(PS2440) BUDOPRUTUG, A LOW-FUCOSYLATED ANTI-CD19 MONOCLONAL ANTIBODY, IN ADULTS WITH PRIMARY IMMUNE THROMBOCYTOPENIA: INITIAL PHASE 1B STUDY RESULTS

Topic: 33. Platelet disorders

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Background

Immune thrombocytopenia (ITP) is a rare autoantibody-mediated disorder characterized by reduced platelets and increased risk of bleeding. While up to 10% of adults may undergo spontaneous remission, others develop persistent disease, often requiring multiple lines of treatment. Budoprutug (TNT119) is an anti-CD19 mAb bioengineered with picomolar binding affinity for CD19 and a low-fucosylated Fc region for enhanced antibody-dependent cell cytotoxicity. CD19 is expressed from the early pro-B stage through maturation and differentiation to plasmablasts and on plasma cell subsets, providing the potential for budoprutug to provide deep and sustained depletion of B cells, including autoantibody-producing cells. Budoprutug was previously evaluated in adults with primary membranous nephropathy, another autoantibody-mediated disease. Budoprutug was well tolerated, with 5/5 evaluable participants experiencing complete peripheral B-cell decreases and complete or partial remission of proteinuria (Cortazar ASN 2024).

Aims

This Phase 1b/2a study is designed to assess ascending doses of budoprutug in adults with primary ITP who failed prior therapy.

Methods

The Phase 1b portion of the study is an open-label dose escalation with 3 dose levels (DL) of IV budoprutug: DL1-250mg, DL2-500mg, DL3-1000mg (NCT07043946). Key inclusion criteria are age >18 years, diagnosis of primary ITP, and platelet (plt) count <30,000/mL (confirmed on two separate occasions, 5-14 days apart) despite ≥1 prior therapy. Key exclusion criteria include CD19+ B cells <80 cells/mL or <40 cells/mL if B-cell depleting treatment was received previously. Budoprutug is administered on Days 1 and 15. Concomitant corticosteroids or thrombopoietin agonists (TPO-RA/TPO) with stable doses ≥14 days prior to Day 1 are allowed. The primary objective is to evaluate safety and tolerability. Secondary objectives include effects on peripheral B-cell depletion using high sensitivity B-cell detection, and plt count.

Results

As of data cut-off, 10 participants (pts) (6 DL1, 4 DL2) had enrolled in the study. The median (range) age was 47 (22-75) years. All pts had persistent or chronic ITP; median (range) duration of ITP was 10 years (0.4-40), with 1 pt (DL2) on concomitant TPO-RA. All pts had 2-4 prior therapies within the last 2 years; 4 pts had prior rituximab and a separate pt had a splenectomy. All pts received the Day 1 and Day 15 doses of budoprutug. After a median (range) follow up of 5 months (3-6) in DL1, and maximum follow up of 43 days (8-43) in DL2, there were no deaths, discontinuations, SAEs, or infusion-related reactions. Figure 1 shows B-cell counts for DL1. Profound decreases occurred following budoprutug administration; median B-cell count at Day 85 was 1 cell/μL. By Day 85, 4/6 pts in DL1 had a platelet response: 1 pt with plt >100,000/μL, 1 pt with plt 50,000-100,000/μL, and 2 pts with plt 30,000-50,000/μL. No pts had bleeding events.

Summary/Conclusion

In this open-label study of budoprutug in previously treated adults with primary ITP, initial data suggest an acceptable tolerability profile and robust B-cell depletion following two doses of budoprutug. Increases in platelet counts were observed in the majority of pts, and no post-baseline bleeding events were reported. The study is continuing with dosing in higher dose cohorts (DL2 and DL3). Additional safety and efficacy data from the study will be presented at the conference.

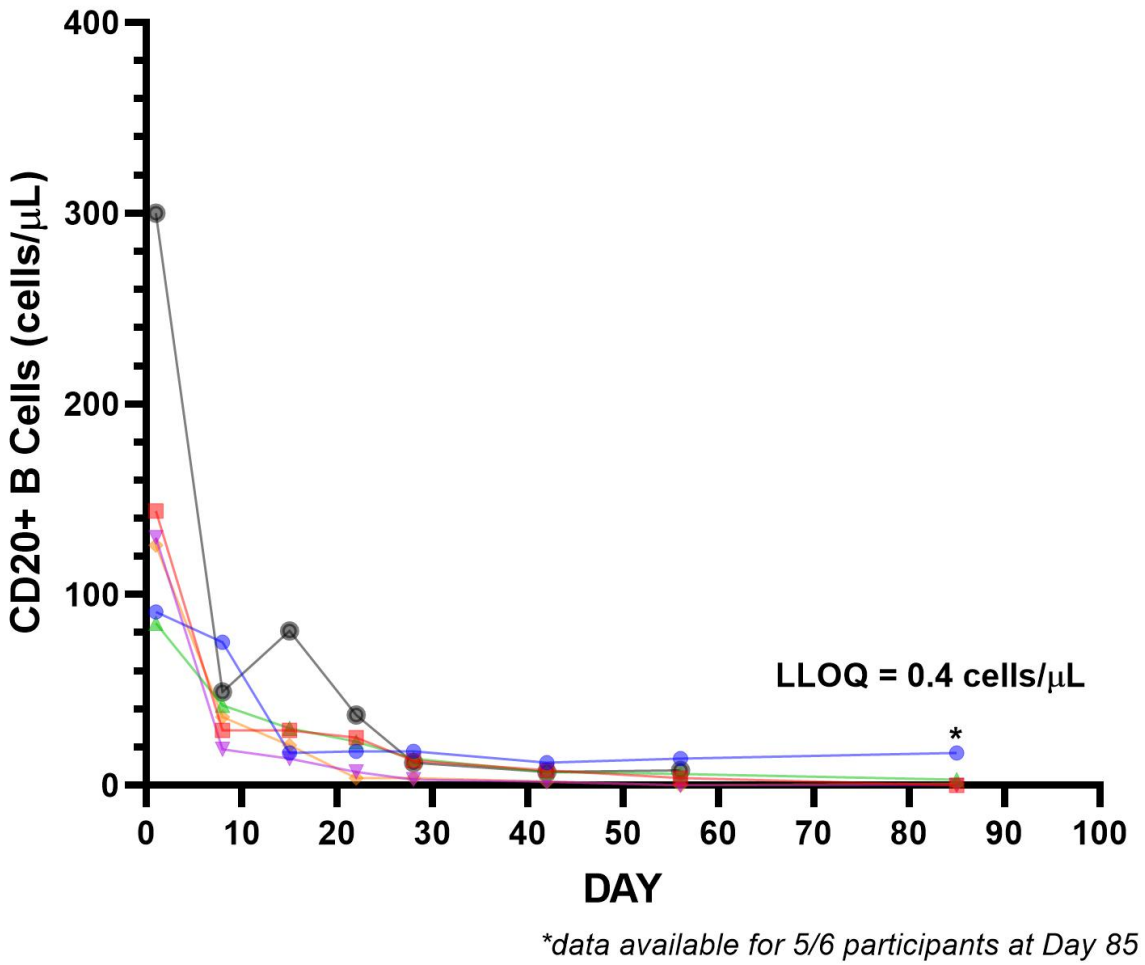

Figure 1. *CD20+ B-cell Counts by Participant (DL1)*