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POSTER ABSTRACTS

627.AGGRESSIVE LYMPHOMAS: CLINICAL AND EPIDEMIOLOGICAL

Population Pharmacokinetics of Subcutaneous Epcoritamab in Relapsed or Refractory B-Cell Non-Hodgkin Lymphoma

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Background: The US FDA approved epcoritamab SC, a CD3xCD20 bispecific antibody developed using the DuoBody ® platform, in May 2023 for the treatment of adults with relapsed or refractory (R/R) diffuse large B-cell lymphoma (DLBCL), not otherwise specified, including DLBCL arising from indolent lymphoma, and high-grade B-cell lymphoma after at least 2 lines of systemic therapy. Here we report the results of a population pharmacokinetic (PK) model-based analysis using data from 2 phase 1/2 clinical trials (EPCORE™ NHL-1 [NCT03625037] and EPCORE NHL-3 [NCT04542824]) evaluating epcoritamab in patients with R/R B-cell non-Hodgkin lymphoma (B-NHL).
Methods: In EPCORE NHL-1 dose expansion and EPCORE NHL-3, epcoritamab SC was administered QW during weeks 1-12 (cycles 1-3), Q2W during weeks 13-36 (cycles 4-9), and Q4W thereafter (cycles ≥10). In EPCORE NHL-1 dose escalation, dosing was QW in cycles 1 and 2, Q2W in cycles 3–6, and Q4W in cycles ≥7. Patients received step-up priming (0.004-0.16 mg), intermediate (0.25-1.6 mg), and full (0.0128-60 mg) doses. A total of 6819 quantifiable PK observations were collected and analyzed from 327 patients (large B-cell lymphoma [LBCL], n=212; indolent B-NHL, n=97; and mantle cell lymphoma, n=18) who received epcoritamab SC. Nonlinear mixed-effects modeling was used for data analysis.
Results: The PK of epcoritamab following SC administration in patients with R/R B-NHL were adequately characterized by a quasi-steady state approximation of a 2-compartment target-mediated drug disposition model with first-order absorption. Among patients with R/R LBCL who received the recommended full dose (48 mg) in EPCORE NHL-1, the estimated median time of maximum concentration (t_{max}) was 4 days (range, 0.3-7) after the first full dose and 2.3 days (range, 0.3-3.2) at the end of weekly dosing (end of cycle 3). The geometric mean (coefficient of variation [CV] %) of the apparent total volume of distribution was 25.6 L (82%). Epcoritamab exposure increased more than proportionally over the range of full doses up to the recommended full dose (1.5-48 mg). For the 48-mg full dose of epcoritamab, the geometric mean (CV%) of terminal half-life at the end of cycle 3 was 22 days (58%), while the geometric mean (CV%) of apparent total clearance after the end of cycle 3 was 0.53 L/day (40%). Body weight was a statistically significant covariate on apparent clearance and central and peripheral volumes of distribution, and age was significant on absorption rate; however, no association was identified between body weight or age and clinical efficacy or safety. After accounting for body weight, no statistically significant effects on epcoritamab PK were observed for age, sex, race, renal or hepatic function, or other disease characteristics. The risk of immunogenicity was low; antidrug antibodies (ADAs) were detected in only 4 (2.6%) of 156 evaluable patients treated with the approved 0.16/0.8/48-mg dosing regimen. No clinically meaningful differences in epcoritamab exposure were observed between ADA-positive patients and ADA-negative patients.
Conclusions: The population PK model appropriately characterized epcoritamab PK in R/R B-NHL. No dosage adjustments are recommended in subpopulations based on body weight, age, sex, race, mild to moderate renal impairment, or mild hepatic impairment.

Disclosures Li: *Genmab:* Current Employment. **Gibiansky:** *Genmab:* Consultancy; *QuantPharm LLC:* Current Employment; *F. Hoffmann-La Roche Ltd:* Consultancy. **Parikh:** *AbbVie:* Current Employment, Current equity holder in publicly-traded company. **van der Linden:** *Genmab:* Current Employment. **Sanghavi:** *Genmab:* Current Employment. **Putnins:** *Genmab:* Current

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