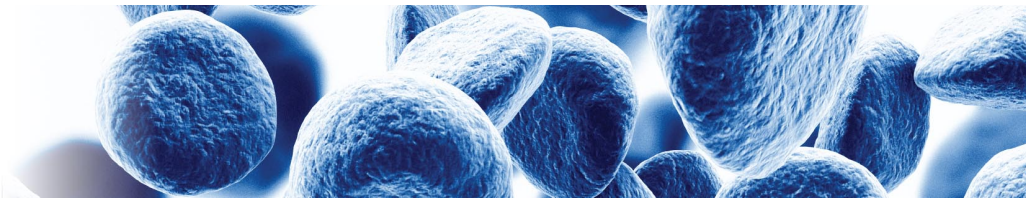

An exploratory, open-label, multicenter study to evaluate safety and efficacy of a two-dose regimen of ATIR101 in patients with a hematologic malignancy, who received a CD34-selected hematopoietic stem cell transplantation from a haploidentical donor

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Introduction: Previous studies demonstrated that donor lymphocytes, selectively depleted of alloreactive T-cells (ATIR101), could be given safely in the haploidentical HSCT setting at doses up to 2x10^6 viable T-cells/kg. In 42 patients a single dose of ATIR101 was given and no grade III/IV acute GVHD has been reported. This confirms the efficacy of the elimination method of allo-reactive T-cells and attributes to its beneficial safety profile. In the ongoing phase 2 study, CRAIR-
007 (NCT01794299), preliminary data shows that addition of ATIR101 at 28 days post-HSCT results in a reduction of transplant-related mortality (TRM) and improvement of overall survival and event-free survival. Incidence of life-threatening infections might be further reduced with the additional of an additional dose of donor lymphocytes.

Material (or patients) and methods: In an open-label, multicenter phase 2 study (CR-AIR-008; NCT02500550), 15 patients with acute myeloid leukemia (AML), acute lymphoblastic leukemia (ALL) or myelodysplastic syndrome (MDS) will undergo a haploidentical HSCT with adjuvant administration of ATIR101. Conditioning regimen consists of either TBI (1200 cGy in 6 fractions) or melphalan (60 mg/m^2 once daily for 2 days), in combination with thiotepa (10 mg/kg),
fludarabine (30 mg/m^2 once daily for 5 days) and ATG (2.5 mg/kg once daily for 4 days). Patients will receive a T-cell depleted graft (CD34+ selection) from a related, haploidentical donor, targeted to contain at least 5×10^6 CD34+ cells/kg but if possible 8-11×10^6 CD34+ cells/kg with a maximum of 3×10^4 CD3+ cells/kg as assessed by flow cytometry. First ATIR101 infusion at a dose of 2x10^6 viable T-cells/kg is given between 28 and 32 days after the HSCT. Patients will receive a second ATIR101 infusion at a dose of 2x10^6 viable T-cells/kg between 70 and 74 days after the HSCT. To assess safety of the second dose administration, the first 6 patients treated will be evaluated for the occurrence of dose limiting toxicity (DLT), defined as acute GVHD grade III/IV within 120 days post HSCT (or within 42 days after

the second ATIR101 infusion in case of prior dose delays).

Results: Regulatory authorities in Canada, Belgium, United Kingdom and Germany have approved the clinical protocol. The study has been initiated and enrolment of the study is expected to continue until May 2016, with first report of safety of the additional dose administration of ATIR101 to be expected before July 2016.

Conclusion: Results of this study will be used to optimize the treatment regimen for a randomized, phase III study, comparing T-cell depleted HSCT + ATIR101 versus T-cell replete HSCT using post transplantation cyclophosphamide (PTCy).

Figure 1: