# Clinical trial results:
# A Single-Arm, Multicenter Phase IIIB Clinical Trial to Evaluate the Safety and Tolerability of Prophylactic Emicizumab in Hemophilia A Patients With Inhibitors

## Summary

| | |
|---|---|
| EudraCT number | 2016-004366-25 |
| Trial protocol | PT GB DE DK HU ES PL FI BE SE NL IT RO |
| Global end of trial date | 19 November 2020 |

### Results information

| | |
|---|---|
| Result version number | v1 (current) |
| This version publication date | 02 June 2021 |
| First version publication date | 02 June 2021 |

## Trial information

### Trial identification

| | |
|---|---|
| Sponsor protocol code | MO39129 |

### Additional study identifiers

| | |
|---|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT03191799 |
| WHO universal trial number (UTN) | - |

Notes:

### Sponsors

| | |
|---|---|
| Sponsor organisation name | F. Hoffmann-La Roche AG |
| Sponsor organisation address | Grenzacherstrasse 124, Basel, Switzerland, CH-4070 |
| Public contact | F. Hoffmann-La Roche AG, F. Hoffmann-La Roche AG, 41 616878333, global.trial_information@roche.com |
| Scientific contact | F. Hoffmann-La Roche AG, F. Hoffmann-La Roche AG, 41 616878333, global.trial_information@roche.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? | Yes |

Notes:

## Results analysis stage

| | |
|---|---|
| Analysis stage | Final |
| Date of interim/final analysis | 19 November 2020 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 19 November 2020 |
| Global end of trial reached? | Yes |
| Global end of trial date | 19 November 2020 |
| Was the trial ended prematurely? | No |

Notes:

## General information about the trial

Main objective of the trial:

The main objective of the trial was to evaluate the overall safety and tolerability of prophylactic administration of emicizumab in patients with congenital hemophilia A who have persistent inhibitors against Factor VIII.

Protection of trial subjects:

This study will be conducted in full conformance with the ICH E6 guideline for Good Clinical Practice and the principles of the Declaration of Helsinki, or the laws and regulations of the country in which the research is conducted, whichever affords the greater protection to the individual. An Informed Consent Form (and Assent Form, when applicable) must be signed and dated by the subject (and the pediatric subject's legally authorized representative, when applicable) before participation in the study.

Background therapy: -

Evidence for comparator: -

| | |
|---|---|
| Actual start date of recruitment | 05 September 2017 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

## Population of trial subjects

### Subjects enrolled per country

| | |
|---|---|
| Country: Number of subjects enrolled | Australia: 7 |
| Country: Number of subjects enrolled | Belgium: 4 |
| Country: Number of subjects enrolled | Brazil: 10 |
| Country: Number of subjects enrolled | Canada: 10 |
| Country: Number of subjects enrolled | Colombia: 5 |
| Country: Number of subjects enrolled | Finland: 2 |
| Country: Number of subjects enrolled | Germany: 13 |
| Country: Number of subjects enrolled | Guatemala: 2 |
| Country: Number of subjects enrolled | Hungary: 3 |
| Country: Number of subjects enrolled | India: 30 |
| Country: Number of subjects enrolled | Israel: 4 |
| Country: Number of subjects enrolled | Italy: 27 |
| Country: Number of subjects enrolled | Mexico: 18 |
| Country: Number of subjects enrolled | Netherlands: 5 |
| Country: Number of subjects enrolled | Panama: 4 |
| Country: Number of subjects enrolled | Poland: 3 |
| Country: Number of subjects enrolled | Portugal: 4 |
| Country: Number of subjects enrolled | Romania: 1 |

| | |
|---|---|
| Country: Number of subjects enrolled | Russian Federation: 11 |
| Country: Number of subjects enrolled | Saudi Arabia: 7 |
| Country: Number of subjects enrolled | Spain: 12 |
| Country: Number of subjects enrolled | Sweden: 4 |
| Country: Number of subjects enrolled | Switzerland: 1 |
| Country: Number of subjects enrolled | United Kingdom: 8 |
| Worldwide total number of subjects | 195 |
| EEA total number of subjects | 78 |

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) | 40 |
| Adults (18-64 years) | 146 |
| From 65 to 84 years | 9 |
| 85 years and over | 0 |

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

A total of 195 patients were enrolled in the clinical trial.

### 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** | 1.5 mg/kg Emicizumab QW |

Arm description:

Participants were enrolled to receive initial weekly doses of prophylactic 3.0 mg/kg emicizumab subcutaneously (SC) for 4 weeks, followed by prophylactic maintenance doses consisting of 1.5 mg/kg emicizumab once a week (QW), administered SC for the remainder of the 2-year treatment period.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Emicizumab |
| Investigational medicinal product code | RO5534262 |
| Other name | Hemlibra; ACE910 |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Emicizumab was administered at a loading dose of 3 milligrams per kilogram (mg/kg) once every week (QW) subcutaneously (SC) for the first 4 weeks followed by a maintenance dose of 1.5 mg/kg QW SC for the remainder of the 2-year treatment period.

| **Number of subjects in period 1** | 1.5 mg/kg Emicizumab QW |
|---|---|
| Started | 195 |
| Received at Least One Dose of Emicizumab | 193 |
| Dose Up-Titrated to 3 mg/kg QW | 2 [1] |
| Completed | 186 |
| Not completed | 9 |
| Adverse event, serious fatal | 2 |
| Consent withdrawn by subject | 4 |
| Physician decision | 2 |
| Lost to follow-up | 1 |

Notes:

[1] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: There was an option for individual subjects to increase their emicizumab dose to 3

mg/kg/week in cases of insufficient control of bleeds on the 1.5 mg/kg/week emicizumab dose.

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | 1.5 mg/kg Emicizumab QW |

Reporting group description:

Participants were enrolled to receive initial weekly doses of prophylactic 3.0 mg/kg emicizumab subcutaneously (SC) for 4 weeks, followed by prophylactic maintenance doses consisting of 1.5 mg/kg emicizumab once a week (QW), administered SC for the remainder of the 2-year treatment period.

| Reporting group values | 1.5 mg/kg Emicizumab QW | Total | |
|---|---|---|---|
| Number of subjects | 195 | 195 | |
| Age categorical<br>Units: Subjects | | | |
| In utero | 0 | 0 | |
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | |
| Newborns (0-27 days) | 0 | 0 | |
| Infants and toddlers (28 days-23 months) | 0 | 0 | |
| Children (2-11 years) | 0 | 0 | |
| Adolescents (12-17 years) | 40 | 40 | |
| Adults (18-64 years) | 146 | 146 | |
| From 65-84 years | 9 | 9 | |
| 85 years and over | 0 | 0 | |
| Age Continuous<br>Units: Years | | | |
| arithmetic mean | 32.2 | | |
| standard deviation | ± 16.6 | - | |
| Sex: Female, Male<br>Units: Participants | | | |
| Female | 0 | 0 | |
| Male | 195 | 195 | |
| Race (NIH/OMB)<br>Units: Subjects | | | |
| American Indian or Alaska Native | 19 | 19 | |
| Asian | 38 | 38 | |
| Native Hawaiian or Other Pacific Islander | 1 | 1 | |
| Black or African American | 7 | 7 | |
| White | 121 | 121 | |
| More than one race | 0 | 0 | |
| Unknown or Not Reported | 9 | 9 | |
| Ethnicity (NIH/OMB)<br>Units: Subjects | | | |
| Hispanic or Latino | 41 | 41 | |
| Not Hispanic or Latino | 143 | 143 | |
| Unknown or Not Reported | 11 | 11 | |

## End points

### End points reporting groups

| | |
|---|---|
| Reporting group title | 1.5 mg/kg Emicizumab QW |

Reporting group description:

Participants were enrolled to receive initial weekly doses of prophylactic 3.0 mg/kg emicizumab subcutaneously (SC) for 4 weeks, followed by prophylactic maintenance doses consisting of 1.5 mg/kg emicizumab once a week (QW), administered SC for the remainder of the 2-year treatment period.

### Primary: Overall Summary of the Number of Participants with Adverse Events, Severity Assessed According to the World Health Organization (WHO) Toxicity Grading Scale

| | |
|---|---|
| End point title | Overall Summary of the Number of Participants with Adverse Events, Severity Assessed According to the World Health Organization (WHO) Toxicity Grading Scale[1] |

End point description:

Investigators sought information on adverse events (AEs) at each contact with participants. The WHO toxicity grading scale was used for assessing AE severity (i.e., intensity of an AE); any AEs not specifically listed in the WHO toxicity grading scale were assessed for severity according to the following grades: Grade 1 is mild; Grade 2 is moderate, Grade 3 is severe; Grade 4 is life-threatening; and Grade 5 is death. Regardless of severity, some AEs may have also met seriousness criteria. The terms "severe" and "serious" are not synonymous; severity and seriousness were independently assessed for each AE. aPCC = activated prothrombin complex concentrate; Hypersens. = hypersensitivity

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

End point timeframe:

From Baseline until study completion (up to 2 years)

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: No formal statistical hypothesis tests were performed, and all analyses were considered descriptive.

| End point values | 1.5 mg/kg Emicizumab QW | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 193[2] | | | |
| Units: Participants | | | | |
| Any Adverse Event (AE) | 163 | | | |
| Fatal AE | 2 | | | |
| Serious AE | 31 | | | |
| AE Leading to Withdrawal from Treatment | 1 | | | |
| AE Leading to Dose Modification/Interruption | 4 | | | |
| AE Leading to Study Discontinuation | 1 | | | |
| Grade 3-5 AE | 39 | | | |
| Related AE | 35 | | | |
| Local Injection Site Reaction | 22 | | | |
| Systemic Hypersens./Anaphylac(tic/toid) Reaction | 0 | | | |
| Thromboembolic Event (TE) | 2 | | | |
| TE Related to aPCC and Emicizumab | 0 | | | |
| Thrombotic Microangiopathy (TMA) | 0 | | | |

| | | | | |
|---|---|---|---|---|
| TMA Related to aPCC and Emicizumab | 0 | | | |
| Cases of Potential Drug-Induced Liver Injury | 0 | | | |
| Suspected Transmission of Infectious Agent by Drug | 0 | | | |

Notes:

[2] - Safety Population: received at least 1 dose of emicizumab.

### Statistical analyses

No statistical analyses for this end point

## Primary: Adverse Events (AEs) Rates per 100 Patient-Years for All-Grade AEs, Serious AEs, and Grade ≥3 AEs

| End point title | Adverse Events (AEs) Rates per 100 Patient-Years for All-Grade AEs, Serious AEs, and Grade ≥3 AEs[3] |
|---|---|

End point description:

Investigators sought information on adverse events (AEs) at each contact with participants. The WHO toxicity grading scale was used for assessing AE severity (i.e., intensity of an AE); any AEs not specifically listed in the WHO toxicity grading scale were assessed for severity according to the following grades: Grade 1 is mild; Grade 2 is moderate, Grade 3 is severe; Grade 4 is life-threatening; and Grade 5 is death. Regardless of severity, some AEs may have also met seriousness criteria. The terms "severe" and "serious" are not synonymous; severity and seriousness were independently assessed for each AE. The AE rate per 100 patient-years was computed as follows: AE Rate = (Number of AEs observed/ Total patient-years at risk)*100. Total patient-years at risk is the sum over all patients of the time intervals (in years) between start of study therapy (study day 1) and the end of follow up.

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

End point timeframe:

From Baseline until study completion (up to 2 years)

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: No formal statistical hypothesis tests were performed, and all analyses were considered descriptive.

| **End point values** | 1.5 mg/kg Emicizumab QW | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 193[4] | | | |
| Units: AEs per 100 patient-years | | | | |
| number (confidence interval 95%) | | | | |
| All-Grade AEs | 211.92 (197.49 to 227.13) | | | |
| Serious AEs | 13.25 (9.83 to 17.46) | | | |
| Grade ≥3 AEs | 17.22 (13.29 to 21.95) | | | |

Notes:

[4] - Safety Population: received at least 1 dose of emicizumab.

### Statistical analyses

No statistical analyses for this end point

## Primary: Number of Participants by Hematology and Biochemistry Laboratory

## Parameter Test Results as Shifts from the WHO Toxicity Grade at Baseline to the Worst WHO Toxicity Grade Post-Baseline

| End point title | Number of Participants by Hematology and Biochemistry Laboratory Parameter Test Results as Shifts from the WHO Toxicity Grade at Baseline to the Worst WHO Toxicity Grade Post-Baseline[5] |
|---|---|

End point description:

The World Health Organization (WHO) toxicity grading scale was used for determining the severity of laboratory abnormalities (i.e., test results outside of the reference range) for hematology and biochemistry parameters; Grade 0 is normal and Grades 1 to 4 represent worsening levels of the parameter outside of the normal range in the specified direction of the abnormality (high and low are above and below the range, respectively). Not every laboratory abnormality qualified as an adverse event (AE). A laboratory test result was reported as an AE if it met any of the following criteria: was accompanied by clinical symptoms; resulted in a change in study treatment; resulted in a medical intervention or a change in concomitant therapy; or was clinically significant in the investigator's judgment. Baseline was defined as the last available assessment prior to first receipt of study drug. Abs = absolute count; SGOT/AST = aspartate aminotransferase; SGPT/ALT = alanine aminotransferase

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

End point timeframe:

Baseline, Weeks 2, 3, and 5; Months 3, 6, 9, 12, and 18; and at Early Termination/Study Completion (up to 24 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: No formal statistical hypothesis tests were performed, and all analyses were considered descriptive.

| **End point values** | 1.5 mg/kg Emicizumab QW | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 193[6] | | | |
| Units: Participants | | | | |
| Hemoglobin, Low - Grade 0 to 0 | 173 | | | |
| Hemoglobin, Low - Grade 0 to 1 | 8 | | | |
| Hemoglobin, Low - Grade 0 to 2 | 4 | | | |
| Hemoglobin, Low - Grade 0 to 4 | 1 | | | |
| Hemoglobin, Low - Grade 1 to 0 | 1 | | | |
| Hemoglobin, Low - Grade 1 to 1 | 2 | | | |
| Hemoglobin, Low - Grade 1 to 2 | 1 | | | |
| Hemoglobin, Low - Grade 1 to 3 | 1 | | | |
| Hemoglobin, Low - Grade 2 to 1 | 1 | | | |
| Hemoglobin, Low - Grade 2 to 3 | 1 | | | |
| Neutrophils, Total (Abs), Low - Grade 0 to 0 | 173 | | | |
| Neutrophils, Total (Abs), Low - Grade 0 to 1 | 13 | | | |
| Neutrophils, Total (Abs), Low - Grade 0 to 2 | 1 | | | |
| Neutrophils, Total (Abs), Low - Grade 0 to 3 | 2 | | | |
| Neutrophils, Total (Abs), Low - Grade 0 to 4 | 2 | | | |
| Neutrophils, Total (Abs), Low - Grade 1 to 1 | 2 | | | |
| Platelets, Low - Grade 0 to 0 | 190 | | | |
| Platelets, Low - Grade 0 to 1 | 2 | | | |
| Platelets, Low - Grade 1 to 0 | 1 | | | |

| | | | | |
|---|---|---|---|---|
| Alkaline Phosphatase, High - Grade 0 to 0 | 187 | | | |
| Alkaline Phosphatase, High - Grade 0 to 1 | 3 | | | |
| Alkaline Phosphatase, High - Grade 0 to 2 | 1 | | | |
| Alkaline Phosphatase, High - Grade 1 to 1 | 2 | | | |
| Bilirubin, High - Grade 0 to 0 | 169 | | | |
| Bilirubin, High - Grade 0 to 1 | 14 | | | |
| Bilirubin, High - Grade 1 to 0 | 3 | | | |
| Bilirubin, High - Grade 1 to 1 | 2 | | | |
| Bilirubin, High - Grade 1 to 2 | 3 | | | |
| Bilirubin, High - Grade 2 to 2 | 2 | | | |
| Blood Urea Nitrogen, High - Grade 0 to 0 | 187 | | | |
| Blood Urea Nitrogen, High - Grade 0 to 1 | 5 | | | |
| Blood Urea Nitrogen, High - Grade 1 to 1 | 1 | | | |
| Calcium (Corrected), High - Grade 0 to 0 | 192 | | | |
| Calcium (Corrected), High - Grade 1 to 2 | 1 | | | |
| Calcium (Corrected), Low - Grade 0 to 0 | 173 | | | |
| Calcium (Corrected), Low - Grade 0 to 1 | 15 | | | |
| Calcium (Corrected), Low - Grade 0 to 2 | 1 | | | |
| Calcium (Corrected), Low - Grade 1 to 0 | 3 | | | |
| Calcium (Corrected), Low - Grade 1 to 1 | 1 | | | |
| Creatinine, High - Grade 0 to 0 | 185 | | | |
| Creatinine, High - Grade 0 to 1 | 5 | | | |
| Creatinine, High - Grade 0 to 2 | 1 | | | |
| Creatinine, High - Grade 1 to 1 | 1 | | | |
| Creatinine, High - Grade 1 to 2 | 1 | | | |
| Glucose, High - Grade 0 to 0 | 148 | | | |
| Glucose, High - Grade 0 to 1 | 28 | | | |
| Glucose, High - Grade 0 to 2 | 6 | | | |
| Glucose, High - Grade 1 to 1 | 2 | | | |
| Glucose, High - Grade 1 to 2 | 3 | | | |
| Glucose, High - Grade 2 to 2 | 1 | | | |
| Glucose, High - Grade 2 to 3 | 1 | | | |
| Glucose, High - Grade 3 to 2 | 1 | | | |
| Glucose, High - Grade 3 to 3 | 2 | | | |
| Glucose, High - Grade 4 to 3 | 1 | | | |
| Glucose, Low - Grade 0 to 0 | 180 | | | |
| Glucose, Low - Grade 0 to 1 | 7 | | | |
| Glucose, Low - Grade 0 to 2 | 4 | | | |
| Glucose, Low - Grade 1 to 0 | 2 | | | |
| Magnesium, Low - Grade 0 to 0 | 188 | | | |
| Magnesium, Low - Grade 0 to 1 | 4 | | | |
| Magnesium, Low - Grade 1 to 1 | 1 | | | |
| Phosphorus, Low - Grade 0 to 0 | 160 | | | |
| Phosphorus, Low - Grade 0 to 1 | 21 | | | |
| Phosphorus, Low - Grade 1 to 0 | 2 | | | |
| Phosphorus, Low - Grade 1 to 1 | 9 | | | |

| | | | | |
|---|---|---|---|---|
| Phosphorus, Low - Grade 1 to 2 | 1 | | | |
| Potassium, High - Grade 0 to 0 | 189 | | | |
| Potassium, High - Grade 0 to 1 | 2 | | | |
| Potassium, High - Grade 0 to 2 | 1 | | | |
| Potassium, High - Grade 0 to 4 | 1 | | | |
| Potassium, Low - Grade 0 to 0 | 184 | | | |
| Potassium, Low - Grade 0 to 1 | 6 | | | |
| Potassium, Low - Grade 1 to 0 | 3 | | | |
| SGOT/AST, High - Grade 0 to 0 | 164 | | | |
| SGOT/AST, High - Grade 0 to 1 | 13 | | | |
| SGOT/AST, High - Grade 0 to 2 | 8 | | | |
| SGOT/AST, High - Grade 1 to 0 | 1 | | | |
| SGOT/AST, High - Grade 1 to 1 | 5 | | | |
| SGOT/AST, High - Grade 1 to 2 | 1 | | | |
| SGOT/AST, High - Grade 1 to 3 | 1 | | | |
| SGPT/ALT, High - Grade 0 to 0 | 158 | | | |
| SGPT/ALT, High - Grade 0 to 1 | 22 | | | |
| SGPT/ALT, High - Grade 0 to 2 | 5 | | | |
| SGPT/ALT, High - Grade 1 to 0 | 1 | | | |
| SGPT/ALT, High - Grade 1 to 1 | 4 | | | |
| SGPT/ALT, High - Grade 1 to 2 | 2 | | | |
| SGPT/ALT, High - Grade 1 to 4 | 1 | | | |
| Sodium, High - Grade 0 to 0 | 178 | | | |
| Sodium, High - Grade 0 to 1 | 7 | | | |
| Sodium, High - Grade 0 to 2 | 2 | | | |
| Sodium, High - Grade 1 to 0 | 4 | | | |
| Sodium, High - Grade 1 to 1 | 2 | | | |
| Sodium, Low - Grade 0 to 0 | 166 | | | |
| Sodium, Low - Grade 0 to 1 | 19 | | | |
| Sodium, Low - Grade 0 to 2 | 2 | | | |
| Sodium, Low - Grade 1 to 0 | 3 | | | |
| Sodium, Low - Grade 1 to 1 | 2 | | | |
| Sodium, Low - Grade 1 to 2 | 1 | | | |

Notes:

[6] - Safety Population: received at least 1 dose of emicizumab.

### Statistical analyses

No statistical analyses for this end point

## Primary: Change from Baseline in Body Temperature at Specified Timepoints

| End point title | Change from Baseline in Body Temperature at Specified Timepoints[7] |
|---|---|

End point description:

Vital signs that were measured included body temperature, pulse and respiratory rates, systolic and diastolic blood pressure, and weight. On treatment days, measurement occurred prior to emicizumab administration.

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

End point timeframe:

Baseline, Weeks 2, 3, and 5; Months 3, 6, 9, 12, and 18; and at Early Termination (ET)/Study Completion (SC)(up to 24 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: No formal statistical hypothesis tests were performed, and all analyses were considered descriptive.

| **End point values** | 1.5 mg/kg Emicizumab QW | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 193[8] | | | |
| Units: degrees Celsius | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (BL) - Value at Visit (n = 193) | 36.33 (± 0.52) | | | |
| Change from BL at Week 2 (n = 190) | 0.04 (± 0.41) | | | |
| Change from BL at Week 3 (n = 191) | 0.03 (± 0.40) | | | |
| Change from BL at Week 5 (n = 191) | 0.03 (± 0.45) | | | |
| Change from BL at Month 3 (n = 187) | 0.04 (± 0.45) | | | |
| Change from BL at Month 6 (n = 183) | 0.07 (± 0.50) | | | |
| Change from BL at Month 9 (n = 184) | 0.06 (± 0.48) | | | |
| Change from BL at Month 12 (n = 182) | 0.07 (± 0.48) | | | |
| Change from BL at Month 18 (n = 176) | 0.10 (± 0.53) | | | |
| Change from BL at ET/SC (n = 163) | 0.08 (± 0.48) | | | |

Notes:

[8] - Safety Population: received at least 1 dose of emicizumab.

## Statistical analyses

No statistical analyses for this end point

## Primary: Change from Baseline in Systolic Blood Pressure at Specified Timepoints

| End point title | Change from Baseline in Systolic Blood Pressure at Specified Timepoints[9] |
|---|---|

End point description:

Vital signs that were measured included body temperature, pulse and respiratory rates, systolic and diastolic blood pressure, and weight. On treatment days, measurement occurred prior to emicizumab administration.

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

End point timeframe:

Baseline, Weeks 2, 3, and 5; Months 3, 6, 9, 12, and 18; and at Early Termination (ET)/Study Completion (SC)(up to 24 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: No formal statistical hypothesis tests were performed, and all analyses were considered descriptive.

| **End point values** | 1.5 mg/kg Emicizumab QW | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 193[10] | | | |
| Units: millimetres of mercury (mmHg) | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (BL) - Value at Visit (n = 193) | 121.1 (± 14.3) | | | |

| | | | | |
|---|---|---|---|---|
| Change from BL at Week 2 (n = 193) | -0.9 (± 11.1) | | | |
| Change from BL at Week 3 (n = 192) | -1.2 (± 10.6) | | | |
| Change from BL at Week 5 (n = 192) | -1.3 (± 12.3) | | | |
| Change from BL at Month 3 (n = 188) | 0.1 (± 11.5) | | | |
| Change from BL at Month 6 (n = 185) | -0.2 (± 13.1) | | | |
| Change from BL at Month 9 (n = 186) | 0.1 (± 13.1) | | | |
| Change from BL at Month 12 (n = 184) | 0.1 (± 13.9) | | | |
| Change from BL at Month 18 (n = 177) | -0.1 (± 13.8) | | | |
| Change from BL at ET/SC (n = 166) | 1.9 (± 14.1) | | | |

Notes:

[10] - Safety Population: received at least 1 dose of emicizumab.

### Statistical analyses

No statistical analyses for this end point

## Primary: Change from Baseline in Diastolic Blood Pressure at Specified Timepoints

| End point title | Change from Baseline in Diastolic Blood Pressure at Specified Timepoints[11] |
|---|---|

End point description:

Vital signs that were measured included body temperature, pulse and respiratory rates, systolic and diastolic blood pressure, and weight. On treatment days, measurement occurred prior to emicizumab administration.

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

End point timeframe:

Baseline, Weeks 2, 3, and 5; Months 3, 6, 9, 12, and 18; and at Early Termination (ET)/Study Completion (SC)(up to 24 months)

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: No formal statistical hypothesis tests were performed, and all analyses were considered descriptive.

| **End point values** | 1.5 mg/kg Emicizumab QW | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 193[12] | | | |
| Units: millimetres of mercury (mmHg) | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (BL) - Value at Visit (n = 193) | 75.5 (± 10.4) | | | |
| Change from BL at Week 2 (n = 193) | -1.2 (± 8.5) | | | |
| Change from BL at Week 3 (n = 192) | -1.0 (± 8.9) | | | |
| Change from BL at Week 5 (n = 192) | -1.2 (± 9.2) | | | |
| Change from BL at Month 3 (n = 188) | -0.3 (± 9.8) | | | |
| Change from BL at Month 6 (n = 185) | -0.7 (± 10.1) | | | |
| Change from BL at Month 9 (n = 186) | -1.3 (± 9.4) | | | |
| Change from BL at Month 12 (n = 184) | -1.2 (± 10.4) | | | |
| Change from BL at Month 18 (n = 177) | -0.9 (± 9.6) | | | |
| Change from BL at ET/SC (n = 166) | 0.0 (± 11.0) | | | |

Notes:

[12] - Safety Population: received at least 1 dose of emicizumab.

## Statistical analyses

No statistical analyses for this end point

## Primary: Change from Baseline in Pulse Rate at Specified Timepoints

| End point title | Change from Baseline in Pulse Rate at Specified Timepoints[13] |
|---|---|

End point description:

Vital signs that were measured included body temperature, pulse and respiratory rates, systolic and diastolic blood pressure, and weight. On treatment days, measurement occurred prior to emicizumab administration.

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

End point timeframe:

Baseline, Weeks 2, 3, and 5; Months 3, 6, 9, 12, and 18; and at Early Termination (ET)/Study Completion (SC)(up to 24 months)

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: No formal statistical hypothesis tests were performed, and all analyses were considered descriptive.

| **End point values** | 1.5 mg/kg Emicizumab QW | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 193[14] | | | |
| Units: beats per minute | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (BL) - Value at Visit (n = 193) | 76.6 (± 11.6) | | | |
| Change from BL at Week 2 (n = 193) | 1.0 (± 9.9) | | | |
| Change from BL at Week 3 (n = 192) | 1.6 (± 11.6) | | | |
| Change from BL at Week 5 (n = 192) | -0.5 (± 11.3) | | | |
| Change from BL at Month 3 (n = 188) | -0.8 (± 10.4) | | | |
| Change from BL at Month 6 (n = 185) | -0.7 (± 11.6) | | | |
| Change from BL at Month 9 (n = 186) | -1.0 (± 11.3) | | | |
| Change from BL at Month 12 (n = 184) | -0.5 (± 12.2) | | | |
| Change from BL at Month 18 (n = 177) | -2.1 (± 12.7) | | | |
| Change from BL at ET/SC (n = 166) | -1.2 (± 11.9) | | | |

Notes:

[14] - Safety Population: received at least 1 dose of emicizumab.

## Statistical analyses

No statistical analyses for this end point

## Primary: Change from Baseline in Respiratory Rate at Specified Timepoints

| End point title | Change from Baseline in Respiratory Rate at Specified Timepoints[15] |
|---|---|

End point description:

Vital signs that were measured included body temperature, pulse and respiratory rates, systolic and diastolic blood pressure, and weight. On treatment days, measurement occurred prior to emicizumab administration.

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

End point timeframe:

Baseline, Weeks 2, 3, and 5; Months 3, 6, 9, 12, and 18; and at Early Termination (ET)/Study Completion (SC)(up to 24 months)

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: No formal statistical hypothesis tests were performed, and all analyses were considered descriptive.

| **End point values** | 1.5 mg/kg Emicizumab QW | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 193[16] | | | |
| Units: breaths per minute | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (BL) - Value at Visit (n = 192) | 17.0 (± 3.1) | | | |
| Change from BL at Week 2 (n = 192) | 0.2 (± 2.2) | | | |
| Change from BL at Week 3 (n = 191) | 0.0 (± 2.3) | | | |
| Change from BL at Week 5 (n = 189) | -0.1 (± 2.5) | | | |
| Change from BL at Month 3 (n = 187) | 0.3 (± 4.7) | | | |
| Change from BL at Month 6 (n = 180) | -0.1 (± 2.5) | | | |
| Change from BL at Month 9 (n = 184) | 0.0 (± 2.7) | | | |
| Change from BL at Month 12 (n = 180) | 0.3 (± 2.9) | | | |
| Change from BL at Month 18 (n = 173) | -0.4 (± 2.7) | | | |
| Change from BL at ET/SC (n = 160) | -0.7 (± 3.1) | | | |

Notes:

[16] - Safety Population: received at least 1 dose of emicizumab.

### Statistical analyses

No statistical analyses for this end point

## Primary: Change from Baseline in Body Weight at Specified Timepoints

| End point title | Change from Baseline in Body Weight at Specified |
|---|---|

End point description:

Vital signs that were measured included body temperature, pulse and respiratory rates, systolic and diastolic blood pressure, and weight. On treatment days, measurement occurred prior to emicizumab administration.

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

End point timeframe:

Baseline, Weeks 2, 3, and 5; Months 3, 6, 9, 12, and 18; and at Early Termination/Study Completion (up to 24 months)

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: No formal statistical hypothesis tests were performed, and all analyses were considered descriptive.

| **End point values** | 1.5 mg/kg Emicizumab QW | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 193[18] | | | |
| Units: kilograms (kg) | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (BL) - Value at Visit (n = 193) | 69.55 (± 16.60) | | | |

| | | | | |
|---|---|---|---|---|
| Change from BL at Week 2 (n = 193) | 0.14 (± 1.06) | | | |
| Change from BL at Week 3 (n = 192) | 0.34 (± 1.18) | | | |
| Change from BL at Week 5 (n = 192) | 0.52 (± 1.56) | | | |
| Change from BL at Month 3 (n = 188) | 0.98 (± 2.44) | | | |
| Change from BL at Month 6 (n = 186) | 1.11 (± 3.20) | | | |
| Change from BL at Month 9 (n = 186) | 1.61 (± 4.08) | | | |
| Change from BL at Month 12 (n = 184) | 1.85 (± 4.88) | | | |
| Change from BL at Month 18 (n = 177) | 2.58 (± 5.56) | | | |
| Change from BL at ET/SC (n = 165) | 3.15 (± 6.78) | | | |

Notes:

[18] - Safety Population: received at least 1 dose of emicizumab.

### Statistical analyses

No statistical analyses for this end point

## Secondary: Model-Based Annualized Bleed Rates (ABR) for Treated Bleeds, All Bleeds, Treated Joint Bleeds, Treated Target Joint Bleeds, and Treated Spontaneous Bleeds

| | |
|---|---|
| End point title | Model-Based Annualized Bleed Rates (ABR) for Treated Bleeds, All Bleeds, Treated Joint Bleeds, Treated Target Joint Bleeds, and Treated Spontaneous Bleeds |

End point description:

The number of bleeds over the efficacy period was analyzed as an ABR using a negative binomial regression model. Treated bleeds: bleeds followed by a hemophilia medication reported to be a "Treatment for bleed". All bleeds: included both treated and non-treated bleeds. Treated joint bleeds: treated bleeds where bleed type was "joint bleed" accompanied by at least one of following symptoms: "increased swelling or warmth of the skin over the joint", "increasing pain" or "decreased range of motion or difficulty using the joint compared with baseline". Treated target joint bleeds: treated joint bleeds that occurred in a target joint, defined as a joint in which ≥3 treated joint bleeds occurred during the 24 weeks prior to study entry. Treated spontaneous bleeds: treated bleeds with no other known contributing factor such as trauma or procedure/surgery. For all bleed types, bleeds due to surgery/procedure were excluded. Bleeds occurring after dose up-titration have been excluded.

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

End point timeframe:

From first dose of emicizumab until dose up-titration or withdrawal from treatment (median [min-max] efficacy period: 103.14 [1.1-108.3] weeks)

| **End point values** | 1.5 mg/kg Emicizumab QW | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 195[19] | | | |
| Units: bleeds per year | | | | |
| number (confidence interval 95%) | | | | |
| Treated Bleeds | 0.5 (0.27 to 0.89) | | | |
| All Bleeds | 1.1 (0.80 to 1.47) | | | |
| Treated Joint Bleeds | 0.4 (0.15 to 0.86) | | | |
| Treated Target Joint Bleeds | 0.2 (0.07 to 0.68) | | | |

| | | | | |
|---|---|---|---|---|
| Treated Spontaneous Bleeds | 0.3 (0.15 to 0.73) | | | |

Notes:

[19] - ITT Population: all enrolled participants.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Mean Calculated Annualized Bleed Rates (ABR) for Treated Bleeds, All Bleeds, Treated Joint Bleeds, Treated Target Joint Bleeds, and Treated Spontaneous Bleeds

| | |
|---|---|
| End point title | Mean Calculated Annualized Bleed Rates (ABR) for Treated Bleeds, All Bleeds, Treated Joint Bleeds, Treated Target Joint Bleeds, and Treated Spontaneous Bleeds |

End point description:

The number of bleeds over the efficacy period was calculated as: ABR = (number of bleeds/number of days during the efficacy period) x 365.25. Treated bleeds: bleeds followed by a hemophilia medication reported to be a "Treatment for bleed". All bleeds: included both treated and non-treated bleeds. Treated joint bleeds: treated bleeds where bleed type was "joint bleed" accompanied by at least one of following symptoms: "increased swelling or warmth of the skin over the joint", "increasing pain" or "decreased range of motion or difficulty using the joint compared with baseline". Treated target joint bleeds: treated joint bleeds that occurred in a target joint, defined as a joint in which ≥3 treated joint bleeds occurred during the 24 weeks prior to study entry. Treated spontaneous bleeds: treated bleeds with no other known contributing factor such as trauma or procedure/surgery. For all types, bleeds due to surgery/procedure and bleeds occurring after dose up-titration were excluded.

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

End point timeframe:

From first dose of emicizumab until dose up-titration or withdrawal from treatment (median [min-max] efficacy period: 103.14 [1.1-108.3] weeks)

| **End point values** | 1.5 mg/kg Emicizumab QW | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 195[20] | | | |
| Units: bleeds per year | | | | |
| arithmetic mean (confidence interval 95%) | | | | |
| Treated Bleeds | 0.6 (0.00 to 4.85) | | | |
| All Bleeds | 1.3 (0.06 to 6.02) | | | |
| Treated Joint Bleeds | 0.4 (0.00 to 4.55) | | | |
| Treated Target Joint Bleeds | 0.3 (0.00 to 4.28) | | | |
| Treated Spontaneous Bleeds | 0.4 (0.00 to 4.49) | | | |

Notes:

[20] - ITT Population: all enrolled participants.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Median Calculated Annualized Bleed Rates (ABR) for Treated Bleeds, All Bleeds, Treated Joint Bleeds, Treated Target Joint Bleeds, and Treated Spontaneous Bleeds

| End point title | Median Calculated Annualized Bleed Rates (ABR) for Treated Bleeds, All Bleeds, Treated Joint Bleeds, Treated Target Joint Bleeds, and Treated Spontaneous Bleeds |
|---|---|

End point description:

The number of bleeds over the efficacy period was calculated as: ABR = (number of bleeds/number of days during the efficacy period) x 365.25. Treated bleeds: bleeds followed by a hemophilia medication reported to be a "Treatment for bleed". All bleeds: included both treated and non-treated bleeds. Treated joint bleeds: treated bleeds where bleed type was "joint bleed" accompanied by at least one of following symptoms: "increased swelling or warmth of the skin over the joint", "increasing pain" or "decreased range of motion or difficulty using the joint compared with baseline". Treated target joint bleeds: treated joint bleeds that occurred in a target joint, defined as a joint in which ≥3 treated joint bleeds occurred during the 24 weeks prior to study entry. Treated spontaneous bleeds: treated bleeds with no other known contributing factor such as trauma or procedure/surgery. For all types, bleeds due to surgery/procedure and bleeds occurring after dose up-titration were excluded.

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

End point timeframe:

From first dose of emicizumab until dose up-titration or withdrawal from treatment (median [min-max] efficacy period: 103.14 [1.1-108.3] weeks)

| **End point values** | 1.5 mg/kg Emicizumab QW | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 195[21] | | | |
| Units: bleeds per year | | | | |
| median (inter-quartile range (Q1-Q3)) | | | | |
| Treated Bleeds | 0.0 (0.00 to 0.00) | | | |
| All Bleeds | 0.0 (0.00 to 1.01) | | | |
| Treated Joint Bleeds | 0.0 (0.00 to 0.00) | | | |
| Treated Target Joint Bleeds | 0.0 (0.00 to 0.00) | | | |
| Treated Spontaneous Bleeds | 0.0 (0.00 to 0.00) | | | |

Notes:

[21] - ITT Population: all enrolled participants.

### Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Participants by the Categorized Number of Bleeds for Treated Bleeds

| End point title | Percentage of Participants by the Categorized Number of Bleeds for Treated Bleeds |
|---|---|

End point description:

Treated bleeds: bleeds followed by a hemophilia medication reported to be a "Treatment for bleed". Bleeds due to surgery/procedure were excluded. The 72-hour rule was implemented: two bleeds of the

same type and at the same anatomical location are counted as one bleed if the second bleed occurs within 72 hours from the last treatment for the first bleed. Included data before up-titration only, for participants whose dose was up-titrated.

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

End point timeframe:

From first dose of emicizumab until dose up-titration or withdrawal from treatment (median [min-max] efficacy period: 103.14 [1.1-108.3] weeks)

| **End point values** | 1.5 mg/kg Emicizumab QW | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 195[22] | | | |
| Units: Percentage of participants | | | | |
| number (confidence interval 95%) | | | | |
| 0 Bleeds | 82.6 (76.5 to 87.6) | | | |
| 1-3 Bleeds | 12.3 (8.0 to 17.8) | | | |
| 4-10 Bleeds | 4.1 (1.8 to 7.9) | | | |
| >10 Bleeds | 1.0 (0.1 to 3.7) | | | |

Notes:

[22] - ITT Population: all enrolled participants.

### Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Participants by the Categorized Number of Bleeds for All Bleeds

| End point title | Percentage of Participants by the Categorized Number of Bleeds for All Bleeds |
|---|---|

End point description:

All bleeds: included both treated and non-treated bleeds. Bleeds due to surgery/procedure were excluded. The 72-hour rule was implemented: two bleeds of the same type and at the same anatomical location are counted as one bleed if the second bleed occurs within 72 hours from the last treatment for the first bleed. Included data before up-titration only, for participants whose dose was up-titrated.

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

End point timeframe:

From first dose of emicizumab until dose up-titration or withdrawal from treatment (median [min-max] efficacy period: 103.14 [1.1-108.3] weeks)

| **End point values** | 1.5 mg/kg Emicizumab QW | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 195[23] | | | |
| Units: Percentage of participants | | | | |
| number (confidence interval 95%) | | | | |

| | | | | |
|---|---|---|---|---|
| 0 Bleeds | 54.9 (47.6 to 62.0) | | | |
| 1-3 Bleeds | 30.3 (23.9 to 37.2) | | | |
| 4-10 Bleeds | 12.3 (8.0 to 17.8) | | | |
| >10 Bleeds | 2.6 (0.8 to 5.9) | | | |

Notes:

[23] - ITT Population: all enrolled participants.

### Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Participants by the Categorized Number of Bleeds for Treated Spontaneous Bleeds

| End point title | Percentage of Participants by the Categorized Number of Bleeds for Treated Spontaneous Bleeds |
|---|---|

End point description:

Treated spontaneous bleeds: treated bleeds with no other known contributing factor such as trauma or procedure/surgery. Bleeds due to surgery/procedure were excluded. The 72-hour rule was implemented: two bleeds of the same type and at the same anatomical location are counted as one bleed if the second bleed occurs within 72 hours from the last treatment for the first bleed. Included data before up-titration only, for participants whose dose was up-titrated.

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

End point timeframe:

From first dose of emicizumab until dose up-titration or withdrawal from treatment (median [min-max] efficacy period: 103.14 [1.1-108.3] weeks)

| End point values | 1.5 mg/kg Emicizumab QW | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 195[24] | | | |
| Units: Percentage of participants | | | | |
| number (confidence interval 95%) | | | | |
| 0 Bleeds | 89.2 (84.0 to 93.2) | | | |
| 1-3 Bleeds | 8.7 (5.2 to 13.6) | | | |
| 4-10 Bleeds | 1.5 (0.3 to 4.4) | | | |
| >10 Bleeds | 0.5 (0.0 to 2.8) | | | |

Notes:

[24] - ITT Population: all enrolled participants.

### Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Participants by the Categorized Calculated Annualized Bleed Rates (ABR) for Treated Bleeds

| End point title | Percentage of Participants by the Categorized Calculated |
|---|---|

| | |
|---|---|
| | Annualized Bleed Rates (ABR) for Treated Bleeds |

End point description:

The number of bleeds over the efficacy period was calculated as an ABR for each participant using the following formula: ABR = (number of bleeds/number of days during the efficacy period) x 365.25. Treated bleeds: bleeds followed by a hemophilia medication reported to be a "Treatment for bleed". Bleeds due to surgery/procedure were excluded. The 72-hour rule was implemented: two bleeds of the same type and at the same anatomical location are counted as one bleed if the second bleed occurs within 72 hours from the last treatment for the first bleed. Included data before up-titration only, for participants whose dose was up-titrated.

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

End point timeframe:

From first dose of emicizumab until dose up-titration or withdrawal from treatment (median [min-max] efficacy period: 103.14 [1.1-108.3] weeks)

| **End point values** | 1.5 mg/kg Emicizumab QW | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 195[25] | | | |
| Units: Percentage of participants | | | | |
| number (confidence interval 95%) | | | | |
| ABR <1 | 90.3 (85.2 to 94.0) | | | |
| ABR 1-3.4 | 6.2 (3.2 to 10.5) | | | |
| ABR 3.5-10 | 2.6 (0.8 to 5.9) | | | |
| ABR >10 | 1.0 (0.1 to 3.7) | | | |

Notes:

[25] - ITT Population: all enrolled participants.

### Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Participants by the Categorized Calculated Annualized Bleed Rates (ABR) for All Bleeds

| | |
|---|---|
| End point title | Percentage of Participants by the Categorized Calculated Annualized Bleed Rates (ABR) for All Bleeds |

End point description:

The number of bleeds over the efficacy period was calculated as an ABR for each participant using the following formula: ABR = (number of bleeds/number of days during the efficacy period) x 365.25. All bleeds: included both treated and non-treated bleeds. Bleeds due to surgery/procedure were excluded. The 72-hour rule was implemented: two bleeds of the same type and at the same anatomical location are counted as one bleed if the second bleed occurs within 72 hours from the last treatment for the first bleed. Included data before up-titration only, for participants whose dose was up-titrated.

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

End point timeframe:

From first dose of emicizumab until dose up-titration or withdrawal from treatment (median [min-max] efficacy period: 103.14 [1.1-108.3] weeks)

| End point values | 1.5 mg/kg Emicizumab QW | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 195[26] | | | |
| Units: Percentage of participants | | | | |
| number (confidence interval 95%) | | | | |
| ABR <1 | 72.3 (65.5 to 78.5) | | | |
| ABR 1-3.4 | 20.5 (15.1 to 26.9) | | | |
| ABR 3.5-10 | 4.6 (2.1 to 8.6) | | | |
| ABR >10 | 2.6 (0.8 to 5.9) | | | |

Notes:

[26] - ITT Population: all enrolled participants.

### Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Participants by the Categorized Calculated Annualized Bleed Rates (ABR) for Treated Spontaneous Bleeds

| End point title | Percentage of Participants by the Categorized Calculated Annualized Bleed Rates (ABR) for Treated Spontaneous Bleeds |
|---|---|

End point description:

The number of bleeds over the efficacy period was calculated as an ABR for each participant using the following formula: ABR = (number of bleeds/number of days during the efficacy period) x 365.25. Treated spontaneous bleeds: treated bleeds with no other known contributing factor such as trauma or procedure/surgery. Bleeds due to surgery/procedure were excluded. The 72-hour rule was implemented: two bleeds of the same type and at the same anatomical location are counted as one bleed if the second bleed occurs within 72 hours from the last treatment for the first bleed. Included data before up-titration only, for participants whose dose was up-titrated.

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

End point timeframe:

From first dose of emicizumab until dose up-titration or withdrawal from treatment (median [min-max] efficacy period: 103.14 [1.1-108.3] weeks)

| End point values | 1.5 mg/kg Emicizumab QW | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 195[27] | | | |
| Units: Percentage of participants | | | | |
| number (confidence interval 95%) | | | | |
| ABR <1 | 95.4 (91.4 to 97.9) | | | |
| ABR 1-3.4 | 2.6 (0.8 to 5.9) | | | |
| ABR 3.5-10 | 1.0 (0.1 to 3.7) | | | |
| ABR >10 | 1.0 (0.1 to 3.7) | | | |

Notes:

[27] - ITT Population: all enrolled participants.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change From Baseline in the Hemophilia Adult Quality of Life (Haem-A-QoL) Questionnaire Total Score at Specified Timepoints, Adult Participants

| End point title | Change From Baseline in the Hemophilia Adult Quality of Life (Haem-A-QoL) Questionnaire Total Score at Specified Timepoints, Adult Participants |
|---|---|

End point description:

The Haem-A-QoL questionnaire was designed for adult participants (greater than or equal to 18 years old) with hemophilia. It consists of 46 items comprising 10 domains: physical health, treatment, work and school, dealing with hemophilia, feelings, familly planning, future, partnerships and sexuality, sports and leisure, and view of yourself. Items are rated by participants with one of five response options: never, seldom, sometimes, often, and always; although, for some items there is also a 'not applicable' option. The Total Score is based on the scores for each domain and ranges from 0 to 100, with lower scores reflective of better quality of life.

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

End point timeframe:

Baseline (Week 1), 3, 6, 12, and 18 months, and at Early Termination (ET) or Study Completion (SC)(up to 24 months)

| **End point values** | 1.5 mg/kg Emicizumab QW | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 155[28] | | | |
| Units: score on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (BL) - Value at Visit (n = 150) | 41.09 (± 16.15) | | | |
| Change from BL at Month 3 (n = 144) | -17.39 (± 12.86) | | | |
| Change from BL at Month 6 (n = 141) | -16.40 (± 14.58) | | | |
| Change from BL at Month 12 (n = 140) | -17.44 (± 14.16) | | | |
| Change from BL at Month 18 (n = 132) | -16.27 (± 15.39) | | | |
| Change from BL at ET/SC (n = 70) | -14.13 (± 13.70) | | | |

Notes:

[28] - Adult participants with a baseline value and a post-baseline value at a given timepoint.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Participants with an Improvement from Baseline Greater Than the Responder Threshold for the Hemophilia Adult Quality of Life (Haem-A-QoL) Questionnaire Total Score at Specified Timepoints

| End point title | Percentage of Participants with an Improvement from Baseline Greater Than the Responder Threshold for the Hemophilia Adult Quality of Life (Haem-A-QoL) Questionnaire Total Score at Specified Timepoints |
|---|---|

End point description:

The Haem-A-QoL questionnaire was designed for adult participants (greater than or equal to 18 years old) with hemophilia. It consists of 46 items comprising 10 domains: physical health, treatment, work and school, dealing with hemophilia, feelings, famillly planning, future, partnerships and sexuality, sports and leisure, and view of yourself. Items are rated by participants with one of five response options: never, seldom, sometimes, often, and always; although, for some items there is also a 'not applicable' option. The Total Score is based on the scores for each domain and ranges from 0 to 100, with lower scores reflective of better quality of life. An improvement larger than the responder threshold was defined as a decrease from baseline of at least 7 points in the Haem-A-QoL Total score.

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

End point timeframe:

At 3, 6, 12, and 18 months

| **End point values** | 1.5 mg/kg Emicizumab QW | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 155[29] | | | |
| Units: Percentage of participants | | | | |
| number (not applicable) | | | | |
| Month 3 (n = 147) | 78.2 | | | |
| Month 6 (n = 145) | 72.4 | | | |
| Month 12 (n = 144) | 70.8 | | | |
| Month 18 (n = 136) | 69.9 | | | |

Notes:

[29] - Adult participants with a post-baseline value at a given timepoint.

### Statistical analyses

No statistical analyses for this end point

## Secondary: Change From Baseline in the Hemophilia Adult Quality of Life (Haem-A-QoL) Questionnaire Physical Health Domain Score at Specified Timepoints, Adult Participants

| End point title | Change From Baseline in the Hemophilia Adult Quality of Life (Haem-A-QoL) Questionnaire Physical Health Domain Score at Specified Timepoints, Adult Participants |
|---|---|

End point description:

The Haem-A-QoL questionnaire was designed for adult participants (greater than or equal to 18 years old) with hemophilia. It consists of 46 items comprising 10 domains: physical health, treatment, work and school, dealing with hemophilia, feelings, famillly planning, future, partnerships and sexuality, sports and leisure, and view of yourself. Items are rated by participants with one of five response options: never, seldom, sometimes, often, and always; although, for some items there is also a 'not applicable' option. Scale scores for each domain range from 0 to 100, with lower scores reflective of better quality of life.

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

End point timeframe:

Baseline (Week 1), 3, 6, 12, and 18 months, and at Early Termination (ET) or Study Completion (SC)(up to 24 months)

| End point values | 1.5 mg/kg Emicizumab QW | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 155[30] | | | |
| Units: score on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (BL) - Value at Visit (n = 150) | 51.13 (± 23.02) | | | |
| Change from BL at Month 3 (n = 144) | -27.36 (± 20.70) | | | |
| Change from BL at Month 6 (n = 141) | -26.10 (± 23.12) | | | |
| Change from BL at Month 12 (n = 140) | -25.21 (± 23.31) | | | |
| Change from BL at Month 18 (n = 132) | -23.14 (± 24.51) | | | |
| Change from BL at ET/SC (n = 70) | -23.29 (± 25.16) | | | |

Notes:

[30] - Adult participants with a baseline value and a post-baseline value at a given timepoint.

### Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Participants with an Improvement from Baseline Greater Than the Responder Threshold for the Hemophilia Adult Quality of Life (Haem-A-QoL) Questionnaire Physical Health Domain Score at Specified Timepoints

| End point title | Percentage of Participants with an Improvement from Baseline Greater Than the Responder Threshold for the Hemophilia Adult Quality of Life (Haem-A-QoL) Questionnaire Physical Health Domain Score at Specified Timepoints |
|---|---|

End point description:

The Haem-A-QoL questionnaire was designed for adult participants (greater than or equal to 18 years old) with hemophilia. It consists of 46 items comprising 10 domains: physical health, treatment, work and school, dealing with hemophilia, feelings, familly planning, future, partnerships and sexuality, sports and leisure, and view of yourself. Items are rated by participants with one of five response options: never, seldom, sometimes, often, and always; although, for some items there is also a 'not applicable' option. Scale scores for each domain range from 0 to 100, with lower scores reflective of better quality of life. An improvement larger than the responder threshold was defined as a decrease from baseline of at least 10 points in the Haem-A-QoL Physical Health domain score.

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

End point timeframe:

At 3, 6, 12, and 18 months

| End point values | 1.5 mg/kg Emicizumab QW | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 155[31] | | | |
| Units: Percentage of participants | | | | |
| number (not applicable) | | | | |
| Month 3 (n = 147) | 79.6 | | | |
| Month 6 (n = 145) | 74.5 | | | |

| | | | | |
|---|---|---|---|---|
| Month 12 (n = 144) | 72.9 | | | |
| Month 18 (n = 136) | 71.3 | | | |

Notes:

[31] - Adult participants with a post-baseline value at a given timepoint.

### Statistical analyses

No statistical analyses for this end point

## Secondary: Change From Baseline in the Hemophilia Adult Quality of Life (Haem-A-QoL) Questionnaire Treatment Domain Score at Specified Timepoints, Adult Participants

| | |
|---|---|
| End point title | Change From Baseline in the Hemophilia Adult Quality of Life (Haem-A-QoL) Questionnaire Treatment Domain Score at Specified Timepoints, Adult Participants |

End point description:

The Haem-A-QoL questionnaire was designed for adult participants (greater than or equal to 18 years old) with hemophilia. It consists of 46 items comprising 10 domains: physical health, treatment, work and school, dealing with hemophilia, feelings, familly planning, future, partnerships and sexuality, sports and leisure, and view of yourself. Items are rated by participants with one of five response options: never, seldom, sometimes, often, and always; although, for some items there is also a 'not applicable' option. Scale scores for each domain range from 0 to 100, with lower scores reflective of better quality of life.

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

End point timeframe:

Baseline (Week 1), 3, 6, 12, and 18 months, and at Early Termination (ET) or Study Completion (SC)(up to 24 months)

| **End point values** | 1.5 mg/kg Emicizumab QW | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 155[32] | | | |
| Units: score on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (BL) - Value at Visit (n = 150) | 39.40 (± 19.89) | | | |
| Change from BL at Month 3 (n = 144) | -23.44 (± 22.07) | | | |
| Change from BL at Month 6 (n = 141) | -21.01 (± 23.74) | | | |
| Change from BL at Month 12 (n = 140) | -22.21 (± 22.57) | | | |
| Change from BL at Month 18 (n = 132) | -20.34 (± 25.37) | | | |
| Change from BL at ET/SC (n = 70) | -21.16 (± 22.31) | | | |

Notes:

[32] - Adult participants with a baseline value and a post-baseline value at a given timepoint.

### Statistical analyses

No statistical analyses for this end point

## Secondary: Change From Baseline in the Hemophilia Adult Quality of Life (Haem-A-QoL) Questionnaire Work and School Domain Score at Specified Timepoints, Adult Participants

| End point title | Change From Baseline in the Hemophilia Adult Quality of Life (Haem-A-QoL) Questionnaire Work and School Domain Score at Specified Timepoints, Adult Participants |
|---|---|

End point description:

The Haem-A-QoL questionnaire was designed for adult participants (greater than or equal to 18 years old) with hemophilia. It consists of 46 items comprising 10 domains: physical health, treatment, work and school, dealing with hemophilia, feelings, familly planning, future, partnerships and sexuality, sports and leisure, and view of yourself. Items are rated by participants with one of five response options: never, seldom, sometimes, often, and always; although, for some items there is also a 'not applicable' option. Scale scores for each domain range from 0 to 100, with lower scores reflective of better quality of life.

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

End point timeframe:

Baseline (Week 1), 3, 6, 12, and 18 months, and at Early Termination (ET) or Study Completion (SC)(up to 24 months)

| **End point values** | 1.5 mg/kg Emicizumab QW | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 155[33] | | | |
| Units: score on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (BL) - Value at Visit (n = 125) | 39.23 (± 25.31) | | | |
| Change from BL at Month 3 (n = 114) | -21.40 (± 26.51) | | | |
| Change from BL at Month 6 (n = 106) | -21.91 (± 27.17) | | | |
| Change from BL at Month 12 (n = 106) | -22.43 (± 25.55) | | | |
| Change from BL at Month 18 (n = 101) | -21.43 (± 26.65) | | | |
| Change from BL at ET/SC (n = 51) | -18.83 (± 29.54) | | | |

Notes:

[33] - Adult participants with a baseline value and a post-baseline value at a given timepoint.

### Statistical analyses

No statistical analyses for this end point

## Secondary: Change From Baseline in the Hemophilia Adult Quality of Life (Haem-A-QoL) Questionnaire Dealing With Hemophilia Domain Score at Specified Timepoints, Adult Participants

| End point title | Change From Baseline in the Hemophilia Adult Quality of Life (Haem-A-QoL) Questionnaire Dealing With Hemophilia Domain Score at Specified Timepoints, Adult Participants |
|---|---|

End point description:

The Haem-A-QoL questionnaire was designed for adult participants (greater than or equal to 18 years old) with hemophilia. It consists of 46 items comprising 10 domains: physical health, treatment, work and school, dealing with hemophilia, feelings, famillly planning, future, partnerships and sexuality, sports and leisure, and view of yourself. Items are rated by participants with one of five response options: never, seldom, sometimes, often, and always; although, for some items there is also a 'not applicable' option. Scale scores for each domain range from 0 to 100, with lower scores reflective of better quality of life.

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

End point timeframe:

Baseline (Week 1), 3, 6, 12, and 18 months, and at Early Termination (ET) or Study Completion (SC)(up to 24 months)

| **End point values** | 1.5 mg/kg Emicizumab QW | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 155[34] | | | |
| Units: score on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (BL) - Value at Visit (n = 150) | 26.61 (± 19.76) | | | |
| Change from BL at Month 3 (n = 144) | 5.32 (± 30.06) | | | |
| Change from BL at Month 6 (n = 141) | 5.73 (± 28.14) | | | |
| Change from BL at Month 12 (n = 140) | 5.24 (± 29.18) | | | |
| Change from BL at Month 18 (n = 132) | 7.70 (± 29.75) | | | |
| Change from BL at ET/SC (n = 70) | 10.60 (± 33.42) | | | |

Notes:

[34] - Adult participants with a baseline value and a post-baseline value at a given timepoint.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change From Baseline in the Hemophilia Adult Quality of Life (Haem-A-QoL) Questionnaire Feelings Domain Score at Specified Timepoints, Adult Participants

| End point title | Change From Baseline in the Hemophilia Adult Quality of Life (Haem-A-QoL) Questionnaire Feelings Domain Score at Specified Timepoints, Adult Participants |
|---|---|

End point description:

The Haem-A-QoL questionnaire was designed for adult participants (greater than or equal to 18 years old) with hemophilia. It consists of 46 items comprising 10 domains: physical health, treatment, work and school, dealing with hemophilia, feelings, famillly planning, future, partnerships and sexuality, sports and leisure, and view of yourself. Items are rated by participants with one of five response options: never, seldom, sometimes, often, and always; although, for some items there is also a 'not applicable' option. Scale scores for each domain range from 0 to 100, with lower scores reflective of better quality of life.

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

End point timeframe:

Baseline (Week 1), 3, 6, 12, and 18 months, and at Early Termination (ET) or Study Completion (SC)(up to 24 months)

| End point values | 1.5 mg/kg Emicizumab QW | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 155[35] | | | |
| Units: score on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (BL) - Value at Visit (n = 150) | 36.25 (± 24.53) | | | |
| Change from BL at Month 3 (n = 144) | -21.22 (± 22.69) | | | |
| Change from BL at Month 6 (n = 141) | -20.88 (± 24.11) | | | |
| Change from BL at Month 12 (n = 140) | -22.37 (± 23.78) | | | |
| Change from BL at Month 18 (n = 132) | -19.55 (± 25.43) | | | |
| Change from BL at ET/SC (n = 70) | -17.95 (± 23.62) | | | |

Notes:

[35] - Adult participants with a baseline value and a post-baseline value at a given timepoint.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change From Baseline in the Hemophilia Adult Quality of Life (Haem-A-QoL) Questionnaire Family Planning Domain Score at Specified Timepoints, Adult Participants

| End point title | Change From Baseline in the Hemophilia Adult Quality of Life (Haem-A-QoL) Questionnaire Family Planning Domain Score at Specified Timepoints, Adult Participants |
|---|---|

End point description:

The Haem-A-QoL questionnaire was designed for adult participants (greater than or equal to 18 years old) with hemophilia. It consists of 46 items comprising 10 domains: physical health, treatment, work and school, dealing with hemophilia, feelings, familly planning, future, partnerships and sexuality, sports and leisure, and view of yourself. Items are rated by participants with one of five response options: never, seldom, sometimes, often, and always; although, for some items there is also a 'not applicable' option. Scale scores for each domain range from 0 to 100, with lower scores reflective of better quality of life.

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

End point timeframe:

Baseline (Week 1), 3, 6, 12, and 18 months, and at Early Termination (ET) or Study Completion (SC)(up to 24 months)

| End point values | 1.5 mg/kg Emicizumab QW | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 155[36] | | | |
| Units: score on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (BL) - Value at Visit (n = 91) | 25.64 (± 28.49) | | | |
| Change from BL at Month 3 (n = 67) | -8.64 (± 20.95) | | | |
| Change from BL at Month 6 (n = 68) | -9.07 (± 20.78) | | | |
| Change from BL at Month 12 (n = 65) | -10.83 (± 22.51) | | | |
| Change from BL at Month 18 (n = 58) | -12.39 (± 25.20) | | | |
| Change from BL at ET/SC (n = 26) | -9.38 (± 24.81) | | | |

Notes:

[36] - Adult participants with a baseline value and a post-baseline value at a given timepoint.

### Statistical analyses

No statistical analyses for this end point

## Secondary: Change From Baseline in the Hemophilia Adult Quality of Life (Haem-A-QoL) Questionnaire Future Domain Score at Specified Timepoints, Adult Participants

| End point title | Change From Baseline in the Hemophilia Adult Quality of Life (Haem-A-QoL) Questionnaire Future Domain Score at Specified Timepoints, Adult Participants |
|---|---|

End point description:

The Haem-A-QoL questionnaire was designed for adult participants (greater than or equal to 18 years old) with hemophilia. It consists of 46 items comprising 10 domains: physical health, treatment, work and school, dealing with hemophilia, feelings, familly planning, future, partnerships and sexuality, sports and leisure, and view of yourself. Items are rated by participants with one of five response options: never, seldom, sometimes, often, and always; although, for some items there is also a 'not applicable' option. Scale scores for each domain range from 0 to 100, with lower scores reflective of better quality of life.

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

End point timeframe:

Baseline (Week 1), 3, 6, 12, and 18 months, and at Early Termination (ET) or Study Completion (SC)(up to 24 months)

| End point values | 1.5 mg/kg Emicizumab QW | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 155[37] | | | |
| Units: score on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (BL) - Value at Visit (n = 150) | 42.70 (± 21.95) | | | |
| Change from BL at Month 3 (n = 144) | -15.56 (± 17.63) | | | |

| | | | | |
|---|---|---|---|---|
| Change from BL at Month 6 (n = 141) | -15.46 (± 17.83) | | | |
| Change from BL at Month 12 (n = 140) | -14.46 (± 20.10) | | | |
| Change from BL at Month 18 (n = 132) | -14.43 (± 19.83) | | | |
| Change from BL at ET/SC (n = 70) | -13.29 (± 19.56) | | | |

Notes:

[37] - Adult participants with a baseline value and a post-baseline value at a given timepoint.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change From Baseline in the Hemophilia Adult Quality of Life (Haem-A-QoL) Questionnaire Partnership and Sexuality Domain Score at Specified Timepoints, Adult Participants

| | |
|---|---|
| End point title | Change From Baseline in the Hemophilia Adult Quality of Life (Haem-A-QoL) Questionnaire Partnership and Sexuality Domain Score at Specified Timepoints, Adult Participants |

End point description:

The Haem-A-QoL questionnaire was designed for adult participants (greater than or equal to 18 years old) with hemophilia. It consists of 46 items comprising 10 domains: physical health, treatment, work and school, dealing with hemophilia, feelings, familly planning, future, partnerships and sexuality, sports and leisure, and view of yourself. Items are rated by participants with one of five response options: never, seldom, sometimes, often, and always; although, for some items there is also a 'not applicable' option. Scale scores for each domain range from 0 to 100, with lower scores reflective of better quality of life.

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

End point timeframe:

Baseline (Week 1), 3, 6, 12, and 18 months, and at Early Termination (ET) or Study Completion (SC)(up to 24 months)

| **End point values** | 1.5 mg/kg Emicizumab QW | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 155[38] | | | |
| Units: score on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (BL) - Value at Visit (n = 150) | 23.17 (± 28.65) | | | |
| Change from BL at Month 3 (n = 144) | -7.35 (± 25.25) | | | |
| Change from BL at Month 6 (n = 141) | -6.03 (± 22.76) | | | |
| Change from BL at Month 12 (n = 140) | -7.74 (± 27.60) | | | |
| Change from BL at Month 18 (n = 132) | -9.72 (± 28.16) | | | |
| Change from BL at ET/SC (n = 70) | -4.05 (± 21.32) | | | |

Notes:

[38] - Adult participants with a baseline value and a post-baseline value at a given timepoint.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change From Baseline in the Hemophilia Adult Quality of Life (Haem-A-QoL) Questionnaire Sports and Leisure Domain Score at Specified Timepoints, Adult Participants

| End point title | Change From Baseline in the Hemophilia Adult Quality of Life (Haem-A-QoL) Questionnaire Sports and Leisure Domain Score at Specified Timepoints, Adult Participants |
|---|---|

End point description:

The Haem-A-QoL questionnaire was designed for adult participants (greater than or equal to 18 years old) with hemophilia. It consists of 46 items comprising 10 domains: physical health, treatment, work and school, dealing with hemophilia, feelings, familly planning, future, partnerships and sexuality, sports and leisure, and view of yourself. Items are rated by participants with one of five response options: never, seldom, sometimes, often, and always; although, for some items there is also a 'not applicable' option. Scale scores for each domain range from 0 to 100, with lower scores reflective of better quality of life.

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

End point timeframe:

Baseline (Week 1), 3, 6, 12, and 18 months, and at Early Termination (ET) or Study Completion (SC)(up to 24 months)

| **End point values** | 1.5 mg/kg Emicizumab QW | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 155[39] | | | |
| Units: score on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (BL) - Value at Visit (n = 114) | 68.86 (± 21.24) | | | |
| Change from BL at Month 3 (n = 89) | -19.65 (± 23.67) | | | |
| Change from BL at Month 6 (n = 83) | -17.63 (± 25.86) | | | |
| Change from BL at Month 12 (n = 87) | -22.56 (± 22.17) | | | |
| Change from BL at Month 18 (n = 76) | -20.20 (± 25.86) | | | |
| Change from BL at ET/SC (n = 42) | -20.65 (± 28.65) | | | |

Notes:

[39] - Adult participants with a baseline value and a post-baseline value at a given timepoint.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change From Baseline in the Hemophilia Adult Quality of Life (Haem-A-QoL) Questionnaire View of Yourself Domain Score at Specified Timepoints, Adult Participants

| End point title | Change From Baseline in the Hemophilia Adult Quality of Life (Haem-A-QoL) Questionnaire View of Yourself Domain Score at Specified Timepoints, Adult Participants |
|---|---|

End point description:

The Haem-A-QoL questionnaire was designed for adult participants (greater than or equal to 18 years old) with hemophilia. It consists of 46 items comprising 10 domains: physical health, treatment, work and school, dealing with hemophilia, feelings, familly planning, future, partnerships and sexuality, sports and leisure, and view of yourself. Items are rated by participants with one of five response options: never, seldom, sometimes, often, and always; although, for some items there is also a 'not applicable' option. Scale scores for each domain range from 0 to 100, with lower scores reflective of better quality of life.

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

End point timeframe:

Baseline (Week 1), 3, 6, 12, and 18 months, and at Early Termination (ET) or Study Completion (SC)(up to 24 months)

| **End point values** | 1.5 mg/kg Emicizumab QW | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 155[40] | | | |
| Units: score on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (BL) - Value at Visit (n = 150) | 43.57 (± 22.05) | | | |
| Change from BL at Month 3 (n = 144) | -13.51 (± 20.63) | | | |
| Change from BL at Month 6 (n = 141) | -15.04 (± 21.19) | | | |
| Change from BL at Month 12 (n = 140) | -15.71 (± 19.88) | | | |
| Change from BL at Month 18 (n = 132) | -15.19 (± 21.88) | | | |
| Change from BL at ET/SC (n = 70) | -9.50 (± 20.70) | | | |

Notes:

[40] - Adult participants with a baseline value and a post-baseline value at a given timepoint.

### Statistical analyses

No statistical analyses for this end point

## Secondary: Change From Baseline in the Hemophilia Quality of Life Short Form (Haemo-QoL-SF) Questionnaire Total Score at Specified Timepoints, Adolescent Participants

| End point title | Change From Baseline in the Hemophilia Quality of Life Short Form (Haemo-QoL-SF) Questionnaire Total Score at Specified Timepoints, Adolescent Participants |
|---|---|

End point description:

The Haemo-QoL-SF was designed as a series of age-related questionnaires to measure health-related quality of life in children and adolescents (12-17 year olds) with hemophilia. This version contains 35 items and covers nine domains considered relevant for children's health-related quality of life: physical health, treatment, sports and school, dealing with hemophilia, feelings, family, friends, other people, and view of yourself. Items are rated by participants with one of five response options: never, seldom, sometimes, often, and always. The Total Score is derived from the scores for all domains and scale scores range from 0 to 100, with a lower score reflective of better health-related quality of life.

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

End point timeframe:

Baseline (Week 1), 3, 6, 12, and 18 months, and at Early Termination (ET) or Study Completion (SC)(up to 24 months)

| **End point values** | 1.5 mg/kg Emicizumab QW | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 40[41] | | | |
| Units: score on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (BL) - Value at Visit (n = 35) | 35.10 (± 12.42) | | | |
| Change from BL at Month 3 (n = 32) | -9.60 (± 12.51) | | | |
| Change from BL at Month 6 (n = 34) | -12.65 (± 12.72) | | | |
| Change from BL at Month 12 (n = 32) | -13.57 (± 13.20) | | | |
| Change from BL at Month 18 (n = 35) | -14.02 (± 11.83) | | | |
| Change from BL at ET/SC (n = 18) | -18.37 (± 17.53) | | | |

Notes:

[41] - Adolescent participants with a baseline value and a post-baseline value at a given timepoint.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Participants with an Improvement from Baseline Greater Than the Responder Threshold for the Hemophilia Quality of Life Short Form (Haemo-QoL-SF) Questionnaire Total Score at Specified Timepoints

| End point title | Percentage of Participants with an Improvement from Baseline Greater Than the Responder Threshold for the Hemophilia Quality of Life Short Form (Haemo-QoL-SF) Questionnaire Total Score at Specified Timepoints |
|---|---|

End point description:

The Haemo-QoL-SF was designed as a series of age-related questionnaires to measure health-related quality of life in children and adolescents (12-17 year olds) with hemophilia. This version contains 35 items and covers nine domains considered relevant for children's health-related quality of life: physical health, treatment, sports and school, dealing with hemophilia, feelings, family, friends, other people, and view of yourself. Items are rated by participants with one of five response options: never, seldom, sometimes, often, and always. The Total Score is derived from the scores for all domains and scale scores range from 0 to 100, with a lower score reflective of better health-related quality of life. An improvement larger than the responder threshold was defined as a decrease from baseline of at least 5 points in the Haemo-QoL-SF Total score.

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

End point timeframe:

At 3, 6, 12, and 18 months

| **End point values** | 1.5 mg/kg Emicizumab QW | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 40[42] | | | |
| Units: Percentage of participants | | | | |
| number (not applicable) | | | | |
| Month 3 (n = 36) | 63.9 | | | |
| Month 6 (n = 37) | 75.7 | | | |
| Month 12 (n = 36) | 75.0 | | | |
| Month 18 (n = 39) | 69.2 | | | |

Notes:

[42] - Adolescent participants with a post-baseline value at a given timepoint.

### Statistical analyses

No statistical analyses for this end point

## Secondary: Change From Baseline in the Hemophilia Quality of Life Short Form (Haemo-QoL-SF) Questionnaire Physical Health Domain Score at Specified Timepoints, Adolescent Participants

| End point title | Change From Baseline in the Hemophilia Quality of Life Short Form (Haemo-QoL-SF) Questionnaire Physical Health Domain Score at Specified Timepoints, Adolescent Participants |
|---|---|

End point description:

The Haemo-QoL-SF was designed as a series of age-related questionnaires to measure health-related quality of life in children and adolescents (12-17 year olds) with hemophilia. This version contains 35 items and covers nine domains considered relevant for children's health-related quality of life: physical health, treatment, sports and school, dealing with hemophilia, feelings, family, friends, other people, and view of yourself. Items are rated by participants with one of five response options: never, seldom, sometimes, often, and always. Scale scores range from 0 to 100, with a lower score reflective of better health-related quality of life.

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

End point timeframe:

Baseline (Week 1), 3, 6, 12, and 18 months, and at Early Termination (ET) or Study Completion (SC)(up to 24 months)

| **End point values** | 1.5 mg/kg Emicizumab QW | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 40[43] | | | |
| Units: score on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (BL) - Value at Visit (n = 35) | 42.14 (± 18.40) | | | |

| | | | | |
|---|---|---|---|---|
| Change from BL at Month 3 (n = 32) | -29.10 (± 20.12) | | | |
| Change from BL at Month 6 (n = 34) | -29.78 (± 17.55) | | | |
| Change from BL at Month 12 (n = 32) | -30.47 (± 20.74) | | | |
| Change from BL at Month 18 (n = 35) | -30.71 (± 18.83) | | | |
| Change from BL at ET/SC (n = 18) | -34.03 (± 25.66) | | | |

Notes:

[43] - Adolescent participants with a baseline value and a post-baseline value at a given timepoint.

### Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Participants with an Improvement from Baseline Greater Than the Responder Threshold for the Hemophilia Quality of Life Short Form (Haemo-QoL-SF) Questionnaire Physical Health Domain Score at Specified Timepoints

| | |
|---|---|
| End point title | Percentage of Participants with an Improvement from Baseline Greater Than the Responder Threshold for the Hemophilia Quality of Life Short Form (Haemo-QoL-SF) Questionnaire Physical Health Domain Score at Specified Timepoints |

End point description:

The Haemo-QoL-SF was designed as a series of age-related questionnaires to measure health-related quality of life in children and adolescents (12-17 year olds) with hemophilia. This version contains 35 items and covers nine domains considered relevant for children's health-related quality of life: physical health, treatment, sports and school, dealing with hemophilia, feelings, family, friends, other people, and view of yourself. Items are rated by participants with one of five response options: never, seldom, sometimes, often, and always. Scale scores range from 0 to 100, with a lower score reflective of better health-related quality of life. An improvement larger than the responder threshold was defined as a decrease from baseline of at least 10 points in the Haemo-QoL-SF Physical Health domain score.

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

End point timeframe:

At 3, 6, 12, and 18 months

| **End point values** | 1.5 mg/kg Emicizumab QW | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 40[44] | | | |
| Units: Percentage of participants | | | | |
| number (not applicable) | | | | |
| Month 3 (n = 36) | 77.8 | | | |
| Month 6 (n = 37) | 78.4 | | | |
| Month 12 (n = 36) | 75.0 | | | |
| Month 18 (n = 39) | 79.5 | | | |

Notes:

[44] - Adolescent participants with a post-baseline value at a given timepoint.

### Statistical analyses

No statistical analyses for this end point

## Secondary: Change From Baseline in the Hemophilia Quality of Life Short Form (Haemo-QoL-SF) Questionnaire Treatment Domain Score at Specified Timepoints, Adolescent Participants

| End point title | Change From Baseline in the Hemophilia Quality of Life Short Form (Haemo-QoL-SF) Questionnaire Treatment Domain Score at Specified Timepoints, Adolescent Participants |
|---|---|

End point description:

The Haemo-QoL-SF was designed as a series of age-related questionnaires to measure health-related quality of life in children and adolescents (12-17 year olds) with hemophilia. This version contains 35 items and covers nine domains considered relevant for children's health-related quality of life: physical health, treatment, sports and school, dealing with hemophilia, feelings, family, friends, other people, and view of yourself. Items are rated by participants with one of five response options: never, seldom, sometimes, often, and always. Scale scores range from 0 to 100, with a lower score reflective of better health-related quality of life.

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

End point timeframe:

Baseline (Week 1), 3, 6, 12, and 18 months, and at Early Termination (ET) or Study Completion (SC)(up to 24 months)

| **End point values** | 1.5 mg/kg Emicizumab QW | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 40[45] | | | |
| Units: score on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (BL) - Value at Visit (n = 35) | 31.61 (± 18.12) | | | |
| Change from BL at Month 3 (n = 32) | -9.38 (± 20.94) | | | |
| Change from BL at Month 6 (n = 34) | -8.64 (± 23.23) | | | |
| Change from BL at Month 12 (n = 32) | -10.74 (± 21.31) | | | |
| Change from BL at Month 18 (n = 35) | -12.68 (± 21.68) | | | |
| Change from BL at ET/SC (n = 18) | -20.83 (± 23.87) | | | |

Notes:

[45] - Adolescent participants with a baseline value and a post-baseline value at a given timepoint.

### Statistical analyses

No statistical analyses for this end point

## Secondary: Change From Baseline in the Hemophilia Quality of Life Short Form (Haemo-QoL-SF) Questionnaire Sports and School Domain Score at Specified Timepoints, Adolescent Participants

| End point title | Change From Baseline in the Hemophilia Quality of Life Short Form (Haemo-QoL-SF) Questionnaire Sports and School Domain Score at Specified Timepoints, Adolescent Participants |
|---|---|

End point description:

The Haemo-QoL-SF was designed as a series of age-related questionnaires to measure health-related quality of life in children and adolescents (12-17 year olds) with hemophilia. This version contains 35 items and covers nine domains considered relevant for children's health-related quality of life: physical health, treatment, sports and school, dealing with hemophilia, feelings, family, friends, other people, and view of yourself. Items are rated by participants with one of five response options: never, seldom, sometimes, often, and always. Scale scores range from 0 to 100, with a lower score reflective of better health-related quality of life.

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

End point timeframe:

Baseline (Week 1), 3, 6, 12, and 18 months, and at Early Termination (ET) or Study Completion (SC)(up to 24 months)

| **End point values** | 1.5 mg/kg Emicizumab QW | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 40[46] | | | |
| Units: score on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (BL) - Value at Visit (n = 35) | 62.32 (± 21.30) | | | |
| Change from BL at Month 3 (n = 32) | -15.82 (± 25.55) | | | |
| Change from BL at Month 6 (n = 34) | -20.04 (± 29.27) | | | |
| Change from BL at Month 12 (n = 32) | -22.07 (± 26.71) | | | |
| Change from BL at Month 18 (n = 35) | -28.21 (± 27.80) | | | |
| Change from BL at ET/SC (n = 18) | -23.61 (± 28.16) | | | |

Notes:

[46] - Adolescent participants with a baseline value and a post-baseline value at a given timepoint.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change From Baseline in the Hemophilia Quality of Life Short Form (Haemo-QoL-SF) Questionnaire Dealing With Hemophilia Domain Score at Specified Timepoints, Adolescent Participants

| End point title | Change From Baseline in the Hemophilia Quality of Life Short Form (Haemo-QoL-SF) Questionnaire Dealing With Hemophilia Domain Score at Specified Timepoints, Adolescent Participants |
|---|---|

End point description:

The Haemo-QoL-SF was designed as a series of age-related questionnaires to measure health-related quality of life in children and adolescents (12-17 year olds) with hemophilia. This version contains 35 items and covers nine domains considered relevant for children's health-related quality of life: physical health, treatment, sports and school, dealing with hemophilia, feelings, family, friends, other people, and view of yourself. Items are rated by participants with one of five response options: never, seldom, sometimes, often, and always. Scale scores range from 0 to 100, with a lower score reflective of better health-related quality of life.

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

End point timeframe:

Baseline (Week 1), 3, 6, 12, and 18 months, and at Early Termination (ET) or Study Completion (SC)(up to 24 months)

| End point values | 1.5 mg/kg Emicizumab QW | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 40[47] | | | |
| Units: score on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (BL) - Value at Visit (n = 35) | 24.11 (± 14.79) | | | |
| Change from BL at Month 3 (n = 32) | -7.23 (± 18.25) | | | |
| Change from BL at Month 6 (n = 34) | -7.72 (± 17.75) | | | |
| Change from BL at Month 12 (n = 32) | -10.35 (± 20.24) | | | |
| Change from BL at Month 18 (n = 35) | -3.39 (± 25.70) | | | |
| Change from BL at ET/SC (n = 18) | -12.50 (± 23.48) | | | |

Notes:

[47] - Adolescent participants with a baseline value and a post-baseline value at a given timepoint.

### Statistical analyses

No statistical analyses for this end point

## Secondary: Change From Baseline in the Hemophilia Quality of Life Short Form (Haemo-QoL-SF) Questionnaire Feelings Domain Score at Specified Timepoints, Adolescent Participants

| End point title | Change From Baseline in the Hemophilia Quality of Life Short Form (Haemo-QoL-SF) Questionnaire Feelings Domain Score at Specified Timepoints, Adolescent Participants |
|---|---|

End point description:

The Haemo-QoL-SF was designed as a series of age-related questionnaires to measure health-related quality of life in children and adolescents (12-17 year olds) with hemophilia. This version contains 35 items and covers nine domains considered relevant for children's health-related quality of life: physical health, treatment, sports and school, dealing with hemophilia, feelings, family, friends, other people, and view of yourself. Items are rated by participants with one of five response options: never, seldom, sometimes, often, and always. Scale scores range from 0 to 100, with a lower score reflective of better health-related quality of life.

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

End point timeframe:

Baseline (Week 1), 3, 6, 12, and 18 months, and at Early Termination (ET) or Study Completion (SC)(up to 24 months)

| End point values | 1.5 mg/kg Emicizumab QW | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 40[48] | | | |
| Units: score on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (BL) - Value at Visit (n = 35) | 26.43 (± 25.10) | | | |
| Change from BL at Month 3 (n = 32) | -9.57 (± 20.08) | | | |
| Change from BL at Month 6 (n = 34) | -16.36 (± 21.54) | | | |
| Change from BL at Month 12 (n = 32) | -13.09 (± 22.80) | | | |
| Change from BL at Month 18 (n = 35) | -15.18 (± 25.51) | | | |
| Change from BL at ET/SC (n = 18) | -23.96 (± 32.67) | | | |

Notes:

[48] - Adolescent participants with a baseline value and a post-baseline value at a given timepoint.

### Statistical analyses

No statistical analyses for this end point

## Secondary: Change From Baseline in the Hemophilia Quality of Life Short Form (Haemo-QoL-SF) Questionnaire Family Domain Score at Specified Timepoints, Adolescent Participants

| End point title | Change From Baseline in the Hemophilia Quality of Life Short Form (Haemo-QoL-SF) Questionnaire Family Domain Score at Specified Timepoints, Adolescent Participants |
|---|---|

End point description:

The Haemo-QoL-SF was designed as a series of age-related questionnaires to measure health-related quality of life in children and adolescents (12-17 year olds) with hemophilia. This version contains 35 items and covers nine domains considered relevant for children's health-related quality of life: physical health, treatment, sports and school, dealing with hemophilia, feelings, family, friends, other people, and view of yourself. Items are rated by participants with one of five response options: never, seldom, sometimes, often, and always. Scale scores range from 0 to 100, with a lower score reflective of better health-related quality of life.

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

End point timeframe:

Baseline (Week 1), 3, 6, 12, and 18 months, and at Early Termination (ET) or Study Completion (SC)(up to 24 months)

| End point values | 1.5 mg/kg Emicizumab QW | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 40[49] | | | |
| Units: score on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (BL) - Value at Visit (n = 35) | 46.07 (± 20.79) | | | |

| | | | | |
|---|---|---|---|---|
| Change from BL at Month 3 (n = 32) | -6.84 (± 15.66) | | | |
| Change from BL at Month 6 (n = 34) | -11.95 (± 20.84) | | | |
| Change from BL at Month 12 (n = 32) | -14.84 (± 23.32) | | | |
| Change from BL at Month 18 (n = 35) | -15.36 (± 21.67) | | | |
| Change from BL at ET/SC (n = 18) | -15.28 (± 19.08) | | | |

Notes:

[49] - Adolescent participants with a baseline value and a post-baseline value at a given timepoint.

### Statistical analyses

No statistical analyses for this end point

## Secondary: Change From Baseline in the Hemophilia Quality of Life Short Form (Haemo-QoL-SF) Questionnaire Friends Domain Score at Specified Timepoints, Adolescent Participants

| | |
|---|---|
| End point title | Change From Baseline in the Hemophilia Quality of Life Short Form (Haemo-QoL-SF) Questionnaire Friends Domain Score at Specified Timepoints, Adolescent Participants |

End point description:

The Haemo-QoL-SF was designed as a series of age-related questionnaires to measure health-related quality of life in children and adolescents (12-17 year olds) with hemophilia. This version contains 35 items and covers nine domains considered relevant for children's health-related quality of life: physical health, treatment, sports and school, dealing with hemophilia, feelings, family, friends, other people, and view of yourself. Items are rated by participants with one of five response options: never, seldom, sometimes, often, and always. Scale scores range from 0 to 100, with a lower score reflective of better health-related quality of life.

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

End point timeframe:

Baseline (Week 1), 3, 6, 12, and 18 months, and at Early Termination (ET) or Study Completion (SC)(up to 24 months)

| **End point values** | 1.5 mg/kg Emicizumab QW | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 40[50] | | | |
| Units: score on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (BL) - Value at Visit (n = 35) | 35.95 (± 26.02) | | | |
| Change from BL at Month 3 (n = 32) | -0.52 (± 24.95) | | | |
| Change from BL at Month 6 (n = 34) | -3.19 (± 28.13) | | | |
| Change from BL at Month 12 (n = 32) | -5.47 (± 27.57) | | | |
| Change from BL at Month 18 (n = 35) | -5.95 (± 36.41) | | | |
| Change from BL at ET/SC (n = 18) | -7.41 (± 31.56) | | | |

Notes:

[50] - Adolescent participants with a baseline value and a post-baseline value at a given timepoint.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change From Baseline in the Hemophilia Quality of Life Short Form (Haemo-QoL-SF) Questionnaire Other People Domain Score at Specified Timepoints, Adolescent Participants

| End point title | Change From Baseline in the Hemophilia Quality of Life Short Form (Haemo-QoL-SF) Questionnaire Other People Domain Score at Specified Timepoints, Adolescent Participants |
|---|---|

End point description:

The Haemo-QoL-SF was designed as a series of age-related questionnaires to measure health-related quality of life in children and adolescents (12-17 year olds) with hemophilia. This version contains 35 items and covers nine domains considered relevant for children's health-related quality of life: physical health, treatment, sports and school, dealing with hemophilia, feelings, family, friends, other people, and view of yourself. Items are rated by participants with one of five response options: never, seldom, sometimes, often, and always. Scale scores range from 0 to 100, with a lower score reflective of better health-related quality of life.

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

End point timeframe:

Baseline (Week 1), 3, 6, 12, and 18 months, and at Early Termination (ET) or Study Completion (SC)(up to 24 months)

| **End point values** | 1.5 mg/kg Emicizumab QW | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 40[51] | | | |
| Units: score on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (BL) - Value at Visit (n = 35) | 21.43 (± 17.50) | | | |
| Change from BL at Month 3 (n = 32) | -2.93 (± 18.72) | | | |
| Change from BL at Month 6 (n = 34) | -5.51 (± 19.08) | | | |
| Change from BL at Month 12 (n = 32) | -8.01 (± 18.53) | | | |
| Change from BL at Month 18 (n = 35) | -6.79 (± 17.51) | | | |
| Change from BL at ET/SC (n = 18) | -11.81 (± 18.55) | | | |

Notes:

[51] - Adolescent participants with a baseline value and a post-baseline value at a given timepoint.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change From Baseline in the Hemophilia Quality of Life Short Form (Haemo-QoL-SF) Questionnaire View of Yourself Domain Score at Specified Timepoints, Adolescent Participants

| End point title | Change From Baseline in the Hemophilia Quality of Life Short Form (Haemo-QoL-SF) Questionnaire View of Yourself Domain Score at Specified Timepoints, Adolescent Participants |
|---|---|

End point description:

The Haemo-QoL-SF was designed as a series of age-related questionnaires to measure health-related quality of life in children and adolescents (12-17 year olds) with hemophilia. This version contains 35 items and covers nine domains considered relevant for children's health-related quality of life: physical health, treatment, sports and school, dealing with hemophilia, feelings, family, friends, other people, and view of yourself. Items are rated by participants with one of five response options: never, seldom, sometimes, often, and always. Scale scores range from 0 to 100, with a lower score reflective of better health-related quality of life.

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

End point timeframe:

Baseline (Week 1), 3, 6, 12, and 18 months, and at Early Termination (ET) or Study Completion (SC)(up to 24 months)

| **End point values** | 1.5 mg/kg Emicizumab QW | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 40[52] | | | |
| Units: score on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (BL) - Value at Visit (n = 35) | 26.07 (± 22.04) | | | |
| Change from BL at Month 3 (n = 32) | -2.73 (± 26.03) | | | |
| Change from BL at Month 6 (n = 34) | -8.27 (± 23.27) | | | |
| Change from BL at Month 12 (n = 32) | -5.08 (± 24.82) | | | |
| Change from BL at Month 18 (n = 35) | -5.89 (± 21.54) | | | |
| Change from BL at ET/SC (n = 18) | -13.19 (± 26.59) | | | |

Notes:

[52] - Adolescent participants with a baseline value and a post-baseline value at a given timepoint.

### Statistical analyses

No statistical analyses for this end point

## Secondary: Change From Baseline in the EuroQoL Five-Dimension-Five Levels Questionnaire (EQ-5D-5L) Index Utility Score at Specified Timepoints

| End point title | Change From Baseline in the EuroQoL Five-Dimension-Five Levels Questionnaire (EQ-5D-5L) Index Utility Score at Specified Timepoints |
|---|---|

End point description:

The EQ-5D-5L is a generic, self-reported, preference-based health utility measure that consists of six

questions and is used to assess health status and inform pharmacoeconomic evaluations. The index utility score is based on the participant's assessment of their health on five scales: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. It ranges from -0.224 to 1, with 0 corresponding to death and 1 corresponding to full health; negative values correspond to health states worse than death. Higher scores indicate better quality of life.

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

End point timeframe:

Baseline (Week 1), 3, 6, 12, and 18 months, and at Early Termination (ET) or Study Completion (SC)(up to 24 months)

| **End point values** | 1.5 mg/kg Emicizumab QW | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 195[53] | | | |
| Units: score on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (BL) - Value at Visit (n = 188) | 0.67 (± 0.23) | | | |
| Change from BL at Month 3 (n = 182) | 0.08 (± 0.18) | | | |
| Change from BL at Month 6 (n = 178) | 0.11 (± 0.18) | | | |
| Change from BL at Month 12 (n = 176) | 0.09 (± 0.19) | | | |
| Change from BL at Month 18 (n = 170) | 0.07 (± 0.21) | | | |
| Change from BL at ET/SC (n = 89) | 0.10 (± 0.22) | | | |

Notes:

[53] - All participants with a baseline value and a post-baseline value at a given timepoint.

### Statistical analyses

No statistical analyses for this end point

## Secondary: Change From Baseline in the EuroQoL Five-Dimension-Five Levels Questionnaire (EQ-5D-5L) Quality-of-Life Visual Analogue Scale (VAS) Score at Specified Timepoints

| End point title | Change From Baseline in the EuroQoL Five-Dimension-Five Levels Questionnaire (EQ-5D-5L) Quality-of-Life Visual Analogue Scale (VAS) Score at Specified Timepoints |
|---|---|

End point description:

The EQ-5D-5L is a generic, self-reported, preference-based health utility measure that consists of six questions and is used to assess health status and inform pharmacoeconomic evaluations. The visual analogue scale (VAS) ranges from 0 to 100 points, on which the participant self-assesses their current health status; 0 being the worst health you can imagine and 100 being the best health you can imagine. Higher scores are reflective of better health.

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

End point timeframe:

Baseline (Week 1), 3, 6, 12, and 18 months, and at Early Termination or Study Completion (up to 24 months)

| End point values | 1.5 mg/kg Emicizumab QW | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 195[54] | | | |
| Units: score on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (BL) - Value at Visit (n = 188) | 71.01 (± 19.41) | | | |
| Change from BL at Month 3 (n = 182) | 8.02 (± 18.70) | | | |
| Change from BL at Month 6 (n = 177) | 10.27 (± 17.24) | | | |
| Change from BL at Month 12 (n = 176) | 10.69 (± 18.18) | | | |
| Change from BL at Month 18 (n = 170) | 9.49 (± 21.08) | | | |
| Change from BL at ET/SC (n = 89) | 14.52 (± 17.91) | | | |

Notes:

[54] - All participants with a baseline value and a post-baseline value at a given timepoint.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Participants who Preferred the New Emicizumab Treatment or the Old Hemophilia Treatment, or Without Treatment Preference, as Assessed by the EmiPref Questionnaire

| End point title | Percentage of Participants who Preferred the New Emicizumab Treatment or the Old Hemophilia Treatment, or Without Treatment Preference, as Assessed by the EmiPref Questionnaire |
|---|---|

End point description:

The EmiPref questionnaire asked participants to specify the treatment they would prefer to continue to receive after receiving treatment with their previous episodic or prophylactic regimen and subcutaneous (SC) emicizumab, or if they had no preference. The 95% confidence intervals were calculated for one sample binomial using the Pearson-Clopper method.

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

End point timeframe:

Month 3

| End point values | 1.5 mg/kg Emicizumab QW | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 179[55] | | | |
| Units: Percentage of participants | | | | |
| number (confidence interval 95%) | | | | |
| Prefer the New Study Drug Treatment (Emicizumab) | 96.6 (92.85 to 98.76) | | | |
| Prefer my Old Hemophilia Treatment | 0.6 (0.01 to 3.07) | | | |
| Have no Preference | 2.8 (0.91 to 6.40) | | | |

Notes:

[55] - All participants who responded to this questionnaire.

### Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Participants with Anti-Drug Antibodies (ADAs) Against Emicizumab at Anytime Post-Baseline

| End point title | Number of Participants with Anti-Drug Antibodies (ADAs) Against Emicizumab at Anytime Post-Baseline |
|---|---|

End point description:

'Total ADA Negative' is the sum of all subjects who tested negative for ADA in the 2 following categories: 'ADA Negative', those who are pre-dose ADA negative or are missing pre-dose ADA data and who have all negative post-dose ADA results; and 'ADA Negative (Treatment Unaffected)', a subset who are pre-dose ADA positive but do not have a ≥4-fold increase in post-dose ADA levels compared to baseline measurement. 'Total ADA Positive' is the sum of all subjects who tested positive for ADA in the 2 following categories: 'ADA Positive (Treatment Boosted)', those who are pre-dose ADA positive and have a ≥4-fold increase in post-dose ADA levels compared to baseline measurement; and 'ADA Positive (Treatment Induced)', those who are pre-dose ADA negative or missing data and who have at least one post-dose ADA positive sample.

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

End point timeframe:

Baseline (Week 1), Week 5, and at 3, 6, 9, 12, and 18 months, and at early termination/study completion (up to 24 months)

| **End point values** | 1.5 mg/kg Emicizumab QW | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 193[56] | | | |
| Units: Participants | | | | |
| Total ADA Negative (Neg + Neg Unaffected) | 183 | | | |
| ADA Negative | 180 | | | |
| ADA Negative (Treatment Unaffected) | 3 | | | |
| Total ADA Positive (Boosted + Induced) | 10 | | | |
| ADA Positive (Treatment Boosted) | 2 | | | |
| ADA Positive (Treatment Induced) | 8 | | | |

Notes:

[56] - Safety Population: received at least 1 dose of emicizumab.

### Statistical analyses

No statistical analyses for this end point

## Secondary: Mean Trough Plasma Concentrations of Emicizumab at Specified Timepoints

| End point title | Mean Trough Plasma Concentrations of Emicizumab at |
|---|---|

| | |
|---|---|
| | Specified Timepoints |

End point description:

The trough concentration is a measure of the plasma concentration of a study drug at the end of of the dosage interval.

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

End point timeframe:

Pre-dose at Weeks 2, 3, and 5, Months 3, 6, 12, and 18, and at treatment discontinuation (up to 2 years)

| **End point values** | 1.5 mg/kg Emicizumab QW | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 193[57] | | | |
| Units: micrograms per millilitre (µg/mL) | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 2 (n = 188) | 16.7 (± 5.5) | | | |
| Week 3 (n = 190) | 30.7 (± 9.2) | | | |
| Week 5 (n = 187) | 52.4 (± 15.5) | | | |
| Month 3 (n = 186) | 52.5 (± 18.3) | | | |
| Month 6 (n = 183) | 53.4 (± 19.3) | | | |
| Month 12 (n = 183) | 54.2 (± 20.6) | | | |
| Month 18 (n = 171) | 53.6 (± 18.3) | | | |
| Treatment Discontinuation (n = 154) | 54.6 (± 19.0) | | | |

Notes:

[57] - PK Population: received at least 1 dose of emicizumab and had at least 1 post-baseline result.

## Statistical analyses

No statistical analyses for this end point

## Adverse events

| Adverse events information | |
|---|---|
| Timeframe for reporting adverse events: | |
| From Baseline until study completion (up to 2 years) | |
| Assessment type | Systematic |

| Dictionary used | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 23.1 |

| Reporting groups | |
|---|---|
| Reporting group title | 1.5 mg/kg Emicizumab QW |

Reporting group description:

Participants received initial weekly doses of prophylactic 3.0 mg/kg emicizumab subcutaneously (SC) for 4 weeks, followed by prophylactic maintenance doses consisting of 1.5 mg/kg emicizumab once a week (QW), administered SC for the remainder of the 2-year treatment period.

| Serious adverse events | 1.5 mg/kg Emicizumab QW | | |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 31 / 193 (16.06%) | | |
| number of deaths (all causes) | 2 | | |
| number of deaths resulting from adverse events | | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| ADENOCARCINOMA OF COLON | | | |
| subjects affected / exposed | 1 / 193 (0.52%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| BLADDER NEOPLASM | | | |
| subjects affected / exposed | 1 / 193 (0.52%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Vascular disorders | | | |
| HAEMATOMA | | | |
| subjects affected / exposed | 1 / 193 (0.52%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| HAEMORRHAGE | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 193 (0.52%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Surgical and medical procedures | | | |
| CENTRAL VENOUS CATHETER REMOVAL | | | |
| subjects affected / exposed | 1 / 193 (0.52%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| EPISTAXIS | | | |
| subjects affected / exposed | 1 / 193 (0.52%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| PNEUMONIA ASPIRATION | | | |
| subjects affected / exposed | 1 / 193 (0.52%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 1 | | |
| Product issues | | | |
| DEVICE DISLOCATION | | | |
| subjects affected / exposed | 1 / 193 (0.52%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Injury, poisoning and procedural complications | | | |
| FEMUR FRACTURE | | | |
| subjects affected / exposed | 2 / 193 (1.04%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| FIBULA FRACTURE | | | |
| subjects affected / exposed | 1 / 193 (0.52%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| FRACTURED SACRUM | | | |

| | | | | |
|---|---|---|---|---|
| subjects affected / exposed | 1 / 193 (0.52%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| HEAD INJURY | | | | |
| subjects affected / exposed | 1 / 193 (0.52%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 1 | | | |
| HIP FRACTURE | | | | |
| subjects affected / exposed | 1 / 193 (0.52%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| INJURY | | | | |
| subjects affected / exposed | 1 / 193 (0.52%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| JOINT INJURY | | | | |
| subjects affected / exposed | 1 / 193 (0.52%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| LOWER LIMB FRACTURE | | | | |
| subjects affected / exposed | 1 / 193 (0.52%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| MULTIPLE INJURIES | | | | |
| subjects affected / exposed | 1 / 193 (0.52%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 1 | | | |
| POST PROCEDURAL HAEMORRHAGE | | | | |
| subjects affected / exposed | 1 / 193 (0.52%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| TIBIA FRACTURE | | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 193 (0.52%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| WOUND DEHISCENCE | | | |
| subjects affected / exposed | 2 / 193 (1.04%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| WOUND HAEMATOMA | | | |
| subjects affected / exposed | 1 / 193 (0.52%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cardiac disorders | | | |
| ACUTE MYOCARDIAL INFARCTION | | | |
| subjects affected / exposed | 1 / 193 (0.52%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Nervous system disorders | | | |
| GENERALISED TONIC-CLONIC SEIZURE | | | |
| subjects affected / exposed | 1 / 193 (0.52%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| TENSION HEADACHE | | | |
| subjects affected / exposed | 1 / 193 (0.52%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Blood and lymphatic system disorders | | | |
| THROMBOCYTOPENIA | | | |
| subjects affected / exposed | 1 / 193 (0.52%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastrointestinal disorders | | | |
| ABDOMINAL COMPARTMENT SYNDROME | | | |

| | | | | |
|---|---|---|---|---|
| subjects affected / exposed | 1 / 193 (0.52%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 1 | | | |
| DIVERTICULUM INTESTINAL HAEMORRHAGIC | | | | |
| subjects affected / exposed | 1 / 193 (0.52%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| GASTROINTESTINAL HAEMORRHAGE | | | | |
| subjects affected / exposed | 1 / 193 (0.52%) | | | |
| occurrences causally related to treatment / all | 0 / 5 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| RETROPERITONEAL HAEMATOMA | | | | |
| subjects affected / exposed | 1 / 193 (0.52%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Hepatobiliary disorders | | | | |
| SUBCAPSULAR HEPATIC HAEMATOMA | | | | |
| subjects affected / exposed | 1 / 193 (0.52%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Renal and urinary disorders | | | | |
| NEPHROTIC SYNDROME | | | | |
| subjects affected / exposed | 1 / 193 (0.52%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| RENAL PAIN | | | | |
| subjects affected / exposed | 1 / 193 (0.52%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| URETEROLITHIASIS | | | | |
| subjects affected / exposed | 1 / 193 (0.52%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |

| | | | |
|---|---|---|---|
| Musculoskeletal and connective tissue disorders | | | |
| HAEMARTHROSIS | | | |
| subjects affected / exposed | 1 / 193 (0.52%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| HAEMATOMA MUSCLE | | | |
| subjects affected / exposed | 2 / 193 (1.04%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Infections and infestations | | | |
| ABSCESS | | | |
| subjects affected / exposed | 1 / 193 (0.52%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| APPENDICITIS | | | |
| subjects affected / exposed | 1 / 193 (0.52%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| CATHETER SITE ABSCESS | | | |
| subjects affected / exposed | 2 / 193 (1.04%) | | |
| occurrences causally related to treatment / all | 1 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| DEVICE RELATED INFECTION | | | |
| subjects affected / exposed | 1 / 193 (0.52%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| INFECTED SKIN ULCER | | | |
| subjects affected / exposed | 1 / 193 (0.52%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| PNEUMONIA | | | |
| subjects affected / exposed | 1 / 193 (0.52%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

| | | | |
|---|---|---|---|
| WOUND INFECTION | | | |
| subjects affected / exposed | 1 / 193 (0.52%) | | |
| 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 %

| **Non-serious adverse events** | 1.5 mg/kg Emicizumab QW | | |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 104 / 193 (53.89%) | | |
| Injury, poisoning and procedural complications | | | |
| FALL | | | |
| subjects affected / exposed | 12 / 193 (6.22%) | | |
| occurrences (all) | 16 | | |
| LIMB INJURY | | | |
| subjects affected / exposed | 10 / 193 (5.18%) | | |
| occurrences (all) | 12 | | |
| Nervous system disorders | | | |
| HEADACHE | | | |
| subjects affected / exposed | 29 / 193 (15.03%) | | |
| occurrences (all) | 52 | | |
| General disorders and administration site conditions | | | |
| PYREXIA | | | |
| subjects affected / exposed | 21 / 193 (10.88%) | | |
| occurrences (all) | 26 | | |
| INJECTION SITE REACTION | | | |
| subjects affected / exposed | 22 / 193 (11.40%) | | |
| occurrences (all) | 29 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| COUGH | | | |
| subjects affected / exposed | 12 / 193 (6.22%) | | |
| occurrences (all) | 13 | | |
| Musculoskeletal and connective tissue disorders | | | |
| ARTHRALGIA | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed<br>occurrences (all) | 33 / 193 (17.10%)<br>52 | | |
| Infections and infestations<br>NASOPHARYNGITIS<br>subjects affected / exposed<br>occurrences (all)<br><br>INFLUENZA<br>subjects affected / exposed<br>occurrences (all) | <br><br>30 / 193 (15.54%)<br>47<br><br><br>16 / 193 (8.29%)<br>25 | | |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---|---|
| 02 June 2017 | Protocol v2.0: the protocol was amended mainly to provide additional guidance on continued access to emicizumab. |
| 09 March 2018 | Protocol v3.0: the protocol was amended mainly to provide additional safety and efficacy data based on completed and ongoing emicizumab clinical trials. Additional minor changes were made to improve clarity and consistency. |

Notes:

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported