Table 1

Sex (M/F)	98/102
Median age	51 (18-72)
Age > 50	53%
KPS > 80%	64%
HCT-CI Score >4	19%

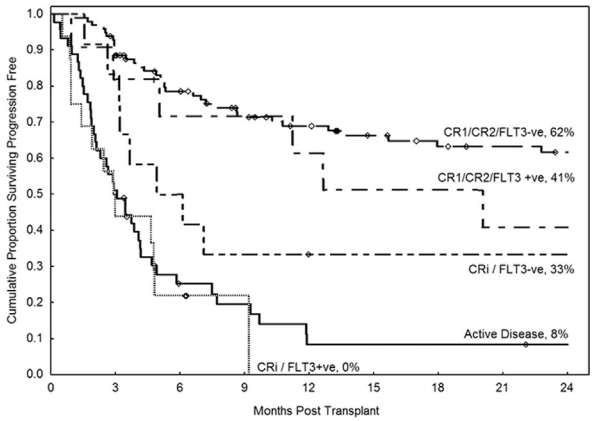

Figure 1A. Progression-free survival.

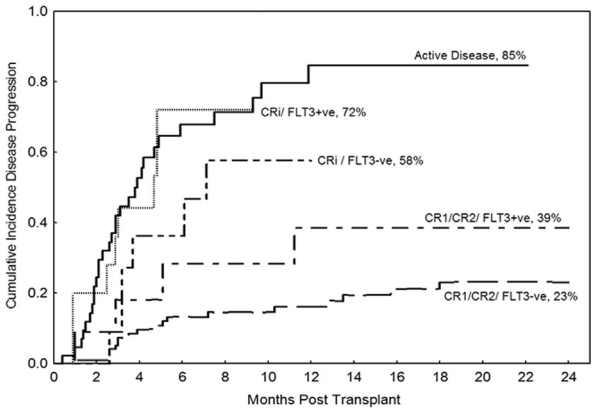

Figure 1B. Cumulative incidence of relapse for *FiT3+ve* pts by disease status at transplant.

(Table1). All donor sources were included: 63 matched sibling (MSD), 95 10/10 MUD, 11 9/10 MUD, 18 cord blood (CB), and 13 haploidentical (Haplo).

Results: The majority of pts received myeloablative conditioning (n=170; busulfan-based n=148). Disease status at AlloSCT was: CR1 (n=99), CR2 (n=20), CR with incomplete count recovery or hypoplastic marrow or CR3 (CRi; n=31), and active disease (AD; n=50). Thirty percent of pts received a FLT3 inhibitor before AlloSCT. After a median follow-up of 27 mo, the 2-year (2Y) OS and PFS rates were 43% and 41%, respectively. Relapse-related mortality was the main cause of death (68%). Remission and FLT3 status at the time of AlloSCT were significantly associated with PFS. Compared to CR1 pts, PFS was not different in CR2 [HR 1.5, p=0.3], but it was worse in CRi (HR 3.9, p<0.001) and AD pts (HR 5.9, p<0.001). The 2Y PFS was highest in CR1/2 FLT3−ve pts (62%) compared to the other groups: CR1/2 FLT3+ve (41%, p=0.3); CRi FLT3−ve (33%, p=0.01); CRi FLT3+ve (0%, p<0.001); AD (8% p<0.001) (Figures 1A, 1B). On multivariate analysis, independent predictors of worse PFS included: AD [HR 4.5, p<0.001], CRi FLT3+ve [HR 7.2, p<0.001], KPS≤80 [HR2.1, p<0.001], HCT-CI>4 [HR 1.6, p=0.05], and unrelated donor source [HR 1.6, p=0.05]. No difference in PFS was found between Haplo and MSD donor sources (HR=0.9, p=0.9). No significant association was identified by age, conditioning intensity or use of a FLT3 inhibitor prior to transplant. Post-transplant FLT3 status was available for 105 of 190 evaluable pts by day 30. Among them, 7 pts had detectable FLT3 PCR and 5/7 pts (71%) relapsed.

Conclusion: Morphologic remission and FLT3 PCR status at the time of transplant are key predictors of relapse risk in pts with FLT3+ AML. Patients who achieved a morphologic CR with an undetectable FLT3 by PCR at the time of SCT had the best outcomes and should undergo an AlloSCT without delay. Although the experience is limited, Haplo transplants had similar outcomes to MSD transplants. Prospective clinical trials with FLT3 inhibitors post-transplant are warranted at least for pts with AD or persistent FLT3+ on PCR at transplant.

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Comparing the Results of Non-TBI Hematopoietic Stem Cell Transplantation in Pediatric Patients with Acute Lymphoblastic Leukemia (ALL) with and without CNS Involvement

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Introduction: There are limited data on the impact of hematopoietic stem cell transplant (HSCT) conditioning regimen, especially without total body radiation (TBI) in pediatric patients with acute lymphoblastic leukemia (ALL) with central nervous system (CNS) involvement. The aim of this study is compare the results of HSCT using non-TBI conditioning regimen in ALL patients aged ≤18 years with or without CNS involvement.

Patients and Methods: Records of 183 patients with ALL (128 male; 55 female) with a median age of 14.1±3.7 years who had undergone HSCT were studied and classified in two groups: with and without CNS involvement. Long-term consequence of the HSCT consisting of leukemia free survival (LFS), the overall survival (OS), relapse and transplant-related mortality (TRM) was compared in the two groups.

Results: A total of 183 ALL patients (148 without CNS involvement and 35 with CNS involvement) underwent HSCT in our center using a TBI-free conditioning containing Busulfan and Cyclophosphomide. The median time of follow up was 42.1 months. Estimated probability on relapse at 4 year was 51.4% in patients with CNS involvement and 42.1% in patients without CNS involvement (p=0.588). Regarding survival analysis, 4-year OS and LFS in all patients was 44.4% (SE:2.5%) and 39.7%(SE:2.5%). In multivariate analysis there were no significant differences in OS and LFS between two groups (p=0.839, p=894) nor was there a difference in relapse probability (HR:1.20, 95%CI:0.69-2.1, p=0.513) and TRM (HR:0.44, 95%CI:0.10-1.92, p=0.286).

Conclusion: HSCT using a non TBI conditioning regimen in ALL are similar with studies using TBI containing regimens. Furthermore HSCT leads to similar clinical outcomes and long-term survival in the ALL pediatric patients with or without CNS involvement.

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Safety and Efficacy of Ibrutinib in Patients with Relapsed/Refractory (R/B) Chronic Lymphocytic Leukemia (CLL)/Small Lymphocytic Lymphoma (SLL) Who Have Undergone Prior Allogeneic Stem Cell Transplant

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Introduction: Patients with CLL who relapse after allogeneic hematopoietic stem cell transplantation (alloHCT) are difficult to treat with chemotherapy due to impaired hematopoietic reserve, infections, and concern for graft-versus-host disease (GVHD). Ibrutinib (Imbruvica®) is approved in the USA for patients with CLL or MCL who have received ≥1 prior therapy and for patients with CLL with del17p. In preclinical studies, ibrutinib reversed established chronic GVHD (cGVHD). We evaluated the safety and efficacy of ibrutinib in a subset of patients with prior alloHCT.

Methods: Data were collected for R/R patients with prior alloHCT enrolled in 1 of 4 clinical trials (PCYC-1102, PCYC-1109, PCYC-1112, and PCYC-1117). PCYC-1112 and PCYC-1117 only enrolled patients >6 months post-HCT and without GVHD. Efficacy evaluations included overall response rate (ORR; iwCLL criteria), duration of response (DOR), progression-free survival (PFS), and overall survival (OS). Safety evaluations included adverse events (AEs), including serious AEs (SAEs).

Results: 16 patients from 4 clinical trials had prior alloHCT (median age, 54.5 y; 16 patients with ECOG performance status 0 or 1; 10 patients with del17p, 3 with del11q, 12 patients with ≥4 prior therapies). Median time since the most recent HCT was 27 months (range, 8-115). Baseline neutropenia, anemia, and thrombocytopenia were reported in 31%, 25%, and 38%, respectively. Median time on ibrutinib was 18.1 months (range, 0.4-38.8), with 12 patients being treated for >12 months. At data cut-off, 11 patients were continuing treatment. Reasons for discontinuation included disease progression (n = 2), AEs (n = 2), and consent withdrawal (n = 1). Investigator-assessed responses included 2 complete responses, 9 partial responses (PRs), and 3 PRs with lymphocytosis, resulting in a best ORR of 87.5%. Median DOR, PFS, and OS were not reached at a median follow-up of 23 months. The 24-month PFS and OS rates were 77% and 75%, respectively. Treatment-emergent grade ≥3 SAEs were observed in 11 patients and included infections (n = 6) and febrile neutropenia, atrial flutter, colitis, perirenal hematoma, subdural hematoma, postprocedural hemorrhage, hypercalcemia, bone lesion, syncope, hematuria, urinary retention, and dyspnea (n = 1 each; some events reported for the same patient). The only AE leading to ibrutinib discontinuation was pneumonia (n = 2); both were fatal events. Two additional deaths occurred on study due to disease progression at 24 and 28 months.

Conclusion: Ibrutinib was well tolerated in patients who had prior alloHCT, with a safety profile similar to that observed in the overall R/R CLL population. Best ORR (87.5%) is consistent with results observed in the overall/broader population. These data support the use of ibrutinib in CLL patients with prior alloHCT, and its exploration in treatment of cGVHD is ongoing (NCT 02195869).

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Allogeneic Transplant for Acute Biphenotypic Leukemia: Characteristics and Outcome in the CIBMTR Database

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Treatment related mortality	n=80	
1-year		15 (8-24)%
2-year		17 (9-26)%
3-year		17 (9-26)%
Disease free survival	n=80	
1-year		70 (60-80)%
2-year		62 (50-72)%
3-year		60 (48-71)%
Overall survival	n=84	
1-year		78 (69-87)%
2-year		69 (59-79)%
3-year		65 (54-75)%

The 3-year overall survival was 61% (95%CI, 46-74%) in My+B group and 73% (95%CI, 54-88%) in My+T group. At three years post transplant, 75%, 48%, and 60% survival rates were observed in younger than 20, 20-40, and older than 40 years age groups, respectively. No notable differences in 3-year overall survival among those transplanted in CR1 and CR2 (64% and 69%, respectively). Patients with normal/intermediate cytogenetics (n=44) and those with bcr/abl+/poor cytogenetics (n=27) had similar 3-year survival rates: 62% and 70%, respectively. In conclusion, allogeneic transplant is a valid treatment option for patients with ABiL and should be explored in patients without significant comorbidities. A study in a larger context is planned.

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Acute biphenotypic leukemias (bearing markers of myeloid and lymphoid origin, ABiL) are rare (2-5% of all acute leukemias) and are considered puzzling both with regard to their cell of origin as well as to the optimal treatment approach. The diagnostic criteria for ABiL were revised by the World Health Organization (WHO) in 2008. In the pediatric age group, the prognosis of ABiL is reported to be intermediate between acute lymphoblastic and acute myeloid leukemia. In the adult age group, ABiL generally has an unfavorable prognosis. As far as allogeneic transplant for ABiL is concerned, only small series of cases have been published to date.

In the current study, the CIBMTR database was queried for patients with ABiL who received an allogeneic transplant between 1996 and 2013 being younger than 70 years of age (n=468). Patients with primary induction failure (n=19) and transplanted in relapse (n=27) were excluded. After detailed review of pathology, cytogenetic and flow cytometry reports, of 241 cases submitted as ABiL, those without complete data to confirm WHO criteria (n=157) were excluded. Of 84 cases with complete immunophenotyping data for review, 48 co-expressed Myeloid and B-lymphoid markers (M+B) and 28 Myeloid and T-lymphoid markers (M+T). The median age of the patients was 19 years, 56% were male, the median WBC at diagnosis was 17 000, 36% received a bone marrow, 33% a peripheral blood graft and 31% cord blood stem cells. The conditioning regimen was myeloablative in 87% and RIC/NMA in 10% of cases.

Treatment outcomes are shown below:

LYMPHOMA/MULTIPLE MYELOMA

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Positive Pre-Allogeneic Hematopoietic Cell Transplantation (alloHCT) PET Scan in Patients with Non-Hodgkin Lymphoma (NHL) Predicts Higher Risk of Relapse but Has No Impact on Survival

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