

Safety and efficacy of romiplostim in splenectomized and nonsplenectomized patients with primary immune thrombocytopenia

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Supplementary Table S1. Infection terms

Possible opportunistic infection	Systemic infection
Candida infection*	Bacteremia
<i>Clostridium difficile</i> colitis	Bacterial sepsis
Coccidioidomycosis	Fungal sepsis**
Cytomegalovirus infection	<i>Klebsiella</i> sepsis
Esophageal candidiasis	Pneumococcal sepsis
Fungal infection*	Pseudomonal sepsis**
Fungal sepsis**	Sepsis
Fungal skin infection*	Septic shock
Genital infection fungal	Staphylococcal bacteremia
Herpes ophthalmic	Thrombophlebitis septic
Herpes pharyngitis	Urosepsis
Herpes simplex*	
Herpes virus infection*	
Herpes zoster*	
Oral candidiasis	
Oral fungal infection	
Oropharyngitis fungal	
Pseudomonal sepsis**	
<i>Pseudomonas</i> infection	
Urinary tract infection fungal	
<i>Varicella</i> *	
Vulvovaginal mycotic infection	

*Term was counted as a possible opportunistic infection but could also be a routine infection.

**Term could be a possible opportunistic infection or systemic infection.

Romiplostim in primary ITP by prior splenectomy

Supplementary Table S2. Thrombotic events

n (r)	Nonsplenectomized		Splenectomized		All patients	
	Romiplostim	Placebo/SOC	Romiplostim	Placebo/SOC	Romiplostim	Placebo/SOC
	N=655 1129.7 pt-yr	N=106 97.7 pt-yr	N=391 702.0 pt-yr	N=27 11.2 pt-yr	N=1046 1831.8 pt-yr	N=133 108.8 pt-yr
Thrombotic event by type						
Acute myocardial infarction	2 (0.2)	-	2 (0.3)	-	4 (0.2)	-
Blindness transient	1 (0.1)	-	-	-	1 (<0.1)	-
Carotid artery occlusion	-	1 (1.0)	-	-	-	1 (0.9)
Cerebrovascular accident	6 (0.5)	-	1 (0.1)	-	7 (0.4)	-
Cerebrovascular disorder	-	1 (1.0)	-	-	-	1 (0.9)
Coronary artery occlusion	1 (0.1)	-	-	-	1 (<0.1)	-
Deep vein thrombosis	9 (0.8)	1 (1.0)	10 (1.4)	-	19 (1.0)	1 (0.9)
Hemiparesis	1 (0.1)	-	1 (0.1)	-	2 (0.1)	-
Intestinal infarction	-	-	1 (0.1)	-	1 (<0.1)	-
Intracranial venous sinus thrombosis	1 (0.1)	-	-	-	1 (<0.1)	-
Ischemic stroke	1 (0.1)	-	1 (0.1)	-	2 (0.1)	-
Myocardial infarction	6 (0.5)	-	2 (0.3)	-	8 (0.4)	-
Peripheral arterial occlusive disease	-	-	1 (0.1)	-	1 (<0.1)	-
Peripheral embolism	1 (0.1)	-	1 (0.1)	-	2 (0.1)	-
Portal vein thrombosis	2 (0.2)	-	3 (0.4)	-	5 (0.3)	-
Pulmonary embolism	7 (0.6)	-	7 (1.0)	1 (8.9)	14 (0.8)	1 (0.9)
Pulmonary thrombosis	2 (0.2)	-	-	-	2 (0.1)	-
Splenic infarction	1 (0.1)	-	-	-	1 (<0.1)	-

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Thrombophlebitis	5 (0.4)	-	1 (0.1)	-	6 (0.3)	-
Thrombophlebitis superficial	2 (0.2)	-	3 (0.4)	-	5 (0.3)	-
Thrombosis	1 (0.1)	-	3 (0.4)	-	4 (0.2)	-
Thrombosis in device	-	-	1 (0.1)	-	1 (<0.1)	-
Transient ischemic attack	2 (0.2)	-	3 (0.4)	-	5 (0.3)	-
Transverse sinus thrombosis	-	-	1 (0.1)	-	1 (<0.1)	-
Venous thrombosis	-	2 (2.0)	1 (0.1)	-	1 (<0.1)	2 (1.8)
Venous thrombosis limb	1 (0.1)	-	1 (0.1)	-	2 (0.1)	-
Last prior platelet count, x10 ⁹ /L*						
<20	4 (0.4)	1 (1.0)	7 (1.0)	1 (8.9)	11 (0.6)	2 (1.8)
<30	6 (0.5)	1 (1.0)	7 (1.0)	1 (8.9)	13 (0.7)	2 (1.8)
<50	8 (0.7)	2 (2.0)	10 (1.4)	1 (8.9)	18 (1.0)	3 (2.8)
50 to <100	7 (0.6)	1 (1.0)	7 (1.0)	-	14 (0.8)	1 (0.9)
100 to <200	20 (1.8)	-	9 (1.3)	-	29 (1.6)	-
200 to <400	14 (1.2)	1 (1.0)	12 (1.7)	-	26 (1.4)	1 (0.9)
≥400	3 (0.3)	1 (1.0)	6 (0.9)	-	9 (0.5)	1 (0.9)
Median (Q1, Q3)	141.5	71.0	156.0	3.0	150.0	52.5
	(77.0, 249.0)	(34.0, 376.0)	(75.0, 285.0)	(3.0, 3.0)	(77.0, 260.0)	(10.0, 376.0)

n: number of events; N: total number of patients; pt-yr: total patient-years on study; Q1: quartile 1; Q3: quartile 3; r: rate per 100 patient-years; SOC: standard of care.

Note: a single patient could have more than one thrombotic event.

*Platelet count closest to the thrombotic event within the prior 3 months.

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Supplementary Table S3. Thrombotic events and time over platelet count thresholds

	Nonsplenectomized		Splenectomized		All patients	
	No thrombotic event	Thrombotic event	No thrombotic event	Thrombotic event	No thrombotic event	Thrombotic event
Romiplostim	N=616	N=39	N=361	N=30	N=977	N=69
Percentage of time platelet count was $\geq 50 \times 10^9/L$						
Mean (SD)	74.4 (25.1)	71.5 (25.5)	59.7 (32.2)	67.1 (18.7)	69.0 (28.8)	69.6 (22.7)
Median (Q1, Q3)	83.3 (67.8, 91.7)	78.6 (68.2, 90.0)	72.7 (34.4, 86.1)	71.1 (52.0, 78.1)	80.4 (57.1, 90.1)	75.0 (63.0, 87.5)
Percentage of time platelets count was $\geq 200 \times 10^9/L$						
Mean (SD)	19.8 (20.5)	15.6 (16.2)	20.5 (21.0)	22.4 (17.6)	20.0 (20.7)	18.6 (17.0)
Median (Q1, Q3)	13.6 (3.0, 30.9)	11.5 (0.0, 27.3)	15.6 (0.0, 34.2)	22.7 (5.3, 33.3)	13.8 (2.1, 32.3)	17.4 (0.0, 31.7)
Placebo/SOC	N=102	N=4	N=26	N=1	N=128	N=5
Percentage of time platelet count was $\geq 50 \times 10^9/L$						
Mean (SD)	33.6 (32.4)	40.8 (36.6)	9.5 (16.7)	11.1 (-)	28.6 (31.3)	34.9 (34.4)
Median (Q1, Q3)	27.3 (0.0, 63.2)	39.2 (12.5, 69.2)	0.0 (0.0, 15.4)	11.1 (11.1, 11.1)	16.7 (0.0, 52.6)	25.0 (11.1, 53.3)
Percentage of time platelet count was $\geq 200 \times 10^9/L$						
Mean (SD)	8.2 (16.7)	18.8 (37.5)	2.2 (6.2)	0.0 (-)	6.9 (15.3)	15.0 (33.5)
Median (Q1, Q3)	0.0 (0.0, 8.3)	0.0 (0.0, 37.5)	0.0 (0.0, 0.0)	0.0 (0.0, 0.0)	0.0 (0.0, 4.8)	0.0 (0.0, 0.0)

Q1: quartile 1; Q3: quartile 3; SD: standard deviation; SOC: standard of care.