Abstract: P1117

Title: GLOFITAMAB PLUS R-CHOP OR POLATUZUMAB VEDOTIN-R-CHP IS DELIVERABLE AND YIELDS HIGH OVERALL RESPONSE IN PATIENTS <=65 YEARS OF AGE WITH HIGH-RISK DLBCL OR HGBL: INTERIM ANALYSIS OF THE COALITION STUDY

Abstract Type: Poster Presentation

Session Title: 19. Aggressive Non-Hodgkin lymphoma - Clinical

Background:

More effective treatments are needed for patients (pts) with high-risk (HR) DLBCL, where response at 3-years is ~50%. Intensification of R-CHOP chemotherapy has not improved outcomes. Furthermore, pts with HR disease are frequently excluded from trials due to disease burden and the need for rapid treatment initiation, an independent predictor of poor outcome (Maurer, JCO 2018).

Glofitamab is a CD20/CD3 bispecific antibody achieving a 39% complete remission (CR) rate in R/R DLBCL (Dickinson, NEJM 2023).

Aims:

We present an interim analysis of an ongoing investigator-initiated, parallel-arm, multi-centre phase I/II study of glofitamab in combination with R-CHOP or polatuzumab vedotin-R-CHP in younger pts with HR DLBCL.

Methods:

Eligible pts include untreated DLBCL, age 18-65 years, and at least one HR feature: IPI ≥3, NCCN-IPI ≥4, or proven double-hit status. To minimise treatment delay, enrolment is allowed after 1 cycle of R-CHOP and ECOG<4 at baseline or <2 at C2 is permitted. Pts receive 5 cycles of glofitamab (2.5 mg & 10 mg step-up in C2, 30 mg in C3-6) in combination with either R-CHOP (Arm A) or Pola-R-CHP (Arm B), followed by 2 cycles of glofitamab consolidation.

Primary endpoints are safety, relative dose intensity (RDI) and rates of treatment discontinuation. Responses are evaluated by Lugano criteria after cycles 2, 4 and 6 and then 3-6 monthly. Adverse events (AEs) are graded using CTCAE V5.0, except cytokine-release syndrome (CRS) and neurotoxicity (ICANS) graded by ASTCT criteria.

Results:

Fifty-five of a planned 80 pts are enrolled; 47 have received at least one dose of study treatment at data cut-off Nov 1, 2022 (25 Arm A, 22 Arm B). Of treated pts, 42 (89%) have *de novo* DLBCL/HGBL and 5 (11%) have transformed indolent lymphoma. Median age was 52 years (range 24-65), IPI was ≥3 in 81%, NCCN-IPI was ≥4 in 81%, and 96% of patients had stage III-IV disease. The median total metabolic tumour volume was 673 cm^3 (IQR 249-1221 cm^3). Median time from diagnosis to first dose of R-CHOP was 15 days (IQR 11-21.5).

Grade (Gr) ≥3 AEs were seen in 10/25 (40%) (Arm A) and 11/21 (52%) (Arm B). There were no Gr 5 AEs. Febrile neutropenia was observed in 1/25 (4%) and 6/21 (29%) and CRS Gr 1 in 5/25 (20%) and 5/21 (24%), respectively. There was 1 episode of Gr 2 CRS in Arm A after 10 mg glofitamab and no Gr 3-4 events. Peripheral neuropathy was limited to Gr 1-2 and occurred in 11/25 (44%) and 5/21 (24%) respectively. No ICANS was observed.

The RDI was ≥90% for cyclophosphamide, doxorubicin, polatuzumab vedotin, vincristine and glofitamab in 93%, 93%, 100%, 76% and 88% of patients, respectively. There was 1 dose interruption of doxorubicin following a myocardial infarction, and 3 interruptions to glofitamab dosing, 2 for infection and 1 for rash.

41 treated pts had at least 1 efficacy assessment, with best overall response rate 100%. Of 25 pts who reached the

end of induction (EOI) assessment, 19 (76%) demonstrated CR, 5 (20%) PR and 1 (5%) PD. To date, only one patient had PD during post-treatment follow up (best response CR). At a median follow up of 3.7 months (mo), the estimated PFS at 6-mo was 91% (Figure). Of the 5 pts with PR at EOI, none has progressed with median follow up 6.1 mo.

Summary/Conclusion:

Glofitamab with R-CHOP or Pola-R-CHP was deliverable with moderate rates of low-grade CRS and maintenance of RDI. The ability to enrol after 1 cycle of R-CHOP resulted in short time to treatment initiation and pragmatic inclusion of pts with high burden disease. Efficacy appears promising in this HR patient population. Updated results and ctDNA analysis will be presented.