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704.CELLULAR IMMUNOTHERAPIES: EARLY PHASE CLINICAL TRIALS AND TOXICITIES

Efficacy and Safety of Inaticabtagene Autoleucel in Children with Relapsed/Refractory (R/R) B-cell Acute Lymphoblastic Leukemia in China

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Introduction: Acute lymphoblastic leukemia (ALL) is the most common malignancy in children. Despite long-term survival rates of 85~90% for newly diagnosed patients(pts) in children with ALL, approximately 20% of pts experience relapsed or refractory (R/R) disease. These R/R ALL cases have poor prognoses, remaining a significant cause of mortality among children. Inaticabtagene Autoleucel(Inati-cel) is an autologous CD19 CAR-T therapy first approved by the NMPA in 2023 for adult pts with R/R B-cell ALL. The safety and efficacy of Inati-cel in children with R/R B-cell ALL are not yet established.
Methods: The trial (NCT05667506) in Chinese children aged 3-18 years with R/R B-cell ALL is a single-arm, phase Ib/II, multicenter, open-label study. Pts underwent leukapheresis to obtain T cells for Inati-cel manufacturing. They received a single infusion of Inati-cel at a target dose of 1×10^6 CAR + viable T-cells/kg (±20%) after lymphodepletion with cyclophosphamide and fludarabine. The primary objectives were to assess the safety, dose-limiting toxicities (DLTs), and the recommended dose in pivotal trial; The primary efficacy endpoint was the overall response rate (ORR) of complete response (CR) and CR with incomplete hematological recovery (CRi) within three months post-infusion.
Results: From April 3, 2023, to June 14, 2024, 17 pts were enrolled and underwent leukapheresis, with no manufacturing failure reported. Twelve pts received Inati-cel infusion and had at least one efficacy assessment. The median age was 12.5 years (range: 6-17). Among the 12 pts diagnosed with B-cell ALL, 25.0% (3/12) were primary refractory, and 66.7% (8/12) had relapsed or refractory after median 2 lines prior therapies, and 1 patient (8.3%) had an early relapse (<18 months from diagnosis). Bone marrow (BM) blasts before infusion ranged from 5.0% to 97.5%, with 41.7% (5/12) having >50% blasts.
All 12 pts (100%) achieved response including CR (N=6, 50.0%) or CRi (N=6, 50.0%) at 28 days post-infusion, all (100%) being Minimal Residual Disease (MRD) negative. With a median follow-up of 2.0 months (range: 0.9+ to 13.3+), 5 pts maintained a response for at least three months with sustained MRD negativity, and no relapse were reported;11 pts remained alive. One patient withdrew at two months post-infusion and died of cardiogenic shock during conditioning therapy before HSCT. Median duration of remission (DOR), relapse-free survival (RFS), and overall survival (OS) have not been reached.
No unexpected or fatal adverse events (AEs) were reported during follow-up. The most frequent Grade ≥3 treatment-emergent AEs were hematologic toxicity. CRS occurred in 91.7% of pts (N=11), with one patient experiencing Grade≥3

CRS, The median CRS onset was seven days (range: 2-10) and lasted seven days (range: 2-34). Two pts experienced Grade 3-4 ICANS, with a median onset of 10.5 days (range: 9-12) and a median duration of 14 days (range: 10-18). All CRS and ICANS cases were resolved without sequelae. Among the 6 pts in the phase Ib stage, one patient had a DLT event observed, related to high tumor burden and severe Grade 4 CRS, and was deemed manageable by the Steering Committee.
CAR T-cell expansion occurred in all pts with a median time to maximum expansion (T max) of 15 days (range: 9-23), and a peak copy number (Cmax) of 1.24×10^5 copies/μg gDNA.
Conclusion: This trial demonstrates that Inati-cel is safe and effective in heavily treated children with R/R B-cell ALL. A pivotal trial evaluating Inati-cel at a target dose of 1×10^6 cells/kg (±20%) in children with R/R B-ALL is underway.
*On behalf of Copenhagen Hospital Biobank and International Epidemiology Lymphoma Consortium

Disclosures No relevant conflicts of interest to declare.

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