864 5-Year Follow-up Analysis from ZUMA-5: A Phase 2 Trial of Axicabtagene Ciloleucel (Axi-Cel) in Patients with Relapsed/Refractory Indolent Non-Hodgkin Lymphoma

Program: Oral and Poster Abstracts
Type: Oral
Session: 623. Mantle Cell, Follicular, Waldenstrom's, and Other Indolent B Cell Lymphomas: Clinical and Epidemiological: Clinical Trials for Marginal Zone Lymphoma, Waldenstrom's Macroglobulinemia and Hairy Cell Leukemia
Hematology Disease Topics & Pathways:
Research, Clinical trials, Lymphomas, Non-Hodgkin lymphoma, Clinical Research, Chimeric Antigen Receptor (CAR)-T Cell Therapies, Diseases, Indolent lymphoma, Treatment Considerations, Biological therapies, Lymphoid Malignancies, Study Population, Human

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Abstract

Introduction:

Axi-cel is an autologous anti-CD19 chimeric antigen receptor (CAR) T-cell therapy approved for relapsed/refractory (R/R) follicular lymphoma (FL) based on the Phase 2 ZUMA-5 trial in patients (pts) with R/R indolent non-Hodgkin lymphoma (iNHL; FL and marginal zone lymphoma [MZL]). With a median follow-up of >52 mo, median progression-free survival (PFS)

was 57.3 mo in pts with FL and 46.9 mo in pts with MZL. No new safety signals were observed (Neelapu et al. ASH 2023. Abstract 4868). Here, we report an updated analysis from ZUMA-5 after a median follow-up of >64 mo.

Methods:

Eligible pts with R/R FL or MZL after ≥2 lines of therapy (including an anti-CD20 monoclonal antibody plus an alkylating agent) underwent leukapheresis followed by lymphodepletion and axi-cel infusion at a dose of 2×10^6 CAR T cells/kg. The primary endpoint was overall response rate. Time-to-event outcomes were assessed per investigator in all enrolled pts. Exploratory analyses included lymphoma-specific survival using competing risk assessment (deaths unrelated to lymphoma including progression or study treatment complications were competing risks) and identification of covariates associated with ongoing response.

Results:

A total of 159 pts (FL: 127, MZL: 31) were enrolled, with a median follow-up at data cutoff (March 31, 2024) of 64.6 mo (range, 32.3-81.4; FL: 65.7, MZL: 55.8). Median duration of response (DOR) was 60.4 mo (95% CI, 39.7-not estimable [NE]; FL: 60.4, MZL: not reached [NR]), with estimated 60-mo DOR of 53.4% (95% CI, 43.9-62.0; FL: 52.2%, MZL: 60.0%). Among pts who achieved a complete response (CR), 58% remained in CR at the time of data cutoff. Median PFS was 62.2 mo (95% CI, 34.9-NE; FL: 57.3, MZL: NR), with 50.4% achieving the 60-mo landmark (FL: 49.8%, MZL: 53.9%). Median PFS was NR among pts with CR (n=120; 95% CI, 62.2-NE); among pts with partial response, median PFS was 6.9 mo (n=23; 95% CI, 4.5-12.4). PFS rates at 60 mo in pts with FL were consistent regardless of high-risk characteristics, including progression <2 y from initiating first anti-CD20–containing chemoimmunotherapy (POD24). Median time to next therapy was NR in all pts with iNHL (95% CI, 38.6-NE; consistent by disease type), with a 60-mo estimated rate of 53.3% (95% CI, 45.0-60.9; FL: 54.0%, MZL: 50.9%). At data cutoff, 55% of pts (n=87) were alive with no new anticancer therapy. The median overall survival (OS) was NR (95% CI, NE-NE; consistent by disease type), and the 60-mo OS estimate was 69.0% (95% CI, 60.8-75.8; FL: 68.9, MZL: 71.1).

Among pts with FL, the 60-mo cumulative incidence of progression or lymphoma-specific death was 35.1%, and the cumulative incidence of non–lymphoma-specific deaths was 15.1%. In addition, the cumulative incidence of lymphoma-specific death at 60 mo was 15.6%, with a cumulative incidence of non-lymphoma-specific death of 15.6%. Only 4 pts progressed >24 mo post-leukapheresis. One pt progressed after the data cutoff of the 4-y analysis; no pts died of disease progression after the prior analysis.

Among treated pts (n=152; 124 FL; 28 MZL), 3 new events not related to axi-cel were reported after the 4-y analysis, including Grade 3 metastasis, Grade 1 bladder cancer, and Grade 4 myelodysplastic syndrome (a serious adverse event). One pt died of pneumonia, unrelated to axi-cel. At any time on trial, a total of 47 pts died due to progressive disease (n=14), secondary malignancies (n=6), infections (n=15), or other/unknown (n=12).

Treated pts in ongoing response at the 60-mo data cutoff had higher median post-infusion peak CAR T-cell expansion (59.41 cells/μL) and area under the curve within the first 28 d after treatment ($AUC_{0\text{-}28}$; 696.92 cells/μL×d) than those who relapsed (30.45 cells/μL and 362.68 cells/μL×d) or nonresponders (22.18 cells/μL and 269.82 cells/μL×d). The total number of

infused CCR7+CD45RA+ T cells, indicative of naive phenotype, was associated with improved response.

Conclusions:

After a median follow-up of more than 5 y in ZUMA-5, treatment with axi-cel continued to demonstrate durable response and long-term survival in pts with R/R iNHL. No new safety signals emerged. Over half of pts were alive at data cutoff without need of subsequent therapy. After the prior analysis, there were no lymphoma-specific deaths, and only 1 late progression event occurred in FL, indicating the curative potential of axi-cel in iNHL.

SN and JC contributed equally.

Disclosures: Neelapu: *Sellas Life Sciences:* Consultancy; *Carsgen:* Consultancy; *Sana Biotechnology:* Consultancy, Research Funding; *Merck:* Consultancy; *Bristol Myers Squibb:* Consultancy, Research Funding; *Caribou Biosciences:* Consultancy; *Synthekine:* Consultancy; *Chimagen:* Consultancy; *Kite, a Gilead Company:* Consultancy, Research Funding; *Athenex:* Consultancy; *Allogene:* Consultancy, Research Funding; *ImmunoACT:* Consultancy; *Fosun Kite:* Consultancy; *bluebird bio:* Consultancy; *Appia Bio:* Consultancy; *Anthenex:* Consultancy; *Astellas Pharma:* Consultancy; *GlaxoSmithKline:* Consultancy; *Adicet Bio:* Consultancy, Research Funding; *Precision Biosciences:* Research Funding; *Takeda:* Consultancy; *Orna Therapeutics:* Consultancy; *MorphoSys:* Consultancy; *Incyte:* Consultancy; *Janssen:* Consultancy; *Cargo Therapeutics:* Research Funding; *Longbow Immunotherapy:* Current holder of stock options in a privately-held company. **Chavez:** *Cellectis:* Consultancy; *GenMab:* Consultancy, Research Funding; *Allogene:* Consultancy; *Kite, a Gilead Company:* Consultancy; *BeiGene:* Consultancy, Honoraria, Speakers Bureau; *Abbvie:* Consultancy; *ADC Therapeutics:* Consultancy; *Novartis:* Consultancy; *Janssen:* Honoraria; *AstraZeneca:* Consultancy; *Lilly:* Honoraria, Speakers Bureau; *Merck:* Research Funding. **Sehgal:** *Cytoagents:* Research Funding; *Chimagen:* Research Funding; *Gilead Sciences:* Research Funding; *Bristol Myers Squibb:* Research Funding; *PeerView Live:* Speakers Bureau. **Epperla:** *Merck:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees; *ADC Therapeutics:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees; *Genentech:* Speakers Bureau; *Novartis:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees, Speakers Bureau; *Incyte Corporation:* Research Funding; *Lilly:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees, Research Funding; *BeiGene:* Research Funding, Speakers Bureau; *AstraZeneca:* Research Funding. **Ulrickson:** *Bristol Myers Squibb:* Consultancy; *ADC Therapeutics.:* Consultancy; *Miltenyi Biomedicine:* Honoraria; *Stemline:* Consultancy; *Autolus:* Consultancy. **Bachy:** *Incyte:* Honoraria, Membership on an entity's Board of Directors or advisory committees; *Janssen:* Consultancy, Honoraria; *Novartis:* Honoraria, Other: Personal Fees; *AbbVie, Roche, Takeda:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees; *Amgen:* Research Funding; *BeiGene:* Honoraria, Membership on an entity's Board of Directors or advisory committees; *Bristol Myers Squibb:* Honoraria, Other: Personal Fees, Research Funding; *ADC Therapeutics:* Honoraria; *Pfizer:* Honoraria, Other: Personal Fees; *Kite, a Gilead Company:* Consultancy, Honoraria, Other: Personal Fees. **Munshi:** *Incyte:* Consultancy, Honoraria, Speakers Bureau; *Sanofi:* Consultancy, Honoraria; *Kite, a Gilead Company:* Honoraria, Speakers Bureau. **Casulo:** *AbbVie:* Consultancy, Honoraria; *Genmab:* Research Funding; *Gilead Sciences, Secura Bio:* Research Funding; *Verastem:* Research Funding; *Genentech:* Consultancy, Honoraria, Research Funding; *Bristol*

Myers Squibb: Consultancy, Honoraria, Research Funding. **Maloney:** *Genentech:* Consultancy, Honoraria; *Caribou Biosciences:* Consultancy; *Navan Technologies:* Current equity holder in private company, Honoraria; *Janssen:* Consultancy; *Kite, a Gilead Company:* Consultancy, Research Funding; *Chimeric Therapeutics:* Honoraria; *Gilead Sciences:* Honoraria; *ImmPACT Bio:* Honoraria; *Interius:* Honoraria; *Lyell Immunopharma:* Honoraria; *Novartis:* Honoraria; *Celgene:* Research Funding; *Bristol Myers Squibb:* Consultancy, Honoraria, Research Funding; *Juno Therapeutics:* Patents & Royalties: rights to royalties from Fred Hutch for patents licensed to Juno, Research Funding; *Legend Biotech:* Research Funding; *A2 Biotherapeutics:* Current holder of stock options in a privately-held company. **Reshef:** *Atara Biotherapeutics:* Research Funding; *Immatics:* Research Funding; *TScan:* Consultancy, Research Funding; *Abbvie:* Research Funding; *Precision Biosciences:* Research Funding; *Sana Biotechnology:* Consultancy; *Incyte:* Consultancy, Research Funding; *Sanofi:* Research Funding; *J&J:* Research Funding; *BMS:* Research Funding; *Orca Bio:* Consultancy; *Autolus*: Consultancy; *Gilead Sciences:* Consultancy, Research Funding; *Bayer:* Consultancy; *Quell Biotherapeutics:* Consultancy; *Synthekine:* Research Funding; *Genentech:* Research Funding; *TCR2:* Research Funding; *CareDx:* Research Funding; *Takeda:* Research Funding; *Cabaletta:* Research Funding; *Allogene:* Consultancy. **Leslie:** *Janssen:* Consultancy, Membership on an entity's Board of Directors or advisory committees, Speakers Bureau; *Kite, a Gilead Company:* Consultancy, Membership on an entity's Board of Directors or advisory committees, Speakers Bureau; *Lily:* Consultancy, Membership on an entity's Board of Directors or advisory committees, Speakers Bureau; *Beigene:* Consultancy, Membership on an entity's Board of Directors or advisory committees, Speakers Bureau; *ADC Therapeutics:* Consultancy; *Epizyme:* Consultancy, Membership on an entity's Board of Directors or advisory committees, Speakers Bureau; *TG Therapeutics:* Consultancy, Speakers Bureau; *Astrazeneca:* Consultancy, Membership on an entity's Board of Directors or advisory committees, Speakers Bureau; *Roche/Genenetech:* Consultancy, Speakers Bureau; *Genmab:* Consultancy, Membership on an entity's Board of Directors or advisory committees, Speakers Bureau; *Evolveimmune:* Consultancy; *AbbVie:* Consultancy, Membership on an entity's Board of Directors or advisory committees, Speakers Bureau; *Merck:* Consultancy, Membership on an entity's Board of Directors or advisory committees; *Pharmacyclics:* Consultancy, Membership on an entity's Board of Directors or advisory committees, Speakers Bureau; *Seagen:* Consultancy, Membership on an entity's Board of Directors or advisory committees, Speakers Bureau; *BMS:* Consultancy; *Karyopharm:* Consultancy. **Oluwole:** *ADC:* Consultancy, Speakers Bureau; *Epizyme:* Consultancy; *Kite, a Gilead Company:* Consultancy, Research Funding, Speakers Bureau; *TGR:* Consultancy; *Nektar:* Consultancy; *Novartis:* Consultancy; *Allogene:* Research Funding; *Daichi Sankyo:* Research Funding; *Bioheng:* Consultancy; *AbbVie:* Consultancy; *Gilead Sciences:* Consultancy, Honoraria; *Caribou Biosciences:* Consultancy; *Cargo:* Consultancy; *Pfizer:* Consultancy, Honoraria, Research Funding. **Yakoub-Agha:** *Kite, a Gilead Company:* Honoraria, Other: Travel Support; *Janssen:* Honoraria; *Bristol Myers Squibb:* Honoraria; *Novartis:* Honoraria. **Wulff:** *Kite, a Gilead Company:* Current Employment; *Gilead Sciences:* Current equity holder in publicly-traded company. **Shen:** *Atara:* Patents & Royalties; *Gilead Sciences:* Current equity holder in publicly-traded company; *Kite, a Gilead Company:* Current Employment, Patents & Royalties. **Zhang:** *Kite, a Gilead Company:* Current Employment. **Poddar:** *Kite, a Gilead Company:* Current Employment, Other: Travel Support; *Gilead Sciences:* Current equity holder in publicly-traded company; *UCLA:* Patents & Royalties. **Miao:** *Gilead Sciences:* Current equity holder in publicly-traded company; *Kite, a Gilead Company:* Current Employment. **Nikolajeva:** *Biotech:* Ended employment in the past 24 months; *IQVIA:* Ended employment in the past 24 months; *Kite, a*

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