

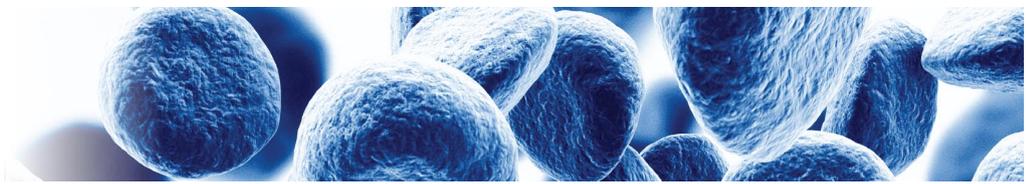
An exploratory, open-label study to evaluate the safety and feasibility of ATIR201, a T-lymphocyte enriched leukocyte preparation depleted *ex vivo* of host alloreactive T-cells (using photodynamic treatment), as adjuvant treatment to a T-cell depleted haploidentical hematopoietic stem cell transplantation in patients with beta-thalassemia major

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Introduction: Previous studies demonstrated that donor lymphocytes, selectively depleted of alloreactive T-cells (ATIR), could be given safely in adult patients receiving a haploidentical HSCT. In 42 patients a single dose of ATIR, at doses up to 2×10^6 viable T-cells/kg, was given and no grade III/IV acute GVHD has been reported. This confirms the efficacy of the elimination method of alloreactive T-cells and attributes to its beneficial safety profile. In an ongoing phase 2 study, CR- AIR-007 (NCT01794299), infusion 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. Adjunctive treatment with donor lymphocytes in patients receiving a T-cell depleted, haploidentical HSCT for non-malignant diseases such as beta thalassemia major, could provide early immunological support and better immune reconstitution in the absence of GVHD.

Patients and Methods: In an open-label, multicenter phase 2 study (CR-BD-001; EudraCT 2016-002959-17), 10 patients age ≥ 2 years and ≤ 25 years with beta thalassemia major will undergo a haploidentical HSCT with adjunctive administration of ATIR201. Patients will receive a T-cell depleted graft (CD34-selected, or CD3/CD19 depleted, or TCR- $\alpha\beta$ depleted, depending on the experience of the study center) from a related, haploidentical donor, Patient conditioning will be myeloablative following standard practices at the study center. ATIR201 infusion at a dose of 2×10^6 viable T-cells/kg is given between 28 and 32 days after the HSCT. To assess safety, patients will be evaluated for the occurrence of dose limiting toxicity (DLT), defined as acute GVHD grade III/IV within 180 days post HSCT. Efficacy will be



primarily evaluated by transfusion-free survival (TFS), occurrence of severe infections, and time to T-cell reconstitution, taking into account hematologic and sustained engraftment. All patients will be closely monitored for CMV, EBV and Adenovirus titers, with initiation of pre-emptive treatment upon rising blood titers.

Results & Conclusion: Regulatory authorities in the United Kingdom and Germany have approved this clinical study protocol. Enrolment of the study is expected to continue during 2017, with first report of safety of ATIR201 to be expected first half 2018.