AdvanTIG-101: A Phase 1b/2 Study of Ociperlimab (anti-TIGIT) Plus Tislelizumab (anti-PD-1) or Rituximab in Relapsed/Refractory Diffuse Large B-Cell Lymphoma

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Background: PD-L1 expression is associated with worse clinical outcome in pts with R/R DLBCL. In preclinical and clinical studies of solid tumors, co-inhibition of PD-1 and T-cell immunoreceptor with immunoglobulin and immunoreceptor tyrosine-based inhibitor motif domains (TIGIT) enhanced antitumor activity of anti-PD-1. Ociperlimab (OCI; BGB-A1217) is a humanized monoclonal antibody (mAb) that binds TIGIT with high specificity and affinity, blocking the interaction with its ligands on tumor cells (TCs). TIGIT blockade may also promote NK cell activation and may synergize the therapeutic mAb-mediated (eg, rituximab [ritux]) ADCC activity.

Aims: AdvanTIG-101 (NCT05267054) investigated the efficacy and safety of OCI + the anti-PD-1 tislelizumab (TIS) or ritux in R/R DLBCL.

Methods: Eligible pts (aged ≥18 with R/R DLBCL, ECOG PS ≤2) were allocated to 2 cohorts to receive OCI + TIS (Cohort 1) or OCI + ritux (Cohort 2). Primary objectives were safety/tolerability and RP2D; other objectives included preliminary antitumor activity (per investigator), PK, host immunogenicity, and association of PD-L1 expression and other exploratory biomarkers with antitumor activity.

Results: As of Aug 30, 2024, 53 pts (n=24, Cohort 1; n=29, Cohort 2) were enrolled and treated. Median age was 65; 81.1% of pts had non-germinal center B-cell subtype; 84.9% had advanced disease stage (III-IV) at study entry; median prior line of therapy was 1 (range, 1–6); 54.7% were refractory to last line of therapy. Median study follow-up was 9.0 months (range, 0.2–28.0).

OCI + TIS or OCI + ritux was generally well tolerated and toxicities were manageable (**Table**). In Cohort 1, the most common TEAEs were neutrophil count decreased (8/24; 33.3%; n=4, Grade ≥3), WBC count decreased (7/24; 29.2%; n=3, Grade ≥3) and lymphocyte count decreased (6/24; 25.0%; n=1, Grade ≥3). In Cohort 2, the most common TEAEs were neutrophil count decreased (9/29; 31.0%; n=3, Grade ≥3), anemia (9/29; 31.0%; n=1, Grade ≥3), WBC count decreased (7/29; 24.1%; n=1, Grade ≥3), and platelet count decreased (7/29; 24.1%; n=0, Grade ≥3). Three pts (Cohort 2) experienced TR-TEAEs leading to treatment discontinuation (cardiac failure; immune-mediated enterocolitis; interstitial lung disease). One pt experienced a TR-TEAE leading to death (cardiac failure; Cohort 2).

Overall, OCI + TIS or OCI + ritux showed limited antitumor activity. ORR was 17.4% (95% CI, 5.0-38.8%) in Cohort 1 (3 CR, 1 PR) and 18.5% (6.6-38.1%) in Cohort 2 (2 CR, 3 PR). Median overall time to response was ~2 months.

PK data for OCI were available for all pts and were consistent with previously reported OCI PK data. Of 47 tested pts, 33 (70.2%) had ≥1% PD-L1$^+$ TCs, including 5 pts with high expression of PD-L1 (≥50%). 41/44 tested pts (93.2%) had ≥1% TIGIT$^+$ immune cells. Although TIGIT was rarely expressed in TCs in previous reports, 18/44 (40.9%) pts had TIGIT positive staining in ≥1% TCs; 3 pts had ≥50% TIGIT$^+$ TCs.

Conclusion: OCI + TIS or OCI + ritux showed acceptable safety and tolerability in R/R DLBCL. Limited antitumor activity was observed; additional combination strategy with selected biomarkers may be explored to expand this benefit.

Safety Table

n (%)	**Cohort 1 (n=24)**	**Cohort 2 (n=27)**
Any TEAE	24 (100)	28 (96.6)
Grade ≥3	10 (41.7)	13 (44.8)
Leading to treatment modification	1 (4.2)	8 (27.6)
Leading to discontinuation	1 (4.2)	4 (13.8)
Leading to death	2 (8.3)	2 (6.9)
TR-TEAE, any	18 (75.0)	25 (86.2)
Grade ≥3	5 (20.8)	11 (37.9)

SAE, any	9 (37.5)	8 (27.6)
Treatment related	5 (20.8)	6 (20.7)
DLT	1 (16.7)*	0
imAE	4 (16.7)	5 (17.2)
IRR	4 (16.7)	1 (3.4)

*Among the 6 DLT-evaluable patients; febrile neutropenia.

AE, adverse event; DLT, dose-limiting toxicity; imAE, immune-mediated adverse event; IRR, infusion-related reaction; SAE, serious adverse event; TEAE, treatment-emergent adverse event; TR-TEAE, treatment-related treatment-emergent adverse event.