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POSTER ABSTRACTS

626.AGGRESSIVE LYMPHOMAS: PROSPECTIVE THERAPEUTIC TRIALS

Efficacy of Subcutaneous Epcoritamab Vs Tisa-Cel in R/R LBCL CAR T-Naive and CAR T-Eligible Patients: An Indirect Comparison

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Background: Epcoritamab is a subcutaneous, off-the-shelf, T-cell-engaging CD3xCD20 bispecific antibody (bsAb) with powerful single-agent activity and a manageable safety profile in relapsed/refractory (R/R) large B-cell lymphoma (LBCL), recently approved in the US for the treatment of adults with R/R diffuse large B-cell lymphoma (DLBCL), not otherwise specified, including DLBCL arising from indolent lymphoma, and high-grade B-cell lymphoma after ≥2 lines of systemic therapy. While chimeric antigen receptor T-cell therapy (CAR T) has demonstrated remarkable efficacy in R/R LBCL, there are still barriers to wide adoption, including logistical restrictions and manufacturing limitations. In the absence of head-to-head clinical trial data comparing CAR T with T-cell-engaging bsAbs, we conducted an indirect treatment comparison between CAR T-naive patients treated with epcoritamab in EPCORE NHL-1 (NCT03625037), including a subgroup of CAR T-eligible patients, identified according to ZUMA-1 (NCT02348216) eligibility criteria and utilized in a prior unanchored, matching-adjusted indirect comparison (MAIC) of epcoritamab and axicabtagene ciloleucel (axi-cel) in patients with R/R DLBCL (Thieblemont et al EHA 2023 #P1154), and patients treated with tisagenlecleucel (tisa-cel) in the JULIET trial (NCT02445248). The CAR T-eligible population was of interest for the comparison of epcoritamab vs tisa-cel as it was most similar in baseline clinical characteristics and comparable to patients examined in CAR T trials.
Methods: Published data on the overall response rate (ORR), complete response (CR) rate, digitized progression-free survival (PFS), and overall survival (OS) for tisa-cel from JULIET publications were used in MAIC vs individual patient-level data (IPD) of CAR T-naive and CAR T-eligible patients from EPCORE NHL-1 (Nov 2022 data cut). Analyses were adjusted for imbalances in the following baseline characteristics between IPD from EPCORE NHL-1 and aggregate data from JULIET: age 65 years or older, gender, Eastern Cooperative Oncology Group performance status, disease stage, DLBCL, refractory to last therapy, and prior autologous stem cell transplant. Kaplan-Meier methodology was used to estimate survival.
Results: A total of 96 CAR T-naive patients from EPCORE NHL-1 were included in the analysis, with an effective sample size of 33 CAR T-naive patients after adjustment. The CAR T-eligible subgroup from EPCORE NHL-1 included 57 patients with an effective sample size of 21 patients after adjustment. After adjustment there was a significant difference in ORR for epcoritamab vs tisa-cel (77.9% vs 53.0%, respectively; difference [95% confidence interval (CI)]: 24.8% [9.5, 40.2]; *P*=0.002) in the CAR T-naive cohort, and in CR rate (52.3% vs 39.1%, respectively; difference [95% CI]: 13.2% [5.9, 32.3]; *P*=0.174). Also, in the CAR T-naive cohort there was a trend toward PFS benefit for epcoritamab vs tisa-cel after adjustment (hazard ratio [HR]: 0.725; 95% CI: 0.447, 1.177; *P*=0.194) and OS (HR: 0.611; 95% CI: 0.356, 1.049; *P*=0.074). In the CAR T-eligible subgroup there was a significant difference in ORR (80.8% vs 53.0%, respectively; difference [95% CI] 27.7% [11.0, 44.4]; *P*=0.001) and CR rate (61.9% vs 39.1%, respectively; difference [95% CI]: 22.8% [1.5, 44.1]; *P*=0.036) for epcoritamab vs tisa-cel after adjustment. Also, there was a statistically significant survival benefit for OS (HR: 0.450; 95% CI: 0.227, 0.891; *P*=0.022) and a numerical trend toward benefit for PFS (HR: 0.548; 95% CI: 0.300, 1.003; *P*=0.051) when comparing epcoritamab vs tisa-cel after adjustment.

Conclusion: In the absence of head-to-head data, this MAIC of the R/R LBCL CAR T-naive cohort and the eligible subgroup treated with epcoritamab vs tisa-cel demonstrated improved response rates and survival outcomes. This study underscores the therapeutic potential of epcoritamab as a novel, subcutaneous, off-the-shelf, core therapy for the treatments of patients with R/R LBCL. Indirect comparisons can be biased by cross-trial differences and further comparisons with longer follow-up are warranted.

Disclosures Salles: *Owkin:* Current holder of *stock options* in a privately-held company; *Nordic Nanovector:* Consultancy; *Nurix:* Consultancy; *Orna:* Consultancy; *Novartis:* Consultancy; *Merck:* Consultancy, Honoraria; *Kite/Gilead:* Consultancy; *ATB Therapeutics:* Consultancy; *Loxo/Lilly:* Consultancy; *BMS/Celgene:* Consultancy; *BeiGene:* Consultancy; *Debiopharm:* Consultancy; *AbbVie:* Consultancy, Honoraria; *Ipsen:* Consultancy, Research Funding; *Molecular Partners:* Consultancy; *EPIZYME:* Consultancy; *Genentech, Inc./F. Hoffmann-La Roche Ltd:* Consultancy, Research Funding; *Janssen:* Consultancy, Research Funding; *Incyte:* Consultancy; *Genmab:* Consultancy. **Fox:** *Genmab:* Consultancy, Membership on an entity's Board of Directors or advisory committees; *AbbVie:* Consultancy. **Wang:** *AbbVie:* Current Employment, Current holder of *stock options* in a privately-held company. **Sail:** *AbbVie:* Current Employment, Current holder of *stock options* in a privately-held company. **Alshreef:** *AbbVie:* Current Employment, Current holder of *stock options* in a privately-held company. **Moran:** *AbbVie:* Current Employment. **Mutebi:** *Genmab:* Current Employment, Current holder of *stock options* in a privately-held company. **Blaedel:** *Genmab:* Current Employment, Current holder of *stock options* in a privately-held company. **Chirikov:** *OPEN Health:* Current Employment. **Wang:** *OPEN Health:* Current Employment. **Thieblemont:** *Kyte, Gilead, Novartis, BMS, Abbvie, F. Hoffmann-La Roche Ltd, Amgen:* Honoraria; *Roche:* Consultancy, Membership on an entity's Board of Directors or advisory committees, Other: Travel Expenses, Research Funding; *Paris University, Assistance Publique, hopitaux de Paris (APHP):* Current Employment; *Bayer:* Honoraria; *Incyte:* Honoraria, Membership on an entity's Board of Directors or advisory committees; *Takeda:* Honoraria, Membership on an entity's Board of Directors or advisory committees; *Kite:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees, Other: Travel Expenses; *AbbVie:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees, Other: Travel Expenses; *Gilead Sciences:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees, Other: Travel Expenses; *Hospira:* Research Funding; *Cellectis:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees, Other: Travel Expenses; *Amgen:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees, Other: Travel Expenses; *Novartis:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees, Other: Travel Expenses; *BMS/Celgene:* Consultancy, Membership on an entity's Board of Directors or advisory committees, Other: Travel Expenses, Research Funding; *Janssen:* Honoraria, Other: Travel Expenses.

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