Selective depletion of alloreactive T-cells while retaining virus-specific and memory T-cells from haploidentical donor lymphocytes

Menno van der Hoorn1, Maartje Geraedts1, Angela M. Krackhardt2, Johan Maertens3, Irwin Walker4, Halvard Bönig5, Denis-Claude Roy6, Jeroen Rovers1, Manfred Rüdiger1, Jurjen Velthuis1.

1 Kiadis Pharma, Amsterdam-Duivendrecht, The Netherlands; 2 Medical Department, Klinikum Rechts der Isar, Technische Universität München, Munich, Germany; 3 Department of Haematology, University Hospital Gasthuisberg, Leuven, Belgium; 4 Department of Medicine, McMaster University, Hamilton, Ontario, Canada; 5 Institute for Transfusion Medicine and Immunohematology of the Goethe University and German Red Cross Blood Service Baden-Württemberg-Hesse, Frankfurt, Germany; 6 Hôpital Maisonneuve-Rosemont, Montreal, Canada

Introduction

Haploidentical donor grafts may resolve the shortage of sufficient available HLA-matched donors for treatment of leukemia patients with a HSCT. Current techniques do not allow for such a procedure as the presence of donor T-cells will cause severe GvHD and absence or suppression of T-cells will lead to occurrence of opportunistic infections and potential relapse. Kiadis Pharma developed ATIR101, a cell based medicinal product consisting of selectively allo-depleted donor T-cells, though the use of photodynamic therapy (fig 1). In the present study, we investigated whether ATIR101, that was infused in patients (n=23) in a Phase II clinical trial (CR-AIR-007; NCT01794299) had all the desired features to promote immune protection while not eliciting GvHD in patients that received a haploidentical HSCT.

ATIR101 product desired characteristics

- ATIR101 consists essentially of T-cells (fig 2)
- ATIR101 has retained the presence of memory and naïve T-cells (fig 3)
- ATIR101 is selectively depleted of recipient-reactivity only (fig 4)
- ATIR101 has retained pathogen specific T-cells (fig 5)

Results

ATIR101 and the original donor cells were phenotyped for the presence of:
- T-cells (CD3+), Monocytes (CD14+), NK-cells (CD3-CD16/15+), B-cells (CD19+)
- ATIR101 is strongly enriched for T-cells (>90%).

![Cellular subsets in donor and ATIR101](Image)

Conclusion

ATIR101 adjunctive therapy provides a broad T-cell immunotherapy that can offer effective immune protection without eliciting life-threatening GvHD. It obviates the need for immunosuppressive agents even in the high-risk haploidentical stem cell transplantation population.

Clinical Results

At 6 months follow up, none of patients treated in CR-AIR-007 revealed grade III/IV acute GvHD, and no relapses and only two cases of TRM were observed, both occurring beyond day 100 post HSCT. The present study demonstrates that ATIR101 is able to promote immune protection while not eliciting GvHD in patients that received a haploidentical HSCT.