Abstract: S237

Title: ENGLUMAFUSP ALFA (CD19/4-1BBL) COMBINED WITH GLOFITAMAB IS SAFE AND SHOWS HIGH EFFICACY IN PATIENTS WITH R/R AGGRESSIVE B-NHL: FINAL RESULTS OF THE DOSE-ESCALATION PART OF PHASE1 TRIAL BP41072

Abstract Type: Oral Presentation

Session Title: Aggressive lymphoma - Targeted drug therapy

Background:

Glofitamab (anti-CD20xCD3) has demonstrated significant efficacy in patients (pts) with relapsed/refractory B-cell Non-Hodgkin Lymphoma (r/r B-NHL) and is approved after at least two prior treatment lines. The combination of glofitamab with englumafusp alfa, an antibody-like fusion protein that simultaneously targets CD19 on B cells and 4-1BB on T cells, has shown a strong synergy in preclinical models. We present final dose escalation data of BP41072, a phase 1b study combining englumafusp alfa with glofitamab in pts with r/r B-NHL after at least one prior treatment.

Aims:

BP41072 (NCT04077723) is a first-in-human trial evaluating the safety, tolerability, pharmacokinetics/dynamics and preliminary activity of englumafusp alfa in combination with glofitamab.

Methods:

Pts with r/r B-NHL received glofitamab step up dosing (2.5/10/30mg) in cycles 1/2 after a single obinutuzumab dose (1000mg). One week after, patients started with englumafusp alfa and received both agents the same day from C3D1 onwards Q3W. Both compounds were administered intravenously with a fixed treatment duration (maximum 12 cycles). Dose escalation was conducted using a mCRM EWOC. Response rates were assessed using Lugano criteria.

Results:

At CCOD October 25th 2023, 134 pts r/r B-NHL were enrolled of which 83 pts had aggressive r/r B-NHL (treated as outlined above), including 60 diffuse large B-cell lymphoma (DLBCL), 18 transformed follicular lymphoma (trFL), 3 transformed other indolent NHL and 2 FL grade 3B. Englumafusp alfa doses ranged from 0.35 up to 75mg with a maximum tolerated dose level not reached. Pts had a median age of 63, were 41% female, 47% ECOG 1, and primarily stage IV disease (50.6%). Pts had a median of 3 prior treatment lines (range 1-8), and were 19.3% primary refractory, and 49.4% had prior CAR-T cell therapy.

Across the 134 safety-evaluable pts (all histologies), the most common adverse events were cytokine release syndrome (CRS, 55.2%), anemia (32.1%), COVID-19 (26.9%) and neutropenia (25.4%). Grade 5 events were reported in 9 (6.7%) pts (related to study treatment n=3). A Grade 5 pneumocystis jirovecci pneumonia, related to glofitamab, was qualified as dose-limiting toxicity (n=1).

CRS events were mostly grade 1 (48.5% pts). Grade 2 events occurred in 13.4% pts and grade 3 in a single pt. CRS was mostly confined to the first two glofitamab doses (2.5mg/10mg) with only 7 (5.2%) pts having CRS (all grade 1) related to englumafusp alfa alone. No additive or synergistic safety signals as a result of combining englumafusp alfa with glofitamab were identified.

Across all doses investigated, complete response rates (CRR) and best overall response rate (BORR) were 57% and 67% for all r/r B-NHL patients (2L+, N= 83). Corresponding results for CAR-T-naïve pts (2L+, N=41) were 66%/73% and 77%/77% for all CAR-T-naïve pts who received only one prior therapy (N=13).

Serum concentrations from pts who received at least one dose of englumafusp alfa and with at least one

quantifiable pharmacokinetic (PK) measure were included in a population PK analysis. For intermediate doses tested, clinical PK falls within the in vivo efficacious dose range of englumafusp alfa.

Pharmacodynamically, we observed expansion of activated and memory CD8+ T cells, with limited expansion of terminally differentiated PD1+ CD8+ T cells in blood, in association with the deepening of the ctDNA response over time.

Summary/Conclusion:

These are the first clinical data demonstrating that combining a T-cell engager with a bispecific antibody-like fusion protein delivering a strong costimulatory signal is safe and efficacious in B-NHL pts. A dose expansion study is currently underway.

Keywords: Non-Hodgkin’s lymphoma, B cell lymphoma, Diffuse large B cell lymphoma, Malignant lymphoma