

S207 EFFICACY AND SAFETY OF A THIRD GENERATION CD20 CART (MB-106) FOR TREATMENT OF RELAPSED/REFRACTORY FOLLICULAR LYMPHOMA (FL)

Topic: 18. Indolent and mantle-cell non-Hodgkin lymphoma - Clinical

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Background: Follicular lymphoma (FL) is incurable and novel treatments with high efficacy and low toxicity are needed. Chimeric antigen receptor T-cells (CAR-T) targeting CD19 are effective, and axicabtagene ciloleucel is currently approved by FDA for treatment of patients (pts) with relapsed FL, but toxicities like cytokine-release syndrome (CRS) and immune effector cell-associated neurotoxicity syndrome (ICANS) may limit its use. MB-106 is a fully human 3rd-generation CD20-targeted CAR-T product with both 4-1BB and CD28 costimulatory domains.

Aims: We present the results of the FL cohort from our ongoing phase I/II clinical trial investigating MB-106 for B-cell lymphoma/CLL.

Methods: Pts with R/R B-cell malignancies including FL were eligible after confirmation of CD20 expression. Prior treatment with CD19 CAR-T is permitted. Lymphodepletion (LD) consists of cyclophosphamide (Cy) ± fludarabine (Flu). CAR-T cells are administered at one of 4 dose levels (DL): DL1: 3.3×10^5 , DL2: 1×10^6 , DL3: 3.3×10^6 , DL4: 1×10^7 CAR T cells/kg. A continual reassessment method dose escalation design was used to find the maximally tolerated dose. CAR-T was infused in the outpatient setting except for the first pt of each dose cohort (overnight observation). Initial treatment response is assessed on day 28 and best response is reported here. CRS and ICANS are graded per ASTCT.

Results: Between Dec 2019 and Dec 2021, 16 pts with FL were treated and had day 28 assessment. Median age was 61.5 years (range: 45 – 81). High-risk features included pts with progression of disease within 24 months of first-line chemotherapy (POD24) (n=11; 69%), history of histologic transformation (n=3; 19%), prior treatment with a CD19 targeted CAR-T (n=1; 6%). 6 pts (37.5%) had a PI3 kinase inhibitor. Median time between leukapheresis and LD was 15 days (range: 9-21) and 2 pts received bridging therapy with lenalidomide (1) and high-dose corticosteroids (1). All DLs were reached (DL0=1, DL1=1, DL2=4, DL3=7, DL4=2), with no dose-limiting toxicities. All CRS events were grade 1 (n=4; 25%) or grade 2 (n=1; 6%), with no grade ≥ 3 CRS events. There was no occurrence of ICANS of any grade. No pts had tumor lysis syndrome or Gr 3-4 infections. In the first 28 days, thrombocytopenia (Gr 3-4: 12.5%) and neutropenia (Gr 3-4: 94%) were common but there were no bleeding complications, and the rate of febrile neutropenia was 25%. Overall response (ORR) rate was 94% (15/16) and a complete response (CR) rate was 75% (12/16). Pts who received DL3 or DL4, had an ORR 100% and CR rate of 89%. The single patient who had previously been treated with a CD19 targeted CAR-T achieved a CR. With median follow-up of 10 months, one patient died, from complications of myelodysplastic syndrome (MDS) while still in remission; the MDS was attributed to the prior treatments (7 lines of chemo-based therapy and radioimmunotherapy). Most of the remissions are ongoing and 4 pts have relapsed during the follow-up median 7 months after treatment (range 3-10.5). CAR T cells were detectable by flow cytometry at last available timepoint (up to 2 years) for 15 of 16 patients. One patient had undetectable CAR T cells by day 201.

Summary/Conclusion: Treatment with MB-106, a third generation CD20 targeting CAR-T, resulted in high ORR and CR rates and CAR-T persistence in FL pts and was associated with favorable safety profile with no occurrence of Gr

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3 or Gr 4 CRS and no ICANS event of any grade. A multicenter trial for treatment of B-cell malignancies including FL will start enrollment in 2022.

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