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POSTER ABSTRACTS

705.CELLULAR IMMUNOTHERAPIES: LATE PHASE AND COMMERCIALLY AVAILABLE THERAPIES

Axicabtagene Ciloleucel (Axi-Cel) in Patients with Relapsed/Refractory Indolent Non-Hodgkin Lymphoma: 4-Year Follow-up from the Phase 2 ZUMA-5 Trial

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Introduction: ZUMA-5 is a multicenter Phase 2 study of axi-cel autologous anti-CD19 chimeric antigen receptor (CAR) T-cell therapy in patients with relapsed/refractory (R/R) indolent non-Hodgkin lymphoma (iNHL; follicular lymphoma [FL] and marginal zone lymphoma [MZL]). After a median of ≥3 years of follow-up, medians of progression-free survival (PFS) in patients with FL and MZL were 40.2 months and not reached, respectively, and no new safety signals were observed (Neelapu et al. ASH 2022. Abstract 4660). Here, we report updated outcomes from ZUMA-5 after a median follow-up of ≥4 years.
Methods: Eligible patients had R/R FL or MZL after ≥2 lines of therapy including an anti-CD20 monoclonal antibody plus an alkylating agent. Patients underwent leukapheresis at enrollment, then received lymphodepletion and axi-cel infusion (2×10^6 CAR T cells/kg). The primary endpoint was overall response rate (ORR; complete response [CR] + partial response [PR]). Time-to-event endpoints were assessed by investigators in all enrolled patients. Exploratory analyses included lymphoma-specific survival, using competing risk assessment, in which deaths unrelated to progression, axi-cel, or lymphodepletion were competing risks.
Results: In 159 enrolled patients (FL: 127, MZL: 31) at data cutoff (March 31, 2023), median follow-up was 52.5 months (range, 20.3-69.4; FL: 53.7, MZL: 43.8). The ORR in enrolled patients remained consistent with prior analyses (90% ORR, 75% CR rate). Median duration of response (DOR) was 55.5 months (95% CI, 38.6-not estimable; FL: 55.5, MZL: not reached). Medians for DOR were 60.4 months in those with a best response of CR and 4.9 months in those with a PR. At data cutoff, responses were ongoing in 48% of patients, consistent by disease type. Median PFS was 57.3 months (95% CI, 34.9-not estimable; FL: 57.3, MZL: 46.9); estimated 48-month PFS rate was 52% (FL: 53%, MZL: 47%; Figure 1). After data cutoff of the prior analysis, 1 patient with FL had disease progression. PFS rates at 48 months in patients with FL were consistent regardless of high-

risk characteristics, including progression <2 years from initiating first anti-CD20-containing chemoimmunotherapy (POD24). Median time to next therapy was 62.2 months (95% CI, 37.8-not estimable; FL: 62.2, MZL: 46.9). Median overall survival (OS) was not reached (95% CI, 62.2-not estimable); 48-month OS rate was 72% (FL: 72%, MZL: 68%).

Among enrolled patients with FL, the 48-month cumulative incidence of lymphoma-specific progression or death was 34%, while the cumulative incidence of competing risks was 13% (Figure 2). Additionally, the cumulative incidence of lymphoma-specific death at 48 months was 14%; the cumulative incidence of other or unknown death was 14%.

After the 3-year analysis, among 152 treated patients (124 FL; 28 MZL), 6 experienced serious adverse events, 1 of which was related to axi-cel (FL, Grade 3 myelodysplastic syndrome). No new neurologic events, hypogammaglobulinemia cases, Grade ≥3 cytopenias, or Grade ≥3 infections occurred. Seven additional patients died due to progression (n=2; both patients received subsequent therapy after progression), new malignancy (n=1; not axi-cel related), and other causes (n=4; 2 cardiac arrest, 1 infection, and 1 unknown).

Among treated patients with FL, those with ongoing response at 48 months continued to have higher median postinfusion CAR T-cell expansion by peak (52.2 cells/μL) and area under the curve (583.6 cells/μL×days) than those who relapsed (29.6 cells/μL and 337.6 cells/μL×days) or had no response (25.4 cells/μL and 269.9 cells/μL×days). Additionally, those with ongoing response had a higher proportion of naive (CCR7+CD45RA+) T cells in axi-cel product (25%) than relapsed (13%) or nonresponding patients (9%). Similar trends were observed in MZL.

Conclusions: With a median ≥4 years of follow-up in ZUMA-5, axi-cel demonstrated continued durable response and long-term survival in patients with R/R FL and R/R MZL. Late progression or lymphoma-specific death was uncommon in FL, suggesting curative potential for those patients. The long-term safety profile of axi-cel was manageable.

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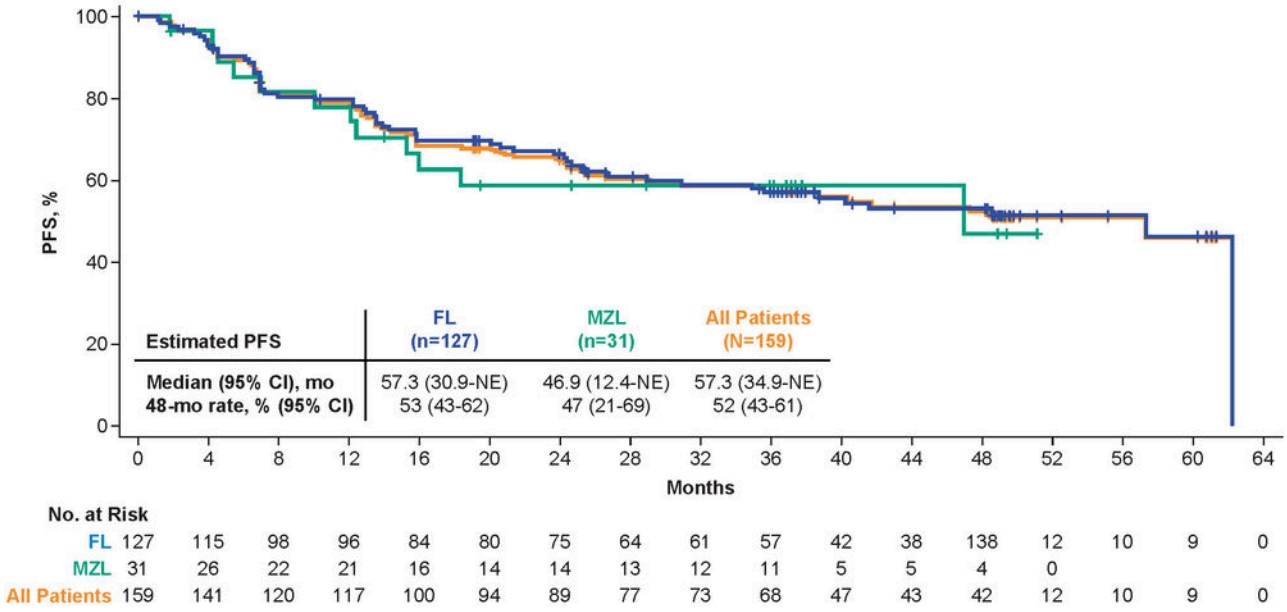
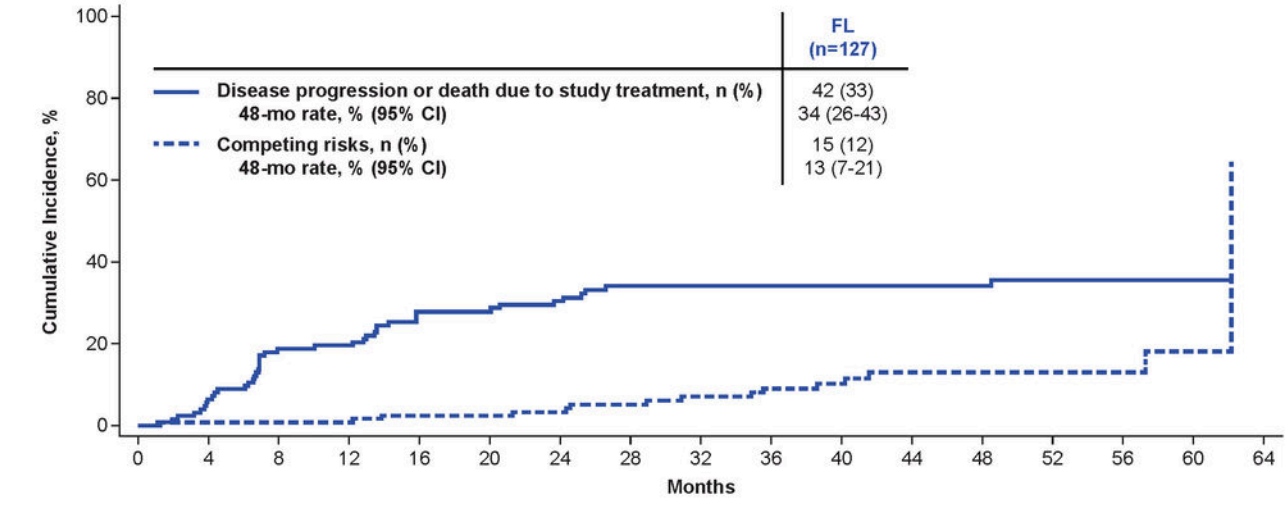
Figure 1. Progression-Free Survival



No. at Risk

FL	127	115	98	96	84	80	75	64	61	57	42	38	138	12	10	9	0
MZL	31	26	22	21	16	14	14	13	12	11	5	5	4	0			
All Patients	159	141	120	117	100	94	89	77	73	68	47	43	42	12	10	9	0

Figure 2. Cumulative Incidence of Lymphoma-Specific Progression or Death in Patients With Follicular Lymphoma



FL, follicular lymphoma; mo, month; MZL, marginal zone lymphoma; NE, not estimable; NR, not reached; PFS, progression-free survival.

Figure 1

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