Abstract: P1131

Title: AZD0486, A NOVEL CD19XCD3 T-CELL ENGAGER, SHOWS DURABLE RESPONSES IN PATIENTS WITH RELAPSED/REFRACTORY FOLLICULAR LYMPHOMA: UPDATE ON EFFICACY AND SAFETY

Abstract Type: Poster Presentation

Topic: Indolent and mantle-cell non-Hodgkin lymphoma - Clinical

Background:

AZD0486 (formerly TNB-486), a novel, IgG4 fully human CD19xCD3 bispecific T-cell engager (TCE) (Malik-Chaudhry, et al. *MAbs*. 2021), is being evaluated in a phase 1 study for patients (pts) with relapsed/refractory (R/R) B-cell non-Hodgkin lymphoma (B-NHL).

Aims:

To present updated data for pts with R/R follicular lymphoma (FL) treated with AZD0486 in the ongoing first-in-human, phase 1, dose-escalation trial (NCT04594642).

Methods:

Pts with R/R CD19+ B-NHL who received ≥2 prior lines of therapy were eligible. AZD0486 was administered in escalating doses in either a single target dose (day [D]1, D15 0.03–2.4 mg), single step-up dosing (1SUD) (D1 0.27–1 mg, D15 0.8–10 mg), or double SUD (2SUD) (D1 0.27 mg, D8 1 mg, D15 2.4–7.2 mg) schedules. AZD0486 was given intravenously every 2 weeks in 28-D cycles (C) for up to 2 years (yrs). Monthly dosing was considered for pts in complete response (CR) after C6. Responses were assessed by central imaging review using RECIL 2017 criteria. Cytokine release syndrome (CRS) and immune effector cell–associated neurotoxicity syndrome (ICANS) were graded by 2019 ASTCT criteria (Lee, et al. *Biol Blood Marrow Transplant*. 2019).

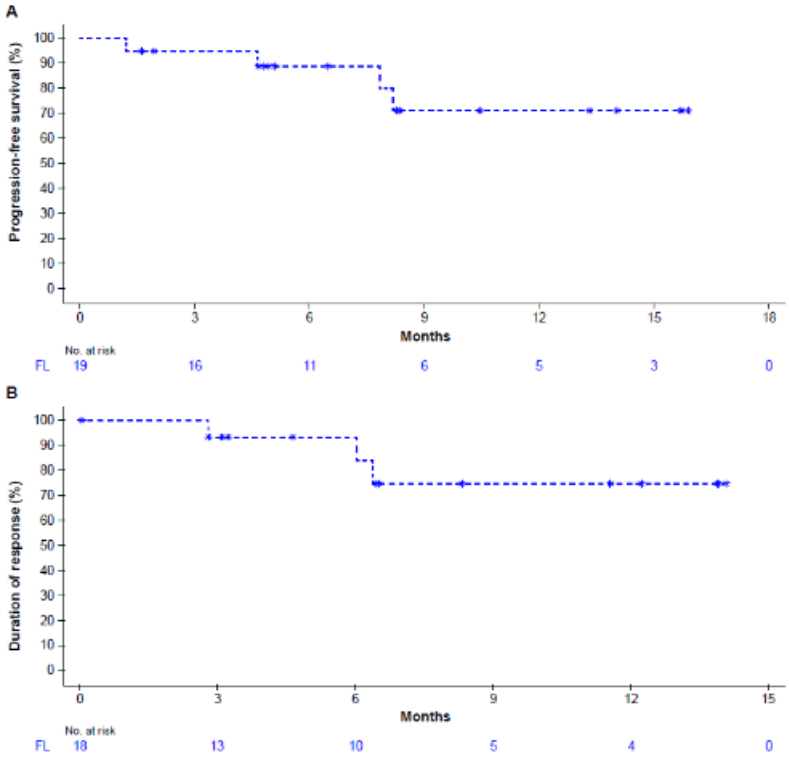
Results:

As of September 29, 2023, 29 pts with R/R FL received AZD0486 at target doses of 0.8 mg (n=5), 2.4 mg (n=14), 7.2 mg (n=7), or other (n=3; 1 each of 0.03, 0.09, and 10 mg); 11 pts received 2SUD. Median age was 65 (range, 33–86) yrs, 59% of pts were male, and 72% of pts had stage III/IV disease. Median prior lines of therapy was 3 (range, 2–9), 5 (17%) pts received prior chimeric antigen receptor T-cell therapy (CAR-T), and 2 (7%) received prior CD20 TCE therapy. Overall, 10/29 (34%) pts had progression of disease within 2 yrs (POD24) with prior therapy. The overall response rate/CR rate for evaluable pts who received doses ≥0.8 mg (n=24) and ≥2.4 mg (n=19) were 92%/79% and 95%/84%, respectively. At doses of ≥2.4 mg, CR rate was 5/5 (100%) for pts with CD20-negative disease, 3/3 (100%) for pts refractory to last line of therapy, 1/2 (50%) for pts who previously received anti-CD19 CAR-T, and 2/2 (100%) for pts with prior CD20 TCE therapy. With median follow-up of 10.5 (range, 1.5–30.7) mo, estimated 9-mo progression-free survival was 71% (**Figure**), 9-mo duration of response was 75% (**Figure**), and 9-mo overall survival was 90%. The most common grade 3/4 treatment-related adverse events (AEs) in >5% of pts with FL across all cohorts were lymphopenia (34%), neutropenia (14%), ICANS (7%), and hypertension (7%). Infections occurred in 15 (52%) pts, mostly COVID-19 (31%). Four (14%) pts had grade ≥3 infections (3 COVID-19 pneumonia and 1 left calf abscess). Among pts who received the 2SUD regimen (n=11), there were 2 grade 1 CRS events (18%) and no ICANS events; all CRS events resolved. There were no drug discontinuations due to treatment-related AEs. Among patients treated with 2SUD (n=11), complete peripheral blood B-cell depletion occurred within 48 hours (hr) of the first priming dose in 91% of patients. The remaining patient had complete B-cell depletion after the target dose of 2.4 mg. AZD0486 also caused transient T-cell margination in peripheral blood with a median 95% reduction in T-cell counts at 6 hr after the end of infusion of first priming dose and T cells returning to baseline levels by 48 hr.

Summary/Conclusion:

AZD0486 is active and well tolerated with 2SUD mitigating CRS and ICANS events in pts with R/R FL. Durable responses were observed with long-term follow-up of up to 31 mo. Later-phase studies of AZD0486 as monotherapy and in combination regimens are planned.

Figure. (A) Progression-free survival and (B) duration of response in patients with R/R FL treated with AZD0486.



Keywords: First in-men, Dose escalation, Follicular lymphoma, Bispecific