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POSTER ABSTRACTS

704.CELLULAR IMMUNOTHERAPIES: EARLY PHASE AND INVESTIGATIONAL THERAPIES

Long-Term Efficacy and Safety of Obecabtagene Autoleucel (obe-cel) in Adult Patients (pts) with Relapsed/Refractory B-cell Acute Lymphoblastic Leukemia ([R/R B-ALL]; Pooled Analysis from ALLCAR19 and FELIX Phase Ib Studies) or Other B-cell Malignancies (ALLCAR19 Extension Study)

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Background: Obe-cel is an autologous CD19 chimeric antigen receptor (CAR) T cell product designed to reduce toxicity and improve persistence through a fast off-rate CD19 binding domain. The clinical activity of obe-cel has been explored in adults with R/R B-ALL in a Phase I study (ALLCAR19, NCT02935257; Roddie C et al. J Clin Oncol 2021) and a Phase Ib/II study (FELIX, NCT04404660; Roddie C et al. J Clin Oncol 2023;41[16 Suppl]:7000). Additionally, obe-cel has been tested in pts with R/R B-cell chronic lymphocytic leukemia (B-CLL) and R/R B-cell non-Hodgkin lymphoma (B-NHL) (ALLCAR19 extension; Roddie C et al. Blood 2022;140[1 Suppl]:7452-3). Pts from the ALLCAR19 and FELIX Phase Ib studies are in long-term follow up (≥22 mos), and the ALLCAR19 extension has been recruiting for 3 years. We report an analysis of long-term efficacy and safety data from the ALLCAR19 and FELIX Phase Ib studies, as well as data from the ALLCAR19 extension.
Methods: ALLCAR19 is a multicenter, non-randomized, open-label Phase I study in pts aged ≥16 years with B-cell malignancies. ALLCAR19 initially recruited pts with R/R B-ALL but was then amended (extension study) to also include pts with

R/R B-CLL and R/R B-NHL. FELIX is a global, single-arm Phase Ib/II study enrolling pts aged ≥18 years with R/R B-ALL.Study designs have been presented previously. Obe-cel was administered as a split dose in pts with B-ALL (target dose 410 × 10^6 CAR T cells) and pts with CLL (target dose 230 × 10^6 CAR T cells), and as a single infusion in pts with B-NHL (target dose 200 × 10^6 CAR T cells); the pt populations in the two studies were similar. Pts with B-ALL from the ALLCAR19 and FELIX Phase Ib studies are being followed long term for disease progression and survival. For this analysis, data in pts with B-ALL from the ALLCAR19 and FELIX Phase Ib studies were pooled. Data in pts with CLL or B-NHL are presented from the ALLCAR19 extension study.

Results: *Outcomes in pts with R/R B-ALL:* Data in pts with B-ALL were pooled (20 pts from ALLCAR19 [data cut-off Jun 26, 2023] and 16 from FELIX Phase Ib [data cut-off Mar 16, 2023]). The median age of the pooled cohort was 41.5 (range 18 to 74) years and pts had received a median of 3 (range 2 to 6) prior lines of treatment. Twenty-nine of the 36 pts (81%) achieved complete remission (CR)/CR with incomplete hematologic recovery post obe-cel infusions, per investigator assessment. The event-free survival rate was 64% at 6 mos and 49% at 12 mos. With a median follow up of 43 (range 19 to 62) mos, 13/36 pts (36%) remain in remission (8 from ALLCAR19; 5 from FELIX Phase Ib). Among these 13 ongoing responders, 2 (15%) had consolidation with allogeneic hematopoietic stem cell transplantation (allo-HSCT). Ten of the 11 ongoing responders (91%) who did not receive allo-HSCT still had detectable CAR T cells at the last follow up. All ongoing remissions were measurable residual disease negative at last available assessment. The estimated 2-, 3- and 4-year overall survival rates were 44%, 39% and 39%, respectively.

Outcomes in pts with R/R B-CLL/B-NHL: The extension phase of the ALLCAR19 study enrolled 35 pts with B-CLL or B-NHL, of which 26 (B-CLL n=5; B-NHL n=21) received obe-cel (data cut-off Jun 26, 2023). The median age of this combined cohort was 61 (range 39 to 79) years and pts had received a median of 3 (range 2 to 8) prior lines of treatment. At a median follow up of 24 mos, the overall response rate for this cohort was 92% (n=24), and 58% of responders (n=14) were alive without disease progression at last follow up.

Late toxicity: Of the 11 long-term R/R B-ALL responders who had not received consolidation allo-HSCT, 10 have ongoing B-cell aplasia. Of the 14 ongoing responders in the R/R B-CLL/B-NHL cohort, 12 have ongoing B-cell aplasia (<20 B cells/μl). Of note, ongoing B-cell aplasia did not correlate with an increased risk of late serious infection. No other long-term toxicity ascribed to obe-cel was reported.

Conclusions: The combined analysis of data from the ALLCAR19 and FELIX Phase Ib studies shows long-term efficacy and safety of obe-cel in pts with R/R B-ALL, with approximately one-third of pts still in remission without consolidative allo-HSCT after a median follow up of >3 years. Durable responses of >2 years were also seen in pts with R/R B-CLL and R/R B-NHL.B-cell aplasia was commonly found in long-term follow up of obe-cel recipients, but without a corresponding rise in serious late infections. Obe-cel can effect durable long-term remissions in B-cell malignancies.

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