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PROMISING TOLERABILITY AND EFFICACY RESULTS FROM DOSE-ESCALATION IN AN ONGOING PHASE IB/II STUDY OF MOSUNETUZUMAB WITH POLATUZUMAB VEDOTIN FOR RELAPSED/REFRACTORY B-CELL NON-HODGKIN'S LYMPHOMA

Topic: 19. Aggressive Non-Hodgkin lymphoma - Clinical

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Background:

Mosunetuzumab (M), a full-length, humanized, IgG1 bispecific antibody targeting CD20 and CD3, has shown promising efficacy and safety as monotherapy for relapsed/refractory (R/R) B-cell non-Hodgkin's lymphoma (B-NHL) (NCT02500407; Assouline, et al. ASH 2020). The combination of M with the anti-CD79b antibody-drug conjugate, polatuzumab vedotin (Pola), showed synergistic anti-lymphoma activity in a mouse xenograft model. These data supported a Phase Ib/II, open-label, multicenter trial of M-Pola for R/R B-NHL (GO40516, NCT03671018).

Aims: To present early clinical data from the Phase Ib cohort of the GO40516 study.

Methods: Patients (pts) with R/R follicular lymphoma (FL; grade [Gr] 1–3a) or aggressive NHL (aNHL), including *de novo* diffuse large B-cell lymphoma (DLBCL), transformed FL (trFL) and FL Gr 3b (FL3b), received Cycle (C) 1 step-up doses of M on Day (D) 1 (1mg) and D8 (2mg), the target dose on C1D15, then continued at the target dose on C2D1 onwards. M was given every 21 days for eight cycles (or 17 cycles if stable disease or a partial response after C8). Pola (1.8mg/kg) was given with M on D1 of each cycle for six cycles.

Results: As of November 17, 2020, 22 pts had received M-Pola (M target doses: 9mg, n=7; 20mg, n=3; 40mg, n=6; 60mg [with D1 dose of 30mg from C3 onwards], n=6). Pts had DLBCL (n=12), FL (n=3), FL3b (n=3) and trFL (n=4). Pt characteristics include: median age of 70 (38–81) years; median of 3 (1–10) prior lines of therapy; 7 (32%) pts had prior chimeric antigen-receptor T-cell (CAR-T) therapy; 17 (77%) and 19 (86%) pts had disease refractory to last prior therapy and prior anti-CD20 therapy, respectively. Median follow-up duration was 9.6 (0.7–23.7) months. The most frequent treatment-related adverse events (AEs) were neutropenia (45.4%), fatigue, nausea and diarrhea (all 36.4%). Cytokine release syndrome (CRS) was observed in 2 pts (9.1%; both Gr 1 by American Society for Transplantation and Cellular Therapy 2019 criteria). One dose-limiting toxicity (Gr 3 new onset atrial fibrillation) was observed in the 40mg cohort. The maximum tolerated dose was not exceeded. The most common Gr ≥3 and serious AEs were both neutropenia, observed in 8 (36.4%) and 3 (13.6%) pts, respectively. Two (9.3%) Gr 5 AEs occurred: sudden cardiac death (n=1) and respiratory failure (n=1); neither was deemed treatment related. No immune effector cell-associated neurotoxicity was observed. The **Table** shows preliminary efficacy data.

Image:

Table: Preliminary efficacy in the dose-escalation cohort.

Response, n (%)	All pts (n=22)	aNHL pts (n=19)	Post-CAR-T pts (n=7)	FL pts (n=3)
Overall response rate	15 (68.2)	12 (63.2)	4 (57.1)	3 (100)
Complete response rate	12 (54.5)	9 (47.4)	2 (28.6)	3 (100)

Summary/Conclusion: These data indicate that M-Pola has an acceptable safety profile, with no Gr ≥2 CRS observed, and promising efficacy in pts with R/R NHL with predominantly aggressive disease. The Phase II expansion cohort in R/R DLBCL is ongoing, with no mandatory hospitalization required.

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