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POSTER ABSTRACTS

613.ACUTE LYMPHOBLASTIC LEUKEMIAS: THERAPIES EXCLUDING ALLOGENEIC TRANSPLANTATION

Sustained Remission and Decreased Severity of CAR T-Cell Related Adverse Events: An Updated Report on the Pivotal Study of Inaticabtagene Autoleucel (Inati-cel; CNCT19) Treatment in Adult Patients with Relapsed/Refractory B-Cell Acute Lymphoblastic Leukemia (r/r B-Cell ALL) in China

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Introduction: CAR-T cell therapies have shown promising efficacy in patients with relapsed or refractory B-cell malignancies. We have developed a unique autologous CD19-specific second-generation chimeric antigen receptor (CAR) T-cell product, Inaticabtagene autoleucel (Inati-cel; CNCT19), featuring a patent-protected CD19 scFv derived from clone HI19α (distinct from the commonly used FMC63) and a 4-1BB/CD3-ζ costimulatory domain. In November 2023, Inati-cel received approval in China for adult patients with r/r B-cell ALL. Previously, we have reported the results of a phase 2 clinical trial of administrating Inati-cel in patients with r/r B-cell ALL, Thirty-two of 39 (82.1%) patients achieved MRD-negative overall remission rate (ORR), comprising complete response (CR) and CR with incomplete hematological recovery (CRi), and a median duration of remission (DOR) and overall survival (OS) have not been reached (Ying Wang et al. ASH, 2022). Here, we provide updated efficacy and safety data for 48 patients. This trial was registered with Clinicaltrials.gov (NCT04684147).
Methods: Patients underwent leukapheresis to obtain T cells for Inati-cel manufacturing. Inati-cel was infused 2 to 14 days after lymphodepletion with cyclophosphamide and fludarabine. A single infusion of Inati-cel at a target dose of 0.5×10^8 (±20%) CAR T cells was administered. The primary endpoint was ORR at the end of Month 3 after Inati-cel infusion, assessed centrally. Other endpoints included minimal residual disease (MRD) negative rate, DOR, relapse-free survival (RFS), and OS.
Results: A total of 92 patients with r/r B-cell ALL was screened, and 67 patients were ultimately enrolled in the study. Forty-eight patients underwent lymphodepletion and received Inati-cel treatment. The median age of all treated patients was 32 years (range, 18-58years), with 54.2% being male. All patients were refractory (81.2%) or relapsed (18.8%) after multiple lines of prior therapy, with 72.9% having received 2 or more previous therapies, and 16.4% had previously received hematopoietic stem cell transplantation (HSCT). At screening, 77.1% of patients had more than 25% blasts in the bone marrow, and 60.4% had

high-risk cytogenetic abnormalities including *Ph+*, *TP53* deletion or mutation, *MLL* rearrangement, *IKZF1* alteration, *Ph*-like, or *E2A-PBX1* fusion gene.

Efficacy

As of the data cutoff date of 2 April 2024, with a median follow-up of 23.7 months (IQR, 6.2 - 23.7), 41 out of 48 patients (85.4%) achieved MRD-negative ORR after Inati-cel infusion, including 35 patients (72.9%) with CR and 6 (12.5%) with CRi. At the end of Month 3 post-infusion, 34 patients (70.8%) remained in CR (60.4%) or CRi (10.4%). The median DOR, both with and without censoring patients at subsequent allo-HSCT, was 20.7 months (95% CI, 6.4-not estimable with censoring, 9.5-not estimable without censoring). The median RFS was 12.4 months (95% CI, 5.2-not estimable). Median OS was not reached, with an estimated 2-year OS rate of 55.2% (95% CI, 38.2%, 69.3%). Sixteen patients survived more than 24 months, and the longest DOR exceeding 24 months without subsequent anti-cancer therapy, and persistently detectable Inati-cel in blood.

Safety

The most common adverse events (AEs) of special interest were cytokine release syndrome (CRS) and immune effector cell-associated neurotoxicity syndrome (ICANS). Grade 3 or higher CRS and ICANS occurred in 12.5% and 6.2% of patients, respectively, with all patients recovering without sequelae. No deaths were attributed to CRS or ICANS

Conclusions: Inati-cel CAR-T cell therapy achieved a high MRD-negative ORR in adult patients with r/r B-cell ALL, with 85.4% of patients reaching CR/CRi post-infusion and demonstrating durable remission. The safety profile was favorable, with a low incidence of grade 3 or higher CRS and ICANS. With its distinct CAR structure containing a unique CD19 scFv (HI19a), Inati-cel provides effective treatment with potential long-term clinical benefits for adult patients with r/r B-cell ALL.

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