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POSTER ABSTRACTS

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

EPCORE FL-1: Phase 3 Trial of Subcutaneous Epcoritamab with Rituximab and Lenalidomide (R ^{2}) Vs R ^{2} Alone in Patients with Relapsed or Refractory Follicular Lymphoma

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Background: Follicular lymphoma (FL) is the most common form of indolent non-Hodgkin lymphoma (NHL). Several treatment options are approved by the US Food and Drug Administration for second- or later-line FL therapy, including rituximab + lenalidomide (R ^{2}). However, advanced-stage FL remains incurable and new treatment options for relapsed or refractory (R/R) disease are needed. Epcoritamab, a subcutaneously administered, bispecific antibody that binds CD3 on T lymphocytes and CD20 on B cells, induces potent and selective T-cell-mediated killing of malignant CD20 $^{+}$ B cells (van der Horst et al, *Blood Cancer J* 2021). In the first-in-human, phase 1/2 EPCORE NHL-1 trial (NCT03625037) in heavily pretreated patients with B-cell NHL (N=68), epcoritamab showed manageable safety and promising single-agent anti-tumor activity (Hutchings et al, *Lancet* 2021). Among 10 patients with R/R FL, objective response rate (ORR) was 90% (95% CI: 55-100) and complete response (CR) rate was 50%. In the ongoing phase 1b/2 trial evaluating epcoritamab + R ^{2} for R/R FL (EPCORE NHL-2 arms 2a and 2b; NCT04663347), ORR was 98% among 104 efficacy-evaluable patients, with a complete metabolic response in 87%. Most cytokine release syndrome (CRS) events were low grade (n=111; grade 1-2, 46%; grade 3, 2%) and occurred in cycle 1; all CRS events resolved with routine management. These encouraging data, and the distinct mechanisms of action of epcoritamab and R ^{2}, support ongoing evaluation of this combination for its potential to improve clinical outcomes in patients with R/R FL. The phase 3 EPCORE FL-1 trial was designed to evaluate epcoritamab in combination with R ^{2} vs R ^{2} alone in patients with R/R FL with ≥1 prior line of anti-lymphoma therapy. We present an updated protocol, reflecting recent developments and revisions implemented in this study.

Study Design and Methods: EPCORE FL-1 (NCT05409066) is a global, randomized, open-label, multicenter phase 3 trial designed to evaluate efficacy and safety of epcoritamab in combination with R ^{2} vs R ^{2} alone in patients with R/R FL. Adult patients must have histologically confirmed classic FL (previously grades 1 to 3a FL) stage II, III, or IV with a CD20 $^{+}$ tumor on a representative biopsy based on local pathology report and no evidence of histologic transformation. Patients must have R/R disease after ≥1 prior anti-lymphoma regimen that contained an anti-CD20 monoclonal antibody in combination with chemotherapy; patients receiving only prior anti-CD20 monoclonal antibody monotherapy and/or radiation are not eligible. Other key eligibility criteria include Eastern Cooperative Oncology Group performance status 0 to 2, fluorodeoxyglucose positron emission tomography-avid disease, and ≥1 measurable disease site per Lugano 2014 criteria. Lenalidomide-refractory FL (best response to lenalidomide of stable or progressive disease or progressive disease within 6 months of completion of lenalidomide) is excluded. Approximately 520 patients will be enrolled and randomized 1:1 to receive a full dose of epcoritamab in combination with R ^{2} or R ^{2} alone (**Figure**); the trial is currently enrolling in 2 arms, Arms A & C. Based on emerging safety and efficacy data, Arm B has been closed to enrollment and the recommended dose of epcoritamab in combination with R ^{2} is 48 mg. Epcoritamab will be subcutaneously administered using a step-up dosing regimen to full dose in cycle 1 (28 days/cycle). Full dose of epcoritamab will be administered weekly in cycles 2-3 and monthly from cycle 4 onward for up to 12 cycles of treatment. Patients will be serially assessed for disease progression at prespecified intervals. The primary endpoint is progression-free survival assessed by independent review committee (IRC) per Lugano criteria. Key secondary efficacy end-

points include CR rate (by IRC per Lugano criteria), overall survival, and minimal residual disease negativity. Other efficacy endpoints include best overall response, duration of response, duration of complete response, time to progression, event-free survival, time to next anti-lymphoma treatment, and patient-reported outcomes. Safety endpoints include incidence and severity of treatment-emergent adverse events and adverse events of special interest. Exploratory endpoints include assessments of pharmacodynamic and pharmacokinetic data. The study opened for enrollment in 2022 in North America, South America, Europe, Africa, Asia, and Australia.

Disclosures Falchi: *Genentech:* Consultancy, Other: Advisory Board, Research Funding; *Abbvie:* Consultancy, Other: Advisory Board, Research Funding; *AstraZeneca:* Consultancy; *Roche:* Consultancy, Research Funding; *Seagen:* Other: Advisory Board; *ADC Therapeutics:* Other: Advisory Board; *Genmab:* Consultancy, Research Funding. **Morschhauser:** *AbbVie:* Consultancy, Other: Advisory Board; *BMS:* Consultancy, Other: Advisory Board; *Celgene:* Other: Advisory Board; *Janssen:* Honoraria; *Gilead:* Consultancy, Other: Advisory Board; *Roche:* Consultancy, Honoraria, Other: Advisory Board; *Incyte:* Other: Advisory Board; *Epizyme:* Other: Advisory Board; *Novartis:* Consultancy, Other: Advisory Board; *Genmab:* Consultancy, Other: Advisory Board. **Linton:** *AbbVie:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees, Research Funding, Speakers Bureau; *Genmab:* Consultancy, Membership on an entity's Board of Directors or advisory committees, Research Funding; *Takeda:* Research Funding; *Hoffman-La Roche:* Honoraria, Membership on an entity's Board of Directors or advisory committees, Research Funding; *Roche:* Consultancy; *BeiGene:* Consultancy, Membership on an entity's Board of Directors or advisory committees; *BMS:* Consultancy, Membership on an entity's Board of Directors or advisory committees, Speakers Bureau; *Celgene:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees; *Gilead:* Consultancy, Membership on an entity's Board of Directors or advisory committees. **Galderisi:** *AbbVie:* Current Employment. **Quadri:** *AbbVie:* Current Employment. **Zeng:** *AbbVie:* Current Employment. **Hoehn:** *Genmab:* Current Employment, Current equity holder in publicly-traded company. **Seymour:** *Hoffmann-La Roche:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees, Speakers Bureau; *Janssen:* Honoraria, Membership on an entity's Board of Directors or advisory committees; *AbbVie:* Honoraria, Membership on an entity's Board of Directors or advisory committees, Research Funding, Speakers Bureau; *AstraZeneca:* Honoraria, Membership on an entity's Board of Directors or advisory committees; *BMS:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees; *Beigene:* Honoraria, Membership on an entity's Board of Directors or advisory committees, Speakers Bureau; *Gilead:* Honoraria, Membership on an entity's Board of Directors or advisory committees; *Genor Bio:* Membership on an entity's Board of Directors or advisory committees; *TG Therapeutics:* Consultancy; *F. Hoffmann-La Roche Ltd:* Research Funding.

Figure. Study design.

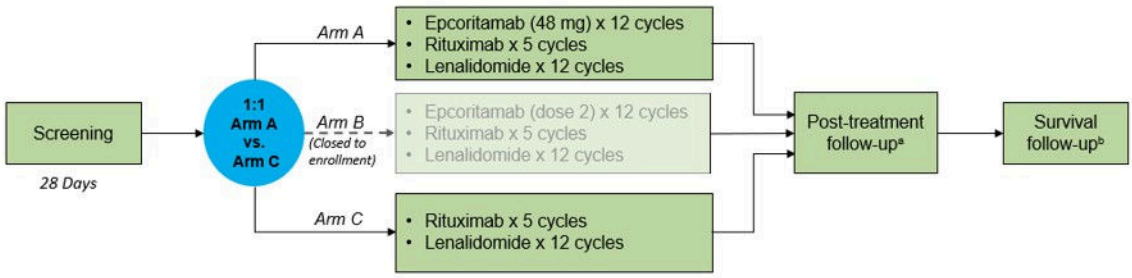

Figure 1

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