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ORAL ABSTRACTS

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

Mosunetuzumab Monotherapy Demonstrates Durable Efficacy with a Manageable Safety Profile in Patients with Relapsed/Refractory Follicular Lymphoma Who Received ≥2 Prior Therapies: Updated Results from a Pivotal Phase II Study

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Abstract Background: Mosunetuzumab (Mosun) is a CD20xCD3 T-cell engaging bispecific monoclonal antibody (Bi-mAb) that redirects T cells to eliminate malignant B cells. Mosun is the first Bi-mAb approved for the treatment of patients (pts) with relapsed/refractory (R/R) follicular lymphoma (FL; EMA 2022) and is a fixed-duration treatment that can be administered in an outpatient setting. In a Phase II study (NCT02500407), Mosun demonstrated a high rate of complete response (CR) with a manageable safety profile in pts with R/R FL who had received ≥2 prior therapies (Budde et al. Lancet Oncol 2022). Here, we present updated data for this cohort after a median follow-up of 27 months.
Methods: Pts with FL grade (gr) 1-3a, who had received ≥2 prior therapies (including an anti-CD20 antibody and an alkylator) were enrolled. Intravenous Mosun was administered in 21-day cycles with step-up dosing in Cycle (C) 1 (Day [D] 1, 1mg; C1D8, 2mg; C1D15/C2D1, 60mg; C3D1 and onwards, 30mg). Pts achieving a CR by C8 completed treatment without additional cycles; those with a partial response or stable disease received a further nine cycles (17 total). Hospitalization following infusion was not required. The primary endpoint was CR rate determined by an Independent Review Committee. Post-hoc analyses were performed to compare efficacy outcomes with Mosun vs last prior therapy, and assess the correlation between cytokine release syndrome (CRS) and tumor response.
Results: Ninety pts with R/R FL and ≥2 prior therapies were enrolled. Median age was 60 years (range: 29-90), and 77% of pts had stage III/IV disease. Median number of prior lines of therapy was three (range: 2-10); 53% of pts were double refractory to prior anti-CD20 therapy and alkylator therapy; and 52% of pts had progressive disease within 24 months from the start of their first-line therapy. As of May 20, 2022, median time on study was 26.7 months (range: 2.0-36.2); 54 pts (60%) had completed

initial treatment and 36 pts (40%) had discontinued initial treatment (25 pts [28%] due to progressive disease). Two pts (2%) were undergoing retreatment, 72 pts (80%) were in follow-up, and 16 pts (18%) had discontinued the study.
In all 90 pts, investigator (INV)-assessed objective response rate (ORR) and CR rate were 77.8% (95% CI: 67.8-85.9) and 60.0% (95% CI: 49.1-70.2), respectively. Median duration of response (DOR) and duration of CR (DOCR) were not reached (NR); 79.5% of complete responders remained in remission for at least 24 months based on Kaplan-Meier estimates. Median progression-free survival (PFS) per INV assessment was NR; 24-month PFS was 51.4% (95% CI: 39.4-63.3). The efficacy of Mosun was compared with that of pts' last prior therapy: most pts (63%) received chemoimmunotherapy as their last prior therapy, and the remainder received PI3K inhibitor-containing regimens (8%), anti-CD20 antibodies plus lenalidomide (2%), CAR-T therapy (2%), or other therapies. Response rates, PFS, DOR, DOCR and time to next therapy or death were all improved with Mosun compared with last prior therapy (**Table; Figure**).
No new CRS events, or fatal, serious, or gr ≥3 adverse events (AEs) were reported since the previous analysis, and no evidence of chronic toxicity was observed. Overall, the rate of AEs leading to discontinuation was low (4.4%) and no treatment-related gr 5 AEs were observed. CRS events (44.4% of pts) were mostly confined to C1 (84.5% of events) and 97.2% were gr 1/2 in severity; all CRS events resolved. No correlation was observed between the occurrence of CRS and tumor response. ORR was 77.5% and 78.0%, respectively, in pts with or without CRS events.
Conclusions: In this updated analysis, with a median follow-up of 27 months, durable responses continued to be observed with Mosun in pts with R/R FL. Compared with pts' last prior therapy, Mosun demonstrated higher ORR and CR rates, with longer DOR, DOCR, PFS and time to next therapy, although limitations should be noted for retrospective comparisons and the absence of standardized imaging assessment for the last prior therapy. The safety profile, characterized by a low rate of AEs leading to treatment discontinuation and predominantly low-grade CRS events, was consistent with previous reports and supports the administration of Mosun as an outpatient regimen. Clinical response was observed regardless of occurrence of CRS, suggesting the Mosun dose and schedule used is effective at dissociating cytokine toxicity from treatment efficacy.

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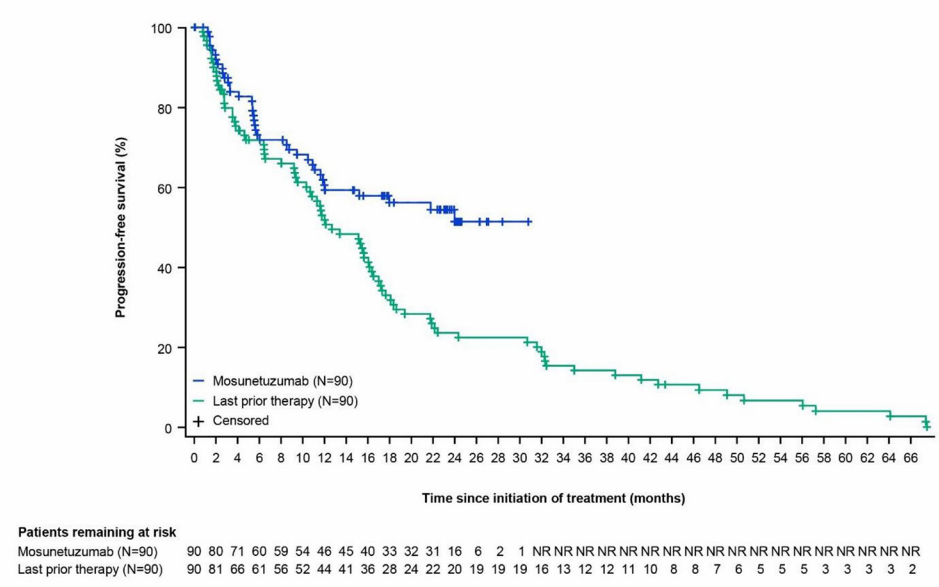
Table: Summary of efficacy with mosunetuzumab and last prior therapy received

Efficacy endpoints assessed by investigators	R/R FL N=90	
	Mosunetuzumab	Last prior therapy
ORR, % (95% CI)	77.8 (67.8–85.9)	55.6 (44.7–66.0)
CR, % (95% CI)	60.0 (49.1–70.2)	35.6 (25.7–46.4)
Median DOR, months (95% CI)	NR (22.8–NR)	11.8 (10.3–16.9)
24-month event-free rate, % (95% CI)	60.8 (46.8–74.2)	28.6 (16.0–41.3)
Median DOCR, months (95% CI)	NR (NR–NR)	15.1 (11.2–26.3)
24-month event-free rate, % (95% CI)	79.5 (66.7–92.2)	34.4 (17.9–50.8)
Median PFS, months (95% CI)	NR (12.0–NR)	12.6 (10.3–16.3)
24-month event-free rate, % (95% CI)	51.4 (39.4–63.3)	23.5 (14.5–32.5)
Median TTNT, months (95% CI)	NR (18.0–NR)	16.8 (14.4–20.4)
24-month event-free rate, % (95% CI)	55.3 (44.6–66.1)	33.3 (23.6–43.1)

CI, confidence interval; CR, complete response; DOCR, duration of complete response; DOR, duration of response in all responders; FL, follicular lymphoma; NR, not reached; ORR, objective response rate; PFS, progression-free survival; R/R, relapsed/refractory; TTNT, time to next therapy or death.

Figure: Progression-free survival (investigator assessed) with mosunetuzumab vs last prior therapy



NR, not reached.

Figure 1.

Gilead/Kite, Genmab, Janssen, MEI, Morphosys, Novartis, Takeda: Honoraria; *BMS, Caribou Biosciences, Epizyme, Genentech, Gilead/Kite, Genmab, Janssen, IGM Biosciences, Novartis, Takeda:* Research Funding. **Wei:** *F. Hoffmann La Roche, Ltd.:* Current equity holder in private company, Current holder of *stock options* in a privately-held company, Patents & Royalties; *Genentech, Inc.:* Current Employment. **Yin:** *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; *Genentech, Inc.:* Current Employment, Patents & Royalties. **To:** *Genentech, Inc.:* Current Employment, Current equity holder in publicly-traded

company. **Huang:** *F. Hoffmann La Roche, Ltd:* Current Employment. **Penuel:** *Genentech, Inc.:* Current Employment, Current equity holder in publicly-traded company.

OffLabel Disclosure: Mosunetuzumab is a CD20xCD3 bispecific antibody that redirects T cells to engage and eliminate malignant B cells. Mosunetuzumab is an investigational agent in the United States.

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