ELSEVIER

Blood 144 (2024) 1631–1633

The 66th ASH Annual Meeting Abstracts

POSTER ABSTRACTS

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

Glofitamab Induces High Response Rates and Durable Remissions in Patients (Pts) with Heavily Pretreated Relapsed/Refractory (R/R) Mantle Cell Lymphoma (MCL), Including Those with a Poor Prognosis: Subgroup Results from a Phase I/II Study

Tycel J. Phillips, MD[1], *Marek Trněný*[2], *Carmelo Carlo-Stella, MD*[3], *Jan Maciej Zaucha*[4], *Tomasz Wrobel*[5], *Fritz Offner, MD PhD*[6], *Michael J. Dickinson, MBBS, DMedSci*[7], *Monica Tani*[8], *Michael Crump, MD*[9], *Nancy L. Bartlett, MD*[10], *Joaquín Martínez-Lopez*[11], *Paolo Corradini, MD*[12], *Estefania Mulvihill*[13], *Alessia Bottos, PhD*[13], *Derrick Kaufman*[14], *James Relf*[15], *Fabiola Bene Tchaleu*[14], *Alexandra Bazeos*[15], *Linda Lundberg*[13], *Franck Morschhauser, MD PhD*[16]

[1] City of Hope National Medical Center, Duarte, CA
[2] Charles University, Prague, Czech Republic
[3] Humanitas University and IRCCS Humanitas Research Hospital, Milan, Italy
[4] Medical University of Gdańsk, Gdańsk, Poland
[5] Wroclaw Medical University, Wroclaw, Poland
[6] Universitair Ziekenhuis Gent, Gent, Belgium
[7] Peter MacCallum Cancer Centre, Melbourne, Australia
[8] Ospedale Santa Maria delle Croci, Ravenna, Italy
[9] Princess Margaret Hospital, Toronto, Canada
[10] Siteman Cancer Center, Washington University, St. Louis, MO
[11] Hospital Universitario 12 de Octubre, Spanish National Cancer Research Center (CNIO), Complutense University Madrid, imas12, Madrid, Spain
[12] University of Milan and Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy
[13] F. Hoffmann-La Roche Ltd, Basel, Switzerland
[14] Genentech, Inc., South San Francisco, CA
[15] Roche Products Ltd, Welwyn, United Kingdom
[16] Centre Hospitalier Universitaire de Lille, Lille, France

Background: Pts with R/R MCL continue to have a poor prognosis, especially those whose disease has become R/R to Bruton tyrosine kinase inhibitor (BTKi)-containing therapies. Additional treatments are needed for pts with R/R MCL. Glofitamab is a CD20xCD3 T-cell-engaging bispecific antibody that is approved for the treatment of pts with R/R diffuse large B-cell lymphoma who have received ≥2 prior lines of therapy. In an ongoing Phase I/II study (NP30179; NCT03075696), fixed-duration glofitamab monotherapy induced high response rates and durable remissions, and had a manageable safety profile, in heavily pretreated pts with R/R MCL (Phillips et al. ASCO 2024). We report updated results for the R/R MCL cohort, including efficacy in clinically and/or histologically defined high-risk subgroups, as well as initial analysis of minimal residual disease (MRD).
Methods: Eligible pts were those with R/R MCL who had received ≥1 prior line of therapy. All pts received obinutuzumab pretreatment (1000mg or 2000mg) on Cycle (C) 1 Day (D) 1. Glofitamab was then given as step up doses on C1D8 (2.5mg) and C1D15 (10mg) and at the target dose (16mg or 30mg) on D1 of each subsequent cycle (C2-12). Investigators assessed the tumor response using Lugano 2014 criteria. Formalin-fixed paraffin-embedded tumor biopsies were classified as classical, blastoid or pleomorphic and analyzed by immunohistochemistry for Ki-67 or p53 expression. MRD was evaluated in genomic or plasma DNA by clonoSEQ.
Results: As of May 17, 2024, 60 pts received treatment (safety population; median age: 72 years, range: 41-86). Most pts (86.7%) had Ann Arbor stage III or IV disease at entry. The median number of prior lines of therapy was 2 (range: 1-5); 46.7% of pts had received ≥3 prior therapies and 55.0% had received ≥1 prior BTKi therapy. The majority of pts (73.3%) were refractory to their last prior therapy and 51.7% were refractory to any prior BTKi. Among pts with an evaluable baseline biopsy, 53.0% (25/46) had ≥1 high-risk histological feature, defined as blastoid morphology, Ki-67 expression >50% or p53 expression >50%.

Median overall survival (OS) follow-up was 24.2 months (range: 0-50) at cut-off. In the intent-to-treat population of all enrolled pts (N=61), the overall response rate was 82% and complete response (CR) rate was 77%. Median time to response was 42 days (range: 29-164) and median duration of CR (DOCR) was 46.5 months (range: 1-47), with 57.4% of complete responders still in response at cut-off. Median progression-free survival (PFS) was 18.0 months (95% CI: 11.3, not estimable [NE]) and median OS was NE (95% CI: 21.6, NE).

Response rates were consistent in patient subgroups defined by baseline clinical characteristics. CR rates were: 76% and 78% in those aged <70 (n=25) and ≥70 (n=36) years; 80%, 78%, and 75% in those with 1 (n=15), 2 (n=18) and ≥3 (n=28) prior lines of therapy; 71% and 85% in those with (n=34) and without (n=27) prior BTKi exposure; and 76% and 81% in those who were (n=45) and were not (n=16) refractory to their last prior therapy, respectively. Among pts with an evaluable baseline biopsy, CR rates were 68.0% and 81.0% in those with (n=25) and without (n=21) ≥1 high-risk features. In detail, CR rates were: 60% and 73% in those with (n=5) and without (n=37) blastoid morphology; 68% and 78% in those with (n=19) and without (n=27) Ki-67 expression >50%; and 67% and 76% in those with (n=9) and without (n=37) p53 expression >50%. Median DOCRs in those with or without ≥1 high-risk features were 21.5 months (95% CI: 17.7, NE) and 19.2 months (95% CI:17.4, 42.8), respectively.

Landmark analyses indicated that most pts who were in CR at end of treatment (EOT) were progression free and alive at 18 months after EOT (PFS rate: 71.8%; OS rate: 83.0%). A trackable MRD clone was identified in 17/31 (54.8%) pts in CR at EOT. Among these pts, 11/12 (91.6%) with evaluable samples had undetectable MRD at C3. Exploratory data on B-cell recovery and Ig levels after EOT will be presented.

No new or unexpected safety signals were reported.

Conclusions: Glofitamab induces high response rates in pts with heavily pretreated R/R MCL, including those who have clinical and/or histological features associated with poor prognosis. Clinical and molecular remissions are achieved early in the course of treatment, with durable responses lasting beyond the length of the treatment.

Disclosures Phillips: *Genmab:* Consultancy; *TG Therapeutics:* Consultancy; *Gilead Sciences:* Consultancy; *Celgene:* Consultancy; *Kite/Gilead:* Consultancy; *Curis:* Consultancy; *ADC Therapeutics:* Consultancy; *Lymphoma & Myeloma Connect:* Honoraria; *Pharmacyclics/Janssen:* Research Funding; *AbbVie:* Research Funding; *Bayer:* Consultancy, Research Funding; *Genentech:* Consultancy; *Incyte:* Consultancy; *Pharmacyclics:* Consultancy; *Seattle Genetics:* Consultancy, Honoraria. **Trněný:** *Takeda, Bristol-Myers Squibb, Incyte, Abbvie, Amgen, Roche, Gilead Sciences, Janssen, MorphoSys, Novartis, Genmab, SOBI, Autolus, Caribou Biosciences:* Consultancy; *Janssen, Gilead Sciences, Takeda, Bristol-Myers Squibb, Amgen, Abbvie, Roche, MorphoSys, Novartis, SOBI, Swixx BioPharma:* Honoraria; *Gilead Sciences, Takeda, Bristol-Myers Squibb, Roche, Janssen, Abbvie, SOBI:* Other: Travel, Accommodations, Expenses. **Carlo-Stella:** *ADC Therapeutics, Roche, Sanofi:* Research Funding; *AstraZeneca, Celgene/Bristol-Myers Squibb, Incyte, Janssen Oncology, Takeda, Novartis, ADC Therapeutics, Roche, Gilead, SOBI, Merck Sharp & Dohme:* Honoraria; *Janssen Oncology:* Honoraria, Membership on an entity's Board of Directors or advisory committees; *Takeda:* Honoraria; *Genmab:* Membership on an entity's Board of Directors or advisory committees; *Abbvie:* Membership on an entity's Board of Directors or advisory committees; *ADC Therapeutics:* Consultancy, Honoraria, Research Funding; *Gilead:* Honoraria; *SOBI:* Honoraria, Membership on an entity's Board of Directors or advisory committees; *Merck Sharp & Dohme:* Honoraria, Membership on an entity's Board of Directors or advisory committees; *Celgene/BMS:* Honoraria, Membership on an entity's Board of Directors or advisory committees; *Karyopharm Therapeutics:* Membership on an entity's Board of Directors or advisory committees; *Sanofi:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees, Research Funding; *Roche:* Honoraria, Membership on an entity's Board of Directors or advisory committees, Research Funding; *AstraZeneca:* Honoraria, Membership on an entity's Board of Directors or advisory committees; *Novartis:* Honoraria, Membership on an entity's Board of Directors or advisory committees; *Scenic Biotech:* Membership on an entity's Board of Directors or advisory committees; *Incyte:* Honoraria; *Humanitas University, Milano (Italy):* Current Employment; *Sanofi, ADC Therapeutics:* Consultancy; *Sanofi, ADC Therapeutics, Celgene/Bristol-Myers Squibb, Karyopharm Therapeutics, Roche, Novartis, Scenic Biotech, Janssen Oncology, Merck Sharp & Dohme, SOBI, AbbVie, Genmab, AstraZeneca:* Membership on an entity's Board of Directors or advisory committees. **Zaucha:** *Takeda, BMS, Gilead, Novartis, Pfizer, Amgen, Roche, Janssen, BeiGene:* Consultancy; *BMS, Takeda:* Research Funding; *Pierre Fabre:* Honoraria; *Roche, AbbVie:* Membership on an entity's Board of Directors or advisory committees. **Wrobel:** *Roche:* Research Funding; *AstraZeneca:* Honoraria; *Abbvie, Amgen, Beigene, Gilead, Johnson and Johnson, Novartis, Roche:* Speakers Bureau. **Dickinson:** *Roche:* Consultancy, Honoraria, Speakers Bureau; *Adicet Bio:* Consultancy, Honoraria; *Genmab:* Consultancy, Honoraria, Speakers Bureau; *Novartis:* Consultancy, Honoraria, Speakers Bureau; *Kite:* Consultancy, Honoraria, Speakers Bureau; *Gilead:* Consultancy, Honoraria, Speakers Bureau. **Tani:** *Roche, Abbvie, Jansen-Cilag, Incyte, BeiGene, Takeda:* Membership on an entity's Board of Directors or advisory committees; *AstraZeneca SpA:* Membership on an entity's Board of Directors or advisory committees. **Crump:** *Roche:* Research Funding; *Canada's Drug Agency (CADTH):* Honoraria; *Epizyme/Ipsen:* Research Funding; *Kyte/Gilead:* Honoraria. **Bartlett:** *Genmab:* Membership on an entity's Board of Directors or advisory committees, Research Funding; *Gilead:* Research Funding; *Celegne:* Research Funding; *BMS:* Research Funding; *Kite Pharm:* Membership on an entity's Board of Directors or advisory committees, Research Funding; *Millennium:* Research Funding; *Roche/Genentech:* Membership on an entity's Board of Directors or advisory committees, Research Funding; *Washington University School of Medicine:* Current Employment; *AbbVie:* Membership on an entity's Board of Directors or advisory committees; *Pfizer:* Membership on an entity's Board of Directors or advisory committees; *Seattle Genetics:* Research Funding; *Forty Seven:* Research Funding; *ADC Therapeutics:* Research Funding; *Foresight Diagnostics:* Membership on an entity's Board of Directors or advisory committees; *Pharmacyclics:* Research Funding; *Janssen:* Research Funding; *Autolus:* Research Funding. **Martínez-Lopez:** *Roche:*

Consultancy, Honoraria; *Amgen:* Consultancy, Honoraria; *BMS:* Consultancy, Honoraria; *Janssen:* Consultancy, Honoraria, Research Funding; *Incity:* Research Funding; *Kite:* Consultancy, Honoraria; *Pfizer:* Consultancy, Honoraria, Research Funding. **Corradini:** *AbbVie:* Other: Honoraria (for consultancy, participation in advisory boards, or lectures); support for travel and accommodations; *Takeda:* Other: Honoraria (for consultancy, participation in advisory boards, or lectures); support for travel and accommodations; *SOBI:* Other: Honoraria (for consultancy, participation in advisory boards, or lectures); *Pfizer:* Other: Honoraria (for consultancy, participation in advisory boards, or lectures); *Roche:* Other: Honoraria (for consultancy, participation in advisory boards, or lectures); support for travel and accommodations; *Sanofi:* Other: Honoraria (for consultancy, participation in advisory boards, or lectures); *Incyte:* Other: Honoraria (for consultancy, participation in advisory boards, or lectures); *Janssen:* Other: Honoraria (for consultancy, participation in advisory boards, or lectures); support for travel and accommodations; *Kyowa Kirin:* Other: Honoraria (for consultancy, participation in advisory boards, or lectures); *Novartis:* Other: Honoraria (for consultancy, participation in advisory boards, or lectures); support for travel and accommodations; *Amgen:* Other: Honoraria (for consultancy, participation in advisory boards, or lectures); support for travel and accommodations; *Celgene:* Other: Honoraria (for consultancy, participation in advisory boards, or lectures); support for travel and accommodations; *GlaxoSmithKline:* Other: Honoraria (for consultancy, participation in advisory boards, or lectures); *Daiichi Sankyo:* Other: Honoraria (for consultancy, participation in advisory boards, or lectures); *Gilead/Kite:* Other: Honoraria (for consultancy, participation in advisory boards, or lectures); support for travel and accommodations; *Bristol Myers Squibb:* Other: Support for travel and accommodations. **Mulvihill:** *F. Hoffmann-La Roche Ltd:* Current Employment, Current equity holder in publicly-traded company, Divested equity in a private or publicly-traded company in the past 24 months. **Bottos:** *F. Hoffmann-La Roche Ltd:* Current Employment, Current equity holder in private company, Current holder of *stock options* in a privately-held company, Ended employment in the past 24 months. **Kaufman:** *Genentech:* Current Employment; *Roche/Genentech:* Current equity holder in publicly-traded company. **Relf:** *F-star Therapeutics:* Divested equity in a private or publicly-traded company in the past 24 months; *F. Hoffmann-La Roche Ltd:* Current equity holder in publicly-traded company, Divested equity in a private or publicly-traded company in the past 24 months; *Roche Products Ltd:* Current Employment. **Bene Tchaleu:** *Genentech, Inc.:* Current Employment, Current holder of *stock options* in a privately-held company. **Bazeos:** *F. Hoffmann-La Roche Ltd:* Current Employment. **Lundberg:** *F. Hoffmann-La Roche Ltd:* Current Employment, Current equity holder in publicly-traded company, Current holder of *stock options* in a privately-held company, Patents & Royalties. **Morschhauser:** *Roche/Genentech:* Consultancy, Honoraria, Other: Payment for Expert Testimony, Honoraria for Scientific Lectures; *Genmab:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees; *Novartis:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees; *AstraZeneca:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees; *Epizyme:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees; *AbbVie:* Consultancy, Membership on an entity's Board of Directors or advisory committees; *Bristol Myers Squibb:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees; *Kite/Gilead Sciences:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees; *Eisai:* Honoraria; *Chugai:* Honoraria; *Servier:* Consultancy.

Off Label 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.

https://doi.org/10.1182/blood-2024-200018