Abstract Submission

33. Platelets disorders

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A PHASE 1B, OPEN-LABEL, DOSE-ESCALATION STUDY OF PRTX-100, A HIGHLY PURIFIED FORM OF STAPHYLOCOCCAL PROTEIN A (SPA), IN ADULT PATIENTS WITH PERSISTENT/CHRONIC IMMUNE THROMBOCYTOPENIA (ITP)

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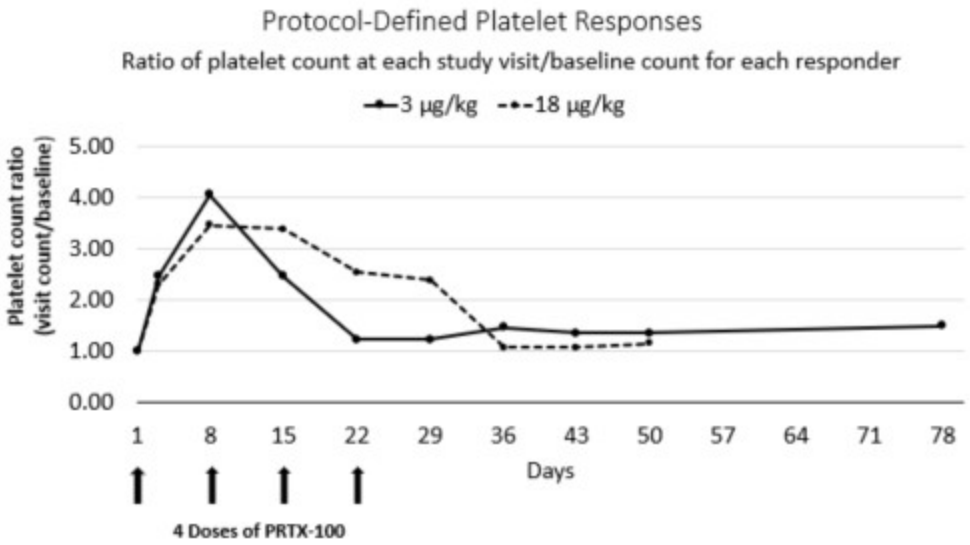
Background: ITP is a rare autoimmune bleeding disorder characterized by isolated thrombocytopenia caused by antibody-dependent platelet destruction and impaired platelet production. Various therapies (eg glucocorticoids, IV immunoglobulin, and thrombopoietin receptor agonists) are available but are limited by inadequate efficacy, side effects and/or cost. PRTX-100 is a highly purified form of SpA that binds to human B-lymphocytes and monocytes and modulates immune processes. Preclinical data indicate that PRTX-100 may have the potential to treat ITP by reducing immune-mediated platelet destruction (Kapur et al., Br J Haematol 2017).

Aims: We present safety and efficacy data from the first four dosing cohorts of patients with refractory ITP enrolled in a phase 1b open-label study (PRTX-100-203).

Methods: Adults with persistent or chronic ITP who had received at least one prior ITP treatment and had either a platelet count <30,000/μL (if not receiving any ITP therapy) or <50,000/μL (if receiving a constant dose of permitted ITP treatment) were eligible. PRTX-100 was administered via a 30-min infusion (60 min if total dose >500 μg) on Days 1, 8, 15 and 22 in a standard 3+3 dose-escalation study design. Starting dose was 3 μg/kg with subsequent dose increases to 6, 12, 18 and 24 μg/kg. Primary objective: to characterize safety of up to five dose levels of PRTX-100. Safety analyses: adverse events (AEs), serious AEs, infusion reactions, clinical laboratory tests, vital signs, physical findings and electrocardiograms. Efficacy endpoints include platelet response (increased platelet count ≥30,000/μL and at least doubling of baseline count in patients with a baseline count <30,000/μL; or, in patients with a baseline count ≥30,000/μL and <50,000/μL, an increase in count to ≥50,000/μL and at least a doubling of baseline count or an increase to >100,000/μL). Secondary objectives include immunogenicity and pharmacokinetics.

Results: Data are available from 13 patients enrolled in the first four dosing cohorts: 3 μg/kg (n=3), 6 μg/kg (n=4), 12 μg/kg (n=3), and 18 μg/kg (n=3). There were 6 women and 7 men (10 Caucasian, 1 Asian, 2 other) with an age range of 21 to 81 years and most had a splenectomy. Two patients in the 6 μg/kg cohort discontinued the study (1 due to a serious unrelated grade 4 worsening of ITP after receiving 2 doses of PRTX-100; 1 due to non-compliance with study visits after receiving 3 doses of PRTX-100). All 11 remaining patients received 4 doses of PRTX-100. Two serious or higher-grade AEs were seen in this group: unrelated grade 4 mouth bleeding (n=1), unrelated grade 3 axonal neuropathy (n=1). Two grade 1 infusion reactions occurred: itching rash at the infusion site (n=1); pruritus (n=1). Laboratory events: grade 3/4 hyperglycaemia, grade 3 lymphocytopenia, and grade 4 abnormal urine glucose (n=1 patent); grade 3 hypophosphatemia and grade 4 abnormal urine glucose (n=1); grade 3 cholesterol increase (n=1). Five patients had increased platelet counts as early as Day 3. Two patients had a protocol-defined platelet response at the 3 μg/kg and 18 μg/kg doses (see Figure). A further 5 patients had an increase in their counts, although not to the level of response.

Image/Pictures:



Summary/Conclusion: Data from the first four cohorts of patients treated with PRTX-100 demonstrate an acceptable safety profile. Platelet counts were elevated in several patients and two patients so far have achieved a platelet response. Enrolment into the last dosing cohort (24 µg/kg) is ongoing and updated data will be included in any presentation.

Keywords: Bleeding, Immune thrombocytopenia (ITP), Platelet count, Therapy