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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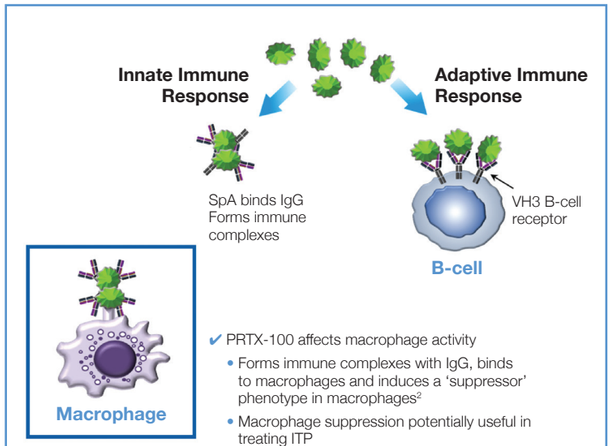
#PF658

Introduction

- ITP is a rare autoimmune bleeding disorder characterized by isolated thrombocytopenia caused by antibody-dependent platelet destruction and impaired platelet production.
- Various therapies (e.g. 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.[1]
- In this poster we present safety and efficacy data from five dosing cohorts of patients with refractory ITP enrolled in a phase 1b open-label study (PRTX-100-203).

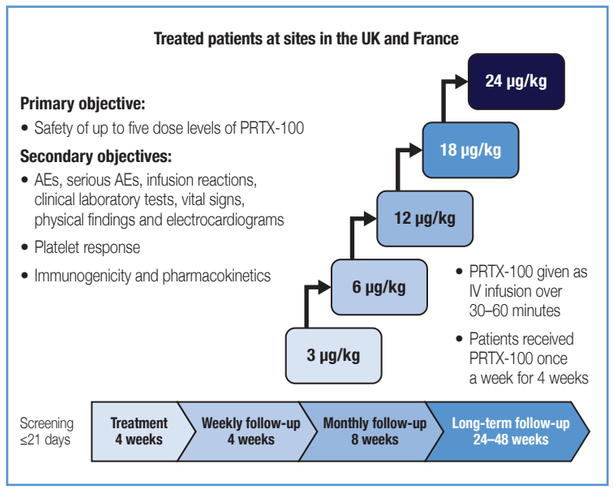
Figure 1. Mechanism of action



Methods

- Eligible patients were 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).
- PRTX-100 was administered via a 30-minute infusion (60 minutes 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.

Figure 2. Phase 1b study design



Patient disposition

- Two patients in the 6 µg/kg cohort discontinued the study (one due to a serious unrelated grade 4 worsening of ITP after receiving two doses of PRTX-100; one due to non-compliance with study visits after receiving three doses of PRTX-100) and one patient in the 24 µg/kg cohort after receiving one dose of PRTX-100 (due to an infusion reaction).
- All 12 remaining patients received four doses of PRTX-100.

Table 1. Baseline demographics

Age	Gender	Previous treatments	Baseline platelet count*	Dose cohort (µg/kg)
71	F	Splenectomy, corticosteroids, IVIg, eltrombopag, romiplostim, rituximab, dapsone	5,667	3
52	F	Corticosteroids	28,000	3
64	M	Corticosteroids, IVIg	16,000	3
76	M	Corticosteroids, dapsone	19,000	6
68	M	Splenectomy, corticosteroids, IVIg, danatrol, disulone, cyclosporine, cyclophosphamide	7,667	6
41	F	Corticosteroids, danatrol	22,333	6
33	F	Corticosteroids, IVIg	15,333	6
40	M	Splenectomy, corticosteroids, eltrombopag, rituximab	8,667	12
30	M	Corticosteroids, IVIg, mycophenolate	7,500	12
50	F	Rituximab	7,333	12
82	F	Splenectomy, corticosteroids, IVIg, cyclosporine, danazol, R-CVP chemotherapy	15,000	18
63	M	Corticosteroids	17,667	18
22	M	Corticosteroids, IVIg, romiplostim, rituximab	32,000	18
32	F	Corticosteroids, IVIg, eltrombopag, romiplostim, mycophenolate	4,000	24
57	M	Splenectomy, corticosteroids, IVIg, eltrombopag, romiplostim, rituximab, mycophenolate	3,000	24

*Baseline platelet count is average of 2–3 pre-treatment platelet counts.

Efficacy overview

- Two patients had a protocol-defined platelet response, one at in the 3 µg/kg dose cohort and the other at 18 µg/kg cohort.
- A further eight patients had an increase in their counts, although not to the level of response.
- Five patients had increased platelet counts as early as 2 days following initial dosing.

Figure 3. Maximum effect in PRTX-100-treated patients#

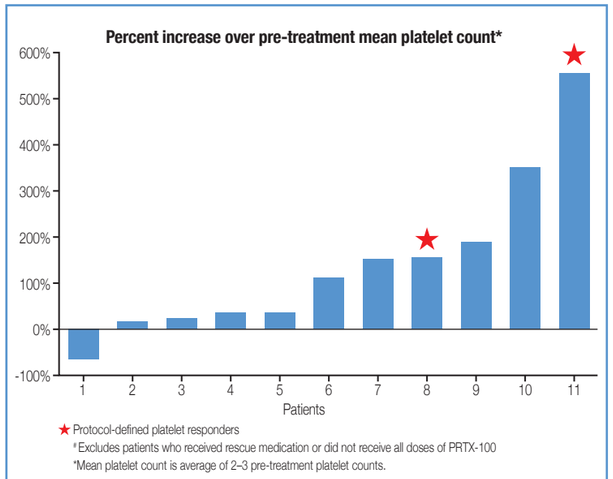
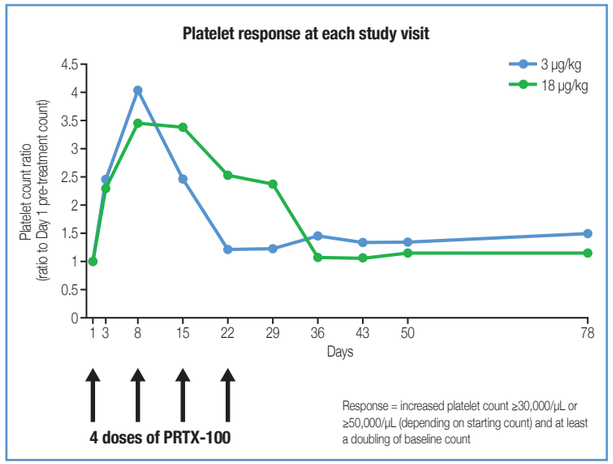


Figure 4. Platelet response over time in per protocol responders



Safety overview

- At least one treatment-related AE was reported in 12 of 15 patients.
- 0-3 treatment-related AEs were observed in most patients. One patient (18 µg/kg) had 19 AEs and another patient (24 µg/kg) had 11 AEs.

Table 2. Treatment-related adverse events in >1 patient (n=15)

Adverse event	Number of patients
Nausea	4
Bone and muscle pain, arthralgia	3
Headache	3
Acute infusion reaction*	3
Abdominal pain	2
Rash	2
Skin discoloration	2

*Grade 1 itching rash at the infusion site (n=1), grade 1 pruritus (n=1), and grade 3 abdominal pain (n=1).

Table 3. Severity of treatment-related adverse events

Total number of treatment-related AEs	n=46 n (%)
Grade 1	16 (35)
Grade 2	28 (61)
Grade 3	2 (4)*
Grade 4	0

*Abdominal pain, infusion reaction.

- Five serious or higher-grade AEs were observed:
  - unrelated grade 4 mouth bleeding (n=1)
  - unrelated grade 4 worsening of ITP (n=1)
  - unrelated grade 3 axonal neuropathy (n=1)
  - grade 3 acute infusion reaction (n=1)
  - grade 3 abdominal pain (n=1).

Table 4. Grade 3/4 laboratory abnormalities

Laboratory analysis	Grade	Number of patients
Abnormal urine glucose	4	2
Hyperglycemia	3	1
Lymphocytopenia	3	1
Cholesterol increase	3	1
Hypophosphatemia	3	1

Conclusions

- Data from five dose cohorts of patients treated with PRTX-100 demonstrate an acceptable safety profile for this therapy.
- Platelet counts were elevated in several patients and two patients achieved a protocol defined platelet response.
- The most common AEs were nausea, bone and muscle pain & arthralgia, headache, acute infusion reactions, abdominal pain, rash and skin discoloration.
- Most AEs were mild to moderate in severity.
- These data, along with data from another ongoing trial in patients with ITP, will be used to guide the further development of PRTX-100 in ITP.

References

1. Kapur et al. Br J Haematol 2017.
2. MacLellan et al. Arthritis & Rheumatism 2011.
3. Kim et al. mBio 2015.

Acknowledgements

- The patients and their families.
- The study investigators, and their coordinators and nurses.