source: 119 PB/31 BM) were retrospectively analyzed. Their diagnoses were 90 acute leukemia, 30 CML, 6 MDS and 24 other diseases. Multiplex PCR method was performed to amplify 16 STR loci (D3S1358, HUMvWA, D16S539, D2S1338, Amelogenin, D8S1179, D21S11, D18S51, D19S433, THO1, FGA, D7S820, CSF1PO, D13S317, TPOX, D5S818) (ABI Prism 3130). The loci examined were classified as complete matched (CM), partially matched (PM), and fully mismatched (FMM) between donors and recipients.

Results: The loci of D13S317, D18S51 and D2S1338 were the most informative, while the loci of TPOX and CSF1PO were the least. The incidence of acute GvHD was 46.7% (n = 69), which acute severe GvHD (grII-IV) was observed in only 31 patients. Chronic GvHD was developed in 63.4% patients. The incidence of grII-IV GvHD was higher in patient with CM in TPOX loci (p = 0.02). Chronic GvHD was more frequent in the patients with PM in D5S818 loci than those with CM or MM (p = 0.016). While PM D21S11 increased TRM, MM or PM in D5S818 loci decreased the TRM. In our cohort analysis, 2-year probability of disease-free survival(DFS) and overall survival(OS) were 58.1 ± 5.5% and 67.5 ± 4.4%, respectively. The CM in D21D11 locus (p = 0.07) and PM in D5S818 locus (p = 0.009) prolonged the probability of DFS. In multivariate analysis, these loci had an impact on DFS (p = 0.055 ve p = 0.005). D19S433 and D5S818 loci had an effect on the OS. We repeated similar analyses into two groups, mismatched (MM) group, which FMM and PM was accepted as a whole group or CM group, while the incidence of grII-IV GvHD was higher in patients with CM of D18S51 and TPOX loci, the chronic GvHD was more frequent in those with CM D5S820 loci. Similar as the first analyses MM in D21S11 and CM in D5S818 affected both TRM and DFS. Besides, MM in FGA locus decreased TRM and prolonged DFS. The impact of D5S818 on the OS also continued, additionally D19S433 had minimal effect on the OS. In conclusion, some disparities of STR loci might affect the transplantation outcome; however, these results should be analyzed together with other co-variates and on multicenter basis.

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AN EVALUATION OF DNA METHYLATION CHANGES IN A PHASE I CLINICAL TRIAL OF LOW-DOSE 5-AZACITIDINE (AZA) GIVEN AS MAINTENANCE THERAPY AFTER ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION (HSCT)

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DNA methylation of CpG Islands is a frequently found epigenetic alteration in AML and MDS that leads to deranged gene activity. Inhibition of the enzyme DNA methyltransferase is associated with hypomethylation, and possibly, restoration of normal function to genes critical for differentiation and proliferation. AZA is a DNA hypomethylating agent that may induce increased tumor immunogenicity, potentially magnifying the GVL effect. Lower doses are likely to be better tolerated after HSCT and to be effective inducers of hypomethylation. We hypothesized that AZA after HSCT will lower relapse rates, and designed a phase I clinical trial that also uses a molecular surrogate endpoint for dose finding. Here we describe methylation changes in patients so treated.

Pts with AML or high-risk MDS not in first remission (CR) are eligible. Three doses of AZA were studied: 8, 16, and 24 mg/m^2 daily × 5 starting on day + 42. DNA was extracted from mononuclear cells of 22 pts that received AZA. The methylation status of long interspersed nuclear elements (LINE) was analyzed by pyrosequencing as a surrogate marker of global DNA methylation before and after AZA administration. Gene specific methylation changes were studied using a methylated CpG island amplification(MCA)/CpG array.

Median age was 57 years. Diagnoses were MDS (n = 4) and AML(n = 18). Disease status at HSCT: CR, 18% (n = 4), and active disease, 82%(n = 18). LINE methylation results were as follows: baseline: 44.51%; on cycle 1, 5th day of AZA: 24 mg/m^2 = 43.58%; 16 mg/m^2: 36.93%; 8 mg/m^2: 42.86%. Two pts have relapsed while on AZA. There has been no major drug-related toxicity and no increase in GVHD incidence. Analysis of gene-specific methylation is ongoing.

AZA in doses up to 24 mg/m^2 can be safely administered early after HSCT. Given the lack of toxicity and low levels of changes in DNA methylation observed, we are currently investigating higher doses.

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ROLE OF EXTENSIVE SPLENOMEGALY IN PATIENTS WITH MYELOFIBROSIS UNDERGOING A REDUCED INTENSITY ALLOGENEIC STEM CELL TRANSPLANT

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Allogeneic stem cell transplantation has been shown to restore normal hematopoiesis in patients with intermediate or high risk primary myelofibrosis (PMF) or myelofibrosis preceeded by polycythemia vera or essential thrombocythemia. However, in patients with PMF and extensive splenomegaly it is not clear whether transplant is associated with an unacceptable risk or if splenectomy should be performed prior to transplant. In this study, ten consecutive patients with myelofibrosis who were not splenectomized received an allogeneic hematopoietic stem cell transplantation (HSCT) from related or unrelated donors and were periodically monitored by ultrasound or CT scan for 12 months after transplant to assess the kinetics of the reduction of splenomegaly. These findings were correlated with the time to resolution of marrow fibrosis, time to engraftment and clinical outcome. Over a 12 month period a progressive reduction in spleen size was observed in all the patients and paralleled the reduction in marrow fibrosis. Of 10 patients, 5 with a splenic longitudinal diameter >30 cm showed a more prolonged time to engraftment ANC > 0.5 × 10^9/L (d 19 ± 5 vs 13 ± 2, p = 0.05) and platelet > 20 × 10^9/L (d 75 ± 104 vs 11 ± 2, p = 0.06). However, of the 5 patients with more extensive splenomegaly only 2 experienced delayed engraftment of platelets (d 77 and 256, respectively). Full donor chimerism was observed in all patients within 60 days after transplantation regardless of the size of the spleen. At a median follow-up of 51 months (range: 2–81) all the patients are alive but 1 who died of a TTP like syndrome 2 months after transplant and had a small spleen at the time of transplant. A clinical CR has been documented in 7 patients and 2 have achieved clinical improvement according to to the criteria established by the International Working Group for Myelofibrosis Research and Treatment (IWG-MRT). These findings suggest that allogeneic HSCT with RIC regimen can be safely performed in patients with extensive splenomegaly. Although in these patients the time to achieve a full hematopoietic engraftment may be prolonged, the significant risk of morbidity and mortality associated with splenectomy may be avoided.

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EFFECT OF SUBSTITUTING FLUDARABINE AND THYMOGLOBULIN FOR CYCLOPHOSPHAMIDE IN BUSULFAN-BASED CONDITIONING REGIMENS ON T-CELL CHIMERISM AND OUTCOMES AFTER ALLOGENEIC HEMATOPOIETIC CELL TRANSPLANTATION (HCT)

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Substitution of cyclophosphamide by agents such as fludarabine and thymoglobulin in busulfan-based conditioning regimens has been used to reduce complications after allogeneic HCT. We performed a retrospective analysis of outcomes among 348 patients