

The study listed may include approved and non-approved uses, formulations or treatment regimens. The results reported in any single study may not reflect the overall results obtained on studies of a product. Before prescribing any product mentioned in this Register, healthcare professionals should consult prescribing information for the product approved in their country.

<b>Study No.:</b> TRA108057
<b>Title:</b> An open-label repeat dosing study of eltrombopag olamine (SB 497115 GR) in adult subjects, with chronic idiopathic thrombocytopenic purpura (ITP). <b>REPEAT. Repeated ExPosure To Eltrombopag in Adults with Idiopathic Thrombocytopenic Purpura.</b>
<b>Rationale:</b> Idiopathic thrombocytopenic purpura is a disease characterized by autoantibody-induced platelet destruction and reduced platelet production, leading to a chronically low peripheral blood platelet count (<150,000/l). Current therapy for thrombocytopenia is unsatisfactory and is associated with significant morbidity and mortality. The administration of an oral agonist of the thrombopoietin receptor (TPO-R), such as eltrombopag, could reduce the severity and duration of thrombocytopenia, reduce the requirement for steroids, splenectomy and/or platelet transfusions. This open-label repeat dosing study evaluated the efficacy, safety, pharmacodynamic effect and durability of eltrombopag when administered in a cyclic, intermittent dosing schedule.
<b>Phase:</b> II
<b>Study Period:</b> 14 March 2007 to 24 June 2008
<b>Study Design:</b> Multi-center, open-label, single-group, repeat-dose study, to evaluate the efficacy, safety and consistency of response following repeated, intermittent dosing of eltrombopag over 3 cycles of therapy, as measured by platelet counts in adults with previously treated chronic ITP. A cycle was defined as an up to 6-week on-therapy period followed by an up to 4-week off-therapy period.
<b>Centres:</b> Subjects were enrolled in 25 centers located in a total of 9 countries in North America, Europe, Australia, and Asia.
<b>Indication:</b> Chronic idiopathic thrombocytopenic purpura (ITP).
<b>Treatment:</b> All subjects received a starting dose of eltrombopag 50 mg in 3 cycles of repeated, intermittent dosing. A cycle was defined as an eltrombopag on-therapy period of up to 6 weeks and an off-therapy period for up to 4 weeks. The dose could be increased to 75 mg eltrombopag on or after Day 22 of each cycle.
<b>Objectives:</b> The primary objective of this study was to evaluate the effect of eltrombopag on platelet counts when administered during 3 cycles of repeated, intermittent treatment.
<b>Primary Outcome/Efficacy Variable:</b> The primary endpoint was consistency (durability of response) defined as the proportion of subjects who responded to eltrombopag treatment in Cycle 2 or 3 (given they responded in Cycle 1). Response was defined as a platelet count $\geq 50$ Gi/L and at least 2x baseline at Day 43 or at treatment discontinuation for subjects who withdrew early due to achieving a platelet count $>200$ Gi/L.
<b>Secondary Outcome/Efficacy Variable(s):</b> <ul style="list-style-type: none"> <li>• Proportion of subjects achieving a platelet count of <math>\geq 50</math> Gi/L and at least 2x baseline in at least 80% of assessments during weeks 2-6 of study treatment in each cycle</li> <li>• Pharmacodynamic parameters of platelet count (baseline, peak and trough) over 3 cycles</li> <li>• Proportion of subjects requiring rescue treatment (defined as a composite of: new ITP medication, increased dose of a concomitant ITP medication from baseline, platelet transfusion, and/or splenectomy) over the 3 cycles</li> <li>• Safety and tolerability assessments included adverse event (AE) collection, clinical laboratory evaluations, concomitant medications, physical examinations, 12-lead electrocardiograms, and detailed ocular examinations</li> <li>• Effect of repeated intermittent dosing of eltrombopag on anti-platelet antibody levels using the indirect PaKAuto Assay (detects serum glycoprotein-specific antigens; GPIIb/IIIa, Ib/IX, and</li> </ul>

<p>la/IIa) carried out by The Blood Center of Southeastern Wisconsin</p> <ul style="list-style-type: none"> <li>Incidence and severity of bleeding signs and symptoms measured using the World Health Organization (WHO) Bleeding Scale and the ITP Bleeding Score</li> </ul>			
<p><b>Statistical Methods:</b> No statistical hypothesis testing was envisaged. All data collected was summarized using appropriate descriptive statistics. The proportion of subjects with a positive response in either Cycle 2 or Cycle 3 given they had a positive response in Cycle 1 was calculated together with 95% confidence intervals for the observed proportion. The Intent-to-Treat (ITT) population comprised of all the subjects who were dispensed study medication. The primary population for efficacy analysis was a subset of the ITT population, defined as all subjects who entered the study, received at least 1 dose of the study medication, and responded in Cycle 1. The Per-Protocol Population was defined as all subjects who were dispensed study medication and responded in Cycle 1 and who did not have any full protocol violations (as defined in the Research Analysis Plan [RAP]). All safety analyses were performed using the Safety Population, which included all subjects who entered the study and received at least 1 dose of study medication.</p>			
<p><b>Study Population:</b> Male and female subjects <math>\geq 18</math> years of age with previously treated chronic ITP, as defined according to the American Society of Hematology/British Committee for Standards in Hematology guidelines, who had platelet counts between <math>\geq 20</math> Gi/L and <math>\leq 50</math> Gi/L, on the Day 1 visit (or within 24 hours prior to dosing on Day 1) and who had received 1 or more prior ITP therapies were eligible for inclusion in this study.</p>			
<b>Number of Subjects:</b>		<b>Eltrombopag 50 mg</b>	
Planned, N		50	
Entered, N		66	
Completed, n (%)		48 (73)	
Total Number Of Subjects Withdrawn, N (%)		18 (27)	
Withdrawn due to non-response in Cycle 1 (per protocol)		9 (14)	
Withdrawn due to Adverse Events, n (%)		1 (2)	
Withdrawn due to Investigator Decision, n (%)		1 (2)	
Withdrawn due to Subject's decision, n (%)		2 (3)	
Withdrawn due to Lack of Efficacy, n (%)		2 (3)	
Withdrawn for other reasons, n (%)		3 (5)	
<b>Demographics</b>		<b>Eltrombopag 50 mg</b>	
N (ITT)		66	
Females: Males		45 : 21	
Median Age, years (Min-Max)		50.5 (20-79)	
White, n (%)		53 (80)	
Asian, n (%)		10 (15)	
Other, n (%)		3 (5)	
<b>Primary Efficacy Results:</b>			
The summary of subjects with platelet counts greater than or equal to 50 Gi/L and at least 2x baseline after up to 42 days of dosing (ITT population), is presented below			
	<b>Eltrombopag 50 mg</b>		
	<b>Cycle 1 (N=66)</b>	<b>Cycle 2 (N=55)</b>	<b>Cycle 3 (N=51)</b>
Evaluable	65	54	51
Responders, n(%)	52 (80)	43 (80)	39 (76)
The summary of subjects with platelet counts greater than or equal to 50 Gi/L and at least 2x baseline after up to 42 days of dosing (subjects responded in Cycle 1) [ITT Population], is presented below			
	<b>Eltrombopag 50 mg</b>		

	Cycle 1 (N=52)	Cycle 2 (N=52)	Cycle 3 (N=49)
Evaluable	52	51	49
Responders, n (%)	52 (100)	41 (80)	38 (78)
<b>The primary endpoint - analysis of responders in Cycle 1 and in Cycle 2 or 3 (ITT Population)</b>			
	<b>Eltrombopag 50 mg</b>		
<b>Evaluable in Cycle 1, n</b>	65		
<b>Response in Cycle 1, n (%)</b>	52 (80)		
Evaluable in Cycle 2 or 3, n	52		
<b>Responders in Cycle 1 and in Cycle 2 or 3, n (%)</b>	45 (87)		
Proportion	0.87		
95% CI for Proportion (Exact Methods)	(0.74, 0.94)		
<b>Analysis of responder in Cycle 1 and in Cycle 2 and 3 (ITT Population)</b>			
	<b>Eltrombopag 50 mg</b>		
Evaluable in Cycle 2 and 3,	48		
<b>Responders in Cycle 1 and in Cycle 2 and 3, n (%)</b>	34 (71)		
Proportion	0.71		
95% CI for Proportion (Exact Methods)	(0.56, 0.83)		
<b>Secondary Outcome Variable(s) :</b>			
<ul style="list-style-type: none"> <li>The subjects responding for at least 80% of assessments during Weeks 2-6 – (ITT Population, Subjects Responding in Cycle 1, Observed Data) is summarized in the table below</li> </ul>			
	Cycle 1 (N=52)	Cycle 2 (N=52)	Cycle 3 (N=49)
Evaluable, n	48	45	43
≥80% of assessments met criteria, n (%)	38 (79)	35 (78)	30 (70)
<ul style="list-style-type: none"> <li>The platelet count (Gi/L) peaks and troughs (subjects responded in Cycle 1) + TT Population (Observed Data) is summarized in the table below</li> </ul>			
	<b>Eltrombopag 50 mg</b>		
<b>Observed Platelet Levels</b>	<b>Cycle 1 (N=52)</b>	<b>Cycle 2 (N=52)</b>	<b>Cycle 3 (N=49)</b>
<b>Baseline, n</b>	52	51	49
Mean (SD)	33.5 (12.77)	27.8 (15.82)	32.4 (26.8)
Median (Min, Max)	33.0 (7.0-82.0)	25.0 (0.0-66.0)	26.0 (8.0-167.0)
<b>On-therapy Period</b>			
<b>Highest, n</b>	52	52	49
Mean (SD)	225.8 (134.69)	209.1 (115.08)	175.6 (82.54)
Median (Min, Max)	200.5 (52.0-762.0)	196.0 (31.0-613.0)	174.0 (10.0-366.0)
<b>Lowest, n</b>	52	52	49
Mean (SD)	94.1 (67.52)	99.6 (91.51)	78.6 (72.69)
Median (Min, Max)	72.0 (6.0-354.0)	67.5 (7.0-454.0)	59.0 (2.0-344.0)
<b>Off-therapy Period</b>			
<b>Highest, n</b>	52	52	49
Mean (SD)	157.2 (148.83)	141.8 (143.37)	144.9 (116.12)
Median (Min, Max)	118.5 (0.0-662.0)	92.5 (12.0-701.0)	125.0 (26.0-594.0)
<b>Lowest, n</b>	52	52	49
Mean (SD)	23.3 (11.54)	25.6 (13.81)	26.7 (24.21)

Median (Min, Max)	21.0 (0.0-59.0)	22.5 (8.0-75.0)	22.0 (0.0-123.00)			
<ul style="list-style-type: none"> <li>No subject received a rescue medication during treatment with eltrombopag or during the off therapy periods between Cycles 1 and 2 or Cycles 2 and 3</li> <li>The anti-platelet antibody samples analyzed are summarized in the table below</li> </ul>						
	<b>Baseline (screening or Day 1)</b>	<b>On-Therapy</b>		<b>Off-Therapy (following last dose of treatment)</b>		
		<b>Cycle 2</b>	<b>Cycle 3</b>	<b>4 Week FU</b>	<b>3 Month FU</b>	<b>6 Month FU</b>
<b>Number of samples</b>	64	44	44	45	18	18
<b>Number of subjects with positive results</b>	12	6	7	8	2	3
The majority of samples tested were negative at baseline and remained negative over the course of treatment for antibodies to glycoproteins Ia/IIa, Ib/IX, and IIb/IIIa. Of the 18% of subjects with detectable anti-platelet antibody, there was no systemic change in the detectable anti-platelet antibody levels during the REPEAT study.						
<ul style="list-style-type: none"> <li>The WHO Grade Bleeding Scale, Grades 0 vs. Grades 1-4 (ITT Population) are summarized in the table below</li> </ul>						
	<b>WHO Grade<sup>a</sup></b>	<b>Cycle 1 (N=52) n (%)</b>	<b>Cycle 2 (N=52) n (%)</b>	<b>Cycle 3 (N=49) n (%)</b>		
<b>On-therapy</b>						
<b>Week 0 (Day 1)</b>						
n		52	52	49		
	Grade 0	26 (50)	21 (40)	32 (65)		
	Grade 1 -4	26 (50)	31 (60)	17 (35)		
<b>Week 1 (Day 8)</b>						
n		51	51	49		
	Grade 0	34 (67)	36 (71)	37 (76)		
	Grade 1 -4	17 (33)	15 (29)	12 (24)		
<b>Week 2 (Day 15)</b>						
n		47	45	43		
	Grade 0	35 (74)	38 (84)	32 (74)		
	Grade 1 -4	12 (26)	7 (16)	11 (26)		
<b>Week 3 (Day 22)</b>						
n		33	32	33		
	Grade 0	28 (85)	25 (78)	26 (79)		
	Grade 1 -4	5 (15)	7 (22)	7 (21)		
<b>Week 4 (Day 29)</b>						
n		31	28	29		
	Grade 0	23 (74)	22 (79)	24 (83)		
	Grade 1 -4	8 (26)	6 (21)	5 (17)		
<b>Week 5 (Day 36)</b>						
n		28	26	29		
	Grade 0	24 (86)	20 (77)	24 (83)		
	Grade 1 -4	4 (14)	6 (23)	5 (17)		
<b>Week 6 (Day 43)</b>						
n		25	26	27		
	Grade 0	22 (88)	22 (85)	22 (81)		

	Grade 1 -4	3 (12)	4 (15)	5 (19)
<b>Off-therapy</b>				
<b>Week 1 (Day 8)</b>				
n		47	45	48
	Grade 0	37 (79)	35 (78)	42 (88)
	Grade 1 -4	10 (21)	10 (22)	6 (13)
<b>Week 2 (Day 15)</b>				
n		37	35	46
	Grade 0	26 (70)	25 (71)	31 (67)
	Grade 1 -4	11 (30)	10 (29)	15 (33)
<b>Week 3 (Day 22)</b>				
n		29	30	46
	Grade 0	19 (66)	19 (63)	30 (65)
	Grade 1 -4	10 (34)	11 (37)	16 (35)
<b>Week 4 (Day 29)</b>				
n		7	12	48
	Grade 0	5 (71)	9 (75)	30 (63)
	Grade 1 -4	2 (29)	3 (25)	18 (38)
a. Grade 0 (No Bleeding), Grade 1 (Petechiae), Grade 2 (Mild Blood Loss), Grade 3 (Gross Blood Loss), Grade 4 (Debilitating Blood Loss)				
<ul style="list-style-type: none"> <li>The ITP Bleeding Scores (Responders in Cycle 1, ITT Population) for all 10 categories are summarized in the table below</li> </ul>				
Visit	Grade <sup>a</sup>	Cycle 1 (N=52) n (%)	Cycle 2 (N=52) n (%)	Cycle 3 (N=49) n (%)
<b>Category- Skin, petechiae</b>				
<b>On-therapy</b>				
<b>Wk 0 (Day 1)</b>				
n		51	52	49
	0	34 (67)	36 (69)	39 (80)
	1	15 (29)	16 (31)	10 (20)
	2	2 (4)	0	0
<b>Wk 1 (Day 8)</b>				
n		51	51	48
	0	41 (80)	44 (86)	42 (88)
	1	9 (18)	4 (8)	5 (10)
	2	1 (2)	3 (6)	1 (2)
<b>Wk 2 (Day 15)</b>				
n		47	45	42
	0	41 (87)	43 (96)	39 (93)
	1	5 (11)	2 (4)	2 (5)
	2	1 (2)	0	1 (2)
<b>Wk 3 (Day 22)</b>				
n		33	32	33
	0	32 (97)	27 (84)	32 (97)
	1	1 (3)	4 (13)	1 (3)
	2	0	1 (3)	0
<b>Wk 4 (Day 29)</b>				
n		31	29	29
	0	31 (100)	25 (86)	28 (97)
	1	0	4 (14)	1 (3)
	2	0	0	0

<b>Wk 5 (Day 36)</b>				
n		28	26	29
	0	27 (96)	21 (81)	28 (97)
	1	1 (4)	5 (19)	1 (3)
	2	0	0	0
<b>Wk 6 (Day 43)</b>				
n		25	25	27
	0	25 (100)	23 (92)	27 (100)
	1	0	2 (8)	0
	2	0	0	0
<b>Off-therapy</b>				
<b>Wk 1 (Day 8)</b>				
n		47	45	48
	0	45 (96)	39 (87)	45 (94)
	1	2 (4)	6 (13)	3 (6)
	2	0	0	0
<b>Wk 2 (Day 15)</b>				
n		36	35	46
	0	30 (83)	30 (86)	41 (89)
	1	6 (17)	5 (14)	4 (9)
	2	0	0	1 (2)
<b>Wk 3 (Day 22)</b>				
n		29	30	46
	0	27 (93)	26 (87)	39 (85)
	1	2 (7)	4 (13)	6 (13)
	2	0	0	1 (2)
<b>Wk 4 (Day 29)</b>				
n		7	12	48
	0	7 (100)	11 (92)	39 (81)
	1	0	1 (8)	8 (17)
	2	0	0	1 (2)
<b>Visit</b>	<b>Grade<sup>a</sup></b>	<b>Cycle 1 (N=52) n (%)</b>	<b>Cycle 2 (N=52) n (%)</b>	<b>Cycle 3 (N=49) n (%)</b>
<b>Category- Skin, ecchymosis</b>				
<b>On-therapy</b>				
<b>Wk 0 (Day 1)</b>				
n		51	52	49
	0	29 (57)	25 (48)	35 (71)
	1	18 (35)	26 (50)	13 (27)
	2	4 (8)	1 (2)	1 (2)
<b>Wk 1 (Day 8)</b>				
n		51	51	48
	0	38 (75)	35 (69)	34 (71)
	1	13 (25)	15 (29)	13 (27)
	2	0	1 (2)	1 (2)
<b>Wk 2 (Day 15)</b>				
n		47	45	42
	0	39 (83)	37 (82)	32 (76)
	1	8 (17)	8 (18)	9 (21)
	2	0	0	1 (2)

<b>Wk 3 (Day 22)</b>				
n		33	32	33
	0	28 (85)	25 (78)	27 (82)
	1	5 (15)	6 (19)	6 (18)
	2	0	1 (3)	0
<b>Wk 4 (Day 29)</b>				
n		31	29	29
	0	24 (77)	24 (83)	25 (86)
	1	7 (23)	5 (17)	4 (14)
	2	0	0	0
<b>Wk 5 (Day 36)</b>				
n		28	26	29
	0	25 (89)	23 (88)	23 (79)
	1	3 (11)	3 (12)	6 (21)
	2	0	0	0
<b>Wk 6 (Day 43)</b>				
n		25	25	27
	0	22 (88)	22 (88)	25 (93)
	1	3 (12)	3 (12)	2 (7)
	2	0	0	0
<b>Off-therapy</b>				
<b>Wk 1 (Day 8)</b>				
n		47	45	48
	0	42 (89)	37 (82)	42 (88)
	1	5 (11)	8 (18)	6 (13)
	2	0	0	0
<b>Wk 2 (Day 15)</b>				
n		36	35	46
	0	26 (72)	24 (69)	37 (80)
	1	9 (25)	11 (31)	9 (20)
	2	1 (3)	0	0
<b>Wk 3 (Day 22)</b>				
n		29	30	46
	0	17 (59)	20 (67)	30 (65)
	1	10 (34)	9 (30)	14 (30)
	2	2 (7)	1 (3)	2 (4)
<b>Wk 4 (Day 29)</b>				
n		7	12	48
	0	6 (86)	9 (75)	31 (65)
	1	0	3 (25)	15 (31)
	2	1 (14)	0	2 (4)
<b>Visit</b>	<b>Grade<sup>a</sup></b>	<b>Cycle 1 (N=52) n (%)</b>	<b>Cycle 2 (N=52) n (%)</b>	<b>Cycle 3 (N=49) n (%)</b>
<b>Category- Oral</b>				
<b>On-therapy</b>				
<b>Wk 0 (Day 1)</b>				
n		51	52	49
	0	44 (86)	44 (85)	45 (92)
	1	7 (14)	7 (13)	4 (8)
	2	0	1 (2)	0

<b>Wk 1 (Day 8)</b>				
n		51	51	48
	0	48 (94)	48 (94)	44 (92)
	1	3 (6)	2 (4)	2 (4)
	2	0	1 (2)	2 (4)
<b>Wk 2 (Day 15)</b>				
n		47	45	42
	0	45 (96)	42 (93)	40 (95)
	1	2 (4)	3 (7)	2 (5)
	2	0	0	0
<b>Wk 3 (Day 22)</b>				
n		33	32	33
	0	32 (97)	29 (91)	31 (94)
	1	1 (3)	3 (9)	2 (6)
	2	0	0	0
<b>Wk 4 (Day 29)</b>				
n		31	29	29
	0	29 (94)	27 (93)	29 (100)
	1	2 (6)	2 (7)	0
	2	0	0	0
<b>Wk 5 (Day 36)</b>				
n		28	26	29
	0	26 (93)	24 (92)	29 (100)
	1	2 (7)	2 (8)	0
	2	0	0	0
<b>Wk 6 (Day 43)</b>				
n		25	25	27
	0	22 (88)	23 (92)	26 (96)
	1	3 (12)	2 (8)	1 (4)
	2	0	0	0
<b>Off-therapy</b>				
<b>Wk 1 (Day 8)</b>				
n		47	45	48
	0	44 (94)	43 (96)	47 (98)
	1	3 (6)	2 (4)	1 (2)
	2	0	0	0
<b>Wk 2 (Day 15)</b>				
n		36	35	46
	0	36 (100)	30 (86)	43 (93)
	1	0	5 (14)	3 (7)
	2	1 (3)	0	0
<b>Wk 3 (Day 22)</b>				
n		29	30	46
	0	25 (86)	27 (90)	41 (89)
	1	4 (14)	3 (10)	5 (11)
	2	0	0	0
<b>Wk 4 (Day 29)</b>				
n		7	12	48
	0	6 (86)	10 (83)	45 (94)
	1	1 (14)	2 (17)	3 (6)
	2	0	0	0

Visit	Grade <sup>a</sup>	Cycle 1 (N=52) n (%)	Cycle 2 (N=52) n (%)	Cycle 3 (N=49) n (%)
<b>Category- Epistaxis</b>				
<b>On-therapy</b>				
<b>Wk 0 (Day 1)</b>				
n		51	52	49
	0	46 (90)	47 (90)	46 (94)
	1	5 (10)	4 (8)	3 (6)
	2	0	1 (2)	0
<b>Wk 1 (Day 8)</b>				
n		51	51	48
	0	50 (98)	50 (98)	47 (98)
	1	1 (2)	1 (2)	1 (2)
	2	0	0	0
<b>Wk 2 (Day 15)</b>				
n		47	45	42
	0	45 (96)	44 (98)	42 (100)
	1	2 (4)	1 (2)	0
	2	0	0	0
<b>Wk 3 (Day 22)</b>				
n		33	32	33
	0	33 (100)	31 (97)	33 (100)
	1	0	1 (3)	0
	2	0	0	0
<b>Wk 4 (Day 29)</b>				
n		31	29	29
	0	31 (100)	28 (97)	28 (97)
	1	0	1 (3)	1 (3)
	2	0	0	0
<b>Wk 5 (Day 36)</b>				
n		28	26	29
	0	28 (100)	25 (96)	27 (93)
	1	0	1 (4)	1 (3)
	2	0	0	1 (3)
<b>Wk 6 (Day 43)</b>				
n		25	25	27
	0	25 (100)	23 (92)	24 (89)
	1	0	2 (8)	3 (11)
	2	0	0	0
<b>Off-therapy</b>				
<b>Wk 1 (Day 8)</b>				
n		47	45	48
	0	45 (96)	44 (98)	47 (98)
	1	2 (4)	1 (2)	1 (2)
	2	0	0	0
<b>Wk 2 (Day 15)</b>				
n		36	35	46
	0	36 (100)	34 (97)	46 (100)
	1	0	1 (3)	0
	2	0	0	0

<b>Wk 3 (Day 22)</b>				
n		29	30	46
	0	28 (97)	29 (97)	42 (91)
	1	1 (3)	1 (3)	2 (4)
	2	0	0	2 (4)
<b>Wk 4 (Day 29)</b>				
n		7	12	48
	0	7 (100)	12 (100)	45 (94)
	1	0	0	3 (6)
	2	0	0	0
<b>Visit</b>	<b>Grade<sup>a</sup></b>	<b>Cycle 1 (N=52) n (%)</b>	<b>Cycle 2 (N=52) n (%)</b>	<b>Cycle 3 (N=49) n (%)</b>
<b>Category- Ocular</b>				
<b>On-therapy</b>				
<b>Wk 0 (Day 1)</b>				
n		51	52	49
	0	51 (100)	52 (100)	49 (100)
	1	0	0	0
	2	0	0	0
<b>Wk 1 (Day 8)</b>				
n		51	51	48
	0	51 (100)	49 (96)	48 (100)
	1	0	1 (2)	0
	2	0	1 (2)	0
<b>Wk 2 (Day 15)</b>				
n		47	45	42
	0	47 (100)	45 (100)	42 (100)
	1	0	0	0
	2	0	0	0
<b>Wk 3 (Day 22)</b>				
n		33	32	33
	0	33 (100)	32 (100)	33 (100)
	1	0	0	0
	2	0	0	0
<b>Wk 4 (Day 29)</b>				
n		31	29	29
	0	31 (100)	29 (100)	29 (100)
	1	0	0	0
	2	0	0	0
<b>Wk 5 (Day 36)</b>				
n		28	26	29
	0	28 (100)	26 (100)	29 (100)
	1	0	0	0
	2	0	0	0
<b>Wk 6 (Day 43)</b>				
n		25	25	27
	0	25 (100)	25 (100)	27 (100)
	1	0	0	0
	2	0	0	0
<b>Off-therapy</b>				

<b>Wk 1 (Day 8)</b>				
n		47	45	48
	0	46 (98)	45 (100)	48 (100)
	1	1 (2)	0	0
	2	0	0	0
<b>Wk 2 (Day 15)</b>				
n		36	35	46
	0	36 (100)	35 (100)	46 (100)
	1	0	0	0
	2	0	0	0
<b>Wk 3 (Day 22)</b>				
n		29	30	46
	0	29 (100)	30 (100)	45 (98)
	1	0	0	1 (2)
	2	0	0	0
<b>Wk 4 (Day 29)</b>				
n		7	12	48
	0	7 (100)	12 (100)	48 (100)
	1	0	0	0
	2	0	0	0
<b>Visit</b>	<b>Grade<sup>a</sup></b>	<b>Cycle 1 (N=52) n (%)</b>	<b>Cycle 2 (N=52) n (%)</b>	<b>Cycle 3 (N=49) n (%)</b>
<b>Category- GI</b>				
<b>On-therapy</b>				
<b>Wk 0 (Day 1)</b>				
n		51	52	49
	0	50 (98)	52 (100)	48 (98)
	1	1 (2)	0	1 (2)
	2	0	0	0
<b>Wk 1 (Day 8)</b>				
n		51	51	48
	0	50 (98)	51 (100)	48 (100)
	1	1 (2)	0	0
	2	0	0	0
<b>Wk 2 (Day 15)</b>				
n		47	45	42
	0	47 (100)	45 (100)	42 (100)
	1	0	0	0
	2	0	0	0
<b>Wk 3 (Day 22)</b>				
n		33	32	33
	0	32 (97)	32 (100)	33 (100)
	1	1 (3)	0	0
	2	0	0	0
<b>Wk 4 (Day 29)</b>				
n		31	29	29
	0	31 (100)	28 (97)	29 (100)
	1	0	1 (3)	0
	2	0	0	0
<b>Wk 5 (Day 36)</b>				

<b>n</b>		28	26	29
	0	28 (100)	24 (92)	29 (100)
	1	0	2 (8)	0
	2	0	0	0
<b>Wk 6 (Day 43)</b>				
<b>n</b>		25	25	27
	0	25 (100)	24 (96)	27 (100)
	1	0	1 (4)	0
	2	0	0	0
<b>Off-therapy</b>				
<b>Wk 1 (Day 8)</b>				
<b>n</b>		47	45	48
	0	45 (96)	43 (96)	48 (100)
	1	2 (4)	2 (4)	0
	2	0	0	0
<b>Wk 2 (Day 15)</b>				
<b>n</b>		36	35	46
	0	35 (97)	35 (100)	46 (100)
	1	1 (3)	0	0
	2	0	0	0
<b>Wk 3 (Day 22)</b>				
<b>n</b>		29	30	46
	0	28 (97)	30 (100)	46 (100)
	1	1 (3)	0	0
	2	0	0	0
<b>Wk 4 (Day 29)</b>				
<b>n</b>		7	12	48
	0	7 (100)	11 (92)	48 (100)
	1	0	1 (8)	0
	2	0	0	0
<b>Visit</b>	<b>Grade<sup>a</sup></b>	<b>Cycle 1 (N=52) n (%)</b>	<b>Cycle 2 (N=52) n (%)</b>	<b>Cycle 3 (N=49) n (%)</b>
<b>Category- Genitourinary</b>				
<b>On-therapy</b>				
<b>Wk 0 (Day 1)</b>				
<b>n</b>		51	52	49
	0	50 (98)	50 (96)	48 (98)
	1	1 (2)	1 (2)	0
	2	0	0	0
	Missing	0	1 (2)	1 (2)
<b>Wk 1 (Day 8)</b>				
<b>n</b>		51	51	48
	0	51 (100)	51 (100)	48 (100)
	1	0	0	0
	2	0	0	0
<b>Wk 2 (Day 15)</b>				
<b>n</b>		47	45	42
	0	45 (96)	44 (98)	42 (100)
	1	0	0	0
	2	1 (2)	0	0

	Missing	1 (2)	1 (2)	0
<b>Wk 3 (Day 22)</b>				
n		33	32	33
	0	33 (100)	30 (94)	32 (97)
	1	0	0	0
	2	0	1 (3)	0
	Missing	0	1 (3)	1 (3)
<b>Wk 4 (Day 29)</b>				
n		31	29	29
	0	30 (97)	28 (97)	29 (100)
	1	0	0	0
	2	0	0	0
	Missing	1 (3)	1 (3)	0
<b>Wk 5 (Day 36)</b>				
n		28	26	29
	0	28 (100)	26 (100)	29 (100)
	1	0	0	0
	2	0	0	0
<b>Wk 6 (Day 43)</b>				
n		25	25	27
	0	25 (100)	25 (100)	27 (100)
	1	0	0	0
	2	0	0	0
<b>Off-therapy</b>				
<b>Wk 1 (Day 8)</b>				
n		47	45	48
	0	47 (100)	44 (98)	46 (96)
	1	0	0	0
	2	0	1 (2)	0
	Missing	0	0	2 (4)
<b>Wk 2 (Day 15)</b>				
n		36	35	46
	0	35 (97)	33 (94)	45 (98)
	1	0	1 (3)	1 (2)
	2	0	0	0
	Missing	1 (3)	1 (3)	0
<b>Wk 3 (Day 22)</b>				
n		29	30	46
	0	28 (97)	29 (97)	45 (98)
	1	1 (3)	0	0
	2	0	0	0
	Missing	0	1 (3)	1 (2)
<b>Wk 4 (Day 29)</b>				
n		7	12	48
	0	7 (100)	11 (92)	47 (98)
	1	0	0	1 (2)
	2	0	0	0
	Missing	0	1 (8)	0
<b>Visit</b>	<b>Grade<sup>a</sup></b>	<b>Cycle 1 (N=52) n (%)</b>	<b>Cycle 2 (N=52) n (%)</b>	<b>Cycle 3 (N=49) n (%)</b>

<b>Category- Gynecologic</b>				
<b>On-therapy</b>				
<b>Wk 0 (Day 1)</b>				
n		51	52	49
	0	13 (25)	14 (27)	13 (27)
	1	1 (2)	0	0
	2	0	1 (2)	1 (2)
	Missing	37 (73)	37 (71)	35 (71)
<b>Wk 1 (Day 8)</b>				
n		51	51	48
	0	13 (25)	13 (25)	13 (27)
	1	0	1 (2)	0
	2	0	0	1 (2)
	Missing	38 (75)	37 (73)	34 (71)
<b>Wk 2 (Day 15)</b>				
n		47	45	42
	0	12 (26)	11 (24)	10 (24)
	1	0	0	0
	2	0	0	0
	Missing	35 (74)	34 (76)	32 (76)
<b>Wk 3 (Day 22)</b>				
n		33	32	33
	0	7 (21)	8 (25)	8 (24)
	1	0	0	0
	2	0	0	0
	Missing	26 (79)	24 (75)	25 (76)
<b>Wk 4 (Day 29)</b>				
n		31	29	29
	0	7 (23)	7 (24)	5 (17)
	1	0	0	0
	2	0	0	0
	Missing	24 (77)	22 (76)	24 (83)
<b>Wk 5 (Day 36)</b>				
n		28	26	29
	0	6 (21)	6 (23)	5 (17)
	1	0	0	0
	2	0	1 (4)	0
	Missing	22 (79)	19 (73)	24 (83)
<b>Wk 6 (Day 43)</b>				
n		25	25	27
	0	4 (16)	7 (28)	4 (15)
	1	0	0	0
	2	0	0	0
	Missing	21 (84)	18 (72)	23 (85)
<b>Off-therapy</b>				
<b>Wk 1 (Day 8)</b>				
n		47	45	48
	0	12 (26)	13 (29)	15 (31)
	1	0	0	0
	2	0	0	0
	Missing	35 (74)	32 (71)	33 (69)

<b>Wk 2 (Day 15)</b>				
n		36	35	46
	0	10 (28)	10 (29)	14 (30)
	1	0	1 (3)	0
	2	0	0	0
	Missing	26 (72)	25 (71)	32 (70)
<b>Wk 3 (Day 22)</b>				
n		29	30	46
	0	7 (24)	7 (23)	13 (28)
	1	0	0	0
	2	0	0	1 (2)
	Missing	22 (76)	23 (77)	32 (70)
<b>Wk 4 (Day 29)</b>				
n		7	12	48
	0	3 (43)	5 (42)	15 (31)
	1	0	0	0
	2	0	0	0
	Missing	4 (57)	7 (58)	33 (69)
<b>Visit</b>	<b>Grade<sup>a</sup></b>	<b>Cycle 1 (N=52) n (%)</b>	<b>Cycle 2 (N=52) n (%)</b>	<b>Cycle 3 (N=49) n (%)</b>
<b>Category- Pulmonary</b>				
<b>On-therapy</b>				
<b>Wk 0 (Day 1)</b>				
n		51	52	49
	0	51 (100)	52 (100)	49 (100)
	1	0	0	0
	2	0	0	0
<b>Wk 1 (Day 8)</b>				
n		51	51	48
	0	51 (100)	51 (100)	48 (100)
	1	0	0	0
	2	0	0	0
<b>Wk 2 (Day 15)</b>				
n		47	45	42
	0	47 (100)	45 (100)	42 (100)
	1	0	0	0
	2	0	0	0
<b>Wk 3 (Day 22)</b>				
n		33	32	33
	0	33 (100)	32 (100)	33 (100)
	1	0	0	0
	2	0	0	0
<b>Wk 4 (Day 29)</b>				
n		31	29	29
	0	31 (100)	29 (100)	29 (100)
	1	0	0	0
	2	0	0	0
<b>Wk 5 (Day 36)</b>				
n		28	26	29
	0	28 (100)	26 (100)	29 (100)

	1	0	0	0
	2	0	0	0
<b>Wk 6 (Day 43)</b>				
n		25	25	27
	0	25 (100)	25 (100)	27 (100)
	1	0	0	0
	2	0	0	0
<b>Off-therapy</b>				
<b>Wk 1 (Day 8)</b>				
n		47	45	48
	0	45 (100)	45 (100)	48 (100)
	1	0	0	0
	2	0	0	0
<b>Wk 2 (Day 15)</b>				
n		36	35	46
	0	36 (100)	35 (100)	46 (100)
	1	0	0	0
	2	0	0	0
<b>Wk 3 (Day 22)</b>				
n		29	30	46
	0	29 (100)	30 (100)	46 (100)
	1	0	0	0
	2	0	0	0
<b>Wk 4 (Day 29)</b>				
n		7	12	48
	0	7 (100)	12 (100)	48 (100)
	1	0	0	0
	2	0	0	0
<b>Visit</b>	<b>Grade<sup>a</sup></b>	<b>Cycle 1 (N=52) n (%)</b>	<b>Cycle 2 (N=52) n (%)</b>	<b>Cycle 3 (N=49) n (%)</b>
<b>Category- Intracerebral hemorrhage</b>				
<b>On-therapy</b>				
<b>Wk 0 (Day 1)</b>				
n		51	52	49
	0	51 (100)	52 (100)	49 (100)
	1	0	0	0
	2	0	0	0
<b>Wk 1 (Day 8)</b>				
n		51	51	48
	0	51 (100)	51 (100)	48 (100)
	1	0	0	0
	2	0	0	0
<b>Wk 2 (Day 15)</b>				
n		47	45	42
	0	47 (100)	45 (100)	42 (100)
	1	0	0	0
	2	0	0	0
<b>Wk 3 (Day 22)</b>				
n		33	32	33

	0	33 (100)	32 (100)	33 (100)
	1	0	0	0
	2	0	0	0
<b>Wk 4 (Day 29)</b>				
n		31	29	29
	0	31 (100)	29 (100)	29 (100)
	1	0	0	0
	2	0	0	0
<b>Wk 5 (Day 36)</b>				
n		28	26	29
	0	28 (100)	26 (100)	29 (100)
	1	0	0	0
	2	0	0	0
<b>Wk 6 (Day 43)</b>				
n		25	25	27
	0	25 (100)	25 (100)	27 (100)
	1	0	0	0
	2	0	0	0
<b>Off-therapy</b>				
<b>Wk 1 (Day 8)</b>				
n		47	45	48
	0	47 (100)	45 (100)	48 (100)
	1	0	0	0
	2	0	0	0
<b>Wk 2 (Day 15)</b>				
n		36	35	46
	0	36 (100)	35 (100)	46 (100)
	1	0	0	0
	2	0	0	0
<b>Wk 3 (Day 22)</b>				
n		29	30	46
	0	29 (100)	30 (100)	46 (100)
	1	0	0	0
	2	0	0	0
<b>Wk 4 (Day 29)</b>				
n		7	12	48
	0	7 (100)	12 (100)	48 (100)
	1	0	0	0
	2	0	0	0
a=Screening visit indicates worst ever lifetime event in category; all other visits indicate subject reported bleeding since last visit				
<b>Safety Results:</b> All the adverse events (AEs) and serious AEs (SAEs) occurring from the day that subjects received investigational product until completion of the study (including the follow-up period) were recorded. On- or off-therapy AEs reported by 5% or more of subjects across the study are summarised in the following table (Safety Population)				
<b>Preferred Term</b>	<b>All Cycles</b>			
	<b>On therapy</b>		<b>Off therapy</b>	
	<b>N=66</b>		<b>N=65</b>	
	<b>n (%)</b>		<b>n (%)</b>	
Subjects with any AE(s)	45 (68)		41 (63)	
Headache	14 (21)		5 (8)	

Diarrhea	7 (11)	4 (6)		
Fatigue	6 (9)	6 (9)		
Nasopharyngitis	6 (9)	6 (9)		
Arthralgia	4 (6)	1 (2)		
Nausea	4 (6)	2 (3)		
Vomiting	4 (6)	1 (2)		
Back pain	3 (5)	5 (8)		
Insomnia	3 (5)	1 (2)		
Pain in extremity	3 (5)	2 (3)		
Upper respiratory tract infection	3 (5)	3 (5)		
<b>Serious Adverse Events, during on-therapy period plus 1 day, n (%) [n considered by the investigator to be related to study medication]: Safety Population</b>				
	Cycle 1 (N=66) n (%)	Cycle 2 (N=55) n (%)	Cycle 3 (N=51) n (%)	All Cycles (N=66) n (%)
Subject with any SAE	0	1 (2) [0]	0	1 (2) [0]
Pneumonia	0	1 (2) [0]	0	1 (2) [0]
<b>Serious Adverse Events, started during an off-therapy period, n (%) [n considered by the investigator to be related to study medication]: Safety Population</b>				
	Cycle 1 (N=65) n (%)	Cycle 2 (N=55) n (%)	Cycle 3 (N=51) n (%)	All Cycles (N=65) n (%)
Subject with any SAE	0	1 (2) [0]	0	1 (2) [0]
Abdominal pain upper	0	1 (2) [0]	0	1 (2) [0]
<b>Serious Adverse Events, started &gt;1 to 30 day after last dose of eltrombopag, n (%) [n considered by the investigator to be related to study medication]: Safety Population</b>				
	Eltrombopag 50 mg (N=66)			
Subject with any SAE	1 (2) [0]			
Pancreatic carcinoma	1 (2) [0]			
<b>Serious Adverse Events, started &gt;30 days after last dose of eltrombopag, n (%) [n considered by the investigator to be related to study medication]: Safety Population</b>				
	Eltrombopag 50 mg (N=66)			
Subjects with any SAE	1 (2) [0]			
Mouth hemorrhage	1 (2) [0]			
Ear hemorrhage	1 (2) [0]			
Epistaxis	1 (2) [0]			
Fatal SAEs: There were no deaths reported during the on-therapy period or during the 4-week follow-up period of the study. However, one subject who reported an SAE of pancreatic carcinoma died 6 and one-half months post-therapy from that cancer.				
<b>Conclusion:</b> Treatment with eltrombopag demonstrated consistency of response in repeated cycles of treatment, as 87% of ITP subjects who responded in Cycle 1 also responded in Cycle 2 or Cycle 3.				
<b>Publications:</b> None				