Abstract: S233

Title: MOSUNETUZUMAB DEMONSTRATES CLINICALLY MEANINGFUL OUTCOMES IN HIGH-RISK PATIENTS WITH HEAVILY PRE-TREATED R/R FL AFTER ≥3 YEARS OF FOLLOW-UP: SUBGROUP ANALYSIS OF A PIVOTAL PHASE II STUDY

Abstract Type: Oral Presentation

Session Title: Follicular and mantle cell lymphoma - Role of bispecifics

Background:

In a pivotal Phase II study (NCT02500407) mosunetuzumab, a CD20xCD3 T-cell engaging bispecific antibody, demonstrated high rates of complete responses (CRs) with a manageable safety profile in patients (pts) with relapsed/refractory (R/R) follicular lymphoma (FL) and ≥2 prior lines of therapy (Budde, et al. Lancet Oncol 2022; Schuster, et al. Blood 2023).

Aims:

To present a subgroup analysis of the Phase II study, evaluating the efficacy and safety of mosunetuzumab monotherapy in high-risk pts with heavily pre-treated R/R FL after ≥3 years of follow-up.

Methods:

Eligible pts with R/R FL Grade (Gr) 1–3a and ≥2 prior therapies were enrolled; methods were previously described (Budde, et al. Lancet Oncol 2022). All pts provided informed consent. Subgroups evaluated for efficacy and safety included pts with a history of progression of disease within 24 months (POD24) from the start of first-line therapy, pts receiving mosunetuzumab in third (3L) vs fourth or later line (4L+), and pts aged ≥65 years. Endpoints included complete response (CR; as best response) rate, objective response rate, median duration of response, duration of CR (DOCR), progression-free survival (PFS), overall survival, time-to-next-treatment (TTNT) and safety.

Results:

As of May 2, 2023, 90 pts had received mosunetuzumab; 52% had POD24, 61% had received mosunetuzumab as 4L+ therapy, and 33% were aged ≥65 years. CR rates in pts with POD24 (60%), pts aged ≥65 years (67%) and 4L+ pts (55%; Table) were consistent with the overall population (60%). Median DOCR was not reached (NR) in the overall population, in pts with POD24 and pts aged ≥65 years, but was 33.0 months in 4L+ pts. Also, a numerically lower 30-month DOCR rate was observed in 4L+ (66%) vs 3L (77%) pts. The 3-year PFS rate was 44% in pts with POD24 and 47% in pts aged ≥65 years, consistent with the overall population (43%). A lower 3-year PFS rate was observed in 4L+ (36%) vs 3L (54%) pts. The median TTNT was NR in any of the high-risk subgroups. The safety profile across subgroups was consistent with the overall safety cohort. The incidence of cytokine release syndrome events was modestly higher in pts with POD24 (51%) and 4L+ pts (47%) compared with the overall safety cohort (44%), but lower in pts aged ≥65 years (30%). In the overall safety cohort, any-grade infections occurred in 51% of pts; after Cycle (C) 8, 8 events were reported in 8 pts (C9: 2/16 [12.5%], C10: 2/15 [13.3%], C12: 2/13 [15.4%], C13: 1/12 [8.3%], C17: 1/11 [9.1%]). Gr ≥3 infections were observed in 17% of pts. Most common Gr ≥3 infections were pneumonia (3%), upper respiratory tract infection (2%), septic shock (2%) and COVID-19 (2%). Most serious infections (14/19 [74%]) occurred in the first 4 cycles; after C8, 3 events were reported in 3 pts (C10: 1/15 [6.7%], C12: 1/13 [7.7%], C17: 1/11 [9.1%]). Serious infections concurrent with neutropenia were rare (1%). Adverse events of hypogammaglobulinemia were reported in 2% of pts; immunoglobulin treatment was initiated in 9% of pts. Biomarkers, including peripheral blood T cells, natural killer cells, cytokines, tumor-localized CD20+ B cells and CD8+ T cells, were similar across subgroups, consistent with the observed clinical activity.

Summary/Conclusion:

In this subgroup analysis, fixed-duration mosunetuzumab monotherapy showed durable remissions and clinically meaningful survival outcomes in high-risk pts with heavily pre-treated R/R FL, including those with POD24. The safety profile was manageable and consistent across all subgroups, including pts aged ≥65 years, and supports outpatient administration.

Table. Efficacy outcomes across subgroups

Subgroups	POD24 status		Line of therapy		Age		Overall population (N=90)
Efficacy endpoints	POD24 (n=47)	Non-POD24 (n=43)	3L therapy (n=35)	4L+ therapy (n=55)	<65 years (n=60)	≥65 years (n=30)	
ORR, n (%) [95% CI]	38 (80.9) [66.7–90.9]	32 (74.4) [58.8–86.5]	30 (85.7) [69.7–95.2]	40 (72.7) [59.0–83.9]	45 (75.0) [62.1–85.3]	25 (83.3) [65.3–94.4]	70 (77.8) [67.8–85.9]
CR, n (%) [95% CI]	28 (59.6) [44.3–73.6]	26 (60.5) [44.4–75.0]	24 (68.6) [50.7–83.2]	30 (54.5) [40.6–68.0]	34 (56.7) [43.2–69.4]	20 (66.7) [47.2–82.7]	54 (60.0) [49.1–70.2]
Median DOR, months (95% CI)	NR (10.6–NE)	35.9 (20.7–NE)	NR (11.9–NE)	34.5 (16.5–NE)	NR (16.5–NE)	35.9 (13.7–NE)	35.9 (18.7–NE)
Median DOCR, months (95% CI)	NR (18.7–NE)	NR (31.5–NE)	NR (NE–NE)	33.0 (18.7–NE)	NR (33.0–NE)	NR (18.7–NE)	NR (33.0–NE)
Median PFS, months (95% CI)	17.8 (12.0–NE)	26.3 (11.8–NE)	NR (12.0–NE)	18.1 (11.8– 37.3)	17.8 (9.4–NE)	25.8 (15.2–NE)	24.0 (12.0–NE)
36-month PFS, % (95% CI)	43.9 (28.2–59.5)	42.0 (25.0–59.0)	54.3 (37.0–71.5)	36.3 (21.8–50.7)	41.5 (27.3–55.8)	46.9 (28.1–65.8)	43.2 (31.8–54.7)
Median OS, months (95% CI)	NR (NE)	NR (NE)	NR (NE)	NR (NE)	NR (NE)	NR (NE)	NR (NE)
36-month OS, % (95% CI)	84.2 (72.1–96.3)	81.0 (69.1–92.9)	84.9 (72.7–97.2)	81.7 (70.5–92.8)	81.2 (70.6–91.9)	86.4 (74.0–98.8)	82.9 (74.6–91.2)
Median TTNT, months (95% CI)	NR (16.2–NE)	NR (16.0–NE)	NR (18.1–NE)	NR (13.9–NE)	19.4 (9.7–NE)	NR (NE)	NR (19.4–NE)

3L, third line; 4L+, fourth or later line; CI, confidence interval; CR, complete response; DOCR, duration of complete response; DOR, duration of response; NE, not evaluable; NR, not reached; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; POD24, progression of disease within 24 months from the start of first-line therapy; TTNT, time-to-next-treatment.

Keywords: Follicular lymphoma, Antibody, Bispecific