Abstract: S262

Title: SAFETY AND EFFICACY OF OBECABTAGENE AUTOLEUCEL (OBE-CEL), A FAST-OFF RATE CD19 CAR IN RELAPSED/REFRACTORY ADULT B-CELL ACUTE LYMPHOBLASTIC LEUKAEMIA:TOP LINE RESULTS OF THE PIVOTAL FELIX STUDY

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Session Title: Gene therapy and cellular immunotherapy - Clinical

Background:

Obe-cel (AUTO1) is an autologous CD19CAR with a fast off-rate CD19 binding domain designed to reduce CAR-T immunotoxicity and improve persistence. Its clinical activity has been tested in r/r paediatric and adult B-ALL trials (CARPALL, Ghorashian S et al., Nat Med 2019; ALLCAR19, Roddie C et al., JCO 2021) and more recently in adults with r/r B-cell malignancies (NCT02935257).

Aims:

Here, we present data from adult r/r B-ALL patients treated with obe-cel in the pivotal FELIX study (NCT04404660).

Methods:

FELIX is an open-label, multi-centre, global, single-arm Phase Ib/II study enrolling r/r B-ALL patients with morphological disease (≥5% BM blasts), measurable residual disease (MRD) (≥0.1% to <5% BM blasts), or isolated extramedullary disease (Cohorts A, B and C). CAR-T products were generated using an automated closed process from fresh leukapheresate. Patients underwent bridging therapy as necessary and lymphodepletion with fludarabine (4x30mg/m2) and cyclophosphamide (2x500mg/m2). Patients received a target dose of 410E+6 CAR T cells as a split dose on Day 1 and Day 10. The dosing schedule is based on the % BM blasts performed locally prior to the pre-conditioning. Primary endpoint was overall remission rate (ORR) defined as proportion of patients achieving CR/CRi by central assessment.

Results:

As of 9th September 2022, a pre-specified interim analysis was conducted based on the first 50 patients infused in Cohort A who have been followed for 3 months or discontinued before month 3. The median age was 50 years (range 20-81), 22% had Ph+ B-ALL. The median number of prior lines of treatment was 2 (range 1-5), 42% underwent prior transplant. At screening, patients had a median of 55% BM blasts (range 6-96%) and 26% had EMD. The geometric mean of peak CAR expansion was 126147.6 copies/ug genomic DNA. Persistence was ongoing in majority of responders at last follow-up. Based on central assessment, the CR/CRi was 70% [95% CI: 55%, 82%] (p-value < 0.0001).

As of 9th September 2022, a total of 92 patients received obe-cel and were evaluable for safety. 63% developed any grade CRS (3% Grade ≥3) at a median of 9 days post-infusion and a median duration of 5 days. Any grade ICANS was observed in 23% (8% Grade ≥3) at a median of 15 days post-infusion and of median duration 8 days. Other common Grade≥3 adverse events regardless of causality were febrile neutropenia (25%) and anaemia (20%).

Summary/Conclusion:

The pre-specified interim analysis of the FELIX study demonstrated that obe-cel for adult r/r B-ALL is safe with low rates of Grade >3 CRS and/or ICANS, even in patients with high burden disease. Obe-cel is effective with high CR/CRi rates and ongoing CAR T persistence in the majority of responders. The trial has completed dosing of all patients in Cohort A. Additional data and longer follow up will be reported at the conference.

Keywords: Cancer immunotherapy, CD19, CAR-T, B cell acute lymphoblastic leukemia