

# ABSTRACTS FROM THE 43RD ANNUAL MEETING OF THE EUROPEAN SOCIETY FOR BLOOD AND MARROW TRANSPLANTATION: WORKING PARTIES (WP001-WP022)

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## ALWP

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### WP001

#### Specific cell-therapy for reducing relapse risk after allo HCT

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Haematopoietic stem cell transplantation (HSCT) is an effective and consolidated therapy for many patients with high risk haematological malignancies. The potential of allogeneic HSCT is strictly dependent by donor immune system, particularly alloreactive T lymphocytes. The possibility to obtain graft-versus-tumour effect (GvL), without developing graft-versus-host-disease (GvHD), represents so far a constant and attractive challenge for allogeneic HSCT, the most exploited cellular adoptive immunotherapy of cancer and leukemia. Gene transfer technologies are promising tools for manipulation of donor T cell immunity to enforce the GvL and foster immune reconstitution, while avoiding or controlling GvHD. Viral-mediated transfer of T-cell receptor (TCRs) and chimeric antigen receptor (CARs) targeting leukemia-expressed antigens are in clinical development in both acute lymphoblastic leukemia (ALL) and acute myeloid leukemia (AML). A more established cell therapy modality is represented by donor lymphocytes transduced with suicide gene such as herpes simplex virus thymidine kinase (HSV-TK) and caspase to offer a wide anti-leukemia immune repertoire while offering a potential control of graft-versus-host disease (GvHD). Results of preclinical and clinical studies of post-transplant adoptive cell therapy have become a real option for disease relapse prevention and treatment after HSCT.

**Disclosure of conflict of interest:** None declared.

### WP002

#### Acute myeloid leukemia with FLT3 mutation: a therapeutic window for targeted therapy after allogeneic hematopoietic cell transplantation (alloHCT)

J Esteve, M Labopin, S Brunet, C Schmid, X Poiré, A Bazarbachi, V Rocha, M Mohty and A Nagler on behalf of the Acute Leukemia Working Party (ALWP) of EBMT  
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Internal tandem duplication of FLT3 gene (FLT3-ITD) confers a high relapse risk (RR) and poor outcome. Several studies indicate a clinical benefit of performance of an alloHCT in first complete response (CR1) in patients harboring FLT3-ITD. Nonetheless, the higher relapse risk associated to FLT3-ITD persists after alloHCT, and prevention of relapse after transplantation is a priority issue. Since FLT3 mutations can be targeted with diverse tyrosine kinase inhibitors, different

strategies of post-transplant FLT3 inhibition are currently being explored. The ALWP have addressed different studies aimed to elucidate the impact of FLT3-ITD on transplant outcome, and is conducting a study aimed to analyze the potential benefit of sorafenib in this setting. FLT3-ITD arose as an independent adverse prognostic factor in patients with normal karyotype AML undergoing alloHCT in first CR1, evidenced by a higher RR and inferior leukemia-free survival (LFS) and survival (OS), regardless of NPM1 mutational status and transplant procedure characteristics such as conditioning regimen or donor source. Nonetheless, the results obtained in patients with FLT3-ITD AML after alloHCT in CR1 compared favorably with those observed in patients receiving other post-remission therapy. An analysis focused on FLT3-ITD AML patients  $\geq 60$  year-old, most of which received a reduced-intensity conditioning, showed a 2-year OS of 54%, pointing to a true clinical benefit for this patient population when transplant was performed in an early phase. Interestingly, the results of the RATIFY trial demonstrated that the addition of midostaurin to conventional AML-type chemotherapy in FLT3-mutated AML translated into an improved outcome also in patients undergoing alloHCT in CR1. Moreover, a recent, limited retrospective study showed a markedly relapse reduction and improved OS and LFS in patients receiving sorafenib after alloHCT, without increased GvHD and NRM. In this context, the ALWP is currently conducting a retrospective analysis of the results of administration of sorafenib prior and after alloHCT. In conclusion, the deleterious effect of FLT3-ITD persists in patients undergoing alloHCT, although alloHCT in CR1 arises as the best currently available therapy. The use of FLT3 inhibitors in pre-transplant therapy and as post-transplant maintenance seems a promising strategy to prevent relapses and improve overall outcome.

**Disclosure of conflict of interest:** None declared.

### WP003

#### Is there a role for allogeneic stem cell transplantation for t(3;3) (q21;q26)/inv(3) (q21;q26) acute myeloid leukemia? A report from the ALWP of the EBMT

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Acute Leukemia Working Party

AML with t(3;3) (q21;q26.2)/inv (3) (q21;q26.2) (3q26 AML) is listed as a separate entity in WHO 2008 and 2016 classification and is regarded as very high risk leukemia with extremely poor survival. Median survival of patients with 3q26 AML is reported to be about 10 months. To determine effectiveness of allogeneic hematopoietic stem cell transplantation (alloHSCT) and analyze factors influencing outcome. We studied 106 patients reported to the ALWP of the EBMT with confirmed and verified 3q26 AML. Median follow up for surviving patients was 47 months (range 14-171) and the median age at

[WP003]

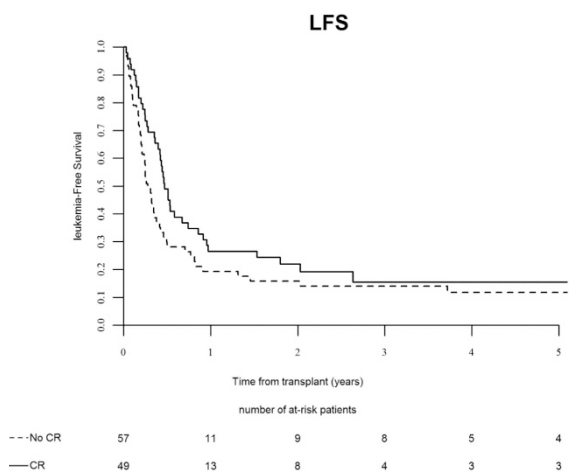


Figure 1. LFS according to disease status at transplantation ( $P=0.05$ ).

transplant was 46 years. Inv(3) was present in 66% and t(3;3) in 34% of cases, respectively. Most frequent concomitant cytogenetic aberrations were chromosome 7 monosomy and complex karyotype. Fifty-seven patients were transplanted in active disease and 49 in complete remission (CR). Two-year leukemia-free survival (LFS), overall survival (OS), relapse incidence (RI), non-relapse mortality (NRM) and graft-versus-host disease-free relapse-free survival (GRFS) probabilities were 19%, 24%, 64%, 17% and 13%, respectively. LFS and OS probabilities were higher for patients transplanted in CR versus those transplanted in active disease: 21.9% vs. 15.8% ( $P=0.05$ ) and 32% vs. 17.5% ( $P=0.06$ ), respectively. In multivariable Cox analysis CR at transplantation was the only factor associated with LFS and OS. CR at transplantation was also the only independent significant factor for decreased NRM ( $P=0.02$ ) and improved GRFS ( $P=0.01$ ). The current study in rather big cohort of patients with 3q26 AML demonstrates that long-term disease control may be achieved with alloHSCT in subgroup of patients, especially those transplanted in remission.

**Disclosure of conflict of Interest:** None declared.

#### Reference

1. Arber DA, Orazi A, Hasserjian R *et al.* The 2016 revision of the World Health Organization classification of myeloid neoplasms and acute leukemia. *Blood* 2016; **127**: 2391–2405.

#### WP004

##### Translating recent cancer genome discoveries to patient tailored clinical intervention protocols

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In recent years, systematic genome-profiling studies have successfully delivered a near complete audit of the genes that cause cancer implicating >400 recurrently mutated genes. These causative mutations have uncovered the molecular underpinnings that drive each tumour's biology and, by extension, its clinical features and treatment response, a concept underpinning the vision of precision medicine. Opportunities for direct translation of such findings include enhanced diagnostic accuracy through molecular profiling, early diagnosis, refined classification and importantly

WP003

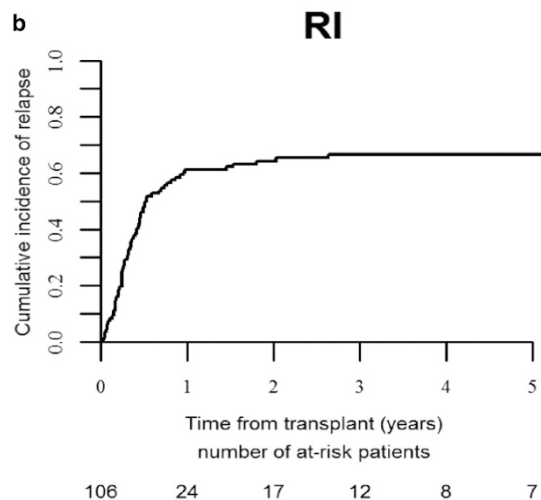
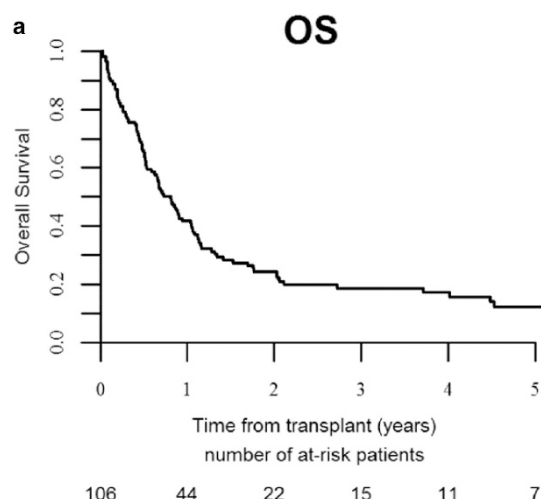


Figure 2. Overall survival (a) and cumulative incidence of relapse (b).

personalized forecasts of a patient's prognosis to support therapeutic decision making. However, the complexity of cancer genomes, which often are genetically and clonally diverse impose significant complications to the narrative of precision medicine. In collaboration with the German Austrian AML Study Group (AML-SG) we have recently performed an in depth molecular characterization of 1540 clinically annotated AML patients. Formal statistical modelling approaches were used to study the genomic and clinical inter-relationships and how these can inform patient tailored clinical management. We show that large knowledge banks of well annotated clinical cohorts, coupled with detailed molecular annotation can deliver refined risk estimates tailored to individual patient status and that inform from the composite molecular architecture that defines a patient tumour. Critical considerations arising from these findings will be discussed alongside emerging data on serial profiling and importantly novel therapeutic agents under clinical investigation.

**Disclosure of conflict of interest:** None declared.

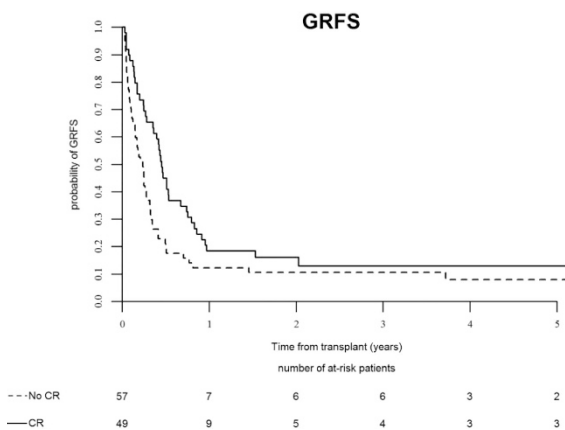


Figure 3. Graft-versus-host disease-free, relapse-free survival according to disease status at transplantation ( $P=0.01$ ).

#### WP005

##### Bad cytogenetic leukemia: transplant or not?

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Cytogenetic analysis is the most powerful prognostic marker of acute myeloid leukemia (AML), and a karyotypic finding classified as high-risk is a well-established indication for early allogeneic stem cell transplantation (allo-SCT). Nevertheless, cytogenetics keeps its prognostic impact even after allo-SCT and the benefit of allo-SCT might be limited to a subgroup of selected patients. Adverse cytogenetic risk group includes a very heterogeneous population and prognosis may be then further stratified according to specific genetic abnormalities such as monosomal karyotype (MK), abnormalities of chromosome 17 p (*abn(17p)*), 11q23 rearrangements or inversion of chromosome 3 (*inv(3)*). The potential benefit of allo-SCT might differ between these diverse AML subtypes. Within the Acute Leukemia Working Party of the EBMT, several studies have been conducted to address the role of allo-SCT in different cytogenetic subgroups. *Poor-risk cytogenetic* AML has been estimated with a 2-year leukemia-free survival (LFS) of 38% after allo-SCT. *MK* has been associated with a worse outcome than CK, with less than 5% survival after chemotherapy alone. Allo-SCT performed in first complete remission (CR1) improves outcome with a 3-year LFS of 29%. Conditioning intensity did not impact on survival. Allo-SCT in patients with *abn(17p)* AML in CR1 translated into a 2-year-LFS of 24%. The presence of *-5/5q-* in combination of *abn(17p)* worsened further the results with a 2-year LFS of 11% after allo-SCT. Patients harbouring *11q23 rearrangements* such as *t(10;11)* and *t(6;11)* showed a 2-year overall survival after allo-SCT of 40% and 24%, respectively. The presence of *inv(3)* was associated with a limited 2-year LFS of 22% after allo-SCT if performed in remission. All those studies showed acceptable toxicities with a 2-year non-relapse mortality around 17%. In conclusions, allo-SCT induces 20 to 30% of long-lasting remission in selected patients harbouring those specific cytogenetic features. Relapse remains the major limitation and prophylactic interventions should then be implemented early after allo-SCT to improve overall results. Introduction of new drugs or post-transplantation immune strategies should be confirmed in the next future as new models to increase the benefit of allo-SCT in these AML subtypes.

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## ADWP

#### WP006

##### Plasma cell depletion strategies in autoimmune disease

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Immunologic memory provides protective immunity against recurrent pathogens, but it can also contribute to chronic inflammation in systemic autoimmune diseases (AID), such as systemic lupus erythematosus (SLE) and systemic sclerosis (SSc). Our research group previously identified long-lived plasma cells (PCs), as an essential component of the autoreactive memory (Hiepe *et al.*, 2011). They are harbored in dedicated niches in the bone marrow or inflamed tissue where they continuously secrete autoantibodies. Their targeting represents a therapeutic challenge. In contrast to short-lived plasmablasts and their precursor memory B cells, long-lived PCs are refractory to immunosuppressive and B cell depleting therapies. Previously, mechanistic studies provided the proof-of-concept that the depletion of the autoreactive immunologic memory (including long-lived PCs) with immunoadjuvant using anti-thymocyte globulin (ATG) is a requisite for curative therapeutic concepts in AID (Alexander *et al.*, 2009). Subsequently, more specific PC depleting strategies have been proposed. They comprise either (i) their direct targeting with proteasome inhibition or monoclonal antibodies, such as anti-CD38, (ii) targeting of soluble PC survival factors, such as APRIL with TACI-Ig (Atacicept) and (iii) targeting of the PC niche, e.g. with CXCR4 blockade or VLA-4 inhibition. Meanwhile, pilot clinical trials demonstrated a therapeutically relevant PC depletion with the proteasome inhibitor Bortezomib in SLE (Alexander *et al.*, 2015) and anti-NMDA receptor encephalitis (Scheibe *et al.*, 2016), but PC regeneration was rapid after Bortezomib discontinuation due to B cell hyperactivity in SLE, which could be inhibited in preclinical trials using B cell depletion or immunosuppression (Taddeo *et al.*, 2015). In addition, Atacicept treatment was associated with a significant reduction in serum immunoglobulin (IgG, IgM) levels and autoantibody production in SLE but this trial had to be discontinued prematurely due to increased infection rates. Overall, these data indicate the therapeutic relevance of PC depletion in AID but also emphasize (i) the need for thorough monitoring of total and protective serum immunoglobulin levels and (ii) the rationale to combine PC depletion with therapeutic strategies to prevent their regeneration in systemic autoimmunity for sustained clinical remissions.

**Disclosure of conflict of interest:** None declared.

#### WP007

##### Northwestern university experience of HSCT for multiple sclerosis—what has been learned in the last 20 years?

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Before attempting HSCT for MS, we performed hematopoietic stem cell transplants (HSCT) in mice with experimental autoimmune encephalomyelitis (EAE), an animal model of MS. HSCT in the relapsing remitting stage of EAE resulted in sustained reversal of disability, while in the progressive phase of EAE, HSCT had no beneficial effect (1). In retrospect, the results of HSCT for EAE foretold the outcome of HSCT for patients with MS. The results of our first human trial confirmed the EAE data in that HSCT in secondary progressive MS (SPMS), even using an aggressive myeloblastic regimen of cyclophosphamide, antithymocyte globulin, and total body irradiation, and CD34 selection, failed to improve neurologic disability (2). Immune analysis confirmed a new and diverse T cell repertoire following transplant. However, immune regeneration occurred without neurologic improvement reaffirming that SPMS is a

neurodegenerative disease that does not respond to immune based therapies. To perform HSCT in relapsing remitting multiple sclerosis (RRMS), we choose a safer non-myeloablative regimen of two immune specific drugs already documented to benefit relapsing remitting MS, i.e. cyclophosphamide and alemtuzumab (without CD34 selection). The regimen was well-tolerated and following HSCT neurologic disability (EDSS) markedly improved (EDSS < 1.0 or more) (3). No pharmacologic drug therapy, including alemtuzumab, had ever achieved the goal of EDSS improvement by 1.0 or more points. However, this transplant regimen was complicated by an 18% incidence of late idiopathic thrombocytopenic purpura (ITP) that could occur up to 3 years after HSCT. In hope of decreasing the incidence of late ITP, we changed the conditioning regimen from cyclophosphamide/alemtuzumab to cyclophosphamide/rabbit anti-thymocyte globulin (ATG) (without CD34 selection) which resulted in the same marked sustained drug-free improvement in EDSS of > 1.0 points after HSCT, and the incidence of late ITP, although not completely eliminated, was significantly reduced to 2% compared to 18% after cyclo-phosphamide/alemtuzumab conditioning (6). Importantly, solumedrol was needed to break late ATG-related fever that occurred on days 1-5 post HSCT (2-6 days after the last ATG dose), because upon long-term follow-up analysis sustained fever during transplant resulted in significantly worse long-term neurologic disability (4). The Multiple Sclerosis International Stem Cell Transplant (MIST) trial involving four sites (Chicago, Sao Paulo, Sheffield, and Uppsala) and 110 patients has completed enrollment and results will be forthcoming.

**Disclosure of conflict of interest:** None declared.

#### WP008

##### **Hematopoietic stem cell transplantation in Crohn's disease**

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*University Hospitals Leuven, Belgium*

Crohn's Disease (CD) is a chronic relapsing inflammatory bowel disease associated with high morbidity and mortality and reduced quality of life. Despite the impressive clinical introduction of several new and active immunosuppressive and immunomodulatory therapies, some patients will show insufficient response or loss of response to previous treatments. According to current recommendations autologous hematopoietic stem cell transplantation (AHSCT) can be considered in severe (based on general performance state and CD-specific scores) refractory (to at least three immunosuppressive/biological agents) CD. Although the number of patients treated with AHSCT is rather limited, available—prospective and retrospective—literature data show AHSCT can be considered both safe and efficacious in patients with severe refractory CD. However, despite these promising results, many questions and unresolved issues have remained. These include optimal timing for AHSCT, patient selection, determination of accurate end points, benefit of maintenance therapy, altered responsiveness to classical treatment, long term efficacy and side effects. Future clinical trials and long term follow up will be absolutely mandatory to answer these questions.

**Disclosure of conflict of interest:** None declared.

#### WP009

##### **HSCT in autoimmune diseases (ADs): activity and trends within the first 20 years of the EBMT ADWP**

*J Snowden, M Badoglio*

*ADWP*

HSCT has been evolving for 20 years as a treatment for severe ADs. The EBMT has been central to these developments. Using data reported to the EBMT registry, we summarize the evolution, trends and long-term outcomes in patients who had undergone autologous and allogeneic HSCT for ADs from

1994 to December 2016. Among 2227 HSCT procedures there were 2071 patients undergoing first autologous HSCT, with median age 37 years (3-76) and 113 patients undergoing allogeneic HSCT, with median age 12 years (< 1 to 62). Patients were registered from 254 centres in 40 countries, 61% were female, 11% were < 18 and 51 patients 2nd or 3rd HSCT procedures. Indications included 926 patients with multiple sclerosis (MS), 633 patients with connective tissue disorders, 186 patients with inflammatory arthritis (IA), 54 patients with vasculitis, 198 patients with inflammatory bowel disease (IBD), 100 patients with haematological immune cytopenias and 20 patients with type 1 diabetes. Ninety-two patients were treated for other neurological diseases including chronic inflammatory demyelinating polyneuropathy (36), neuromyelitis optica (24) and myasthenia gravis (7). The predominant countries of activity were Italy, Germany, Sweden, United Kingdom, the Netherlands, Spain, France, Australia and Poland who made up around three quarters of the activity, although some other countries contributed highly based on per head of population. Registration is now hitting 200 registrations annually in tandem with the publication of EBMT 2012 guidelines and a number of RCTs (Snowden *et al.*, 2012; Kelsey *et al.*, 2016; Bell *et al.*, 2017). In conjunction with clinical data, we are beginning to understand the mechanisms behind the 'immune reboot' (Snowden *et al.*, 2016). Survival curves support basic biological differences in the responses of AD to allogeneic and autologous HSCT. In summary, HSCT for AD has now become established in some indications and should be considered alongside modern biological therapies. After 20 years, there is now a case for future ADWP focus to be on "Implementation Science" to drive the field into routine, fully-resourced high-quality clinical practice. Further clinical trials to improve the safety and efficacy of HSCT, along with multi-disciplinary guidelines and health economic evaluations, will be essential.

**Disclosure of conflict of interest:** None declared.

## CMWP

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#### WP010

##### **IMiDs, proteasome-inhibitors and antibodies as part of a transplant-package for multiple myeloma**

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Important studies have recently reaffirmed the integral role of high-dose chemotherapy and autologous haematopoietic cell transplantation (AHCT) in the management of multiple myeloma. The routine use of novel agent-based induction therapies has resulted in improved responses before transplantation, and numbers of AHCTs have continued to increase in younger and older myeloma patients in recent years. In addition to prolonged post-transplant maintenance therapies that largely aim to extend the duration of remission, time-limited consolidation with novel agents is being investigated as a strategy to primarily increase the depth of response following AHCT. I will discuss recent advances and potential future directions in incorporating novel agents into the AHCT package. The discussion will predominantly focus on the application of "immunomodulatory" drugs, proteasome inhibitors, and antibodies as post-transplant consolidation therapy, and how such approaches impact on the depth of response and duration of remission. I will also consider how these agents and other new experimental therapies may be used in the immediate peri-transplant period, and what impact consolidation and maintenance strategies may have on clonal evolution and metabolic adaptation of myeloma cells.

**Disclosure of conflict of interest:** Consultancy/Advisory board for Takeda, Novartis.



#### WP011

##### **JAK inhibitors before, during and after stem cell transplantation for myelofibrosis**

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Over the last decade, there has been a significant increase in the number of patients with Myelofibrosis (MF) undergoing allogeneic stem cell transplantation (SCT). The introduction of JAK inhibitors into the clinical arena has revolutionized the available therapeutic options for MF. Many patients with MF who subsequently undergo a SCT have had previous exposure to one or more of these agents. To date, there have been multiple retrospective reports of the outcomes of patients treated with JAK inhibitors who have subsequently underwent an allogeneic SCT procedure 1–3. In this presentation, I will discuss the many questions concerning how JAK inhibitor therapy best integrates into the pre-, peri- and post-SCT period. The potential benefits and risks of JAK inhibitors will be discussed in the pre-SCT period. We will discuss the optimal timing of JAK inhibitor discontinuation prior to SCT and whether a patient with a well-matched donor responding well to JAKi therapy should proceed directly to SCT or wait until loss of response/intolerance. Furthermore, I will consider the role of JAK inhibitors during the transplant conditioning and peri-engraftment period. Lastly, I will discuss the role of JAK inhibitors post-SCT –in the management of Graft-Versus-Host-Disease, as a consolidation agent to aid control of splenomegaly and modulation of graft function, as maintenance therapy and also as a bridge to a second SCT where required.

**Disclosure of conflict of interest:** Speaker fees from Novartis and JAZZ Pharmaceuticals.

#### WP012

##### **BTK, BCL2 or PI3K inhibitors combined with allogeneic stem cell transplantation for patients with chronic lymphocytic leukemia**

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For patients with refractory courses of Chronic Lymphocytic Leukemia (CLL) allogeneic hematopoietic cell transplantation (alloHCT) provides the best long-term disease control and can lead to cure. In the past years, the approval of the Bruton-Tyrosinase-inhibitor Ibrutinib (Ib), the phosphatidylinositol 3-kinase- $\delta$  inhibitor, Idelalisib (Idela), and the B-cell Lymphoma-2 inhibitor, Venetoclax (Ven), have led to fundamental changes of the treatment algorithms of patients with CLL. Especially Ib and Ven have few side effects and are generally very well tolerated. Patients on Idela are at somewhat greater risk of side effects such as colitis, hepatitis, and pneumonitis. Comparative trials with alloHCT have not been performed. Against this background, the place of alloHCT in the treatment of algorithm of patients with high-risk relapsed or refractory CLL will be discussed. In large registry studies sustained disease-control at 10 years after alloHCT was observed in 28% (95%-CI, 25% to 31%) of patients and the survival probability was 35% (95%-CI, 32% to 38%). 1. Taking into account individual information on risk factors which predict low 2-year non-relapse mortality, the balance may tip towards preferring alloHCT above the sequential use of the new drugs for certain groups of patients. EBMT has launched a couple of studies which aim at investigating the outcome of alloHCT in patients who had received ibrutinib or idelalisib prior to alloHCT showing promising results. Further information is available on the integration of ibrutinib as pre-emptive

or relapse treatment after alloHCT. 2. Especially the immunomodulatory characteristics of ibrutinib mediated also through inhibition of the interleukin-2-inducible T-cell kinase are appealing for patients with CLL suffering from chronic graft-versus-host disease (GVHD)3. In summary, defining the optimal timing for alloHCT for individual patients became a challenging task due to promising alternative options for patients with high-risk CLL. Integration of the new drugs as induction therapy prior to alloHCT and for the prevention and treatment of relapse and chronic GVHD gives a promising prospective.

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#### WP013

##### **HSCT for adult cerebral adrenoleukodystrophy**

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The adult cerebral form of X-linked adrenoleukodystrophy (ACALD) is characterized by a rapidly progressing inflammatory demyelination in the brain, typically leading to death within a few years after onset. Boys with the childhood cerebral form demonstrate long-term neurological benefit from allogeneic hematopoietic stem cell transplantation (HSCT), but anecdotal results in adults had been inconclusive. Data from 14 adult males treated with allogeneic HSCT for ACALD on a compassionate basis had been collected. Diagnosis was based on ALD-trait and cerebral demyelinating lesions with gadolinium enhancement in MRI. In addition to ACALD 5 patients demonstrated severe motor disability (EDSS  $\geq 6$ ) from the chronic neuronopathic form of ALD, adrenomyeloneuropathy. 12 patients received bone marrow ( $n = 10$ ) or peripheral stem cells ( $n = 2$ ) from a matched donor after myeloablative conditioning, whereas 2 patients were transplanted with cord blood after reduced-intensity conditioning. Median age at HSCT was 34 years. Altogether 12 patients engrafted and 8 survived (57%) with a median follow-up of 65 months. Death was infection-related ( $n = 3$ ), or due to disease progression ( $n = 3$ ). Deterioration of motor and bladder dysfunction ( $n = 12$ ) as well as behavioural changes ( $n = 8$ ) were typical complications during transplantation. All 8 survivors showed arrest of progressive cerebral demyelination and prevention of severe loss of neurocognition. Severe motor dysfunction (EDSS  $\geq 6$ ) and advanced involvement of corticospinal tracts before transplantation were predictive for a poor outcome. This series was recently extended by 7 additional HSCTs in Berlin. 5 survivors suggest a potential survival rate of  $> 70\%$  and prevention of cognitive decline in about 50% of patients. The additional data further confirmed advanced adrenomyeloneuropathy prior to HSCT as a strong negative predictor. The study indicates the feasibility and potential long-term benefit of allogeneic HSCT for ACALD patients. Further studies are warranted to optimize patient and donor selection as well as conditioning regimens.

**Disclosure of conflict of interest:** None declared.

**WP014****HSCT for SCID in the 21st century: an update from SCETIDE**

*A Lankester on behalf of WP-IE and SCETIDE*

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In almost half a century, hematopoietic stem cell transplantation (HSCT) has evolved as an increasingly successful treatment for children with severe combined immune deficiency. Previous reports from SCETIDE have demonstrated that overall survival after HSCT for SCID has gradually improved in time (Gennery *et al*, *JACI* 2010). In the most recent period this is particularly reflected in the improved survival following matched unrelated donor HSCT, which now approaches survival in matched sibling donor transplantation. Increasingly, and in addition to traditional phenotypic classification, SCID patients can be classified based on genetic diagnosis which allows for analysis of HSCT outcome in patients belonging to specific subgroups. Data will be presented on the HSCT outcome results for SCID patients transplanted in the period 2006\_2014 ( $n=497$ ). The impact of donor type, genetic diagnosis, conditioning and GvHD on HSCT outcome will be discussed with particular focus on the influence on immune reconstitution and long term immune function.

**Disclosure of conflict of interest:** None declared.

**WP015****HSCT for monogenic autoimmune disorders**

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The genomic revolution has led to the discovery of monogenic disorders that lead to loss of self-tolerance. The challenge is to evaluate such patients and decide on the best treatment options. These disorders have very variable phenotypes and clinical features which may be due to the patient environment, infection and other modifier genes but should be suspected in patients with a combination of any of the following features: lymphadenopathy, organomegaly, lymphoproliferation, cytopaenias, skin rashes, enteropathy, endocrinopathies, joint inflammation and infections. Some specific treatments for specifically affected pathways are available but, for definitive cure, if the defect is in the hematopoietic stem cell then transplant is a viable option. The dilemma is to know which patients should be transplanted and when. It is better to transplant younger patients before organ damage and severe infection and inflammation occur. Low toxicity regimens are increasingly preferred but care needs to be taken to maximize GvHD prophylaxis but also to procure high levels of stable donor chimerism. Ultimately the decision to transplant needs to be made according to the phenotype not the genotype of the patient following careful discussion with the patient and their family. The risks of using specific immunomodulatory agents long-term need to be balanced against the risks of HSCT, and these agents may be very useful for optimizing the condition of patients prior to HSCT leading to better outcomes. Further studies are needed on the long-term outcome of the non-transplanted and transplanted patients including their quality of life. The talk will review transplant outcomes of a number of these newly discovered disorders.

**Disclosure of conflict of interest:** None.

**WP016****Infectious diseases (IDWP): How much should we worry about viral respiratory tract infections in HSCT recipients?**

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Viral respiratory tract infections (VRTI) are an important cause of morbidity and mortality after HSCT. Since rapid molecular diagnostic methods have become widely available, the management of VRTI is increasingly challenging. First, the spectrum of respiratory viruses has widened, since in addition to influenza, parainfluenza e respiratory syncytial virus (RSV), novel multiplex assays detect also rhinoviruses, coronaviruses, adenoviruses and, more recently discovered, bocavirus and metapneumovirus. Second, clinicians are faced with virological identification of pathogens responsible for clinical pictures of very different severity, ranging from slightly symptomatic upper respiratory tract infections to severe pneumonia. Complications of VRTI include bacterial superinfection, respiratory failure and long term immune-mediated lung disorders such as idiopathic pneumonia syndrome, bronchiolitis obliterans syndrome and bronchiolitis obliterans organizing pneumonia. An association between influenza and aspergillosis has been described after 2009 H1N1 epidemics. Most of VRTI occur during winter and early spring, with seasonal outbreaks of influenza and RSV, and more even distribution for other viruses. Nosocomial outbreaks are possible and should be actively avoided in centres caring for transplant patients through isolation measures and vaccination against influenza. Vaccination should be provided to healthcare workers, patients' household contacts and patients who are 4–6 months after transplant. In case of influenza, empirical or targeted therapy with antivirals is warranted and viral shedding might be prolonged. Antiviral prophylaxis of severely immunocompromised patients during outbreaks might be chosen in selected cases. Administration of ribavirin via aerosol or orally has been recommended for selected patients with RSV infection and its activity has been also reported for other respiratory viruses.

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**WP017****Introduction to activities and initiatives of infectious diseases working party EBMT**

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Infectious Diseases Working Party (IDWP) is a transversal Working Party, with scientific interests involving various diseases. The IDWP objectives are: (1) to organize high level accredited educational activities related to infectious diseases of HSCT; (2) to design and support prospective studies in the field of infectious diseases; (3) to generate high quality retrospective studies addressing different issues related to infectious diseases management and therapy; (4) to generate guidelines related to the management of infectious diseases. Currently ongoing prospective non-interventional studies run by IDWP: (1) Current treatment of HCV infection after HSCT, (2) Pneumocystis jirovecii pneumonia (PcP) after allogeneic HSCT, (3) Impact of pre-existing invasive aspergillosis on allogeneic stem cell transplantation (IPAT). This Report summarizes also general data of abstracts submitted to

EBMT-2017: Infectious diseases every year belongs to the Top-5 areas of interest. A total number of 88 abstracts were submitted for infectious complications to EBMT-2017. Their characteristics: 59 (66%) retrospective studies, 29 (34%) prospective studies. 13 (15%) abstracts reported the results of multicenter studies (including 2 RTC Phase II and Phase III studies, 1 from EBMT-IDWP, others from Poland, France, Italy, China, Germany). 8 (9%) were case reports, 2 in-vitro study and 1 meta-analysis. 67 (76%) abstracts concerned adults, 17 (19%) children, 4 (5%) mixed populations. 61 abstracts (69%) focused on allogeneic transplant, 12 (13%) on autologous transplant, 15 (18%) on auto/allo-transplant. Viral infections were studied in 42 (49%) abstracts (7 abstracts related to: letermovir, maribavir or brincidofovir), fungal infections in 19 (21%), bacterial infections in 22 (24%) (fecal microbiota transplantation in 2), parasite 1, and various infections in 4 (5%); with vaccination being the focus in 3 abstracts. The objective of 41 (46%) abstracts was epidemiology/risk factors/survival, diagnosis 9 (10%), prophylaxis 12 (13%), immunity 3 (4%), therapy 26 (31%) including adoptive immunotherapy 2 (2%), and economy 2 (2%). In conclusion, most abstracts reported retrospective studies involving single-centers, with viral infections representing the most frequent area of interest.

**Disclosure of conflict of interest:** None declared.

## PDWP

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### WP018

#### Outcome of children developing grade III-IV acute graft-versus-host disease after allogeneic hematopoietic stem cell transplantation

*A Bertaina, F Locatelli, A Lawitschka, A Balduzzi, J-H Dalle, P Sedlacek, A Willasch, I Yaniv, C Peters and P Bader on behalf of the EBMT Paediatric Diseases Working Party*

Information on the outcome of paediatric patients experiencing acute GvHD (aGvHD) is limited. For this reason, we conducted a retrospective analysis on 2519 children, transplanted between 2004 and 2014, who developed grade III-IV aGvHD and were reported to EBMT registry. Median year at transplantation was 2009. 826 children had a non-malignant disorder, while 1689 had malignancies. The donor was an HLA-identical sibling in 707 cases and an UD in 1081 cases. Umbilical cord blood (UCBT) was employed as stem cell source in 396 cases, while a relative other than a compatible sibling was utilized in 202 cases. Overall, 1281 patients were given bone marrow (BM), while 800 received peripheral blood stem cells (PBSC). Grade III aGvHD occurred in 1607 patients (64%), while grade IV aGvHD was diagnosed in 908 (36%). Chronic GvHD occurred in 649 patients (26%). It was extensive in 333 (13%) and of limited severity in 269 (11%). At time of last follow-up, 1341 patients were alive (53%), while 1178 were dead (47%). Fifty-seven patients were lost to the follow-up. Relapse of the original disorder occurred in 219 children (19.7%). Transplant-related causes were responsible for the death of 902 patients (76.5%), while 6 (0.5%) patients developed a secondary malignancy. The 3-year Kaplan-Meier probability of OS was 46.7% (CI 95, 44.1-49.5) and 50.9% in patients affected by malignant and non-malignant disorders, respectively. Patients who received as stem cell source BM had a better outcome in comparison to those who received PBSC (3-year OS, 53.2 vs 40.4%,  $P < 0.0001$ ). In the overall cohort, in comparison to patients who developed limited cGvHD, the extensive form of the disease had a detrimental effect on the outcome, being the 3-year OS 74.2% and 41.6%, respectively ( $P < 0.0001$ ). The 3-year Kaplan-Meier probability of non-relapse mortality (NRM) was 37.4% and 45.9% in malignant and non-malignant disorders, respectively. These data indicate that the occurrence of grade III-IV aGvHD is associated with a

dismal outcome also in paediatric patients. Although the outcome of children experiencing grade III-IV aGvHD is improving over time, strategies aimed at preventing this immune-mediated complication and at optimizing its treatment are desirable.

**Disclosure of conflict of interest:** None declared.

### WP019

#### Progress in pediatric chronic graft-versus-host disease (cGvHD) biomarkers

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**Introduction:** cGvHD remains a major long term complication of BMT. To minimize this problem validated cGvHD biomarkers are needed for better diagnosis, prognosis, prediction, and response to therapy evaluation. Progress in the validation of cGvHD biomarkers have been limited by the quality of samples and clinical data, sufficient patient numbers, and reproducibility by more than one research group. Multiple variables including donor source, previous acute GvHD, and TBI may impact on cGvHD biomarker interpretation further complicating biomarker application in clinical trials and practice. Because if these issues, larger multicenter trials performed in a standardized fashion with close collaboration are required. **Material and Methods:** Through the PBMTCC, we have a network of 25 pediatric BMT centers in Canada, US, and Europe entitled the Applied Biomarkers in Late Effects (ABLE). The study collects high quality samples and clinical data allowing for discovery and validation assays of cGvHD prognostic, predictive, and diagnostic biomarkers. The process involves central adjudication of the clinical data to ensure accurate cGvHD assignment. Samples are processed in a standardized manner with a streamlined enrollment design.

**Results:** The project has enrolled the initial goal of 300 children and adolescents with a cGvHD prevalence of approximately 22%. The sample submission rate is 92% of all samples on continuing patients ( $\geq 100$  days). Two findings are that (a) many cases classified as cGvHD are actually late aGvHD and (b) a number of clinical criteria considered to define cGvHD many times do not meet the NIH cGvHD criteria. We will present preliminary results of the initial 100 patients and contrast with previous adult studies. We will present the next generation study validation design and how the current design was leveraged for additional studies. **Conclusion:** The ABLE study design has resulted in a rapid accrual of high quality biomarker samples and clinical data from a large number of pediatric BMT centers. The study has yielded findings that will result in improved future study design and will yield clinical validation and discovery data.

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### WP020

#### Previously published

### WP021

#### Outcome of children developing grade III-IV acute graft-versus-host disease after allogeneic hematopoietic stem cell transplantation

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improving over time, strategies aimed at preventing this immune-mediated complication and at optimizing its treatment are desirable.

**Disclosure of conflict of interest:** None declared.

## CMWP

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### WP022

#### Hypomethylating agents pre- and post-transplantation for MDS

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The only curative treatment for patients with higher risk MDS remains the allogeneic hematopoietic stem cell transplant (HSCT). Firstly, not all patients with a donor can be transplanted because of disease progression or comorbidity. Secondly, HSCT is the source of potential complications related to the transplant as well as disease progression. Because hypomethylating agents (HMA) have been reported to induce remission able to extend life expectancy in MDS patients, they are frequently used in these patients, including those who will receive a transplant. HMA might be an option either to improve control disease before HSCT and/or to prevent relapse after HSCT. Based on the review of the literature, this presentation proposes to give some clue on the place of HMA before and after HSCT.

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