data also suggest that permanent alopecia can be seen with non-busulfan containing regimens. One important observation was patients usually accept permanent alopecia as the price for the cure and find ways to hide it unless they are questioned about. This may be responsible for underestimation of the true incidence of permanent alopecia after HDC. Our findings may also have medico legal and psychosocial implications that need to be taken into consideration when consenting patients for HSCT.

134

NO EVIDENCE FOR INCREASED TRANSPLANT RELATED TOXICITY IN PH+ CHRONIC MYELOGENOUS LEUKEMIA (CML) AND ACUTE LYMPHOBLASTIC LEUKEMIA (ALL) WITH PRIOR EXPOSURE TO DASATINIB

Leiba, M.[1], Shimoni, A.[1], Guilhot, F.[2], Martineau, G.[2], Renaud, M.[2], Francois, S.[2], Hardan, I.[1], Nagler, A.[1] [1]Chaim Sheba Medical Center, Tel Hashomer, Israel; [2]Oncology Hematology and Cell Therapy CHU La Miletrie, Poitiers, France.

SCT is frequently used as salvage or curative therapy in patients (pts) with advanced CML or Ph+ ALL previously treated with Imatinib. While one study showed higher incidence of GVHD, VOD and TRM, most studies have demonstrated that Imatinib therapy prior to SCT does not adversely affect SCT outcome. Dasatinib is a SRC/ABL kinase inhibitor currently being used in pts with Imatinib-resistant. Most of these pts will eventually undergo SCT, raising the question of whether Dasatinib therapy may adversely affect SCT outcome. We report eight pts: CML – 6 (CP1-4, low sokal score –3, high sokal score –1, CP2-1, AP-1) and Ph+ ALL –2 who received Dasatinib prior to alloSCT (n=7) or autoSCT (n=1). Donors were matched siblings –4 or unrelated –2 or mismatch related (haploSCT) –1. 5 were male and 3 female with a median age of 46.5 (16-56) years. First line therapies included Hydroxyurea & Interferon or chemotherapy followed by Imatinib for the CP CML and advanced CML/Ph+ ALL pts, respectively. All pts subsequently received Dasatinib 70mg x 2/day due to resistance to Imatinib, resulting in complete hematological response in all, as well as complete (n=5) or partial cytogenetic response (CyR) (n=2) prior to SCT. One pt did not achieve CyR prior to SCT. The pts were conditioned with either a myeloablative (n=5) or a reduced intensity protocol (n=3). GVHD prophylaxis consisted of CSA and MTX (n=6) or complete T-cell depletion (n=1). Pts received a mobilized peripheral blood stem cell graft with 11.4–19.8 $\times$ 10^6 CD34+ cells/ kg. The pt who underwent autoSCT was successfully mobilized (2 apheresis cycles yielding 5.7 $\times$ 10^6 CD34+/kg). Dasatinib was stopped 6 days before mobilization. All pts engrafted reaching ANC $>$ 0.5×10^9/L on day +14 (11-21) and PLT $>20\times10^9$/L on day +12.5 (11-17). Chimerism was 99.4 – 100%. Transplant related toxicities were minimal. Only 1 pt developed severe mucositis. No pt developed hyperbilirubinemia or VOD. There was no increased risk of infections. Acute GVHD (Gr II) was observed in only 1 pt, while 2 developed extensive chronic GVHD. With a median followup of 8.5 (2-13) months, 6 pts are alive, 5 in CR, while 2 died of disease progression. We may conclude that in pts undergoing SCT following Dasatinib there is no evidence that Dasatinib adversely affect post SCT outcome as no increased transplant related organ toxicities, non-engraftment, GVHD or infections were observed. Larger studies are obviously indicated to confirm our preliminary results.

135

ONCE-DAILY ADMINISTRATION OF MODIFIED-RELEASE TACROLIMUS CAPSULE (MR) FOR THE PROPHYLAXIS OF GRAFT-VERSUS-HOST-DISEASE (GVHD) AFTER UNRELATED DONOR BONE MARROW TRANSPLANTATION (BMT)

Okamoto, S.[1], Gondo, H.[2], Imamura, M.[3], Kodera, Y.[4] [1]Keio University Hospital, Tokyo, Japan; [2]Saga Prefectural Hospital Koseikan, Saga, Japan; [3]Hokkaido University Hospital, Sapporo, Japan; [4]Japanese Red Cross Nagoya First Hospital, Nagoya, Japan.

The safety and efficacy profiles of tacrolimus capsule, twice-daily (BID) administration of Prograf® (PRG), in patients received allogeneic stem cell transplantation are well defined. MR is an extended-release formulation of tacrolimus which is administered once-daily (QD). QD dosing regimen could improve compliance and convenience while maintaining the potency of immune suppression. Studies in renal and liver transplantation indicated that the MR formulation given QD and PRG administered BID showed a similar exposure ($AUC_{0\text{-}24}$) and correlation between $AUC_{0\text{-}24}$ and C_{min}.

We here report the efficacy, safety and pharmacokinetics (PK) of MR in patients who underwent allogeneic BMT from HLA-matched unrelated donors. PRG was started as continuous i.v. at a dose of 0.03mg/kg from 1 to 3 days before BMT, MTX was also given on days 1, 3 and 6. The infusion of tacrolimus was switched to QD oral administration of MR 38.0 days (24-87 days) after BMT. The blood sampling for PK was collected 8-60 days after administration of MR. A total of 20 patients received BMT, and 15 of them received MR. The diagnosis included AML (3), CML(3), MDS (3), ML (2), ATL (1), CNL (1), Waldenstrom's Macroglobulinemia (1) and Myelofibrosis (1). All 15 patients received TBI, together with cyclophosphamide (13), or cytarabine (1), or melphalan (1) as conditioning. Acute GVHD was graded according to the modified Gluksberg grading system.

Before day 100 post-BMT, 7 of 15 (46.7%) patients developed grade II-IV acute GVHD, and 3 (20.0%) developed grade III-IV acute GVHD. Three patients developed grade II-IV acute GVHD (2 grade II and 1 grade III) after conversion to MR. At one year post-BMT, cumulative incidence of chronic GVHD was 51.0%, and the cumulative overall survival rate was 93.3%. All adverse drug reactions observed during the administration of MR were already known as those of PRG. PK profile of MR was evaluated in 13 patients. $AUC_{0\text{-}24}$ and C_{min} were 217.56±100.01 ng.h/mL and 6.03±2.65 ng/mL, respectively. Co-efficiency between $AUC_{0\text{-}24}$ and C_{min} was highly correlated (r=0.8679) as studies in renal and liver transplantation.

These results suggest that QD administration of MR is effective as an alternative to BID administration of PRG capsule for the prophylaxis of acute and chronic GVHD in unrelated donor BMT. Ongoing studies are aiming to evaluate the relapse and survival rates over one year in BMT as well as the long-term benefits of MR in multiple types of organ transplantation.

136

LATE-ONSET NONINFECTIOUS PULMONARY COMPLICATIONS AFTER ALLOGENEIC BONE MARROW TRANSPLANTATION IN BRAZIL: INCIDENCE, CLINICAL FEATURES AND INFLUENCE OF TUBERCULOSIS

Fermino, F.A.[1], Oliveira, J.S.R.[1,2] [1]Universidade Federal de Sao Paulo, Sao Paulo, Brazil; [2]Hospital Santa Marcelina, São Paulo, Brazil.

Despite advances in the management of bone marrow transplantation (BMT), pulmonary complications have been developed in 40-60% of patients, influencing morbidity and mortalitality. Late-onset noninfectious pulmonary complications (LONIPC) include a number of different entities and an association with chronic graft-versus-host disease (GVHD) has been noted for almost all of them. Among 253 patients who underwent allogeneic BMT at Universidade Federal de São Paulo and Hospital Santa Marcelina, 159 of them survived at least 6 months, 16 (10%) fulfilled the diagnostic criteria of LONIPC. There was a significant association between pulmonary infectious ($p=0,01$), acute and chronic GVHD and the development of LONIPC ($p=0,038$ and $0,043$, respectively). The frequency of Tuberculosis (Tb) among our patients was 3,7%. Two patients with previous Tb fulfilled criteria for LONIPC. We believe that the pulmonary symptoms and lung function tests presented by our patients can be attributed to Tb sequelae. However, it was not possible to exclude LONIPC since biopsy was not performed. On the other hand, it is necessary to determine if in Brazil and other endemic areas of Tb, the pulmonary biopsy can provide the correct diagnosis in similar cases. In view of theses findings, we conclude that the LONIPC is an important complication after allogenic BMT, chronic and acute GVHD is significantly associated with this complication and Tb sequelae can be a differential diagnosis with LONIPC mainly in endemic areas. These results have implications for the care of pacients who developed respiratory symptoms after BMT.