Prolonged Survival Can be Achieved By Primary Plasma Cell Leukemia and Multiply-Refractory Multiple Myeloma Patients with Responding Disease Prior to Melphalan/Total Body Irradiation-Conditioned Myeloablative Allogeneic Hematopoietic Cell Transplantation

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Background: Primary plasma cell leukemia (pPCL) and multiply-refractory multiple myeloma (MM) are plasma cell dyscrasias with a median survival of <1 year without aggressive treatment. Prolonged remission can be achieved following allogeneic hematopoietic cell transplantation (alloHCT) in this population, although survival may be compromised by treatment-related mortality (TRM). With the intention of providing long-term disease control, we have offered a myeloablative conditioning regimen containing melphalan 100 mg/m² and 9 Gy of total body irradiation (MEL100/TBI9) followed by alloHCT to patients with these diseases.

Methods: Seven patients with pPCL and 2 patients with multiply-refractory MM underwent MEL100/TBI9 alloHCT at the University of Pennsylvania between June 2009 and January 2013. MEL was given as a single infusion of 100 mg/m² on day -3 and TBI as 150 cGy twice daily on days -2, -1 and 0. Palifermin was given on days -4 (60 mg/kg) and 0 (180 mg/kg) for prevention of mucositis. Methotrexate and tacrolimus were used for graft-versus-host-disease (GVHD) prophylaxis. Therapies pre- and post-alloHCT were given at the discretion of the treating physician.

Results: The median number of therapies pre-alloHCT was 3.5 (range 1-10) including bortezomib in 7 patients and high-dose melphalan in 2 patients. Karnofsky Performance Status pre-alloHCT was <80 in 4 patients. The median age at alloHCT was 48 years (range 42-57). The donor source was a HLA-matched sibling in 5 patients and a 10/10 HLA-matched unrelated donor in 4 patients. Disease response pre-alloHCT was very good partial response (VGPR) or better in 4 patients, partial response (PR) for 3 patients and stable disease/progressive disease (SD/PD) for 2 patients. Lenalidomide maintenance was given post-alloHCT to 3 patients. Acute GVHD of the intestine (3 patients; grade II, III and unknown) and skin (1 patient; grade II) as well as chronic GVHD of the oral cavity (2 patients; mild, moderate), skin (1 patient; moderate) and eyes (1 patient; moderate) was observed. With a median length of follow-up of 31.6 months post-alloHCT (range 6.7-49.9) for patients surviving >100 days (n=6), the median event-free survival (EFS) was 28.2 months and the median overall survival (OS) was not yet reached. As shown in Figure I, patients achieving VGPR or better prior to alloHCT experienced prolonged EFS and OS. TRM was experienced by 3 patients (2 with SD/PD and 1 with PR pre-alloHCT), with all deaths occurring within approximately 30 days post-alloHCT due to sepsis.

Conclusions: In pPCL and multiply-refractory MM patients demonstrating response to prior therapy, consolidation with MEL100/TBI9 alloHCT can result in long-term survival without severe toxicity. MEL100/TBI9 should be analyzed prospectively either alone or in comparison to alternative alloHCT conditioning regimens in this patient population.

Outcomes of Relapse of AML Post Allogeneic Transplantation in the Era of Hypomethylating Agents: An Analysis of 162 Allogeneic Transplants from a Single Center

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Allogeneic hematopoietic cell transplantation (allo-HCT) can be curative in many patients with intermediate and high risk AML. However, patients with AML who relapse post allo-HCT typically have a dismal prognosis with limited therapeutic options. The activity and minimal toxicity associated with hypomethylating agents (hypomeths) makes them potentially useful in the management of post allo-HCT relapsed AML patients. However, their use in this setting has not been...
Variable Success Rates of Haplo-Cord Transplants in High Risk Patients: A Minimum Serotherapy Exposure Is a Prerequisite for Sustainable Engrafting

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Combining a CD34+ selected haplo-graft with a full graft cord blood (CB) unit is a cell support procedure that can make single CB available as a donor source to a larger proportion of patients. Early haplo-donor cell engraftment may serve as a myeloid bridge until sustainable CB-engraftment. In addition it has been hypothesized that haplo-derived innate anti-tumor activity (e.g. NK- / γδ-T-cells through other cell selection techniques) plus CB could be a platform for multi-modal anti-tumor activity in high-risk malignancies. The latter in the context of omitting serotherapy. The impact of serotherapy-exposure on the success of "haplo-myeloid bridge to CB engraftment" is however unknown.

Methods: Since 2009 in the UMC Utrecht 2 haplo-CB protocols were open; 1) active infection and/or known difficult engraftment without a conventional donor available: CB + CD34+selected Haplo-id donor (5milj CD34+/kg); 2) Poor risk malignancies, not eligible to other treatment protocols: CB + CD19/CD52CR depleted haplo-id donor (5milj CD34+/kg). Conditioning regimens: 1st HCT busulfan (targeted cumulative exposure of 90mg*h/L)+ Fludarabine (Flu)+ Tymglobulin (ATG) in protocol 1 or Flu/Cyclophosphamide (Cy)/TBI as RIC-alternative; 2nd HCT Treosulfan, Flu+Campath (TreoFluCamp: protocol 1). G-CSF was given from day +7. Patients received GVHD-profilaxis with CsA and pred 1 mg/kg. Active-ATG levels and Campath levels were measured as described previously (Jol et al. BMT 2012). The association of serotherapy-exposure for the endpoints overall survival (OS), non-relapse mortality (NRM), neutrophil recovery and graft failure (GF) was analyzed. GF was defined as either "early loss of Haplo and no engraftment of the CB" or secondary loss of both grafts. Logrank testing was used in statistical analyses.

Results: 22 patients were included (18 protocol 1; 4 protocol 2); 20 patients received FluBu (15 ATG, 1 Campath), 1 TreoFluCamp and 1 FluCyTBI. Median nucleated cell dose was 4.1 x 10e7/kg (2.0-20.0). There was a cumulative incidence (CI) of GF was however 43 ±11%. The median "active ATG-AUC" (area under the curve) was 17 IU*day/L (1 pat no Campath FluCamp and 1 FluCyTBI. Median nucleated cell dose was 4.1 x 10e7/kg (2.0-20.0). There was a cumulative incidence (CI) of GF was however 43 ±11%. The median "active ATG-AUC" (area under the curve) was 17 IU*day/L (1 pat no Campath FluCamp and 1 FluCyTBI. Median nucleated cell dose was 4.1 x 10e7/kg (2.0-20.0). There was a cumulative incidence (CI) of GF was however 43 ±11%. The median "active ATG-AUC" (area under the curve) was 17 IU*day/L (1 pat no Campath FluCamp and 1 FluCyTBI. Median nucleated cell dose was 4.1 x 10e7/kg (2.0-20.0). There was a cumulative incidence (CI) of GF was however 43 ±11%. The median "active ATG-AUC" (area under the curve) was 17 IU*day/L (1 pat no Campath FluCamp and 1 FluCyTBI. Median nucleated cell dose was 4.1 x 10e7/kg (2.0-20.0). There was a cumulative incidence (CI) of GF was however 43 ±11%. The median "active ATG-AUC" (area under the curve) was 17 IU*day/L (1 pat no Campath FluCamp and 1 FluCyTBI. Median nucleated cell dose was 4.1 x 10e7/kg (2.0-20.0). There was a cumulative incidence (CI) of GF was however 43 ±11%. The median "active ATG-AUC" (area under the curve) was 17 IU*day/L (1 pat no Campath FluCamp and 1 FluCyTBI. Median nucleated cell dose was 4.1 x 10e7/kg (2.0-20.0). There was a cumulative incidence (CI) of GF was however 43 ±11%. The median "active ATG-AUC" (area under the curve) was 17 IU*day/L (1 pat no Campath FluCamp and 1 FluCyTBI. Median nucleated cell dose was 4.1 x 10e7/kg (2.0-20.0). There was a cumulative incidence (CI) of GF was however 43 ±11%. The median "active ATG-AUC" (area under the curve) was 17 IU*day/L (1 pat no Campath FluCamp and 1 FluCyTBI. Median nucleated cell dose was 4.1 x 10e7/kg (2.0-20.0). There was a cumulative incidence (CI) of GF was however 43 ±11%. The median "active ATG-AUC" (area under the curve) was 17 IU*day/L (1 pat no Campath FluCamp and 1 FluCyTBI. Median nucleated cell dose was 4.1 x 10e7/kg (2.0-20.0). There was a cumulative incidence (CI) of GF was however 43 ±11%. The median "active ATG-AUC" (area under the curve) was 17 IU*day/L (1 pat no Campath FluCamp and 1 FluCyTBI. Median nucleated cell dose was 4.1 x 10e7/kg (2.0-20.0). There was a cumulative incidence (CI) of GF was however 43 ±11%. The median "active ATG-AUC" (area under the curve) was 17 IU*day/L (1 pat no Campath FluCamp and 1 FluCyTBI. Median nucleated cell dose was 4.1 x 10e7/kg (2.0-20.0). There was a cumulative incidence (CI) of GF was however 43 ±11%. The median "active ATG-AUC" (area under the curve) was 17 IU*day/L (1 pat no Campath FluCamp and 1 FluCyTBI. Median nucleated cell dose was 4.1 x 10e7/kg (2.0-20.0). There was a cumulative incidence (CI) of GF was however 43 ±11%. The median "active ATG-AUC" (area under the curve) was 17 IU*day/L (1 pat no Campath FluCamp and 1 FluCyTBI. Median nucleated cell dose was 4.1 x 10e7/kg (2.0-20.0). There was a cumulative incidence (CI) of GF was however 43 ±11%. The median "active ATG-AUC" (area under the curve) was 17 IU*day/L (1 pat no Campath FluCamp and 1 FluCyTBI. Median nucleated cell dose was 4.1 x 10e7/kg (2.0-20.0). There was a cumulative incidence (CI) of GF was however 43 ±11%. The median "active ATG-AUC" (area under the curve) was 17 IU*day/L (1 pat no Campath FluCamp and 1 FluCyTBI. Median nucleated cell dose was 4.1 x 10e7/kg (2.0-20.0). There was a cumulative incidence (CI) of GF was however 43 ±11%. The median "active ATG-AUC" (area under the curve) was 17 IU*day/L (1 pat no Campath FluCamp and 1 FluCyTBI. Median nucleated cell dose was 4.1 x 10e7/kg (2.0-20.0). There was a cumulative incidence (CI) of GF was however 43 ±11%. The median "active ATG-AUC" (area under the curve) was 17 IU*day/L (1 pat no Campath FluCamp and 1 FluCyTBI. Median nucleated cell dose was 4.1 x 10e7/kg (2.0-20.0).