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Poster Session

CLINICAL CARE - ACUTE AND CHRONIC GVHD, INFECTIOUS COMPLICATIONS AND IMMUNE RECONSTITUTION OF TRANSPLANTATION POSTER I

Thymic Recovery After Allogeneic Hematopoietic Cell Transplantation with Nonmyeloablative Conditioning Might Be Limited to Patients Younger Than 60 Years of Age.

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Background: Nonmyeloablative conditioning followed by allogeneic hematopoietic cell transplantation (HCT) has been increasingly used as treatment for elderly patients with hematologic malignancies. It has been suspected that T cell reconstitution would be impaired in elderly patients given nonmyeloablative conditioning because of age-related thymic atrophy. Here, we investigated long term lymphocyte reconstitution and thymic function in 80 patients given allogeneic peripheral blood stem cells (PBSC) after nonmyeloablative conditioning.

Patients and Methods: Median age at transplant was 57 years (range 10-71). Conditioning regimen consisted of 2 Gy total body irradiation (TBI) with (n=46) or without (n=20) added fludarabine, 4 Gy TBI with fludarabine (n=6), or cyclophosphamide plus fludarabine (n=8). Thirty-three of the 80 patients received grafts from HLA-matched related donors, 22 from HLA-matched unrelated donors, and 25 from HLA-mismatched related or unrelated donors. PBSC were unmanipulated in 56 patients, CD8-depleted in 19 others, and CD34-selected in the remaining 5 patients. GVHD prophylaxis consisted of mycophenolate mofetil and cyclosporine or tacrolimus. Immune recovery was assessed between 1 and 8.5 years after HCT by signal-joint T-cell receptor excision circle (sjTREC) quantification (221 samples), and flow cytometry. Further, in order to demonstrate a potential thymic recovery, sjTREC level changes from day 100 to days 365 and 730 were also assessed by using Wilcoxon signed rank tests.

Results: There was a close correlation between sjTREC levels and naive CD4+ T cells (defined as

CD4+CD45RA+) counts (P<0.0001). An inverse correlation was observed between the levels of sjTREC/ml and the recipient's age (R=-0.41, p<0.0001). Interestingly, sjTREC levels increased from day 100 to 1 and 2 years after transplantation in patients ≤ 50 (n=23; P=0.02 and P=0.04, respectively), and in those 51-60 years of age (n=35; P=0.17 and P=0.06, respectively), but not in patients >60 (n=22; P=0.3 and P=0.3, respectively) (Figure 1). Similarly, naïve CD4 T cell counts increased from day 100 to 1 and 2 years after transplantation in patients ≤50 (n=23; P=0.01 and P=0.3, respectively), and in those 51-60 years of age (n=35; P=0.5 and P<0.001, respectively), but not in patients >60 (n=22; P=0.9 and P=1.0, respectively). In multivariate analyses, older patient age (P<0.001), extensive chronic GVHD (P<0.001), and prior (resolved) extensive chronic GVHD (P=0.008) were associated with low sjTREC levels, while older patient age (P<0.001), and extensive chronic GVHD (P<0.001) were associated with low naïve CD4 T cell counts.

Conclusions: Our data suggest that thymic neo-generation of T cells occurred from day 100 onwards in patients under 60. However, the levels of sjTREC remained low for patients above 60. Further, chronic GVHD has a dramatic impact on thymic function, as observed after myeloablative conditioning.

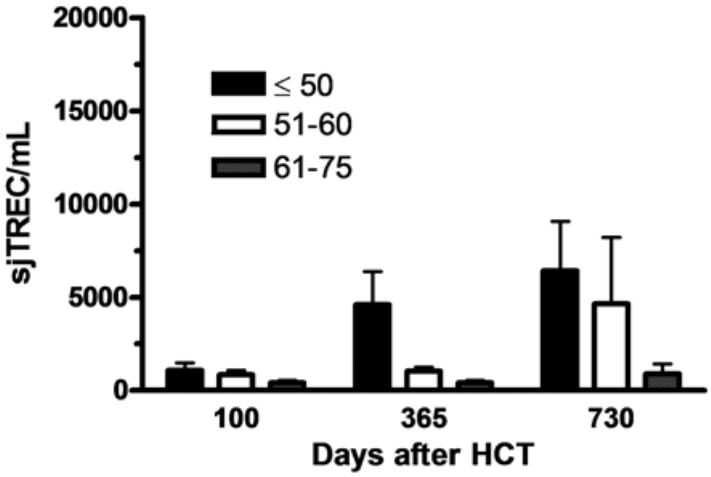

Figure 1. Evolution of sjTREC concentration according to patient age at HCT.

Disclosures: No relevant conflicts of interest to declare.

Footnotes

* Asterisk with author names denotes non-ASH members.

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