Abstract: P1157

Title: PHASE II STUDY OF GLOFITAMAB, POSELTINIB AND LENALIDOMIDE IN PATIENTS WITH RELAPSED/REFRACTORY DIFFUSE B CELL LYMPHOMAS

Abstract Type: Poster Presentation

Session Title: Aggressive Non-Hodgkin lymphoma - Clinical

Background:

Despite the groundbreaking introduction of rituximab for the treatment of diffuse large B cell lymphoma (DLBCL), approximately 30% of the patients ultimately experience refractory / relapse (R/R) disease and so far myriads attempts to improve survival outcomes have not yielded firm positive results.

Glofitamab is a T-cell engaging bispecific antibody with a novel 2:1 configuration conferring bivalency for CD20 and monovalency for CD3 that is both effective and tolerable in patients with R/R B-cell lymphomas. On the other hand, it is a well-known fact that the lenalidomide plus BTK inhibitor combination has a synthetic lethality against DLBCL. One of the major advantage of such combination is the absence of cytotoxic agents that may lead to unmanageable toxicities and dose limitations.

Aims:

We planned to test the efficacy and safety of glofitamab in combination with lenalidomide and poseltinib.

Methods:

This is an open-label single arm phase II study with intent to recruit 76 participants (ClinicalTrials.gov Identifier: NCT05335018). CD20 positive DLBCL (DLBCL NOS, HGBCL, trFL) patients older than 19 years of age with history of exposure to anti-CD20 agents are deemed eligible for screening. Major exclusion criteria include (1) BCL6(-) and MYC(+) disease; (2) previous exposure to glofitamab; (3) 4 or more lines of prior therapies.

The treatment schedules and durations are shown in Figure. To mitigate the risk of glofitamab associated cytokine release syndrome, obinutuzumab premedication and cycle 1 step-up dosing was implemented. From cycle 2, glofitama b 30mg is given on day 1 of each cycle. Lenalidomide 20mg is given daily from day 1-14 of each cycle. Poseltinib 40mg is given twice daily from day 1-21 of each cycle. Each cycle is 28 days. The primary endpoint is overall response rate. The secondary endpoints include duration of response, complete response rate, progression free survival, overall survival and treatment related adverse events.

Results:

Herein, we report the initial safety and efficacy data of the first 6 patients in the safety cohort (Table). The median time from first diagnosis to study enrollment was 25 months, with median of 2 prior lines of therapy (range 1-3).

There was 1 event of cytokine release syndrome grade 1, which resolved without sequalae. The most common adverse event was skin rash (2 grade 2, 1 grade 1) which did not require study drug modifications. Neutropenia occurred in 2 patients, but no dose adjustment was necessary. One patient with a previous history of prior COVID19 infection after TNB-486 (CD19/CD3 bispecific) clinical trial, despite receiving vaccination prior to this study enrollment, experienced COVID19 reactivation after cycle 1. Glofitamab D8 and D15 doses were skipped, and both lenalidomide and posetinib were stopped for 14 days. The patient recovered and underwent full doses of subsequent therapies. After DSMB clearance, we are now enrolling patients in the expansion phase.

For tumor response, all 6 patients achieved objective response per Lugano criteria at the end of cycle 2 (3 CR, 3 PR). Based on the best overall response, there were 4 confirmed CR and the median duration of response 4 months (Table).

Summary/Conclusion: Glofitamab, poseltinib and lenalidomide (GPL) is promising combination for the

treatment of R/R DLBCL.

(Table)

Age/ Sex	Disease	Previous treatment history	Diagnosis to study enrollment	Adverse events C1	Adverse events C2	Adverse events C3	Interim response evaluation after C2	Current status
70/M	DLBCL, nGCB	RCHOP#6	30M	None	None	Skin rash, Gr 2	CR	CR Consent withdrawal after C7
70/F	DLBCL, nGCB	RCHOP#6→ PBR#2 → ICE#2	18M	Neutropenia, Gr4 Thrombocytopenia, Gr3	None	Neutropenia, Gr4	PR	CR C9 ongoing
60/F	DLBCL, nGCB	RCHOP#6→ ICE#6 → PBR#3	21M	Skin rash, Gr1	None	Skin rash, Gr 2	CR	CR Consent withdrawal after C4
43/M	DLBCL, nGCB	RCHOP#6 →ICE#3+ASCT →TNB-486 trial#3	42M	COVID19 reactivation	None	None	PR	PD Off trial
42/M	tDLBCL	RCHOP#6	52M	Skin rash, Gr 1	Skin rash, Gr 1	Skin rash, Gr 1	CR	CR C5 ongoing
70/F	DLBCL, GCB	RCHOP#2	2M	CRS, Gr 1	Neutropenia, Gr 3 Anemia, Gr 1	None	PR	PR C4 ongoing

Keywords: Refractory, DLBCL, Bispecific