PB2115 TRIAL IN PROGRESS: A RANDOMIZED PHASE II STUDY OF MB-CART2019.1 COMPARED TO STANDARD OF CARE THERAPY IN PATIENTS WITH RELAPSED/REFRACTORY DLBCL INELIGIBLE FOR AUTOLOGOUS STEM CELL TRANSPLANTATION

Topic: 19. Aggressive Non-Hodgkin lymphoma - Clinical

Peter Borchmann1, Peter Vandenberghe2, Alvaro Urbano3, Corinne Hailour4, Francois Lemonnier4, Laimonas Griškevičius5, Sebastian Maury4, Silke Holtkamp6, Birte Friedrichs6, Gregor Zadoyan6, Linda Hanssens6, Corinne Brilliant7, Ulf Bethke7, Mario Assenmacher7, Iris Bürger7, Barbara Philippe7, Toon Overstijns6, Ulrich Jäger8, Marie José Kersten9

1 Department of Internal Medicine I, University Hospital of Cologne, Cologne, Germany; 2 Department of Hematology, University Hospital Leuven, Leuven, Belgium; 3 Institut Cliníc de Malalties Hematologiques i Oncologiques (ICMHO), Hospital Clinic de Barcelona, Barcelona, Spain; 4 AP-HP, Henri Mondor University Hospital, Créteil, France; 5 Santaros Klinikos, Vilnius University Hospital, Vilnius, Lithuania; 6 Miltenyi Biomedicine GmbH, Bergisch Gladbach, Germany; 7 Miltenyi Biotec B.V. & Co. KG, Bergisch Gladbach, Germany; 8 Department of Hematology and Hemostaseology, University Hospital Vienna, Vienna, Austria; 9 Department of Hematology, Amsterdam University Medical Centers, Amsterdam, Netherlands

Background:

A tandem CAR T-cell product (MB-CART2019.1) targeting CD20 and CD19 antigens has been developed and has shown superior efficacy as compared to each single-CAR in pre-clinical models. MB-CART2019.1 is manufactured in a 13-day process and consists of autologous CD4 and CD8 enriched T-cells, which are transduced with a lentiviral vector that encodes the CAR construct for both CD20 and CD19 single chain variable fragments. The CAR incorporates 4-1BB and CD3ζ signaling domains. The safety of MB-CART2019.1 was investigated in a Phase I dose finding study (NCT03870945) in mainly elderly patients with relapsed or refractory (r/r) B-cell lymphoma. It demonstrated encouraging safety with a low incidence of neurotoxicity and cytokine release syndrome accompanied by first evidence of efficacy, which provide the rationale of this Phase II trial.

Aims:

This study is a pivotal Phase II randomized, multi-center, open-label study with two arms evaluating the efficacy and safety of MB-CART2019.1 compared to standard of care (SoC) therapy in participants with r/r diffuse large B-cell lymphoma (DLBCL) who are not eligible for high-dose chemotherapy (HDC) and autologous stem cell transplantation (ASCT).

Methods:

The primary endpoint of the trial is progression-free survival. Key secondary endpoints include event-free survival, best complete response rate, duration of response and overall survival. Secondary endpoints in the experimental arm include persistence of MB-CART2019.1, phenotype and immune cell compositions, and anti-MB-CART2019.1 antibodies. Safety endpoints include frequency and severity of adverse events as well as the use of tocilizumab and/or high-dose steroids. PET-CTs are performed for response assessment by an Independent Review Committee according to the Lugano 2014 criteria. A total of 168 adult patients with r/r DLBCL will be randomized in a 1:1 ratio to receive MB-CART2019.1 or SoC therapy. In the experimental arm, patients are treated with a dose of 2.5 × 10⁶ CAR+ T-cells per kg body weight based on the recommended dose in the Phase I trial. MB-CART2019.1 is infused as a fresh product (day 0) after a lymphodepleting chemotherapy regimen consisting of fludarabine 30 mg/m² body surface area (BSA) and cyclophosphamide 300mg/m² BSA (each from day -5 to day -3 prior to MB-CART2019.1 infusion). The comparator treatment consists of either R-GemOx (rituximab, gemcitabine and oxaliplatin) or BR (rituximab and bendamustine) plus polatuzumab vedotin, pre-defined to a maximum of 10% of enrolled patients. Main criteria for...
inclusion are i) histologically proven DLBCL and associated subtypes, according to the WHO 2016 classification ii) patients with either refractory disease after first-line chemoimmunotherapy or relapsed disease within < 12 months from the completion of first-line therapy, and iii) patients ineligible to receive HDC followed by ASCT due to age ≥ 65 years and/or documented organ dysfunction.

**Results:**

Final results regarding the primary endpoint are expected by end of 2023.

**Summary/Conclusion:**

This trial evaluates the superiority of 2nd-line CAR T-cell treatment with MB-CART2019.1 compared to SoC in an elderly high-risk population of patients with r/r DLBCL and early relapse. It is planned to be performed in up to 50 clinical trial sites in 10 countries in Europe. The study is actively enrolling patients since August 2021. Clinical trial information: NCT04844866.