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EFFICACY AND SAFETY OF TISAGENLECLEUCEL IN ADULT PATIENTS WITH RELAPSED/REFRACTORY FOLLICULAR LYMPHOMA: PRIMARY ANALYSIS OF THE PHASE 2 ELARA TRIAL

Topic: 18. Indolent and mantle-cell non-Hodgkin lymphoma - Clinical

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Background: Most patients with relapsed/refractory follicular lymphoma (r/r FL) experience multiple relapses and progressively worse clinical outcomes with each line of therapy, underlining a need for novel therapies. Tisagenlecleucel has demonstrated durable responses and manageable safety in adult patients with r/r diffuse large B-cell lymphoma.

Aims: To report the primary analysis of ELARA (NCT03568461), an international, single-arm phase 2 trial of tisagenlecleucel in adult patients with r/r FL.

Methods: Eligible patients (≥18 years) had r/r FL (grades 1-3A) after ≥2 lines of therapy or had failed autologous stem cell transplant. Bridging therapy was permitted followed by disease assessment prior to tisagenlecleucel infusion. Patients received tisagenlecleucel (0.6-6×108 CAR+ viable T cells) after lymphodepleting chemotherapy. The primary endpoint was complete response rate (CRR) by central review per Lugano 2014 criteria. Secondary endpoints included overall response rate (ORR), duration of response (DOR), progression-free survival (PFS), overall survival, safety, and cellular kinetics. Predefined primary analysis occurred when ≥90 treated patients had ≥6 months of follow-up.

Results: As of September 28, 2020, 98 patients were enrolled and 97 received tisagenlecleucel (median follow-up, 10.6 months). At study entry, median age among treated patients was 57 years (range, 29-73), 85% had stage III-IV

disease, 60% had a FLIPI score ≥3, 65% had bulky disease, and 42% had LDH greater than the upper limit of normal. The median number of prior therapies was 4 (range, 2-13); 78% of patients were refractory to their last treatment (76% to any ≥2 prior regimens) and 60% progressed within 2 years of initial anti-CD20-containing treatment. Of 94 patients evaluable for efficacy, the CRR was 66% (95% CI, 56-75) and the ORR was 86% (95% CI, 78-92). CRRs/ORRs were comparable among key high-risk subgroups. Estimated DOR (CR) and PFS rates at 6 month were 94% (95% CI, 82-98) and 76% (95% CI, 65-84), respectively. Of 97 patients evaluable for safety, 65% experienced grade ≥3 adverse events within 8 weeks post-infusion, most commonly neutropenia (28%) and anemia (13%). Any-grade cytokine release syndrome (per Lee scale) occurred in 49% of patients (grade ≥3, 0%). Any-grade neurological events (per CTCAE v4.03) occurred in 9% of patients (grade 3, 0%; grade 4, 1 patient and recovered). Three patients died from progressive disease.

Cellular kinetic parameters for tisagenlecleucel were estimated using transgene levels (by qPCR) in peripheral blood. Median maximal expansion (C_{max}) and exposure during the first 28 days following infusion ($AUC_{0\text{-}28d}$) were similar between responders (CR or partial response) and non-responders (stable or progressive disease). Maximum transgene levels were reached by a median of 10 days in responders and 12.9 days in non-responders; transgene persistence was detected up to 370 days and 187 days, respectively.

Summary/Conclusion: These data demonstrate the efficacy and acceptable safety of tisagenlecleucel in patients with r/r FL, including high-risk patients after multiple lines of prior therapy, and suggest that tisagenlecleucel may be a promising therapy for patients with r/r FL.

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