HLA-haploidentical allografting with high-dose post-transplant cyclophosphamide: clinical outcomes and immunereconstitution.

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HLA-haploidentical allografting with high-dose post-transplant cyclophosphamide: clinical outcomes and immune-reconstitution.

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Preferred Method of Presentation: Oral or Poster Presentation

Introduction: HLA-haploidentical allografting is a potential cure in patients (pts) without a HLA-identical donor

Materials (or patients) and methods: Between April 2010 and November 2014, 41 pts (median age 50, r 21-71 years) with hematologic malignancies (33 acute leukemias; n=2 CML; n=6 lymphomas) were transplanted from a HLA-haploidentical donor. Fifty% had advanced disease at the time of transplant. Eight pts had received a previous allograft. Conditioning was either reduced-intensity (11 pts) with fludarabine (30 mg/m^2/day for 5 days), cyclophosphamide (Cy) (14.5 mg/Kg/day for 2 days) and single dose 2 Gy TBI, or myeloablative (29 pts) with thiotepa (TT) (5 mg/Kg/day for 2 days), fludarabine (50 mg/m^2/day for 3 days) and i.v. Busulphan (Bu) (3.2 mg/Kg/day for 3 days) or thiotepa-fludarabine-melphalan (140 mg/m^2/day) (1 patient), followed by T-cell replete bone marrow (34 pts) or peripheral blood stem cells (7 pts). Post-transplant immunosuppression consisted of Cy, 50 mg/Kg/day on days +3 and +4, followed by mycophenolate mofetil and FK-506. G-CSF was administered from day +5 until engraftment. In 22 (54%) pts, T-cell reconstitution and thymic activity were studied for the first 2 years post-transplant. T-cells subsets in both the CD4+ and CD8+ T cell compartments were evaluated by flow-cytometry: naïve (CD45RO - and CD27 +); central memory (CD45RO + CD27 +); effector memory (CD45RO - CD27 -); and revertant (CD45RA + CD45RO +). Thymic function through T-cell receptor rearrangement excision circles (TRECs) was measured by RT quantitative PCR on DNA extracted from peripheral mononuclear cells and from sorted CD4+ and CD8+ T cells. Here we present preliminary data on thymic output and naïve CD4+ T cell recovery

Results: Neutrophil recovery occurred at a median of 17 days. Incidence of acute grade II-IV and III-IV GVHD was 28,2% and 7,6%. Blood stream infections were documented in 13 pts (7 gram+ bacteria; 6 gram- bacteria). Six had probable invasive fungal infection, in 2 cases after prophylaxis with micafungin and in 4 with azoles. CMV reactivation occurred in 21 and EBV reactivation, successfully treated with rituximab, in 1. At a median follow-up of 501 days (r 18-1278 days), 19 pts (67%) are alive, 11 (58%) in complete remission. Median OS and DFS at 2 years were 46% and 34%. Overall, 14 pts (34%) died of relapse and 8 pts (19%) of transplant related mortality (TRM). The probability of TRM was 16% at 100 days and 26% at 1 year. (CD4+CD27+CD45RA+) Naïve T cells decreased from a median of 23.92/ul at day 28 to 1.8/ul at day 90, then gradually increased to 3.8/ul, 3.9/ul, 8.7/ul at 6, 12 and 18 months, respectively. Median TREC copies/100 ng DNA from sorted CD4+ cells decreased from 14.5 (r 0-202.2) pre-transplant to 4.4 (r 0-49.2) at day 90, than increased to 9.5 (r 0-134.2), 24.8 (r 2.7-83), 41.5 (r 5.5-102.2) and 47.41 (r 31.5-584.3) at 6, 12, 18 and 24 months, respectively. In healthy donors, median TREC copies/100 ng DNA was 74.5 in sorted CD4+cells

Conclusion: Feasibility of HLA-haploidentical transplantation with high-dose post-transplant Cy in heavily pretreated pts was confirmed. Thymic activity and immune recovery of naïve CD4+ T cells were slow and less robust when compared with transplants from HLA identical donors. Longer follow-up on a larger series of pts is needed to evaluate long-term outcomes and correlate clinical issues with immunological data

Disclosure of Interest: None Declared

Keywords: cyclophosphamide, haploidentical hematolopoietic stem cell transplantation, immune reconstitution, thymus