Successful Treatment of Thrombocytopenia with Staphylococcal Protein A (PRTX- 100) in a Murine Model of Immune Thrombocytopenia (ITP)

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Immune thrombocytopenia (ITP) is an autoimmune bleeding disorder in which autoantibodies and autoreactive T cells target the destruction of platelets and megakaryocytes in the spleen and bone marrow. Several therapeutic options e.g. steroids, IVIg, Rituximab and thrombopoietin mimetics, are available for patients but inadequate efficacy, side effects and/or expense can make them undesirable. PRTX-100 is a highly purified formulation of Staphylococcal Protein A that has been evaluated in clinical trials with rheumatoid arthritis patients. Here, we analyzed the efficacy of PRTX-100 in raising platelet counts in a well-established murine model of ITP that demonstrates both antibody- and T cell-mediated thrombocytopenia. Platelet glycoprotein (GP) IIIa (CD61) knockout (KO) mice were immunized with $CD61^+$ platelets and ITP was initiated by transfer of their splenocytes into severe combined immunodeficient (SCID) mice. On day 10, post transfer, the SCID mice were treated with either placebo, 1g/kg IVIg (ip, biweekly) or doses of PRTX-100 (iv, biweekly, 2.5-250 ug/kg) and platelet counts were measured weekly. Results show that control SCID mice transferred with $1x10^4$ splenocytes from immune CD61 KO mice became thrombocytopenic at day 7 post-transfer and remained extremely thrombocytopenic throughout the 28 day protocol (3 mice died from bleeding diatheses). Similar observations were found with SCID mice given placebo. In contrast, however, transferred SCID mice treated with either IVIg or the PRTX-100 doses had platelet counts that increased to within normal levels within 1-2 weeks after treatment and none of the mice died (Table 1).

Table 1. Platelet counts (mean ± SD) in SCID ITP mice (N=3-8/group) treated with the indicated compounds.

Treatment	Pre-bleed	Day 14	Day 21	Day 28
No treatment	848 ± 202	89 ± 46	51 ± 42	78 ± 51
Placebo (250 ug/kg)	848 ± 202	113 ± 59	46 ± 20	63 ± 40
IVIg (1 g/kg)	848 ± 202	290 ± 211	490 ± 289	698 ± 350
PRTX-100 (250 ug/kg)	848 ± 202	101 ± 37	303 ± 112	505 ± 226
PRTX-100 (25 ug/kg)	848 ± 202	203 ± 88	290 ± 67	254 ± 70
PRTX-100 (2.5 ug/kg)	848 ± 202	275 ± 202	405 ± 289	631 ± 401

These results demonstrate that PRTX-100 was effective in elevating platelet counts in a murine model of human ITP and support the proof of principle that PRTX-100 may be beneficial in patients with ITP.