



Clinical trial results:

Prospective Follow-up Study for Patients who Completed Study ALX0681-C301 (HERCULES) to Evaluate Long-term Safety and Efficacy of Caplacizumab (Post-HERCULES)

Summary

| | |
|--------------------------|-------------------------------|
| EudraCT number | 2016-001503-23 |
| Trial protocol | AT ES HU GB CZ BE FR DE NL IT |
| Global end of trial date | 23 October 2020 |

Results information

| | |
|--------------------------------|---|
| Result version number | v2 (current) |
| This version publication date | 05 January 2023 |
| First version publication date | 06 November 2021 |
| Version creation reason | <ul style="list-style-type: none">• Correction of full data setUpdated safety optional field |

Trial information

Trial identification

| | |
|-----------------------|----------|
| Sponsor protocol code | LTS16371 |
|-----------------------|----------|

Additional study identifiers

| | |
|------------------------------------|-----------------------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT02878603 |
| WHO universal trial number (UTN) | - |
| Other trial identifiers | Post-HERCULES: ALX0681-C302 |

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | Sanofi-aventis Recherche & Développement |
| Sponsor organisation address | 1 avenue Pierre Brossolette, Chilly Mazarin Cedex, France, 91385 |
| Public contact | Trial Transparency Team, Sanofi aventis recherche & développement, Contact-US@sanofi.com |
| Scientific contact | Trial Transparency Team, Sanofi aventis recherche & développement, Contact-US@sanofi.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 | 18 December 2020 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 23 October 2020 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

- To evaluate long-term safety and efficacy of caplacizumab.
- To evaluate safety and efficacy of repeated use of caplacizumab.
- To characterise long-term impact of acquired thrombotic thrombocytopenic purpura (aTTP).

Protection of trial subjects:

Subjects were fully informed of all pertinent aspects of the clinical trial as well as the possibility to discontinue at any time in language and terms appropriate for the subject and considering the local culture. During the course of the trial, subjects were provided with individual subject cards indicating the nature of the trial the subject is participating, contact details and any information needed in the event of a medical emergency. Collected personal data and human biological samples were processed in compliance with the Sanofi-Aventis Group Personal Data Protection Charter ensuring that the Group abides by the laws governing personal data protection in force in all countries in which it operates.

Background therapy: -

Evidence for comparator: -

| | |
|---|------------------|
| Actual start date of recruitment | 06 October 2016 |
| Long term follow-up planned | Yes |
| Long term follow-up rationale | Efficacy, Safety |
| Long term follow-up duration | 3 Years |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|--------------------|
| Country: Number of subjects enrolled | Austria: 4 |
| Country: Number of subjects enrolled | Belgium: 4 |
| Country: Number of subjects enrolled | Switzerland: 1 |
| Country: Number of subjects enrolled | United Kingdom: 19 |
| Country: Number of subjects enrolled | Hungary: 6 |
| Country: Number of subjects enrolled | Canada: 11 |
| Country: Number of subjects enrolled | Turkey: 7 |
| Country: Number of subjects enrolled | Czechia: 3 |
| Country: Number of subjects enrolled | France: 7 |
| Country: Number of subjects enrolled | Israel: 5 |
| Country: Number of subjects enrolled | Spain: 12 |
| Country: Number of subjects enrolled | United States: 18 |
| Country: Number of subjects enrolled | Italy: 7 |

| | |
|------------------------------------|-----|
| Worldwide total number of subjects | 104 |
| EEA total number of subjects | 43 |

Notes:

Subjects enrolled per age group

| | |
|---|----|
| In utero | 0 |
| Preterm newborn - gestational age < 37 wk | 0 |
| 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) | 95 |
| From 65 to 84 years | 9 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

Study was conducted at 43 active sites in 13 countries. A total of 104 subjects who completed Study ALX0681-C301 (HERCULES; NCT02553317) were enrolled between 06-October-2016 and 27-October-2017 in this current study: LTS16371 (ALX0681-C302).

Pre-assignment

Screening details:

Subjects who were randomised to caplacizumab/placebo and received caplacizumab for recurrence of acquired thrombotic thrombocytopenic purpura (aTTP) in ALX0681-C301 were enrolled in Caplacizumab group, and subjects randomised to placebo in ALX0681-C301 were enrolled under Standard of Care (SoC) group in the current study LTS16371.

Period 1

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

Arms

| | |
|------------------------------|--|
| Are arms mutually exclusive? | Yes |
| Arm title | Standard of Care (Treated in Study C301) |

Arm description:

Subjects who completed study ALX0681-C301 with SoC (plasma exchange [PE], corticosteroid and other immunosuppressive agents) treatment were enrolled in study LTS16371. Subjects upon each recurrence of aTTP in LTS16371 and not meeting any criteria (namely: pregnancy, history of severe and/or serious hypersensitivity reaction to investigational medicinal product [IMP], withdrawal before receiving IMP, received more than 1 PE) were treated with caplacizumab initial 10 mg intravenous (IV) dose followed by a daily 10 milligrams (mg) subcutaneous (SC) injections during the period of PE and for 30 days after stop of PE (and eventually 28-day extension period, if needed). Subjects with or without recurrence were followed up twice yearly up to maximum of 36 months in LTS16371.

| | |
|--|---|
| Arm type | Experimental |
| Investigational medicinal product name | Caplacizumab |
| Investigational medicinal product code | ALX-0081 |
| Other name | |
| Pharmaceutical forms | Powder and solvent for solution for injection |
| Routes of administration | Intravenous bolus use , Subcutaneous use |

Dosage and administration details:

- First day of treatment: 10 mg IV injection prior to PE followed by a 10 mg SC injection after completion of PE. - Subsequent days of treatment during PE: daily 10 mg SC injection following PE. - Treatment after PE period: daily 10 mg SC injections for 30 days (and eventually 28-day extension period, if needed).

| | |
|--|-----------------------|
| Investigational medicinal product name | SoC treatment |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

- PE with plasma (e.g., fresh frozen plasma, solvent detergent/viral-inactivated plasma, cryosupernatant).
- Corticosteroid treatment.
- Use of other immunosuppressive agents (e.g., rituximab).

| | |
|------------------|--------------------------------------|
| Arm title | Caplacizumab (Treated in Study C301) |
|------------------|--------------------------------------|

Arm description:

Subjects who completed study ALX0681-C301 and received caplacizumab with PE and

immunosuppressive agents were enrolled in study LTS16371. Subjects upon each recurrence of aTTP in LTS16371 and not meeting any criteria (namely: pregnancy, history of severe and/or serious hypersensitivity reaction to IMP, withdrawal before receiving IMP, received more than 1 PE) were treated with caplacizumab initial 10 mg IV dose followed by a daily 10 mg SC injections during the period of PE and for 30 days after stop of PE (and eventually 28-day extension period, if needed). Subjects with or without recurrence were followed up twice yearly up to maximum of 36 months in LTS16371.

| | |
|--|---|
| Arm type | Experimental |
| Investigational medicinal product name | Caplacizumab |
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Dosage and administration details:

- First day of treatment: 10 mg IV injection prior to PE followed by a 10 mg SC injection after completion of PE. - Subsequent days of treatment during PE: daily 10 mg SC injection following PE. - Treatment after PE period: daily 10 mg SC injections for 30 days (and eventually 28-day extension period, if needed).

| Number of subjects in period 1 | Standard of Care (Treated in Study C301) | Caplacizumab (Treated in Study C301) |
|---------------------------------------|---|---|
| Started | 29 | 75 |
| Completed | 23 | 70 |
| Not completed | 6 | 5 |
| Consent withdrawn by subject | 1 | 1 |
| Physician decision | - | 3 |
| Lost to follow-up | 4 | 1 |
| Other (Death) | 1 | - |

Baseline characteristics

Reporting groups

| | |
|-----------------------|--|
| Reporting group title | Standard of Care (Treated in Study C301) |
|-----------------------|--|

Reporting group description:

Subjects who completed study ALX0681-C301 with SoC (plasma exchange [PE], corticosteroid and other immunosuppressive agents) treatment were enrolled in study LTS16371. Subjects upon each recurrence of aTTP in LTS16371 and not meeting any criteria (namely: pregnancy, history of severe and/or serious hypersensitivity reaction to investigational medicinal product [IMP], withdrawal before receiving IMP, received more than 1 PE) were treated with caplacizumab initial 10 mg intravenous (IV) dose followed by a daily 10 milligrams (mg) subcutaneous (SC) injections during the period of PE and for 30 days after stop of PE (and eventually 28-day extension period, if needed). Subjects with or without recurrence were followed up twice yearly up to maximum of 36 months in LTS16371.

| | |
|-----------------------|--------------------------------------|
| Reporting group title | Caplacizumab (Treated in Study C301) |
|-----------------------|--------------------------------------|

Reporting group description:

Subjects who completed study ALX0681-C301 and received caplacizumab with PE and immunosuppressive agents were enrolled in study LTS16371. Subjects upon each recurrence of aTTP in LTS16371 and not meeting any criteria (namely: pregnancy, history of severe and/or serious hypersensitivity reaction to IMP, withdrawal before receiving IMP, received more than 1 PE) were treated with caplacizumab initial 10 mg IV dose followed by a daily 10 mg SC injections during the period of PE and for 30 days after stop of PE (and eventually 28-day extension period, if needed). Subjects with or without recurrence were followed up twice yearly up to maximum of 36 months in LTS16371.

| Reporting group values | Standard of Care (Treated in Study C301) | Caplacizumab (Treated in Study C301) | Total |
|------------------------------------|--|--|-------|
| Number of subjects | 29 | 75 | 104 |
| Age categorical Units: Subjects | | | |

| | | | |
|---|----------------|----------------|----|
| Age continuous Units: years arithmetic mean standard deviation | 51.5 ± 14.8 | 46.0 ± 11.9 | - |
| Gender categorical Units: Subjects | | | |
| Female | 23 | 51 | 74 |
| Male | 6 | 24 | 30 |
| Race (NIH/OMB) Units: Subjects | | | |
| American Indian or Alaska Native | 0 | 0 | 0 |
| Asian | 0 | 3 | 3 |
| Native Hawaiian or Other Pacific Islander | 0 | 0 | 0 |
| Black or African American | 6 | 13 | 19 |
| White | 21 | 52 | 73 |
| More than one race | 0 | 2 | 2 |
| Unknown or Not Reported | 2 | 5 | 7 |

End points

End points reporting groups

| | |
|-----------------------|--|
| Reporting group title | Standard of Care (Treated in Study C301) |
|-----------------------|--|

Reporting group description:

Subjects who completed study ALX0681-C301 with SoC (plasma exchange [PE], corticosteroid and other immunosuppressive agents) treatment were enrolled in study LTS16371. Subjects upon each recurrence of aTTP in LTS16371 and not meeting any criteria (namely: pregnancy, history of severe and/or serious hypersensitivity reaction to investigational medicinal product [IMP], withdrawal before receiving IMP, received more than 1 PE) were treated with caplacizumab initial 10 mg intravenous (IV) dose followed by a daily 10 milligrams (mg) subcutaneous (SC) injections during the period of PE and for 30 days after stop of PE (and eventually 28-day extension period, if needed). Subjects with or without recurrence were followed up twice yearly up to maximum of 36 months in LTS16371.

| | |
|-----------------------|--------------------------------------|
| Reporting group title | Caplacizumab (Treated in Study C301) |
|-----------------------|--------------------------------------|

Reporting group description:

Subjects who completed study ALX0681-C301 and received caplacizumab with PE and immunosuppressive agents were enrolled in study LTS16371. Subjects upon each recurrence of aTTP in LTS16371 and not meeting any criteria (namely: pregnancy, history of severe and/or serious hypersensitivity reaction to IMP, withdrawal before receiving IMP, received more than 1 PE) were treated with caplacizumab initial 10 mg IV dose followed by a daily 10 mg SC injections during the period of PE and for 30 days after stop of PE (and eventually 28-day extension period, if needed). Subjects with or without recurrence were followed up twice yearly up to maximum of 36 months in LTS16371.

Primary: Percentage of Subjects With Acquired Thrombotic Thrombocytopenic Purpura (aTTP-) Related Events

| | |
|-----------------|--|
| End point title | Percentage of Subjects With Acquired Thrombotic Thrombocytopenic Purpura (aTTP-) Related Events ^[1] |
|-----------------|--|

End point description:

aTTP-related events were defined as: aTTP-related death, recurrence of aTTP (defined as recurrent thrombocytopenia requiring initiation of daily PE) or at least one major thromboembolic event (e.g., myocardial infarction, cerebrovascular accident, pulmonary embolism or deep venous thrombosis). Percentage of subjects with at least one of aTTP-related events during the study were reported in this endpoint. Analysis was performed on efficacy intention-to-observe (efficacy ITO) population which included subjects who were enrolled in LTS16371 and did not experience an aTTP recurrence in previous study ALX0681-C301 or prior to the beginning of LTS16371.

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

From Baseline up to 36 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: As the endpoint was descriptive in nature, no statistical analysis was provided.

| End point values | Standard of Care (Treated in Study C301) | Caplacizumab (Treated in Study C301) | | |
|-------------------------------|--|--------------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 29 | 49 | | |
| Units: percentage of subjects | | | | |
| number (not applicable) | 37.9 | 8.2 | | |

Statistical analyses

No statistical analyses for this end point

Primary: Number of Acquired Thrombotic Thrombocytopenic Purpura-related Events

| | |
|-----------------|--|
| End point title | Number of Acquired Thrombotic Thrombocytopenic Purpura-related Events ^[2] |
|-----------------|--|

End point description:

aTTP-related events were defined as: aTTP-related death, recurrence of aTTP (defined as recurrent thrombocytopenia requiring initiation of daily PE) or at least one major thromboembolic event (e.g., myocardial infarction, cerebrovascular accident, pulmonary embolism or deep venous thrombosis). Analysis was performed on efficacy ITO population which included subjects who were enrolled in LTS16371 and did not experience an aTTP recurrence in previous study ALX0681-C301 or prior to the beginning of LTS16371.

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

From Baseline up to 36 months

Notes:

[2] - 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: As the endpoint was descriptive in nature, no statistical analysis was provided.

| End point values | Standard of Care (Treated in Study C301) | Caplacizumab (Treated in Study C301) | | |
|-----------------------------|--|--------------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 29 | 49 | | |
| Units: aTTP-related events | 11 | 4 | | |

Statistical analyses

No statistical analyses for this end point

Primary: Time to First Acquired Thrombotic Thrombocytopenic Purpura-related Events

| | |
|-----------------|--|
| End point title | Time to First Acquired Thrombotic Thrombocytopenic Purpura-related Events ^[3] |
|-----------------|--|

End point description:

Time to first aTTP-related events was defined as the duration of time (in days) from Baseline up to first aTTP-related event in LTS16371. Subjects without an event during LTS16371 were censored at the end of the study. Kaplan-Meier method was used for the analysis. Analysis was performed on efficacy ITO population which included subjects who were enrolled in LTS16371 and did not experience an aTTP recurrence in previous study ALX0681-C301 or prior to the beginning of LTS16371. Here, '99999' was used as a space filler which indicates that median and 95% confidence interval (CI) data were not calculated due to very few subjects with events.

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

From Baseline up to 36 months

Notes:

[3] - 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: As the endpoint was descriptive in nature, no statistical analysis was provided.

| End point values | Standard of Care (Treated in Study C301) | Caplacizumab (Treated in Study C301) | | |
|----------------------------------|--|--------------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 29 | 49 | | |
| Units: days | | | | |
| median (confidence interval 95%) | 99999 (845.00 to 99999) | 99999 (99999 to 99999) | | |

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With aTTP related Deaths Reported During the Study

| | |
|-----------------|--|
| End point title | Number of Subjects With aTTP related Deaths Reported During the Study ^[4] |
|-----------------|--|

End point description:

Analysis was performed on efficacy ITO population which included subjects who were enrolled in LTS16371 and did not experience an aTTP recurrence in previous study ALX0681-C301 or prior to the beginning of LTS16371.

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

From Baseline up to 36 months

Notes:

[4] - 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: As the endpoint was descriptive in nature, no statistical analysis was provided.

| End point values | Standard of Care (Treated in Study C301) | Caplacizumab (Treated in Study C301) | | |
|-----------------------------|--|--------------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 29 | 49 | | |
| Units: subjects | 1 | 0 | | |

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With Recurrence of Disease (aTTP)

| | |
|-----------------|---|
| End point title | Percentage of Subjects With Recurrence of Disease (aTTP) ^[5] |
|-----------------|---|

End point description:

Recurrence of aTTP was defined as recurrent thrombocytopenia requiring initiation of daily PE. Analysis was performed on efficacy ITO population which included subjects who were enrolled in LTS16371 and did not experience an aTTP recurrence in previous study ALX0681-C301 or prior to the beginning of LTS16371.

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

From Baseline up to 36 months

Notes:

[5] - 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: As the endpoint was descriptive in nature, no statistical analysis was provided.

| End point values | Standard of Care (Treated in Study C301) | Caplacizumab (Treated in Study C301) | | |
|-------------------------------|--|--------------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 29 | 49 | | |
| Units: percentage of subjects | | | | |
| number (not applicable) | 27.6 | 8.2 | | |

Statistical analyses

No statistical analyses for this end point

Primary: Number of Disease (aTTP) Recurrence Reported During the Study

| | |
|-----------------|--|
| End point title | Number of Disease (aTTP) Recurrence Reported During the Study ^[6] |
|-----------------|--|

End point description:

Recurrence of aTTP was defined as recurrent thrombocytopenia requiring initiation of daily PE. Analysis was performed on efficacy ITO population which included subjects who were enrolled in LTS16371 and did not experience an aTTP recurrence in previous study ALX0681-C301 or prior to the beginning of LTS16371.

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

From Baseline up to 36 months

Notes:

[6] - 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: As the endpoint was descriptive in nature, no statistical analysis was provided.

| End point values | Standard of Care (Treated in Study C301) | Caplacizumab (Treated in Study C301) | | |
|-----------------------------|--|--------------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 29 | 49 | | |
| Units: aTTP recurrence | 8 | 4 | | |

Statistical analyses

No statistical analyses for this end point

Primary: Time to Recurrence of Disease (aTTP)

| | |
|-----------------|---|
| End point title | Time to Recurrence of Disease (aTTP) ^[7] |
|-----------------|---|

End point description:

Time to first recurrence of disease (aTTP) was defined as the duration of time (in days) from Baseline up to first recurrence of aTTP event in LTS16371. Recurrence of aTTP: defined as recurrent thrombocytopenia requiring initiation of daily PE. Subjects without an event during LTS16371 were censored at the end of the study. Kaplan-Meier method was used for the analysis. Analysis was

performed on efficacy ITO population which included subjects who were enrolled in LTS16371 and did not experience an aTTP recurrence in previous study ALX0681-C301 or prior to the beginning of LTS16371. Here, '99999' was used as a space filler which indicates that median and 95% CI data were not calculated due to very few subjects with events.

| | |
|-------------------------------|---------|
| End point type | Primary |
| End point timeframe: | |
| From Baseline up to 36 months | |

Notes:

[7] - 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: As the endpoint was descriptive in nature, no statistical analysis was provided.

| End point values | Standard of Care (Treated in Study C301) | Caplacizumab (Treated in Study C301) | | |
|----------------------------------|--|--------------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 29 | 49 | | |
| Units: days | | | | |
| median (confidence interval 95%) | 99999 (1280.00 to 99999) | 99999 (99999 to 99999) | | |

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With Major Thromboembolic Events Including Thrombotic Thrombocytopenic Purpura (TTP)

| | |
|-----------------|--|
| End point title | Percentage of Subjects With Major Thromboembolic Events Including Thrombotic Thrombocytopenic Purpura (TTP) ^[8] |
|-----------------|--|

End point description:

Major thromboembolic events (e.g., myocardial infarction, cerebrovascular accident, pulmonary embolism, or deep venous thrombosis) were assessed based on Standardised Medical Dictionary for Regulatory Activities (MedDRA) Query (SMQ). Reported major thromboembolic events included TTP recurrences. Analysis was performed on efficacy ITO population which included subjects who were enrolled in LTS16371 and did not experience an aTTP recurrence in previous study ALX0681-C301 or prior to the beginning of LTS16371.

| | |
|-------------------------------|---------|
| End point type | Primary |
| End point timeframe: | |
| From Baseline up to 36 months | |

Notes:

[8] - 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: As the endpoint was descriptive in nature, no statistical analysis was provided.

| End point values | Standard of Care (Treated in Study C301) | Caplacizumab (Treated in Study C301) | | |
|-------------------------------|--|--------------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 29 | 49 | | |
| Units: percentage of subjects | | | | |
| number (not applicable) | 37.9 | 8.2 | | |

Statistical analyses

No statistical analyses for this end point

Primary: Number of Major Thromboembolic Events Including Thrombotic Thrombocytopenic Purpura

| | |
|-----------------|--|
| End point title | Number of Major Thromboembolic Events Including Thrombotic Thrombocytopenic Purpura ^[9] |
|-----------------|--|

End point description:

Major thromboembolic events (e.g., myocardial infarction, cerebrovascular accident, pulmonary embolism, or deep venous thrombosis) were assessed based on SMQ. Reported major thromboembolic events included TTP recurrences. Analysis was performed on efficacy ITO population which included subjects who were enrolled in LTS16371 and did not experience an aTTP recurrence in previous study ALX0681-C301 or prior to the beginning of LTS16371.

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

From Baseline up to 36 months

Notes:

[9] - 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: As the endpoint was descriptive in nature, no statistical analysis was provided.

| End point values | Standard of Care (Treated in Study C301) | Caplacizumab (Treated in Study C301) | | |
|------------------------------------|--|--------------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 29 | 49 | | |
| Units: major thromboembolic events | 11 | 4 | | |

Statistical analyses

No statistical analyses for this end point

Primary: Time to First Major thromboembolic event

| | |
|-----------------|--|
| End point title | Time to First Major thromboembolic event ^[10] |
|-----------------|--|

End point description:

Time to first major thromboembolic event was defined as the duration of time (in days) from Baseline up to first major thromboembolic event in LTS16371. Subjects without an event during LTS16371 were censored at the end of the study. Kaplan-Meier method was used for the analysis. Analysis was performed on efficacy ITO population which included subjects who were enrolled in LTS16371 and did not experience an aTTP recurrence in previous study ALX0681-C301 or prior to the beginning of LTS16371. Here, '99999' was used as a space filler which indicates that median and 95% CI data were not calculated due to very few subjects with events.

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

From Baseline up to 36 months

Notes:

[10] - 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: As the endpoint was descriptive in nature, no statistical analysis was provided.

| End point values | Standard of Care (Treated in Study C301) | Caplacizumab (Treated in Study C301) | | |
|----------------------------------|--|--------------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 29 | 49 | | |
| Units: days | | | | |
| median (confidence interval 95%) | 99999 (845.00 to 99999) | 99999 (99999 to 99999) | | |

Statistical analyses

No statistical analyses for this end point

Primary: Cognitive Function: Repeatable Battery for the Assessment of Neuropsychological Status (RBANS) Total Absolute Score at Baseline, 36 Months Follow-up Visit, and Change From Baseline in RBANS Total Score at 36 Months Follow-up Visit

| | |
|-----------------|--|
| End point title | Cognitive Function: Repeatable Battery for the Assessment of Neuropsychological Status (RBANS) Total Absolute Score at Baseline, 36 Months Follow-up Visit, and Change From Baseline in RBANS Total Score at 36 Months Follow-up Visit ^[11] |
|-----------------|--|

End point description:

The RBANS is a 30-minute comprehensive screening test with five individual domains (immediate memory, delayed memory, attention, language, and visuospatial ability) to examine the cognitive mental status of a subject. Scores from all individual domain were aggregated into a total score and thus RBANS total score ranged from 40 to 160, where higher scores reflected better performance. Analysis was performed on efficacy ITO population which included subjects who were enrolled in LTS16371 and did not experience aTTP recurrence in previous study ALX0681-C301 or prior to the beginning of LTS16371. Here, 'n' = subjects with available data for each specified category.

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Baseline, 36 Months follow-up visit

Notes:

[11] - 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: As the endpoint was descriptive in nature, no statistical analysis was provided.

| End point values | Standard of Care (Treated in Study C301) | Caplacizumab (Treated in Study C301) | | |
|--------------------------------------|--|--------------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 26 | 38 | | |
| Units: units on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (n = 26, 38) | 89.7 (± 20.3) | 92.7 (± 14.9) | | |
| At 36 Months (n = 12, 32) | 98.0 (± 16.6) | 96.5 (± 17.0) | | |
| Change at 36 Months (n = 12, 32) | 2.1 (± 8.7) | 4.2 (± 8.9) | | |

Statistical analyses

No statistical analyses for this end point

Primary: Health-Related Quality of Life (HRQoL): Change From Baseline in Headache Impact Test (HIT-6) Total Scores at Month 12, 24, and 36 Follow-up Visits

| | |
|-----------------|--|
| End point title | Health-Related Quality of Life (HRQoL): Change From Baseline in Headache Impact Test (HIT-6) Total Scores at Month 12, 24, and 36 Follow-up Visits ^[12] |
|-----------------|--|

End point description:

HIT-6 is an easy to administer assessment that was used as a clinical evaluation of the impact of headache on a subject's QoL in both clinical practice and clinical research. The questionnaire included 6 questions covering the 6 areas of functioning most impacted in headache sufferers including pain, role functioning (the ability to carry out usual activities), social functioning, vitality (energy/ fatigue), cognitive functioning, and psychological/emotional distress. Total HIT-6 scores (sum of all individual questions) ranged from 36 (best outcome) to 78 (worst outcome), where higher scores indicated worse condition. Analysis was performed on efficacy ITO population which included subjects who were enrolled in LTS16371 and did not experience aTTP recurrence in previous study ALX0681-C301 or prior to the beginning of LTS16371. Here, 'n' = subjects with available data for each specified category.

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Baseline, Month 12, 24, and 36 Follow-up visits

Notes:

[12] - 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: As the endpoint was descriptive in nature, no statistical analysis was provided.

| End point values | Standard of Care (Treated in Study C301) | Caplacizumab (Treated in Study C301) | | |
|--------------------------------------|--|--------------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 29 | 49 | | |
| Units: units on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (n = 29, 49) | 45.0 (± 10.0) | 48.2 (± 9.9) | | |
| Change at 12 Months (n = 20, 43) | 0.9 (± 6.5) | 0.1 (± 7.0) | | |
| Change at 24 Months (n = 19, 45) | 1.2 (± 8.2) | -0.6 (± 8.7) | | |
| Change at 36 Months (n = 14, 43) | 0.6 (± 7.9) | 1.4 (± 7.5) | | |

Statistical analyses

No statistical analyses for this end point

Primary: Health-Related Quality of Life: Change From Baseline in 36-Item Short Form questionnaire (SF-36) Health Survey - Physical Functioning Domain Scores at Month 12, 24, and 36 Follow-up Visits

| | |
|-----------------|---|
| End point title | Health-Related Quality of Life: Change From Baseline in 36- |
|-----------------|---|

End point description:

The SF-36 consisted of 36 items that was summarised into 8 domains: physical functioning, social functioning, role functioning/physical, role functioning/emotional, emotional well-being, energy/fatigue, pain, general health and an additional single item covering change in health status. Physical functioning domain scores ranged from 0 (worst value) to 100 (best value), with higher scores reflecting better health status. Change from baseline in physical functioning domain score at months 12, 24, and 36 were reported in this endpoint. Analysis was performed on efficacy ITO population which included subjects who were enrolled in LTS16371 and did not experience aTTP recurrence in previous study ALX0681-C301 or prior to the beginning of LTS16371. Here, 'n' = subjects with available data for each specified category.

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Baseline, Month 12, 24, and 36 Follow-up visits

Notes:

[13] - 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: As the endpoint was descriptive in nature, no statistical analysis was provided.

| End point values | Standard of Care (Treated in Study C301) | Caplacizumab (Treated in Study C301) | | |
|--------------------------------------|--|--------------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 29 | 49 | | |
| Units: units on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (n = 29, 49) | 68.3 (± 28.9) | 74.1 (± 23.6) | | |
| Change at 12 Months (n = 20, 46) | 1.3 (± 16.8) | 1.5 (± 24.1) | | |
| Change at 24 Months (n = 20, 45) | -0.8 (± 18.2) | 5.7 (± 19.3) | | |
| Change at 36 Months (n = 15, 43) | 5.7 (± 17.4) | 6.2 (± 18.9) | | |

Statistical analyses

No statistical analyses for this end point

Primary: Health-Related Quality of Life: Change From Baseline in 36-Item Short Form questionnaire Health Survey - Role Functioning/Physical Domain Scores at Month 12, 24, and 36 Follow-up Visits

| | |
|-----------------|---|
| End point title | Health-Related Quality of Life: Change From Baseline in 36-Item Short Form questionnaire Health Survey - Role Functioning/Physical Domain Scores at Month 12, 24, and 36 Follow-up Visits ^[14] |
|-----------------|---|

End point description:

The SF-36 consisted of 36 items that was summarised into 8 domains: physical functioning, social functioning, role functioning/physical, role functioning/emotional, emotional well-being, energy/fatigue, pain, general health and an additional single item covering change in health status. Role Functioning/Physical domain scores ranged from 0 (worst value) to 100 (best value), with higher scores reflecting better health status. Change from baseline in role functioning/physical domain score at months 12, 24, and 36 were reported in this endpoint. Analysis was performed on efficacy ITO population which included subjects who were enrolled in LTS16371 and did not experience aTTP recurrence in previous study ALX0681-C301 or prior to the beginning of LTS16371. Here, 'n' = subjects with available data for each specified category.

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Baseline, Month 12, 24, and 36 Follow-up visits

Notes:

[14] - 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: As the endpoint was descriptive in nature, no statistical analysis was provided.

| End point values | Standard of Care (Treated in Study C301) | Caplacizumab (Treated in Study C301) | | |
|--------------------------------------|--|--------------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 29 | 49 | | |
| Units: units on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (n = 29, 49) | 60.1 (± 31.9) | 65.9 (± 30.6) | | |
| Change at 12 Months (n = 19, 46) | -5.3 (± 19.3) | 7.7 (± 35.4) | | |
| Change at 24 Months (n = 20, 45) | 4.1 (± 24.1) | 7.1 (± 28.0) | | |
| Change at 36 Months (n = 15, 43) | 5.8 (± 20.0) | 3.6 (± 28.6) | | |

Statistical analyses

No statistical analyses for this end point

Primary: Health-Related Quality of Life: Change From Baseline in 36-Item Short Form questionnaire Health Survey - Role Functioning/Emotional Domain Scores at Month 12, 24, and 36 Follow-up Visits

| | |
|-----------------|--|
| End point title | Health-Related Quality of Life: Change From Baseline in 36-Item Short Form questionnaire Health Survey - Role Functioning/Emotional Domain Scores at Month 12, 24, and 36 Follow-up Visits ^[15] |
|-----------------|--|

End point description:

The SF-36 consisted of 36 items that was summarised into 8 domains: physical functioning, social functioning, role functioning/physical, role functioning/emotional, emotional well-being, energy/fatigue, pain, general health and an additional single item covering change in health status. Role functioning/emotional domain scores ranged from 0 (worst value) to 100 (best value), with higher scores reflecting better health status. Change from baseline in role functioning/emotional domain score at months 12, 24, and 36 were reported in this endpoint. Analysis was performed on efficacy ITO population which included subjects who were enrolled in LTS16371 and did not experience aTTP recurrence in previous study ALX0681-C301 or prior to the beginning of LTS16371. Here, 'n' = subjects with available data for each specified category.

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Baseline, Month 12, 24, and 36 Follow-up visits

Notes:

[15] - 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: As the endpoint was descriptive in nature, no statistical analysis was provided.

| End point values | Standard of Care (Treated in Study C301) | Caplacizumab (Treated in Study C301) | | |
|--------------------------------------|--|--------------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 29 | 49 | | |
| Units: units on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (n = 29, 49) | 75.3 (± 25.6) | 75.0 (± 29.4) | | |
| Change at 12 Months (n = 19, 46) | -13.2 (± 31.0) | 1.6 (± 38.0) | | |
| Change at 24 Months (n = 20, 45) | -1.3 (± 32.5) | 0.9 (± 33.7) | | |
| Change at 36 Month (n = 15, 43) | -4.4 (± 20.6) | -3.7 (± 29.6) | | |

Statistical analyses

No statistical analyses for this end point

Primary: Health-Related Quality of Life: Change From Baseline in 36-Item Short Form questionnaire Health Survey - Energy/Fatigue Domain Scores at Month 12, 24, and 36 Follow-up Visits

| | |
|-----------------|--|
| End point title | Health-Related Quality of Life: Change From Baseline in 36-Item Short Form questionnaire Health Survey - Energy/Fatigue Domain Scores at Month 12, 24, and 36 Follow-up Visits ^[16] |
|-----------------|--|

End point description:

The SF-36 consisted of 36 items that was summarised into 8 domains: physical functioning, social functioning, role functioning/physical, role functioning/emotional, emotional well-being, energy/fatigue, pain, general health and an additional single item covering change in health status. Energy/fatigue domain scores ranged from 0 (worst value) to 100 (best value), with higher scores reflecting better health status. Change from baseline in energy/fatigue domain score at months 12, 24, and 36 were reported in this endpoint. Analysis was performed on efficacy ITO population which included subjects who were enrolled in LTS16371 and did not experience aTTP recurrence in previous study ALX0681-C301 or prior to the beginning of LTS16371. Here, 'n' = subjects with available data for each specified category.

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Baseline, Month 12, 24, and 36 Follow-up visits

Notes:

[16] - 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: As the endpoint was descriptive in nature, no statistical analysis was provided.

| End point values | Standard of Care (Treated in Study C301) | Caplacizumab (Treated in Study C301) | | |
|--------------------------------------|--|--------------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 29 | 49 | | |
| Units: units on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (n = 29, 49) | 50.9 (± 21.2) | 52.4 (± 20.9) | | |
| Change at 12 Months (n = 20, 45) | -0.3 (± 18.3) | 2.0 (± 20.7) | | |
| Change at 24 Months (n = 20, 45) | 5.9 (± 21.4) | 0.6 (± 21.7) | | |
| Change at 36 Months (n = 15, 43) | 7.5 (± 21.3) | 3.9 (± 18.7) | | |

Statistical analyses

No statistical analyses for this end point

Primary: Health-Related Quality of Life: Change From Baseline in 36-Item Short Form questionnaire Health Survey - Emotional well-being Domain Scores at Month 12, 24, and 36 Follow-up Visits

| | |
|-----------------|--|
| End point title | Health-Related Quality of Life: Change From Baseline in 36-Item Short Form questionnaire Health Survey - Emotional well-being Domain Scores at Month 12, 24, and 36 Follow-up Visits ^[17] |
|-----------------|--|

End point description:

The SF-36 consisted of 36 items that was summarised into 8 domains: physical functioning, social functioning, role functioning/physical, role functioning/emotional, emotional well-being, energy/fatigue, pain, general health and an additional single item covering change in health status. Emotional well-being domain scores ranged from 0 (worst value) to 100 (best value), with higher scores reflecting better health status. Change from baseline in emotional well-being domain score at months 12, 24, and 36 were reported in this endpoint. Analysis was performed on efficacy ITO population which included subjects who were enrolled in LTS16371 and did not experience aTTP recurrence in previous study ALX0681-C301 or prior to the beginning of LTS16371. Here, 'n' = subjects with available data for each specified category.

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Baseline, Month 12, 24, and 36 Follow-up visits

Notes:

[17] - 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: As the endpoint was descriptive in nature, no statistical analysis was provided.

| End point values | Standard of Care (Treated in Study C301) | Caplacizumab (Treated in Study C301) | | |
|--------------------------------------|--|--------------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 29 | 49 | | |
| Units: units on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (n = 29, 49) | 72.1 (± 18.3) | 70.1 (± 20.7) | | |
| Change at 12 Months (n = 20, 45) | -9.3 (± 18.2) | -2.5 (± 21.1) | | |
| Change at 24 Months (n = 20, 45) | -3.3 (± 18.9) | -2.0 (± 21.3) | | |
| Change at 36 Months (n = 15, 43) | -0.7 (± 14.6) | -1.5 (± 19.3) | | |

Statistical analyses

No statistical analyses for this end point

Primary: Health-Related Quality of Life: Change From Baseline in 36-Item Short Form questionnaire Health Survey - Social Functioning Domain Scores at Month 12,

24, and 36 Follow-up Visits

| | |
|-----------------|--|
| End point title | Health-Related Quality of Life: Change From Baseline in 36-Item Short Form questionnaire Health Survey - Social Functioning Domain Scores at Month 12, 24, and 36 Follow-up Visits ^[18] |
|-----------------|--|

End point description:

The SF-36 consisted of 36 items that was summarised into 8 domains: physical functioning, social functioning, role functioning/physical, role functioning/emotional, emotional well-being, energy/fatigue, pain, general health and an additional single item covering change in health status. Social functioning domain scores ranged from 0 (worst value) to 100 (best value), with higher scores reflecting better health status. Change from baseline in social functioning domain score at months 12, 24, and 36 were reported in this endpoint. Analysis was performed on efficacy ITO population which included subjects who were enrolled in LTS16371 and did not experience aTTP recurrence in previous study ALX0681-C301 or prior to the beginning of LTS16371. Here, 'n' = subjects with available data for each specified category.

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Baseline, Month 12, 24, and 36 Follow-up visits

Notes:

[18] - 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: As the endpoint was descriptive in nature, no statistical analysis was provided.

| End point values | Standard of Care (Treated in Study C301) | Caplacizumab (Treated in Study C301) | | |
|--------------------------------------|--|--------------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 29 | 49 | | |
| Units: units on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (n = 29, 49) | 74.6 (± 25.3) | 74.0 (± 28.5) | | |
| Change at 12 Months (n = 20, 46) | -10.6 (± 26.7) | 1.6 (± 35.1) | | |
| Change at 24 Months (n = 20, 45) | 0.0 (± 27.5) | -0.8 (± 33.8) | | |
| Change at 36 Months (n = 15, 43) | 0.8 (± 18.0) | -2.6 (± 31.9) | | |

Statistical analyses

No statistical analyses for this end point

Primary: Health-Related Quality of Life: Change From Baseline in 36-Item Short Form questionnaire Health Survey - Pain Domain Scores at Month 12, 24, and 36 Follow-up Visits

| | |
|-----------------|--|
| End point title | Health-Related Quality of Life: Change From Baseline in 36-Item Short Form questionnaire Health Survey - Pain Domain Scores at Month 12, 24, and 36 Follow-up Visits ^[19] |
|-----------------|--|

End point description:

The SF-36 consisted of 36 items that was summarised into 8 domains: physical functioning, social functioning, role functioning/physical, role functioning/emotional, emotional well-being, energy/fatigue, pain, general health and an additional single item covering change in health status. Pain domain scores ranged from 0 (worst value) to 100 (best value), with higher scores reflecting better health status. Change from baseline in pain domain score at months 12, 24, and 36 were reported in this endpoint. Analysis was performed on efficacy ITO population which included subjects who were enrolled in LTS16371 and did not experience aTTP recurrence in previous study ALX0681-C301 or prior to the beginning of LTS16371. Here, 'n' = subjects with available data for each specified category.

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Baseline, Month 12, 24, and 36 Follow-up visits

Notes:

[19] - 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: As the endpoint was descriptive in nature, no statistical analysis was provided.

| End point values | Standard of Care (Treated in Study C301) | Caplacizumab (Treated in Study C301) | | |
|--------------------------------------|--|--------------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 29 | 49 | | |
| Units: units on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (n = 29, 49) | 68.4 (± 31.7) | 68.0 (± 23.5) | | |
| Change at 12 Months (n = 20, 46) | -1.8 (± 30.4) | 0.3 (± 33.6) | | |
| Change at 24 Months (n = 20, 45) | -9.4 (± 32.5) | 5.0 (± 24.9) | | |
| Change at 36 Months (n = 15, 43) | -5.2 (± 21.5) | 3.7 (± 25.6) | | |

Statistical analyses

No statistical analyses for this end point

Primary: Health-Related Quality of Life: Change From Baseline in 36-Item Short Form Questionnaire (SF-36) Health Survey - General Health Domain Scores at Month 12, 24, and 36 Follow-up Visits

| | |
|-----------------|--|
| End point title | Health-Related Quality of Life: Change From Baseline in 36-Item Short Form Questionnaire (SF-36) Health Survey - General Health Domain Scores at Month 12, 24, and 36 Follow-up Visits ^[20] |
|-----------------|--|

End point description:

The SF-36 consisted of 36 items that was summarised into 8 domains: physical functioning, social functioning, role functioning/physical, role functioning/emotional, emotional well-being, energy/fatigue, pain, general health and an additional single item covering change in health status. General Health domain scores ranged from 0 (worst value) to 100 (best value), with higher scores reflecting better health status. Change from baseline in general health domain score at months 12, 24, and 36 were reported in this endpoint. Analysis was performed on efficacy ITO population which included subjects who were enrolled in LTS16371 and did not experience aTTP recurrence in previous study ALX0681-C301 or prior to the beginning of LTS16371. Here, 'n' = subjects with available data for each specified category.

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Baseline, Month 12, 24, and 36 Follow-up visits

Notes:

[20] - 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: As the endpoint was descriptive in nature, no statistical analysis was provided.

| End point values | Standard of Care (Treated in Study C301) | Caplacizumab (Treated in Study C301) | | |
|--------------------------------------|--|--------------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 29 | 49 | | |
| Units: units on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (n = 29, 49) | 66.4 (± 18.5) | 53.1 (± 19.3) | | |
| Change at 12 Months (n = 20, 46) | -4.0 (± 19.8) | 4.9 (± 19.0) | | |
| Change at 24 Months (n = 20, 45) | -1.5 (± 17.9) | 4.8 (± 20.9) | | |
| Change at 36 Months (n = 15, 43) | -4.7 (± 11.1) | 3.6 (± 17.3) | | |

Statistical analyses

No statistical analyses for this end point

Primary: Health-Related Quality of Life: Change From Baseline in 36-Item Short Form Questionnaire (SF-36) Health Survey - Change in Health Status Scores at Month 12, 24, and 36 Follow-up Visits

| | |
|-----------------|--|
| End point title | Health-Related Quality of Life: Change From Baseline in 36-Item Short Form Questionnaire (SF-36) Health Survey - Change in Health Status Scores at Month 12, 24, and 36 Follow-up Visits ^[21] |
|-----------------|--|

End point description:

The SF-36 consisted of 36 items that was summarised into 8 domains: physical functioning, social functioning, role functioning/physical, role functioning/emotional, emotional well-being, energy/fatigue, pain, general health and an additional single item covering change in health status. Change in health status scores ranged from 0 (worst value) to 100 (best value), with higher scores reflecting better health status. Change from baseline in change in health status score at months 12, 24, and 36 were reported in this endpoint. Analysis was performed on efficacy ITO population which included subjects who were enrolled in LTS16371 and did not experience aTTP recurrence in previous study ALX0681-C301 or prior to the beginning of LTS16371. Here, 'n' = subjects with available data for each specified category.

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Baseline, Month 12, 24, and 36 Follow-up visits

Notes:

[21] - 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: As the endpoint was descriptive in nature, no statistical analysis was provided.

| End point values | Standard of Care (Treated in Study C301) | Caplacizumab (Treated in Study C301) | | |
|--------------------------------------|--|--------------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 29 | 49 | | |
| Units: units on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (n = 29, 49) | 45.7 (± 31.4) | 53.6 (± 34.2) | | |
| Change at 12 Months (n = 20, 46) | 30.0 (± 40.2) | 20.1 (± 44.0) | | |
| Change at 24 Months (n = 20, 45) | 21.3 (± 36.5) | 10.6 (± 39.0) | | |
| Change at 36 Months (n = 15, 43) | 16.7 (± 33.6) | 4.7 (± 37.1) | | |

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With Drug-Induced Treatment-emergent (TE) Antidrug Antibodies (ADA) Positive Response

| | |
|-----------------|--|
| End point title | Percentage of Subjects With Drug-Induced Treatment-emergent (TE) Antidrug Antibodies (ADA) Positive Response ^[22] |
|-----------------|--|

End point description:

Drug-induced TE ADA positive was based on the outcome of a tiered assay approach that included a modified ADA (mADA) method to eliminate the effects of pre-existing antibodies (pre-Ab). TE ADA responses reported here included both pre-Ab positive and negative responses. A subject was considered as drug-induced TE ADA positive if post-dose samples were positive, regardless of the status of pre-dose samples in the ADA and modified ADA assay. Analysis was performed on overall ITO population which included subjects who were enrolled in LTS16371, grouped by whether they received caplacizumab during previous study ALX0681-C301 versus those who never received caplacizumab before enrollment in LTS16371.

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

From Baseline up to 36 months

Notes:

[22] - 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: As the endpoint was descriptive in nature, no statistical analysis was provided.

| End point values | Standard of Care (Treated in Study C301) | Caplacizumab (Treated in Study C301) | | |
|-------------------------------|--|--------------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 29 | 75 | | |
| Units: percentage of subjects | | | | |
| number (not applicable) | 0 | 10.7 | | |

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Adverse Events (AEs) and Serious Adverse Events (SAEs)

| | |
|-----------------|--|
| End point title | Number of Subjects With Adverse Events (AEs) and Serious Adverse Events (SAEs) ^[23] |
|-----------------|--|

End point description:

An AE was any untoward medical occurrence in a clinical study subject administered a medicinal product and which did not necessarily had to have a causal relationship with the treatment. An SAE was any untoward medical occurrence that at any dose: resulted in death, was life-threatening, required inpatient hospitalisation or prolongation of existing hospitalisation, resulted in persistent or significant disability/incapacity, was a congenital anomaly/birth defect, was a medically important event. Analysis was performed on overall ITO population which included subjects who were enrolled in LTS16371,

grouped by whether they received caplacizumab during previous study ALX0681-C301 versus those who never received caplacizumab before enrollment in LTS16371.

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

From Baseline up to 36 months

Notes:

[23] - 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: As the endpoint was descriptive in nature, no statistical analysis was provided.

| End point values | Standard of Care (Treated in Study C301) | Caplacizumab (Treated in Study C301) | | |
|----------------------------------|--|--------------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 29 | 75 | | |
| Units: subjects | | | | |
| At least one AE | 26 | 68 | | |
| At least one SAE | 16 | 28 | | |
| At least one AE leading to death | 1 | 0 | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From Baseline up to 36 months

Adverse event reporting additional description:

Analysis was performed on overall ITO population which included subjects who were enrolled in LTS16371, grouped by whether they received caplacizumab during previous study ALX0681-C301 versus those who never received caplacizumab before enrollment in LTS16371.

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

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 22.0 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|--------------------------------------|
| Reporting group title | Caplacizumab (Treated in Study C301) |
|-----------------------|--------------------------------------|

Reporting group description:

Subjects who completed study ALX0681-C301 and received caplacizumab with PE and immunosuppressive agents were enrolled in study LTS16371. Subjects upon each recurrence of aTTP in LTS16371 and not meeting any criteria (namely: pregnancy, history of severe and/or serious hypersensitivity reaction to IMP, withdrawal before receiving IMP, received more than 1 PE) were treated with caplacizumab initial 10 mg IV dose followed by a daily 10 mg SC injections during the period of PE and for 30 days after stop of PE (and eventually 28-day extension period, if needed). Subjects with or without recurrence were followed up twice yearly up to maximum of 36 months in LTS16371.

| | |
|-----------------------|--|
| Reporting group title | Standard of Care (Treated in Study C301) |
|-----------------------|--|

Reporting group description:

Subjects who completed study ALX0681-C301 with SoC (plasma exchange [PE], corticosteroid and other immunosuppressive agents) treatment were enrolled in study LTS16371. Subjects upon each recurrence of aTTP in LTS16371 and not meeting any criteria (namely: pregnancy, history of severe and/or serious hypersensitivity reaction to investigational medicinal product [IMP], withdrawal before receiving IMP, received more than 1 PE) were treated with caplacizumab initial 10 mg intravenous (IV) dose followed by a daily 10 milligrams (mg) subcutaneous (SC) injections during the period of PE and for 30 days after stop of PE (and eventually 28-day extension period, if needed). Subjects with or without recurrence were followed up twice yearly up to maximum of 36 months in LTS16371.

| Serious adverse events | Caplacizumab (Treated in Study C301) | Standard of Care (Treated in Study C301) | |
|--|--|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 28 / 75 (37.33%) | 16 / 29 (55.17%) | |
| number of deaths (all causes) | 0 | 1 | |
| number of deaths resulting from adverse events | | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Breast Cancer | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 1 / 75 (1.33%) | 0 / 29 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|--|----------------------------------|----------------------------------|--|
| Invasive Ductal Breast Carcinoma alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 75 (1.33%) 0 / 1 0 / 0 | 0 / 29 (0.00%) 0 / 0 0 / 0 | |
| Plasma Cell Myeloma alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 75 (1.33%) 0 / 1 0 / 0 | 0 / 29 (0.00%) 0 / 0 0 / 0 | |
| Renal Cell Carcinoma alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 75 (0.00%) 0 / 0 0 / 0 | 1 / 29 (3.45%) 0 / 1 0 / 0 | |
| Transitional Cell Carcinoma alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 75 (0.00%) 0 / 0 0 / 0 | 1 / 29 (3.45%) 0 / 1 0 / 0 | |
| Surgical and medical procedures Abortion Induced alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 2 / 75 (2.67%) 0 / 2 0 / 0 | 0 / 29 (0.00%) 0 / 0 0 / 0 | |
| Cholecystectomy alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 75 (1.33%) 0 / 1 0 / 0 | 0 / 29 (0.00%) 0 / 0 0 / 0 | |
| Pregnancy, puerperium and perinatal conditions Abortion Spontaneous | | | |

| | | | |
|--|----------------|----------------|--|
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 2 / 75 (2.67%) | 0 / 29 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pre-Eclampsia | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 1 / 75 (1.33%) | 0 / 29 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Reproductive system and breast disorders | | | |
| Colpocele | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 1 / 75 (1.33%) | 0 / 29 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hysterocele | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 1 / 75 (1.33%) | 0 / 29 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Acute Respiratory Failure | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 75 (0.00%) | 1 / 29 (3.45%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Psychiatric disorders | | | |
| Psychotic Disorder | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 1 / 75 (1.33%) | 0 / 29 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Injury, poisoning and procedural | | | |

| | | | |
|--|----------------|----------------|--|
| complications | | | |
| Allergic Transfusion Reaction | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 1 / 75 (1.33%) | 0 / 29 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac disorders | | | |
| Acute Myocardial Infarction | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 75 (0.00%) | 1 / 29 (3.45%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Angina Unstable | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 75 (0.00%) | 1 / 29 (3.45%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pericarditis | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 75 (0.00%) | 1 / 29 (3.45%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nervous system disorders | | | |
| Haemorrhage Intracranial | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 1 / 75 (1.33%) | 0 / 29 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ischaemic Stroke | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 1 / 75 (1.33%) | 0 / 29 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Migraine | | | |

| | | | |
|--|------------------|-----------------|--|
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 75 (0.00%) | 1 / 29 (3.45%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Seizure | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 75 (0.00%) | 1 / 29 (3.45%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Blood and lymphatic system disorders | | | |
| Lymphadenitis | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 1 / 75 (1.33%) | 0 / 29 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Thrombotic Thrombocytopenic Purpura | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 11 / 75 (14.67%) | 8 / 29 (27.59%) | |
| occurrences causally related to treatment / all | 0 / 21 | 0 / 9 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Gastrointestinal disorders | | | |
| Gastrointestinal Haemorrhage | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 1 / 75 (1.33%) | 0 / 29 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ileus | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 75 (0.00%) | 1 / 29 (3.45%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal and urinary disorders | | | |
| Glomerulonephritis Membranous | | | |

| | | | |
|--|----------------|----------------|--|
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 75 (0.00%) | 1 / 29 (3.45%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Haematuria | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 1 / 75 (1.33%) | 0 / 29 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Haemorrhage Urinary Tract | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 1 / 75 (1.33%) | 0 / 29 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal Infarct | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 75 (0.00%) | 1 / 29 (3.45%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Musculoskeletal and connective tissue disorders | | | |
| Back Pain | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 75 (0.00%) | 2 / 29 (6.90%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Osteoarthritis | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 1 / 75 (1.33%) | 0 / 29 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| Appendicitis | | | |
| alternative dictionary used: MedDRA 22.0 | | | |

| | | | |
|---|----------------|----------------|--|
| subjects affected / exposed | 1 / 75 (1.33%) | 0 / 29 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cellulitis | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 1 / 75 (1.33%) | 0 / 29 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatitis Viral | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 75 (0.00%) | 1 / 29 (3.45%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Localised Infection | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 75 (0.00%) | 1 / 29 (3.45%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lower Respiratory Tract Infection | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 1 / 75 (1.33%) | 0 / 29 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Meningitis Aseptic | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 1 / 75 (1.33%) | 0 / 29 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ophthalmic Herpes Zoster | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 1 / 75 (1.33%) | 0 / 29 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|--|----------------------------------|----------------------------------|--|
| Pneumonia alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 2 / 75 (2.67%) 0 / 3 0 / 0 | 0 / 29 (0.00%) 0 / 0 0 / 0 | |
| Pneumonia Pneumococcal alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 75 (1.33%) 0 / 1 0 / 0 | 0 / 29 (0.00%) 0 / 0 0 / 0 | |
| Upper Respiratory Tract Infection alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 75 (0.00%) 0 / 0 0 / 0 | 1 / 29 (3.45%) 0 / 1 0 / 0 | |
| Urinary Tract Infection alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 75 (1.33%) 0 / 1 0 / 0 | 0 / 29 (0.00%) 0 / 0 0 / 0 | |

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

| Non-serious adverse events | Caplacizumab (Treated in Study C301) | Standard of Care (Treated in Study C301) | |
|--|--|--|--|
| Total subjects affected by non-serious adverse events subjects affected / exposed | 58 / 75 (77.33%) | 22 / 29 (75.86%) | |
| Investigations Adamts13 Activity Decreased alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences (all) Blood Cholesterol Increased alternative dictionary used: MedDRA 22.0 | 13 / 75 (17.33%) 13 | 0 / 29 (0.00%) 0 | |

| | | | |
|--|--|--|--|
| subjects affected / exposed occurrences (all) | 4 / 75 (5.33%) 4 | 0 / 29 (0.00%) 0 | |
| Injury, poisoning and procedural complications Contusion alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences (all) | 2 / 75 (2.67%) 2 | 2 / 29 (6.90%) 2 | |
| Vascular disorders Hypertension alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences (all) | 1 / 75 (1.33%) 1 | 3 / 29 (10.34%) 3 | |
| Nervous system disorders Dizziness alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences (all) Headache alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences (all) Paraesthesia alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences (all) Seizure alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences (all) | 10 / 75 (13.33%) 10 16 / 75 (21.33%) 17 4 / 75 (5.33%) 4 1 / 75 (1.33%) 1 | 2 / 29 (6.90%) 2 9 / 29 (31.03%) 9 5 / 29 (17.24%) 5 2 / 29 (6.90%) 2 | |
| General disorders and administration site conditions Asthenia alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences (all) Fatigue | 0 / 75 (0.00%) 0 | 2 / 29 (6.90%) 2 | |

| | | | |
|--|---|---|--|
| <p>alternative dictionary used: MedDRA 22.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Pyrexia</p> <p>alternative dictionary used: MedDRA 22.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>7 / 75 (9.33%)</p> <p>7</p> <p>3 / 75 (4.00%)</p> <p>3</p> | <p>1 / 29 (3.45%)</p> <p>1</p> <p>3 / 29 (10.34%)</p> <p>3</p> | |
| <p>Immune system disorders</p> <p>Drug Hypersensitivity</p> <p>alternative dictionary used: MedDRA 22.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Hypersensitivity</p> <p>alternative dictionary used: MedDRA 22.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>4 / 75 (5.33%)</p> <p>5</p> <p>1 / 75 (1.33%)</p> <p>1</p> | <p>2 / 29 (6.90%)</p> <p>2</p> <p>2 / 29 (6.90%)</p> <p>2</p> | |
| <p>Gastrointestinal disorders</p> <p>Abdominal Pain</p> <p>alternative dictionary used: MedDRA 22.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Abdominal Pain Upper</p> <p>alternative dictionary used: MedDRA 22.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Constipation</p> <p>alternative dictionary used: MedDRA 22.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Diarrhoea</p> <p>alternative dictionary used: MedDRA 22.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Nausea</p> <p>alternative dictionary used: MedDRA 22.0</p> | <p>3 / 75 (4.00%)</p> <p>3</p> <p>4 / 75 (5.33%)</p> <p>4</p> <p>5 / 75 (6.67%)</p> <p>5</p> <p>5 / 75 (6.67%)</p> <p>5</p> | <p>2 / 29 (6.90%)</p> <p>2</p> <p>3 / 29 (10.34%)</p> <p>3</p> <p>1 / 29 (3.45%)</p> <p>1</p> <p>5 / 29 (17.24%)</p> <p>5</p> | |

| | | | |
|--|---|---|--|
| <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Toothache</p> <p>alternative dictionary used: MedDRA 22.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>7 / 75 (9.33%)</p> <p>7</p> <p>1 / 75 (1.33%)</p> <p>1</p> | <p>1 / 29 (3.45%)</p> <p>1</p> <p>2 / 29 (6.90%)</p> <p>2</p> | |
| <p>Respiratory, thoracic and mediastinal disorders</p> <p>Cough</p> <p>alternative dictionary used: MedDRA 22.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>7 / 75 (9.33%)</p> <p>7</p> | <p>3 / 29 (10.34%)</p> <p>3</p> | |
| <p>Skin and subcutaneous tissue disorders</p> <p>Erythema</p> <p>alternative dictionary used: MedDRA 22.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Pruritus</p> <p>alternative dictionary used: MedDRA 22.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Rash</p> <p>alternative dictionary used: MedDRA 22.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Urticaria</p> <p>alternative dictionary used: MedDRA 22.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>0 / 75 (0.00%)</p> <p>0</p> <p>6 / 75 (8.00%)</p> <p>7</p> <p>5 / 75 (6.67%)</p> <p>5</p> <p>4 / 75 (5.33%)</p> <p>4</p> | <p>2 / 29 (6.90%)</p> <p>2</p> <p>1 / 29 (3.45%)</p> <p>1</p> <p>0 / 29 (0.00%)</p> <p>0</p> <p>1 / 29 (3.45%)</p> <p>1</p> | |
| <p>Musculoskeletal and connective tissue disorders</p> <p>Arthralgia</p> <p>alternative dictionary used: MedDRA 22.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Back Pain</p> <p>alternative dictionary used:</p> | <p>8 / 75 (10.67%)</p> <p>8</p> | <p>2 / 29 (6.90%)</p> <p>2</p> | |

| | | | |
|---|----------------|-----------------|--|
| MedDRA 22.0 | | | |
| subjects affected / exposed | 4 / 75 (5.33%) | 2 / 29 (6.90%) | |
| occurrences (all) | 4 | 2 | |
| Infections and infestations | | | |
| Bronchitis | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 5 / 75 (6.67%) | 0 / 29 (0.00%) | |
| occurrences (all) | 5 | 0 | |
| Herpes Zoster | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 2 / 75 (2.67%) | 2 / 29 (6.90%) | |
| occurrences (all) | 2 | 2 | |
| Influenza | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 7 / 75 (9.33%) | 3 / 29 (10.34%) | |
| occurrences (all) | 7 | 3 | |
| Lower Respiratory Tract Infection | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 4 / 75 (5.33%) | 2 / 29 (6.90%) | |
| occurrences (all) | 4 | 2 | |
| Nasopharyngitis | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 6 / 75 (8.00%) | 6 / 29 (20.69%) | |
| occurrences (all) | 6 | 6 | |
| Rhinitis | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 2 / 75 (2.67%) | 2 / 29 (6.90%) | |
| occurrences (all) | 2 | 2 | |
| Tonsillitis | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 1 / 75 (1.33%) | 2 / 29 (6.90%) | |
| occurrences (all) | 1 | 2 | |
| Tooth Abscess | | | |
| alternative dictionary used: MedDRA 22.0 | | | |

| | | | |
|---|--|--|--|
| <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Upper Respiratory Tract Infection</p> <p>alternative dictionary used: MedDRA 22.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Urinary Tract Infection</p> <p>alternative dictionary used: MedDRA 22.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>0 / 75 (0.00%)</p> <p>0</p> <p>7 / 75 (9.33%)</p> <p>7</p> <p>4 / 75 (5.33%)</p> <p>5</p> | <p>2 / 29 (6.90%)</p> <p>2</p> <p>3 / 29 (10.34%)</p> <p>3</p> <p>3 / 29 (10.34%)</p> <p>3</p> | |
| <p>Metabolism and nutrition disorders</p> <p>Hypercholesterolaemia</p> <p>alternative dictionary used: MedDRA 22.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Iron Deficiency</p> <p>alternative dictionary used: MedDRA 22.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Hypokalaemia</p> <p>alternative dictionary used: MedDRA 22.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>2 / 75 (2.67%)</p> <p>2</p> <p>5 / 75 (6.67%)</p> <p>5</p> <p>2 / 75 (2.67%)</p> <p>2</p> | <p>2 / 29 (6.90%)</p> <p>2</p> <p>1 / 29 (3.45%)</p> <p>1</p> <p>2 / 29 (6.90%)</p> <p>2</p> | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported