



## Clinical trial results:

### A Phase 2, Interventional, Single Arm Study Describing Platelet Responses and ITP Remission Rates in Adult Subjects with Immune Thrombocytopenia Purpura Receiving Romiplostim

#### Summary

|                          |                   |
|--------------------------|-------------------|
| EudraCT number           | 2010-019987-35    |
| Trial protocol           | IT DE GB ES FR CZ |
| Global end of trial date | 26 December 2013  |

#### Results information

|                                |              |
|--------------------------------|--------------|
| Result version number          | v1 (current) |
| This version publication date  | 20 June 2016 |
| First version publication date | 30 July 2015 |

#### Trial information

##### Trial identification

|                       |          |
|-----------------------|----------|
| Sponsor protocol code | 20080435 |
|-----------------------|----------|

##### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT01143038 |
| WHO universal trial number (UTN)   | -           |

Notes:

#### Sponsors

|                              |   |
|------------------------------|---|
| Sponsor organisation name    | Amgen Inc.  |
| Sponsor organisation address | One Amgen Center Drive, Thousand Oaks, United States, 91320                           |
| Public contact               | IHQ Medical Info-Clinical Trials, Amgen (EUROPE) GmbH, MedInfoInternational@amgen.com |
| Scientific contact           | IHQ Medical Info-Clinical Trials, Amgen (EUROPE) GmbH, MedInfoInternational@amgen.com |

Notes:

#### Paediatric regulatory details

|  |    |
|--|----|
| Is trial part of an agreed paediatric investigation plan (PIP)       | No |
| Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial? | No |
| Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial? | No |

Notes:

## Results analysis stage

|  |                  |
|--|------------------|
| Analysis stage                                       | Final            |
| Date of interim/final analysis                       | 26 December 2013 |
| Is this the analysis of the primary completion data? | No               |
| Global end of trial reached?                         | Yes              |
| Global end of trial date                             | 26 December 2013 |
| Was the trial ended prematurely?                     | No               |

Notes:

## General information about the trial

Main objective of the trial:

To describe the number of months with a subject platelet response over a 12 month treatment period

Protection of trial subjects:

This study was conducted in accordance with applicable FDA and International Conference on Harmonisation (ICH) Good Clinical Practice (GCP) regulations/guidelines. A copy of the protocol, the proposed informed consent, and all other subject information and/or recruitment materials were submitted to the IEC or IRB of each study center for approval. The investigator or a designee obtained written informed consent from their subjects or legally acceptable representatives after adequate explanation of the aims, methods, anticipated benefits, and potential hazards of the study and before any protocol-specific screening procedures were conducted or investigational product was administered.

Background therapy: -

Evidence for comparator: -

|   |                  |
|---|------------------|
| Actual start date of recruitment                          | 30 November 2010 |
| Long term follow-up planned                               | No               |
| Independent data monitoring committee (IDMC) involvement? | No               |

Notes:

## Population of trial subjects

### Subjects enrolled per country

|                                      |                    |
|--------------------------------------|--------------------|
| Country: Number of subjects enrolled | Poland: 15         |
| Country: Number of subjects enrolled | Spain: 8           |
| Country: Number of subjects enrolled | United Kingdom: 3  |
| Country: Number of subjects enrolled | Czech Republic: 12 |
| Country: Number of subjects enrolled | France: 5          |
| Country: Number of subjects enrolled | Germany: 11        |
| Country: Number of subjects enrolled | Italy: 11          |
| Country: Number of subjects enrolled | Australia: 3       |
| Country: Number of subjects enrolled | United States: 7   |
| Worldwide total number of subjects   | 75                 |
| EEA total number of subjects         | 65                 |

Notes:

### Subjects enrolled per age group

|  |   |
|--|---|
| In utero                               | 0 |
| Preterm newborn - gestational age < 37 | 0 |

|  |    |
|--|----|
| wk                                       |    |
| Newborns (0-27 days)                     | 0  |
| Infants and toddlers (28 days-23 months) | 0  |
| Children (2-11 years)                    | 0  |
| Adolescents (12-17 years)                | 0  |
| Adults (18-64 years)                     | 61 |
| From 65 to 84 years                      | 12 |
| 85 years and over                        | 2  |

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

Ninety-eight adult subjects with ITP were screened for the study; 23 subjects were considered screen failures. Seventy-five subjects were enrolled and received at least 1 dose of romiplostim.

### Period 1

|                              |                                |
|------------------------------|--------------------------------|
| Period 1 title               | Overall Study (overall period) |
| Is this the baseline period? | Yes                            |
| Allocation method            | Not applicable                 |
| Blinding used                | Not blinded                    |

### Arms

|           |             |
|-----------|-------------|
| Arm title | Romiplostim |
|-----------|-------------|

Arm description:

Participants received romiplostim administered weekly by subcutaneous injection during the 12-month treatment period. The starting dose was 1 µg/kg with weekly dose increases continued in increments of 1 µg/kg/week to a maximum dose of 10 µg/kg in an attempt to reach a target platelet count of  $\geq 50 \times 10^9/L$ .

|  |                                   |
|--|-----------------------------------|
| Arm type                               | Experimental                      |
| Investigational medicinal product name | Romiplostim                       |
| Investigational medicinal product code | AMG 531                           |
| Other name                             | Nplate                            |
| Pharmaceutical forms                   | Powder for solution for injection |
| Routes of administration               | Subcutaneous use                  |

Dosage and administration details:

Romiplostim was administered weekly by subcutaneous injection. The starting dose of romiplostim was 1 µg/kg; weekly dose increases continued in increments of 1 µg/kg/week to a maximum dose of 10 µg/kg in an attempt to reach a target platelet count of  $\geq 50 \times 10^9/L$ . Dose adjustments were allowed during the treatment period to maintain a platelet count between  $50 \times 10^9/L$  and  $200 \times 10^9/L$ .

| Number of subjects in period 1      | Romiplostim |
|-------------------------------------|-------------|
| Started                             | 75          |
| Completed                           | 59          |
| Not completed                       | 16          |
| Consent withdrawn by subject        | 4           |
| Death                               | 1           |
| Other                               | 1           |
| Adverse event                       | 3           |
| Lost to follow-up                   | 2           |
| Requirement for alternative therapy | 4           |
| Protocol deviation                  | 1           |



## Baseline characteristics

### Reporting groups

|                       |             |
|-----------------------|-------------|
| Reporting group title | Romiplostim |
|-----------------------|-------------|

Reporting group description:

Participants received romiplostim administered weekly by subcutaneous injection during the 12-month treatment period. The starting dose was 1 µg/kg with weekly dose increases continued in increments of 1 µg/kg/week to a maximum dose of 10 µg/kg in an attempt to reach a target platelet count of  $\geq 50 \times 10^9/L$ .

| Reporting group values                    | Romiplostim | Total |  |
|---|-------------|-------|--|
| Number of subjects                        | 75          | 75    |  |
| Age categorical                           |             |       |  |
| Units: Subjects                           |             |       |  |
| < 65 years                                | 61          | 61    |  |
| ≥ 65 years                                | 14          | 14    |  |
| Age continuous                            |             |       |  |
| Units: years                              |             |       |  |
| arithmetic mean                           | 44.5        |       |  |
| standard deviation                        | ± 18.17     | -     |  |
| Gender categorical                        |             |       |  |
| Units: Subjects                           |             |       |  |
| Female                                    | 44          | 44    |  |
| Male                                      | 31          | 31    |  |
| Race                                      |             |       |  |
| Units: Subjects                           |             |       |  |
| American Indian or Alaska Native          | 0           | 0     |  |
| Asian                                     | 1           | 1     |  |
| Black (or African American)               | 1           | 1     |  |
| Native Hawaiian or Other Pacific Islander | 0           | 0     |  |
| White                                     | 72          | 72    |  |
| Other                                     | 0           | 0     |  |
| Unknown                                   | 1           | 1     |  |
| Ethnicity                                 |             |       |  |
| Units: Subjects                           |             |       |  |
| Hispanic/Latino                           | 6           | 6     |  |
| Not Hispanic/Latino                       | 69          | 69    |  |
| Time since ITP diagnosis                  |             |       |  |
| Units: months                             |             |       |  |
| median                                    | 2.2         |       |  |
| full range (min-max)                      | 0.1 to 6.6  | -     |  |
| Platelet count at screening               |             |       |  |
| Units: $\times 10^9/L$                    |             |       |  |
| arithmetic mean                           | 19.78       |       |  |
| standard deviation                        | ± 15.8      | -     |  |

## End points

### End points reporting groups

|  |             |
|--|-------------|
| Reporting group title  | Romiplostim |
| Reporting group description:<br>Participants received romiplostim administered weekly by subcutaneous injection during the 12-month treatment period. The starting dose was 1 µg/kg with weekly dose increases continued in increments of 1 µg/kg/week to a maximum dose of 10 µg/kg in an attempt to reach a target platelet count of $\geq 50 \times 10^9/L$ . |             |

### Primary: Number of Months with Platelet Response During the 12-Month Treatment period

|   |   |
|---|---|
| End point title   | Number of Months with Platelet Response During the 12-Month Treatment period <sup>[1]</sup> |
| End point description:<br>The primary endpoint was the number of months a subject achieved a platelet response during the 12-month treatment period. A platelet response for any 1 month was defined as the median of platelet counts measured in the month $\geq 50 \times 10^9/L$ .<br>Platelet counts within 4 weeks following a rescue medication use or following splenectomy were considered non-response. Months without any platelet count measurement and months following splenectomy were considered as months with no platelet response.<br>Safety Analysis Set includes all subjects who have received at least 1 dose of romiplostim. |   |
| End point type  | Primary   |
| End point timeframe:<br>12 months   |   |

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: A formal hypothesis was not tested in this study. The primary analysis of the primary and secondary endpoints was descriptive.

| End point values                 | Romiplostim       |  |  |  |
|----------------------------------|-------------------|--|--|--|
| Subject group type               | Reporting group   |  |  |  |
| Number of subjects analysed      | 75 <sup>[2]</sup> |  |  |  |
| Units: months                    |                   |  |  |  |
| arithmetic mean (standard error) | 9.2 ( $\pm 0.4$ ) |  |  |  |

Notes:

[2] - Safety Analysis Set

### Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of subjects with ITP remission

|  |   |
|--|---|
| End point title  | Percentage of subjects with ITP remission |
| End point description:<br>ITP remission was defined as all platelet counts $\geq 50 \times 10^9/L$ in the absence of romiplostim and all other therapies dosed with the intent to treat ITP for at least 6 months. |   |
| End point type   | Secondary                                 |
| End point timeframe:<br>12 months  |   |

|                                  |                   |  |  |  |
|----------------------------------|-------------------|--|--|--|
| <b>End point values</b>          | Romiplostim       |  |  |  |
| Subject group type               | Reporting group   |  |  |  |
| Number of subjects analysed      | 75 <sup>[3]</sup> |  |  |  |
| Units: percentage of subjects    |                   |  |  |  |
| number (confidence interval 95%) | 32 (21.7 to 43.8) |  |  |  |

Notes:

[3] - Safety analysis set

### Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of subjects with splenectomy during the 12-month treatment period

|                        |  |
|------------------------|--|
| End point title        | Percentage of subjects with splenectomy during the 12-month treatment period |
| End point description: |  |
| End point type         | Secondary  |
| End point timeframe:   |  |
| 12 months              |  |

|                                  |                   |  |  |  |
|----------------------------------|-------------------|--|--|--|
| <b>End point values</b>          | Romiplostim       |  |  |  |
| Subject group type               | Reporting group   |  |  |  |
| Number of subjects analysed      | 75 <sup>[4]</sup> |  |  |  |
| Units: percentage of subjects    |                   |  |  |  |
| number (confidence interval 95%) | 1.3 (0 to 7.2)    |  |  |  |

Notes:

[4] - Safety analysis set

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects who developed antibodies to romiplostim

|   |  |
|---|--|
| End point title   | Number of subjects who developed antibodies to romiplostim |
| End point description:  |  |
| The number of subjects developing antibody formation (defined as negative at baseline and positive at post-baseline, transient or persistent) to romiplostim, endogenous thrombopoietin (eTPO), and thrombopoietin mimetic peptide (TMP, the peptide component of romiplostim) was summarized |  |
| End point type  | Secondary  |
| End point timeframe:  |  |
| 12 months   |  |



|  |                   |  |  |  |
|--|-------------------|--|--|--|
| <b>End point values</b>                | Romiplostim       |  |  |  |
| Subject group type                     | Reporting group   |  |  |  |
| Number of subjects analysed            | 69 <sup>[5]</sup> |  |  |  |
| Units: subjects                        |                   |  |  |  |
| Antibodies to romiplostim              | 2                 |  |  |  |
| Antibodies to TPO                      | 1                 |  |  |  |
| Antibodies to TMP                      | 2                 |  |  |  |
| Neutralizing antibodies to romiplostim | 1                 |  |  |  |
| Neutralizing antibodies to TPO         | 0                 |  |  |  |
| Neutralizing antibodies to TMP         | 0                 |  |  |  |

Notes:

[5] - Safety analysis set participants with available results

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of subjects with adverse events

|                 |  |
|-----------------|--|
| End point title | Number of subjects with adverse events |
|-----------------|--|

End point description:

An adverse event is defined as any untoward medical occurrence in a clinical trial subject. The event does not necessarily have a causal relationship with study treatment. A serious adverse event is defined as an adverse event that meets at least one of the following serious criteria:

- fatal
- life threatening (places the subject at immediate risk of death)
- requires in-patient hospitalization or prolongation of existing hospitalization
- results in persistent or significant disability/incapacity
- congenital anomaly/birth defect
- other significant medical hazard.

Whether an adverse event was treatment related (TRAE) or not was determined by investigator.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

From first dose date of romiplostim to end of study (up to 24 months).

|  |                   |  |  |  |
|--|-------------------|--|--|--|
| <b>End point values</b>                            | Romiplostim       |  |  |  |
| Subject group type                                 | Reporting group   |  |  |  |
| Number of subjects analysed                        | 75 <sup>[6]</sup> |  |  |  |
| Units: subjects                                    |                   |  |  |  |
| All treatment-emergent adverse events              | 63                |  |  |  |
| Serious adverse events                             | 17                |  |  |  |
| Leading to discontinuation of romiplostim          | 4                 |  |  |  |
| Leading to discontinuation from study              | 3                 |  |  |  |
| Fatal adverse events                               | 0                 |  |  |  |
| Treatment-related treatment-emergent adverse event | 21                |  |  |  |

|   |   |  |  |  |
|---|---|--|--|--|
| Treatment-related serious adverse events        | 3 |  |  |  |
| TRAEs leading to discontinuation of romiplostim | 2 |  |  |  |
| TRAEs leading to discontinuation from study     | 2 |  |  |  |
| Treatment-related fatal adverse events          | 0 |  |  |  |

Notes:

[6] - Safety analysis set

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

From first dose date of romiplostim to end of study (up to 24 months)

|                 |            |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

### Dictionary used

|                 |        |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

|                    |      |
|--------------------|------|
| Dictionary version | 16.1 |
|--------------------|------|

### Reporting groups

|                       |             |
|-----------------------|-------------|
| Reporting group title | Romiplostim |
|-----------------------|-------------|

Reporting group description:

Participants received romiplostim administered weekly by subcutaneous injection during the 12-month treatment period. The starting dose was 1 µg/kg with weekly dose increases continued in increments of 1 µg/kg/week to a maximum dose of 10 µg/kg in an attempt to reach a target platelet count of  $\geq 50 \times 10^9/L$ .

| Serious adverse events  | Romiplostim      |  |  |
|---|------------------|--|--|
| Total subjects affected by serious adverse events                   |                  |  |  |
| subjects affected / exposed   | 17 / 75 (22.67%) |  |  |
| number of deaths (all causes)                                       | 1                |  |  |
| number of deaths resulting from adverse events                      |                  |  |  |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                  |  |  |
| Non-Hodgkin's lymphoma  |                  |  |  |
| subjects affected / exposed   | 1 / 75 (1.33%)   |  |  |
| occurrences causally related to treatment / all                     | 0 / 1            |  |  |
| deaths causally related to treatment / all                          | 0 / 0            |  |  |
| Papillary thyroid cancer  |                  |  |  |
| subjects affected / exposed   | 1 / 75 (1.33%)   |  |  |
| occurrences causally related to treatment / all                     | 0 / 2            |  |  |
| deaths causally related to treatment / all                          | 0 / 0            |  |  |
| Vascular disorders  |                  |  |  |
| Peripheral vascular disorder  |                  |  |  |
| subjects affected / exposed   | 1 / 75 (1.33%)   |  |  |
| occurrences causally related to treatment / all                     | 0 / 1            |  |  |
| deaths causally related to treatment / all                          | 0 / 0            |  |  |
| Respiratory, thoracic and mediastinal disorders                     |                  |  |  |
| Pleuritic pain  |                  |  |  |

|   |                |  |  |
|---|----------------|--|--|
| subjects affected / exposed                     | 1 / 75 (1.33%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Psychiatric disorders                           |                |  |  |
| Delirium tremens                                |                |  |  |
| subjects affected / exposed                     | 1 / 75 (1.33%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Investigations                                  |                |  |  |
| Transaminases increased                         |                |  |  |
| subjects affected / exposed                     | 1 / 75 (1.33%) |  |  |
| occurrences causally related to treatment / all | 1 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Injury, poisoning and procedural complications  |                |  |  |
| Tendon rupture                                  |                |  |  |
| subjects affected / exposed                     | 1 / 75 (1.33%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Cardiac disorders                               |                |  |  |
| Atrial fibrillation                             |                |  |  |
| subjects affected / exposed                     | 1 / 75 (1.33%) |  |  |
| occurrences causally related to treatment / all | 0 / 2          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Nervous system disorders                        |                |  |  |
| Reversible ischaemic neurological deficit       |                |  |  |
| subjects affected / exposed                     | 1 / 75 (1.33%) |  |  |
| occurrences causally related to treatment / all | 1 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Blood and lymphatic system disorders            |                |  |  |
| Idiopathic thrombocytopenic purpura             |                |  |  |
| subjects affected / exposed                     | 1 / 75 (1.33%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Thrombocytopenia                                |                |  |  |

|   |                |  |  |
|---|----------------|--|--|
| subjects affected / exposed                     | 1 / 75 (1.33%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Gastrointestinal disorders                      |                |  |  |
| Abdominal pain                                  |                |  |  |
| subjects affected / exposed                     | 1 / 75 (1.33%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Faecaloma                                       |                |  |  |
| subjects affected / exposed                     | 1 / 75 (1.33%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Gastritis                                       |                |  |  |
| subjects affected / exposed                     | 1 / 75 (1.33%) |  |  |
| occurrences causally related to treatment / all | 1 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Skin and subcutaneous tissue disorders          |                |  |  |
| Dapsone syndrome                                |                |  |  |
| subjects affected / exposed                     | 1 / 75 (1.33%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Renal and urinary disorders                     |                |  |  |
| Renal failure acute                             |                |  |  |
| subjects affected / exposed                     | 1 / 75 (1.33%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Endocrine disorders                             |                |  |  |
| Hypothyroidism                                  |                |  |  |
| subjects affected / exposed                     | 1 / 75 (1.33%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Infections and infestations                     |                |  |  |
| Erysipelas                                      |                |  |  |

|   |                |  |  |
|---|----------------|--|--|
| subjects affected / exposed                     | 1 / 75 (1.33%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |

Frequency threshold for reporting non-serious adverse events: 5 %

| <b>Non-serious adverse events</b>                     | Romiplostim      |  |  |
|---|------------------|--|--|
| Total subjects affected by non-serious adverse events |                  |  |  |
| subjects affected / exposed                           | 50 / 75 (66.67%) |  |  |
| Vascular disorders                                    |                  |  |  |
| Haematoma   |                  |  |  |
| subjects affected / exposed                           | 8 / 75 (10.67%)  |  |  |
| occurrences (all)                                     | 9                |  |  |
| Hypertension  |                  |  |  |
| subjects affected / exposed                           | 6 / 75 (8.00%)   |  |  |
| occurrences (all)                                     | 7                |  |  |
| Nervous system disorders                              |                  |  |  |
| Dizziness   |                  |  |  |
| subjects affected / exposed                           | 4 / 75 (5.33%)   |  |  |
| occurrences (all)                                     | 5                |  |  |
| Headache  |                  |  |  |
| subjects affected / exposed                           | 13 / 75 (17.33%) |  |  |
| occurrences (all)                                     | 18               |  |  |
| General disorders and administration site conditions  |                  |  |  |
| Asthenia  |                  |  |  |
| subjects affected / exposed                           | 5 / 75 (6.67%)   |  |  |
| occurrences (all)                                     | 6                |  |  |
| Fatigue   |                  |  |  |
| subjects affected / exposed                           | 6 / 75 (8.00%)   |  |  |
| occurrences (all)                                     | 7                |  |  |
| Ear and labyrinth disorders                           |                  |  |  |
| Vertigo   |                  |  |  |
| subjects affected / exposed                           | 4 / 75 (5.33%)   |  |  |
| occurrences (all)                                     | 7                |  |  |
| Eye disorders   |                  |  |  |

|   |  |  |  |
|---|--|--|--|
| Conjunctivitis<br>subjects affected / exposed<br>occurrences (all)  | 4 / 75 (5.33%)<br>4  |  |  |
| Gastrointestinal disorders<br>Diarrhoea<br>subjects affected / exposed<br>occurrences (all)   | 4 / 75 (5.33%)<br>4  |  |  |
| Respiratory, thoracic and mediastinal disorders<br>Cough<br>subjects affected / exposed<br>occurrences (all)<br><br>Epistaxis<br>subjects affected / exposed<br>occurrences (all)   | 7 / 75 (9.33%)<br>7<br><br>6 / 75 (8.00%)<br>8                             |  |  |
| Skin and subcutaneous tissue disorders<br>Pruritus<br>subjects affected / exposed<br>occurrences (all)<br><br>Petechiae<br>subjects affected / exposed<br>occurrences (all)<br><br>Rash<br>subjects affected / exposed<br>occurrences (all) | 4 / 75 (5.33%)<br>5<br><br>7 / 75 (9.33%)<br>13<br><br>4 / 75 (5.33%)<br>6 |  |  |
| Musculoskeletal and connective tissue disorders<br>Arthralgia<br>subjects affected / exposed<br>occurrences (all)<br><br>Myalgia<br>subjects affected / exposed<br>occurrences (all)  | 11 / 75 (14.67%)<br>14<br><br>4 / 75 (5.33%)<br>4                          |  |  |
| Infections and infestations<br>Influenza<br>subjects affected / exposed<br>occurrences (all)<br><br>Nasopharyngitis   | 7 / 75 (9.33%)<br>10   |  |  |

|                                   |                  |  |  |
|-----------------------------------|------------------|--|--|
| subjects affected / exposed       | 10 / 75 (13.33%) |  |  |
| occurrences (all)                 | 11               |  |  |
| Rhinitis                          |                  |  |  |
| subjects affected / exposed       | 4 / 75 (5.33%)   |  |  |
| occurrences (all)                 | 5                |  |  |
| Upper respiratory tract infection |                  |  |  |
| subjects affected / exposed       | 6 / 75 (8.00%)   |  |  |
| occurrences (all)                 | 9                |  |  |



## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date            | Amendment  |
|-----------------|--|
| 15 January 2013 | <ul style="list-style-type: none"><li>- The study schema was updated to illustrate and clarify the various treatment scenarios.</li><li>- Clarification was made to describe the various treatment periods and their definitions.</li><li>- Clarification was made in the language throughout the protocol for medications for ITP given either concomitantly or as rescue medications.</li><li>- Updates to pregnancy, antibody testing parameters, and contraception requirements were updated per the current Amgen requirements.</li><li>- Updates were made to the serious adverse event reporting language in Section 9.2 per the current Amgen safety requirements.</li></ul> |

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported