ABSTRACTS FROM THE 43RD ANNUAL MEETING OF THE EUROPEAN SOCIETY FOR BLOOD AND MARROW TRANSPLANTATION: PHYSICIANS ABSTRACTS (O001–O010)

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Van Bekkum Award

O001

Impact of MRD before and after allogeneic hematopoietic cell transplantation (HCT) of childhood ALL by FC and RQ-PCR: a retrospective study on behalf of COG, the PBMTC, the I-BFM, the PDWP of the EBMT and the Westhafen-intercontinental-group

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Studies to date of MRD detection pre-/post-HCT in children with ALL include insufficient numbers for multivariate analyses and lack comparison of methodologies (flow cytometry (FC) vs. RQ-PCR). Patients and Methods: Patients (pts) ($N = 747$) were treated in Europe, North America and Australia between 09/99 and 05/16. MRD was assessed prior to HCT and on or near days +30, +60, +100, +180, +365 and beyond after HCT. Pts were in CR1 ($n = 275$), CR2 ($n = 410$), >CR3 ($n = 53$) or non-remission (NR) ($n = 7$). 586 pts had pre-B ALL, 145 had T-cell ALL and 16 had bi-lineage or bi-phenotypic AL. Grafts were sibling (MSD; $n = 227$), unrelated (MUD; $n = 314$), mismatched (MMD, $n = 75$) or cord blood ($n = 128$) Pts were placed in 4 groups for analysis according to MRD level: (1) no detectable MRD (=MRD negative), (2) MRD positive $< 10E-4$ (=MRD low positive), (3) MRD positive $\geq 10E-4 < 10E-3$ (=MRD high positive) and (4) MRD positive $\geq 10E-3$ (=MRD very high positive). A further analysis compared those tested by FC ($n = 272$ pre- and 775 post-HCT) with those tested by RQ-PCR (381 pre- and 1532 post-HCT). Results: Pts showed a 4y-pEFS of 55%, 4y-pOS of 60%, a CIR of 31% and a CI-NRM of 13%. MRD: Pre-HCT MRD was available in 648 pts. MRD very high, high, low and negative pts showed a 4 yr-pEFS of 28%, 47%, 62% and 67% ($P < 0.001$). Pts with a very high pre-HCT MRD had a 2.44-fold increased HR for relapse and a 1.96 increased risk of TRM ($P < 0.001$); pts with high MRD had a 1.85-fold increased risk of relapse which was similar in pts with low MRD compared with MRD negative pts. Cox Regression analysis showed that pre-HCT MRD and remission status both significantly influenced survival. Post-HCT MRD was analyzed as time-dependent covariates. 4y-pEFS at day +30 for MRD very high, MRD high, MRD low and MRD negative pts were: 32%, 44%, 59% and 66%, respectively ($P = 0.001$); at day +60 0%, 40%, 47% and 64%, respectively ($P < 0.001$); at day +90 29%, 42%, 69% and 65%, respectively ($P < 0.001$); at day +180 10%, 17%, 40% and 79%, respectively ($P < 0.001$); and at day +365 0%, 40%, 36% and 87%, respectively ($P < 0.001$). Very high and high MRD at all time points post-HCT led to higher relapse. Comparison between FC and PCR MRD: At all pre- and post-HCT time points both FC and RQ-PCR levels $\geq 10^{-4}$ were highly predictive of relapse. At pre- and post-HCT points where adequate numbers were available for comparison, RQ-PCR values $\geq 10^{-4} \leq 10^{-3}$ better predicted outcomes compared to FC (e.g. pre-HCT FC HR 1.26, RQ-PCR 2.41; d+30 FC HR 1.33, RQ-PCR 2.53; day +365 FC HR 3.54, RQ-PCR 31.84, all points $P < 0.05$).The predictive value of MRD post-transplant could be clearly confirmed by the analysis using area under the curve (AUC) survival analysis. Multivariable cox regression analysis confirmed the high association between MRD and outcome. GVHD and outcome: Univariate KM estimates showed that pts with no GVHD, GVHD I, II, III and IV had a 4y-pEFS of 43%, 67%, 65%, 56% and 29% ($P < 0.001$), and a CIR of 44%, 24%, 26%, 21% and 12% ($P < 0.001$). GVHD was significantly correlated to EFS, relapse and TRM. There was a clear interaction between aGVHD and MRD. At all time-points landmark analysis showed that MRD positive pts with GVHD had a superior pEFS compared to MRD positive pts without GVHD. Summary: This large study confirmed that MRD pre- and post-HCT is a powerful predictor for survival. These results suggest MRD measurement pre-/post-HCT could be used to guide post-HCT interventions.

Disclosure of conflict of interest: None.

Basic Science Award

O002

Previously published

O003

The UM171 cord blood expansion trial: smaller, better HLA matched cords in short 7 day fedbatch cultures already provide clinical and cost benefits

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Cord blood (CB) transplants are hampered by low cell dose and high transplant related mortality (TRM). UM171, a novel and potent agonist of hematopoietic stem cell (HSC) self-renewal could solve this major limitation, allowing for CB's important qualities as lower risk of chronic GVHD and relapse to prevail. Hence, we initiated a phase I-II clinical trial for patients (pts) in need of a HSC transplant but lacking an HLA identical donor to test the safety and efficacy of UM171 expanded CB (eCB). The procedure was designed to be non-labor intensive and of short duration (no longer than the conditioning regimen) for it to be clinically viable. Pts received a myeloablative or functionally myeloablative conditioning regimen. On day(D)-7 of transplant, the CB was thawed and CD34+ selected. The CD34− component was cryopreserved and infused at transplant. The CD34+ component was placed in a closed culture system with UM171 and culture media was injected once a day until D0, when cells were washed and infused. This fed-batch culture system allowed for small culture volumes, making the procedure less expensive and laborious. The first pts also received a second nonmanipulated CB (nCB) until eCB engraftment was documented in 2 pts. Subsequent pts would only receive a single eCB with a dose de-escalation study to access smaller, better HLA matched CBs. Between 5–11/2016, the first 7 out of 25 pts (23–63 years old) were transplanted, 3 with double CBs and 4 with single eCB. Median culture volume at the end of expansion was 660 mL. The median viable (v)CD34 fold expansion was 34 and that of vCD34+CD201+ was 176. We recently identified CD201 as a more specific marker for HSCs compared to CD34 during UM171 expansion. There was no infusional toxicity. Median first day of 100 and 500 neutrophils were D+10 (8–16) and D+17 (10–19), respectively. As infused (i) vCD34 dose is the best predictor of neutrophil engraftment with non-eCB, we constructed an algorithm to predict engraftment based on ivCD34. We can therefore infer that neutrophil engraftment improved by a median of 5 days thanks to UM171 expansion based on vCD34 dose at thaw of the CB to be expanded. In addition, because cell dose requirements were lower, 4 out of 7 patients were transplanted with a better HLA matched CB compared to standard criteria. No grade 3-4 GVHD or TRM was observed. These results favorably compare to those of other expansion trials which utilize much larger (up to 30 L) and longer (up to 21 days) cultures. Moreover, and in contrast to others, we have already moved into single eCB transplants and are currently embarking onto our dose reduction study to use smaller, better HLA matched CBs, proven to reduce TRM. Furthermore, when compared to other HSC sources (our own data 2011-15), UM171 eCB provides an advantage for engraftment, hospitalization length and days of fever (Table1). Despite very preliminary data, it is already clear that a 7-day UM171 single eCB protocol is feasible and appears to provide clinical benefit beyond faster engraftment with fewer infectious complications and better HLA matching, all the while saving production and hospitalization costs. In conclusion, this 1st in human trial documents the potency of UM171 and potentially positions eCB as a viable HSC source in high risk hematologic malignancies. Results will be updated at the meeting.

Disclosure of conflict of interest: Sauvageau, Marinier and Zandstar own stock in ExCellThera. Caudrelier is an employee of ExCellThera. ExCellThera has the license for UM171. Cohen, Roy and Lachance would receive royalties if Um171 were successful and making a profit.

[O003] Table 1

Table 1 medians	*Hospitalization days*	*Day neutrophil ⩾ 500*	*Last day of fever before engraftment*	*Day platelet engraftment*
eCB	42	17	6	35
CB	60	20	15	42
Peripheral blood	39	17	10	20
Marrow	45	23	NA	28

O004

Letermovir (LET) for prevention of cytomegalovirus (CMV) infection: results from a phase III randomized, double-blind, placebo (PBO)-controlled trial in adult allogeneic hematopoietic cell transplant (alloHCT) recipients

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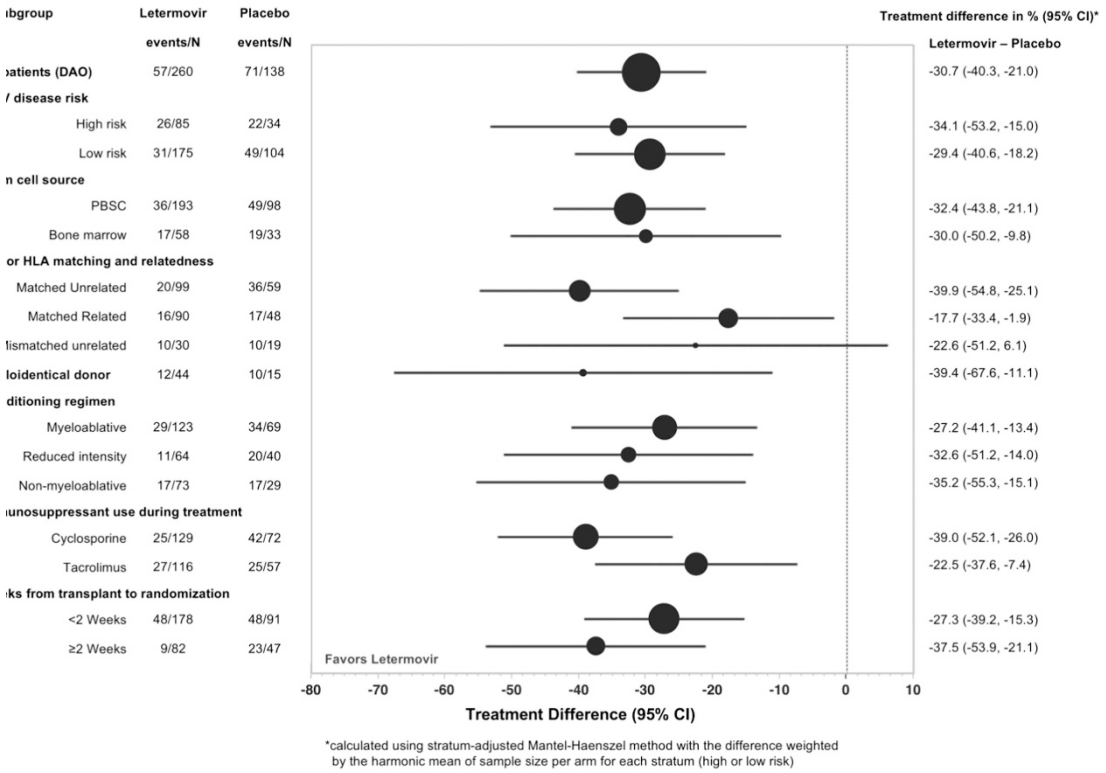
Introduction: No safe and effective antiviral drug suitable for CMV prophylaxis is available in alloHCT. LET is a new antiviral that inhibits the human CMV terminase complex. The objectives of this trial were to evaluate the efficacy and safety of LET for prevention of clinically significant CMV infection (CS-CMVi), defined as CMV disease or confirmed CMV viremia leading to preemptive treatment (PET) through W24 after alloHCT. **Materials and Methods:** Adult CMV seropositive alloHCT recipients with undetectable plasma CMV DNA within 5 days of randomization were randomized 2:1 to receive LET or PBO through W14 (D+100) post-HCT, stratified by study site and CMV disease risk. Study drug had to start by D+28 post-HCT. LET was dosed at 480 mg/d (or 240 mg/d for subjects receiving cyclosporine due to drug-drug interaction). Subjects were assessed weekly through W14, biweekly through W24, and every other month through W48. Plasma CMV DNA obtained at each visit was assayed in a central laboratory. Central or local CMV assay results could be used to start PET. The primary endpoint was the stratum-adjusted proportion of subjects without detectable CMV DNA at treatment initiation (primary cohort) who developed CS-CMVi through W24 post-HCT. Subjects who discontinued the study before W24 for any reason or had missing outcomes at W24 were considered failures for the primary endpoint. The data-as-observed (DAO) approach was used for the subgroup analyses presented (subjects with missing values for a particular endpoint were excluded), and reflect subgroup LET antiviral efficacy not confounded by missing data or subjects discontinuing early from the study. All AEs in treated subjects were included in the safety analyses through 14 d after the last dose of study drug. **Results:** From June 2014 to March 2016, 570 subjects were

Figure 1 [O004]:

Figure 1. Proportion of subjects with CS-CMVi Through Week 24 post-HCT
Selected subject characteristics, DAO approach



*calculated using stratum-adjusted Mantel-Haenszel method with the difference weighted by the harmonic mean of sample size per arm for each stratum (high or low risk)

randomized, 5 did not receive study drug and 70 had detectable CMV DNA at randomization. Study arms were well balanced. In the primary cohort, 57/325 (37.5%) LET-treated subjects developed CS-CMVi or were considered failures compared to 71/170 (60.6%) receiving PBO by W24 post-HCT ($P < 0.0001$). Results were similar among all randomized, treated subjects (153/373, 41.0% vs. 123/192, 64.1%; $P < 0.0001$). Significant reductions of CS-CMVi were seen in subjects at High and Low risk for CMV. Similarly, LET treated subjects receiving different conditioning regimen intensities, different stem cell sources, and donor types had reduced rates of CS-CMVi compared to PBO subjects (Figure 1). However, there was a numerically smaller between-treatment difference in CS-CMVi rates in subjects of Asian origin: LET 13/35; 37.1% vs 6/11; 54.5% (treatment difference −11.5; 95% CI −48.1, 25.1). 7.1% of LET subjects had documented quantifiable CMV viremia at W14 compared to 38.8% in PBO subjects. The corresponding percentages at W24 were 21.5% and 41.8%. GVHD risk was similar between LET and PBO treated subjects either by W14 (38.8% vs. 41.8%) or by W24 (48.9% vs. 54.7%). The W24 all-cause mortality was 10.2% and 15.1% for LET and PBO treated subjects, respectively. No increased myelotoxicity or nephrotoxicity was observed with LET. AEs more commonly reported in LET than PBO subjects were vomiting, peripheral edema, atrial arrhythmias, and sALT levels > 5xULN.
Conclusions: LET prophylaxis through D+100 was efficacious and well tolerated in reducing clinically significant CMV infections through W24 post-HCT.
Disclosure of conflict of interest: P Ljungman: Merck site investigator and research funding, AiCuris advisory board AiCuris; FM Marty: Merck site investigator, consultancy and research funding; R Chemaly: Merck site investigator, consultancy and research funding, AiCuris research funding; J Maertens: Merck site investigator, consultancy and research funding; RF Duarte: Merck site investigator, speakers bureau, consultancy, and research funding; V Teal, H Wan, NA Kartsonis: Merck employees and stock ownership; RY Leavitt: Merck employee; C Badshah: Merck employee and stock ownership.

O005
Previously published

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O006
Application of the disease risk index for risk stratification of allogeneic hematopoietic stem cell transplantation in a large cohort of the European Society for Blood and Marrow Transplantation (EBMT)

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Introduction: The success of an allogeneic hematopoietic stem cell transplantation (HSCT) is highly dependent on the disease and disease status at transplantation. The Disease Risk Index (DRI) (Armand et. al., Blood, 2012/2014) integrates various combinations of these 2 key features, stratifying patients into 4 distinct risk groups. It could potentially promote informed decision and may be used for designing prospective trials and analyzing retrospective data when dealing with a heterogeneous patient population. The DRI has yet to be validated on a large international cohort. Furthermore, there is need to account for additional disease and disease status combinations not included in the original index. In the current analysis we sought to validate the DRI in a large independent European cohort. Furthermore, we explored how it could be extended to additional hematologic malignancies not originally considered. **Methods**: Patients with hematologic malignancies undergoing a first allogeneic HSCT between the years 2000-2015 in centers reporting to the EBMT were analyzed. DRI categories were assigned according to disease and disease status at time of HSCT. Kaplan Meier curves were utilized to evaluate 2-year overall survival (OS) and event free survival (EFS) following HSCT. Relapse incidence (RI), considering death as a competing event, was calculated by cumulative incidence curves. The Log-rank and Fine and Grey tests were used to compare DRI strata. Hazard ratios (HR) were estimated by a Cox model, accounting for competing events when indicated. Combinations of disease and disease status at HSCT not originally included in the DRI were assigned to risk categories according to the mortality risk. **Results**: A total of 73,348 patients from 423 centers were included. The median age was 48. Among various hamtologic malignancies the most frequent indications for transplantation were acute lymphoblastic leukemia (18%), acute myeloid leukemia (AML) (29%), and non-Hodgkins lymphoma (10%). The low, intermediate (Int), high and very (V) high DRI categories corresponded with 18%, 57%, 16% and 9% of the population, respectively, suggesting that the Int group could be further partitioned. The same categories were associated with decreasing 2-year OS and EFS and increasing RI (Figure). In a multivariate analysis DRI was the strongest determinant of survival; the Int risk category was associated with an OS HR of 1.3, high risk 2.17, and V. high risk 2.99, relative to low risk. Risk categories were assigned to hematologic conditions, including sec-AML, which were not previously considered in the DRI (Table). **Conclusions**: In this massive European cohort we demonstrate that the DRI is robust tool for stratifying heterogeneous populations undergoing an allogeneic HSCT. The groupings suggested by the DRI corresponded with distinct risk groups for mortality, EFS and relapse. Furthermore, we have expanded the DRI's utility by introducing hematologic conditions not originally considered.

Table 1 [O006]

Disease	*Status*	N	*% 2-year OS*	*HR[a]*	*New DRI category[b]*
Sec-AML	Early	5409	50	1.5	Int
	Advanced	2690	31	2.7	V.high
Mixed-phenotype Acute Leukemia	Early	617	57	1.2	Int
	Advanced	127	31	2.6	V.high
MDS/MPN	Early	918	53	1.4	Int
	Advanced	298	37	2.2	V.high

[a]Reference is AML intermediate risk cytogenetics at complete remission. [b]Categories were determined according to the HR.

Disclosure of conflict of interest: None.

O007

Fecal microbiota transplantation in patients with blood disorders inhibits gut colonization with antibiotic-resistant bacteria: results of a prospective, single-center study

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Introduction: Gut microbiome is believed to affect outcomes of patients after allogeneic hematopoietic cell transplantation (alloHCT). Recently, we identified gut colonization with antibiotic-resistant bacteria (ARBs) as an independent risk factor for post-alloHCT morbidity and mortality (Bilinski et al. BBMT 2016). We hypothesized that reintroduction of commensal flora by fecal microbiota transplantation (FMT) could be used to eradicate ARBs from the gut in order to improve outcomes of alloHCT in the future. **Material and Methods**: Participants colonized with ARBs were treated with

Figure 1 [0006]:

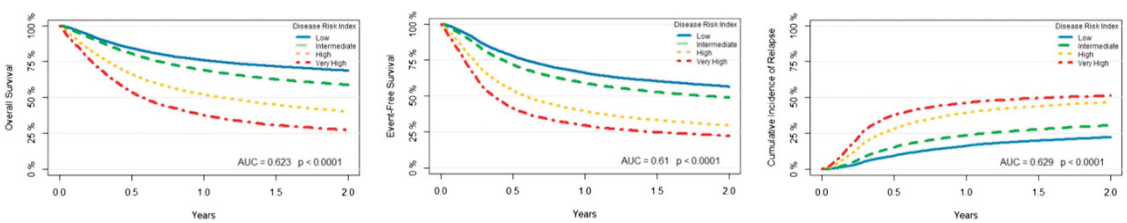

Figure 1 [0007]

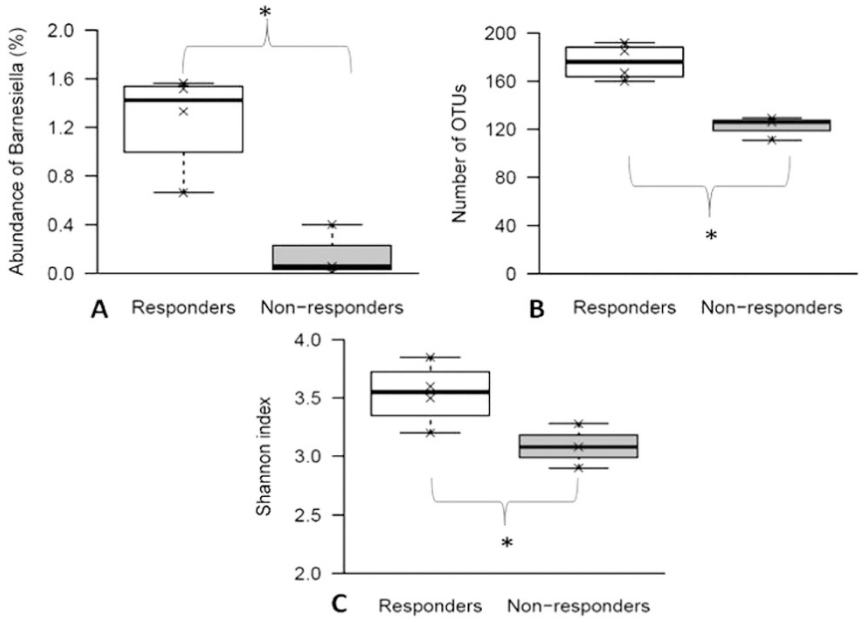

Figure 1. Analysis of NGS data from samples obtained from the transplanted fecal material donated to patients who were colonized with *Klebsiella pneumoniae* NDM1+. The white bars represent participants who were decolonized after FMT (n=4) and the gray bars represent participants who were not decolonized (n=3). (**A**) Proportion of *Barnesiella* spp. in the samples. *p=0·009. (**B**) Richness of the microbiome, as assessed using the number of OTUs. *p=0·003. (**C**) Diversity of the microbiome, as assessed using the Shannon index. *p=0·06. FMT – fecal microbiotal transplantation; NGS – next-generation sequencing; OTU – operational taxonomic unit.

intraduodenal FMT according to a prospective protocol (NCT02461199). Decolonization was defined as two negative subsequent cultures and negative qPCR (when applicable). The primary endpoint was complete decolonization at one month after FMT (decolonization from all ARBs). Secondary endpoints included safety assessments and partial decolonization (decolonization from $\geqslant 1$ ARBs). Microbiome sequencing was performed to investigate the influence of microbial composition of the transplanted material on the outcome of FMT. **Results**: We report the results of 25 FMT procedures performed in 20 patients colonized with median of 2 (range, 1-4) ARBs. The diagnosis was acute myeloblastic leukemia ($n=5$), acute graft-versus-host disease (GvHD) ($n=4$), chronic GvHD ($n=2$), multiple myeloma ($n=3$) and other ($n=6$). FMT was performed before and after alloHCT in 3 and 7 patients, respectively. 40% of patients had neutropenia ($<1.8\times10^9$/L) at the time of the procedure. The gut-colonizing ARBs included *K.pneumoniae* (*Kp*) NDM1 ($n=14$), *E. coli* ESBL ($n=11$), carbapenem-resistant *Kp* ($n=3$), *Pseudomonas aeruginosa* MBL ($n=2$), carbapenem-resistant *Enterobacter cloacae* ($n=2$), carbapenem-resistant *P. aeruginosa* ($n=2$), *Kp* ESBL ($n=2$), vancomycin-resistant *Enterococci* ($n=2$) and other ($n=3$). There were no severe adverse events related to FMT. Complete decolonization was achieved in 15/25 (60%) and partial decolonization in 20/25 (80%) cases at 1 month after FMT. Including repeated procedures, 15/20 patients (75%) achieved complete decolonization. Complete decolonization rate was significantly higher in patients not treated with antibiotics within 1 week after FMT (11/14, 79%) compared with those treated with antibiotics (4/11, 36%, $P<0.05$). In 17 patients, qPCR was used to investigate whether ARBs with a gene encoding carbapenemase were eradicated and negative results were obtained in 53% of cases. The most abundant pathogen *K. pneumoniae* was found to be eradicated after 10/19 (53%) FMTs at one month including 5/6 patients with *K. pneumoniae* NDM1, who did not take antibiotics (83%). The microbiome sequencing (16SrRNA) revealed that stool donated to patients who eliminated *K. pneumoniae* NDM1 was characterized by significantly higher number of operational taxonomic units ($P=0.003$) and a higher abundance of *Barnesiella* spp. ($P=0.009$, Fig. 1), compared to non-responders. **Conclusions**: Fecal microbiota transplantation is safe in patients with blood disorders including those before and after alloHCT. This biological method allows to decolonize majority of patients from ARBs. Administration of antibiotics shortly following FMT decreases success rate. Eradication of *Klebsiella pneumoniae* NDM1 may depend on the abundance of *Barnesiella* spp. in transplanted fecal material. Thus, FMT may constitute a valid tool to fight colonization with ARBs and for modulation of gut microbiome in patients with blood disorders.

Disclosure of conflict of interest: There is no conflict of interest.

O008

Inotuzumab ozogamicin (InO) versus standard of care (SC) for relapsed/refractory (R/R) acute lymphoblastic leukemia (ALL) in the phase 3 INOVATE trial: outcomes in patients who received post-study hematopoietic stem cell transplantation (HSCT)

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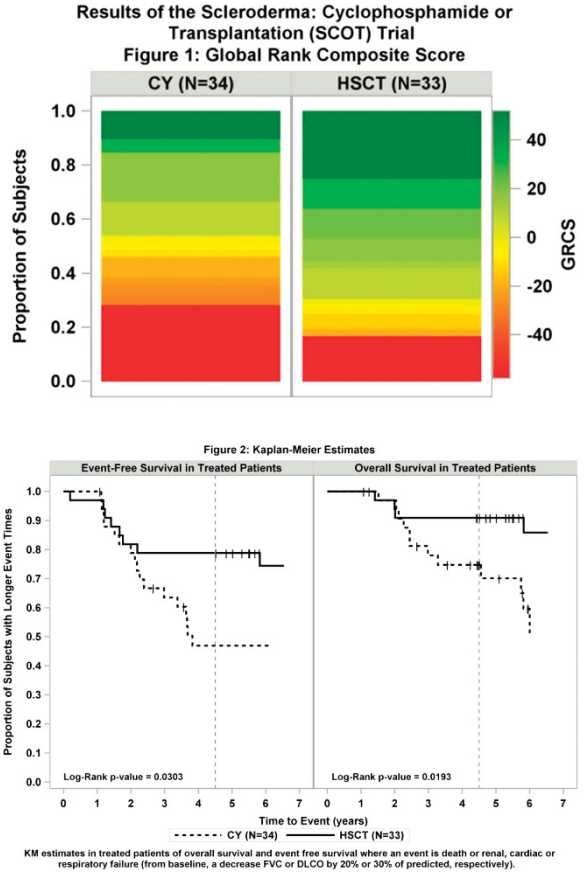
Introduction: Inotuzumab Ozogamicin (InO) demonstrated superior response vs standard of care (SC) in patients (pts) with relapsed/refractory (R/R) acute lymphoblastic leukemia (ALL) in the ongoing INOVATE study (NCT01564784). Intent-to-treat (ITT) analyses of the first 218 of 326 pts randomized showed higher complete remission (CR), including CR with incomplete hematological recovery (CRi) rates for InO vs SC pts (81% [95% CI 72–88] vs 29% [21–39]; 2-sided $P < 0.0001$; Kantarjian *NEJM* 2016). Among pts with CR/CRi, more InO vs SC pts achieved minimal residual disease (MRD) negativity by flow cytometry (78% vs 28%; $P < 0.0001$). Clinical and safety outcomes for pts who proceeded to HSCT are presented. **Methods**: Adults with CD22-positive ALL receiving salvage 1 or 2 treatment were randomized 1:1 to InO (starting dose 1.8 mg/m^2/cycle; 0.8 mg/m^2 on day 1; 0.5 mg/m^2 on days 8 and 15 of a 21–28 day cycle) or SC (FLAG, AraC+mitoxantrone, or HIDAC). Clinical outcomes were assessed by ITT in pts who proceeded to HSCT (InO, $N = 164$; SC, $N = 162$), while safety was assessed in pts who received ≥ 1 dose of study drug (InO, $N = 164$; SC, $N = 143$). Predictors of overall survival (OS), determined by stepwise Cox regression modelling, and veno-occlusive disease (VOD), determined by logistic regression modelling, are shown. Data as of 3/8/16 are presented. Multivariate analyses (MVA) on other major HSCT outcomes will be analyzed after longer follow-up. **Results**: InO pts received a median of 3 (range 1-6) and SC pts 1 (1-4) cycle(s). Significantly more InO vs SC pts received follow-up HSCT (47% [77/164] vs 20% [33/162]; 1-sided $P < 0.0001$). Of the 110 pts who proceeded to HSCT, 6 InO and 15 SC pts received additional reinduction/ salvage therapy before HSCT. Median post-HSCT survival follow-up was 11 months (range 0.5–35). Most pts received allogeneic HSCT (InO, 100%; SC, 91%) and myeloablative conditioning (InO, 66%; SC, 64%). Overall incidence of post-HSCT non-relapse mortality (NRM) was higher in InO vs SC pts (38% vs 24%), whereas relapse rates were lower in InO vs SC pts (31% vs 42%). We failed to detect significant differences in PFS and OS between InO and SC pts. However, we noted that the risk of death between InO vs SC varied before and after 15 months post-HSCT. At 12 months post-HSCT, the probability of OS was 44% (95% CI 33–55) vs 64% (44–78) in InO vs SC pts, respectively. At 24 months, the probabilities were 39% (95% CI 28–50) vs 29% (11–49) in InO vs SC pts, respectively. Among baseline and post-baseline covariates investigated, only MRD negativity and pre-HSCT platelet levels ≥ 100X10^9/L were associated (2-sided; $P < 0.05$) with improved OS in InO pts on MVA. VOD after HSCT was observed in 22% (17/77) of InO pts (fatal, $n = 5$) and 3% (1/32) of SC pts (none were fatal). Five InO pts with VOD had pre-study HSCT. The median onset of VOD for InO pts was 15 days post-HSCT (range 3–57). MVA showed dual alkylator conditioning regimens and age ≥ 55 years were associated (2-sided; $P < 0.05$) with increased risk of VOD in InO pts. **Conclusions**: Administration of InO in R/R ALL is an effective treatment as a bridge to HSCT with the possibility of long-term cure. A greater proportion of InO pts proceeded to HSCT and had lower relapse rates vs SC pts. However, the high post-HSCT NRM in InO pts resulted in failure to detect significant differences in PFS and OS, although more InO pts were long-term survivors. Strategies to lower post-HSCT NRM in pts receiving InO, including VOD, should be evaluated.

Clinical Trial Registry: INOVATE study (NCT01564784).

Disclosure of conflict of interest: David Marks reports consultancy/advisory boards (Pfizer Inc) and consultancy/ advisory boards/lectures (Amgen); Matthias Stelljes reports consultancy, advisory boards, research support (Pfizer); Giovanni Martinelli reports no conflicts of interest; Nicola Gökbuget reports speaker honoraria, research support (Pfizer, Amgen); Hagop M Kantarjian reports research grants (Pfizer Inc, Amgen, Astex, Novartis, BMS); Dan DeAngelo reports ad-board (Pfizer Inc); Anjali Advani reports consultant and research funding (Pfizer Inc); Ryan D Cassaday reports consultancy, research support (Pfizer Inc) and consultancy (Amgen); Akil Merchant reports consultant and research funding (Pfizer Inc); Tao Wang reports employee and stock owner (Pfizer Inc); Fausto Loberiza reports employee and stock owner (Pfizer Inc); Barbara Sleight reports employee and stock owner (Pfizer Inc); Erik Vandendries reports employee and stock owner (Pfizer Inc); Partow Kebriaei reports no conflicts of interest.

Disclosure of conflict of interest: None for the presentation, since the trial was supported by NIH and there were no proprietary products.

Figure 1 [0008]



ISCT-EBMT Award

O009
Previously published

Jian-Jian Luan

O010
Allogeneic hematopoietic stem cell transplantation outcomes after nivolumab monotherapy for +relapsed/ refractory hodgkin lymphoma (CheckMate 039 and CheckMate 205)

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L Giulino-Roth[10], L Castagna[11], K Kato[12], M Popa McKiver[13], A Sumbul[12], L Zhu[12], M Trneny[14], MC Minnema[15], A Rueda[16], D Cunningham[17], N Reddy[18], A Younes[19] and A Santoro[20]
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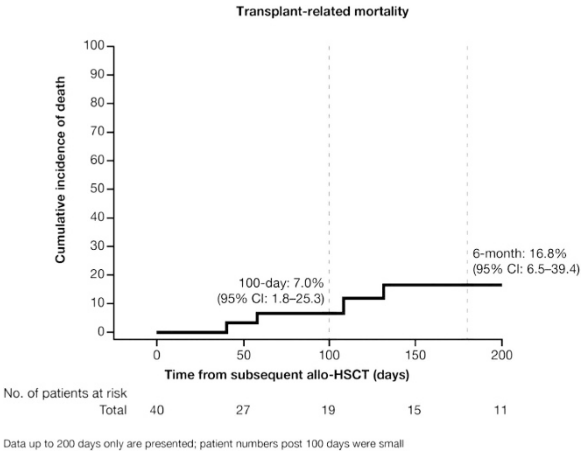
Introduction: Hodgkin lymphoma (HL) patients (pts) who have relapsed after autologous hematopoietic stem cell transplantation (HSCT) and received nivolumab (nivo), a PD-1 checkpoint inhibitor, may achieve adequate disease control with nivo (Ansell *et al*., *N Engl J Med* 2015; Younes *et al*., *Lancet Oncol* 2016) or subsequent therapy and, in some cases, can be eligible for potentially curative treatment with allogeneic (allo)-HSCT. However, US Prescribing Information recommends monitoring for allo-HSCT complications after nivo, eg, hyperacute graft-versus-host disease (GVHD), grade (G) 3–4 GVHD, steroid-requiring febrile syndrome (SRFS), and other immune-mediated reactions. **Methods**: This post-hoc analysis evaluated allo-HSCT safety outcomes in HL pts who received prior nivo therapy in clinical studies: CheckMate 039 ($n = 23$) and CheckMate 205 ($n = 243$). Outcomes data (eg, transplantation date, GVHD, and tumor assessment) were collected prospectively in CheckMate 205 and retrospectively in CheckMate 039. Transplant characteristics (eg, stem cell source, preparative regimen, and post-allo-HSCT safety data) were collected retrospectively. Transplant-related mortality (TRM) was defined as death by any reason other than disease progression. SRFS was defined as steroid-responsive, non-infectious fever that could be accompanied by skin, joint, or liver symptoms. Cumulative incidence of TRM and acute GVHD was assessed by the Kaplan-Meier method. **Results**: Forty pts ($n = 5$, CheckMate 039; $n = 35$, CheckMate 205) who received allo-HSCT after nivo were included. Median (range) age was 34 (18–62) years, pts received 4 (2–9) therapies prior to nivo, and time from last nivo dose to allo-HSCT was 42 (11–411) days. Additional therapy between nivo and allo-HSCT was received by 25%. Stem cell source was peripheral blood in 33 pts and bone marrow in 7. Fifteen percent received stem cells from a matched HLA-identical sibling, 3% 1 HLA-mismatched relation, 30% a haploidentical relation, and 43% an unrelated donor (10%, donor not reported). Myeloablative conditioning was used in 10% and reduced-intensity conditioning in 68%; conditioning regimen was unreported in 23%. In-vivo T-cell depletion was performed in 10 pts, 3 with anti-thymocyte globulin, 7 with alemtuzumab. After allo-HSCT, 6 deaths, all from TRM, occurred; median (range) time from allo-HSCT to death was 120 (40–441) days. No deaths due to disease progression occurred. Any-grade GVHD occurred in 18 pts (45%), G2-4 GVHD in 13 (33%), and G4 GVHD in 7 (18%; including 2 cases of unknown grade, imputed to G4). The organ most commonly affected by any grade GVHD was skin. The 6-mo Kaplan-Meier estimates (95% CI) of TRM (Figure), G2–4 and G3–4 acute GVHD, were 16.8% (6.5–39.4), 41.5% (24.7–63.7), and 25.7% (12.4–48.7), respectively. There were 6 cases of SRFS, 2 of chronic GVHD, 2 of encephalitis (G3 lymphocytic encephalitis and G3 suspected viral encephalitis; both resolved with treatment), and 1 of hepatic veno-occlusive disease (died of multi-organ GVHD). **Conclusions**: Our results suggest that nivo treatment does not preclude subsequent allo-HSCT. Monitoring of pts undergoing allo-HSCT post-PD-1 blockade is recommended for detection and management of early/severe GVHD. Follow-up in a larger number of pts is ongoing to help establish pt characteristics, clinical factors, and treatment timings that may influence outcomes. Study funding: Bristol-Myers Squibb.

Figure 1 [0010]



Data up to 200 days only are presented; patient numbers post 100 days were small

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