S257 A PHASE 1, FIRST-IN-HUMAN, DOSE-ESCALATION CLINICAL TRIAL OF MEMORY-ENRICHED CD30-CAR T-CELL THERAPY FOR THE TREATMENT OF RELAPSED OR REFRACTORY HODGKIN LYMPHOMA AND CD30+ T-CELL LYMPHOMA

Topic: 25. Gene therapy, cellular immunotherapy and vaccination - Clinical

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Background:

Up to 30% of Hodgkin lymphoma (HL) patients are refractory or relapse (R/R) after first treatment and their prognosis is poor. We have developed a refined CD30-CAR-T (HSP-CAR30) targeting a proximal epitope within the CD30 molecule to overcome soluble CD30 and generated products enriched in memory T-cells to ensure efficient engraftment, persistence and enhancement of antitumor efficacy (Alvarez-Fernández et al, 2021). Here, we report the results of our Phase 1 study evaluating HSP-CAR30 for the treatment of R/R HL and CD30+ T-cell non-Hodgkin lymphoma (T-NHL) (NCT04653649).

Aims:

Primary endpoints were to assess safety of HSP-CAR30 and to establish maximum tolerated dose (MTD) recommended for the following Phase 2. Secondary objectives include best response rates after infusion.

Methods:

We conducted a phase 1 dose-escalation study in 11 patients with R/R HL or CD30+ T-NHL. HL patients were R/R to treatments including chemotherapy, brentuximab and anti-PD-1 antibodies, while T-NHL patients were R/R to at least 2 chemotherapy treatments. T-cells were transduced with a lentivirus encoding a second-generation 4-1BB costimulated CAR, containing a scFv directed against an epitope from the proximal non-cleavable part of CD30 protein. Three cell-dose levels were evaluated: DL1 (3x10^6/kg), DL2 (5x10^6/kg) and DL3 (10x10^6/kg) CAR30+ T-cells.

Results:

From February 2021 to December 2021, 11 patients (9 HL and 2 CD30+ T-NHL) were enrolled and underwent leukapheresis. Of these, 10 patients received HSP-CAR30: 3 patients at DL1, 3 at DL2 and 4 at DL3. Demographic characteristics and baseline disease features are summarized in the Table. Median age was 49.9 years (range 21–65). Median number of prior lines of treatment was 4.6 (range 3–7). One patient did not received treatment due to lack of T-cell expansion. All patients received LD before infusion, fludarabine/bendamustine in HL patients (n=8) and fludarabine/cyclophosphamide in T-NHL (n=2). Mean HSP-CAR30 expression was 94.79±3,38% (±SD). Memory T-cell subset comprised 93.07±4,8% (±SD) in CD4+ and 91.64±4,9% (±SD) in CD8+. Mean time to HSP-CAR30 cell peak level across all doses was 29 days (range 6–98). CAR+ T-cells were detectable by flow cytometry up to 11 months after infusion. HSP-CAR30 infusion was well tolerated; there were no dose limiting toxicities (DLTs). Relevant adverse events are shown in the Table. Grade 1 cytokine release syndrome (CRS) was observed in 6 (60%) patients. No patient developed neurotoxicity. Self-limited skin rash was seen in 4 (40%) patients. One patient with history of cytomegalovirus (CMV) infections had CMV pneumonia. Another patient developed pulmonary tuberculosis. At data cutoff (February 21st, 2021), the median follow-up was 204 days (60–351). Best objective response was 100%, including 5 (50%) patients with complete response (CR), all with HL (DL1=1; DL2=3; DL3= 1).
Three patients have died of progressive disease (2 T-NHL and 1 HL). There were no non-relapse mortality events. Median PFS and median overall survival (OS) was not reached. Six-month PFS for HL patients was 75%.

Summary/Conclusion:
This is the first European academic CART clinical trial evaluating a T-cell memory-enriched CART 30. Our Phase 1 study provides evidence for feasibility and safety of HSP-CAR30. Additionally, HSP-CAR30 has shown promising efficacy in heavily treated HL patients that is being explored in a phase 2 trial already started.