ClinicalTrials.gov Protocol Registration and Results System (PRS) Receipt
Release Date: 11/21/2012

ClinicalTrials.gov ID: NCT00370331

Study Identification

Unique Protocol ID:	TRA102537
Brief Title:	RAISE: Randomized Placebo-Controlled Idiopathic Thrombocytopenic Purpura (ITP) Study With Eltrombopag
Official Title:	A Randomized, Double-blind, Placebo-controlled Phase III Study, to Evaluate the Efficacy, Safety and Tolerability of Eltrombopag Olamine (SB-497115-GR), a Thrombopoietin Receptor Agonist, Administered for 6 Months as Oral Tablets Once Daily in Adult Subjects With Previously Treated Chronic ITP.
Secondary IDs:	

Study Status

Record Verification:	November 2012
Overall Status:	Completed
Study Start:	November 2006
Primary Completion:	July 2008 [Actual]
Study Completion:	July 2008 [Actual]

Sponsor/Collaborators

Sponsor:	GlaxoSmithKline
Responsible Party:	Sponsor
Collaborators:	

Oversight

FDA Regulated?:	Yes

Applicable Trial?:	Section 801 Clinical Trial? Yes Delayed Posting? No
IND/IDE Protocol?:	Yes
IND/IDE Information:	Grantor: CDER IND/IDE Number: 63,293 Serial Number: 0003 Has Expanded Access? No
Review Board:	Approval Status: Approved Approval Number: 23153 Board Name: Quorum Central IRB Board Affiliation: No affiliation Phone: 206-448-4082 Email: info@quorumreview.com
Data Monitoring?:	
Plan to Share Data?:	
Oversight Authorities:	United Kingdom: Medicines and Healthcare Products Regulatory Agency United States: Food and Drug Administration

Study Description

Brief Summary:	The rationale for this Phase III study is to evaluate the 6 month safety and efficacy of eltrombopag in the treatment of previously treated subjects with chronic ITP. The starting dose of eltrombopag, 50 mg, once daily was selected based upon the observed efficacy, safety and pharmacokinetics in a dose-finding Study (TRA100773). This Phase III study is a randomized, double-blind, placebo-controlled, Phase III study, to evaluate efficacy, safety and tolerability of eltrombopag, initially administered as 50 mg oral tablets once daily for six months in adult subjects with previously treated chronic ITP. Subjects will be randomized 2:1, eltrombopag to placebo, and will be stratified based upon splenectomy status, use of ITP medication at baseline and baseline platelet count less than or equal to 15,000/μL. Subjects will receive study medication for 6 months, during which the dose of study medication may be adjusted based upon individual platelet counts. In addition, subjects may taper off concomitant ITP medications and may receive any rescue treatments as dictated by local standard of care. After discontinuation of study medication, subjects will complete follow-up visits at weeks 1, 2, 4 and months 3 and 6.
Detailed Description:	A randomized, double-blind, placebo-controlled phase III study, to evaluate the efficacy, safety and tolerability of eltrombopag olamine (SB-497115-GR), a thrombopoietin receptor agonist, administered for 6 months as oral tablets once daily in adult subjects with previously treated chronic idiopathic thrombocytopenic purpura (ITP).

Conditions

Conditions:	Purpura, Thrombocytopenic, Idiopathic
Keywords:	ITP idiopathic

platelets
purpura
thrombocytopenia
Idiopathic Thrombocytopenic Purpura
thrombocytopenic

Study Design

Study Type:	Interventional
Primary Purpose:	Treatment
Study Phase:	Phase 3
Intervention Model:	Parallel Assignment
Number of Arms:	2
Masking:	Double Blind (Subject, Caregiver, Investigator, Outcomes Assessor)
Allocation:	Randomized
Endpoint Classification:	Safety/Efficacy Study
Enrollment:	197 [Actual]

Arms and Interventions

Arms	Assigned Interventions
Experimental: Treatment arm plus standard of care Subjects will initiate treatment with 50 mg eltrombopag or matching placebo once daily. Based upon the subjects platelet count at each visit, the dose of eltrombopag may be adjusted either up or down.	Drug: eltrombopag Subjects will initiate treatment with either 50 mg eltrombopag or matching placebo once daily. Based upon the subjects platelet count at each visit, the dose of eltrombopag may be adjusted either up or down. Other Names: • eltrombopag
Placebo Comparator: placebo plus standard of care Subjects will initiate treatment with 50 mg eltrombopag or matching placebo once daily. Based upon the subjects platelet count at each visit, the dose of eltrombopag may be adjusted either up or down.	Drug: Placebo Subjects will initiate treatment with either 50 mg eltrombopag or matching placebo once daily. Based upon the subjects platelet count at each visit, the dose of eltrombopag may be adjusted either up or down

Outcome Measures

[See Results Section.]

Eligibility

Minimum Age: 18 Years

Maximum Age:

Gender: Both

Accepts Healthy Volunteers?: No

Criteria: Inclusion criteria:

- A subject will be eligible for inclusion in this study only if all of the following criteria apply:
- Subject has signed and dated a written informed consent.
- Adults (≥18 years) diagnosed with chronic ITP according to the American Society for Hematology/British Committee for Standards in Hematology (ASH/BCSH) guidelines [George, 1996; BCSH, 2003], and platelet count < 30,000/μL on Day 1 (or within 24 hours prior to dosing on Day 1). In addition, a peripheral blood smear should support the diagnosis of ITP with no evidence of other causes of thrombocytopenia (e.g. pseudothrombocytopenia, myelofibrosis). The physical examination should not suggest any disease which may cause thrombocytopenia other than ITP.
- Subjects who have previously received one or more prior ITP therapies. Previous treatments for ITP include but are not limited to corticosteroids, immunoglobulins, azathioprine, danazol, cyclophosphamide and/or rituximab.
- Subjects must have either initially responded (platelet count > 100,000/μL) to a previous ITP therapy or have had a bone marrow examination consistent with ITP within 3 years to rule out myelodysplastic syndromes or other causes of thrombocytopenia.
- Previous therapy for ITP with immunoglobulins (IVIg and anti-D) must have been completed at least 1 week prior to randomization and the platelet count must show a clear downward trend after the last treatment with immunoglobulins. Previous treatment for ITP with splenectomy, rituximab and cyclophosphamide must have been completed at least 4 weeks prior to randomization, or clearly be ineffective.
- Subjects treated with concomitant ITP medication (e.g. corticosteroids or azathioprine) must be receiving a dose that has been stable for at least 4 weeks prior to randomization. Subjects treated with cyclosporine A, mycophenolate mofetil or danazol must be receiving a dose that has been stable for at least 3 months prior to randomization. The medication should be continued with a stable dose for the initial 6 weeks of study "Concomitant ITP Therapy")
- Prothrombin time (PT/INR) and activated partial thromboplastin time (aPTT) must be within 80 to 120% of the normal range with no history of hypercoagulable state.
- A complete blood count (CBC), within the reference range (including WBC differential not indicative of a disorder other than ITP), with the following exceptions:
- < 30,000 platelets/μL on Day 1 (or within 24 hours of Day 1) is required for inclusion,
- Hemoglobin: Subjects with hemoglobin levels between 10 g/dL (100 g/L) and the lower limit of normal are eligible for inclusion, if anemia is clearly attributable to ITP (excessive blood loss).
- ANC ≥ 1500/μL (1.5 x 10^9/L) is required for inclusion (elevated WBC/ANC due to steroid treatment is acceptable).
- The following clinical chemistries MUST NOT exceed the upper limit of normal (ULN) reference range by more than 20%: creatinine, ALT, AST, total bilirubin, and alkaline phosphatase. In addition, total albumin must not be below the lower limit of normal (LLN) by more than 10%.
- Subject is practicing an acceptable method of contraception (documented in chart). Female subjects (or female partners of male subjects) must either be of non-childbearing potential (hysterectomy, bilateral oophorectomy, bilateral tubal ligation or post-menopausal > 1 year), or of childbearing potential and use one of the following highly effective methods of

contraception (i.e., Pearl Index <1.0%) from two weeks prior to administration of study medication, throughout the study, and 28 days after completion or premature discontinuation from the study:

- Complete abstinence from intercourse;
- Intrauterine device (IUD);
- Two forms of barrier contraception (diaphragm plus spermicide, and for males condom plus spermicide);
- Male partner is sterile prior to entry into the study and is the only partner of the female;
- Systemic contraceptives (combined or progesterone only). Subject is able to understand and comply with protocol requirements and instructions and intends to complete the study as planned.

Exclusion criteria:

- A subject will NOT be eligible for inclusion in this study if any of the following criteria apply:
- Any clinically relevant abnormality, other than ITP, identified on the screening examination or any other medical condition or circumstance, which in the opinion of the investigator makes the subject unsuitable for participation in the study or suggests another primary diagnosis (e.g., thrombocytopenia is secondary to another disease).
- Concurrent malignant disease and/or history of cancer treatment with cytotoxic chemotherapy and/or radiotherapy.
- Any prior history of arterial or venous thrombosis (stroke, transient ischemic attack, myocardial infarction, deep vein thrombosis or pulmonary embolism), AND ≥ two of the following risk factors: hormone replacement therapy, systemic contraception (containing estrogen), smoking, diabetes, hypercholesterolemia, medication for hypertension, cancer, hereditary thrombophilic disorders (e.g., Factor V Leiden, ATIII deficiency, etc), or any other family history of arterial or venous thrombosis.
- Pre-existing cardiovascular disease (congestive heart failure, New York Heart Association [NYHA] Grade III/IV), or arrhythmia known to increase the risk of thromboembolic events (e.g. atrial fibrillation), or subjects with a QTc >450 msec.
- Female subjects who are nursing or pregnant (positive serum or urine b-human chorionic gonadotrophin pregnancy test) at screening or pre-dose on Day 1.
- History of alcohol/drug abuse.
- Treatment with an investigational drug within 30 days or five half-lives (whichever is longer) preceding the first dose of study medication.
- Subject treated with drugs that affect platelet function (including but not limited to aspirin, clopidogrel and/or NSAIDs) or anti-coagulants for > 3 consecutive days within 2 weeks of the study start and until the end of the study.
- History of platelet agglutination abnormality that prevents reliable measurement of platelet counts.
- All subjects with secondary immune thrombocytopenia, including those with laboratory or clinical evidence of HIV infection, anti-phospholipid antibody syndrome, chronic hepatitis B infection, hepatitis C virus infection, or any evidence for active hepatitis at the time of subject screening. If a potential subject has no clinical history that would support HIV infection or hepatitis infection, no further laboratory screening is necessary; however, standard medical practice would suggest further evaluation of patients who have risk factors for these infections.
- Previous participation in a clinical study with eltrombopag.
- Patients planning to have cataract surgery.
- In France, a subject is neither affiliated with nor a beneficiary of a social security category.

Contacts/Locations

Study Officials: GSK Clinical Trials
Study Director

GlaxoSmithKline

Locations: Ukraine
GSK Investigational Site
Dnipropetrovsk, Ukraine, 49102

United States, California
GSK Investigational Site
Los Angeles, California, United States, 90033

United States, Washington
GSK Investigational Site
Tacoma, Washington, United States, 98405

United Kingdom
GSK Investigational Site
Rhyl, Denbighshire, United Kingdom

United States, Texas
GSK Investigational Site
Dallas, Texas, United States, 75137

Spain
GSK Investigational Site
Palma de Mallorca, Spain, 07014

United Kingdom
GSK Investigational Site
London, United Kingdom, NW1 2BU

Germany
GSK Investigational Site
Giessen, Hessen, Germany, 35392

GSK Investigational Site
Berlin, Berlin, Germany, 13353

United Kingdom
GSK Investigational Site
Leed, United Kingdom, LS1 3EX

United States, Ohio
GSK Investigational Site
Cleveland, Ohio, United States, 44106

Canada, Quebec

GSK Investigational Site
Montreal, Quebec, Canada, H2L 4M1

Peru
GSK Investigational Site
Lima, Lima, Peru, Lima 41

France
GSK Investigational Site
Pessac, France, 33604

Finland
GSK Investigational Site
Kuopio, Finland, 70210

Greece
GSK Investigational Site
Athens, Greece, 10676

GSK Investigational Site
Athens, Greece, 15123

Russian Federation
GSK Investigational Site
St Petersburg, Russian Federation, 193024

United States, California
GSK Investigational Site
San Francisco, California, United States, 94143

United States, District of Columbia
GSK Investigational Site
Washington, District of Columbia, United States, 20007

United Kingdom
GSK Investigational Site
Manchester, United Kingdom, M13 9WL

Canada, Quebec
GSK Investigational Site
Greenfield Park, Quebec, Canada, J4V 2H1

Russian Federation
GSK Investigational Site
Moscow, Russian Federation, 125167

Poland
GSK Investigational Site
Opole, Poland, 45-372

Italy
GSK Investigational Site
Padova, Veneto, Italy, 35128

United States, Georgia
GSK Investigational Site
Savannah, Georgia, United States, 31405

Peru
GSK Investigational Site
Lima, Peru, Lima 27

United Kingdom
GSK Investigational Site
London, United Kingdom, E1 1BB

GSK Investigational Site
Morriston, United Kingdom, SA6 6NL

Ukraine
GSK Investigational Site
Lviv, Ukraine, 79044

Russian Federation
GSK Investigational Site
Novosibirsk, Russian Federation, 630087

United States, Texas
GSK Investigational Site
Lubbock, Texas, United States, 79410

United Kingdom
GSK Investigational Site
Reading, United Kingdom, RG1 5AN

Canada, Ontario
GSK Investigational Site
Weston, Ontario, Canada, M9N 1N8

Poland
GSK Investigational Site
Krakow, Poland, 31-501

United States, New York
GSK Investigational Site
New York, New York, United States, 10065

Czech Republic
GSK Investigational Site
Brno, Czech Republic, 625 00

Netherlands
GSK Investigational Site
Amersfoort, Netherlands, 3816 CP

China
GSK Investigational Site
Tianjin, China, 300020

Poland
GSK Investigational Site
Slupsk, Poland, 76-200

Taiwan
GSK Investigational Site
Taipei, Taiwan, 100

United States, Massachusetts
GSK Investigational Site
Boston, Massachusetts, United States, 02114

Italy
GSK Investigational Site
Albano Laziale (Roma), Lazio, Italy, 00041

United States, Oregon
GSK Investigational Site
Portland, Oregon, United States, 97227

France
GSK Investigational Site
Caen, France, 14033

Canada, Newfoundland and Labrador
GSK Investigational Site
Saint John's, Newfoundland and Labrador, Canada, A1B 3V6

New Zealand
GSK Investigational Site

Auckland, New Zealand, 1701

Czech Republic
GSK Investigational Site
Olomouc, Czech Republic, 775 20

United States, New York
GSK Investigational Site
New York, New York, United States, 10029

France
GSK Investigational Site
Créteil, France, 94010

Taiwan
GSK Investigational Site
Taipei, Taiwan, 114

United States, California
GSK Investigational Site
Duarte, California, United States, 91010

Poland
GSK Investigational Site
Torun, Poland, 87-100

Ukraine
GSK Investigational Site
Kyiv, Ukraine, 04112

United States, Missouri
GSK Investigational Site
St. Louis, Missouri, United States, 63110

United States, Virginia
GSK Investigational Site
Arlington, Virginia, United States, 22205

Slovakia
GSK Investigational Site
Martin, Slovakia, 036 59

Germany
GSK Investigational Site
Muenchen, Bayern, Germany, 80639

GSK Investigational Site
Hannover, Niedersachsen, Germany, 30625

Netherlands
GSK Investigational Site
Zwolle, Netherlands, 8025 AB

Italy
GSK Investigational Site
Bologna, Emilia-Romagna, Italy, 40138

Canada, Ontario
GSK Investigational Site
Hamilton, Ontario, Canada, L8N 3Z5

United States, Oklahoma
GSK Investigational Site
Lawton, Oklahoma, United States, 73505

New Zealand
GSK Investigational Site
Auckland, New Zealand, 1309

United Kingdom
GSK Investigational Site
Plymouth, Devon, United Kingdom, PL6 8DH

Poland
GSK Investigational Site
Legnica, Poland, 59-200

Italy
GSK Investigational Site
Napoli, Campania, Italy, 80131

Tunisia
GSK Investigational Site
Sousse, Tunisia, 4000

New Zealand
GSK Investigational Site
Christchurch, New Zealand, 8011

Poland
GSK Investigational Site
Gdansk, Poland, 80-952

Taiwan
GSK Investigational Site
Taipei, Taiwan, 110

Slovakia
GSK Investigational Site
Kosice, Slovakia, 041 90

Poland
GSK Investigational Site
Wroclaw, Poland, 50-367

Italy
GSK Investigational Site
Vicenza, Veneto, Italy, 36100

New Zealand
GSK Investigational Site
Grafton, New Zealand, 1003

United States, Georgia
GSK Investigational Site
Atlanta, Georgia, United States, 30341

United States, Washington
GSK Investigational Site
Seattle, Washington, United States, 98109

Hong Kong
GSK Investigational Site
Shatin, Hong Kong

Austria
GSK Investigational Site
Vienna, Austria, A-1090

Italy
GSK Investigational Site
Milano, Lombardia, Italy, 20132

Czech Republic
GSK Investigational Site
Praha 2, Czech Republic, 128 20

Slovakia
GSK Investigational Site

Presov, Slovakia, 080 01

United States, Pennsylvania
GSK Investigational Site
Willow Grove, Pennsylvania, United States, 19090

United Kingdom
GSK Investigational Site
Taunton, Somerset, United Kingdom, TA1 5DA

Vietnam
GSK Investigational Site
Ho Chi Minh, Vietnam

Denmark
GSK Investigational Site
Odense, Denmark, 5000

Netherlands
GSK Investigational Site
Nijmegen, Netherlands, 6525 GA

References

Citations: Haselboeck J, Pabinger I, Ay C, Koder S, Panzer S. Platelet Activation and Function during Eltrombopag Treatment in Immune Thrombocytopenia. [Ann Hematol]. 2011;

Cheng G, Saleh MN, Marcher C, Vasey S, Mayer B, Aivado M, Arning M, Stone NL, Bussel JB. Eltrombopag for management of chronic immune thrombocytopenia (RAISE): a 6-month, randomised, phase 3 study. [Lancet].2011;377(9763):393-402.

Links:

Study Data/Documents:

Study Results

Participant Flow

Reporting Groups

	Description
Placebo	Matching placebo tablets taken once a day

	Description
Eltrombopag 50 mg QD	Eltrombopag 50 mg oral tablets taken once a day (QD)

Overall Study

	Placebo	Eltrombopag 50 mg QD
Started	62	135
Completed	55	112
Not Completed	7	23
Adverse Event	4	13
Withdrawal by Subject	2	4
Lost to Follow-up	0	3
Lack of Efficacy	0	1
Non-compliance	0	1
Protocol Violation	1	1

Baseline Characteristics

Reporting Groups

	Description
Placebo	Matching placebo tablets taken once a day
Eltrombopag 50 mg QD	Eltrombopag 50 mg oral tablets taken once a day (QD)

Baseline Measures

	Placebo	Eltrombopag 50 mg QD	Total
Number of Participants	62	135	197
Age, Continuous [units: years] Mean (Standard Deviation)	51.0 (14.72)	46.5 (15.61)	47.9 (15.45)
Gender, Male/Female [units: participants]			
Female	43	93	136
Male	19	42	61

	Placebo	Eltrombopag 50 mg QD	Total
Race/Ethnicity, Customized [units: participants]			
African American/African	1	2	3
American Indian/Alaska native	4	8	12
East Asian	10	19	29
South-East Asian	3	2	5
Native Hawaiian or other Pacific Islander	0	1	1
White/Arabic/North African	2	6	8
White/Caucasian/European	42	95	137
Mixed Race	0	2	2
Stratification variable [1] [units: Participants]			
Use of ITP medication at randomization	31	63	94
Splenectomy at randomization	21	50	71
Platelet count less or equal 15,000 per microliter	30	67	97

[1] Subjects were stratified at randomization based on current use of idiopathic thrombocytopenic purpura (ITP) medication, splenectomy status, and baseline platelet count

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Percentage of Responders
Measure Description	The percentage of evaluable participants who achieved a platelet response (defined as a platelet count between 50,000 and 400,000 microliter) at each nominal on-therapy day and 4 weeks post-treatment
Time Frame	Baseline; each on-therapy treatment day; Weeks 10, 14, 18, 22, and 26; and Weeks 1, 2, and 4 post-treatment
Safety Issue?	No

Analysis Population Description

Intent-to-Treat (ITT) Population: all randomized participants

Reporting Groups

	Description
Placebo	Matching placebo tablets taken once a day
Eltrombopag 50 mg QD	Eltrombopag 50 mg oral tablets taken once a day (QD)

Measured Values

	Placebo	Eltrombopag 50 mg QD
Number of Participants Analyzed	62	135
Percentage of Responders [units: Percentage of participants]		
Baseline	2	1
Day 8	7	37
Day 15	8	46
Day 22	8	51
Day 29	10	49
Day 36	8	56
Day 43	14	54
Week 10	17	52
Week 14	18	46
Week 18	17	46
Week 22	19	49
Week 26	17	52
1 Week Follow-up	15	42
2 Week Follow-up	18	22
4 Week Follow-up	14	20

Statistical Analysis 1 for Percentage of Responders

Statistical Analysis Overview	Comparison Groups	Placebo, Eltrombopag 50 mg QD
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.001
	Comments	[Not specified]
	Method	Other [Repeated measures model for binary data]
	Comments	Repeated measures model for binary data using Generalized Estimating Equations (GEE)
Method of Estimation	Estimation Parameter	Odds Ratio (OR)
	Estimated Value	8.2
	Confidence Interval	(2-Sided) 99% 3.59 to 18.73
	Estimation Comments	[Not specified]

2. Secondary Outcome Measure:

Measure Title	Summary of Median Platelet Counts
Measure Description	Platelet counts were measured by blood draw.
Time Frame	Baseline; Day 8 through Week 26 on-treatment; and 1, 2, 4 week follow-up visits
Safety Issue?	No

Analysis Population Description

ITT Population

Reporting Groups

	Description
Placebo	Matching placebo tablets taken once a day
Eltrombopag 50 mg QD	Eltrombopag 50 mg oral tablets taken once a day (QD)

Measured Values

	Placebo	Eltrombopag 50 mg QD
Number of Participants Analyzed	62	135
Summary of Median Platelet Counts [units: platelets/microliter (ul)] Median (Full Range)		
Baseline	16,000 (2000 to 87,000)	16,000 (0 to 78,000)
Day 8	17,500 (3000 to 354,000)	36,000 (1000 to 593,000)
Day 15	18,000 (2000 to 214,000)	54,000 (2000 to 750,000)
Day 22	18,500 (1000 to 271,000)	54,000 (1000 to 507,000)
Day 29	18,000 (3000 to 313,000)	53,000 (1000 to 400,000)
Day 36	19,000 (4000 to 297,000)	60,000 (1000 to 952,000)
Day 43	20,000 (3000 to 275,000)	59,000 (1000 to 545,000)
Week 10	20,000 (0 to 293,000)	61,500 (1000 to 433,000)
Week 14	17,500 (1000 to 303,000)	60,000 (1000 to 409,000)
Week 18	20,500 (2000 to 281,000)	61,000 (3000 to 363,000)
Week 22	23,000 (1000 to 315,000)	72,000 (3000 to 408,000)
Week 26	23,000 (2000 to 315,000)	73,500 (1000 to 429,000)
1 Week Follow-up	19,000 (0 to 323,000)	38,500 (1000 to 409,000)
2 Week Follow-up	18,000 (1000 to 340,000)	21,000 (1000 to 434,000)
4 Week Follow-up	18,000 (1000 to 301,000)	24,000 (1000 to 446,000)

3. Secondary Outcome Measure:

Measure Title	Percentage of Participants Initiating Rescue Treatment On-therapy
Measure Description	Percentage of participants initiating new ITP medication, an increased dose of concomitant ITP medication from baseline, platelet transfusion, or splenectomy.
Time Frame	Anytime from Day 1 to Week 26
Safety Issue?	No

Analysis Population Description
All participants randomized to receive placebo or eltrombopag treatment

Reporting Groups

	Description
Placebo	Matching placebo tablets taken once a day
Eltrombopag 50 mg QD	Eltrombopag 50 mg oral tablets taken once a day (QD)

Measured Values

	Placebo	Eltrombopag 50 mg QD
Number of Participants Analyzed	62	135
Percentage of Participants Initiating Rescue Treatment On-therapy [units: Percentage of participants]		
Participants who received rescue treatment	40	18
Participants who did not receive rescue treatment	60	82

4. Secondary Outcome Measure:

Measure Title	Maximum and Total Weeks of Platelet Response
Measure Description	Response is defined as a platelet count between 50,000 and 400,000 platelets per microliter.
Time Frame	Day 1 through Week 26 on-treatment
Safety Issue?	No

Analysis Population Description
ITT Population

Reporting Groups

	Description
Placebo	Matching placebo tablets taken once a day
Eltrombopag 50 mg QD	Eltrombopag 50 mg oral tablets taken once a day (QD)

Measured Values

	Placebo	Eltrombopag 50 mg QD
Number of Participants Analyzed	62	135
Maximum and Total Weeks of Platelet Response [units: Weeks] Median (Full Range)		
Maximum continuous Response	0 (0 to 25)	8.1 (0 to 26)
Cumulative Response	0 (0 to 25)	10.9 (0 to 26)

5. Secondary Outcome Measure:

Measure Title	Percentage of Participants With a Reduction in Use of Baseline ITP Medication
Measure Description	Percentage of participants who experienced a reduction in their baseline concomitant ITP medication use
Time Frame	From Day 1 through Week 26 on-treatment
Safety Issue?	No

Analysis Population Description

ITT Population

Reporting Groups

	Description
Placebo	Matching placebo tablets taken once a day
Eltrombopag 50 mg QD	Eltrombopag 50 mg oral tablets taken once a day (QD)

Measured Values

	Placebo	Eltrombopag 50 mg QD
Number of Participants Analyzed	60	134
Percentage of Participants With a Reduction in Use of Baseline ITP Medication [units: Percentage of participants]		
Participants who reduced/discontinued ITP therapy	32	59
Participants not reducing/discont. ITP therapy	68	41

6. Secondary Outcome Measure:

Measure Title	WHO Bleeding Scale
Measure Description	Summary of World Health Organization (WHO) bleeding scores at each nominal visit. WHO Grades 1-4 = any bleeding; WHO Grades 2-4 = clinically significant bleeding
Time Frame	Baseline, all nominal visits on-therapy defined as Day 8, Day 15, Day 22, Day 29, Day 36, Day 43, Week 10, Week 14, Week 18, Week 22, Week 26, and 1, 2 and 4 week follow-up visits
Safety Issue?	No

Analysis Population Description

ITT Population

Reporting Groups

	Description
Placebo	Matching placebo tablets taken once a day
Eltrombopag 50 mg QD	Eltrombopag 50 mg oral tablets taken once a day (QD)

Measured Values

	Placebo	Eltrombopag 50 mg QD
Number of Participants Analyzed	62	135
WHO Bleeding Scale [units: Percentage of participants]		
Baseline, WHO Grades 1-4	77	73
Day 8, WHO Grades 1-4	73	56
Day 15, WHO Grades 1-4	68	39
Day 22, WHO Grades 1-4	67	38
Day 29, WHO Grades 1-4	56	37
Day 36, WHO Grades 1-4	66	23
Day 43, WHO Grades 1-4	59	23
Week 10, WHO Grades 1-4	49	22
Week 14, WHO Grades 1-4	57	23
Week 18, WHO Grades 1-4	59	22

	Placebo	Eltrombopag 50 mg QD
Week 22, WHO Grades 1-4	46	18
Week 26, WHO Grades 1-4	56	22
1 Week Follow-up, WHO Grades 1-4	59	28
2 Week Follow-up, WHO Grades 1-4	56	50
4 Week Follow-up, WHO Grades 1-4	59	46
Baseline, WHO Grades 2-4	28	22
Day 8, WHO Grades 2-4	20	16
Day 15, WHO Grades 2-4	22	8
Day 22, WHO Grades 2-4	21	11
Day 29, WHO Grades 2-4	19	10
Day 36, WHO Grades 2-4	19	7
Day 43, WHO Grades 2-4	19	5
Week 10, WHO Grades 2-4	13	9
Week 14, WHO Grades 2-4	17	5
Week 18, WHO Grades 2-4	18	2
Week 22, WHO Grades 2-4	10	8
Week 26, WHO Grades 2-4	15	7
1 Week Follow-up, WHO Grades 2-4	20	11
2 Week Follow-up, WHO Grades 2-4	18	16
4 Week Follow-up, WHO Grades 2-4	21	13

7. Secondary Outcome Measure:

Measure Title	HR-QoL Instrument and Domain Scores From the SF-36v2 Questionnaire at Baseline, Week 6, Week 14, and Week 26 or Early Discontinuation From Study Treatment
Measure Description	Health-related quality of life (HR-QoL) patient reported outcomes from the short form-36v2 (SF-36v2) questionnaire. Scores could range from 0 (worst possible) to 100 (best possible).
Time Frame	Baseline, Week 6, Week 14, and Week 26/Early Withdrawal

Safety Issue?	No

Analysis Population Description
ITT Population

Reporting Groups

	Description
Placebo	Matching placebo tablets taken once a day
Eltrombopag 50 mg QD	Eltrombopag 50 mg oral tablets taken once a day (QD)

Measured Values

	Placebo	Eltrombopag 50 mg QD
Number of Participants Analyzed	62	135
HR-QoL Instrument and Domain Scores From the SF-36v2 Questionnaire at Baseline, Week 6, Week 14, and Week 26 or Early Discontinuation From Study Treatment [units: Points on a scale (0-100)] Mean (Standard Deviation)		
SF-36v2 physical function, Baseline	75.0 (21.7)	73.1 (26.8)
SF-36v2 physical function, Week 6	76.5 (20.8)	78.0 (24.4)
SF-36v2 physical function, Week 14	77.6 (20.0)	78.9 (22.5)
SF-36v2 physical funct., Week 26/Early Withdrawal	75.8 (22.6)	80.6 (21.7)
SF-36v2 physical role, Baseline	64.5 (26.7)	64.5 (30.5)
SF-36v2 physical role, Week 6	66.9 (25.4)	73.7 (27.4)
SF-36v2 physical role, Week 14	67.2 (25.8)	72.9 (24.9)
SF-36v2 physical role, Week 26/Early Withdrawal	67.5 (27.1)	73.7 (25.4)
SF-36v2 bodily pain, Baseline	70.0 (23.2)	75.2 (27.8)
SF-36v2 bodily pain, Week 6	69.9 (25.9)	78.5 (25.4)
SF-36v2 bodily pain, Week 14	68.3 (24.8)	77.6 (25.8)
SF-36v2 bodily pain, Week 26/Early Withdrawal	68.5 (25.0)	75.7 (26.6)
SF-36v2 general health, Baseline	53.7 (21.8)	56.0 (21.3)
SF-36v2 general health, Week 6	55.9 (21.4)	59.7 (21.5)

	Placebo	Eltrombopag 50 mg QD
SF-36v2 general health, Week 14	52.8 (23.2)	59.3 (20.7)
SF-36v2 general health, Week 26/Early Withdrawal	53.3 (24.9)	57.3 (23.1)
SF-36v2 vitality, Baseline	56.7 (20.2)	55.1 (26.3)
SF-36v2 vitality, Week 6	59.0 (20.0)	62.1 (22.7)
SF-36v2 vitality, Week 14	56.8 (22.3)	61.0 (22.4)
SF-36v2 vitality, Week 26/Early Withdrawal	57.5 (22.4)	60.0 (23.3)
SF-36v2 social function, Baseline	76.1 (21.7)	72.7 (28.3)
SF-36v2 social function, Week 6	78.0 (21.4)	77.6 (26.2)
SF-36v2 social function, Week 14	73.4 (25.8)	78.4 (22.6)
SF-36v2 social function, Week 26/Early Withdrawal	75.0 (25.8)	79.0 (24.2)
SF-36v2 emotional role, Baseline	73.4 (25.4)	69.1 (30.9)
SF-36v2 emotional role, Week 6	73.1 (24.6)	77.5 (25.9)
SF-36v2 emotional role, Week 14	73.3 (22.9)	74.1 (25.2)
SF-36v2 emotional role, Week 26/Early Withdrawal	71.5 (26.5)	76.9 (25.4)
SF-36v2 mental health, Baseline	70.3 (18.7)	68.0 (21.0)
SF-36v2 mental health, Week 6	71.7 (18.3)	71.8 (19.0)
SF-36v2 mental health, Week 14	68.6 (20.4)	70.6 (19.3)
SF-36v2 mental health, Week 26/Early Withdrawal	68.6 (22.8)	70.2 (21.6)
SF-36v physical component summary, Baseline	45.6 (8.3)	46.9 (9.7)
SF-36v physical component summary, Week 6	46.2 (8.3)	48.7 (9.0)
SF-36v physical component summary, Week 14	46.3 (8.3)	49.0 (8.1)
SF-36v physical component summary, Week 26/ EW	46.2 (8.1)	48.7 (8.6)
SF-36v2 mental component summary, Baseline	46.4 (10.1)	44.3 (12.6)
SF-36v2 mental component summary, Week 6	46.8 (10.0)	47.2 (11.1)
SF-36v2 mental component summary, Week 14	45.3 (11.1)	46.2 (11.3)
SF-36v2 mental component summary, Week 26/ EW	45.2 (12.3)	46.5 (12.4)

8. Secondary Outcome Measure:

Measure Title	HR-QoL Instrument and Domain Scores From the FACIT-F Questionnaire at Baseline, Week 6, Week 14, and Week 26 or Early Discontinuation From Study Treatment
Measure Description	Health-related quality of life (HR-QoL) patient reported outcomes from the functional assessment of chronic illness therapy fatigue (FACIT-F) questionnaire. Scores could range from 0 (worst possible) to 52 (best possible).
Time Frame	Baseline, Week 6, Week 14, and Week 26/Early Withdrawal
Safety Issue?	No

Analysis Population Description

ITT Population

Reporting Groups

	Description
Placebo	Matching placebo tablets taken once a day
Eltrombopag 50 mg QD	Eltrombopag 50 mg oral tablets taken once a day (QD)

Measured Values

	Placebo	Eltrombopag 50 mg QD
Number of Participants Analyzed	62	135
HR-QoL Instrument and Domain Scores From the FACIT-F Questionnaire at Baseline, Week 6, Week 14, and Week 26 or Early Discontinuation From Study Treatment [units: Points on a scale (0-52)] Mean (Standard Deviation)		
Baseline	36.3 (9.0)	36.0 (12.2)
Week 6	38.3 (8.2)	39.2 (9.7)
Week 14	36.9 (10.2)	39.5 (9.9)
Week 26/Early Withdrawal	37.0 (11.3)	39.2 (10.1)

9. Secondary Outcome Measure:

Measure Title	HR-QoL Instrument and Domain Scores for the FACT-Th Questionnaire at Baseline, Week 6, Week 14, and Week 26 or Early Discontinuation From Study Treatment
Measure Description	Health-related quality of life (HR-QoL) patient reported outcomes from the functional assessment of cancer therapy thrombocytopenia (FACT-Th) questionnaire (six selected items). Scores could range from 0 (worst possible) to 24 (best possible).
Time Frame	Baseline, Week 6, Week 14, and Week 26/Early Withdrawal
Safety Issue?	No

Analysis Population Description
ITT Population

Reporting Groups

	Description
Placebo	Matching placebo tablets taken once a day
Eltrombopag 50 mg QD	Eltrombopag 50 mg oral tablets taken once a day (QD)

Measured Values

	Placebo	Eltrombopag 50 mg QD
Number of Participants Analyzed	62	135
HR-QoL Instrument and Domain Scores for the FACT-Th Questionnaire at Baseline, Week 6, Week 14, and Week 26 or Early Discontinuation From Study Treatment [units: Points on a scale (0-24)] Mean (Standard Deviation)		
Baseline	14.8 (5.8)	13.5 (5.8)
Week 6	15.1 (5.7)	15.9 (6.0)
Week 14	15.3 (5.4)	16.7 (5.6)
Week 26/Early Withdrawal	15.3 (6.0)	16.0 (6.1)

10. Secondary Outcome Measure:

Measure Title	HR-QoL Instrument and Domain Scores From the MEI-SF Questionnaire at Baseline, Week 6, Week 14, and Week 26 or Early Discontinuation From Study Treatment

Measure Description	Health-related quality of life (HR-QoL) patient reported outcomes from the motivation and energy inventory-short form (MEI-SF) questionnaire. Scores could range from 0 (worst possible) to 72 (best possible).
Time Frame	Baseline, Week 6, Week 14, and Week 26/Early Withdrawal
Safety Issue?	No

Analysis Population Description
ITT Population

Reporting Groups

	Description
Placebo	Matching placebo tablets taken once a day
Eltrombopag 50 mg QD	Eltrombopag 50 mg oral tablets taken once a day (QD)

Measured Values

	Placebo	Eltrombopag 50 mg QD
Number of Participants Analyzed	62	135
HR-QoL Instrument and Domain Scores From the MEI-SF Questionnaire at Baseline, Week 6, Week 14, and Week 26 or Early Discontinuation From Study Treatment [units: Points on a scale (0-72)] Mean (Standard Deviation)		
Baseline	71.3 (17.2)	72.7 (21.4)
Week 6	73.4 (16.4)	76.2 (19.5)
Week 14	71.1 (20.5)	76.9 (20.5)
Week 26/Early Withdrawal	72.0 (21.7)	76.7 (20.2)

Reported Adverse Events

Time Frame	[Not specified]
Additional Description	62 participants were randomized to the placebo arm, but only 61 took study medication and are analyzed in the Safety Population.

Reporting Groups

	Description
Placebo	Matching placebo tablets taken once a day
Eltrombopag 50 mg QD	Eltrombopag 50 mg oral tablets taken once a day (QD)

Serious Adverse Events

	Placebo	Eltrombopag 50 mg QD
	Affected/At Risk (%)	Affected/At Risk (%)
Total	11/61 (18.03%)	16/135 (11.85%)
Blood and lymphatic system disorders		
Haemorrhagic anaemia [A] †	0/61 (0%)	1/135 (0.74%)
Eye disorders		
Cataract [A] †	2/61 (3.28%)	2/135 (1.48%)
Cataract subcapsular [A] †	1/61 (1.64%)	0/135 (0%)
Retinal haemorrhage [A] †	1/61 (1.64%)	0/135 (0%)
Gastrointestinal disorders		
Duodenal ulcer haemorrhage [A] †	0/61 (0%)	1/135 (0.74%)
Gastrointestinal haemorrhage [A] †	1/61 (1.64%)	0/135 (0%)
Intra-abdominal haemorrhage [A] †	0/61 (0%)	1/135 (0.74%)
Infections and infestations		
Cellulitis [A] †	1/61 (1.64%)	0/135 (0%)
Orchitis [A] †	1/61 (1.64%)	0/135 (0%)
Urinary tract infection [A] †	0/61 (0%)	1/135 (0.74%)
Injury, poisoning and procedural complications		
Hand fracture [A] †	1/61 (1.64%)	0/135 (0%)
Spinal compression fracture [A] †	0/61 (0%)	1/135 (0.74%)

	Placebo	Eltrombopag 50 mg QD
	Affected/At Risk (%)	Affected/At Risk (%)
Investigations		
Alanine aminotransferase (ALT) increased [A] †	1/61 (1.64%)	1/135 (0.74%)
Aspartate aminotransferase (AST) increased [A] †	0/61 (0%)	1/135 (0.74%)
Heart rate increased [A] †	1/61 (1.64%)	0/135 (0%)
Renal function test abnormal [A] †	1/61 (1.64%)	0/135 (0%)
Transaminases increased [A] †	0/61 (0%)	1/135 (0.74%)
Metabolism and nutrition disorders		
Hyperkalaemia [A] †	1/61 (1.64%)	0/135 (0%)
Hypokalaemia [A] †	0/61 (0%)	1/135 (0.74%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)		
Rectosigmoid cancer [A] †	0/61 (0%)	1/135 (0.74%)
Nervous system disorders		
Brain stem haemorrhage [A] †	1/61 (1.64%)	0/135 (0%)
Headache [A] †	0/61 (0%)	3/135 (2.22%)
Loss of consciousness [A] †	0/61 (0%)	1/135 (0.74%)
Renal and urinary disorders		
Haemorrhage urinary tract [A] †	1/61 (1.64%)	0/135 (0%)
Urogenital haemorrhage [A] †	1/61 (1.64%)	0/135 (0%)
Reproductive system and breast disorders		
Menorrhagia [A] †	1/61 (1.64%)	0/135 (0%)
Respiratory, thoracic and mediastinal disorders		
Pulmonary embolism [A] †	0/61 (0%)	2/135 (1.48%)

	Placebo	Eltrombopag 50 mg QD
	Affected/At Risk (%)	Affected/At Risk (%)
Pulmonary infarction [A] †	0/61 (0%)	1/135 (0.74%)
Respiratory tract haemorrhage [A] †	1/61 (1.64%)	0/135 (0%)
Vascular disorders		
Aortic aneurysm [A] †	0/61 (0%)	1/135 (0.74%)
Deep vein thrombosis [A] †	0/61 (0%)	1/135 (0.74%)
Thrombophlebitis superficial [A] †	0/61 (0%)	1/135 (0.74%)

† Indicates events were collected by systematic assessment.
A Term from vocabulary, MedDRA

Other Adverse Events

Frequency Threshold Above Which Other Adverse Events are Reported: 5%

	Placebo	Eltrombopag 50 mg QD
	Affected/At Risk (%)	Affected/At Risk (%)
Total	56/61 (91.8%)	120/135 (88.89%)
Eye disorders		
Conjunctival haemorrhage [A] †	3/61 (4.92%)	3/135 (2.22%)
Gastrointestinal disorders		
Abdominal pain upper [A] †	5/61 (8.2%)	7/135 (5.19%)
Constipation [A] †	6/61 (9.84%)	6/135 (4.44%)
Diarrhoea [A] †	6/61 (9.84%)	17/135 (12.59%)
Dyspepsia [A] †	5/61 (8.2%)	2/135 (1.48%)
Nausea [A] †	4/61 (6.56%)	17/135 (12.59%)
Vomiting [A] †	1/61 (1.64%)	10/135 (7.41%)
General disorders		
Fatigue [A] †	8/61 (13.11%)	13/135 (9.63%)

	Placebo	Eltrombopag 50 mg QD
	Affected/At Risk (%)	Affected/At Risk (%)
Oedema peripheral [A] †	6/61 (9.84%)	2/135 (1.48%)
Infections and infestations		
Cellulitis [A] †	4/61 (6.56%)	1/135 (0.74%)
Influenza [A] †	3/61 (4.92%)	7/135 (5.19%)
Nasopharyngitis [A] †	12/61 (19.67%)	14/135 (10.37%)
Pharyngitis [A] †	1/61 (1.64%)	9/135 (6.67%)
Upper respiratory tract infection [A] †	7/61 (11.48%)	14/135 (10.37%)
Urinary tract infection [A] †	4/61 (6.56%)	8/135 (5.93%)
Investigations		
Alanine aminotransferase (ALT) increased [A] †	3/61 (4.92%)	9/135 (6.67%)
Aspartate aminotransferase (AST) increased [A] †	2/61 (3.28%)	7/135 (5.19%)
Musculoskeletal and connective tissue disorders		
Arthralgia [A] †	3/61 (4.92%)	9/135 (6.67%)
Back pain [A] †	3/61 (4.92%)	9/135 (6.67%)
Myalgia [A] †	2/61 (3.28%)	8/135 (5.93%)
Neck pain [A] †	4/61 (6.56%)	2/135 (1.48%)
Pain in extremity [A] †	6/61 (9.84%)	9/135 (6.67%)
Nervous system disorders		
Dizziness [A] †	6/61 (9.84%)	5/135 (3.7%)
Headache [A] †	20/61 (32.79%)	40/135 (29.63%)
Psychiatric disorders		
Insomnia [A] †	5/61 (8.2%)	3/135 (2.22%)

	Placebo	Eltrombopag 50 mg QD
	Affected/At Risk (%)	Affected/At Risk (%)
Respiratory, thoracic and mediastinal disorders		
Cough [A] †	5/61 (8.2%)	7/135 (5.19%)
Epistaxis [A] †	6/61 (9.84%)	7/135 (5.19%)
Oropharyngeal pain [A] †	3/61 (4.92%)	9/135 (6.67%)
Skin and subcutaneous tissue disorders		
Ecchymosis [A] †	4/61 (6.56%)	2/135 (1.48%)
Pruritus [A] †	6/61 (9.84%)	5/135 (3.7%)

† Indicates events were collected by systematic assessment.
A Term from vocabulary, MedDRA

Limitations and Caveats

[Not specified]

More Information

Certain Agreements:

Principal Investigators are NOT employed by the organization sponsoring the study.

There IS an agreement between the Principal Investigator and the Sponsor (or its agents) that restricts the PI's rights to discuss or publish trial results after the trial is completed.

GSK agreements may vary with individual investigators, but will not prohibit any investigator from publishing. GSK supports the publication of results from all centers of a multi-center trial but requests that reports based on single-site data not precede the primary publication of the entire clinical trial.

Results Point of Contact:

Name/Official Title: GSK Response Center
Organization: GlaxoSmithKline
Phone: 866-435-7343
Email: