Transplant Recpients: Single Center Experience

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Background: The incidence and causes of thrombotic events during hematopoietic stem cell transplantation (HSCT) are not well definied[1]. Predisposing factors could be related to patient (underlying disease, previous thrombosis, infections) [2,3,4] transplant (conditioning regimen, GVHD) and central venous catheter (CVC).

Methods: We retrospectively analyzed thrombotic events after transplantation in 1203 patients receiving HSCT in our center from January-2000 to August-2020. They were categorized: upper deep vein thrombosis (DVT), lower DVT and pulmonary thromboembolism (PE), diagnosed by Doppler ultrasound and CT Angiography or pulmonary perfusion scintigraphy.

Results: Population`s characteristics and transplant procedure: see Table 1.

Thrombotic events ocurred in 44 of 1203 (3.6%), as previously reported[5,6]. 79% (35) were upper extremity DVT

all catheter-related, 5% (2) lower extremity DVT and 16% (7) PE.

75% (33) were allogeneic transplants, 68% (30) with myeloablative regimens.

Median platelet count was 120x109/L (4-583x109/L). Eighteen (41%) had <100x109/L platelets.

Regarding PE, 71% were bilateral, all in allogenic HSCT. Four had chronic GVHD, 2 with pulmonary involvement. Median time from transplantation to PE was 1 year (3 months-7 years). Median anticoagulation time was 7 months (27 days to indefinite). Two (29%) received indefinite anticoagulation and one for 27 days due to fatal outcome.

There were 2 lower DVT, both lymphomas with femoropopliteal thrombosis, one during conditioning and the other at 120 days postransplant.

In catheter-related DVT, there were no differences regarding either catheter or thrombosis location and 57% occurred in non-tunneled CVCs. Median time from transplantation to DVT was 28 days, (0 days-8 years); 74% (26) in first 100 days of transplantation, and 69% (18) in <30 days. In 74% (26) catheter was removed. 66% (23) were anticoagulated with low molecular weight heparin (LMWH) adjusted to platelet count. Twelve patients did not receive treatment, 7 due to active bleeding or severe thrombopenia and 5 because of terminal status. No hemorrhagic events were observed. Median anticoagulation time was 3 months (1 month-indefinite), 70% (16) ≤ 3 months, 26% (6) 3-6 months and one indefinite anticoagulation.

Six (17%) patients had also catheter-related infection; 5 due to Gram-positive and one Gram-negative bacteria. In all cases, catheter was replaced. Most catheter infections occurred in allo-transplants 67% (4).

Table 1.	Mediana (range)/n(%)
Age / Sex (Female/Male)	52 (21-68) / 15 (34%) / 29 (66%)
Nº Cardiovascular risk factors: 1 / 2 /3	16 (36%) / 7 (16%) / 1(2%)
Underlying disease: AML/MDS/ALL	10 (22%) / 7 (16%) / 7 (16%)
NHL/ MM/ PCL	9 (20%) / 7 (16%) / 2 (5%)
Aplastic anemia	2 (5%)
HSCT: Autologous/Allogeneic	11 (25%) / 33 (75%)
Conditioning Regimen: Myeloablative/RIC	30 (68%) / 14 (32%)
GVHD Prophilaxys: CsA + MTX/ CsA + MMF + Cy post	25 (78%) / 7 (22%)
Prethrombosis GVHD: NO/ YES	32 (73%) / 12 (27%)

Conclusions: Thrombosis is a transplant associated complication. We observed a low incidence of 3.6%, most in allogeneic transplants. The majority were catheter related thrombosis. Adjusted LMWH and catheter removal are the most widely used treatment,but always requiring individualized management.

Disclosure: The authors declare not to have any interest conflicts.

P148.

Evaluation of Intestinal Permeability in Candidates For Allohct And in Early Post-Transplant Period by Sugar Absorbtion Test: Interim Analysis of The Single-Center Prospective Study

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Background: Integrity of the intestinal barrier is maintained mainly by the trophic and immunomodulating functions of certain species of bacteria and its metabolites. Conditioning reduces the occurrence of these species, leading to the intestinal barrier dysfunction and translocation of microorganisms into the circulation.

Methods: 32 consecutive patients admitted for alloHCT were enrolled in the study. The intestinal barrier permeability was analyzed using the sugar absorption test (SAT) on day -7 (prior to conditioning) and on day +7 after alloHCT. The current analysis covers the group evaluable at both time points ($n = 26$). Samples from 6 h urine collection after the intake of 500 mL water solution containing 7.5 g lactulose and 2 g mannitol were analyzed using a gas chromatograph with a FID detector to obtain the lactulose to mannitol ratio (LMR). The physiological ratio was considered <0.035. All the patients consented to participation and the study was approved by the local IRB Board.

Results: 62% of evaluable patients were male, median age was 54 (19-67), 46% suffered from acute myeloid leukemia and 65% underwent myeloablative conditioning. The median LMR before the conditioning for the whole group was 0.033 (0.0 - 1.084). 10 of those patients had already elevated LMR at the baseline, before conditioning (median 0.049, 0.039-1.084) while in remaining 16 it was within the normal range (median 0.029), (0.0–0.034). 21 out of 26 patients (81%) had increased intestinal permeability (above the normal range) on day +7 and median LMR for the whole group was significantly increased compared to the baseline (0.058, 0.000 - 2.068, $p < 0.001$). Patients with increased permeability before transplantation experienced

comparable rise in LMR compared to patients with normal ratio before transplantation (median Δ LMR for two groups 0.016, NS).

There were no statistical differences in LMR at the baseline and at day +7 between groups that underwent myeloablative or non-myeloablative conditioning, among women and men, and patients younger and older than 60 years old. Among all patients 8 had confirmed bacterial infection within 30 days after alloHCT, and these patients had higher median ΔLMR 0.069 (-0,001-2,027) compared with those who did not experienced this complication (median ΔLMR=0.012) (-0,021 0,648), ($p = 0.009$). The evaluation of correlation of LMR and ΔLMR with biomarkers of intestinal permeability (zonulin, calprotecin, β-defensin) and microbiome analysis is ongoing and the study is still recruiting.

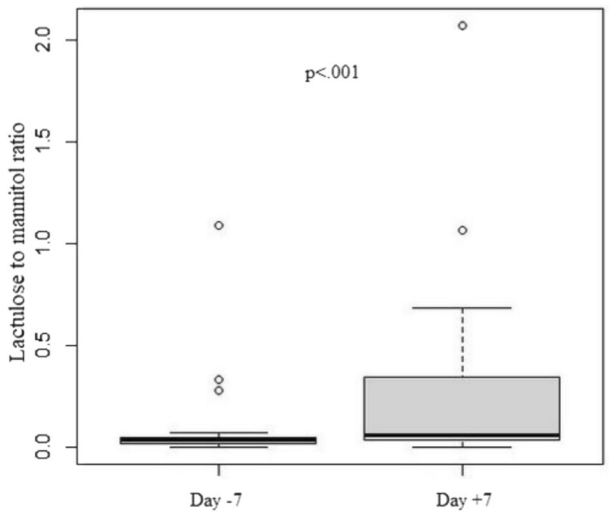

Figure 1 Difference in intestinal permeability before (day -7) and after (day +7) alloHCT expressed as lactulose to mannitol ratio. Results correspond to patients evaluable at both time points.

Conclusions: AlloHCT candidates have frequently disrupted intestinal barrier and increased intestinal permeability, which may be quantified as LMR after SAT. Conditioning leads to the further increase in intestinal permeability, which may promote microbial translocation to the bloodstream and systemic infections.

Clinical Trial Registry:.

Disclosure: This research was financed by the National Science Center (competition PRELUDIUM 15).

P149.

Anicteric Presentation of Severe Hepatic Veno-Occlusive Disease (VOD) with Multiorgan Dysfunction (MOD)- A Pediatric Case Report

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Background: VOD is a potentially fatal complication of hematopoietic stem cell transplantation (HSCT). For years, hyperbilirubinemia has been acknowledged as its dominant symptom. However, in context of increasing number of anicteric cases of VOD in children, and current modification of the diagnostic criteria for VOD, the importance of hyperbilirubinemia is uncertain.

Methods: We are reporting a 3 years old girl who underwent allogeneic BMT from a matched sibling donor for high-risk ALL. Conditioning regimen consisted of Busulfan, Fludarabine and Thiotepa (dosage acc. to SmPC). Baseline abdominal ultrasound (US) and serum markers of liver function were normal. Patient had no previous history of hepatotoxicity.

Results: Starting from day +6, refractory thrombocytopenia (RT) was observed. On day +12, abdominal US revealed ascites and hepatomegaly, indicating moderate VOD. Bilirubin level was 0.6 mg/dL, AST: 23U/l, ALT: 12U/l. Defibrotide (DF) 25mg/kg/d and diuretics were administered immediately. On day +17, progression to very severe VOD was observed: rapid weight gain, cumulative ascites, new-onset cognitive impairment, and pulmonary dysfunction resulting in increased oxygen demand. Bilirubin was 1.4mg/dL, AST: 1333U/l, ALT: 789U/l. Patient was not feverish nor presented any skin rash; inflammatory markers were negative. On day +18 further increase in weight and severe coagulation impairment with a need for coagulation factors replacement were observed. Bilirubin raised to 1.7 mg/dL, being the highest value noted in this patient. However low, it has doubled over 48h, being a predictor of an unfavorable outcome. Urine output was unsatisfactory despite high doses of diuretics; Creatinine level remains normal while urea serum level surged to 150 mg/dL, suggesting diminished renal blood flow and a preliminary phase of hepato-renal syndrome. On day +19, the patient presented with relevant constipation and hematemesis; the abdominal US revealed massive ascites and mild pleural effusion. Despite unequivocal indications, the decision to perform peritoneal drainage was suspended due to severe, symptomatic coagulation impairment. Instead, diuretics were increased up to the maximum daily dose, and pentoxifylline in continuous infusion was administered to improve renal blood flow and force diuresis. To decrease intra-abdominal pressure, the stomach was emptied through a naso-gastric tube, and enema was performed. A significant turnaround was observed in days 21-25: gradual weight normalization, negative fluid balance, and improvement in mental and pulmonary function. Abdominal US on day +29 revealed minimal hepatomegaly

and no ascites. The patient remained transfusion-dependent, presenting symptoms of consumptive RT. Therefore, DF administration was prolonged until complete VOD resolution on day +44. Stable, well, and VOD-free, the patient was discharged home on day +53.

Conclusions: Hyperbilirubinemia is not a mandatory symptom of VOD even in the most severe cases. Pentoxifylline might prevent hepatorenal syndrome in VOD patients when peritoneal drainage is hazardous. Despite the severity and the dynamics of VOD, we observed quick and complete recovery, possibly due to preemptive treatment with DF. Persistent RT, being a manifestation of ongoing VOD, should indicate maintenance of treatment with DF even in the absence of other symptoms. To reduce the risk of busulfan-associated toxicity, TDM should be implemented especially in young children.

Disclosure: Nothing to declare.

Non-infectious Late Effects, Quality of Life and Fertility

P150.

Impact of Age in Early And Late Complications After An Allogeneic Transplant in Elderly Patients

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Background: Allogeneic transplant (HSCT) may be a curative treatment for elderly patients, although it is uncommon in patients over 65 years old due to poor outcomes and high post-transplant toxicity. The aim of this study is to examine complications and toxicity after HSCT in patients aged 60 to 65 years compare to patients over 65.

Methods: We performed a single-center retrospective analysis of 70 patients over 60 years old transplanted with an allogeneic peripheral blood stem cells transplant between 2013 and September 2020.

Results: 52/70 patients were included in the 60-65 years group, with a median of 62; and 18/70 in the >65 years group, with a median age of 67 (66-69). Baseline characteristics of entire cohort are reflected in Table 1.

77% of the patients >65 received an haploidentic transplant, whereas in 60-65 the donor type was equally distributed in haploidentic, MSD and MUD (Table1). All of >65 received a reduced intensity transplant whereas 3 patients in the 60-65 had a myeloablative conditioning. GvHD prophylaxis included post-transplant methotrexate and cyclosporine for myeloablative conditioning and cyclosporine and mycophenolate mofetil for reduced intensity; haploidentic types also received post-transplant cyclophosphamide and unrelated types received ATG.

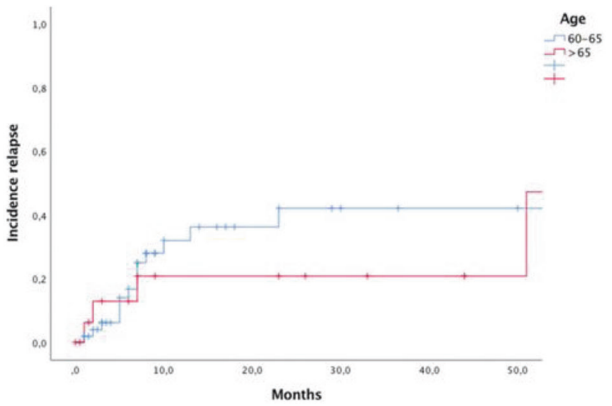
3 patients 60-65 and 1 patient >65 presented primary graft failure (p>0.05), with no differences regarding donor type. Incidence of acute graft versus host disease (aGvHD) was 66% in 60-65, 28.8% presented at grade III-IV; in >65, the incidence was 29.4%, 5.6% developing high grade ($p < 0.05$). cGvHD oscillated between 47 and 60%, with nearly 30% of the patients presenting moderate or severe disease (p>0.05). Neither donor type, gender or CMV disparity showed significant impact on aGvHD or cGvHD.

30% of the patients 60-54 had a proven/probable invasive fungal infection (IFI) versus 12% of the patients >65 (p>0.05), being higher among patients with high dose use of corticoids ($p < 0.05$). Thrombotic microangiopathy was found in 6% of HSCT in both groups and over 70% presented cytomegalovirus reactivation, with no significant differences between the groups.

There was an estimated 2-yo relapse rate of 42% for 60-65 and 21% for >65, with a HR 0.94 (CI 95% 0.34-2.65) (Figure 1).

Table1. Basal characteristics of patients. Abbreviations: AML, Acute Myeloid Leukemia; MDS, myelodisplasic syndrome; NHL, non-Hodgin lymphoma; F, female; M, male; N negative; P, positive; MSD, matched sibling donor; MUD, matched unrelated donor.

	60-65 ($n = 52$)	>65 ($n = 18$)	p
GENDER, male n (%)	35 (71.2%)	14 (77.8%)	>0.05
DIAGNOSIS n (%)			
AML	24 (46.2%)	7 (38.9%)	>0.05
MDS	26 (30.8%)	7 (38.9%)	
NHL	6 (11.5%)	1 (5.6%)	
Others	6 (11.5%)	3 (16.7%)	
GENDER DISPARITY RECIPIENT/DONOR			
Non disparity	30 (68.2%)	6 (40%)	>0.05
F/M	8 (18.2%)	4 (26.7%)	
M/F	6 (13.6%)	5 (33.3%)	
CMV PRE-HSCT R/D n(%)			
N/P	2 (4.5%)	-	>0.05
P/N	9 (20.5%)	1 (6.7%)	
P/P	33 (75%)	14 (93.3%)	
DONOR TYPE n (%)			
MSD	2 (4.5%)	2 (11.1%)	<0.05
Haploidentic	9 (20.5%)	14 (77.8%)	
MUD	33 (75%)	2 (11.1%)	
CONDITIONING			
Reduced-intensity	45 (93.8%)	18 (100%)	>0.05
Mieloablative	3 (6.3%)	-	



Conclusions: In our population, patients >65 years did not present more post-HSCT complications than patients 60-65. No significant differences were found either between donor types. Therefore, HSCT should be considered in elderly and fit patients when indicated avoiding limitations regarding just age or having an identical HLA donor.

Disclosure: Nothing to declare.

P151.

Osteonecrosis in Patients Undergoing Hematopoietic Stem Cells Transplant: A Single-Center Study of Incidence, Risk Factors, Characteristics And Evolution

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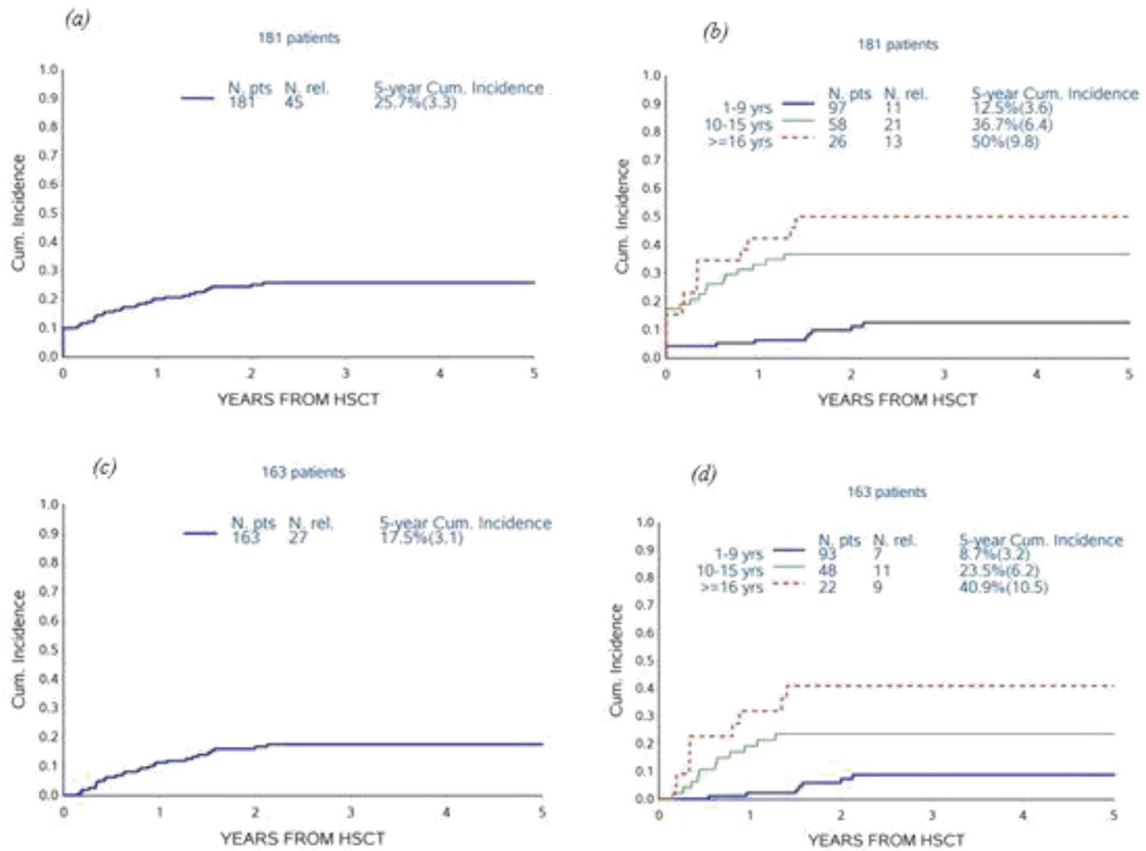
Background: Osteonecrosis (AVN) is a frequent and severe complication in children undergoing HSCT. AVN incidence varies widely among studies (4-44%) and its classification and management are still controversial.

Methods: This study includes patients <21 years transplanted in our Institution, between March 2012 and

Five-year cumulative incidence of avascular necrosis overall (a) and according to age (b) and after HSCT (c) and after HSCT according to age (d)



December 2017. AVN was diagnosed upon symptoms and monitored by MRI, classified according to the Niinimäki and Steinberg grading, with the former scoring every AVN lesion at any site and the latter scoring AVN lesions of the convex surfaces in the lower limbs only. Transplant-related risk factors for AVN were analyzed after excluding patients affected prior to HSCT. AVN evolution was assessed.

Results: 45 of the 181 transplanted patients developed AVN before (18) or after HSCT (27). The overall 5-year cumulative incidence of AVN (5 yr CI-AVN) was 25.7% (SD: 3.3) (Fig. 1). The 5-yr CI-AVN diagnosed after HSCT was 17.5% (SD: 3.1), significantly increased by age (1-9 year old: 8.7%, SD: 3.2; 10-15 years old: 23.5%, SD: 6.2; ≥16 years old: 40.9%, SD: 10.5; $p < 0.001$), as shown in Figure 1, and was associated with TBI ($p < 0.001$) and aGvHD of any grade ($p = 0.002$).200 MRIs were assessed and a total of 307 lesions were detected overtime, with a median of 5 lesions per patient (1-18, IQ 2-11). The knee resulted the most affected joint, followed by the ankle and the hip. During the follow-up, the total number of lesions increased from 307, detected at the first MRI, to 380, with a median of 8 lesions per patient (1-22, IQ 4-13). A high percentages of diaphyseal involvement was found in our population, but, since they were asymptomatic and didn't worsen, they were judged as non-clinically relevant. In 37 patients, who performed more than one MRI overtime, we evaluated the evolution of the lesions. Our data showed that convex surfaces were more severely and most frequently involved compared with concave surfaces. In terms of hip involvement, no lesions were detected in the acetabular roof (concave surface) but in 2, which regressed to grade 0 during follow-up, whereas more frequent, higher grade and worse evolution (4 grade III and 9 grade IV by Steinberg) occurred in the femoral head (convex surface) involved. 16/45 (36%) patients underwent surgery, mainly through the core decompression technique. The knee was the most frequently operated district. 5/12 patients with available clinical follow-up reported pain resolution after surgery.

Conclusions: Our study underlines the high risk of AVN in transplanted patients and age, TBI and aGVHD as significative risk factors. The Steinberg classification gives relevant information on AVN extension and quality of the lesion, possibly predicting their prognosis. Our findings suggest that convex surfaces are more frequently involved and are at major risk of severe lesions.

Disclosure: Nothing to declare.

P152.

Secondary Malignancies After Autologous Hematopoietic Stem Cell Transplantation

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Background: After autologous hematopoietic stem cell transplantation (ASCT), long-term survivors are at considerable risk for secondary malignancies, especially therapy-related myeloid neoplasms, which is related to the type and intensity of chemotherapy received prior to and during conditioning and HSCT, with a cumulative incidence that can exceed 10%.

Methods: Retrospective analysis of secondary malignancies in patients who underwent ASCT from January 2008 to November 2020 in a single institution. Median follow-up was 93 months. Statistical analysis was performed using SPSS v26.

Results: A total of 501 patients underwent ASCT during this period and 22 (4.4%) developed a secondary malignancy. Of these, 15 patients (68.2%) were male, the median age at the time of the second cancer diagnosis was 59 years and the median age at the time of the first ASCT was 62 years. Three patients (13.6%) had undergone a second ASCT, at a median age of 68 years. Overall, 14 patients (63.6%) were transplanted due to multiple myeloma (MM), 6 patients (27.3%) due to non-Hodgkin lymphoma (NHL) and 2 patients (9.1%) due to Hodgkin lymphoma (HL). MM patients had a median of 1 therapeutic regimen prior to transplant: in 71.5% a Bortezomib-based regimen, 14.2% Bortezomib- and Lenalidomide-based regimens, 14.2% anthracycline-based therapies and three patients received radiotherapy (RT). Nine patients (64.3%) received maintenance therapy with an immunomodulatory drug following ASCT. All 3 patients who underwent a second ASCT received maintenance therapy with Lenalidomide (one of these patients underwent tandem ASCT). All NHL transplanted patients had undergone 2 previous chemotherapy regimens, the first anthracycline-based followed by a platinum-based regimen. None had undergone RT. One HL patient had undergone BEACOPP followed by 2 platinum-based regimens while the other underwent ABVD followed by BEACOPP. Both received RT. Melfalan 200mg/m2 was the conditioning regimen used in all MM patients and BEAM in the lymphoma group.

Regarding the secondary malignancies, 21 patients developed 1 type of cancer and 1 patient 2 tumors. Twelve patients (54.5%) presented secondary hematologic malignancies: 8 acute myeloid leukemia and 4 myelodysplastic syndrome. Of the remaining 10 patients, 3 developed skin cancer (1 squamous-cell carcinoma, 1 basal-cell carcinoma and 1 melanoma), 1 colon adenocarcinoma, 1 prostate

adenocarcinoma, 1 germinate line tumor, 1 sarcoma, 1 thyroid carcinoma, 1 larynx carcinoma and 1 patient developed breast carcinoma followed by thyroid carcinoma. Median time between ASCT and the diagnosis of the secondary cancer was 39 months [14–146], with no statistically significant differences between those who developed secondary hematologic (HM) and non-hematologic malignancies (NHM) ($p = 0.741$). Overall, two-thirds of patients died, 83.3% in the HM group and 20% in the NHM group. In the HM group, 5 patients (41.7%) underwent therapy with Azacitidine, of which 80% died. The remaining 7 patients received support therapy. Median overall survival (OS) since the diagnosis of the secondary malignancy was 3 months, with no statistically significant differences between HM and NHM groups ($p = 0.243$).

Conclusions: in our cohort, the incidence of secondary malignancies was lower than that reported by previous studies. Nevertheless, the prognosis of such malignancies remains poor.

Disclosure: Catarina Geraldes received honoraria from lectures and participation on Advisory Boards from Celgene, BMS, Janssen, Amgen, Takeda, Sanofi and Gilead.

P153.

Secondary Malignancies After Allogeneic HSCT in Children

Yulia Skvortsova[1], Larisa Shelikhova[1], Dmitrij Balashov[1], Anna Scherbina[1], Irina Kondratenko[2], Elena Skorobogatova[2], Denis Kachanov[1], Nikolaj Grachev[1], Yulia Rodina[1], Elena Deripapa[1], Ella Kumirova[1], Kirill Voronin[1], Michael Maschan[1], Alexey Maschan[1]

[1]Dmitry Rogachev National Research Center of Pediatric Hematology, Oncology and Immunology, Moscow, Russian Federation, [2]Russian Children's Hospital, Moscow, Russian Federation

Background: Secondary malignancies after allogeneic HSCT is rare but life-threatening late effect with increasing incidence over time.

Methods: We present retrospective analysis of secondary malignant diseases in 2 groups of children and young adults after allogeneic HSCT. Group 1 - 289 children (170 boys, 119 girls) who underwent conventional allogeneic HSCT from 1994 to 2011 at BMT Department of Russian Children's Hospital. Group 2 - 864 children (564 boys, 300 girls), who got allogeneic HSCT with TCRαβ- and CD19-depletion at BMT 1&2 Departments of Dmitry Rogachev National Research Center of Pediatric Hematology, Oncology and Immunology (Moscow, Russia) between 2012 and 2019.

Results: in Group 1 with follow-up period 1-18.5 years (median 7 years) 8 patients (6 boys, 2 girls) developed secondary malignancies (2.8%; cumulative incidence 8.1%; 95% CI 0-16). Three of them had diagnosis of Fanconi anemia and presented oral cancer 14, 11 and 10 years after HSCT. Follow-up was not regular, all started treatment in advanced stages of cancer, one is alive after radical surgical intervention. Two patients died due to disease progression. Other three solid tumors presented: glioblastoma in boy after 2 HSCTs for B-cell lymphoma (7 years after last HSCT); esophagus cancer in young man transplanted in 3rd complete remission of ALL and had severe chronic GVHD (9 years after HSCT); adenocarcinoma of salivary gland in boy with primary immunodeficiency: hyper-IgM syndrome, who got 2 allogeneic HSCTs and developed chronic severe GVHD (5 years after HSCT). Only last patient with earlier stage of cancer treated by surgery survived. Two of 8 young adults presented hematologic malignancies: secondary AML from donor cells in girl transplanted for AML (10 years later) – she got chemotherapy and 2nd allogeneic HSCT and achieved complete remission, secondary Hodgkin lymphoma in boy 6 years after allogeneic HSCT for AML – alive after chemotherapy. So, 4 of 8 patients survived.

In Group 2 with follow-up period 1-8 years (median 3.8 years) secondary malignancies occurred in 6 children - 3 boys and 3 girls (0.7%; cumulative incidence 0.77%; 95% CI 0.34-1.75). Four of them had primary immunodeficiency with genomic instability – 3 patients with Nijmegen syndrome developed 2 cases of rhabdomyosarcoma and 1 T-cell lymphoma 1 year after HSCT (1 patient is alive) and one boy with Kabuki syndrome died from Kaposi sarcoma 1 year after HSCT. One girl transplanted for ALL presented Kaposi sarcoma 1 year later but died from COVID-19 infection. Inflammatory fibroblastic tumor of jejunum was detected in boy with STAT3 defect 4 months after HSCT and was successfully operated. Thus, 2 of 6 patients survived.

Conclusions: Secondary malignancies in children after HSCT develop predominantly in patients with genomic instability or chronic GVHD, have poor treatment response and lead to decrease of survival. Less GVHD incidence after T-cell depletion in Group 2 and shorter follow-up period could explain lower rate of secondary neoplasms. High risk patients should be closely monitored for early detection and prompt treatment. Patients without chromosomal instability develop secondary malignancies mostly in adulthood, so cancer alertness is important.

Disclosure: Nothing to declare.

P154.

Anxiety Symptomatology Progression in Patients with Diagnosis of Malignant Hematological Pathology Who Are Candidates to Receive Intensive Chemotherapy

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Background: Patients who are diagnosed malignant hematological pathology, and who are needed from urgent intensive chemotherapy treatment, may present high anxiety levels. Although this symptomatology is part of an adaptative process, sometimes it may turn into more pathological states, such as a mixed anxiety and depression disorder.

Methods: Patients older than 18 years old and who were going to receive chemotherapy treatment were included from June 2018 to December 2019. Patients presenting any previous diagnosis of any mental disorder according to DSM-IV or ICD 10 were excluded. The Spanish adaptation of the STAI questionnaire was used. This self-administrated instrument is comprised of 2 scales: State (S) anxiety, which is a changeable condition, and Trait (T) anxiety, which indicates a relatively stable anxious propensity among the individual's life. Patients fulfilled the STAI questionnaire twice: First, on their first admission and during the first 72 hours after receiving the diagnosis of the malignant hematological pathology (Moment 1). And second, during the admission prior to the chemotherapy treatment. The final sample was comprised of 45 participants (Women: n = 26; 57.8%; Men: n = 19; 42.2%), from 19 to 79 years old (M = 56.29).

Results: The median duration of admission was 25 days (5-77). The main diagnoses were: Acute Myeloid Leukemia (n = 23; 51.1%), Non-Hodgking Lymphoma (n = 12; 26.7%), Acute Lymphoblastic Leukemia (n = 5; 11.1%), Myelodysplastic Syndrome (n = 2; 4%), and Acute Promyelocytic Leukemia (n = 3; 6.7%). At moment 1, the mean score in state anxiety was 26.42 points, 5.88 points higher than the population scale. This difference was statistically significant (p = 0.04 CI at 95% 20.82-32.02). Regarding women, the difference between the state anxiety score (M = 25.4) and the population scale was not statistically significant (p = 0.47 95% CI 19.50-31.3). At moment 2, the mean score in state anxiety in men was 19.5. This difference was not statistically significant compared to the population scale (p = 0.7 with a 95% Confidence Interval (CI) between 20.82 and 32.02). In women, the mean score was 18.5, which was statistically significant from general population (p = 0.03, with a 95% CI between 14.5 and 24.5).

Conclusions: This exploratory study shows that patients presented a decrease in their anxiety levels throughout the process. Future studies may focus on which strategy is chosen by patients to cope with the diagnosis: Psychological, pharmacological, or even no formal intervention (self-adaptation by natural recovery).

Disclosure: No conflict of interest.

P155.

An Unusual Presentation of Autoimmune Disorders After Allogeneic Stem Cell Transplantation – Amyopathic Dermatomysistis, Primary Biliary Cholangitis And Autoimmune Hemolytic Anemia

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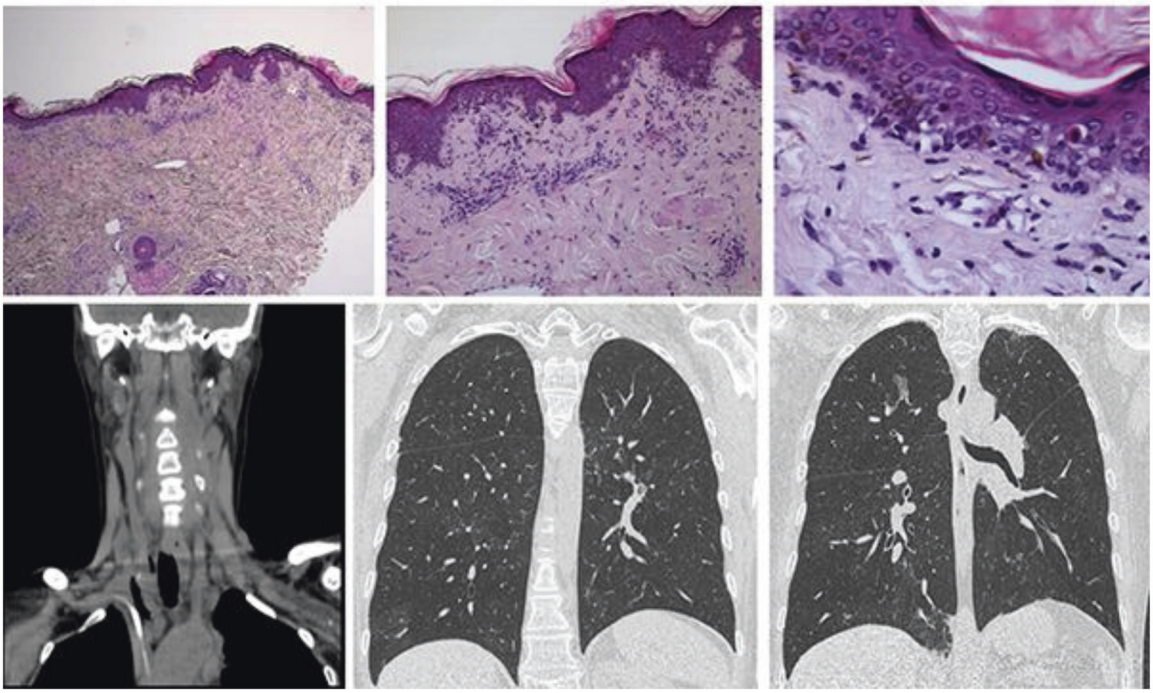
Background: The dysregulation of immune reconstitution following allogeneic stem-cell transplantation (alloSCT) presents classically as chronic graft vs host disease (cGVHD), which frequently resembles an autoimmune disorder. Immunologic phenomena not classified as cGVHD are infrequently recognized and include antibody-mediated immunity against antigens not necessarily host-related. Autoantibodies detected in this setting are usually organ-specific and the concomitant diagnosis of alloreactive dysfunction is uncommon.

Methods: Clinical case report.

Results: A 34-year-old woman with refractory Hodgkin's disease underwent alloSCT from a matched unrelated male donor. 24 months after transplantation she needed continued immunosuppression due to pulmonary and cutaneous cGVHD. At 32 months after SCT, while on low dose immunosuppression, the patient was hospitalized for fatigue, generalized erythematous rash and cytocholestasis. Careful skin examination revealed bilateral heliotrope, Shwal and V signs, Grotton papules, palmar erythema and periungual vasculitis. These signs suggested the diagnosis of dermatomyositis and the following investigation was carried out:.

1) skin biopsy, which revealed perivascular lymphocytic infiltrates at the superficial dermis and epidermal atrophy with focal hydropic degeneration and isolated necrotic keratinocytes (findings that were considered



indistinguishable between cutaneous cGVHD and dermatomyositis);.

2) autoimmune serology, which detected strong positive anti-MAD2 and anti-mithocondrial M2 antibodies (despite immunosuppression);.

3) lung imaging, which was consistent with interstitial lung disease and pneumomediastinum;.

4) myositis was excluded through neurologic examination, serum biochemistry (normal creatinine kinase, myoglobin and aldolase) and electromyography.

Based on these findings, the diagnosis of anti-MDA5 amyopathic dermatomyositis with interstitial lung disease and primary biliary cholangitis were made. After adjusting the dose of immunosuppression, the patient improved her condition; however she soon developed both microangiopathic and positive DAT hemolytic anemia, IgG positive, which resolved with the discontinuation of calcineurin inhibitor and increasing dose of steroids. Due to the presentation of multiple immune phenomena and concern of relapse, chimerism testing was performed, revealing 100% donor cells. Sex chromosome analysis of a paraffin-embedded affected skin specimen was carried out, and there was no evidence of Y chromosomes by FISH and RT-PCR. These findings suggested the coexistence of a complete chimera and tissue infiltrating by host lymphocytes causing autoimmune dermatomyositis. After discharge, the patient started follow-up by a multidisciplinary team and is progressively improving her condition.

Figure 1: Top figures reveal the inflammatory histologic skin changes. Bottom figures reveal pneumomediastinum (left side) and ground glass opacities (right side) detected on coronal-plane thoracic CT scan.

Conclusions: Autoimmune disorders developing after alloSCT are very difficult to distinguish from cGVHD, which frequently arises in this setting, manifesting as an autoimmune-like inflammatory disease. Autoimmune serology testing in selected post-alloSCT patients may help unveil immunologic phenomena that would otherwise be underestimated by chimerism studies. This case highlights an unusual presentation of confirmed autoimmune disorders developing post-alloSCT in a patient with complete donor chimerism.

Disclosure: Nothing to declare.

Pediatric Issues

P156.

Post-Transplant Cyclophosphamide After Allogeneic Hematopoetic Stem Cell Transplantation For Pediatric Hodgkin Lymphoma

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Background: Relapsed or refractory classical Hodgkin lymphoma (R-R cHL) is uncommon in children but still is a challenge for a treating physician. Patients with failure of autologous hematopoietic stem cell transplantation (auto-HSCT) have poor prognosis. In these patients allogeneic hematopoietic stem cell transplantation (allo-HSCT) results in improved outcome compared to chemotherapy alone. Introduction of effective and technically simple graft versus host disease (GVHD) prophylaxis with cyclophosphamide (PTCy) became a game changer in allo-HSCT. Data for this option in pediatric Hodgkin lymphoma are limited.

Methods: in Raisa Gorbacheva Memorial Research Institute of Children Oncology, Hematology and Transplantation, Pavlov First St. Petersburg State Medical University, 13 children with R-R cHL received alloHSCT with PTCy. Median age at diagnosis was 14 years (9-17) and median age at transplantation – 17 years (14-18). Median number of prior therapy lines was 5 (1-6) with autologous HSCT in 6 (46%). Relapsed cHL was diagnosed in 6 patients (46%), refractory in 6 (46%) and 1 (8%) child received allo-HSCT due to unclassified primary immunodeficiency complicated by cHL. According to Lugano criteria remission before allo-HSCT was achieved in 69% ($n = 9$) with complete response in 54% ($n = 7$) and partial response in 15% ($n = 2$). Prior to allo-HSCT immunotherapy with nivolumab was performed in 4 patients (31%) and donor lymphocytes were infused after transplantation in 6 (46%). Fully HLA-matched sibling donor was used in 3 children (23%), fully HLA-matched unrelated donor – 4 (31%), HLA-mismatched (one mismatch) unrelated donor – 3 (23%) and haploidentical donor - 3 (23%). Following conditioning regimen was used: fludarabine 90 mg/m2+ bendamustine 390 mg/m2. PTCy 100 mg/m2 for GVHD prophylaxis was used in all patients (monotherapy for related transplants and in combination with calcineurin inhibitors and/or mTOR inhibitors for unrelated or haploidentical transplants).

Results: with median follow-up of 609 days (301-1636) 4-year OS and PFS were 67% and 52%, respectively. Cumulative incidences of relapse/progression at 4 years and non-relapse mortality were 38% and 15%, respectively. Cumulative incidences of acute and chronic GVHD were 8% and 40%, respectively.

Conclusions: PTCy demonstrated high effectiveness in the prevention of acute GVHD in children with cHL. High levels of chronic GVHD despite PTCy were probably associated with the use of immunotherapy prior and post transplantation.

Disclosure: Nothing to disclose.

P157.

Frequency And Causes of Death After Hematopoietic Stem Cell Transplantation in Children with Non-Malignant Diseases

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Background: Despite the improvements in supportive care, immunosuppression, and infection treatments, morbidity and mortality remain an important problem. This study aims to determine the mortality rates and causes in patients who underwent HSCT with non-malignant diseases.

Methods: Between 2011 and 2020, 1101 children who underwent HSCT due to non-malignant diseases in Medicalpark Göztepe&Antalya Hospitals were evaluated retrospectively.

Results: Median follow-up period is 50 months (6-117months) in alive patients.We lost 192 patients and mortality rate was found as 17.4%.The distribution and mortality rates of cases in respect of diagnosis were found that thalassemia ($n = 410$)4.8%, immune deficiencies ($n = 273$)26%, HLH ($n = 81$)25.2%, aplastic anemia ($n = 63$) 7.5%, Fanconi anemia ($n = 99$) 26.2%, pure red cell aplasia ($n = 29$)24.1%, congenital neutropenia ($n = 13$) 0%, other bone marrow failure syndromes ($n = 20$)15%, adrenoleukodystrophy and metachromatic leukodystrophy ($n = 38$) 28.9%, osteopetrosis ($n = 41$)39%, Hurler disease ($n = 15$)%20 and the other metabolic disorders ($n = 19$)15.8%.

Mortality rates were found in bone marrow ($n = 610$) and peripheral blood stem cell ($n = 326$) groups as 15.4% and 18.7%,respectively. The highest mortality rate was seen in the unrelated cord blood transplantation group ($n = 63$) as% 38.1. The lowest mortality rate was found bone marrow +cord blood ($n = 54$) group which all were MSD.

In respect of donor type and HLA matching, mortality rate was%7 in MSD cases ($n = 357$). In matched related donor group (MRD); mortality rate was 16% in 10/10 MRD cases (n= 131) and 36.8% in 9/10 MRD cases ($n = 19$). Mortality rates were found as 13.7%,%26.8% and 39% in 10/10 MUD cases ($n = 248$), 9/10 MUD cases ($n = 246$) and in haploidentical cases ($n = 100$),respectively.

Infection was the most common cause of death (51%) that was followed by GVHD (10.4%).We have evaluated our patients who were monitored due to GvHD but lost due to intervening infection, with a mortality rate of 13.5%. Other causes of mortality were VOD (4.7%), bleeding (7.3%).

One Fanconi patient has developed ALL after 6 years and was lost. Nine patients were lost because of the primary diseases.Five patients died because of other causes, which were ARDS after rituximab, drug toxicity,post-transplant lymphoproliferative disease, PRES, and idiopathic hyperammonemia.The cause of death of 8 patients who died in the other centers could not be determined.

Regarding the time of death,19.8% of deaths were in the first 30 days,57.8% were in the first 100 days and 87.5% were in the first year.Infection was the leading cause with% 51 of all deaths.The GvHD mortality rate was 8.9% in the first year and increased to 20.8% afterward.

Conclusions: Our center is one of the tertial centers in our country that's why most of the patients were high risk and resistant patients.Mortality rates were lower in congenital neutropenia and thalassemia, higher in immunodeficiency and osteopetrosis cases.The mortality rate was the highest in the use of cord blood as a source of stem cells (38.1%) and 2 times higher than 10/10 MUD compared to 9/10 MUD ($p < 0.001$).The most important causes of death were infection and GVHD.

Careful analysis of data from periodic studies, taking into account multi-center and large group co-morbidity data, will be useful to improve the outcomes of HSCT.

Disclosure: Nothing to declare.

P158.

Risk Factors And Survival of Graft Failure in Pediatric Patients with Hematological Malignancies Treated with Allogeneic Hematopoietic Stem-Cell Transplantation From Haploidentical Donors Using Ex Vivo T-Cell-Depletion

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Background: Graft failure is a rare but potentially severe complication in patients treated with allogeneic hematopoietic stem-cell transplantation (aHSCT). There are very few studies analyzing risk factors when ex-vivo T-cell depletion is used.

Methods: A total of 148 pediatric patients (94 males) diagnosed from hematological malignancies that underwent allogeneic HSCT from haploidentical donors using ex_vivo T-cell depletion between 2005 and 2020 were included. Donors mean age was 40 (range: 2-54) years. All patients received reduced toxicity conditioning based on fludarabine busulphan and thiotepa.

Results: A total of 20 patients (global incidence of 13%) presented graft failure (12 primary and 8 secondary). Only in one case anti-HLA antibodies were positive. Univariate analysis showed that patient age (13% incidence in patients less than 9 years old compared to 3% incidence in 9 years old or more; p= 0.018), disease stage (early stage 15% vs advanced stage 5%; $p = 0.03$), total lymphocyte count pre-aHSCT (15% incidence if 700/mL vs 2% incidence if <700/mL; $p = 0.02$), T-cell count pre-aHSCT (17% if >= 350/mL vs 0% if <350/mL; $p = 0.007$), CD4+ count pre-aHSCT (15% if >= 150/mL vs 2% if <150/mL; $p = 0.006$), and CD8+ count pre-aHSCT (17% if >= 150/mL vs 0% if <150/mL; $p = 0.003$) were associated with increased risk of graft failure. Multivariate analysis showed that T-Cell count (>= 350/mL: HR: 2,6: 1,7-115,5; p= 0.01) and patient age (< 9 years: HR; 5.0: 1.1- 23.4; $p = 0.04$) were associated with graft failure.

A risk score was established based on patient age and T lymphocyte pre-aHSCT with one point each one: patients with one point had a graft failure risk of 5% and 13% if they had two points.

With a mean follow up of 4 years (range: 3 moths – 15 years), the survival rate is 60%, with no significant differences between patients that presented graft failure and patients without this complication.

Conclusions: Our research allows us to identify risk factors (patient age less than 9 years old and T lymphocytes before transplantation) for graft failure in patients undergoing allogenic HSCT from haploidentical donor using exvivo T-cell depletion.

Disclosure: Nothing to declare.

P159.

SVEGF-R1 Levels Are Associated with Endothelial Dysfunction After Pediatric Hematopoietic Stem Cell Transplantation

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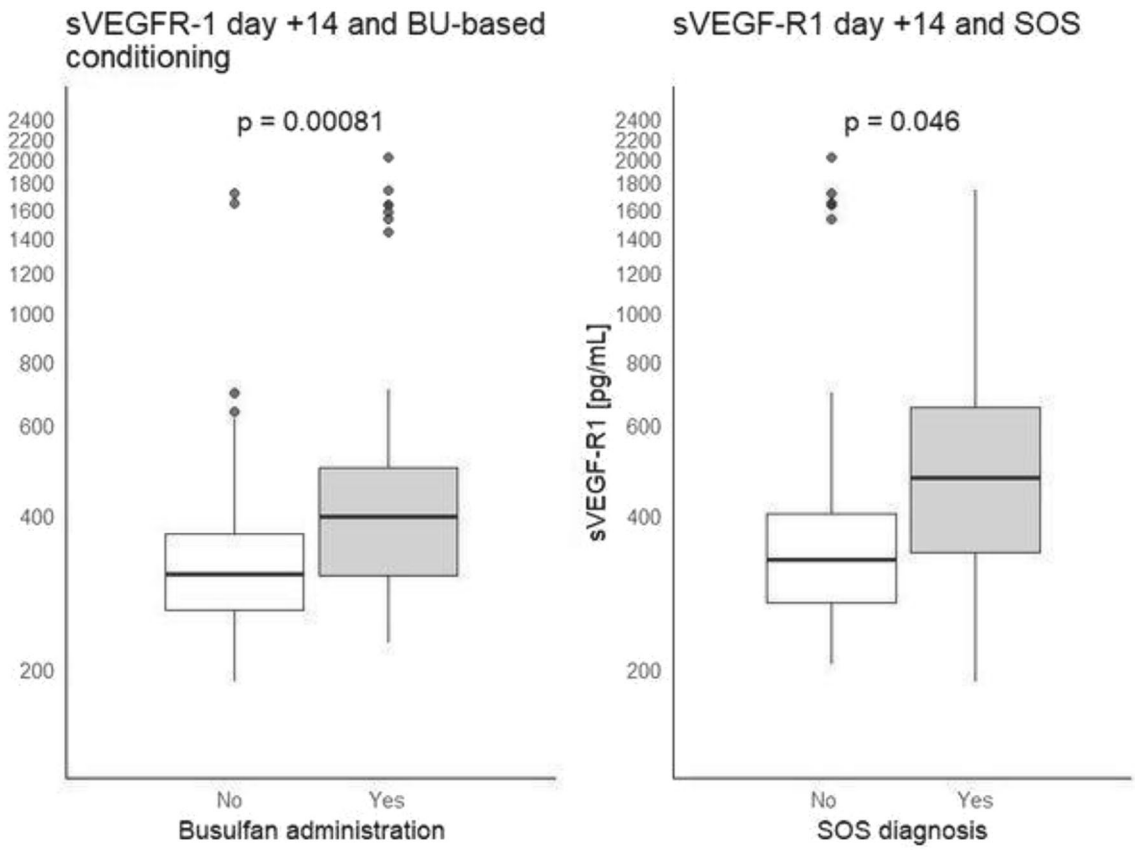
Background: Allogeneic hematopoietic stem cell transplantation (HSCT) is limited by acute toxicities including sinusoidal obstruction syndrome (SOS), acute graft-versus-host disease (aGvHD) and capillary leak syndrome (CLS). These complications are initiated by a dysfunctional vascular endothelium, although the pathophysiology remains incompletely understood. Soluble vascular endothelial growth factor receptor-1 (sVEGF-R1) has previously been associated with endothelial cell activation and damage in patients with trauma and sepsis.

In this study, we investigated plasma levels of sVEGF-R1 as a marker of endothelial dysfunction and its associations with treatment-related complications after pediatric HSCT.

Methods: We included 113 children undergoing HSCT from 2010-2019 in Denmark with a median age of 9.0 years (range: 1.1-17.6); of these 69 patients (61.1%) had malignant diagnoses. All patients were treated with myeloablative conditioning based on either TBI ($n = 27$), busulfan ($n = 50$) or other chemotherapy ($n = 36$). Donors were either MSD ($n = 33$), MUD ($n = 67$) or MMUD ($n = 13$) and grafts were BM ($n = 108$) or PB ($n = 5$). Seven high risk patients received prophylactic defibrotide for SOS.

sVEGF-R1 levels were measured with ELISA prior to conditioning, at day of HSCT and at day +7, +14, +21, +30, and +90 post-transplant.

Results: sVEGF-R1 levels were significantly increased from day +7 compared to pre-HSCT levels and peaked at day +30 (all $p < 0.05$). Patients receiving busulfan as part of conditioning had significantly elevated sVEGF-R1 levels from the day of transplantation until day +90 compared to non-busulfan regimens (all $p < 0.05$, figure A). Seven high-risk patients receiving prophylactic defibrotide showed significantly elevated levels of sVEGF-R1 before conditioning (446.3 pg/mL vs. 281.3 pg/mL, $p = 0.0035$) but did not increase further post-transplant, thereby achieving similar levels after HSCT as patients without defibrotide prophylaxis. Fourteen (12.4%) children were diagnosed with SOS using the modified Seattle criteria at median day +8 (range: +1-+18), and these had significantly higher sVEGF-R1 levels on day +14 (figure B). In a logistic regression analysis, children with increasing levels of sVEGF-R1 at day +14 had increased risk of SOS (OR = 1.94 pr. quartile, $p = 0.036$). Busulfan-based conditioning was also associated with increased risk of SOS in univariate analysis. Conditioning regimens based on busulfan and not including ATG was also associated with SOS. In a multivariable analysis, sVEGF-R1 levels remained associated with SOS after adjustment for ATG (OR = 2.17 pr. quartile, $p = 0.0221$), but was lost when adjusted for busulfan.sVEGF-R1 levels were significantly increased on day +30 in



seven patients with aGvHD grade III-IV (373.5 pg/mL vs. 467 pg/mL, $p = 0.014$). ATG was associated with a lower risk of aGvHD grade III-IV ($p = 0.0229$). In a multivariable logistic regression analysis, sVEGF-R1 levels remained associated with severe aGvHD after adjustment for ATG (OR = 4.21 pr. quartile, $p = 0.0225$). No association was found between sVEGF-R1 levels and CLS ($p > 0.05$).

Conclusions: This study demonstrates that elevated levels of sVEGF-R1 are associated with SOS and aGvHD after HSCT, suggesting that conditioning-induced activation and damage to the endothelium plays a key role in the pathogenesis of these complications. These findings indicate that sVEGF-R1 may prove useful as a biological marker for treatment-related complications and could help guiding treatment and prophylaxis.

Disclosure: Nothing to declare.

P160.

Late Endocrine Effects After Hsct in Children with Nonmalignant Diseases: A Single Center Cohort Analysis

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Background: While many studies have addressed endocrine late effects after pediatric hematopoietic stem cell transplantation (HSCT) for malignant diseases, knowledge is scarce in children transplanted for nonmalignant diseases.

Methods: This retrospective study included 197 children transplanted for a non-malignant disease between January 1997 and November 2018 with at least 2 years of follow up. Endocrine late effects and growth were evaluated. Gonadal dysfunction was defined as transient or permanent elevation of gonadotropins or hypogonadotropic hypogonadism, and only assessed in (post)pubertal patients. Hypothyroidism was defined as low FT4 and/or TSH > 10 mU/L. Growth was assessed in those who had reached near adult height (NAH), excluding those who had received growth hormone treatment.

Results: The study population consisted of 134 males and 63 females. Median age at HSCT was 5.7 years (IQR 2.8-11.3 years) and median follow-up was 6.2 years (IQR 3.0-10.4 years). Underlying diseases were inborn errors of immunity ($n = 74$), hemoglobinopathies ($n = 66$), and bone marrow failure ($n = 57$). The majority of patients had received busulfan-based (46%) or treosulfan-based (34%), mainly myeloablative, conditioning. The remainder was treated with chemotherapy with low dose irradiation (4%), fludarabine with cyclophosphamide (11%), cyclophosphamide (2%), other (2%) or no conditioning (2%).

Gonadal dysfunction occurred in 24 of 44 female patients (55%) from who data were available, and 5 of them recovered (21%). Hormonal substitution was started in 22 of 44 females (50%), and could be stopped in 7/22 (32%), but in two gonadotropins remained elevated. Half of patients with gonadal dysfunction were prepubertal at HSCT. In females that received busulfan-based conditioning 16 of 17 (94%) developed gonadal dysfunction compared to 5 of 15 (33%) with treosulfan-based conditioning.

Gonadal dysfunction occurred in 28 of 66 male patients (42%) from who data were available, and 5 of them recovered (18%). Treatment with testosterone or gonadotropins was started in 6 of 66 males, and could be stopped in 1. Gonadal dysfunction was more common in males (post) pubertal at HSCT, 14 of 21 (67%), compared to those prepubertal at HSCT, 14 of 45 (31%). Three of 15 males treated with a treosulfan-based regimen (20%) developed gonadal dysfunction, all were transient, versus 19 of 39 with a busulfan-based regimen (49%).

Permanent hypothyroidism occurred in 8 of 187 patients (4%). Two had central hypothyroidism. Seven of them received levothyroxine treatment. Transient and subclinical hypothyroidism were more common. All patients with persistent primary hypothyroidism had positive TPO-antibodies.

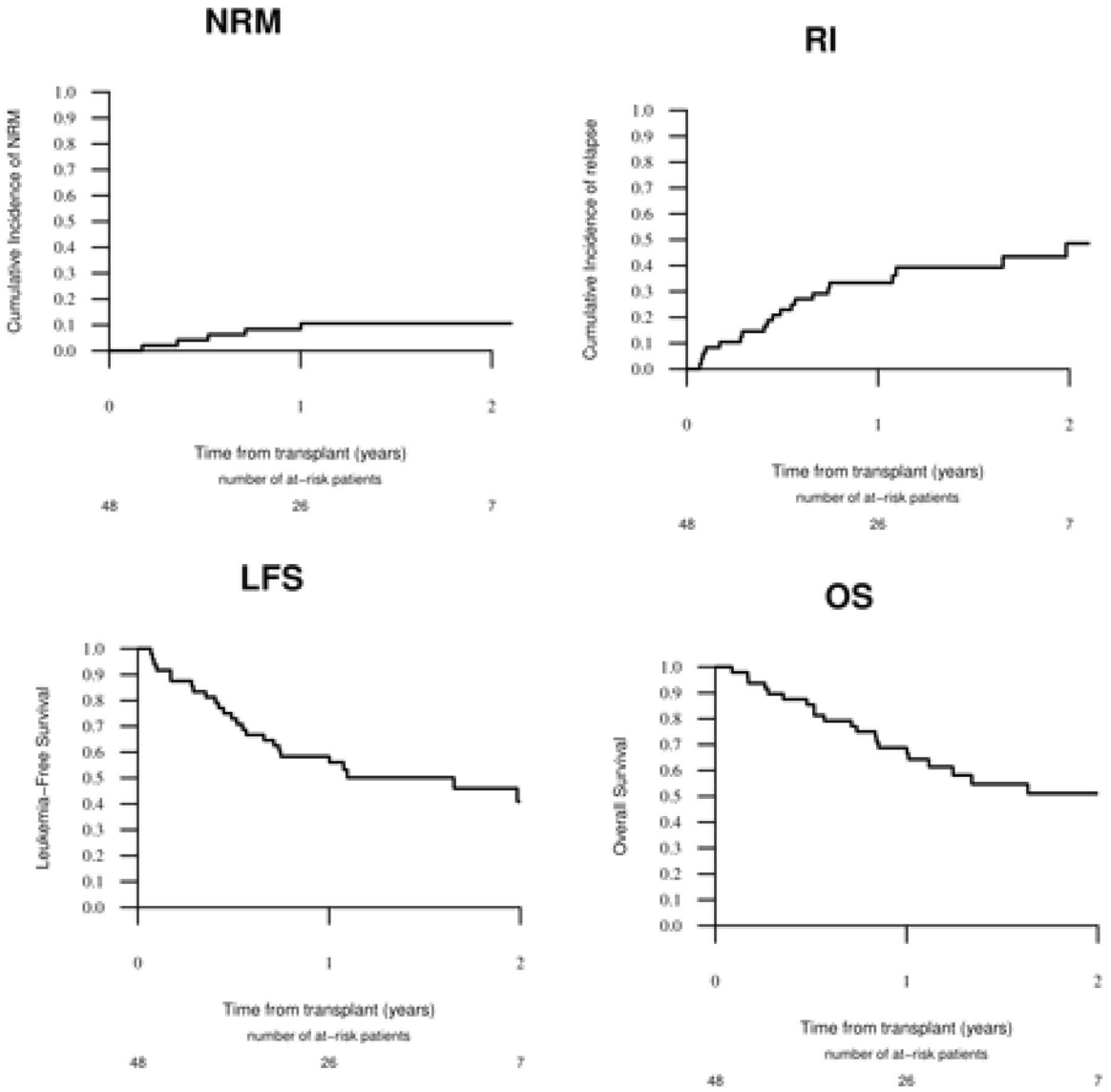
Near adult height below -2 SDS was seen in 13 of 43 males (30%) and 2 of 36 females (6%). The majority of these patients already had a height below -2 SDS before HSCT (73%).

Conclusions: in this study on late endocrine effects after HSCT in children with nonmalignant diseases we demonstrate gonadal dysfunction is the most frequent complication, present in 55% of females and 43% of males. Gonadal dysfunction was more frequent in those conditioned with a busulfan-based regimen than with a treosulfan-based regimen, but sample size was too small to perform a multivariate analysis. Careful long-term endocrine follow-up is indicated in this population.

Disclosure: Nothing to declare.

P161.

Prospective Multicenter Study of A Reduced-Toxicity Myeloablative Conditionning Regimen Using Fludarabine And Full Doses of Iv Busulfan in Pediatric Patients Not Eligible For Myeloablative Regimens



Fanny Rialland[1], Jean-Hugues Dalle[2], Gerard Michel[3], Virginie Gandemer[4], Catherine Paillard[5], Laurence Clement[6], Eolia Brissot[7], Charlotte Jubert[8], Anne Sirvent[9], Pierre-Simon Rohrlich[10], Dominique Plantaz[11], Myriam Labopin[12], Mohamad Mohty[7]

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Background: Reduced-toxicity conditioning (RTC) regimens are a well-established approach in adult patients, offering curative allo-SCT to patients with comorbidities. Because pediatric patients generally tolerate more intensive approaches, myeloablative regimens have continued to be the preferred approach. Data regarding the safety and efficacy of RTC to treat hematologic malignancies in pediatric patients are limited to single institution studies. The role of RTC in pediatric cancer has yet to be defined.

Methods: This prospective multicenter phase 2 trial investigated a so-called RTC regimen based on the combination of intravenous Busulfan (eq 3.2mg/kg/d × 4 days), fludarabine and ATG (5mg/kg total dose) with the aim to deliver high dose myeloablation that would allow optimal disease control while minimizing toxicity, in a subgroup of children at a very high risk for non-relapse-

related mortality (NRM) as previous transplantation, significant organ dysfunction, active fungal infection, or those receiving unrelated donor transplantation in advanced disease phases. The primary endpoint was to assess NRM at 1 year in children and adolescents with hematologic malignancies after such RTC.

Results: A total of 48 patients (24 M, 24 F) were included and analyzed (median age, 13 y; range, 3-24). Diagnoses were: 21 AML, 19 ALL, 2 NHL, 2 HL, 3 MDS, and 1 CML (21 CR1, 24 in CR≥ 2 and 3 in advanced disease). The stem cell source was BM in 30 pts (62.5%), PBSC in 13 (27%) and unrelated CB in 5 (10%). 10 donors (21%) were HLA-matched sibling donors, 33 (69%) were matched-unrelated donors, and 5 were CB (10%). Of note, 14 pts (29%) received a prior allo-SCT.At 1 year, the cumulative incidence of recurrence/disease progression and NRM were 33% (95%CI, 20-47) and 8% (95%CI, 3%-18%), respectively (4 patients died of NRM: 2 GVHD, 1 VOD and 1 pneumonia). with a median follow-up of 23 months (IQR, 13-37), the Kaplan-Meier estimates of overall and disease-free survival at 1 year were 69% (95%CI, 56-82) and 58% (95%CI, 44-72), respectively. The cumulative incidences of grade 2 to 4 aGVHD and cGVHD (all grades) were 30% (95%CI, 18-44) and 22% (95%CI, 11-35), respectively. Patient age, diagnosis, donor type, sex, presence of comorbidities, and the hematopoietic cell transplantation-specific comorbidities index did not appear to have any statistically significant impact on NRM, recurrence/disease progression, disease-free survival, or overall survival.

Conclusions: We conclude that the RTC regimen used in the current prospective trial is safe, with a low NRM rate (<10%) noted among high-risk children and adolescents, paving the way for larger phase 3 trials incorporating novel agents pre and post-allo-SCT.

Clinical Trial Registry: (ClinicalTrials.gov Identifier: NCT01572181).

Disclosure: Nothing to declare.

P162.

TCR Alfa/Beta Depletion For Hsct From Unrelated Donor in Pediatric Patients

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Background: Allogeneic hematopoietic stem cell transplantation (allo-HSCT) from unrelated donor (UD) could be associated with an increased incidence of GvHD when using peripheral blood as a source of hematopoietic cells. Several strategies have been developed in the last years involving selective depletion of T cells in allo-HSCT, as TCR alpha/beta depletion.

Methods: We reported a retrospective analysis of a cohort of 10 pediatric patients who received TCR alfa/beta CD19 allografts from unrelated donors (5 matched and 5 with 1 HLA loci-mismatched) at our center. The indication for HSCT was a malignant disease in all but one patient that was affected by primary immunodeficiency; for this last patient, it was his 3rd HSCT. Five patients were affected by ALL, 2 patients by AML, 1 patient by biphenotypic leukemia, and 1 patient by MDS. The status of the disease at HSCT was CR1 for 3 patients, CR2 for 4 patients, and CR3 for 1 patient. The median age at HSCT was 4 years (1-18). Conditioning was based on Fludarabine, Thiotepa, Melphalan, and Total lymphoid irradiation (TLI) in 8 patients; 2 patients received Thymoglobilin instead of TLI and one patient received Treosulphan instead of Melphalan. GvHD prophylaxis was based on MMF in 8 patients, CsA in 1 patient, and a combination of CsA and MMF in 1 patient. In order to improve immunological recovery, all patients received DLI (manipulated with CD45RA method) since day +30.

CliniMACS® Device was used for TCR alpha/beta and CD19+ depletion. Regarding the composition of the graft, the patients received a median number of 10.1 CD34+ stem cells per kg (5.84-16.67). Moreover, the graft contained a median number of 1.35x10e7/kg gamma delta T cells (0.93-47.1), and a median residual alfa beta T cells after depletion of 1,66x10e4 cells per kg (0.12-10.08). The median count of CD19+ cells infused was 6.1x 10e5 cells per kg. In terms of progenitor stem cell loss after the procedure, we assume a 44.42% loss of CD34+ cells/kg body weight. Referring to the purity of the product after the process of depletion we confirmed >95% in all the procedures.

Results: All patients engrafted at a median of 11 days (9-15); the median time for platelets >20,000 was 12 days (10-28). One patient experienced secondary graft failure in the context of hemophagocytic syndrome and was submitted to a second HSCT. Eight out of 9 patients that maintained the graft showed complete donor chimerism; one patient experienced mixed chimerism. Four patients experienced acute GvHD (grade 1=1 patient; grade 2= 1 patient; grade 3=1 patient; grade 4= 1 patient). No one experienced chronic GvHD. Two patients relapsed at 4.5 and 7.5 months after HSCT respectively and both were submitted to CAR-T therapy and achieved complete remission. with a median follow-up of 329 days (29-754), all patients are alive.

Conclusions: Our experience shows that TCR alpha/beta depletion is safe for HSCT from unrelated donors allowing

early engraftment. The incidence of severe acute GvHD was low and no patient experienced chronic GvHD. Overall survival has been 100% at the time of follow up.

Disclosure: Nothing to declare.

P163.

SARS-COV-2 Serological Status of Pediatric Hsct Recipients: A Single Center Experience

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Background: Eastern France was one of the most affected areas by the COVID-19 pandemic during the first wave in March 2020. It raised concerns about Hematopoietic Stem Cell Transplant (HSCT) recipient's management. From March to June, as EBMT guidelines suggested, we practiced telemedicine, postponed all non-urgent HSCT and elaborated specific circuit for our patients in the hospital. Patients with respiratory symptoms, new oncologic diagnosis or HSCT recipients were tested. Fourty of our patients were tested by SARS-CoV-2 polymerase chain reaction (PCR), with six being positive; only one had mild symptoms. In the French society of pediatric oncology (SFCE) study, as of May 2020, 41 onco-hematology patients were diagnosed with COVID-19 nationally and only one died. Knowing that, we wanted to approach the serological status of our HSCT population.

Methods: Six months after the first wave we performed a SARS-CoV-2 serology for every HSCT recipients who came for a follow-up in Strasbourg University Hospital between October 15, and December 1st. Serology tests were performed using enzyme-linked immunosorbent assay (ELISA) to detect IgG. We collected with their consent clinical, biological and epidemiological data.

Results: Twenty-five allografted children were tested for a serology against SARS-CoV-2. They were at a median time post HSCT of 19 months (2-117). 38% had an HSCT for hematologic malignancy, 38% for an hemoglobinopathy, 13% for aplastic anemia and 13% for an immune deficiency. 15 patients had a normal B lymphocyte level at the time of the serology. Nine had intravenous immunoglobulin supplementation; 15 an immunosuppressive therapy. Three (including 2 with positive PCR in March) were positive. Only one presented mild symptoms, with positive PCR on March 31 (3 months post-HSCT with a poor immunological reconstitution), positive serology initially, and inconclusive 6 months later.

	Negative SARS-CoV-2 serology ($n = 22$)	Positive SARS-CoV-2 serology ($n = 3$)
Hematologic malignancies	8	1
Hemoglobinopathy	8	1
Immune Deficiency	2	1
Aplastic anemia	3	0
Pheno/Geno/Haplo-identical	11/8/3	2/1/0
Median time between HSCT and SARS-CoV-2 serology (months)	18 (2-117)	19 (9-113)
Normal level of B lymphocytes	14	1
Normal level of IgG	21	3
Normal level of IgM	13	3
Immunoglobulins supplementation	9	0
Immunosuppresive therapies	14	1

Conclusions: Despite being severely impacted by SARS-CoV-2 pandemic, no severe form of COVID-19 among our HSCT recipients occurred. It allowed us to reduce the strong preventive measures we initially took in our hospital. This population being used to physical isolation was probably not as exposed as others. Those results are reassuring knowing that vaccination will not be available soon for them. Indeed, vaccine against SARS-CoV-2 is not yet tested on children, vaccination of patients with comorbidities is planned in France on phase 3 of the vaccination protocol and their immunization capacity is probably not sufficient to provide them an effective protection. We wonder then how long after HSCT should we vaccine those patients and whether their vaccination should be planned sooner in the national protocol.

Disclosure: Nothing to declare.

P164.

Safety And Performance of Central Venous Catheters in Pediatric Leukapheresis: A Single Center Experience

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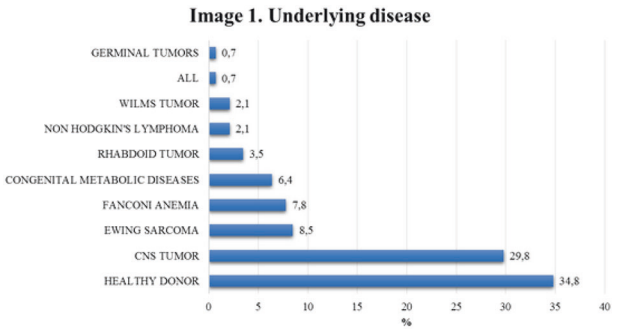
Background: in pediatric population, a central venous catether (CVC) is usually required in order to establish adequate blood flow rates for leukapheresis. In spite of the safety and efficacy of this procedure, a central access may associate more adverse events (AEs), especially in children.

Methods: We retrospectively collected data of 140 pediatric patients and donors (<18 years) *(Image 1)*, who underwent leukapheresis via double lumen central venous catheter between January 2011 and August 2020 at the Hospital Infantil Universitario Niño Jesus. Collection efficiency and safety were analyzed.



Results: in our cohort, donors versus patients proportion was 49/91, 35% and 65%, respectively. The median age was 5 years (range: 5 months-17 years). The median weight was 18 kg (6-69). CVC were most frequently located at jugular vein in 52.1% of cases ($n = 73$), followed by femoral vein in 38.6% ($n = 54$) and subclavian vein in 9.3% ($n = 13$). The median CVC french and length were 7 (range: 3 – 8) and 15 cm (6 – 21), respectively. All CVC were placed without complication. The median of time between CVC placement and apheresis were 1 day (range: 0 – 110). The median duration of CVC placement were 1 day (0 – 518). Mobilization was carried out with granulocyte colony-stimulating factor in 97.8% of children ($n = 137$) and in 19.3% ($n = 27$) the association of plerixafor was needed to optimize mobilization.

The median CD34+/mL prior to apheresis was 56/mL (range: 5-734), median CD34+ yield in apheresis was 5.2 x10^6/kg (0.6-40.9) and collection efficiency was 49.2 (1.9-115.8), respectively.

In 126/140 (90%) of the cohort, there were no CVC-associated AEs. Most common AE in our study was fever in 3.6% ($n = 5$), followed by thrombosis in 2.1% ($n = 3$), bleeding in 2.1% ($n = 3$), local CVC infection in 1.4% ($n = 2$) and CVC replacement after displacement in 0.7% ($n = 1$). There was 1 (0.7%) AEs in the group of healthy donors, corresponding with bleeding following CVC removal. All other AEs occurred in oncologic patients. Blood cultures and catheter tip cultures were tested in patients with fever, local infection or thrombosis. 1.4% ($n = 2$) presented catheter-related bacteriemia, blood and tip cultures positives with coagulase-negative Staphylococcus or Enterococcus faecalis, and 3.6% ($n = 5$) developed catheter-related local infection, with positive tip culture. Sterility testing of 97.1% ($n = 136$) apheresis product was performed. There was microbiological isolation in 1.4% ($n = 2$) without clinical effects. There was significant correlation between patients group and development of CVC-related AEs ($p < 0.0001$). There was no statistically significant difference between cohort baseline characteristics and CVC specifications and CVC-related AEs.

Conclusions: in our study, in 90% of the cases there were no major CVC-related complications during harvest. Of the total AEs observed, 92.8% corresponded to the group of patients and mainly those who had a duration of >3 days after the CVC placement. There was only a minor bleeding AEs in donors group. All infections resolved after CVC removal and systemic antibiotic treatment. Thrombosis events were presented by patients with metastatic CNS tumor and rhabdoid tumor receiving chemotherapy. In our experience, leukapheresis via CVC is a safe procedure with effective performance for PBSC collection in pediatrics.

Disclosure: Nothing to declare.

P165.

Treosulfan – Based Condition Regimen For Stem Cell Transplantation in Patients with Diamond – Blackfan Anemia

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Background: Stem cell transplantation is the only curative option for the hematological Diamond-Blackfan anemia (DBA) phenotype. Data concerning HSCT in DBA utilizing reduced intensity conditioning regimen are still very limited. We present our experience of treosulfan– based conditioning in patients with DBA.

Methods: Nine DBA patients (M:F=6:3), with a median age of 6.3 years (0.98-12.6) were transplanted between July 2012 and March 2020. The clinical phenotype in 8 patients was represented by steroid resistant anemia, and in 1 – MDS; all had iron overload with ferritin levels from 567 to 2974 μg/L (m =1485). The condition was very poor in 1 patient with Karnofsky performance status of 40%. The source of stem cells in 3 cases was BM from MUD (10/10, $n = 1$; 9/10, $n = 1$) or

MRD ($n = 1$); other 6 patients were transplanted with PBSC from MUD (9/10, $n = 1$; 9/10, $n = 4$) or haploidentical donor ($n = 1$). PBSC grafts were TCRab/CD19 depleted.

Conditioning regimens consisted of: 1-Treosulfan 36g/m2 +Fludarabine 150mg/m2, 5 – Treosulfan 42g/m2 + Thiotepa 10mg/kg + Fludarabine150 mg/m2, 1- Treosulfan 42g/m2 + Melphalan 140mg/m2 + Fludarabine 150 mg/m2. Eight patients received serotherapy by ATG. Moreover, we used rituximab (100-375mg/m2 on day -1) to decrease the risk of EBV-PTLD and for additional desensitization.

Posttransplant GVHD prophylaxis after TCRab/CD19 depletion included CNI (3–monotherapy; 1-with MMF +abatacept, 1–with abatacept+tozilizumab) or MMF ($n = 1$). In other cases we used CNI+MMF ($n = 1$), CNI+MMF +abatacept+tozilizumab ($n = 1$), PtCy(+3+4)+CNI +MMF ($n = 1$).

Results: Primary engraftment was achieved in all patients. Eight patients are alive with complete donor chimerism with a follow-up of 9,1-102,4 (m=36,4) months after HSCT; 7 patients free from IST. One patient (with Karnofsky status of 40%) died on day +58 from multiple organ failure as a result of severe toxicity (skin, kidney, endothelial and liver toxicities), disseminated intravascular coagulation and infectious complications (bacterial sepsis and Adv-disease). Three patients had early toxicity, including 1-mucositis grade III, 2- grade III dermatitis, 1-mild VOD. We did not observe any patient with acute GVHD (aGVHD) grade > III and chronic GVHD. aGVHD grade II was diagnosed in 5 patients with complete response to the first line of the IST (2- TCRab/CD19 depletion, 3-non-manipulated grafts). In one of these patients after HSCT with non-manipulated graft, we performed CD34+ selected boost due to graft failure (with full donor chimerism) 6 months after HSCT; later, we observed recurrent aGVHD grade II and Coombs-negative hemolysis afterwards; it remains dependent on immunosuppressive therapy 32 months after HSCT. Moreover, one patient developed severe AIHA after day +100, which resolved after combined IST and splenectomy.

Conclusions: in our experience, the Treo-based conditioning regimen is a feasible and effective technology with low risk of toxicity and TRM for the treatment of DBA patients. However, a larger cohort is needed to evaluate the role of this approach. In addition, it seems that TCRab/CD19 depletion is a good option for these patients due to low incident of potential complications and good outcome of HSCT.

Disclosure: Nothing to declare.

P166.

Allo-HSCT in Treatment of TP53 Mutation-Related MDS/AML in Pediatric Patients – Report of Two Cases

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Background: Gene TP53 is a known locus of mutations which lead to increased risk of numerous malignancies. MDS/AML related to TP53 mutations has been connected with particularly poor prognosis, and allo-HSCT is often the only possible curative treatment option.

Methods: in this report two pediatric patients are described, who had undergone alloHSCT for TP53-related MDS/AML diagnosed as secondary malignancy related to previous oncological therapy.

Patient 1: A fourteen-year-old girl diagnosed with TP53-related secondary MDS transformed into AML M1. Primarily she had been treated for T-NHL and polyposis-related colon cancer. MDS was diagnosed 18 months after starting the treatment for lymphoma. The transformation to AML occured a month after MDS diagnosis. She achieved complete remission after treatment with AML-Interim 2006 Protocol. MUD-HSCT was carried out after conditioning with treosulfan 42 mg/m^2 and fludarabine 150 mg/m^2 plus in vivo T-cell depletion. Cyclosporine and "short" methotrexate were given for GvHD prevention. Engraftment was achieved on day +29.

Patient 2: An eight-year-old boy diagnosed with TP53-related MDS secondary to the treatment for choroid plexus carcinoma (CPC). After first line of CPC treatment, during the next years several subsequent relapses of the disease occured. As a part of the treatment he underwent triple tandem autologous stem cell transplantations in other center. Six months after that, 60 months after primary malignancy discovery, he was diagnosed with MDS. He underwent MUD-HSCT after conditioning with treosulfan 42 mg/m^2 and fludarabine 150 mg/m^2 plus in vivo T-cell depletion. Cyclosporine and "short" methotrexate were given for GvHD prevention. Engraftment was achieved on day +32.

Results: Patient 1 has not experienced life-threatening complications. For the next 3 years she needed immunoglobulin supplementation after receiving rituximab for EBV reactivation. As of today, she is disease-free, with current follow-up being 65 months.

Patient 2 was diagnosed with another relapse of CNS tumor two months after allo-HSCT. Introduced treatment had to be quickly withdrawn because of viral infection reactivations. The patient was qualified for stereotactic radiotherapy. 2 months later, severe thrombocytopenia and increased leukocyte count led to a diagnosis of AML M1. Chemotherapy consisting of thioguanine and low doses of

cytarabine was introduced, but had to be immediately withdrawn due to severe side-effects (pleuropneumonia, acute kidney failure, hydrothorax, pericardial effusion). Because of extremely poor tolerance of implemented therapy the patient was disqualified from causative treatment and started palliative chemotherapy (thioguanine). For two months, until today (follow-up of 12 months), the patient has been staying at home in satisfactory general condition, occasionaly receiving platelet transfusions.

Conclusions: Currently available literature emphasizes therapeutic difficulties in treating TP53-related MDS/AML, however the reports are limited to adult patients only. There is no scientific data available regarding the effectiveness and safety of treating such patients in pediatric population.

The cases shown here suggest that allo-HSCT may be considered as an effective and feasible therapeutic option in children likewise. However, due to a small number of such cases in our report it should rather be considered as a spark for initiating further research.

Disclosure: Nothing to declare.

P167.

Central Line Removal in Allogenic Pediatric Hematopoietic Stem Cell Transplant Patients

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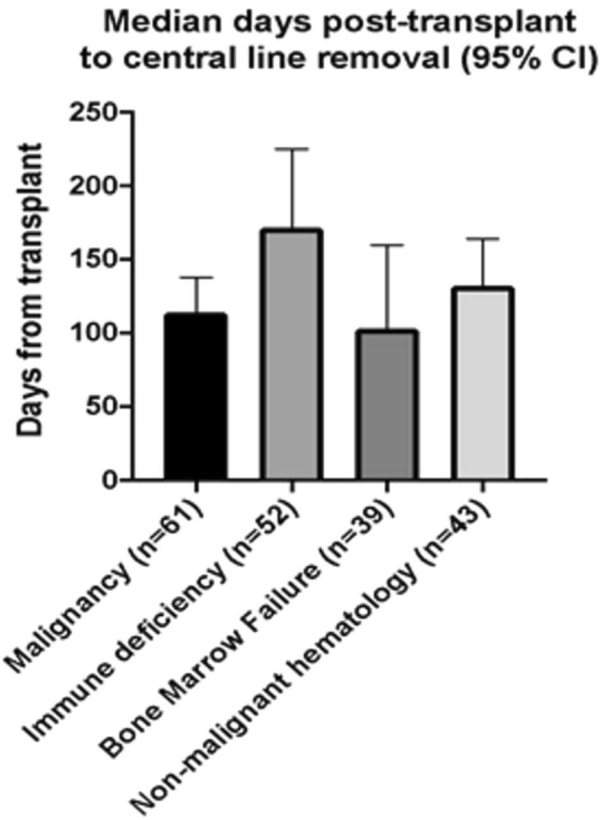
Background: Pediatric hematopoietic stem cell transplant (HSCT) patients typically require central lines for medication administration, lab draws, and transfusions. Protracted central venous catheter (CVC) use has been associated with bloodstream infections, increased healthcare-related costs, and decreased quality of life. While many aspects of HSCT have standardization in practice, line removal in the pediatric population continues to be provider- and institution-specific.

Methods: The standard of care at our center is to place a double lumen external CVC prior to transplant and remove the line "when it is no longer needed". We performed a single-center retrospective cohort study of pediatric HSCT patients (age 0-20) who underwent allogeneic transplantation from 2016-2018 to determine the time from transplant (day 0) to line removal. We excluded from evaluation patients with a diagnosis of Hurler syndrome (due to need for enzyme replacement for 8 weeks after engraftment) and osteopetrosis (due to small sample size [$n = 2$] and significant complications after transplant). We also excluded patients who developed graft failure, who were diagnosed with graft versus host disease (grade 2 or higher), or received autologous HSCT.

Results: 195 patients were included in the analysis. HSCT was performed for malignancy ($n = 61$), immunodeficiency ($n = 52$), bone marrow failure ($n = 39$), and non-malignant hematology ($n = 43$). Median age at HSCT was 6.5 years IQR (2-10) and the median time of line removal from HSCT was 157 days with an IQR of 91-191. Patients undergoing HSCT for an immune deficiency had a significantly increased length of CVC duration (median 171 days, IQR 91-282) than patients with a malignancy (median 114 days, IQR 92-168), bone marrow failure syndrome (103 days, IQR 73-177) and non-malignant hematology diagnosis (median 132, IQR 98-180), ($p = 0.007$) (Figure). Additionally, age at the time of transplant was not associated with CVC duration ($p = 0.1$).



Conclusions: While central line removal continues to vary greatly between institution and provider, there are many complications associated with protracted CVC duration. These include bloodstream infection, accidental line removal, thrombosis, or incorrect positioning leading to extravasation or the line no longer being central. Bloodstream infections continue to be an area of significant concern as there is a well-established association with

prolonged hospitalizations, intensive care admissions, and overall increase in morbidity and mortality. The average and median time for line removal was 5 months, but there was wide variety in practice. Identifying barriers to CVC removal is needed to reduce duration. While in pediatric patients one would expect age to create variations in line removal, no statistical difference was identified. Based on this evaluation, creating a standardized approach with criteria to determine patient-to-patient readiness and feasibility of CVC removal is warranted to limit the well-known and significant complications associated with protracted CVC duration.

Disclosure: Nothing to declare.

Solid Tumors

P168.

High Dose Chemotherapy And Stem-Cell Transplant For Relapsed Germ Cell Tumors: Multicentric Real-World Experience in Argentina

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Background: Germ cell tumors (GCT) are the most common cancer in adolescents and young adults. Most of them are curable even in advances stages with multimodal treatment including cisplatin-based chemotherapy and surgery. Patients who relapse after initial treatment are usually treated with salvage chemotherapy regimens achieving around 50% response rates. High dose chemotherapy (HDCT) followed by autologous stem-cell transplant (ASCT) is also an effective treatment in this setting. This indication is based mainly in large retrospective reports since collecting prospective data is challenging in this disease.

Methods: We conducted a retrospective multicenter analysis including patients with relapse GCT who underwent HDCT followed by ASCT in ten Argentine Bone Marrow Units reporting to Grupo Argentino de Trasplante de Médula Ósea y Terapia Celular (GATMO-TC) from 2011 to 2019. We estimated overall (OS) and progression-free survival (PFS) using Kaplan Meier and difference between groups were compared by log-rank test.

Results: Among 72 patients included, the median age was 32 years (range 15-58). The most frequent primary tumor site was testis ($n = 51$, 70.8%), following by retroperitoneum ($n = 10$, 13.9%), mediastinum ($n = 6$, 8.3%), and others ($n = 5$, 6.9%). Most of patients presented a non-seminoma histology (70%). Twenty-nine (40.3%) patients had poor risk disease by IGCCCG score.

Most patients (87.5%) received ≥2 chemotherapy lines before the HDCT, and 40% received two courses of HDCT and ASCT. Tandem strategy was a decision criterion of each center.

With a median follow-up of 36 months (95% CI 17.7-54.3), the PFS and OS rates at 2 years were 67% and 73%, respectively. Patients harboring responsive diseases to first-line chemotherapy had significant better survival than those without response (cisplatin-refractory) ($p = 0.022$). There were no statistical differences between tandem and non-tandem strategies, maybe since the number of patients in each subgroup was low.

Conclusions: This multicenter retrospective study shows that HDCT with ASCT is an effective treatment even for heavily-pretreated GCT, consistently with the literature. Among poor-responders to first-line chemotherapy, HDCT with ASCT must be the preferred option since this group of patients has worse OS. Prospective trials are needed to confirm this data and to stablish the adequate strategy as regards timing and tandem ASCT.

Disclosure: nothing to declare.

Stem Cell Donor

P169.

Haploidentical vs HLA-Matched Related Donor HSCT For Acute Leukemia And Myelodysplastic Syndrome: A Single-Center Comparison

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Background: Due to fast donor availability and a relatively favorable toxicity profile, haploidentical stem cell transplantation (haplo-SCT) using post-transplant cyclophosphamide (PT-Cy) has become an increasingly utilized alternative in hematological patients lacking an HLA-identical donor. Recent studies demonstrated equal outcomes of haplo-SCT with PT-Cy in terms of overall survival (OS), progression free survival (PFS) or the incidence of severe Graft versus Host Disease (GvHD) compared to matched unrelated donor transplantation (MUD-SCT). In this single center analysis, we compared matched related donor transplantation (MRD-SCT) with haplo-SCT with PT-Cy in patients with acute leukemia and myelodysplastic syndromes (MDS).

Methods: Between January 2010 and July 2019, we retrospectively evaluated 77 adult patients (median age 50 years) with acute leukemia ($n = 55$ with AML, $n = 10$ with ALL and $n = 1$ with biphenotypic leukemia) or MDS ($n = 11$) undergoing haplo-SCT ($n = 37$) or MRD-SCT ($n = 40$) at the Technical University of Munich (TUM). The amount of high risk patients in terms of refractory disease at the time of transplantation were approximately equal in both groups. The objective of this single-center study was to prove the non-inferiority of haplo-SCT compared to MRD-SCT in terms of OS, PFS and GvHD-incidence.

Results: 1-year OS was 58,3% vs 62,9% in MRD-SCT and haplo-SCT respectively ($p = 0{,}567$); cumulative incidences of relapse (death without relapse as a competing risk) was 30% vs 25% after 1 year ($p = 0{,}829$), nonrelapse-mortality (relapse as a competing risk) was 25% vs 24,3% after 1 year ($p = 0{,}787$). There also was no significant difference between MRD- and haplo-HSCT with regards to cumulative incidences of grade III-IV aGvHD (grade I-II aGvHD, death without GvHD and relapse as competing risks) after 1 year (35,1% vs 24,8%; $p = 0{,}359$) and cumulative incidences of extensive cGvHD after 2 years (20% vs 17,3%; $p = 0{,}673$).

Moreover, pneumonia (diagnosed with x-ray or CT) and bloodstream infections did not occur more frequently in one of the groups ($p = 0{,}608$ and $p = 0{,}224$).

However, we found a significant difference ($p < 0{,}05$) between the two groups regarding the median count recovery for platelet and leukocytes (leukocytes >1G/l: 17 vs 21 days; platelet >20G/l: 15 vs 25 days).

Conclusions: in total, we saw no significant differences in OS, PFS, occurrence of GvHD and toxicity in terms of infections comparing MRD-SCT- vs haplo-SCT besides the slower count recovery after haplo-SCT. Thus, haplo-SCT appears to be a safe and reasonable alternative not only to MUD-SCT but also to MRD-SCT.

Disclosure: Nothing to declare.

P170.

Clinical Outcomes in Allogenic Hematopoietic Stem Cell Transplantation From Alternative Donors: Single Center Experience with 9/10 HLA-Mismatched Unrelated, Double Umbilical Cord Blood And Haploidentical Donors

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Background: The increasing use of alternative donors with less stringent HLA-matching has made allogenic hematopoietic stem cell transplantation (aHSCT) more accessible in ethnically diverse populations.

Methods: We retrospectively reviewed 80 consecutive patients undergoing myeloablative aHSCT from alternative donors, including 9/10 HLA-mismatched unrelated (MMUD, $n = 31$), double umbilical blood (dUCB, $n = 33$) or haploidentical donor (Haplo, $n = 16$) at our center between January 2009 and December 2019. The MMUD group received TBI- or Busulfan-based conditioning regimen, graft-versus-host-disease (GVHD) prophylaxis with ATG, methotrexate plus calcineurin inhibitors, and stem cells mostly from peripheral blood source (96.8%). The dUCB group received units with a minimal HLA-match of 6/8, conditioning with TBI(1350 cGy)-fludarabine and GVHD prophylaxis with tacrolimus plus mycophenolate mofetil. The Haplo group received bone marrow sourced stem cells, fludarabine-busulfan±thiotepa conditioning and post-transplant cyclophosphamide, tacrolimus plus mycophenolate mofetil for GVHD prophylaxis.

Results: The median age was similar in all groups with 46 years (range:18-68). Acute leukemia was the most common indication for aHSCT in the 3 groups (58.8%). The median time to neutrophil engraftment (>0.5x10*9/L) was similar with 20, 20 and 24 days in the MMUD, dUCB and Haplo groups respectively ($p = 0.226$). Platelet recovery (>20x10*9/L) was significantly delayed in the dUCB group with a median time of 33.5 days compared to 17 days in the MMUD and 25 days in the Haplo group ($p < 0.001$). One case of primary graft failure occurred in the Haplo group and subsequently had successful engraftment with a second Haplo aHSCT from a different donor.

There was no statistically significant difference in the cumulative incidence (CI) of any type of GVHD between the

different groups. The CI of grade II-IV acute GVHD (aGVHD) at d+100 was 45.2%, 62.1% and 56.3% in the MMUD, dUCB and Haplo groups respectively ($p = 0.315$). The corresponding CI of grade III-IV aGVHD was 19.4%, 17.2% and 18.7% ($p = 0.993$). Similarly, the CI of chronic GVHD (cGVHD) at 1 year was 48.3%, 45.8% and 35.7% while moderate to severe cGVHD was 34.5%, 43.5% and 14.3% in the MMUD, dUCB and Haplo groups respectively ($p = 0.756$ and 0.208).

Donor choice did not have a statistically significant impact on the CI of relapse (CIR), non-relapse mortality (NRM) and overall survival (OS) at 2 years. The CIR at 2 years was 35.3% for MMUD, 16.7% for dUCB and 28.0% for Haplo ($p = 0.317$). The corresponding NRM at 2 years was 17.6%, 28.3% and 29.3%. The OS at 2 years was 66.4%, 65.9% and 45.1% in the MMUD, dUCB and Haplo groups respectively ($p = 0.281$).

Conclusions: We report similar outcomes in patients receiving aHSCT from MMUD, dUBC and Haplo donors at our center which suggests that they all represent feasible options for alternative donors. The MMUD were associated with the numerically highest CIR but lowest NRM, which could potentially be related to the use of ATG. There was also a trend towards higher NRM and lower OS with Haplo. Alternative donor choice should be tailored to the individual patient, with considerations such as treatment delays and cost becoming increasingly important in the context of a global pandemic.

Disclosure: Nothing to declare.

P171.

Haploidentical Stem Cell Transplantation with Post-Transplant Cyclophosphamide For Patients with High-Risk Hematologic Malignancies. A Single Center Experience in Mexico

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Background: Haploidentical stem cell transplantation with post-transplant cyclophosphamide (HaploSCT) can be curative for a variety of high-risk hematologic malignancies. It is an attractive approach for emerging countries in the world because of its cost effectiveness.

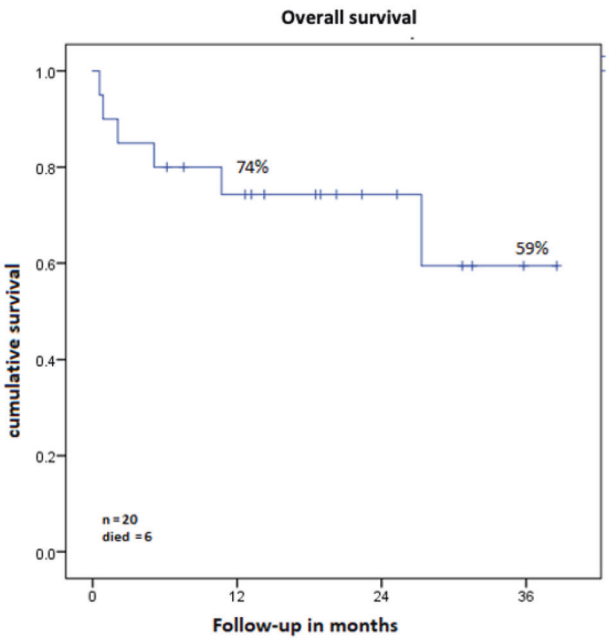
Methods: A retrospective cross-sectional study was performed in twenty patients with high-risk hematologic malignancies who received an HaploSCT between July 2017 and May 2020 at Instituto Nacional de Cancerología, México. Patient files were reviewed for several clinical characteristics, information about the disease, factors regarding the stem cell donor and the procedure itself, searching for possible prognostic factors affecting survival.

Results: Nine patients were female and eleven patients were male, with a median age of 24 years. The most common indication for HaploSCT was high-risk Acute Lymphoblastic Leukemia in 55% of patients. Time from diagnosis to transplant was more than 12 months in 60% of patients and 75% were in complete response at the time of the procedure. Ten percent of transplants were ABO-incompatible (one patient with mayor and one with minor incompatibility). Twenty-five percent of patients were found to have anti-HLA antibodies (2624 – 16676 MFI) and were desensitized using plasma exchange, Rituximab and intravenous Immunoglobulin.

After the stem cell infusion (SCI) 80% presented with cytokine release syndrome, mainly grade I and II. Fifty-five percent of patients had cytomegalovirus reactivation that resolved with antiviral treatment. Seventy percent of patients had successful grafts around day 16 after SCI. We only had one patient with primary graft failure, another patient with secondary graft failure and 20% presented graft dysfunction.

Grade I-II acute GVHD was present in 25% of patients (80% skin and 20% ocular) and grade I-II chronic GVHD presented in 20% of patients, affecting mostly the liver. We found a 30% mortality among our patients, of whom only two patients were relapse related. Relapses were at 10- and 22-months post HaploSCT. Overall survival at 1-year was 74% and 59% at 3-years.

After univariate analysis, we found no prognostic factors affecting survival in our cohort.



Conclusions: in our population HaploSCT using post-transplant cyclophosphamide is associated with low rates of severe graft-versus-host disease and non-relapse mortality. Due to our sample size, we could not identify prognostic factors for survival. Nevertheless, we describe better outcomes that other series.

A thorough patient selection is a key factor for achieving results comparable to those of HLA-matched hematopoietic stem cell transplantation.

Disclosure: Nothing to declare.

Stem Cell mobilization, Collection and Engineering

P172.

Interim Analysis of The Optimob Study: A Non-Interventional Study Across Germany to Evaluate The Mobilization And Collection of Hscs in Poor Mobilizers Ahead of ASCT

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Background: Adequate mobilization of hematopoietic stem cells (HSCs) prior to apheresis (aph) is mandatory in patients suffering from multiple myeloma (MM) or lymphoma eligible for autologous stem cell transplantation (ASCT) to ensure a successful HSC collection. Although treatments with chemotherapy +/- G-CSF (granulocyte-colony stimulating factor) are standardized mobilization strategies, a notable number of patients do not achieve an adequate $CD34^+$ cell count in the peripheral blood (PB) and are therefore classified as poor mobilizer (PM). For those patients, the use of plerixafor (PLX) is indicated to improve mobilization of HSCs. The aim of the OPTIMOB study is to provide insights into the HSC mobilization and apheresis practice in Germany in order to eventually improve mobilization and transplantation strategies particularly for PM patients.

Methods: The OPTIMOB study is an ongoing, prospective, multi-center, non-interventional, observational study, documenting the HSC-mobilization and -collection practice as well as ASCT parameters in German apheresis and transplantation centers. Patients with MM or lymphoma who are eligible for ASCT were included. The main objective of this interim analysis was the evaluation of the PM population. Therefore, analyses were performed for PM patients in general as well as for PM subtypes defined as follows: (1) patient never achieved ≥ 20 $CD34^+$ cells / μL before 1st aph (PM-A), (2) patient received PLX at any time point of mobilization (PM-B), (3) the initially planned HSC yield had to be reduced (PM-C), or (4) patients have not received aph due to low $CD34^+$ count in PB (PM-D).

Results: As of November 2020, 461 patients were included in the study, of which 67% had MM. In total, 173 patients were classified as PM patients (37,6%). Surprisingly, the proportion of PM patients was almost the same in MM and lymphoma. The majority (61,8%) of all patients (PM and GM [good mobilizer] patients) were mobilized with chemotherapy + G-CSF and 25% of all patients received PLX during mobilization. The main reason for using PLX in the PM subtypes was a low $CD34^+$ cell count in PB. After administration of PLX, an at least two-fold increase of $CD34^+$ cells in the PB was observed in all PM subtypes and aph could be performed in more than 90% of all patients. PM patients, receiving PLX during mobilization had a higher mean total $CD34^+$ collection result than PM patients without PLX administration (7.5 $x10^6$ cells/kg body weight (BW) [SD: ± 7.46] vs 5.2 $x10^6$ cells/kg BW [SD: ± 3.70]). 72% of the PM patients treated with PLX ($n = 104$) reached the total planned $CD34^+$ collection target (median 6.0 $x10^6$ cells/kg BW) during aph.

Conclusions: Interim data of the ongoing non-interventional OPTIMOB study provide a comprehensive overview of the "real world" clinical handling of PM patients in Germany. Data support that after addition of PLX to standardized mobilization strategies an adequate mobilization of $CD34^+$ precursors and HSCs is attainable in PM patients.

This non-interventional study is sponsored by Sanofi.

Clinical Trial Registry: BfArM-study number: 7186.

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P173.

Trends in Autologous Stem Cell Mobilisation Practices in Myeloma Patients in Ebmt Centers Between 2008 And 2017

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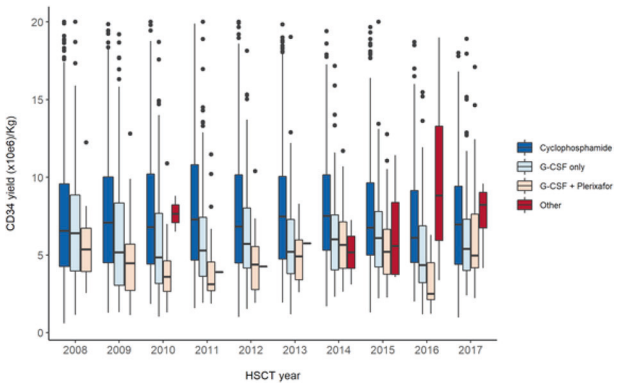
Background: The use of autologous haematopoietic cell transplantation (auto-HCT) in the treatment of myeloma (MM) has continued to increase in EBMT centers over the last ten years. Stem cell mobilisation practices have evolved with the availability of plerixafor which received EMA authorisation in July 2009. There has been wide variation in stem cell mobilisation practice over time and between European countries though there are no published datasets. We performed a retrospective analysis of all patients who underwent first auto-HCT for MM in EBMT centers between 2008 and 2017 inclusive.

Methods: Data on patients were obtained from the EBMT registry. Med-A forms consist of a registration and follow-up forms. More detailed information is captured in Med-B forms. We also analysed national data from the six largest EBMT member states.

Results:



Data was collected on 64,079 patients transplanted in 499 centers in 51 countries. Ages ranged from 18 to 83 years. There were four categories of mobilisation regimen: (1) Cyclophosphamide, (2) G-CSF only, (3) G-CSF+ Plerixafor and, (4) Other (Figure 1). The median overall stem cell yields (CD34 Yield (x10e6)/Kg) were (1) 7.2 (4.69-10.52), (2) 5.5 (3.7-8.02), (3) 4.49 (2.98-6.03) and (4) 7.3 (4.18-9.41) (see Figure).

The median (IQR) CD34 Yield (x10e6/Kg) by gender was 6.53 (4.3-9.8) in men and 6.49 (4.2-9.92) in women ($p = 0.809$).

In univariate analyses, there was a significant effect of age on (log) stem cell yield ($p < 0.001$). According to the estimate for age10, each increase in age of 10 years resulted in a change (decrease) in stem cell yield by [exp (0.1)] 0.905 × 10e6/Kg.

The median (IQR) CD34 Yield (x10e6/Kg) by MM subtype was as follows: IgG: 6.7 (4.31-10.1), IgA: 6.33 (4.26-9.6), light chain: 6.36 (4.1-9.4), and Other: 5.57 (3.99-8.92) ($p = 0.001$).

The use of these four approaches varied widely across Europe during this decade, as follows: France: (1) 41%, (2) 51.2%, (3) 6.7%, and (4) 1.1%; Spain (1) 15.9%, (2) 75.3%, (3) 4.4%, and (4) 4.4%; Italy: (1) 90.7%, (2) 5.5%, (3) 3.1%, and (4) 0.7%; United Kingdom: (1) 70.2%, (2) 23.3%, (3) 5.5%, and (4) 1.0%; Germany (1) 62.3%, (2) 31.2%, (3) 3.7%, and (4) 2.8%; and, Turkey (1) 59.5%, (2) 38.4%, (3) 0.9%, and (4) 1.2%.

We next assessed whether the prior induction regimen affected the yield. The average median (IQR) CD34 Yield (x10e6/Kg) was as follows: CThalDex 5.93 (4.07-8.89), Other 6.76 (4.37-10), PAD 6.05 (3.33-9.31), VAD 6.03 (3.88-9.04), VCD 6.71 (4.64-9.88), VD 5.91 (3.66-8.96), VRD 5.4 (4.08-9.08) and VTD 6.87 (4.77-10) (<0.001).

Conclusions: Stem cell yield was consistently higher with Cyclophosphamide than with G-CSF or G-CSF-Plerixafor. There was a significant decline in stem cell yield with increasing age. The effect of MM subtype and induction regimen on the stem cell collection was minor. Comparison of approaches to stem cell mobilisation across Europe reveals marked national variation. Cyclophosphamide use was highest in Italy, next the UK, Germany, Turkey, France and Spain, in that order. G-CSF usage was highest in Spain. G-CSF-Plerixafor usage exceeded 5% in France and the UK.

Disclosure: Nothing to declare.

P174.

The Impact of The "New Normal" On Stem Cell Laboratory Practices

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Background: Covid-19 pandemic put before us new challenges regarding the procurement and organization of allogeneic hematopoetic progenitor cell (HPC) transplantation. Therefore, securing the cryopreserved graft before start of patient conditioning is recommended to reduce risks due to donor or recipient infection or transport disturbances. Quality control (QC) standards for autologous grafts are well established and translated to allogenic setting but the impact of factors such as prolonged storage and cell concentration during transport on cryopreservation and grafts recovery is not clear. Practice is to begin conditioning immediately after the graft is cryopreserved which opens up new questions regarding QC. New measures created extra workload for the stem cell laboratory and QC unit.

Methods: We investigated the impact of cryopreservation on work load of the stem cell lab and graft QC issues.

Data on allogenic mobilized peripheral blood HPC received, cryopreserved and infused during 2019. Were compared to the first 11 months of 2020.

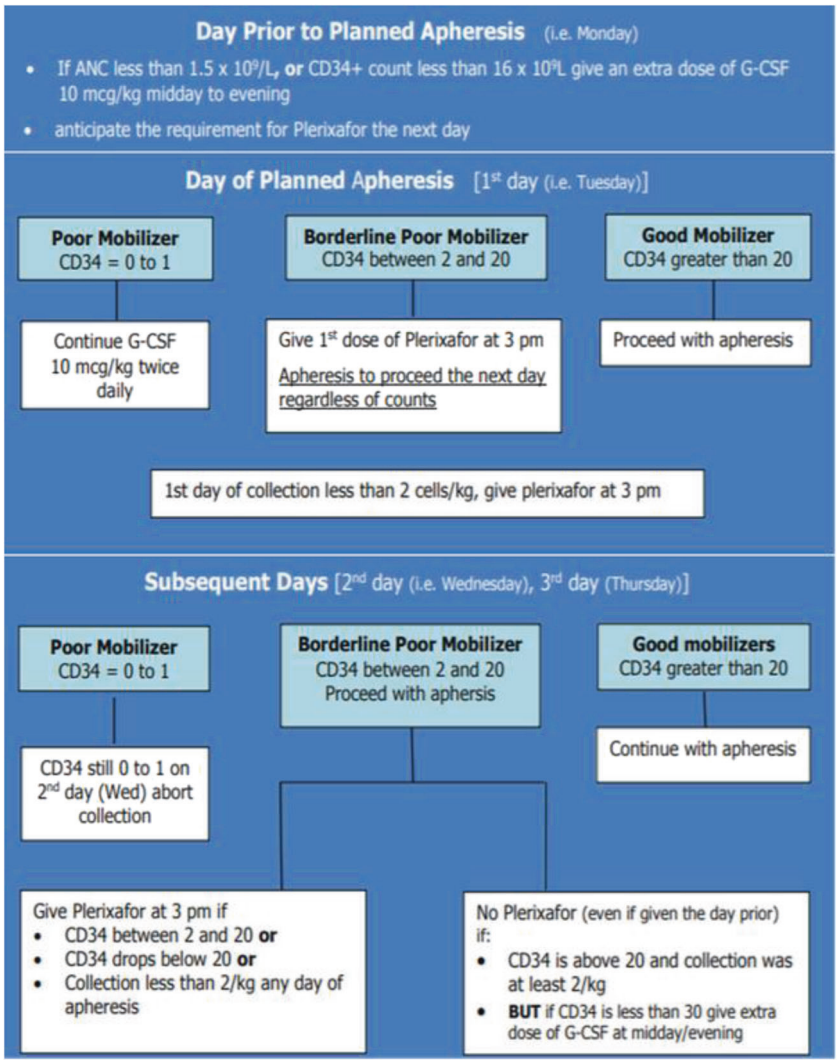
Results: in 2019. we received 25 HPC products for 25 patients which were infused fresh except one which was cryopreserved due to organisational issues of pediatric recipient conditioning. We cryopreserved 82 bags intended for donor lymphocyte infusions (DLI). In the first 3 quarters of 2020. we cryopreserved 129 bags (34 products, 33 patients) for the purpose of transplantation and DLI which is 1,5 times more than previously. By December number of cryopreserved bags went up to 189 (49 patients, 50 products) which is more than twofold higher along with 90 bags thawed and infused. Mean time from collection to cryopreservation was 51 hours (26,5h-67h).

Our standard QC for cryopreserved HPC products includes viability assessment using 7-AAD and colony forming unit assay (CFU). with the start of pandemic, the decision on quality of cryopreserved products relies on acceptable results of flow cytometry analysis of cryovial sample thawed 48 hours after freezing. After informing the transplant unit (TU) of acceptable QC results conditioning is started.

The median of CD45/7AAD viability of 98% (61-100) in native product dropped to 71,5% (30-93) in thawed cryovial sample whilst CD34/7AAD native viability of median 100% (97-100) held at median 96% (2-98) post thaw and the results of CFU assay were in accordance. One product with poor viability and recovery in all cryovials tests was further investigated, transplant bags were analysed only to confirm the total loss of cell viability (CD45/7-AAD 30%, CD34/7-AAD 0,3%). This raised questions of factors that could have contributed such as prolonged time from collection to cryopreservation (>67 hours) and inadequate dilution of fresh cells (>250x109/L WBC). Patient was postponed and haplo transplant was initiated which was complicated with Covid-19 infection of the donor starting GCSF.

Conclusions: Recommended cryopreservation of HPC products is a substantial financial and workload burden for the stem cell laboratory and QC unit. Cryopreservation tends to triple in 2020. and additional thawing procedures take considerable amount of time of overstretched staff working in epidemiologically acceptable shifts. Additional QC results need to be timely and clearly communicated to the TU so that deviations can be resolved before the start of conditioning.

Disclosure: Nothing to declare.



P175.

Plerixafor Mobilization of Hematopoietic Stem Cells in Dialysis Dependent Patients is Safe And Feasible; A Single Center Analysis

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Background: Adequate mobilization of hematopoietic stem cells is essential for successful autologous transplantation. Plerixafor is approved for mobilization of stem cells following treatment with GCSF in patients with lymphoma and multiple myeloma (MM). Dose reduction is needed for patients with renal impairment (eGFR < 50 ml) however it has not been studied in dialysis patients and the use of chemo-mobilization strategies in such cases carries additional risk of toxicity. At our center, we use pre-emptive plerixafor in patients not mobilizing well with GCSF and the aim of this analysis is to examine its safety and efficacy.

Methods: Following IRB approval, adult patients that underwent stem cell mobilization using plerixafor were identified and stratified by renal function. Plerixafor was given in patients if peripheral blood (PB) CD34 count was less than 20 cells/uL after 4 days of GCSF followed by apheresis 11 hours later with deviations permitted at physician discretion. Baseline patient, treatment and outcome characteristics were collected retrospectively

and analysed. Categorical and continuous variables were compared using chi-squared or Kruskal-Wallis, as appropriate.

Results: A total of 23 patients were identified and stratified by renal function into eGFR ≥ 50 or dialysis dependent. Baseline characteristics of age, gender and underlying diagnosis were similar across the two groups whereas ECOG performance status was better in the normal renal function cohort ($p = 0.0045$). Factors that influence collection quality such as diabetes mellitus, number of lines prior to collection and disease status at collection were analysed and were similar between the two cohorts.

The median daily dose of plerixafor was lower in dialysis patients (365 vs 209 mcg/kg; $p = 0.0032$). Efficacy of mobilization, indicated by the median PB CD34 pre- and post-collection, number of collection days as well as the CD34 yield was similar between the two cohorts. Time to neutrophil and platelet engraftment was similar as well however there was one case of secondary engraftment failure following successful engraftment due to development of paralytic ileus followed by septic shock in a dialysis patient. Incidence of adverse events attributable to plerixafor were also similar and all were minor in nature and managed conservatively.

Conclusions: The outcome presented herein is suggestive that plerixafor is effective in dialysis dependent patients without causing excess toxicity. This reports adds further value to the paucity of available literature in this difficult to treat patient population.

Clinical Trial Registry: not applicable.

Disclosure: No relevant disclosures.

P176.

An Algorithmic Approach TO Pre-Emptive Plerixafor Usage with Gcsf Alone For Mobilization of Peripheral Blood Stem Cells in Multiple Myeloma

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Background: We developed an algorithm-based approach in using Plerixafor pre-emptively based on the CD34 count in the peripheral blood during apheresis along with GCSF in patients with Multiple Myeloma to ensure successful stem cell collections, prevent delays of transplant and mobilization failures.

Methods: Patients with Multiple Myeloma who underwent stem cell collection in Saskatoon Cancer Center between April 2012 and December 2017 were included in this analysis. The aim was to collect stem cells enough for two autologous transplants for every patient according to our institutional policy. Peripheral blood CD34 count and absolute neutrophil count (ANC) were tested daily starting from the day before (D0) apheresis until the end of collection or failure. Successful collections were defined as a CD34 count of at least 4x106 cells/kg. On the day of apheresis (D1), if the peripheral blood CD34 count was between 2 and 20x106 cells/L the patients would receive Plerixafor at 3 PM on that day and they would proceed with apheresis the next day. On subsequent days of apheresis, Plerixafor was given according to the algorithm in figure 1.

Results: A total number of 90 consecutive patients were analyzed. All patients started mobilization after induction chemotherapy for at least 4 cycles with Velcade containing chemotherapy, mostly CyBORD, and achieved at least PR. The median age was 61 years (34 to 71 years). In our patient cohort, 88 patients (97.8%) had successful stem cell collection. Two patients failed to mobilise. One patient did not qualify to receive Plerixafor according to our algorithm. The other patient failed to mobilize despite using Plerixafor. Plerixafor was required in 19 patients (21.1%). The number of doses of Plerixafor needed was in the range of 1 to 3. The median number of apheresis days required was 2 (1 to 3 days). A median CD34 count of 6.2 x106 cells/kg was harvested (4.1 to 10.5 x106 cells/kg). Eighty-eight (97.8%) patients received high dose melphalan and underwent autologous stem cell transplant (ASCT). The median time to neutrophil engraftment was 12 days and platelet engraftment was 14 days. The median length of hospitalization was 19 days (10 to 31 days). All patients were alive at 100 days post-transplant.

Conclusions: By using this algorithm based pre-emptive strategy, we were successful in collecting stem cells enough for 2 transplants in Multiple Myeloma patients mobilized by GCSF alone (97.8%). Only 21.1% of the patients required pre-emptive Plerixafor. We were able to reduce the total apheresis days to a maximum of 3 days even for poor mobilizers, avoid delays of transplant in case of failure, and also avoid the toxicity of chemotherapy based mobilization approach. Early engraftment was achieved in all patients. This algorithm-based approach guides us to use Plerixafor only in the cases that would benefit the most and leads to optimal utilization of our resources without compromising patient outcomes.

Disclosure: Nothing to declare.

P177.

A Retrospective Record Review of Mobilization Strategies with And Without Plerixafor For Autologous Stem Cell Transplant in Patients with Multiple Myeloma

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Background: Plerixafor used in combination with colony stimulating factor (G-CSF) was shown to be superior to G-CSF alone in mobilizing peripheral blood stem cells (also referred to as CD34+) for use in autologous hematopoietic stem cell transplantation (ASCT). The objective of this study was to determine clinical outcomes of different mobilization regimens in the era of new treatment options.

Methods: This was a retrospective, multi-center, chart-review study in patients with MM, conducted at 4 high-volume centers in the US between Feb 2018 and Jul 2020. Patients were included if aged ≥18 years, diagnosed with MM and eligible for first ASCT. Patients were attributed to three treatment arms according to mobilization regimen:

- G-CSF+plerixafor.
- G-CSF.
- G-CSF+chemotherapy.

Demographics and baseline characteristics, mobilization regimen, apheresis and transplantation outcomes, and survival status were extracted from medical charts. Differences in outcomes between mobilization regimens were tested for statistical significance with G-CSF+plerixafor as reference.

Results: Overall, 389 patients were included in the database, 310 in the G-CSF+plerixafor, 57 in the G-CSF only and 22 in the G-CSF+chemotherapy arm. Demographic and baseline characteristics were comparable between treatment arms. More patients (26%) in the G-CSF arm had received prior radiotherapy compared with the G-CSF+plerixafor arm (6%). Stage III disease was diagnosed in 54% of patients in the G-CSF+plerixafor arm, 38% of G-CSF patients and 68% of G-CSF +chemotherapy patients (p-value=0.08).

Patients treated with G-CSF+plerixafor had lower blood volumes processed and higher CD34+ yields, especially after the first apheresis session, compared with patients treated with G-CSF alone (Table 1). The same trends were observed when comparing G-CSF+plerixafor to G-CSF +chemotherapy, though the differences were not statistically significant.

Median number of days to neutrophil and platelet engraftment was shorter in the G-CSF+plerixafor arm compared with G-CSF (neutrophils: 12 vs 13 days; p-value<0.001; platelet: 12 vs 18 days; p-value<0.001). Higher CD34+ yields in the G-CSF+plerixafor arm may confer faster engraftment. While CD34+ dose infused during transplantation was not collected, we did observe a significant negative correlation between CD34+ yield (< 12 × 10^6 cells vs > 12 × 10^6 cells) and time to neutrophil and platelet engraftment (p-value<0.001).

The type of mobilization regimen had no significant impact on patient status in terms of relapse or survival at 6 and 12 months follow-up.

Table 1 Apheresis Outcomes

	G-CSF+plerixafor (n = 310)	G-CSF (n = 57)	G-CSF+chemotherapy (n = 22)
Sessions			
median (Q1-Q3)	1.5 (1.0-2.0)	2.0 (1.0-2.0)	2.0 (1.0-2.0)
p–value*	NA	0.25**	0.56**
Volume (l)			
median (Q1-Q3)	24.8 (18.3-42.2)	30.0 (26.0-45.0)	27.0 (15.3-30.5)
p–value*	NA	0.04**	0.65**
CD34+ yield (x 10^6 cells)			
All sessions; median (Q1-Q3)	12.5 (9.8-17.0)	7.6 (5.8-10.8)	10.7 (9.0-26.6)
p–value*	NA	<0.001**	0.52**
1st session; median (Q1-Q3)	9.3 (5.3-14.3)	4.2 (3.2-7.0)	8.0 (4.6-18.6)
p-value*	NA	<0.001**	0.87**

*p–value based on comparison between G-CSF and G-CSF+plerixafor or G-CSF+chemotherapy and G-CSF+plerixafor.

** Wilcoxon Rank Sum.

Conclusions: Plerixafor reduced the burden of apheresis and increased CD34+ yields. Whether higher CD34+ yields relate to CD34+ dose infused and faster engraftment deserves further attention.

Disclosure: JR is member of Sanofi advisory board and acts as consultant to Sanofi; JB received research support from Helsinn and BTG; TM acts as a consultant for Karyopharm, Amgen, Janssen, Adaptive, and Bristol Myers Squibb; SA has not conflict of interest.

P178.

Prediction of The Mobilization Success For Autologous Peripheral Blood Stem Cell Collection in Patients with Malignant Hematologic Diseases

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Background: The goal of peripheral blood stem cell (PBSC) mobilization is collecting an optimum number of cells by leukapheresis with no adverse events. Patients' age and gender, time since last chemotherapy treatment, bone marrow involvement, diagnosis, disease status, previous irradiation/chemotherapy regimens were associated with poor PBSC mobilization, but there is no universal consensus on this matter.

We aimed to identify factors that influence the success of PBSCs mobilization in adult patients with onco-hematologic diseases proposed to autologous transplant between October/2019 and September/2020.

Methods: A retrospective analysis of data was designed to identify possible predictive markers of the mobilization success (CD34+ cells number in the peripheral blood and graft). Chi-squared tests were used for comparing categorical data (p-value <0.05 was considered statistically significant). Poisson regression was performed to determine which factors influence the graft quality.

Results: We analyzed 83 patients: 59% males, 80% ≥50 years; 57% with plasma cell dyscrasia, 33% non-Hodgkin lymphoma (NHL) and 11% Hodgkin lymphoma; 77% had bone marrow invasion. Sixty-six percent were diagnosed in ≤1 year and 55% did ≤1 treatment line; the time between the last treatment date and mobilization was ≤1 month in 66%. Bortezomib was prescribed in 57%, lenalidomide/thalidomide in 47%, R-CHOP in 28%, radiotherapy in 11%. The response rate was 95% (complete in 57%). Six percent had previous mobilization failure and all had ≤2 previous mobilizations.

At leukapheresis time, 80% of patients had WBC≥20.000x10E9/L, 87% had platelets≥100.000x 10E9/L, 7% presented positive infectious disease marker (IDM, anti-HBc) and 72.3% good peripheral venous access. The mean G-CSF dose 17,2 mg/kg/d, 13% did additionally plerixafor. We classified 13.3% very bad mobilizers (<5 CD34+ cells/μl), 12% bad mobilizers (5-10), 22.9% good mobilizers (10-20) and 51.8% very good mobilizers (>20).

Within our population, some factors independently influenced the mobilization success ($p < 0.05$): diagnosis and follow-up time, bone marrow invasion, lenalidomide/thalidomide/bortezomib exposure, number of treatment lines, WBC/platelets counts and G-CSF dosage.

Some variables improved CD34+ harvesting in comparison within the same category: NHL (OR 1.72), female gender (OR 1.41), ≤1 year of disease (OR 1.31), absence of previous pregnancy (OR 1.26), ≤1 month between the last treatment and mobilization (OR 1.11), WBC≥20.000x10E9/L (OR 1.40), platelets≥100.000x10E9/L (OR 1.44), ≤2 previous mobilizations (OR 1.99), <3 volemias (OR 1.7), absence of past history of diabetes (OR 1.27), previous treatment with R-CHOP (OR 1.61).

Some variables worsened CD34+ harvesting in comparison with the reference variable in the same category: <2 treatment lines (OR 0.72), G-CSF <15 kg/d (OR 0.49), bone marrow involvement (OR 0.68) and absence of plerixafor (OR 0.4).

We found three unexpected results that should be considered in a broader cohort: age<25 years (OR 0.42), leukapheresis by peripheral vein (OR 1.19) and absence of IDM (OR 0.74).

There were no major adverse events along mobilization or harvesting.

Conclusions: This study found relevant factors with impact in the mobilization success that should be considered when we are prescribing the mobilization regimen, in order to improve the efficiency in (very) bad mobilizers. Physician expertise is crucial in optimizing the time and the protocol mobilization.

Disclosure: No disclosures.

P179.

Does Use of Biosimilar Zarzio Change Plerixafor Utilization During Stem Cell Mobilization For Autologous Stem Cell Transplant?

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Background: Zarzio® (ZZ) the biosimilar of the granulocyte colony-stimulating factor (G-CSF) filgrastim were approved by the European Medicines Agency (EMA) in 2009 for peripheral blood stem cells (PBSC) mobilization (PBSCM). Comparative studies did not show significant statistical differences with the original filgrastim Neupogen® (NEU) respect to CD34+ cells peak in PB on day 4 of treatment, the total number of CD34+ cells in the final apheresis product, and the median number of apheresis per patient. In our center NEU was used for SCM until April 2016, being replaced for its biosimilar ZZ for the same purpose. Plerixafor (PLEX) requirement in patients mobilized with NEU vs ZZ is still unknown.

Methods: Retrospective analysis of our results in SCM comparing patients receiving NEU vs ZZ alone (G-CSF) or in addition to chemotherapy (G-CSF + Ch) between 2013 and 2020 in a single center. Patients were all ≥ 18 years,

lymphoma and myeloma as underlying hematological disease and they were all scheduled for autologous stem cell transplantation (ASCT). Every patient received G-CSF 8-10 μg/kg for at least 5 days and PLEX was administered when deficient preapheresis CD34+ cell count. We evaluated whether ZZ required PLEX utilization more often for an optimal mobilization in contrast with NEU. Additionally, both group (NEU vs ZZ) were compared in the setting of maximum concentration of peripheral blood CD34+ cells reached after SCM, as well as the necessity of additional mobilization for an optimal apheresis yield. Analysis was done by "IBM SPSS Statistics 20". Patient baseline characteristics were compared between mobilization agents (NEU vs ZZ). Chi-squared and Mann-Whitney U tests were used to prove differences between variables.

Results: 140 patients were analyzed (group NEU=55, group ZZ=85). Baseline characteristics showed no differences between both groups. 20% of patients in ZZ group required PLEX compared to 14.5% in NEU group. Probability of PLEX requirement is 1.15 times higher in ZZ compared to NEU (0.84-1.56), however this analysis did not show significant differences. When comparing PLEX requirement in both groups according to mobilization agent (GCSF vs GCSF+Ch) no differences were also found. Median of maximum circulating CD34+ reached in PB in ZZ group (median = 50, IQR 30.5-107) versus NEU group (median = 70 IQR=55-123) showed no differences. 12.7% of patients in the group NEU required more than one mobilization compared to 15.3% of patients in ZZ group, this analysis resulted not significative.

Conclusions: Our experience revealed no differences between PLEX requirement in patients receiving ZZ for SCM versus those receiving NEU. Patients receiving G-CSF + Ch for mobilization seem to show more PLEX requirement when mobilization agent was ZZ compared to NEU, however our analysis showed no significant differences. In contrast some other authors (Parody et al.) found lower efficacy in ZZ group for patients receiving only G-CSF. Our analysis confirm equality in both groups in the setting of maximum CD34+ reached and number of mobilizations required. Although our results are encouraging, prospective studies are needed to provide more insight into the utilization of secondary agent for SCM.

Disclosure: Nothing to declare.

P180.

Autologous Peripheral Blood Stem Cell Backup Before Haematopoetic Stem Cell Transplantation For Intermediate Osteopetrosis: A Single Center Experience

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Background: Allogeneic haematopoetic stem cell transplantation (alloHSCT) for Malignant Infantile Osteopetrosis (MIOP) is complicated by high primary graft rejection rates. Autologous peripheral blood stem cells (PBSC) collected prior to alloHSCT can rescue patients with non-engraftment. Backup autologous PBSC collection is possible via limited exchange transfusion or venesection in MIOP patients who have leucoerythroblastic blood and large numbers of circulating CD34+ cells secondary to minimal marrow cavities. Intermediate Osteopetrosis (IOP) is a recently published indication for alloHSCT but circulating CD34+ cell numbers and methods for autologous PBSC harvest prior to alloHSCT in IOP patients have not been described. Autologous backup for IOP is not generally performed in Europe but is important in Australia where distance makes emergency grafts harder to procure.

Methods: Two pediatric patients with IOP secondary to C1CN7 mutations underwent autologous PBSC harvest prior to first alloHSCT at The Children's Hospital at Westmead in Sydney in 2019. Peripheral blood was analysed by flow cytometry to measure resting CD34+ count and percentage of mononuclear cells (MNC) (Table 1). As per institutional practice, Granulocyte-colony stimulating factor (G-CSF; 10ug/kg/day) was commenced if the resting CD34+ count was < 20 × 10^6/L and PBSC backup collection proceeded using the MNC procedure on the Spectra Optia when CD34+ count >20 × 10^6/L. The harvest target was >2 × 10^6/kg viable CD34+ cells (vCD34+) measured using modified ISHAGE gating strategy on BD FACS Canto II.

Results: Both patients were male and aged 12-13 years at the time of autologous backup.

Patient 1 (34kg) had a resting CD34+ count of 18 × 10^6/L (0.37% MNC). The theoretical blood volume required to collect 2 × 10^6/kg CD34+ cells using limited exchange transfusion was calculated based on resting CD34+ count and patient weight and was 3.8L. After 3 days of G-CSF, the mobilised CD34+ count was 58 × 10^6/L (0.54% MNC) and 3 × 10^6/kg vCD34+ cells were harvested.

Patient 2 (57kg) had a resting CD34+ count of 10 × 10^6/L (0.17% MNC). The theoretical blood volume required to collect 2 × 10^6/kg CD34+ cells using limited exchange transfusion was 11.4L. Following 4 days of G-CSF, the

CD34+ count was 143 × 10^6/L (0.43% MNC) and 11.6 × 10^6/kg vCD34+ cells were harvested.

Both patients were collected on a single day.

Table 1: Resting CD34+ counts and harvest in IOP

Patient	Age (yrs)	WBC pre mobilisation (x10^9/L)	Resting CD34+ count × 10^6/L (% of MNC)	WBC post mobilisation (x10^6/L)	CD34+ count post mobilisationx 10^6/L (% of MNC)	Total VolumeCollected (mL)	TNC × 10^8/ kg	Harvested fresh vCD34+ × 10^6/kg
1	12	4.9	18 (0.37%)	9.6	58 (0.54%)	69	2.5	3.3
2	13	5.2	10 (0.17%)	39.4	143 (0.32%)	201	6.6	11.6

Conclusions: in our experience, patients with IOP had lower unstimulated CD34+ counts than those previously reported in MIOP patients and were not high enough to allow autologous PBSC collection via limited exchange transfusion. Both patients successfully mobilised with G-CSF and had adequate backup cells collected by apheresis.

Disclosure: Nothing to declare.

Stem Cell Source

P181.

The Blood Donation Before Bone Marrow Harvest Has No Impact On Efficiency of Collection

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Background: Bone marrow donation is a procedure that takes place in a hospital operating room. In many hospitals, autologous red cell units are collected from donor before the harvest and reinfused immediately after the donation to reduce the risk of anemia. The blood donation stimulates hematopoiesis, so it's possible that autotransfusion has an impact on number of collected cells.

The aim of this study is to assess whether blood donation before the harvest has an impact on the total number of nucleated cells in the product.

Methods: Study design: Most of the donors undergo pre-harvest autologous blood collection. The procedure was not carried out if the weight difference is greater than 30kg in favor of the donor. Until March 2020, due to COVID-19, routine blood donations for autotransfusion were suspended. This situation gave an opportunity to assess, if the donation of blood has an impact on the efficiency of BM collection and hemoglobin level in donors' blood after harvest.

Bone marrow was aspirated under general anesthesia, from both pelvic bones. According to the local protocol the volume of marrow and WBC was measured during donation; if the total number of nucleated cells was sufficient, the donation was finished. The collection was also completed, if the total volume of BM reached 15 ml per kg of donor's body weight.

Laboratory analyses: The blood samples for morphology analyses were taken in the day of qualification, one day before and one day after harvest. The samples of BM were taken during donation to measure number of lymphocytes.

Statistics: The Mann–Whitney U-test was used to determine the significance between the cohorts. Differences with p values <0.05 were considered as statistically significant.

Results: Between March and October 2020, 15 BM donations from 15 healthy donors (10 men and 5 women, median age: 35 years, range 20-49 years) were performed; these donors were not referred for autotransfusion. The control group consisted of 34 donors, who underwent harvest between January 2019 and March 2020 (23 men and 11 women, median age 25 years, range 18-41 years). Total volume collected BM was comparable in both groups (median: 1182 ml in first vs 1277 ml in control group).

The level of hemoglobin on the day of qualification was similar in both group: median 15.2 g/dL for donors who had blood donation; and 15.4 g/dL, for donors not referred to autotransfusion. One day before harvest, the first group had statistically lower level of hemoglobin (median 14.1 g/dL vs 14.8 g/dL, $p < 0.001$), however one day after BM collection both groups were comparable (median 11.1 g/dL vs 11.5 g/dL).

Total number of nucleated cells in the product was comparable in both groups: median 204 × 10^8 in donors referred for autotransfusion vs 219 × 10^8 in control group.

Conclusions: Autologous blood transfusion had no impact on Hb levels in blood after BM donation and had no impact on the efficiency of BM harvest. This does not support the routine use of autologous blood transfusion for unrelated BM donors.

Disclosure: Nothing to declare.

P182.

Unmanipulated Haploidentical Transplantation For High Risk Acute Leukemia Using Mobilized Peripheral Blood Stem Cells (PBSC) As Source of Graft: A Single Center Experience

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Background: High risk acute leukemia (HR-AL) are often associated with poor outcome after conventional induction or first salvage chemotherapy. For these patients allogeneic stem cell transplant represent a curative approach. Haploidentical stem cell transplantation (HaploSCT) may be attractive option for patients requiring a hematopoietic stem cell transplant who do not have an related or unrelated HLA-matched donor. We report here the outcome of patients with high-risk acute myeloid (AML) or lymphoblastic (ALL) leukemia who underwent to Haplo-SCT, at single center, outside of clinical trial.

Methods: Between February 2019 and November 2020, 22 HR-AL, 14 (66%) AML and 8 (34%) ALL patients without HLA-matched donor underwent to Haplo-SCT. In all cases graft source was mobilized PBSC; myeloablative (MAC) conditioning regimen consisting of thiotepa, busulfan and fludarabine (TBF) was delivered to 18 patients (81%) and treosulfan and fludarabine in the remaining 4 patients (2 patients > 70 years old and additional 2 because previously transplanted); all patients received post transplant cyclophosphamide (PT-CY) 50 mg/Kg day +3 and day +5 as GvHD prophylaxis combined with cyclosporin (CSA) + micophenolate mofetil in all cases. Twelve patients (60%) were in CR1 and 10 (40%) >RC1 at time of transplant, 4 (19%) had previously been transplanted.

Results: The median age was 49 years (range 24-75). The median number of peripheral CD34+blood cells infused was 6.4 ^{x} 106/Kg (range 4.6-7.8). The median time to neutrophil engraftment > 0.5 ^{x} 109/l and platelet > 20 ^{x} 109/l was 15 days (range 13-17) and 19 (range 13-26) respectively. There was no difference in the median time of engraftment 15 days (range 13-26) for patients ≤ 60 years or older. All but one of the patients achieved full engraftment. The cumulative incidence (CI) of aGvHD grade 0-I, II, III-IV was 80%, 26% and 13% respectively and chronic GVHD (evaluated in 15 patients) was 40%, 20% and 13% for grade 0-I, II, III-IV respectively. After a median follow-up of 240 days (range 20-645) 18 (81%) patients maintained CR with MRD negativity. Four patients with persistent MRD positivity after Haplo-SCT became MRD negative after DLI infusion. Nineteen patients are alive at time of this analysis. Three patients died of progressive disease at day + 30, + 126 and + 127 respectively. The non relapse mortality (NRM) was 0% at day 100 and 1-year. The 1-year overall survival (OS) was 82% (95% CI, 0,66-1) and event free survival (EFS) 78% (95% CI, 0,46-1). No difference statistically significant was observed in median overall survival between patients in RC1 or > RC1; 18,4 (95% CI, 15,6-21,7) versus 18,6 (95% CI, 13.3-23,4) months ($p = 0.95$).

Conclusions: Our results albeit obtained in a single center and on a small series of patients confirm the efficacy of PT-Cy as GVHD prophylaxis after haploidentical mobilized PBSC transplantation with MAC conditioning regimen. The use of mobilized PBSC has demonstrated also in our series rapid engraftment, optimal control of high-risk leukemia with low rates of both chronic and acute extensive GVHD suggesting that this source of graft may replace bone marrow for haploidentical transplantation.

Disclosure: no conflict of interest to declare.