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POSTER ABSTRACTS

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

GLOBRYTE: A Phase III, Open-Label, Multicenter, Randomized Trial Evaluating Glofitamab Monotherapy in Patients with Relapsed or Refractory Mantle Cell Lymphoma

Tycel J. Phillips, MD[1], Matthew Matasar[2], Toby A. Eyre, MBChB, DipMedEd, MRCP, FRCPath, MD[3], Eva Gine, MD[4], Audrey Filézac De L'Étang, PhD[5], Ben Byrne, MSc[6], Linda Lundberg, PhD[5], Alejandra Padovani, BSc[5], Christophe Boetsch, PharmD[5], Alessia Bottos, PhD[5], Naseer Qayum, MDPhD[6]

[1] City of Hope National Medical Center, Duarte, CA
[2] Rutgers Cancer Institute of New Jersey, New Brunswick, NJ
[3] Oxford University Hospitals NHS Foundation Trust, Churchill Cancer Center, Oxford, United Kingdom
[4] Hospital Clínic, Barcelona, Spain
[5] F. Hoffmann-La Roche Ltd, Basel, Switzerland
[6] Roche Products Ltd, Welwyn Garden City, United Kingdom

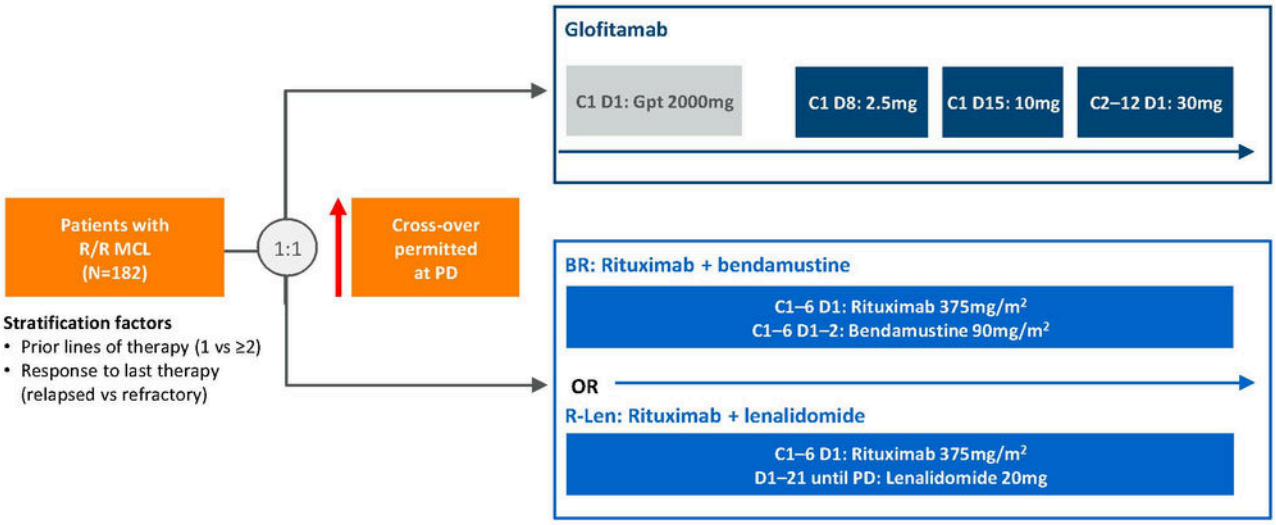
Background and Significance: There is currently no standard of care for patients (pts) with relapsed or refractory (R/R) mantle cell lymphoma (MCL). Although Bruton tyrosine kinase inhibitors (BTKi) have improved clinical outcomes in R/R MCL, there is a high unmet need for new treatment options for pts who do not respond to, or progress through, BTKi therapy. Chimeric antigen receptor (CAR) T-cell therapies, such as brexucabtagene autoleucel, have shown promising outcomes, but alternative systemic therapies are still needed in this pt population. Glofitamab is a CD20xCD3 T-cell-engaging bispecific antibody that redirects T cells to eliminate B cells. A Phase I/II trial of glofitamab monotherapy with step-up dosing (SUD) and obinutuzumab pretreatment (Gpt; 1000 or 2000mg) to mitigate the risk of cytokine release syndrome (CRS) showed high and durable complete response (CR) rates (73.0%) and manageable, mostly low-grade CRS in heavily pretreated pts with R/R MCL (n=37), most of whom had failed prior BTKi therapy (Phillips et al. ASH 2021, Phillips et al. ASH 2022).
Study Design and Methods : The GLOBRYTE study (GO43878; EU CT: 2023-503206-37-00) is a Phase III, open-label, multicenter, randomized, controlled trial that will evaluate the efficacy, safety, pharmacokinetics (PK), and pharmacodynamics (biomarkers) of glofitamab monotherapy in pts with R/R MCL, in comparison with an investigator's choice of rituximab + bendamustine (BR) or rituximab + lenalidomide (R-Len). Pts with histologically confirmed R/R MCL who have received ≥1 prior line of systemic therapy (including a BTKi) and have an Eastern Cooperative Oncology Group performance status of 0-2 are eligible for enrollment. Exclusion criteria include leukemic, non-nodal MCL; prior CAR T-cell therapy or CD20xCD3 bispecific antibodies; primary or secondary central nervous system (CNS) lymphoma or history of CNS lymphoma; and current or prior CNS disease (including stroke or transient ischemic attack in the past 2 years and residual neurologic deficits, epilepsy, or CNS vasculitis). Eligible pts will be randomly assigned (1:1) to receive glofitamab or investigator's choice of BR or R-Len stratified by line of therapy (1 vs ≥2) and response to last therapy (relapsed vs refractory). Pts will receive intravenous (IV) Gpt (2000mg) on Day (D) 1 of Cycle (C) 1, 7 days prior to the first glofitamab dose (Gpt may be split over 2 days as 1000mg doses if needed: the second 1000mg dose must be administered ≥1 day before initial glofitamab treatment). Pts will receive glofitamab for a fixed duration of 12 cycles, unless progressive disease (PD) or unacceptable toxicity occurs earlier. Glofitamab IV SUD will be given on C1D8 (2.5mg), C1D15 (10mg), and then the target dose (30mg) on D1 of C2-12 (21-day cycles). Pts randomized to the investigator's choice will receive 375mg/m^2 IV rituximab on D1 in combination with either 90mg/m^2 IV bendamustine on D1-2 of each cycle (BR for six cycles) or 20mg/day oral lenalidomide on D1-21 of each cycle (R-Len until PD); the cycle length for BR or R-Len is 28 days. Crossover to glofitamab from the investigator's choice is permitted in pts with radiologic confirmation of PD (**Figure**). The primary endpoint is progression-free survival (PFS) determined by independent review committee (IRC). Treatment comparisons will be made with a 2-sided, level 0.05 stratified log-rank test. Secondary endpoints include overall survival (OS); IRC- and investigator-assessed CR rate, objective response rate, duration of response, and duration of CR; PFS (investigator-assessed); safety; health-related quality of life including time to deterioration in physical functioning or fatigue evaluated by the EORTC QLQ-C30; glofitamab PK; and immune response to glofitamab (including presence of anti-drug antibodies). Response will be determined according to Lugano criteria (Cheson et al. J Clin Oncol 2014). Stratified hazard

ratios with 95% confidence intervals (95% CI) will be calculated for PFS and OS, and odds ratios (95% CI) will be calculated for the difference in CR rate and overall response rate between treatment arms. Predictive and prognostic biomarkers (to characterize high-risk subgroups and minimal residual disease kinetics) will also be explored. An estimated 80 sites globally will enroll approximately 182 pts with R/R MCL (glofitamab n=91; BR or R-Len n=91 total) starting in Oct-Nov 2023 (APAC, US, and EU regions).

Disclosures Phillips: *Abbvie, Bayer:* Research Funding; *Abbvie, AstraZeneca, Bayer, Beigene, BMS, Cardinal Health, Epizyme, Incyte, Karyopharm, Pharmacyclics, Seattle Genetics:* Consultancy. **Matasar:** *Regeneron:* Honoraria, Other: Stipends; *Kite:* Honoraria, Other: Stipends; *Teva:* Consultancy; *Immunovaccine Technologies:* Honoraria; *Epizyme:* Other: Stipends; *Celegene:* Honoraria, Other: Stipends; *BMS:* Honoraria, Other: Stipend; *Bayer:* Consultancy, Honoraria, Research Funding; *AstraZeneca:* Honoraria, Other: Stipend; *Takeda:* Consultancy, Honoraria; *Genentech, Inc.:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees, Research Funding; *Juno:* Consultancy; *Merck:* Current equity holder in private company; *ADC Therapeutics:* Consultancy, Honoraria, Other: Stipend; *Seattle Genetics:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees, Research Funding; *F. Hoffmann-La Roche Ltd:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees, Research Funding; *Immunovaccine Technologies:* Research Funding; *Janssen:* Honoraria, Research Funding; *Pharmacyclics:* Honoraria, Research Funding; *Seagen:* Honoraria, Other: stipends. **Eyre:** *PeerView:* Speakers Bureau; *Incyte:* Consultancy, Membership on an entity's Board of Directors or advisory committees, Speakers Bureau; *Loxo Lilly:* Membership on an entity's Board of Directors or advisory committees, Speakers Bureau; *Medscape:* Speakers Bureau; *Gilead:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees, Speakers Bureau; *Janssen:* Consultancy, Honoraria, Speakers Bureau; *Autolus:* Consultancy; *KITE:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees, Speakers Bureau; *Eli Lilly and Company:* Consultancy, Honoraria, Speakers Bureau; *Loxo Oncology:* Consultancy, Honoraria, Other, Speakers Bureau; *Abbvie:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees, Speakers Bureau; *Beigene:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees, Research Funding, Speakers Bureau; *AstraZeneca:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees, Research Funding, Speakers Bureau; *Roche:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees, Speakers Bureau; *Secura Bio:* Membership on an entity's Board of Directors or advisory committees. **Gine:** *Lilly:* Consultancy, Honoraria; *Genmab:* Consultancy, Honoraria; *Janssen:* Consultancy, Honoraria, Research Funding; *Miltenyi:* Consultancy, Honoraria; *Gilead:* Consultancy, Honoraria. **Filézac De L'Étang:** *F. Hoffmann-La Roche Ltd:* Current Employment, Current equity holder in publicly-traded company. **Byrne:** *Roche Products Ltd:* Current Employment, Current equity holder in publicly-traded company, Current holder of *stock options* in a privately-held company. **Lundberg:** *F. Hoffmann La Roche Ltd:* Current Employment, Current equity holder in publicly-traded company; *F. Hoffmann-La Roche Ltd:* Current Employment; *F. Hoffmann-La Roche Ltd:* Current equity holder in publicly-traded company. **Padovani:** *F. Hoffmann La Roche Ltd:* Current Employment, Current holder of *stock options* in a privately-held company. **Boetsch:** *F. Hoffmann La Roche Ltd:* Current Employment, Current holder of *stock options* in a privately-held company. **Bottos:** *F. Hoffmann La Roche Ltd:* Current Employment, Current holder of *stock options* in a privately-held company. **Qayum:** *F. Hoffmann La Roche Ltd:* Current Employment, Current equity holder in private company, Current holder of *stock options* in a privately-held company, Patents & Royalties.

OffLabel Disclosure: Glofitamab (Columvi) is a bispecific CD20-directed CD3 T-cell engager indicated for the treatment of adult patients with relapsed or refractory DLBCL, NOS or large B-cell lymphoma arising from FL, after two or more lines of systemic therapy.

Figure. Study schema



B, bendamustine; C, cycle; D, day; Gpt, obinutuzumab pretreatment; Len, lenalidomide; MCL, mantle cell lymphoma; PD, progressive disease; R/R, relapsed/refractory; R, rituximab. Relapsed disease is defined as disease progression after the last regimen; refractory disease is defined as failure to achieve a partial response or complete response to the last regimen.

Figure 1

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