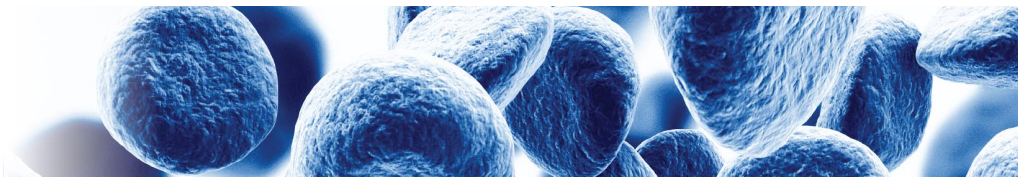

ISCT Annual Meeting 2016 (Abstract P188)

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

Menno van der Hoorn[1], Maartje Geraedts[1], Angela Krackhardt[2], Johan Maertens[3], Irwin Walker[4], Halvard Bönig[5], Denis Claude Roy[6], Jurjen Velthuis[1], Manfred Ruediger1

[1] Kiadis Pharma, Amsterdam-Duivendrecht, 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, ON, 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, QC, Canada

Current HSCT techniques limit the use of haploidentical donor grafts as presence of donor T-cells cause severe GvHD and absence or repression of T-cells will often result in occurrence of opportunistic infections and relapse. Administering T-cells selectively depleted of alloreactive T-cells should reduce the incidence and severity of lethal complications and GvHD and possibly reduce relapse rates.

Here, we investigated whether ATIR, a cell based medicinal product consisting of selectively allo-depleted donor Tcells, had all the desired features, i.e. being selectively depleted of host-reactive T-cells while retaining third-party and anti-pathogen responsiveness. To manufacture ATIR, donor cells were first co-incubated with irradiated recipient cells in a 4-day mixed lymphocyte culture. Upon donor T-cell activation, a photo-active rhodamine derivate (TH9042) that is selectively retained in activated cells was added. Next, cells were exposed to visible light to deplete the TH9042-retaining activated allo-reactive cells.

In vitro studies into the characterization of ATIR showed that treatment of activated donor T-cells with photodynamic purging inhibited host-alloreactive responses measured by T-cell proliferation and INFγ production; by contrast, anti-third party and anti-pathogen responses were preserved. Also virus-specific T-cell multimer analysis showed that these specific T-cells were retained in ATIR.

ATIR is currently being tested in two phase 2 clinical studies (CR-AIR-007; CR-AIR-008) in which it is administered to recipients of a haploidentical HSCT without the use of any immune suppression. An interim analysis conducted at 6 months follow up of the first 10 patients treated in CR-AIR-007 revealed no grade III/IV acute GvHD, no relapses and only two cases of TRM, both occurring beyond day 100 post HSCT. The present study demonstrates that ATIR is indeed able to promote immune protection while not eliciting GvHD in patients that received a haploidentical HSCT.