P1184 PHASE I TRIAL OF MB-CART2019.1 IN PATIENTES WITH RELAPSED OR REFRATORY B-CELL NON-HODGKIN LYMPHOMA: 2 YEAR FOLLOW-UP REPORT

Topic: 19. Aggressive Non-Hodgkin lymphoma - Clinical

Peter Borchmann[1], Anja Lohneis[1], Philipp Gödel[1], Hyatt Balke-Want[1], Christoph Schmid[2], Francis Ayuk[3], Silke Holtkamp[4], Linda Hanssens[4], Gregor Zadoyan[4], Birte Friedrichs[4], Mario Assenmacher[5], Iris Bürger[5], Dina Schneider[6], Toon Overstijns[4], Christof Scheid[7], Udo Holtick[7], Stefan Miltenyi[5], Michael Hallek[1]

[1] Department of Internal Medicine I, University Hospital of Cologne, Cologne, Germany;[2] II. Med. Klinik Hämatologie/Onkologie, Universitätsklinikum Augsburg, Augsburg, Germany;[3] Department of Stem Cell Transplantation, Universitätsklinikum Hamburg-Eppendorf, Hamburg, Germany;[4] Miltenyi Biomedicine GmbH, Bergisch Gladbach, Germany;[5] Miltenyi Biotec B.V. & Co. KG, Bergisch Gladbach, Germany;[6] Lentigen Technology Inc., Gaithersburg, United States;[7] Leukapheresis and Stem Cell Transplant Unit, Department of Internal Medicine I, University Hospital of Cologne, Cologne, Germany

Background:

A tandem chimeric antigen receptor (CAR) targeting CD20 and CD19 (pLTG1497) has shown superior efficacy as compared to each single-CAR in pre-clinical models. MB-CART2019.1 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 incorporating a 4-1BB co-stimulatory domain.

Aims:

This first-in-human, Phase I study had the objective to assess feasibility, safety and toxicity of *ex vivo* generated MB-CART2019.1 in mainly elderly patients (pts) with relapsed or refractory (r/r) CD20 and CD19 positive aggressive B-cell Non-Hodgkin lymphoma (B-NHL) without curative treatment option (NCT03870945).

Methods:

The trial included two predefined dose levels (DL1 1.0×10^6 and DL2 2.5×10^6 CAR T-cells/kg body weight (BW), respectively). In DL1 pts with multiple prior treatment lines were included while in DL2 the patient population was limited to pts with r/r DLBCL and 1 prior line of treatment who were transplant-ineligible. Fludarabine and cyclophosphamide were used for lymphodepletion. Infusion of fresh MB-CART2019.1 was scheduled 14 days after leukapheresis. The primary endpoint was to evaluate the maximum tolerated dose of MB-CART2019.1 as determined by dose limiting toxicities (DLT). Secondary endpoints included adverse events, overall response rate (ORR), maximum concentration (C_{max}), area under the curve (AUC_{d0-d28}), and persistence of CAR T-cells, measured by flow-cytometry.

Results:

A total of 12 pts, 6 per dose level, have been treated in the trial after obtaining informed consent. Median age was 72 y (range 20, 78 y), with 8 pts >70 y. Histologies included aggressive B-NHL (9), transformed follicular lymphoma (2), and mantle cell lymphoma (1). No grade ≥3 cytokine release syndrome (CRS) or neurotoxicity were observed. Haematotoxicity was very limited with no anemia or thrombocytopenia ≥grade 3 beyond day 28 and intermittent neutropenia ≥grade 3 in only two pts beyond week 8 after treatment. No DLT were observed.

The ORR was 75% (3/6 pts in DL1 and 6/6 pts in DL2) with 5/12 pts (3/6 pts in DL1 and 2/6 pts in DL2) achieving PET-CT negative complete remission (CR) (CR-group). Among those 5 pts, all had ongoing CR as radiologically documented by PET-CT or CT at 12 months and all completed a 2-year follow-up visit without evidence of relapse as

per investigator assessment. Patients with only partial response or stable disease as best overall response ultimately progressed.

All pts with CR had a C_{max} ≥450 cells/µL with mean C_{max} 1,092.5 cells/µL (range 460.1, 3,147.0) while pts with no CR had lower values with mean C_{max} of 111.0 cells/µL (3.9, 458.0). Mean AUC_{d0-d28} was 7,901 d*cells/µL (2,399.2; 19,574.7) in the CR-group as opposed to mean AUC_{d0-d28} of 942.0 d*cells/µL (39.3; 3,471.62) in the non-CR group. Mean time of CAR T-cell persistence in the CR-group was 491 days (274, 736 d) and all 5 CR pts had detectable CAR T-cells beyond month 6.

Summary/Conclusion:

As reported previously, recommended dose of MB-CART2019.1 is 2.5×10^6 CAR T-cells/kg BW. Importantly, all 5 pts with CR were still in CR 12 months after treatment and have now completed the 2-year follow-up visit without evidence of relapse. MB-CART2019.1 is currently challenging conventional immune-chemotherapy in a randomized Phase II trial for elderly, non-transplant eligible pts with first progression or relapse of aggressive B-NHL (NCT04844866).

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