

Allogeneic Peripheral Blood Stem Cell Versus Bone Marrow Transplantations: CD34+ Cell Mobilisation, Graft Composition, Immune Reconstitution and Clinical Outcome

Michallet Mauricette

Service d'Hématologie, Hôpital Edouard Herriot, Lyon, France

Abstract

The use of peripheral blood, after G-CSF mobilization, as a source of allogeneic hematopoietic stem cells is being increasingly considered. Some significant data were given by 3 large randomized trials comparing bone marrow (BM) and peripheral blood stem cells (PBSC). Numbers of CD34+ and CD3+ harvested cells were significantly higher in PBSC group and the hematopoietic recovery was significantly faster after PBSC. While the American trial showed significant increased rates of acute GVHD and a higher survival and disease-free survival in favour of PBSC, the 2 other studies showed a significant increase of chronic GVHD after PBSC. The French group investigated whether there was a correlation between cellular composition of PBSC and outcome after transplant. Neither hematological recovery, acute or chronic GVHD, nor disease relapse, were significantly associated with CD3+ cell doses. However, high CD34+ cell doses ($>8.3 \times 10^6/\text{Kg}$) were associated with faster hematopoietic recovery and higher probability of extensive cGVHD at 5 years and DFS was significantly higher in patients receiving low CD34+ cell dose. In parallel, in this study, we evaluated and compared different immune parameters in the graft and after transplantation. Absolute values of mononuclear cells/kg were significantly higher in PBSC grafts than in BM grafts. Analysis of CD25, CD95, HLA-DR and CD45RA expression showed that PBSC grafts T cells exhibited a lower activation level. We found no preferential G-CSF-induced mobilisation of so-called "suppressive" CD3+ cells. In contrast, G-CSF reduced 2- to 3-fold the frequency of IFN-gamma-, IL-2- and TNF-alpha-secreting cells within the NK, NK-T and T-cell subsets and severely reduced the potential for IFN-gamma production at the single-cell level. Thirty days after transplantation, T-cell blood counts were 3-fold higher after PBSC. After PBSC, T cells were less activated, and at day 30 CD4+, CD8+, CD45RA+ counts were correlated with the number of mononuclear cells infused with the graft, this was not observed after BMT. We showed that Anti-A and/or anti-B Ab titers were significantly increased in PBSC vs BMT recipients at day 30 and mostly after minor ABO mismatch transplant. PBSC were significantly associated with increased detection of anti-HLA antibodies early after transplantation. This difference was further increased when analysis was restricted to anti-HLA IgG Ab-negative donor/recipient pairs. The higher number of B cells in the PBSC could be associated with enhanced Ab production early after transplantation. Regarding mini-allotransplants, in France, in a retrospective analysis, we did not show any difference between PBSC and BM in term of disease response, chimerism and overall survival but a significant impact of number of CD34+ cells on early chimerism after transplant. This kind of transplant might include donor lymphocyte infusion (DLI) strategy and we showed in our center that previous PBSC donation selectively impaired the yields of total MNC and total CD3+ cells recovery after donation but did not affect neither CD19+ nor CD3- CD56+ recoveries when compared to the cohort of BM donations. The use of G-CSF mobilised peripheral blood, as a source of allogeneic stem cells is increasingly considered, especially for mini-allotransplants which justify further studies to identify the different biological characteristics of this source and its clinical impact.
