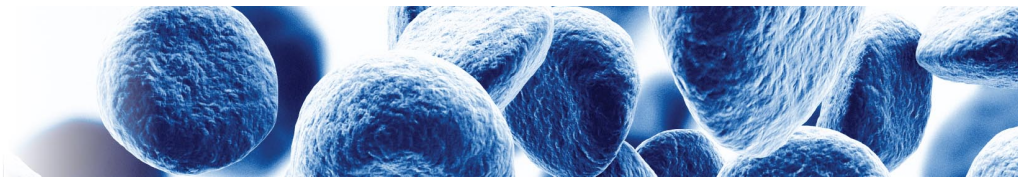

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Phase II clinical trial of Allodepleted T-cell Immunotherapy (ATIR101) post-transplant results in decreased transplant-related mortality and improved survival in acute leukemia patients undergoing T-depleted haploidentical stem cell transplantation

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Introduction: Haploidentical donors may resolve the shortage of available HLA-matched donors for the treatment of blood cancers requiring hematopoietic stem cell transplantation (HSCT). However, to prevent graft-versus-host disease (GVHD), haploidentical HSCT requires alloreactive T-cell depletion. We developed a strategy that allows donor lymphocyte infusion post-HSCT without inducing severe GVHD and maintaining reactivity against viruses and leukemic cells.

Patients and methods: In this open-label, multicenter phase 2 study (CRAIR-007; NCT01794299), 23 patients with median age of 41 years (range 21-64) were treated with ATIR101. Sixteen patients had AML (70%): 11 CR1 and 5 CR2; and 7 patients had ALL (30%): 4 CR1 and 3 CR2/3. Patients underwent myeloablative conditioning, consisting of a] TBI (1200 cGy; n=11) or b] melphalan (120 mg/m^2; n=12), along with thiotepa (10 mg/kg), fludarabine (30 mg/m^2 x 5d) and ATG (2.5mg/kg x 4d). A CD34+ selected stem cell graft from a haploidentical donor was given, containing 11x10^6 CD34+ cells/kg (range;4.7–24.4) and 0.29x10^4 CD3+ cells/kg (range; 0–1.8). In addition, donor lymphocytes were depleted of alloreactive T-cells (ATIR101) using a selective photodepletion technology. ATIR101 was infused at a median of 28 days (range; 28-73) post-HSCT at a fixed dose of 2x10^6 CD3+ cells/kg, without use of post-transplant GVHD prophylaxis.

Results: All patients showed rapid neutrophil and platelet engraftment, both at a median of 12 days (range 8-34 and 9-35, respectively). Median follow-up (as of November 23, 2015)

is 292 days post-HSCT. No patients developed grade III/IV acute GVHD after infusion of ATIR101. Two cases of grade II acute GVHD were reported with a delayed onset, starting only at day 173 and day 247 post-HSCT. When compared to a historic control group (N=35), TRM was significantly lower in patients given ATIR101 with a 6-month TRM for HSCT + ATIR101 of 15% versus 37% for HSCT only (Figure 1). The overall survival of ATIR101 patients was significantly improved with a 1-y survival of 75% in the HSCT+ATIR101 group vs 20% in the control group (Figure 2).

Conclusion: Administration of ATIR101 from a haploidentical donor does not cause severe GVHD without use of prophylactic immune suppression. ATIR101 improves T-cell depleted transplantation outcome, with reduced TRM and improved OS. Moreover, the low number of relapses observed thus far supports the hypothesis of preservation of anti-leukemia T-cells in ATIR101.

Figure 1: