(PS2067) THE PIVOTAL CLINICAL STUDY OF IM19 CAR-T CELLS IN THE TREATMENT OF RELAPSED OR REFRACTORY AGGRESSIVE B-CELL NON-HODGKIN LYMPHOMAS

Topic: 19. Large B cell lymphomas - Clinical

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Background

IM19 is a CD19/4-1BB CAR-T cell product enriched in naïve and memory T cells, which is manufactured in China using a commercial process.

Aims

SD45 is a multicenter, single-arm, open-label phase II pivotal study evaluating the safety and efficacy of IM19 in patients with relapsed/refractory aggressive non-Hodgkin's lymphoma.

Methods

Eligible patients (≥18 years) had histologically confirmed aggressive large B-cell lymphoma (DLBCL NOS, double/triple-hit high-grade B-cell lymphoma, transformed DLBCL, primary mediastinal B-cell lymphoma, follicular lymphoma grade 3B) with ≥2 prior lines of therapy; those with active central nervous system DLBCL were excluded. Written informed consent was obtained from all patients, who underwent leukapheresis with optional investigator-chosen bridging therapy. Lymphodepletion included fludarabine (25-30 mg/m²/day) + cyclophosphamide (250-300 mg/m²/day) for 3 days, followed by a single IM19 infusion (3×10^6/kg). The primary endpoint was 3-month objective response rate (ORR) .

Results

As of data cutoff (31 May 2025), 160 patients were screened at 15 Chinese sites, 116 underwent successful leukapheresis, with an IM19 production success rate of 99.1% (115/116).A total of 101 patients received IM19 infusion (100 standard dose, 1 reduced dose due to infusion set error). Of these, 94 (94%) had DLBCL, 1 (1%) FL grade 3B, 1 (1%) transformed DLBCL, 2 (2%) HGBL, and 2 (2%) other lymphoma (DLBCL combined with FL).Median age was 60 years (21–79), median prior lines 2 (2–9), median production time 8 days, and naïve/memory T-cell proportion >80%.Bridging therapy was used in 69% of patients (median vein-to-vein time: 34 vs. 29 days).
In the efficacy-evaluable population (100 patients), 3-month ORR was 57% (95%CI:46.7%-66.9%); best ORR and CR were 71% (95%CI:61.1%-79.6%) and 41% (95%CI:31.3-51.3%), respectively. Median PFS was 5.98 months (95%CI:5.68m-11.89m), median DOR 10.94 months (95%CI:5.03m-NA).The 1-year OS rate was 63.7% (95%CI: 53.0%–72.7%).Of note, among 10 patients (10%) with post-ASCT relapse, best ORR was 90.0% and best CRR was 80.0%. Among 28 patients aged ≥65 years, best ORR was 75.0%.Among 31 patients (31%) without bridging therapy, best ORR was 77.4% and best CRR was 61.3%.
In the safety population (101 patients), 44.6% developed cytokine release syndrome (CRS), with only 1 grade 3 event (0.9%); immune effector cell-associated neurotoxicity syndrome (ICANS) occurred in 5.0% (all grade 1-2). Grade ≥3 adverse events occurring in ≥10% of patients were neutropenia, leukopenia, lymphopenia, thrombocytopenia, and anemia. No IM19-related deaths were reported.
Among 101 patients with evaluable cellular kinetics, median time to CAR-T peak expansion was 13 days, median peak concentration (Cmax) 96.88cells/μL, and median AUClast 725.37 day×cells/μL. Bridging therapy and lymphodepletion dosage had no significant impact on PK parameters; patients with CRS/ICANS had higher Cmax and AUC0-28d. PK parameters did not differ between patients with 90-day remission and those without.

Summary/Conclusion

IM19 CAR-T demonstrated favorable efficacy and a favorable safety profile (low grade ≥3 CRS/ICANS) in R/R aggressive B-cell NHL patients with diverse histological subtypes and high-risk features. The study population had a high proportion of DLBCL (94%). The slower CAR-T peak expansion (13 days) – potentially due to the high naïve/memory T cell content – may contribute to the excellent safety of IM19, distinguishing it from other CD19 CAR-T products.