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Comparison of immune reconstitution after nonmyeloablative hematopoietic cell transplantation (HCT) with Flu-TBI versus TLI-ATG conditioning

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Background

The BHS transplantation sub-committee has initiated a phase II randomized study comparing two nonmyeloablative conditioning regimen for allogeneic HCT. Here, we report data on immune reconstitution in patients for which cell samples were prospectively collected (n=40).

Patients and methods

The conditioning regimen consisted of either 2 Gy TBI with 90 mg/m² fludarabine (n=21), or 8 Gy TLI plus Thymoglobulin® (ATG) 7.5 mg/kg total dose given from day -11 to day -7 (n=19). Median ages at HCT were 59 yrs and 61 yrs in the TBI and TLI arms, respectively. Immune reconstitution was assessed by immunophenotyping, signal joint T-cell Receptor Excision Circle (sjTREC) quantification, and T-cell receptor Vβ spectratyping.

Results

Absolute T-cell counts were lower in the TLI arm than in the TBI arm on day 28 after HCT (P=0.04) but not thereafter. Further, absolute B cell, as well as CD4+, CD4+CD45RA+ (naïve) and CD4+CD45RO+ (memory) T-cell counts were lower in the TLI arm compared to the TBI arm the first year after HCT (B cells: p=0,0295; others: p<0.0001 with the 2-way ANOVA test). In contrast, reconstitution of CD8+ T cells and NK cells were similar in the 2 groups. SjTREC levels (thymic activity) were higher in the TBI arm than in the TLI arm on day 100 (P=0.002) after HCT evincing higher peripheral expansion of transplanted T cells in the TLI arm, while the diversity of the TCR repertoire was similar (with several oligoclonal Vβ families) in the 2 groups of patients on day 100 after HCT. Treg and iNKT recovery in the 2 arms, as well as data on clearance of Thymoglobulin® in the TLI arm will be presented.

Conclusions

These results suggest that immune recovery is slower in the TLI arm than in the TBI arm.