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ORAL ABSTRACTS

623.MANTLE CELL, FOLLICULAR, AND OTHER INDOLENT B CELL LYMPHOMAS: CLINICAL AND EPIDEMIOLOGICAL

Clinical Outcomes of Patients with Relapsed/Refractory Follicular Lymphoma Treated with Tisagenlecleucel: Phase 2 Elara 3-Year Follow-up

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Background: Tisagenlecleucel is approved in the United States and Europe for adults with relapsed/refractory follicular lymphoma (r/r FL) after ≥2 lines of prior therapy. The primary analysis of the Phase II ELARA trial (median follow-up: 17 months) reported high response rates and a favorable safety profile in heavily pretreated patients with r/r FL. Here we report longer-term efficacy, safety, pharmacokinetic, and exploratory biomarker analyses after a median follow-up of more than 3 years.
Methods: Eligible patients with r/r FL (grades 1-3A) previously treated with ≥2 lines of systemic therapy (including an anti-CD20 monoclonal antibody [mAb] and alkylating agent) received a single tisagenlecleucel infusion ($0.6\text{-}6\times10^{8}$ CAR+ viable T cells). Bridging therapy was permitted. Baseline clinical characteristics and circulating blood naive T cells were correlated with clinical response. Cellular kinetics were assessed using quantitative polymerase chain reaction.
Results: As of March 29, 2023, 97 patients were infused and had a median follow-up of 41 months (range, 34.2-49.7). At baseline, 68% of patients were double refractory to anti-CD20 mAb and alkylating agent, 65% had bulky disease (>7 cm or 3 lesions >3 cm), and 63% had progression of disease within 2 years of frontline systemic therapy (POD24). Comorbidities included cardiac disorders (9%), diabetes (9%), and renal insufficiency (5%). Among 94 patients evaluable for efficacy, best overall response (BOR) of complete response (CR) rate by independent review committee assessment was 68% (95% CI, 57.7%-77.3%) and overall response rate (CR + partial response) 86% (95% CI, 77.5%-92.4%). Median progression-free survival (PFS) was 37 months; 36-month PFS was 53% in all patients and 69% in patients with a BOR of CR. In the POD24 subgroup, 36-month PFS was 50% (n=61) compared with 59% for patients without POD24 (n=33) (Figure). CAR transgene persistence was observed for up to 1290 days. Patients without POD24 had higher median in vivo CAR expansion and longer persistence than patients with POD24. Median duration of response (DOR) was not reached; 64% of responding patients had ongoing response at the time of the 36-month analysis. Among patients with a BOR of CR, 73% had an ongoing response at the time of the 36-month analysis. High baseline levels of circulating CD8+ naive T cells (>2.14% of total T cells) were associated with prolonged PFS and DOR. Median overall survival (OS) and median time to next treatment were not reached. The OS rate at 36 months was 82%, and probability of starting a new treatment at 36 months was 35%. In the POD24 subgroup, 36-month OS rate was 83% compared with 81% in patients without POD24 (Figure). No new safety signals were reported. The most common grade ≥3 adverse events (AEs) were neutropenia (43%) and anemia (19%). The most common serious AEs were cytokine release syndrome (20% [Lee grading]), pneumonia (11%), and febrile neutropenia (8%). To date 18 patients have died during the study (progressive disease, n=8; AE, n=9; euthanasia, n=1).
Conclusions: Patients with r/r FL maintained a high rate of durable responses more than 3 years after tisagenlecleucel infusion, including patients in high-risk subgroups such as POD24. Tisagenlecleucel's safety profile remains favorable with no new safety signals during extended follow-up. Correlative analyses suggest higher baseline levels of CD8+ naive T cells (>2.14%) are associated with improved long-term clinical outcomes.

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Figure. (A) Progression-free survival by POD24, (B) Overall survival by POD24.
NE, not evaluable; POD24, progression of disease within 2 years of frontline systemic therapy.

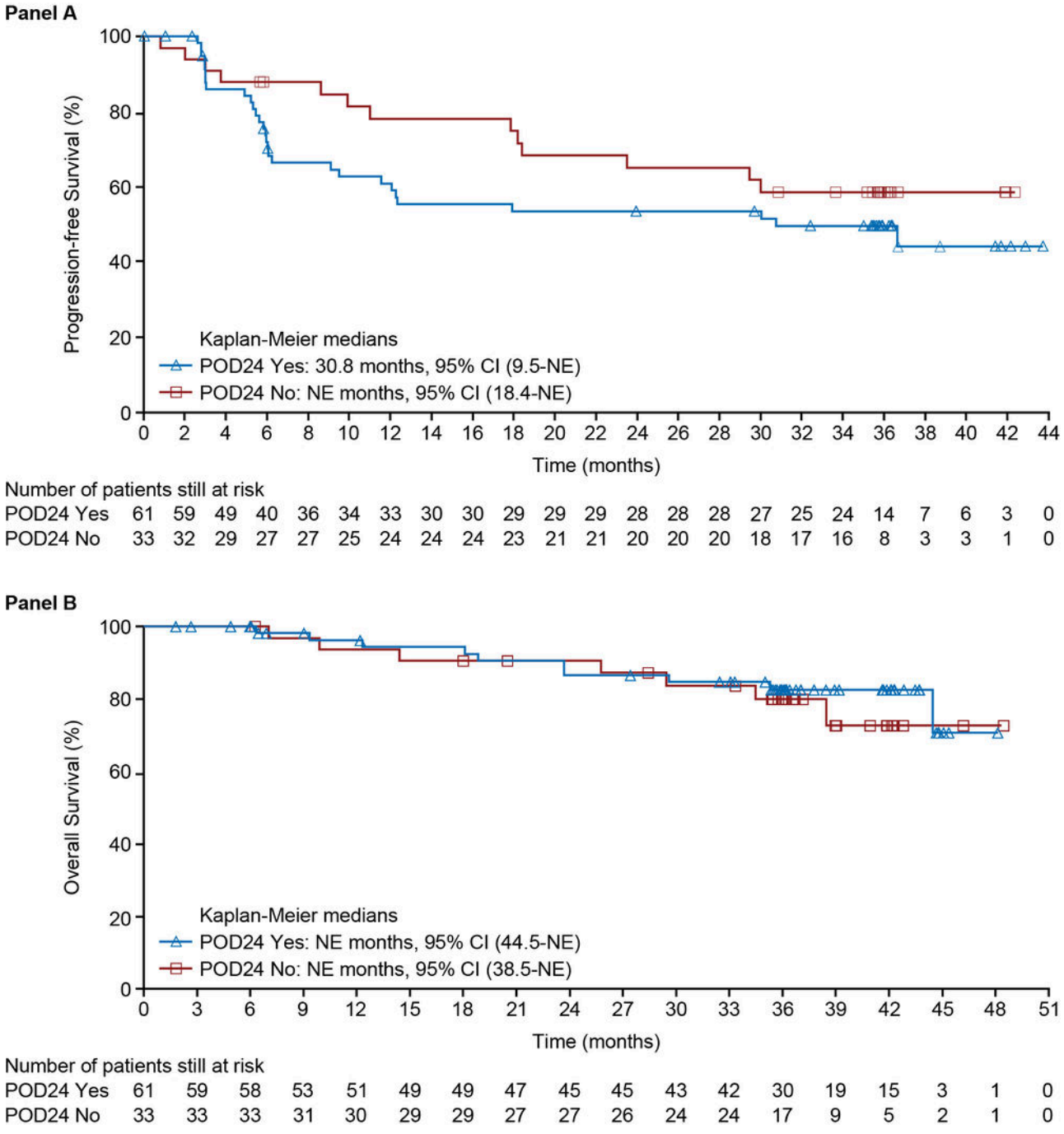

Figure 1

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