Long-term treatment with romiplostim and treatment-free platelet responses in children with chronic immune thrombocytopenia

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Supplementary Data

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Table S1. Serious adverse events.

	All treated patients N=65 n (%)
Thrombocytopenia	4 (6)
Pyrexia	3 (5)
Epistaxis	2 (3)
Headache	2 (3)
Vomiting	2 (3)
Anemia	1 (2)
Asthenia	1 (2)
Asthma	1 (2)
Biliary dyskinesia	1 (2)
Clostridium difficile infection	1 (2)
Contusion	1 (2)
Dehydration	1 (2)
Depression	1 (2)
Febrile neutropenia	1 (2)
Gastroenteritis	1 (2)
Gastrointestinal infection	1 (2)
Gingivitis	1 (2)
Hemangioma	1 (2)
Hematoma	1 (2)
Head injury	1 (2)
Immune thrombocytopenia	1 (2)
Infection	1 (2)
Leukopenia	1 (2)
Meningitis viral	1 (2)
Metapneumovirus infection	1 (2)
Mouth hemorrhage	1 (2)
Pharyngitis streptococcal	1 (2)
Platelet count decreased	1 (2)
Pneumonia mycoplasmal	1 (2)
Post-procedural hemorrhage	1 (2)
Respiratory syncytial virus infection	1 (2)
Subcutaneous abscess	1 (2)
Suicidal ideation	1 (2)
Transfusion reaction	1 (2)
Ulcer hemorrhage	1 (2)
Viral infection	1 (2)
Viral upper respiratory tract infection	1 (2)

Table S2. Serious and/or grade 3 bleeding adverse events.

		Age (years)	Sex	Week	Bleeding adverse events	Duration (days)	Grade	Related	Serious	Actions
Serious bleeding		7	Boy*	95	Hematoma	16	1	N	Y	Hospitalized, no change to romiplostim
				24	Epistaxis and mouth hemorrhage	1	2	N	Y	Hospitalized, no change to romiplostim
		4	Boy	86	Hemorrhage after tonsillectomy (platelet count day before was 191×10^9/L)	1	2	N	Y	Hospitalized, no change to romiplostim
		11	Girl	40	Worsening ITP and contusion	3	1	N	Y	Hospitalized, left the study a few days later for noncompliance
Grade 3 bleeding		7	Boy	12	Worsening epistaxis, concurrent grade 4 thrombocytopenia	2	3	Y	Y	Hospitalized, no change to romiplostim (later D/C as req other Rx)
		3	Girl	3	Bleeding mouth sores	1	3	N	Y	ER
		14	Boy	294	Hematuria	5	3	N	N	ER, no change to romiplostim
		8	Boy	94	Increased petechiae	13	3	N	N	No change to romiplostim (later D/C as req other Rx)

D/C: discontinued; ER: emergency room; ITP: immune thrombocytopenia; N: no; req: required; Rx: therapy; Y: yes.
*This patient reported 499 adverse events.

Table S3. Rescue medications.

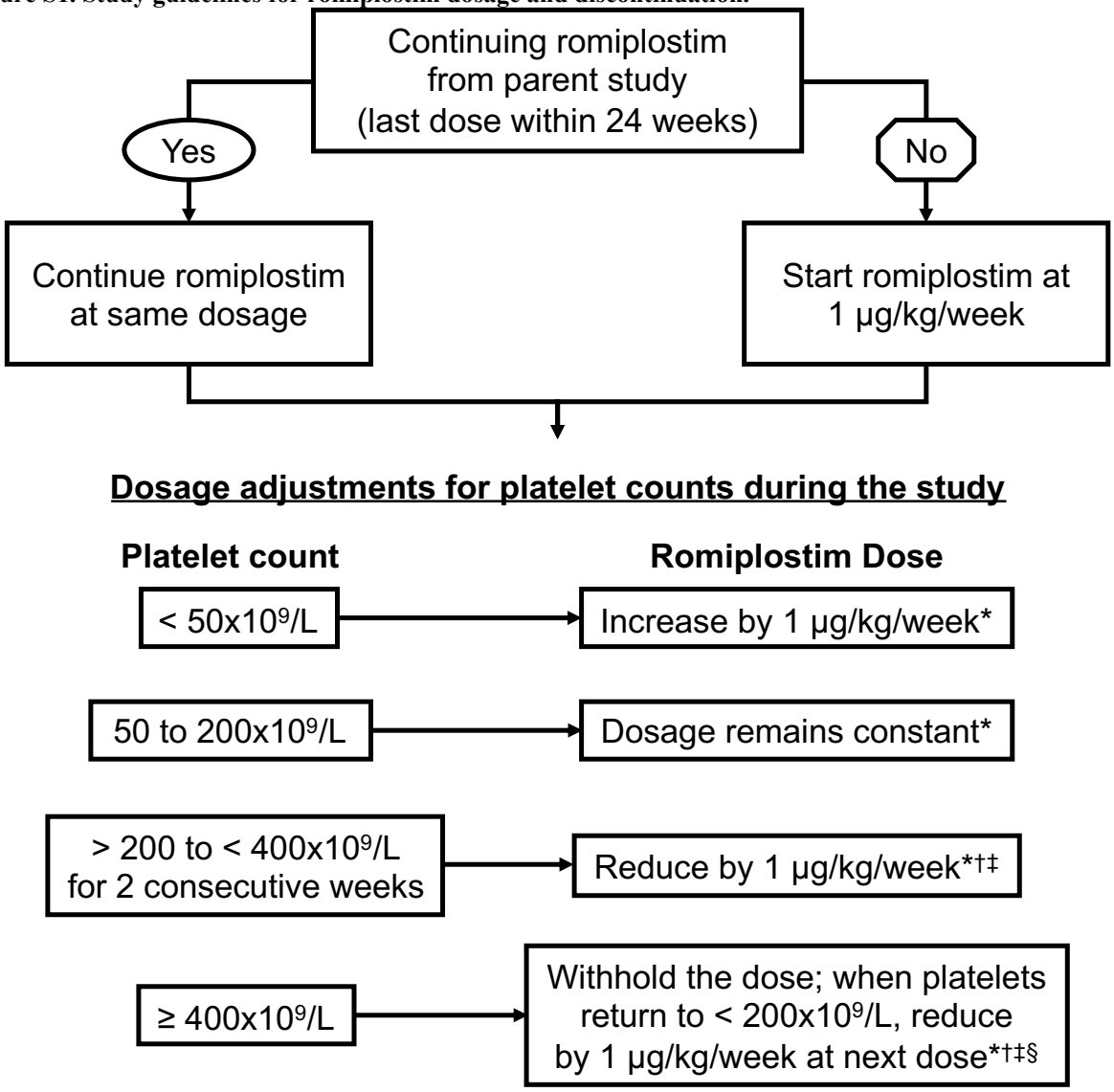
	All treated patients N=65	
	n (%)	Events (rate per 100 pt-yr)
Any use	23 (35)	80 (44)
Intravenous immunoglobulin	11 (17)	31 (17)
Corticosteroids*	13 (20)	31 (17)
Antifibrinolytic (aminocaproic acid or tranexamic acid)	6 (9)	14 (8)
Azathioprine	1 (2)	1 (0.6)
Red blood cell transfusion	1 (2)	1 (0.6)
Platelet transfusion	1 (2)	2 (1)

Pt-yr: patient-years.
*Corticosteroids include prednisone/prednisolone, methylprednisolone, and dexamethasone.

Table S4. Alphabetical list of investigators.

Investigator	Institution	Country
Abish, Sharon	Montreal Children's Hospital	Canada
Barnes, Chris	The Royal Children's Hospital	Australia
Beam, Donald	Cook Children's Medical Center	USA
Bennett, Carolyn	Emory University	USA
Blanchette, Victor	The Hospital for Sick Children	Canada
Bussel, James	New York Presbyterian Hospital, Weill Cornell Medical Center	USA
Callaghan, Michael	Children's Hospital of Michigan	USA
Despotovic, Jenny	Texas Children's Hospital West Tower	USA
Diaz de Heredia Rubio, Cristina	Hospital Universitari Vall d Hebron	Spain
Escoto, Heather	Peyton Manning Children's Hospital at St Vincent	USA
Ford, James	Children's Hospital and Medical Center	USA
Geddis, Amy	University of California at San Diego, Rady Children's Hospital San Diego	USA
Guerrera, Michael	Children's National Medical Center	USA
Ho, Richard	Vanderbilt University Medical Center, Monroe Carell Junior Children's Hospital at Vanderbilt	USA
Ikeda, Alan	Children's Specialty Center of Nevada	USA
Kalpatthi, Ramasubramanian	Children's Mercy Hospital	USA
Nugent, Diane	Children's Hospital of Orange County	USA
Pastore, Yves	Centre Hospitalier Universitaire Sainte-Justine	Canada
Quinn, Charles	Cincinnati Children's Hospital Medical Center	USA
Raj, Ashok	Pediatric Cancer and Blood Disorders Clinic	USA
Ritchey, Arthur	Children's Hospital of Pittsburgh of University of Pittsburgh Medical Center	USA
Rose, Melissa	Nationwide Children's Hospital	USA
Russell, Susan	Sydney Children's Hospital	Australia
Stegner, Martha	University of Texas Southwestern Medical Center	USA
Tarantino, Michael	The Bleeding and Clotting Disorders Institute	USA
Thompson, Alexis	Ann and Robert H Lurie Children's Hospital of Chicago	USA
Velez, Maria	Children's Hospital	USA
Williams, Bronwyn/Roy, John	Children's Health Queensland	Australia

Figure S1. Study guidelines for romiplostim dosage and discontinuation.



Possible reasons to withhold romiplostim doses:

(1) Required - any platelet count is ≥ $400x10^9$/L
(2) Required - current dose is 1 µg/kg/week and a dose reduction is required
(3) Investigator's opinion - the patient maintains an acceptable platelet count ≥ $50x10^9$/L without weekly romiplostim treatment

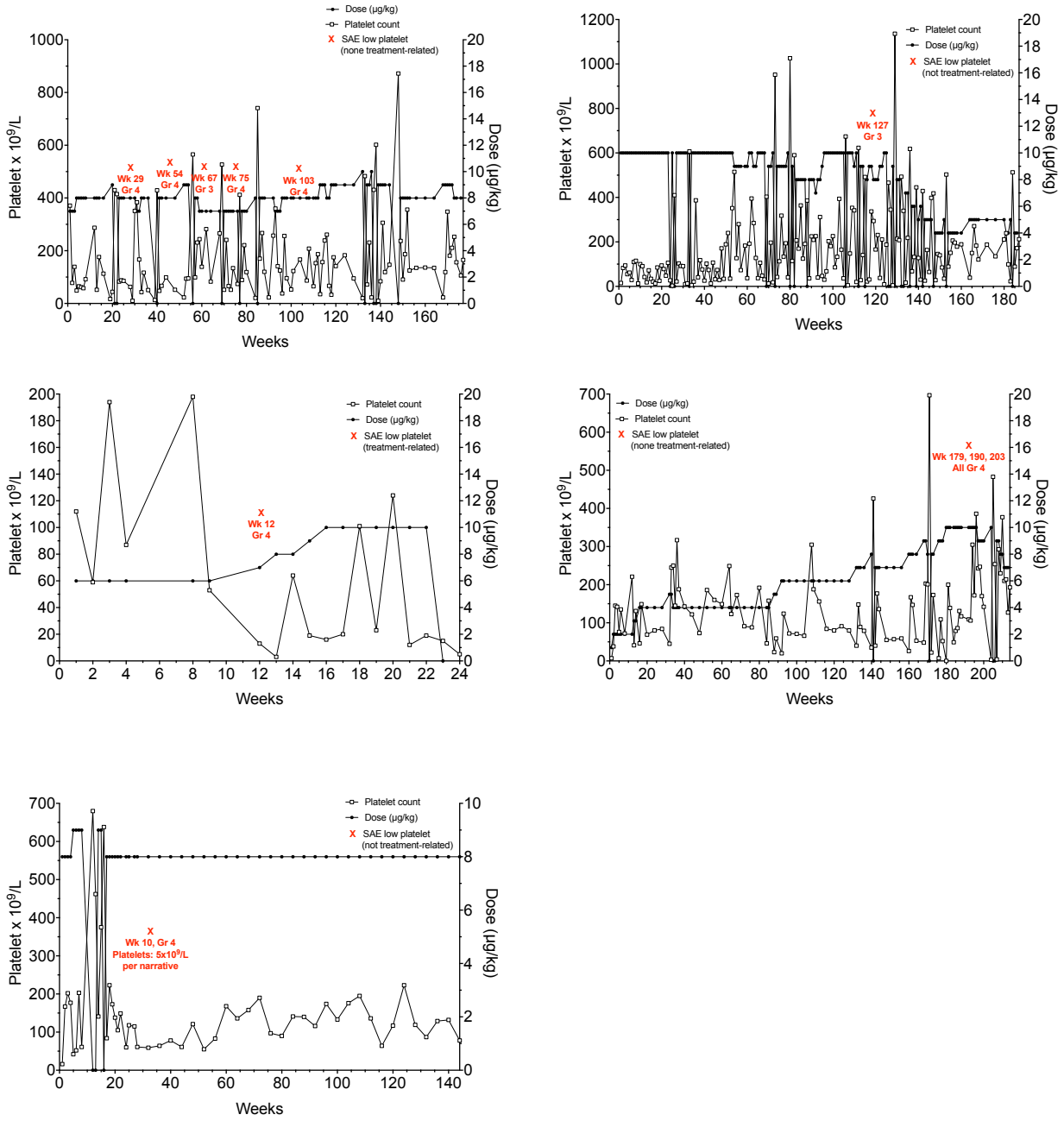
* Romiplostim may be used with other medical ITP therapies. If platelet count is ≥ $50x10^9$/L, other medical ITP therapies may be reduced or discontinued.

† If platelet count is elevated in response to the initiation or increase in dose of another ITP medication, then the same dose of romiplostim should be administered when the platelet count is < $200x10^9$/L.

‡ If the current dose is 1 µg/kg and a dose reduction is required during the treatment period, the dose will be withheld until the platelet count falls to < $50x10^9$/L. Once the platelet count is < $50x10^9$/L, dosing of romiplostim will resume at a dose of 1 µg/kg using the dose adjustment rules above.

§ If platelet count is ≥ $400x10^9$/L due to rescue medications, it is at the discretion of the investigator to reduce the dose of romiplostim by 1 µg/kg.

Figure S2. Platelet counts and romiplostim dosing in patients with an SAE of low platelet count



Gr: grade; plt: platelets; SAE: serious adverse event.

Figure S3A. Rescue medication use over time

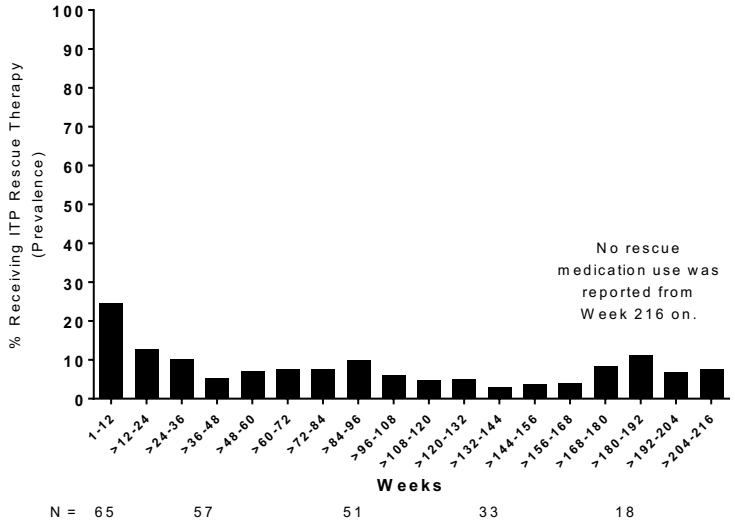
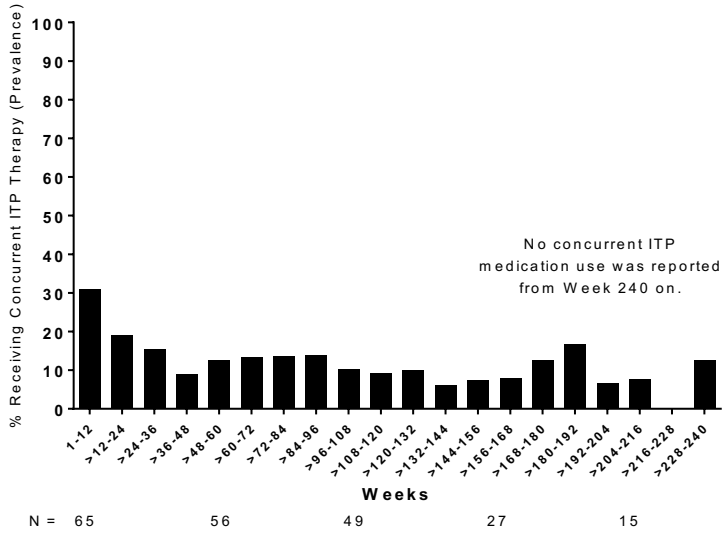
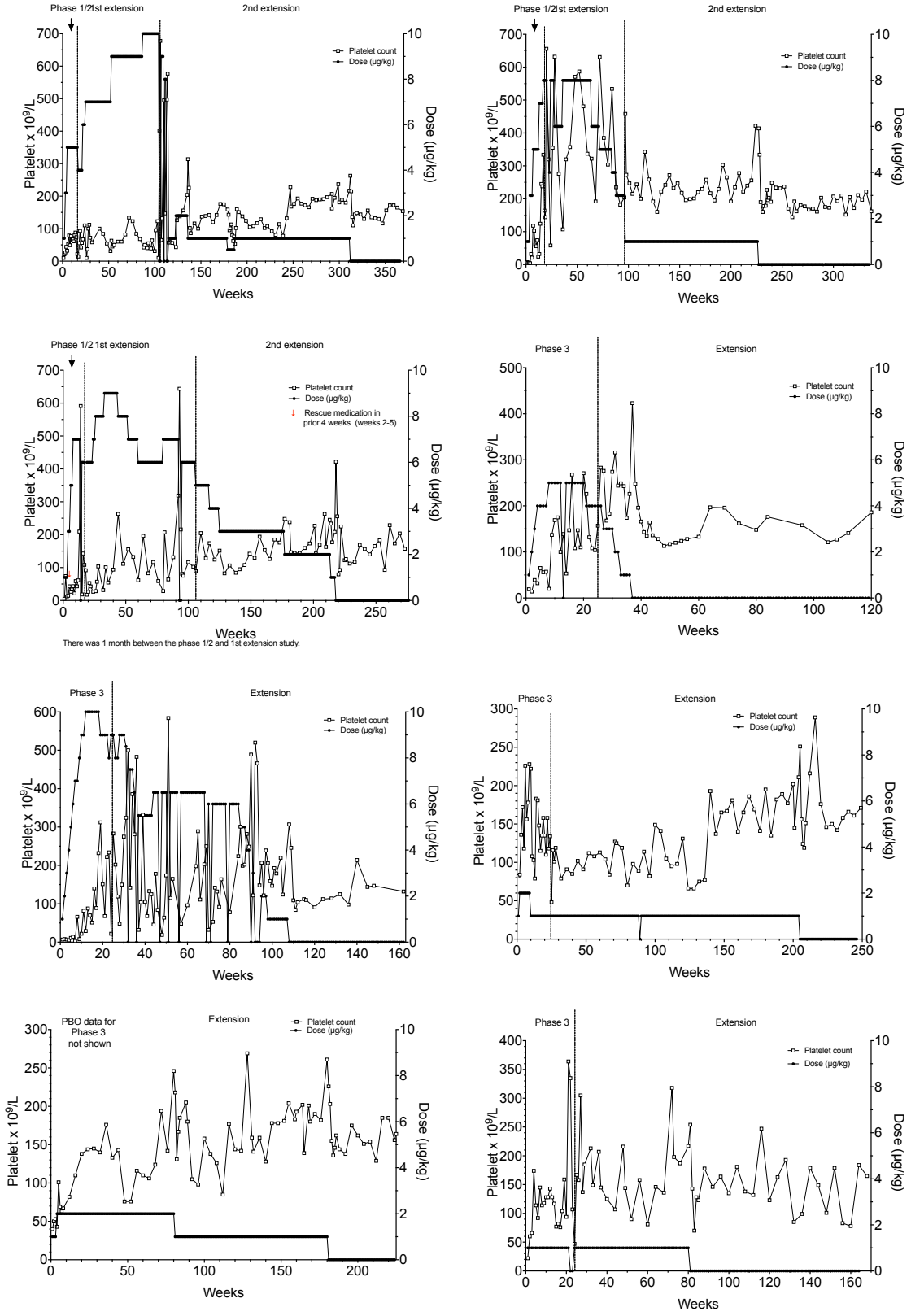


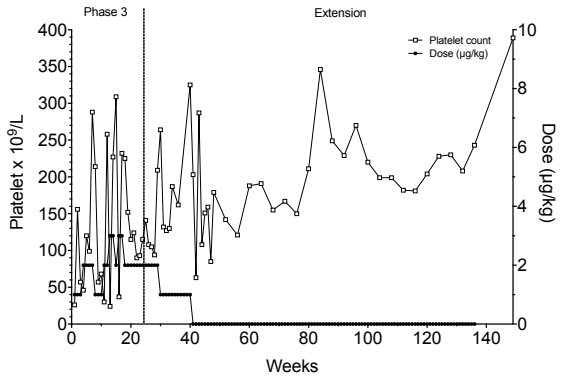
Figure S3B. Concomitant medication use over time

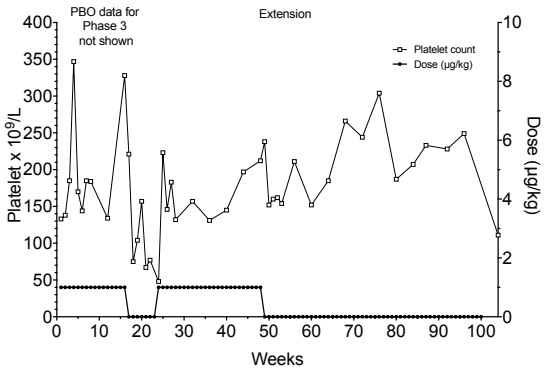


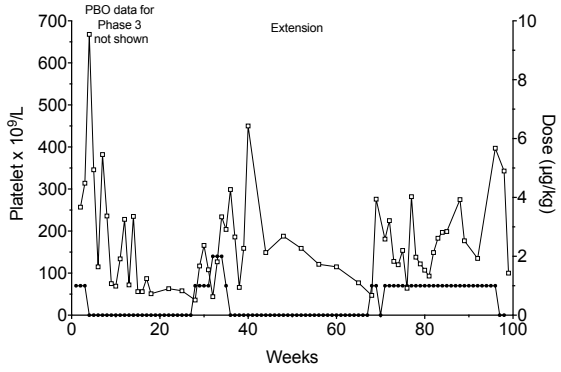
ITP: immune thrombocytopenia.

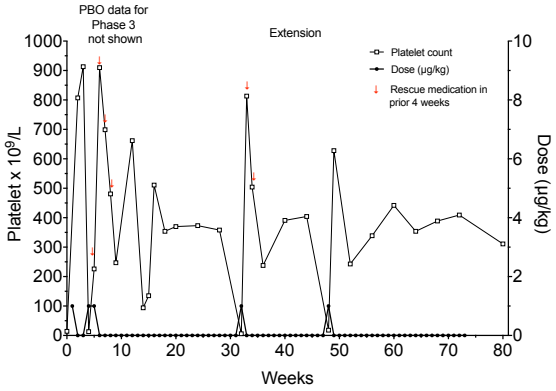
Figure S4. Platelet counts and romiplostim doses for each patient with a treatment-free response.

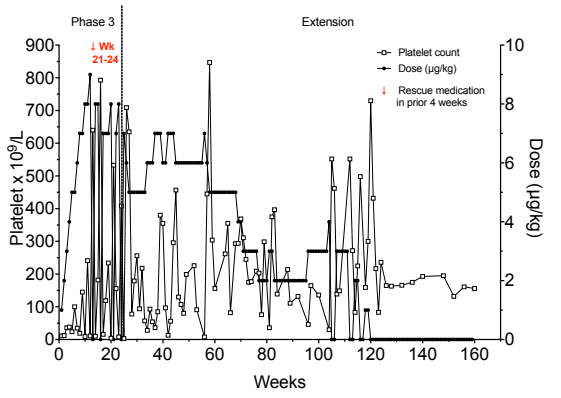


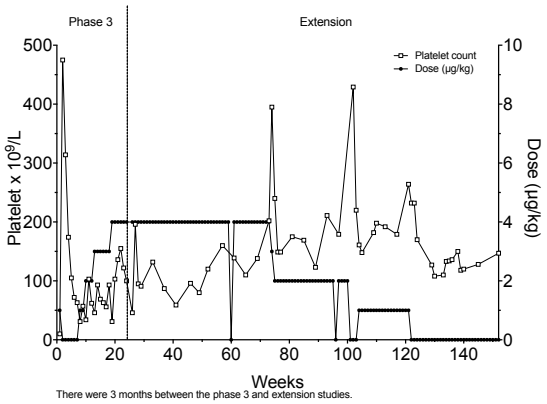




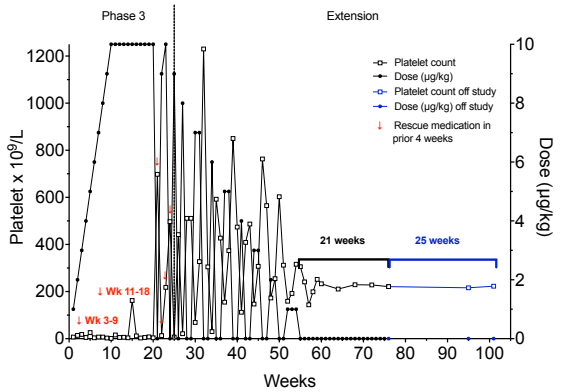








There were 3 months between the phase 3 and extension studies.



PBO: placebo.