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ORAL ABSTRACTS

704.CELLULAR IMMUNOTHERAPIES: EARLY PHASE AND INVESTIGATIONAL THERAPIES

Obecabtagene Autoleucel (obe-cel, AUTO1) for Relapsed/Refractory Adult B-cell Acute Lymphoblastic Leukemia (R/R B-ALL): Pooled Analysis of the Ongoing FELIX Phase Ib/II Study

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Background: Obe-cel is an autologous chimeric antigen receptor (CAR) T cell product with a novel CD19 binding domain CAT conferring a fast antigen off-rate designed to mitigate safety concerns and improve persistence over approved CD19 CAR T therapies. Early results from the pivotal FELIX study Phase IIA cohort (N=94) were recently presented (Roddie C et al. J Clin Oncol 2023;41[16 Suppl]:7000). We report findings from a pooled analysis of all patients (pts) treated to date with obe-cel in the FELIX Phase Ib/II study (NCT04404660), with a focus on pts with low leukemia burden prior to obe-cel infusion.
Methods: The FELIX study enrolled adults with R/R B-ALL at screening with either morphological disease ≥5% bone marrow (BM) blasts (Cohort A), or in ≥2 nd complete remission (CR)/CR with incomplete hematologic recovery (CRi) with measurable residual disease (MRD) (Cohort B), or with isolated extramedullary disease (EMD) (Cohort C). The Phase Ib part of the study enrolled Cohorts A and B; the Phase II part enrolled Cohorts A, B, and C. CAR T products were generated from leukapheresis material using an automated process. Pts received bridging therapy as needed and lymphodepletion with fludarabine (4 × 30mg/m ^{2}) and cyclophosphamide (2 × 500mg/m ^{2}). A target dose of 410 × 10 ^{6} CAR T cells was infused as a split dose on Days 1 and 10 based on pre-lymphodepletion BM blast burden. The primary endpoint was overall remission rate (best response of CR/CRi by independent review). Secondary endpoints included duration of remission (DoR), MRD negative remission rate, safety, and CAR T expansion/persistence. This pooled analysis included data from pts treated with obe-cel across all cohorts in the Phase Ib/II parts of the study. Low leukemia burden was defined as morphological remission per investigator assessment (<5% BM blasts without EMD) as measured at screening or at the start of lymphodepletion.
Results: Between September 2020 and December 2022, 152 pts were enrolled and underwent leukapheresis. As of 16 March 2023, obe-cel was successfully administered to 126/152 (83%) pts (Phase Ib: Cohort A n=13, B n=3; Phase II: Cohort A n=94, B n=9, C n=7). Baseline characteristics at screening (n=126): median age 46.5 (range 20-81) yrs; Philadelphia positive B-ALL 27%; median 2 (range 1-6) prior lines of therapy; prior blinatumomab/inotuzumab 42%/32%; median BM blast burden 37% (range 0-100) including 23% pts with EMD; prior allogeneic stem cell transplant 44%. At a median follow up of 11.0 (range 0.9-30.6) months, the CR/CRi rate was 77% (95/124 response evaluable pts) with CR rate 57% (71/124). Among MRD evaluable responders, 96% achieved MRD negative status by central flow cytometry analysis. Median DoR was not reached at the current follow up. Low rates of Grade (Gr) ≥3 cytokine release syndrome (CRS; 2.4%) and/or Gr ≥3 immune effector cell associated neurotoxicity syndrome (ICANS; 7.1%) were observed. CAR T expansion was similar across the Phase Ib/II cohorts and CAR T persistence was ongoing in the majority of responders at the current follow up.
Preliminary data indicate favorable efficacy and safety in pts with low leukemia burden prior to obe-cel infusion. Among 12 pts with MRD at screening (Cohort B), two pts were not evaluable and 9/10 evaluable pts achieved CR/CRi, with 100% achieving MRD negative status by central flow cytometry analysis post obe-cel. Median DoR was not reached at the current follow up. In this subset, no Gr ≥3 CRS was observed; one pt had Gr ≥3 ICANS.
In a subset of 28 pts (across all cohorts) in morphological remission at the time of lymphodepletion, 24/27 (89%) response evaluable pts achieved CR/CRi and 100% of MRD evaluable responders achieved MRD negative CR/CRi by central flow cytometry analysis post obe-cel. Median DoR was not reached at the current follow up. In this subset, no pts experienced Gr ≥3 CRS/ICANS.
Conclusions: This pooled analysis of data from all pts treated to date in the FELIX study demonstrates high rates of CR/CRi after obe-cel treatment, durable responses (median DoR not reached), and a favorable safety profile. Preliminary data suggest better outcomes in pts with low leukemia burden at screening/lymphodepletion, with higher rates of deep MRD negative complete remission, median DoR not reached at the current follow up, no Gr ≥3 CRS and one Gr ≥3 ICANS. These data support further exploration of CAR T therapy earlier in the treatment algorithm for adults with ALL.

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