Results: The mean number of infused CD34+ve cells was 6.7x 10^6 /kg recipient weight. All patients engrafted rapidly at a median rate of 15 days for neutrophils and 16 days for platelets. Although the total incidence of cGVHD was 43%, only 17% had extensive cGVHD, and the remaining 26% had the limited form which was very well controlled under a small-dose of immuno-suppressive therapy. By sub-group analysis, we found that the vast majority of patients with extensive cGVHD received the initial lower dose of Flu (75mg/m2), and half of them were >30 years old. Since then, we've standardized the dose to be 120mg/m2. At a follow up period of up to 9 years (median 5.9 years), both DFS & OS were 79.2%.
Conclusion: Allografting SAA patients with PBSCs, using the Flu-Cy regimen has a significantly lower cost, with excellent tolerability, and promising outcome regarding engraftment, DFS & OS. The incidence of cGVHD can be considered acceptable, putting in mind the higher patients' age and the initial lower dose of Flu that we've used. However, this approach definitely needs a larger cohort of patients to be randomly compared to the standard Cy-ATG regimen with the use of BM cells.

357

Pre-Transplant Therapy for Patients with Myelodysplastic Syndrome and Post-Transplant Outcome

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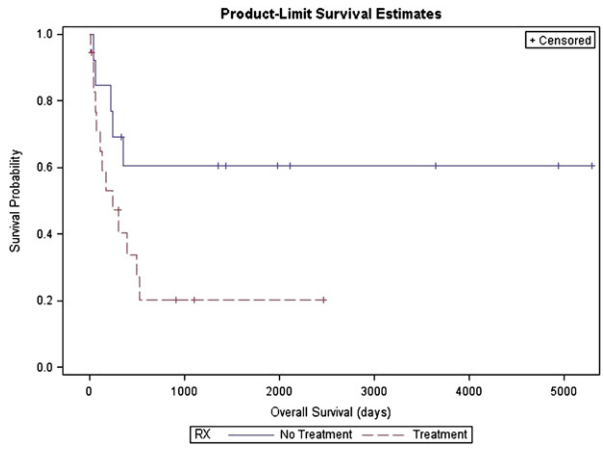
Allogeneic hematopoietic cell transplantation (Allo-HSCT) has proven to have curative potential for myelodysplastic syndrome (MDS). However, relapse post HSCT continues to be a problem. Pre-HSCT cytoreduction with either intensive chemotherapy or hypomethylating agents has been used with limited data on pre- or post-HSCT outcomes. In this report, we evaluated the impact of pre-transplant therapy on post-HSCT outcomes including overall survival (OS) and Progression Free Survival (PFS).
Methods: We retrospectively reviewed 31 patients who underwent allo-HSCT for MDS in our center between 1997 and 2012. Primary objective was to study the impact of therapy pre-HSCT on HSCT outcome. Demographics, disease-related and transplant-related variables were collected. PFS was defined as the time from HSCT to the time of progression, death or last contact whichever occurred first. OS was defined as the time from HSCT to the time of death or last contact. The distributions of PFS and OS were estimated by the Kaplan-Meier method. The log-rank test was used to compare the survival distributions between the two groups. Regression analyses for survival data used Cox proportional hazards model.
Results: Median age at HSCT was 58 years. Median time from diagnosis to HSCT was 145 days. Of the 31 patients, 38.8% had poor cytogenetic abnormalities. Conditioning regimen used was high-dose in 71% or a reduced-intensity in 29%. 18/31 patients (58.1%) received therapy before HSCT. Intensive therapy with cytarabine was used in 3 patients while non-intensive therapy, with hypomethylating agents, median of 4 cycles, were used in 11 patients, Thalidomide or Lenalidomide in 3 patients and hydroxyurea in 1. 13/31 (41.9%) did not get any therapy prior to HSCT.

On univariate analysis, the treatment prior to HSCT had adverse impact on PFS and OS (HR=2.8, P = .0404 and HR=2.8, P = .0387 respectively). In multivariate models, treatment prior to HSCT still emerged as a significant predictor of poor PFS and OS (HR=6.6, P= .0070 and HR=8.1,P = .0037 respectively) after adjusting for age, gender and WHO classification-based Prognostic Scoring System. There was no statistical significant difference in the change in percentage of blasts at diagnosis and just before transplant for those who received therapy compared to those who did not (P = .5496).
Conclusion: In this small cohort from a single center, the results are not in favor of MDS patients receiving therapy prior to HSCT. Prospective study with larger cohort should be conducted to address this issue and taking into consideration disease characteristics in patients who may and may not benefit from pre-transplant therapy. As recently published approximately 85% of bone marrow cells are clonal in MDS regardless of blast count (Walter et al. NEJM 2012) which may explain our result of no difference in blast percentage before or after therapy and should not be used as a surrogate marker.



358

The Serum Galactomannan Index Predicts Mortality in Allogeneic Hematopoietic Stem Cell Transplant Recipients with Probable Pulmonary Invasive Aspergillosis

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Background: Invasive pulmonary aspergillosis (IPA) remains a significant cause of infectious morbidity and mortality in hematopoietic cell transplant (HCT) recipients. The serum and BAL galactomannan (GM) index are widely used mycologic criteria for the diagnosis of IPA; however, their prognostic value at the time of diagnosis is poorly defined. It remains unclear whether IPA patients with a positive serum or BAL GM index have different clinical outcomes than IPA patients with a negative GM index in the corresponding compartment, and whether higher GM index cut-off levels correlate with poor outcome. In this study, we examined the prognostic value of quantitative aspects of both the serum and BAL GM index at the time of IPA diagnosis.
Methods: We retrospectively analyzed a cohort of 100 adult patients with probable IPA (per 2008 revised EORTC criteria) diagnosed in 2004-2010 within 100 days after a first allogeneic HCT. All subjects had a chest CT, a serum GM, and a BAL GM index performed at the time of IPA diagnosis. We

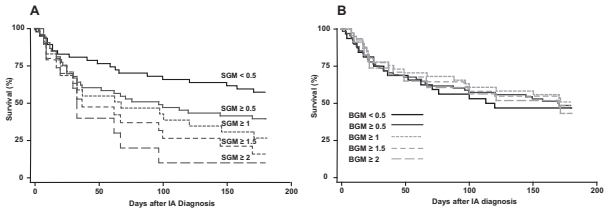

Figure 1. Kaplan Meier survival curve of different magnitudes of serum GM indices (A), and BAL GM indices (B)

evaluated the impact of different GM cut-off levels in serum and BAL on mortality. Kaplan Meier curves were used to estimate survival, and Cox proportional hazards models were used to evaluate univariate and adjusted hazards ratios for 180 day all-cause mortality associated with different serum and BAL GM index cutoff values.

Results: A diagnosis of probable IPA was made by a positive serum GM index (≥ 0.5) alone in 32 patients and a positive BAL GM index (≥ 0.5) alone in 47 patients. In 21 patients, the serum and BAL GM indices were both positive. Overall mortality in all patients was 52% at 180 days. Patients with a positive serum GM index at the time of IPA diagnosis had an increased mortality (60.4%; $n = 53$) compared to patients with a negative serum GM index (42.6%; $n = 47$). In contrast, a positive BAL GM index had no effect on mortality (Figure 1A,B). In addition, the magnitude of the serum GM index was associated with enhanced mortality. When compared to a serum GM index of ≤ 0.5, increasing values of serum GM were associated with an increased HR of 180 day mortality (serum GM ≥ 1: HR = 2.18 (1.15-4.15); serum GM ≥ 1.5: HR = 2.97 (1.53-5.81); serum GM ≥ 2: HR = 3.68 (1.63-8.30)). This result was confirmed in a multivariate analysis that adjusted for acute GVHD, sex, underlying hematologic disease severity, and elevated creatinine. No association was seen with increasing magnitudes of BAL GM indices.

Conclusions: This study shows an increased HR for mortality with increasing cutoffs of serum GM indices, with no corresponding increase in HR with increasing BAL GM indices. We propose that the initial serum GM index value at the time of IPA diagnosis represents both an important prognostic indicator and a valuable covariate in future analyses on outcomes in HCT recipients.

359

Impact of CD 34 Cell Dose and Conditioning Regimens on Donor T-Cell and Myeloid Chimerism After an Alemtuzumab-Based in-Vivo T-Cell Depleted Allogeneic Stem Cell Transplant (SCT)

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Background: Phase II studies suggested that pts who received an in-vivo T-cell depleted (TCD) alloSCT with Alemtuzumab (AL) tended to have less aGVHD.However, the utility of this approach is limited by increased incidence of mixed chimerism which is associated with increased disease recurrence and often require DLI.

Hypothesis: We hypothesize that sub-optimal CD 34 +ve cell dose contribute to mixed chimerism after an in-vivo TCD alloSCT using AL. By identifing an optimal CD 34 +ve cell dose; an in-vivo TCD protocol could maintain the benefit of lowering the incidences of GVHD and minimize mixed chimerism. We also evaluate other patient & treatment characteristics that may contribute to mixed chimerism.

Method: We conducted a retrospective study to evaluate the impact of CD 34 +ve cell dose and patient and treatment characteristics on T-cell and Myeloid chimerism after an in-vivo TCD alloSCT. Between 5/11 & 5/12, 32 consecutive pts underwent an in-vivo TCD alloSCT. F/M: 18/14. The diagnosis included 21 AML/MDS, 4 NHL, 3 MDS & 7 others. Conditioning regimens consisted of Fludarabine/Melphalan:22, Fludarabine/Busulfan: 7 and others in 3. Upon achievement of engraftment, we monitor engraftment by Short tandem repeat monthly with T-cell and Myeloid subsets analysis. We utilize of AL for in-vivo TCD (20 MRD: 30 mg on Day -1; 12 MUD: 30 mg daily on Day -2 & Day -1). All patients also received cyclosporine.

Results: Pts received a median of 4.96 x 10e6 per kg CD 34 positive cells (range 2.45 – 27.22). 30/32 pts achieved neutrophils engraftment except 1 died shortly after SCT from CHF & 1 experienced primary graft failure with day 30 STR showing only 3% donor T-cell chimerism. On Day 30 post-SCT, all evaluable pts had predominately donor T-cell (median 99%; 22/31 (71%) $\geq$ 99%; range 82 to $>$ 99%) and Myeloid Chimerism (28/31 (90%) $\geq$ 99%. 25 pts survived beyond Day 90 and have engraftment data available for analysis . Between Days 90 & 120 analysis, most pts maintain predominant donor myeloid chimerism ($>$ 95%; median 99%); only 11/25 (44%) had maintained $\geq$ 91% donor T-cell chimerism. 7/25 (28%) and 7/25 (28%) had 71-90 % and $\leq$ 70% donor T-cell chimerism respectively. CD 34 +ve Cell dose, disease type, disease status, prior treatment, age, sources of stem cells (MRD vs MUD) and conditioning regimen did not predict for mixed chimerism. While 43% of the patients received Melphalan/Fludarabine; 60% of the patients received a busulfan/fludarbine had donor T-cell chimerism dropped below 80% between day 90-120. Five pts (17%) developed acute GVHD with only 1 (4%) Grade IV aGVHD.

Conclusion: 1. Mixed chimerism is common after in-vivo TCD alloSCT; 2. CD 34 Cell dose, disease type, prior treatment, age, sources of stem cells and conditioning regimen did not predict for mixed chimerism & 3.The high incidences of significant mixed chimerism ($<$ 80%) on day 90 in pts received Bu/Flu is of concerns that warrant close monitoring in future studies.

360

Hematopoietic Stem Cell Transplantation in Myelofibrosis: A Comparison Between Myeloablative and Reduced Intensity Conditioning

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