Poster Presentations–Session II

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CD34+ SELECTED AUTOLOGOUS PERIPHERAL BLOOD STEM CELL TRANSPLANTATION FOR MULTIPLE SCLEROSIS (MS): REPORT OF TOXICITY AND TREATMENT RESULTS AT ONE YEAR OF FOLLOW-UP IN 15 PATIENTS

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Aim: To report the results of a phase II trial to evaluate feasibility and toxicity of CD34+ selected autologous peripheral blood stem cell transplantation (CD34+/ASCT) and treatment results at one year of follow-up. Design and methods. Patients with advanced secondary progressive (SP) or relapsing-remitting (RR) MS and confirmed worsening of the extended disability status scale (EDSS) in the previous year despite interferon or other immunotherapies were included. Peripheral blood stem cells were obtained by leukaphereses after mobilization with cyclophosphamide (Cy) and G-CSF. CD34+ selection was performed by means of Isolex 300 or CliniMACS devices. BCNU, Cy and ATG were administered as conditioning regimen. Results: Fifteen patients (9 SPMS and 6 RRMS) with a median EDSS of 6.0 (4.5-6.5) and a median of 3 (1-7) relapses in the previous year were included. Mobilization was unsuccessful in one patient. During mobilization, one patient presented a transient neurologic deterioration. Main complications during ASCT were engraftment syndrome en three patients, CMV reactivation in one, and two neurologic deterioration coinciding with high-fever related to ATG. Haematological recovery was fast and complete in all cases. At 12 months, the EDSS improved in three patients, worsened in two and remained stable in nine. Despite withdrawal of all immunosuppressive therapy only two patients presented relapses. MRI showed disappearance of enhanced T1 lesions but CSF oligoclonal bands persisted in all evaluated cases. Conclusions: CD34+/ASCT using BCNU, Cy and ATG as conditioning regimen has an acceptable toxicity and clearly reduces the progression of the MS. Further follow-up is necessary to establish the real impact of the procedure on the long-term evolution of the disease.

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IMMUNOABLATIVE THERAPY WITH PURIFIED AUTOLOGOUS STEM CELLS RESCUE FOR THE TREATMENT OF POOR PROGNOSIS MS

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Chronic immune modulation is partially effective in slowing the progression of multiple sclerosis (MS). Intensive conditioning regimens ablate host immunity mediating allograft rejection and thus should be capable of ablating dysfunctional autoreactive immunity. Stringent depletion of immune cells in the graft eliminate GvH reactions and hematopoietic stem cells (HSC) reconstitute a naive graft-derived immune system. As autoimmunity is an acquired defect of the immune system, purified stem cells from patients with autoimmune diseases should reconstitute an immune system free of autoreactivity. We are testing these hypotheses in a phase II study of 24 MS patients. Patients are chosen on the basis of rapid aggressive early disease and failure to respond to approved disease-modifying drugs. Following baseline evaluations and a back-up bone marrow harvest, HSC are mobilized using G-CSF, Decadron and Cyclophosphamide and collected by leukopheresis. Autologous HSC are purified on a CliniMACS. Reinfusion of highly purified HSC follows treatment with Busulphan (~16 mg/kg dose adjusted to AUC of the first dose), Cyclophosphamide (200 mg/kg), and rabbit anti-thymocyte globulin (5 mg/kg). Five patients have been treated. Peripheral blood stem cells (PBSC) were mobilized and collected with nominal toxicity. Immune cell contamination of the purified HSCs were below the level of detection by FACS. The mobilization regimen did not cause worsening of MS by clinical or MRI exam. The expected regimen related toxicities were minimal following peripheral blood stem cell transplant. The MS has remained stable in all patients (3-12 months post transplant). Signs of central nervous system inflammation on MRI have resolved following treatment. All patients remain profoundly deficient in T lymphocytes. Although only early follow-up is available, complete immune ablation with stem cell rescue for MS appears to be well tolerated and no sign of active disease can be detected providing preliminary support for role of immunoablative therapy in autoimmunity.

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RE-INFUSED AUTOLOGOUS GRAFT NATURAL KILLER CELLS CORRELATES WITH ABSOLUTE LYMPHOCYTE COUNT RECOVERY AFTER AUTOLOGOUS STEM CELL TRANSPLANTATION: A PILOT STUDY

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Early absolute lymphocyte count (ALC) has been reported to be a powerful prognostic indicator of survival after autologous stem cell transplantation (ASCT). One possible source affecting ALC recovery includes the re-infused autologous graft lymphocytes (AGL). To assess if the re-infused AGL correlate with ALC recovery post-ASCT, we conducted a pilot study to identify which of the re-infused AGL subsets is most associated with day 15 ALC recovery in three patients with multiple myeloma and four patients with non-Hodgkin's lymphoma. Using the Spearman rank correlation coefficient analysis (r), we compared absolute numbers of CD3, CD4, CD8, CD19, and CD16+/CD56+/CD3- cells/kg of body weight from the apheresis product with ALC (cells/ul) at day 15 post-ASCT. The main lymphocyte subsets identified in the apheresis product were T cells and NK cells. There was no strong correlation between T or B cells from the apheresis product compared with ALC at day 15 post-ASCT (CD3, r=0.21; CD4, r=0.32; CD8, r=0.39; and CD19, r=0.14). However, there was good correlation between NK cells from the apheresis product compared with ALC at day 15 post-ASCT (CD16+/CD56+/CD3-, r=0.77). These data provide preliminary evidence that the number of re-infused autologous NK cells in the apheresis product significantly affect ALC recovery early post-ASCT. However, given the small sample size, our results are primarily hypothesis-generating and subject of further research.

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PARAMETERS FOR OPTIMAL TIMING FOR HEMATOPOIETIC PROGENITOR CELL COLLECTION

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Controversies exist regarding the timing of leukapheresis for peripheral blood progenitor cell (PBPC) collection. Patients are often subjected to multiple procedures to collect sufficient number