ClinicalTrials.gov Protocol Registration and Results System (PRS) Receipt
Release Date: 07/25/2013

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Study Identification

Unique Protocol ID:	TRA108057
Brief Title:	Repeated Exposure to Eltrombopag in Adults With Idiopathic Thrombocytopenic Purpura (REPEAT)
Official Title:	An Open-label Repeat Dosing Study of Eltrombopag Olamine (SB-497115-GR) in Adult Subjects, With Chronic Idiopathic Thrombocytopenic Purpura (ITP)
Secondary IDs:	

Study Status

Record Verification:	May 2012
Overall Status:	Completed
Study Start:	March 2007
Primary Completion:	August 2008 [Actual]
Study Completion:	November 2008 [Actual]

Sponsor/Collaborators

Sponsor:	GlaxoSmithKline
Responsible Party:	Sponsor
Collaborators:	

Oversight

FDA Regulated?:	
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: TBD Board Name: Quorum Central IRB Board Affiliation: No affiliation Phone: 206-448-4082 Email: info@quorumreview.com
Data Monitoring?:	No
Plan to Share Data?:	
Oversight Authorities:	United States: Food and Drug Administration

Study Description

Brief Summary:	This open-label, repeat dosing study, TRA108057, will evaluate the efficacy, safety and tolerability of eltrombopag, when administered in a repeat, cyclic dosing schedule. The study will describe the effect of repeated (3 cycles), intermittent dosing of eltrombopag on the pharmacodynamics and durability of eltrombopag response as measured by the peripheral platelet counts. For more information or to see if you qualify, please visit: http://www.itpstudy.com/gov
Detailed Description:	

Conditions

Conditions:	Purpura, Thrombocytopaenic, Idiopathic
Keywords:	idiopathic thrombocytopenic purpura ITP thrombocytopenia platelets

Study Design

Study Type:	Interventional
Primary Purpose:	Treatment
Study Phase:	Phase 2
Intervention Model:	Single Group Assignment

Number of Arms:	1
Masking:	Open Label
Allocation:	Non-Randomized
Endpoint Classification:	Safety/Efficacy Study
Enrollment:	66 [Actual]

Arms and Interventions

Arms	Assigned Interventions
Experimental: eltrombopag	Drug: eltrombopag experimental Other Names: • eltrombopag

Outcome Measures

[See Results Section.]

Eligibility

Minimum Age:	18 Years
Maximum Age:	
Gender:	Both
Accepts Healthy Volunteers?:	No
Criteria:	Inclusion Criteria:

Subjects eligible for enrolment in the study must meet all of the following criteria:

- Subject has signed and dated a written inform consent.
- Adults (≥18 years) diagnosed with chronic ITP according to the American Society of Hematology/British Committee for Standards in Hematology guidelines, and a platelet count between ≥20 Gi/L and ≤50 Gi/L 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, myelodysplasia). 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 Gi/L) to a previous ITP therapy or have had a bone marrow biopsy consistent with ITP within 3 years to rule out myelodysplastic syndromes or other causes of thrombocytopenia.
- It is important to clearly differentiate the effect of eltrombopag on platelet count from the treatment effects of prior and concomitant ITP therapies. Therefore:

    a. 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.
    b. Subjects treated with concomitant ITP medication (e.g. corticosteroids or azathioprine) must be receiving a dose that has been stable for a 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.
- Prothrombin time and activated partial thromboplastin time must be within 80 to 120% of normal range with no history of hypercoagulable state.
- A complete blood count (CBC), within the reference range (including differential not indicative of a disorder other than ITP), with the following exceptions:
- Platelet count between ≥20 Gi/L and ≤50 Gi/L on Day 1 (or within 24 hours of Day 1) is required for inclusion.
- Hemoglobin: Subjects with hemoglobin levels between 10g/dL (100g/L) and the lower limit of normal are eligible for inclusion, if anemia is clearly attributable to ITP (excessive blood loss).
- Absolute Neutrophil Count (ANC) >1500/mL (1.5 x 10^9/L) is required for inclusion (elevated White Blood Cells/ANC above the reference range due to steroid treatment is acceptable).
- The following clinical chemistries MUST NOT exceed the normal reference range by more than 20%: creatinine, Alanine aminotransferase, Aspartate aminotransferase, total bilirubin, total albumin and alkaline phosphatase.
- 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 of one of the following acceptable methods of contraception 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, Antithrombin III deficiency, etc), or any other family history of arterial or venous thrombosis.
- Pre-existing cardiovascular disease (congestive heart failure, New York Heart Association 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 Non Steroidal Anti Inflammatory Drugs) 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 human immunodeficiency virus (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.
- Subjects 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: Russian Federation
GSK Investigational Site
Moscow, Russian Federation, 125167

Germany
GSK Investigational Site
Berlin, Berlin, Germany, 13353

GSK Investigational Site
Hannover, Niedersachsen, Germany, 30625

References

Citations: Bussel JB, Saleh MN, Vasey SY, Mayer B, Arning M, Stone NL. Repeated short-term use of eltrombopag in patients with chronic immune thrombocytopenia (ITP). Br J Haematol. 2013;160(4):538-546.

This study has not been published in the scientific literature.

Tarantino M, Fogarty P, Mayer B, Vasey SY, Brainsky A. Efficacy of Eltrombopag in Management of Bleeding Symptoms Associated With Chronic Immune Thrombocytopenia. Blood Coagul Fibrinolysis. 2013;24(3):284-296.

Links:

Study Data/Documents:

Study Results

Participant Flow

Reporting Groups

	Description
Treatment Period	Three cycles of treatment. A cycle is defined as an on-therapy period of up to 6 weeks and an off-therapy period of up to 4 weeks.

Cycle 1: Eltrombopag 50 mg Starting Dose

	Treatment Period
Started	66
Completed	55
Not Completed	11
Lack of Efficacy	8
Adverse Event	1
Prolonged Response	1
Relocation	1

Cycle 2: Eltrombopag 50 or 75 mg

	Treatment Period
Started	55
Completed	51
Not Completed	4
Lack of Efficacy	2
Prolonged Response	1
Withdrawal by Subject	1

Cycle 3: Eltrombopag 50 or 75 mg

	Treatment Period
Started	51
Completed	48
Not Completed	3
Lack of Efficacy	1
Withdrawal by Subject	1
Physician Decision	1

Baseline Characteristics

Reporting Groups

	Description
Overall Study Population	Male and female participants greater than or equal to 18 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 greater than or equal to 20 gi/L and less than or equal to 50 Gi/L, on the Day 1 visit (or within 24 hours prior to dosing on Day 1).

Baseline Measures

	Overall Study Population
Number of Participants	66
Age, Continuous [units: years] Mean (Standard Deviation)	49.6 (14.61)

	Overall Study Population
Gender, Male/Female [units: participants]	
Female	45
Male	21
Race/Ethnicity, Customized [units: participants]	
White - White/Caucasian/ European	47
Asian - East Asian	10
White - Arabic/North African	6
African American/African	2
American Indian or Alaska Native	1
Baseline Platelet Count [1] [units: participants]	
Less than 20 giga per liter (Gi/L)	4
20 Gi/L to 30 Gi/L	29
Greater than 30 Gi/L to 50 Gi/L	31
Greater than 50 Gi/L	2
Baseline Splenectomy Status [units: participants]	
Yes	20
No	46
Use of Idiopathic Thrombocytopenic Purpura Medication at Baseline [2] [units: participants]	
Yes	22
No	44

[1] Baseline Platelet Count

[2] Baseline Idiopathic Thrombocytopenic Purpura (ITP) Medication Use

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Number of Participants Who Responded (Platelet Count >=50 Gi/L and >=2x Baseline) to Eltrombopag Treatment in Cycle 2 or Cycle 3 Given Participants Responded in Cycle 1
Measure Description	Complete blood count, platelet count by blood draw
Time Frame	Day 42 of each cycle
Safety Issue?	No

Analysis Population Description

Primary Analysis Population: All participants who entered the study, received at least 1 dose of eltrombopag, and responded in Cycle 1

Reporting Groups

	Description
Cycle 1	Eltrombopag 50 mg starting dose. Participants whose platelet count was below 50 Gi/L were permitted to increase to eltrombopag 75 mg on or after Day 22.
Cycle 2	Same dose of eltrombopag at which participants completed Cycle 1 (eltrombopag 50 or 75 mg)
Cycle 3	Same dose of eltrombopag at which participants completed Cycle 2 (eltrombopag 50 or 75 mg)

Measured Values

	Cycle 1	Cycle 2	Cycle 3
Number of Participants Analyzed	52	51	49
Number of Participants Who Responded (Platelet Count >=50 Gi/L and >=2x Baseline) to Eltrombopag Treatment in Cycle 2 or Cycle 3 Given Participants Responded in Cycle 1 [units: participants]			
Responders	52	41	38
Non-responders	0	10	11

Statistical Analysis 1 for Number of Participants Who Responded (Platelet Count >=50 Gi/L and >=2x Baseline) to Eltrombopag Treatment in Cycle 2 or Cycle 3 Given Participants Responded in Cycle 1

Statistical Analysis Overview	Comparison Groups	Cycle 2, Cycle 3
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Method of Estimation	Estimation Parameter	Other [Proportion of subjects in Cycle 2 or 3]
	Estimated Value	0.87
	Confidence Interval	(2-Sided) 95% 0.74 to 0.94
	Estimation Comments	[Not specified]

2. Secondary Outcome Measure:

Measure Title	Number of Participants Who Responded (Platelet Count Greater Than or Equal to 50 Gi/L and at Least 2x Baseline) for at Least 80 Percent of Their On-therapy Assessments During Weeks 2-6.
Measure Description	CBC, platelet counts
Time Frame	Up to 42 days of dosing
Safety Issue?	No

Analysis Population Description

Cycle 1 responders

Reporting Groups

	Description
Cycle 1	Eltrombopag 50 mg starting dose. Participants whose platelet count was below 50 Gi/L were permitted to increase to eltrombopag 75 mg on or after Day 22.
Cycle 2	Same dose of eltrombopag at which participants completed Cycle 1 (eltrombopag 50 or 75 mg)
Cycle 3	Same dose of eltrombopag at which participants completed Cycle 2 (eltrombopag 50 or 75 mg)

Measured Values

	Cycle 1	Cycle 2	Cycle 3
Number of Participants Analyzed	48	45	43

	Cycle 1	Cycle 2	Cycle 3
Number of Participants Who Responded (Platelet Count Greater Than or Equal to 50 Gi/L and at Least 2x Baseline) for at Least 80 Percent of Their On-therapy Assessments During Weeks 2-6. [units: participants]			
At least 80 percent of assessments met criteria	38	35	30
Less than 80 percent of assessments met criteria	10	10	13

3. Secondary Outcome Measure:

Measure Title	Changes in Participants' Platelet Counts During 3 Cycles of Treatment
Measure Description	Changes from baseline, during on-therapy periods of a cycle, during off-therapy periods of a cycle, and within 4 weeks of permanent discontinuation of eltrombopag treatment.
Time Frame	Up to 1 year
Safety Issue?	No

Analysis Population Description

Intent-to-Treat (ITT) Population: All participants who were dispensed study medication

Reporting Groups

	Description
Cycle 1	Eltrombopag 50 mg starting dose. Participants whose platelet count was below 50 Gi/L were permitted to increase to eltrombopag 75 mg on or after Day 22.
Cycle 2	Same dose of eltrombopag at which participants completed Cycle 1 (eltrombopag 50 or 75 mg)
Cycle 3	Same dose of eltrombopag at which participants completed Cycle 2 (eltrombopag 50 or 75 mg)

Measured Values

	Cycle 1	Cycle 2	Cycle 3
Number of Participants Analyzed	52	52	49
Changes in Participants' Platelet Counts During 3 Cycles of Treatment [units: Gi/L] Median (Full Range)			
Baseline platelet count	33.0 (7.0 to 82.0)	25.0 (0 to 66.0)	26.0 (8.0 to 167.0)

	Cycle 1	Cycle 2	Cycle 3
Highest on-therapy platelet count	200.5 (52.0 to 762.0)	196.0 (31.0 to 613.0)	174.0 (10.0 to 366.0)
Lowest on-therapy platelet count	72.0 (6.0 to 354.0)	67.5 (7.0 to 454.0)	59.0 (2.0 to 344.0)
Highest off-therapy platelet count	118.5 (0 to 662.0)	92.5 (12.0 to 701.0)	125.0 (21.0 to 594.0)
Lowest off-therapy platelet count	21.0 (0 to 59.0)	22.5 (8.0 to 75.0)	22.0 (0 to 187.0)

4. Secondary Outcome Measure:

Measure Title	Number of Participants Who Required Rescue Medication
Measure Description	New idiopathic thrombocytopenic purpura (ITP) medication, increase dose of a concomitant ITP medication from baseline, platelet transfusion, and/or splenectomy
Time Frame	Up to 3 cycles of treatment including follow-up visits following last dose of eltrombopag
Safety Issue?	No

Analysis Population Description

ITT Population

Reporting Groups

	Description
Cycle 1	Eltrombopag 50 mg starting dose. Participants whose platelet count was below 50 Gi/L were permitted to increase to eltrombopag 75 mg on or after Day 22.
Cycle 2	Same dose of eltrombopag at which participants completed Cycle 1 (eltrombopag 50 or 75 mg)
Cycle 3	Same dose of eltrombopag at which participants completed Cycle 2 (eltrombopag 50 or 75 mg)

Measured Values

	Cycle 1	Cycle 2	Cycle 3
Number of Participants Analyzed	66	55	51
Number of Participants Who Required Rescue Medication [units: participants]			
Participants who required rescue treatment	2	2	10
Participants who did not require rescue treatment	64	53	41

5. Secondary Outcome Measure:

Measure Title	Change in Participants Anti-platelet Antibody Levels From Baseline Through Follow-up
Measure Description	Change in participants' anti-platelet antibody levels was measured as the number of samples positive for at least 1 glycoprotein from baseline to follow-up. Serum glycoprotein-specific antigens: GPIIb/IIIa, Ib/IX, and Ia/IIa
Time Frame	Up to 1 year
Safety Issue?	No

Analysis Population Description

Safety Population: any participant who received at least 1 dose of study medication

Reporting Groups

	Description
Overall Study	

Measured Values

	Overall Study
Number of Participants Analyzed	64
Change in Participants Anti-platelet Antibody Levels From Baseline Through Follow-up [units: participants]	
Baseline	12
Cycle 2 on-therapy	6
Cycle 3 on-therapy	7
4-week follow-up	8
3-month follow-up	1
6-month follow-up	3

6. Secondary Outcome Measure:

Measure Title	Number of Participants With the Indicated Bleeding Signs and Symptoms Using the World Health Organization Bleeding Scale

Measure Description	World health Organization (WHO) Bleeding Scale Grade 0 = no bleeding, Grade 1 = petechiae, Grade 2 = mild blood loss, Grade 3 = gross blood loss, Grade 4 = debilitating blood loss.
Time Frame	Baseline, on-treatment visits (Weeks 1-6), off-treatment visits (Weeks 1-4)
Safety Issue?	No

Analysis Population Description

Participants who responded in Cycle 1

Reporting Groups

	Description
Cycle 1	Eltrombopag 50 mg starting dose. Participants whose platelet count was below 50 Gi/L were permitted to increase to eltrombopag 75 mg on or after Day 22.
Cycle 2	Same dose of eltrombopag at which participants completed Cycle 1 (eltrombopag 50 or 75 mg)
Cycle 3	Same dose of eltrombopag at which participants completed Cycle 2 (eltrombopag 50 or 75 mg)

Measured Values

	Cycle 1	Cycle 2	Cycle 3
Number of Participants Analyzed	52	52	49
Number of Participants With the Indicated Bleeding Signs and Symptoms Using the World Health Organization Bleeding Scale [units: participants]			
On-therapy, Week 0 (Day 1), n	52	52	49
On-therapy, Week 0, Grade 0	26	21	32
On-therapy, Week 0, Grades 1-4	26	31	17
On-therapy, Week 0, Grades 2-4	10	10	6
On-therapy, Week 1 (Day 8), n	51	51	49
On-therapy, Week 1, Grade 0	34	36	37
On-therapy, Week 1, Grades 1-4	17	15	12
On-therapy, Week 1, Grades 2-4	4	2	3
On-therapy, Week 2 (Day 15), n	47	45	43
On-therapy, Week 2, Grade 0	35	38	32
On-therapy, Week 2, Grades 1-4	12	7	11

	Cycle 1	Cycle 2	Cycle 3
On-therapy, Week 2, Grades 2-4	4	2	4
On-therapy, Week 3 (Day 22), n	33	32	33
On-therapy, Week 3, Grade 0	28	25	26
On-therapy, Week 3, Grades 1-4	5	7	7
On-therapy, Week 3, Grades 2-4	3	2	2
On-therapy, Week 4 (Day 29), n	31	28	29
On-therapy, Week 4, Grade 0	23	22	24
On-therapy, Week 4, Grade 1-4	8	6	5
On-therapy, Week 4, Grade 2-4	2	2	0
On-therapy, Week 5 (Day 36), n	28	26	29
On-therapy, Week 5, Grade 0	24	20	24
On-therapy, Week 5, Grades 1-4	4	6	5
On-therapy, Week 5, Grades 2-4	1	3	1
On-therapy, Week 6 (Day 43), n	25	26	27
On-therapy, Week 6, Grade 0	22	22	22
On-therapy, Week 6, Grades 1-4	3	4	5
On-therapy, Week 6, Grades 2-4	0	4	1
Off-therapy, Week 1 (Day 8), n	47	45	46
Off-therapy, Week 1, Grade 0	37	35	42
Off-therapy, Week 1, Grades 1-4	10	10	4
Off-therapy, Week 1, Grades 2-4	4	4	0
Off-therapy, Week 2 (Day 15), n	37	35	45
Off-therapy, Week 2, Grade 0	26	25	30
Off-therapy, Week 2, Grades 1-4	11	10	15
Off-therapy, Week 2, Grades 2-4	2	3	2
Off-therapy, Week 3 (Day 22), n	28	30	46
Off-therapy, Week 3, Grade 0	18	19	30

	Cycle 1	Cycle 2	Cycle 3
Off-therapy, Week 3, Grades 1-4	10	11	16
Off-therapy, Week 3, Grades 2-4	2	4	7
Off-therapy, Week 4 (Day 29), n	7	12	48
Off-therapy, Week 4, Grade 0	5	9	30
Off-therapy, Week 4, Grades 1-4	2	3	18
Off-therapy, Week 4, Grades 2-4	1	2	6

7. Secondary Outcome Measure:

Measure Title	Number of Participants With the Indicated Bleeding Signs and Symptoms Using the ITP Bleeding Score
Measure Description	ITP Bleeding Score: Grade 0 = no bleeding, Grade 1 = mild bleeding, Grade 2 = severe bleeding
Time Frame	Baseline, on-treatment visits (Weeks 1-6), off-treatment visits (Weeks 1-4)
Safety Issue?	No

Analysis Population Description

Participants who responded in Cycle 1

Reporting Groups

	Description
Cycle 1	Eltrombopag 50 mg starting dose. Participants whose platelet count was below 50 Gi/L were permitted to increase to eltrombopag 75 mg on or after Day 22.
Cycle 2	Same dose of eltrombopag at which participants completed Cycle 1 (eltrombopag 50 or 75 mg)
Cycle 3	Same dose of eltrombopag at which participants completed Cycle 2 (eltrombopag 50 or 75 mg)

Measured Values

	Cycle 1	Cycle 2	Cycle 3
Number of Participants Analyzed	52	52	49
Number of Participants With the Indicated Bleeding Signs and Symptoms Using the ITP Bleeding Score [units: participants]			
Skin, petechiae, on-therapy, Week 0 (Day 1), n	50	52	49

	Cycle 1	Cycle 2	Cycle 3
Skin, petechiae, on-therapy, Week 0, Grade 0	35	35	39
Skin, petechiae, on-therapy, Week 0, Grade 1	14	17	10
Skin, petechiae, on-therapy, Week 0, Grade 2	1	0	0
Skin, petechiae, on-therapy, Week 1 (Day 8), n	51	51	48
Skin, petechiae, on-therapy, Week 1, Grade 0	41	46	44
Skin, petechiae, on-therapy, Week 1, Grade 1	10	3	3
Skin, petechiae, on-therapy, Week 1, Grade 2	0	2	1
Skin, petechiae, on-therapy, Week 2 (Day 15), n	47	45	42
Skin, petechiae, on-therapy, Week 2, Grade 0	40	43	39
Skin, petechiae, on-therapy, Week 2, Grade 1	7	2	2
Skin, petechiae, on-therapy, Week 2, Grade 2	0	0	1
Skin, petechiae, on-therapy, Week 3 (Day 22), n	33	32	33
Skin, petechiae, on-therapy, Week 3, Grade 0	31	28	32
Skin, petechiae, on-therapy, Week 3, Grade 1	2	4	1
Skin, petechiae, on-therapy, Week 3, Grade 2	0	0	0
Skin, petechiae, on-therapy, Week 4 (Day 29), n	31	28	29
Skin, petechiae, on-therapy, Week 4, Grade 0	30	24	28
Skin, petechiae, on-therapy, Week 4, Grade 1	1	4	1
Skin, petechiae, on-therapy, Week 4, Grade 2	0	0	0
Skin, petechiae, on-therapy, Week 5 (Day 36), n	28	26	29
Skin, petechiae, on-therapy, Week 5, Grade 0	27	21	29
Skin, petechiae, on-therapy, Week 5, Grade 1	1	5	0
Skin, petechiae, on-therapy, Week 5, Grade 2	0	0	0
Skin, petechiae, on-therapy, Week 6 (Day 43), n	24	25	27
Skin, petechiae, on-therapy, Week 6, Grade 0	24	23	27
Skin, petechiae, on-therapy, Week 6, Grade 1	0	2	0
Skin, petechiae, on-therapy, Week 6, Grade 2	0	0	0

	Cycle 1	Cycle 2	Cycle 3
Skin, petechiae, off-therapy, Week 1 (Day 8), n	47	45	48
Skin, petechiae, off-therapy, Week 1, Grade 0	45	39	45
Skin, petechiae, off-therapy, Week 1, Grade 1	2	6	3
Skin, petechiae, off-therapy, Week 1, Grade 2	0	0	0
Skin, petechiae, off-therapy, Week 2 (Day 15), n	36	35	45
Skin, petechiae, off-therapy, Week 2, Grade 0	31	30	40
Skin, petechiae, off-therapy, Week 2, Grade 1	5	5	4
Skin, petechiae, off-therapy, Week 2, Grade 2	0	0	1
Skin, petechiae, off-therapy, Week 3 (Day 22), n	29	30	46
Skin, petechiae, off-therapy, Week 3, Grade 0	27	26	39
Skin, petechiae, off-therapy, Week 3, Grade 1	2	4	7
Skin, petechiae, off-therapy, Week 3, Grade 2	0	0	0
Skin, petechiae, off-therapy, Week 4 (Day 29), n	7	12	48
Skin, petechiae, off-therapy, Week 4, Grade 0	7	12	41
Skin, petechiae, off-therapy, Week 4, Grade 1	0	0	6
Skin, petechiae, off-therapy, Week 4, Grade 2	0	0	1
Skin, ecchymosis, on-therapy, Week 0 (Day 1), n	50	52	49
Skin, ecchymosis, on-therapy, Week 0, Grade 0	31	27	36
Skin, ecchymosis, on-therapy, Week 0, Grade 1	16	25	12
Skin, ecchymosis, on-therapy, Week 0, Grade 2	3	0	1
Skin, ecchymosis, on-therapy, Week 1 (Day 8), n	51	51	48
Skin, ecchymosis, on-therapy, Week 1, Grade 0	39	37	35
Skin, ecchymosis, on-therapy, Week 1, Grade 1	11	13	12
Skin, ecchymosis, on-therapy, Week 1, Grade 2	1	1	1
Skin, ecchymosis, on-therapy, Week 2 (Day 15), n	47	45	42
Skin, ecchymosis, on-therapy, Week 2, Grade 0	42	38	32
Skin, ecchymosis, on-therapy, Week 2, Grade 1	5	7	9

	Cycle 1	Cycle 2	Cycle 3
Skin, ecchymosis, on-therapy, Week 2, Grade 2	0	0	1
Skin, ecchymosis, on-therapy, Week 3 (Day 22), n	33	32	33
Skin, ecchymosis, on-therapy, Week 3, Grade 0	28	24	29
Skin, ecchymosis, on-therapy, Week 3, Grade 1	5	8	4
Skin, ecchymosis, on-therapy, Week 3, Grade 2	0	0	0
Skin, ecchymosis, on-therapy, Week 4 (Day 29), n	31	28	29
Skin, ecchymosis, on-therapy, Week 4, Grade 0	24	24	25
Skin, ecchymosis, on-therapy, Week 4, Grade 1	7	4	4
Skin, ecchymosis, on-therapy, Week 4, Grade 2	0	0	0
Skin, ecchymosis, on-therapy, Week 5 (Day 36), n	28	26	29
Skin, ecchymosis, on-therapy, Week 5, Grade 0	25	23	25
Skin, ecchymosis, on-therapy, Week 5, Grade 1	3	3	4
Skin, ecchymosis, on-therapy, Week 5, Grade 2	0	0	0
Skin, ecchymosis, on-therapy, Week 6 (Day 43), n	24	25	27
Skin, ecchymosis, on-therapy, Week 6, Grade 0	20	22	25
Skin, ecchymosis, on-therapy, Week 6, Grade 1	4	3	2
Skin, ecchymosis, on-therapy, Week 6, Grade 2	0	0	0
Skin, ecchymosis, off-therapy, Week 1 (Day 1), n	47	45	48
Skin, ecchymosis, off-therapy, Week 1, Grade 0	42	38	43
Skin, ecchymosis, off-therapy, Week 1, Grade 1	5	7	5
Skin, ecchymosis, off-therapy, Week 1, Grade 2	0	0	0
Skin, ecchymosis, off-therapy, Week 2 (Day 15), n	36	35	45
Skin, ecchymosis, off-therapy, Week 2, Grade 0	26	24	36
Skin, ecchymosis, off-therapy, Week 2, Grade 1	9	11	9
Skin, ecchymosis, off-therapy, Week 2, Grade 2	1	0	0
Skin, ecchymosis, off-therapy, Week 3 (Day 22), n	29	30	46
Skin, ecchymosis, off-therapy, Week 3, Grade 0	16	20	31

	Cycle 1	Cycle 2	Cycle 3
Skin, ecchymosis, off-therapy, Week 3, Grade 1	11	9	13
Skin, ecchymosis, off-therapy, Week 3, Grade 2	2	1	2
Skin, ecchymosis, off-therapy, Week 4 (Day 29), n	7	12	48
Skin, ecchymosis, off-therapy, Week 4, Grade 0	6	9	31
Skin, ecchymosis, off-therapy, Week 4, Grade 1	0	3	15
Skin, ecchymosis, off-therapy, Week 4, Grade 2	1	0	2
Oral, on-therapy, Week 0 (Day 1), n	50	52	49
Oral, on-therapy, Week 0, Grade 0	46	46	46
Oral, on-therapy, Week 0, Grade 1	4	5	3
Oral, on-therapy, Week 0, Grade 2	0	1	0
Oral, on-therapy, Week 1 (Day 8), n	51	51	48
Oral, on-therapy, Week 1, Grade 0	49	49	46
Oral, on-therapy, Week 1, Grade 1	2	2	2
Oral, on-therapy, Week 1, Grade 2	0	0	0
Oral, on-therapy, Week 2 (Day 15), n	47	45	42
Oral, on-therapy, Week 2, Grade 0	46	43	41
Oral, on-therapy, Week 2, Grade 1	1	2	1
Oral, on-therapy, Week 2, Grade 2	0	0	0
Oral, on-therapy, Week 3 (Day 22), n	33	32	33
Oral, on-therapy, Week 3, Grade 0	33	30	31
Oral, on-therapy, Week 3, Grade 1	0	2	2
Oral, on-therapy, Week 3, Grade 2	0	0	0
Oral, on-therapy, Week 4 (Day 29), n	31	28	29
Oral, on-therapy, Week 4, Grade 0	30	26	29
Oral, on-therapy, Week 4, Grade 1	1	2	0
Oral, on-therapy, Week 4, Grade 2	0	0	0
Oral, on-therapy, Week 5 (Day 36), n	28	26	29

	Cycle 1	Cycle 2	Cycle 3
Oral, on-therapy, Week 5, Grade 0	27	24	29
Oral, on-therapy, Week 5, Grade 1	1	2	0
Oral, on-therapy, Week 5, Grade 2	0	0	0
Oral, on-therapy, Week 6 (Day 43), n	24	25	27
Oral, on-therapy, Week 6, Grade 0	23	23	26
Oral, on-therapy, Week 6, Grade 1	1	2	1
Oral, on-therapy, Week 6, Grade 2	0	0	0
Oral, off-therapy, Week 1 (Day 8), n	47	45	48
Oral, off-therapy, Week 1, Grade 0	45	43	48
Oral, off-therapy, Week 1, Grade 1	2	2	0
Oral, off-therapy, Week 1, Grade 2	0	0	0
Oral, off-therapy, Week 2 (Day 15), n	36	35	45
Oral, off-therapy, Week 2, Grade 0	36	35	45
Oral, off-therapy, Week 2, Grade 1	0	3	3
Oral, off-therapy, Week 2, Grade 2	0	0	0
Oral, off-therapy, Week 3 (Day 22), n	29	30	46
Oral, off-therapy, Week 3, Grade 0	27	29	41
Oral, off-therapy, Week 3, Grade 1	2	1	5
Oral, off-therapy, Week 3, Grade 2	0	0	0
Oral, off-therapy, Week 4 (Day 29), n	7	12	48
Oral, off-therapy, Week 4, Grade 0	7	10	45
Oral, off-therapy, Week 4, Grade 1	0	2	2
Oral, off-therapy, Week 4, Grade 2	0	0	0

Reported Adverse Events

Time Frame	[Not specified]
Additional Description	[Not specified]

Reporting Groups

	Description
Cycle 1	Participants received once-daily treatment for up to 6 weeks, followed by up to 4 weeks off-therapy
Cycle 2	Participants received once-daily treatment for up to 6 weeks, followed by up to 4 weeks off-therapy
Cycle 3	Participants received once-daily treatment for up to 6 weeks, followed by up to 4 weeks off-therapy
More Than 1 to 30 Days After Last Dose	Adverse events >1 to 30 days after last dose (Post-therapy)
More Than 30 Days After Last Dose	Adverse events >30 days after last dose (Post-therapy)
All Cycles	Participants who reported an AE anytime during 3 cycles of treatment. A cycle consisted of once-daily treatment for up to 6 weeks, followed by up to 4 weeks off-therapy.

Serious Adverse Events

	Cycle 1	Cycle 2	Cycle 3	More Than 1 to 30 Days After Last Dose	More Than 30 Days After Last Dose	All Cycles
	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)
Total	0/66 (0%)	1/55 (1.82%)	0/51 (0%)	1/66 (1.52%)	1/66 (1.52%)	4/66 (6.06%)
Ear and labyrinth disorders						
Ear hemorrhage [A] †	0/66 (0%)	0/55 (0%)	0/51 (0%)	0/66 (0%)	1/66 (1.52%)	1/66 (1.52%)
Gastrointestinal disorders						
Abdominal pain upper [A] †	0/66 (0%)	0/55 (0%)	0/51 (0%)	1/66 (1.52%)	0/66 (0%)	1/66 (1.52%)
Mouth Hemorrhage [A] †	0/66 (0%)	0/55 (0%)	0/51 (0%)	0/66 (0%)	1/66 (1.52%)	1/66 (1.52%)
Infections and infestations						
Pneumonia [A] †	0/66 (0%)	1/55 (1.82%)	0/51 (0%)	0/66 (0%)	0/66 (0%)	1/66 (1.52%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)						

	Cycle 1	Cycle 2	Cycle 3	More Than 1 to 30 Days After Last Dose	More Than 30 Days After Last Dose	All Cycles
	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)
Pancreatic carcinoma [A] †	0/66 (0%)	0/55 (0%)	0/51 (0%)	1/66 (1.52%)	0/66 (0%)	1/66 (1.52%)
Respiratory, thoracic and mediastinal disorders						
Epistaxis [A] †	0/66 (0%)	0/55 (0%)	0/51 (0%)	0/66 (0%)	1/66 (1.52%)	1/66 (1.52%)

† 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%

	Cycle 1	Cycle 2	Cycle 3	More Than 1 to 30 Days After Last Dose	More Than 30 Days After Last Dose	All Cycles
	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)
Total	39/66 (59.09%)	30/55 (54.55%)	38/51 (74.51%)	17/66 (25.76%)	7/66 (10.61%)	55/66 (83.33%)
Gastrointestinal disorders						
Abdominal pain upper [A] †	1/66 (1.52%)	1/55 (1.82%)	1/51 (1.96%)	0/66 (0%)	0/66 (0%)	3/66 (4.55%)
Diarrhoea [A] †	6/66 (9.09%)	1/55 (1.82%)	3/51 (5.88%)	1/66 (1.52%)	1/66 (1.52%)	8/66 (12.12%)
Dyspepsia [A] †	1/66 (1.52%)	1/55 (1.82%)	1/51 (1.96%)	1/66 (1.52%)	0/66 (0%)	3/66 (4.55%)
Nausea [A] †	3/66 (4.55%)	3/55 (5.45%)	0/51 (0%)	0/66 (0%)	0/66 (0%)	5/66 (7.58%)
Vomiting [A] †	2/66 (3.03%)	2/55 (3.64%)	1/51 (1.96%)	0/66 (0%)	0/66 (0%)	5/66 (7.58%)
General disorders						
Fatigue [A] †	1/66 (1.52%)	5/55 (9.09%)	7/51 (13.73%)	3/66 (4.55%)	0/66 (0%)	10/66 (15.15%)
Pain [A] †	2/66 (3.03%)	1/55 (1.82%)	0/51 (0%)	0/66 (0%)	0/66 (0%)	3/66 (4.55%)
Infections and infestations						

	Cycle 1	Cycle 2	Cycle 3	More Than 1 to 30 Days After Last Dose	More Than 30 Days After Last Dose	All Cycles
	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)
Gastroenteritis [A] †	1/66 (1.52%)	0/55 (0%)	2/51 (3.92%)	0/66 (0%)	1/66 (1.52%)	3/66 (4.55%)
Nasopharyngitis [A] †	5/66 (7.58%)	2/55 (3.64%)	5/51 (9.8%)	3/66 (4.55%)	1/66 (1.52%)	10/66 (15.15%)
Sinusitis [A] †	2/66 (3.03%)	2/55 (3.64%)	0/51 (0%)	0/66 (0%)	0/66 (0%)	4/66 (6.06%)
Upper respiratory tract infection [A] †	2/66 (3.03%)	1/55 (1.82%)	3/51 (5.88%)	3/66 (4.55%)	0/66 (0%)	5/66 (7.58%)
Injury, poisoning and procedural complications						
Skin laceration [A] †	1/66 (1.52%)	0/55 (0%)	2/51 (3.92%)	0/66 (0%)	0/66 (0%)	3/66 (4.55%)
Investigations						
Alanine aminotransferase increased [A] †	1/66 (1.52%)	1/55 (1.82%)	2/51 (3.92%)	0/66 (0%)	1/66 (1.52%)	3/66 (4.55%)
Helicobacter pylori [A] †	0/66 (0%)	0/55 (0%)	3/51 (5.88%)	2/66 (3.03%)	3/66 (4.55%)	3/66 (4.55%)
Musculoskeletal and connective tissue disorders						
Arthralgia [A] †	3/66 (4.55%)	1/55 (1.82%)	1/51 (1.96%)	1/66 (1.52%)	0/66 (0%)	5/66 (7.58%)
Back pain [A] †	3/66 (4.55%)	4/55 (7.27%)	1/51 (1.96%)	0/66 (0%)	0/66 (0%)	7/66 (10.61%)
Pain in extremity [A] †	3/66 (4.55%)	0/55 (0%)	2/51 (3.92%)	0/66 (0%)	0/66 (0%)	5/66 (7.58%)
Nervous system disorders						
Dizziness [A] †	1/66 (1.52%)	2/55 (3.64%)	1/51 (1.96%)	0/66 (0%)	0/66 (0%)	3/66 (4.55%)
Headache [A] †	9/66 (13.64%)	10/55 (18.18%)	7/51 (13.73%)	5/66 (7.58%)	0/66 (0%)	16/66 (24.24%)
Psychiatric disorders						
Anxiety [A] †	1/66 (1.52%)	1/55 (1.82%)	1/51 (1.96%)	1/66 (1.52%)	0/66 (0%)	3/66 (4.55%)
Insomnia [A] †	2/66 (3.03%)	1/55 (1.82%)	1/51 (1.96%)	0/66 (0%)	0/66 (0%)	3/66 (4.55%)
Respiratory, thoracic and mediastinal disorders						
Epistaxis [A] †	1/66 (1.52%)	2/55 (3.64%)	0/51 (0%)	0/66 (0%)	1/66 (1.52%)	3/66 (4.55%)

† 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.

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