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Introduction: HAPLO-HSCT is a therapeutic option for patients with high-risk hematologic neoplasms with the advantages of quick availability, easy programation and logistics, and a committed donor. It has shown promising results in patients diagnosed with relapsed or refractory Hodgkin's lymphoma (HL) at least comparable to allogeneic transplant from siblings or unrelated donors (Burroughs LM et al. Biol Blood Marrow Transplant 2008; 14:1279-1287).
Patients and Methods: We retrospectively evaluate the results of HAPLO-HSCT with IV Busulfan (BUX) based RIC regimens (Fludarabine 30 mg/m2 x5 days (-6 to -2), Cyclophosphamide14,5 mg/kg x2 days (-6 to -5), BUX 3,2 mg/kg x 1 (BUX1) or 2 days (BUX2) on days -3 to -2) and GVHD prophylaxis based on PT-CY (50 mg/kg on days +3 and +4) and a calcineurin inhibitor plus mycophenolate from day +5 performed in GETH centers to patients diagnosed with relapsed or refractory HL.
Results: From March 2009, 43 HAPLO-HSCT have been performed in patients diagnosed with relapsed or refractory HL in 11 GETH centers. Median age was 31 years (17-53), 67% were males and all were in advanced phases of their disease, after a median of 4 prior treatment lines (2-8). Autologous HSCT was previously employed in 79%, and allogeneic HSCT in 7%. Five patients (11.5%) have received more than 2 prior transplants. Disease status at HAPLO-HSCT evaluated by PET was complete remission in 14 (32%) and persistent disease in 29 (68%). Bone marrow was employed in 11 (26%) and peripheral blood in 32 (74%), without T-cell depletion in all cases. The haploidentical donor was patient's mother (20), father (3), siblings (19) or daughter (1). The RIC regimens employed were BUX1 in 14 (32.5%) and BUX2 in 29 patients (67.5%). Median neutrophils engraftment was day +18 (13-44) and platelets >20K was day +26 (13-150). Graft failure with autologous reconstitution happened only in 1 patient (2.5%). The day +100 cumulative incidence (CI) of non-relapse mortality (NRM) was 7% (3/43) and 16% (7/43) at 1 year post-transplant. The day +100 CI of grade II-IV acute GVHD was 43%, and grade III-IV was 14.5%. Chronic GVHD CI was 26.5% at 1 year, being extensive in 6%. After a median follow-up for survivors of 13 months (3-60), the event-free survival (EFS) was 59.5% and overall survival (OS) was 84%. The 1-year CI of relapse or progression was 25%. Factors related with better 1-year EFS were CR prior to HAPLO-HSCT (93% vs 45%; p=0.017) and receiving less than 4 treatment lines prior to HAPLO-HSCT (100% vs 51.5%; p=0.018). No significant differences were seen when comparing BUX1 against BUX2 in terms of NRM, EFS or OS.
Conclusions: HAPLO-HSCT with PT-CY and BUX based RIC conditioning in relapsed or refractory HL patients, renders long-lasting remissions with acceptable toxicity and GVHD, obtaining better results in those transplanted in CR and with less than 4 treatment lines prior to HAPLO-HSCT.

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FDG-PET Interpreted By Deauville Criteria Prior to Allogeneic Transplantation Predicts Outcomes in Patients with Relapsed or Refractory Hodgkin Lymphoma

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Background: Despite high curative rates with upfront therapy, 20-30% of patients (pts) with Hodgkin lymphoma (HL) experience disease relapse. Survival is further diminished for those who fail autologous stem cell transplantation (ASCT). However a fraction of pts can still be salvaged with allogeneic hematopoietic cell transplantation (allo-HCT).
Methods: In this retrospective cohort study, we investigated the prognostic significance of FDG-PET (interpreted by both standard and Deauville criteria) among 42 consecutive patients with relapsed/refractory (RR) HL undergoing allo-HCT from 2004-2012. All FDG-PET scans were obtained within 4 weeks prior to allo-HCT. The study cohort included recipients of non-myeloablative (NMA) conditioning consisting of fludarabine 150-200 mg/m^2, cyclophosphamide 50 mg/kg and total body irradiation TBI 200 cGy followed by transplantation of umbilical cord blood (n=30; 71%), matched related (n=10; 24%) and unrelated (n=2; 5%) donor grafts.
Results: The median age was 28 years (range, 6-59); 52% were males. Median time from HL diagnosis to allo-HCT was 34.6 months (range, 13.3-228.6) and median follow up of pts was 26.5 months (range, 0.8-97.1). Pts had received a median of 4 lines (range, 3-9) of prior regimens with 83% failing ASCT; only 13 pts (31%) had achieved PET-negative (neg) CR prior to allografting. Blinded re-evaluation of all pre-HCT FDG-PET scans using Deauville 5-point scale (i.e. PET_D-pos if Deauville>3) by independent nuclear medicine physicians confirmed all pre-existing PET-neg reports, but also reclassified 4 prior PET-pos scans as PET_D-neg (kappa coefficient=0.79 [95% CI, 0.61-0.98] for PET_D vs. archived PET). All 17 PET_D-neg pts had significantly better 3-yr post-transplant OS, PFS, and relapse rate as compared to PET_D-pos pts (100% vs. 51%; 76% vs. 17%; 24% vs. 65%, respectively; all p<0.01, Figure). Three out of four reclassified PET_D-neg pts remained alive and in remission after a median follow up of 3.3 years

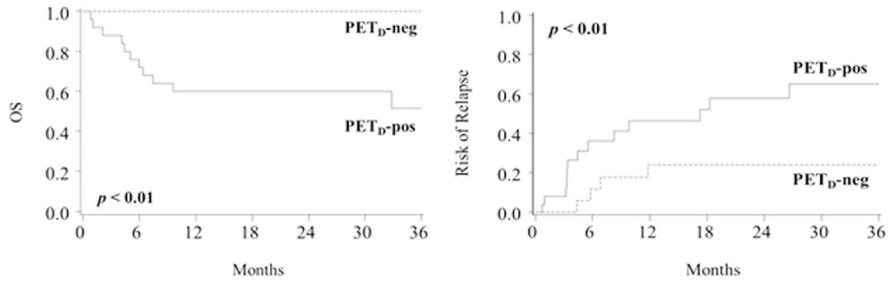

Figure. Overall survival and relapse risk according to pre-transplant FDG-PET status by Deauville criteria.

(range, 1.0-8.0). Three-year non-relapse mortality for all pts was 7% (0% for PET_D-neg vs. 12% for PET_D-pos, p=0.1). Pre-HCT PET_D-neg status remained prognostic for improved 3-yr OS (HR=0.1; 95% CI, 0-0.86) and lower relapse risk (HR=0.34; 95% CI, 0.1-1.0) in the multivariable Cox models.

Conclusions: Our study demonstrates encouraging outcomes achieved with NMA allo-HCT in heavily pre-treated pts (3-yr OS, PFS and relapse of 72% [95% CI, 54%-84%], 40% [95% CI, 24%-55%], 48% [95% CI, 29%-66%], respectively). FDG-PET imaging interpreted by Deauville criteria can serve as a powerful prognostic tool in pts with RR HL considered for NMA allo-HCT.

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Impact of Chromosomal Abnormalities in the Recipients of Allogeneic Hematopoietic Stem Cell Transplantation with Adult T-Cell Leukemia/Lymphoma

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Adult T-cell leukemia/lymphoma (ATLL), which is a human T-lymphotropic virus type I (HTLV-1)-related hematological malignancy, is known as a poorly prognostic disease even with the intensive chemotherapeutic regimens. It is known that ATLL cells normally have chromosomal abnormalities. These abnormalities were various types of numerical aberrations and complex structural abnormalities (Kamada N et al. Cancer Res. 1992). So far only one report showed that the impact of chromosome abnormalities for survival outcomes in ATLL patients who received chemotherapies (Itoyama T et al. Blood 2001). The report suggested that complex karyotype (more than 6 break points) abnormalities of 1p, 1q, 3q, 14q, and 17q was the poorly prognostic factors. Here we have analyzed the impact of chromosomal abnormalities in 26 ATLL patients who received allo-HSCT.

Seventy-two ATLL patients consecutively underwent allo-HSCT from June 2006 to March 2014 at our center. Karyotype study was performed with G-banding stain. Since patients' chromosomal study showed normal karyotype and/or bad proliferation or no information about chromosomal study, 46 of 72 patients were excluded from this study. The rest of 26 patients (13 male, 13 female) were eligible for this study.

The median age of patients was 54 years (34-65). All patients, except one lymphoma type patient, were diagnosed as acute type ATLL. Thirteen of 26 patients were performed unrelated BMT, 8 sibling-BMT, 2 sibling PBSCT and 3 UCB. Eighteen patients used MAC regimens and 8 RIC regimens. With respect to disease status at allo-HSCT, 6 patients were in CR, and 20 non-CR. Specimen materials were from 11 PB, 8 BM, 6 lymph node and 1 pleural effusion, respectively. The median number of numerally chromosomal abnormalities was 2 (0-10), and the median number of structural abnormality was 4 (0-12), respectively. The majorities of numeral abnormalities were defects of sex chromosomes (31%), -14 (24%) and -10 (17%), etc. Structurally, more than 6 break points of the chromosomal abnormalities were seen in 11 patients. Majorities of structural abnormalities were abnormalities of 14q (41%), 1q (28%), 4q (28%) and 7q (28%), etc. The median study observation days was 173 days (12-2895) and an overall survival (OS) was 40.7%. Statistically, no impacts were seen in chromosomal abnormality of more than 6 break points (HR:1.839, 95%CI: 0.67-5.04, P=0.237), abnormalities of 1q (HR: 2.035, 95%CI: 0.718-5.77, P=0.182), 3q (HR: 1.1, 95%CI: 0.312-3.88, P=0.882), 14q (HR: 1.516, 95%CI: 0.565-4.07, P=0.409) and any other chromosomal abnormalities with OS. Also, no statistical impacts were seen in these chromosomal abnormalities with relapse rate and non-relapse mortality after allo-HSCT, respectively.

Although relatively a small number study, the results newly showed that allo-HSCT would have a potential to overcome the poor prognostic risks in chromosomal abnormalities.

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A Randomized Phase III Trial of Busulfan + Melphalan Vs Melphalan Alone for Multiple Myeloma

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Background: Two recent retrospective analyses suggested that a combination of busulfan (Bu) and Mel (Bu-Mel) may be associated with a longer progression-free survival (PFS) compared to Mel alone. In this randomized phase III trial we compared the safety and efficacy of Bu-Mel vs. Mel.

Methods: Patients were randomized to either Bu-Mel or Mel using the Pocock-Simon method. In the Bu-Mel arm, Bu 130 mg/m^2 was infused daily for 4 days, followed by 2 daily doses of Mel at 70 mg/m^2. Mel 200 mg/m^2 was given as a single dose in the Mel only arm. The primary endpoint was Day 90 CR (IMWG criteria) rate.

Results: Ninety-two patients (Bu-Mel: 49, Mel: 43) were enrolled from October 2011 to August 2013. Median ages at auto-HCT were 58.4 and 58.5 years in Bu-Mel and Mel arms, respectively (p=0.75). Ten (20%) and 11 (26%) patients had high-risk chromosomal abnormalities in Bu-Mel vs. Mel, respectively (p=0.62). Forty-four (90%) and 40 (93%) patients received bortezomib-based induction therapy in the Bu-Mel and Mel, respectively (p=0.71). At the time of auto-HCT, 8/0 (16%) and 7/3 (23%) patients were in CR/near (n)CR in Bu-Mel and Mel arms, respectively (p=0.44), Grade 3 non-hematologic toxicity was seen in 41 (84%) and 20 (47%) patients in Bu-Mel and Mel, respectively (p=0.0003). There was no 100-day TRM in either arm. At day 90, 8 (16%) and 15 (35%) patients had achieved a CR (p=0.05), and 13 (27%) and 20 (47%) patients had achieved a CR + nCR (p=0.05) in Bu-Mel and Mel, respectively. At day 90, 7/7 (100%) evaluable patients with CR in Bu-Mel and 14/15 (93%) evaluable patients with CR in Mel also achieved a multiparametric flow cytometric (MFC) CR (p=1.00). Thirty-nine (80%) patients in Bu-Mel and 37 (86%) in Mel received maintenance therapy after day 90 (p=0.58). Median follow up was 15.7 months (range 0.8 – 28.7). No second primary malignancies have been seen in either arm so far. Bayesian multivariable lognormal survival time regression showed significantly better PFS in the Bu-Mel arm (posterior probability of the treatment effect >0.9963, 95% credible interval 0.21-1.70, Figure 1). Median PFS from Day 90 was not reached in the Bu-Mel arm. Median PFS from Day 90 for Mel only was 20 months. One-year survival rates in the Bu-Mel vs Mel arms were 91% (95% CI: 75-97%) and 77% (95% CI: 58-88%),