



Clinical trial results:

A Phase III, Randomized, Multicenter, Open-Label, Active-Comparator Controlled Study to Evaluate the Efficacy and Safety of APL-2 in Patients With Paroxysmal Nocturnal Hemoglobinuria (PNH)

Summary

| | |
|--------------------------|----------------------|
| EudraCT number | 2017-004268-36 |
| Trial protocol | DE BE ES NL FR GB IT |
| Global end of trial date | 13 August 2020 |

Results information

| | |
|--------------------------------|------------------|
| Result version number | v1 (current) |
| This version publication date | 12 November 2021 |
| First version publication date | 12 November 2021 |

Trial information

Trial identification

| | |
|-----------------------|----------|
| Sponsor protocol code | APL2-302 |
|-----------------------|----------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT03500549 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | Apellis Pharmaceuticals, Inc |
| Sponsor organisation address | 100 5th Avenue, Waltham, Massachusetts, United States, MA 02451 |
| Public contact | Apellis Clinical Trial Information Line, Apellis Pharmaceuticals, Inc, 1 833-284-6361, clinicaltrials@apellis.com |
| Scientific contact | Apellis Clinical Trial Information Line, Apellis Pharmaceuticals, Inc, 1 833-284-6361, clinicaltrials@apellis.com |

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

| | |
|--|----------------|
| Analysis stage | Final |
| Date of interim/final analysis | 13 August 2020 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 13 August 2020 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

Evaluation of the efficacy and safety of pegcetacoplan (APL-2) compared with those of eculizumab in subjects with paroxysmal nocturnal hemoglobinuria (PNH) who continued to have Hb levels <10.5 grams per deciliter (g/dL) despite treatment with eculizumab (Soliris®).

Protection of trial subjects:

This research was carried out in accordance with the protocol, applicable regulations, the ethical principles set forth in the Declaration of Helsinki, and the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use Harmonised Guideline for Good Clinical Practice E6 Revision 2. An external, independent data monitoring committee (IDMC) assessed the progress and cumulative safety/tolerability data of the study. The IDMC had the responsibility to conduct a thorough safety assessment at regular predefined intervals during the randomized controlled period (RCP) and open-label treatment phases of the study.

Background therapy: -

Evidence for comparator:

PNH is caused by complement-mediated lysis of erythrocyte clones lacking functional CD55 and CD59 on their surface to protect them against this process. These erythrocytes are particularly susceptible to the membrane attack complex (MAC) and have been shown to lyse readily in the presence of complement activation. Eculizumab is a monoclonal anti-C5 antibody that inhibits the formation of the MAC, and has been approved for the treatment of PNH.

| | |
|---|------------------|
| Actual start date of recruitment | 14 June 2018 |
| Long term follow-up planned | Yes |
| Long term follow-up rationale | Safety, Efficacy |
| Long term follow-up duration | 2 Years |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|-----------------------|
| Country: Number of subjects enrolled | United States: 14 |
| Country: Number of subjects enrolled | Australia: 5 |
| Country: Number of subjects enrolled | Japan: 10 |
| Country: Number of subjects enrolled | United Kingdom: 11 |
| Country: Number of subjects enrolled | Germany: 11 |
| Country: Number of subjects enrolled | France: 16 |
| Country: Number of subjects enrolled | Belgium: 4 |
| Country: Number of subjects enrolled | Spain: 2 |
| Country: Number of subjects enrolled | Canada: 4 |
| Country: Number of subjects enrolled | Russian Federation: 2 |
| Country: Number of subjects enrolled | Korea, Republic of: 1 |

| | |
|------------------------------------|----|
| Worldwide total number of subjects | 80 |
| EEA total number of subjects | 33 |

Notes:

| Subjects enrolled per age group | |
|---|----|
| In utero | 0 |
| Preterm newborn - gestational age < 37 wk | 0 |
| Newborns (0-27 days) | 0 |
| Infants and toddlers (28 days-23 months) | 0 |
| Children (2-11 years) | 0 |
| Adolescents (12-17 years) | 0 |
| Adults (18-64 years) | 63 |
| From 65 to 84 years | 17 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

This was a Phase 3, randomized, multicenter, open-label, active-comparator controlled study. The treatment period of the study consisted of 3 parts: a 4-week run-in period, a 16-week RCP, and a 32-week open-label period.

Pre-assignment

Screening details:

Of the 102 subjects screened, 80 subjects met all the inclusion criteria and none of the exclusion criteria and entered the run-in period. Randomization was stratified by the number of packed red blood cell (PRBC) transfusions within the 12 months prior to Day -28 and platelet count at screening.

Period 1

| | |
|------------------------------|-----------------------------------|
| Period 1 title | Run-in Period (Day -28 to ≤Day 1) |
| Is this the baseline period? | Yes |
| Allocation method | Not applicable |
| Blinding used | Not blinded |

Arms

| | |
|------------------------------|------------------------------|
| Are arms mutually exclusive? | Yes |
| Arm title | Run-in Period: Pegcetacoplan |

Arm description:

During the 4-week run-in period (Day -28 to ≤Day 1) all subjects received twice-weekly subcutaneous (SC) doses of pegcetacoplan 1080 milligrams (mg) in addition to their current dosage of eculizumab treatment.

| | |
|--|-----------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Eculizumab |
| Investigational medicinal product code | |
| Other name | Soliris |
| Pharmaceutical forms | Solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Dosage of eculizumab treatment continued as prescribed regardless of study visit scheduling or the pegcetacoplan administration schedule (ie, it was not required that eculizumab dosing aligned with pegcetacoplan dosing or study visits).

| | |
|--|-----------------------|
| Investigational medicinal product name | Pegcetacoplan |
| Investigational medicinal product code | APL2-302 |
| Other name | |
| Pharmaceutical forms | Solution for infusion |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Pegcetacoplan was administered as a 20 mL SC infusion.

| | |
|------------------|---------------------------|
| Arm title | Run-in Period: Eculizumab |
|------------------|---------------------------|

Arm description:

During the 4-week run-in period (Day -28 to ≤Day 1) all subjects received twice-weekly SC doses of pegcetacoplan 1080 mg in addition to their current dosage of eculizumab treatment.

| | |
|--|-----------------------|
| Arm type | Active comparator |
| Investigational medicinal product name | Eculizumab |
| Investigational medicinal product code | |
| Other name | Soliris |
| Pharmaceutical forms | Solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Dosage of eculizumab treatment continued as prescribed regardless of study visit scheduling or the pegcetacoplan administration schedule (ie, it was not required that eculizumab dosing aligned with pegcetacoplan dosing or study visits).

| | |
|--|-----------------------|
| Investigational medicinal product name | Pegcetacoplan |
| Investigational medicinal product code | APL2-302 |
| Other name | |
| Pharmaceutical forms | Solution for infusion |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Pegcetacoplan was administered as a 20 mL SC infusion.

| Number of subjects in period 1 | Run-in Period: Pegcetacoplan | Run-in Period: Eculizumab |
|---------------------------------------|---------------------------------|------------------------------|
| Started | 41 | 39 |
| Completed | 41 | 39 |

Period 2

| | |
|------------------------------|-------------------------|
| Period 2 title | RCP (Day 1 - Week 16) |
| Is this the baseline period? | No |
| Allocation method | Randomised - controlled |
| Blinding used | Not blinded |

Arms

| | |
|------------------------------|--------------------|
| Are arms mutually exclusive? | Yes |
| Arm title | RCP: Pegcetacoplan |

Arm description:

On Day 1, the subjects were randomized to receive monotherapy with SC infusions of pegcetacoplan 1080 mg twice-weekly or every 3 days up to the end of the open-label period (Week 48).

| | |
|--|-----------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Pegcetacoplan |
| Investigational medicinal product code | APL2-302 |
| Other name | |
| Pharmaceutical forms | Solution for infusion |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Pegcetacoplan was administered as a 20 mL SC infusion.

| | |
|------------------|-----------------|
| Arm title | RCP: Eculizumab |
|------------------|-----------------|

Arm description:

On Day 1, the subjects were randomized to receive monotherapy with their pre-screening stable dose of eculizumab via intravenous infusion every 2 weeks up to the end of the RCP (Week 16).

| | |
|----------|-------------------|
| Arm type | Active comparator |
|----------|-------------------|

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

Dosage and administration details:

Dosage of eculizumab treatment continued as prescribed regardless of study visit scheduling or the pegcetacoplan administration schedule (ie, it was not required that eculizumab dosing aligned with pegcetacoplan dosing or study visits).

| Number of subjects in period 2 | RCP: Pegcetacoplan | RCP: Eculizumab |
|--------------------------------|--------------------|-----------------|
| Started | 41 | 39 |
| Completed | 38 | 39 |
| Not completed | 3 | 0 |
| Adverse event, non-fatal | 3 | - |

Period 3

| | |
|------------------------------|--|
| Period 3 title | Open-label Period (Week 17 to Week 48) |
| Is this the baseline period? | No |
| Allocation method | Not applicable |
| Blinding used | Not blinded |

Arms

| | |
|------------------------------|---|
| Are arms mutually exclusive? | Yes |
| Arm title | Open-label Period: Continue Pegcetacoplan |

Arm description:

On Day 1 of the RCP, the subjects were randomized to receive monotherapy with SC infusions of pegcetacoplan 1080 mg twice-weekly or every 3 days up to the end of the open-label period (Week 48).

| | |
|--|-----------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Pegcetacoplan |
| Investigational medicinal product code | APL2-302 |
| Other name | |
| Pharmaceutical forms | Solution for infusion |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Pegcetacoplan was administered as a 20 mL SC infusion.

| | |
|------------------|---|
| Arm title | Open-label Period: Crossover to Pegcetacoplan |
|------------------|---|

Arm description:

Subjects entered the open-label run-in period where they received pegcetacoplan 1080 mg twice-weekly in addition to eculizumab for 4 weeks (Week 17 to Week 20) before receiving monotherapy with SC infusions of pegcetacoplan 1080 mg twice-weekly or every 3 days up to the end of the open-label period (Week 48).

| | |
|----------|--------------|
| Arm type | Experimental |
|----------|--------------|

| | |
|--|-----------------------|
| Investigational medicinal product name | Pegcetacoplan |
| Investigational medicinal product code | APL2-302 |
| Other name | |
| Pharmaceutical forms | Solution for infusion |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Pegcetacoplan was administered as a 20 mL SC infusion.

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

Dosage and administration details:

Dosage of eculizumab treatment continued as prescribed regardless of study visit scheduling or the pegcetacoplan administration schedule (ie, it was not required that eculizumab dosing aligned with pegcetacoplan dosing or study visits).

| Number of subjects in period 3 | Open-label Period: Continue Pegcetacoplan | Open-label Period: Crossover to Pegcetacoplan |
|---------------------------------------|---|---|
| Started | 38 | 39 |
| Completed | 35 | 32 |
| Not completed | 3 | 7 |
| Adverse event, non-fatal | 3 | 7 |

Baseline characteristics

Reporting groups

| | |
|---|------------------------------|
| Reporting group title | Run-in Period: Pegcetacoplan |
| Reporting group description: | |
| During the 4-week run-in period (Day -28 to ≤Day 1) all subjects received twice-weekly subcutaneous (SC) doses of pegcetacoplan 1080 milligrams (mg) in addition to their current dosage of eculizumab treatment. | |
| Reporting group title | Run-in Period: Eculizumab |
| Reporting group description: | |
| During the 4-week run-in period (Day -28 to ≤Day 1) all subjects received twice-weekly SC doses of pegcetacoplan 1080 mg in addition to their current dosage of eculizumab treatment. | |

| Reporting group values | Run-in Period: Pegcetacoplan | Run-in Period: Eculizumab | Total |
|---|---------------------------------|------------------------------|-------|
| Number of subjects | 41 | 39 | 80 |
| Age categorical | | | |
| Units: Subjects | | | |
| ≤18 years | 0 | 0 | 0 |
| Between 18 and 65 years | 31 | 32 | 63 |
| ≥65 years | 10 | 7 | 17 |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 27 | 22 | 49 |
| Male | 14 | 17 | 31 |
| Ethnicity | | | |
| Units: Subjects | | | |
| Hispanic or Latino | 2 | 1 | 3 |
| Not Hispanic or Latino | 29 | 32 | 61 |
| Unknown or Not Reported | 10 | 6 | 16 |
| Race | | | |
| Units: Subjects | | | |
| Asian | 5 | 7 | 12 |
| Black or African American | 2 | 0 | 2 |
| White | 24 | 25 | 49 |
| Other | 0 | 1 | 1 |
| Not Reported | 10 | 6 | 16 |
| Number of transfusions in the last 12 months prior to Day -28 | | | |
| Units: Subjects | | | |
| <4 | 20 | 16 | 36 |
| ≥4 | 21 | 23 | 44 |
| Platelet count at screening | | | |
| Units: Subjects | | | |
| <100,000 (count/ cubic millimeter [mm ³]) | 12 | 9 | 21 |
| ≥100,000 (count/ mm ³) | 29 | 30 | 59 |

End points

End points reporting groups

| | |
|--|--|
| Reporting group title | Run-in Period: Pegcetacoplan |
| Reporting group description: During the 4-week run-in period (Day -28 to ≤Day 1) all subjects received twice-weekly subcutaneous (SC) doses of pegcetacoplan 1080 milligrams (mg) in addition to their current dosage of eculizumab treatment. | |
| Reporting group title | Run-in Period: Eculizumab |
| Reporting group description: During the 4-week run-in period (Day -28 to ≤Day 1) all subjects received twice-weekly SC doses of pegcetacoplan 1080 mg in addition to their current dosage of eculizumab treatment. | |
| Reporting group title | RCP: Pegcetacoplan |
| Reporting group description: On Day 1, the subjects were randomized to receive monotherapy with SC infusions of pegcetacoplan 1080 mg twice-weekly or every 3 days up to the end of the open-label period (Week 48). | |
| Reporting group title | RCP: Eculizumab |
| Reporting group description: On Day 1, the subjects were randomized to receive monotherapy with their pre-screening stable dose of eculizumab via intravenous infusion every 2 weeks up to the end of the RCP (Week 16). | |
| Reporting group title | Open-label Period: Continue Pegcetacoplan |
| Reporting group description: On Day 1 of the RCP, the subjects were randomized to receive monotherapy with SC infusions of pegcetacoplan 1080 mg twice-weekly or every 3 days up to the end of the open-label period (Week 48). | |
| Reporting group title | Open-label Period: Crossover to Pegcetacoplan |
| Reporting group description: Subjects entered the open-label run-in period where they received pegcetacoplan 1080 mg twice-weekly in addition to eculizumab for 4 weeks (Week 17 to Week 20) before receiving monotherapy with SC infusions of pegcetacoplan 1080 mg twice-weekly or every 3 days up to the end of the open-label period (Week 48). | |
| Subject analysis set title | Treatment Period: Pegcetacoplan |
| Subject analysis set type | Full analysis |
| Subject analysis set description: During the 4-week run-in period (Day -28 to ≤Day 1) all subjects received twice-weekly SC doses of pegcetacoplan 1080 mg in addition to their current dosage of eculizumab treatment. On Day 1, the subjects were randomized to receive monotherapy with SC infusions of pegcetacoplan 1080 mg twice-weekly or every 3 days up to the end of the open-label period (Week 48). | |
| Subject analysis set title | Treatment Period: Eculizumab |
| Subject analysis set type | Full analysis |
| Subject analysis set description: During the 4-week run-in period (Day -28 to ≤Day 1) all subjects received twice-weekly SC doses of pegcetacoplan 1080 mg in addition to their current dosage of eculizumab treatment. On Day 1, the subjects were randomized to receive monotherapy with their pre-screening stable dose of eculizumab via intravenous infusion every 2 weeks up to the end of the RCP (Week 16). Subjects then entered the open-label run-in period where they received pegcetacoplan 1080 mg twice-weekly in addition to eculizumab for 4 weeks (Week 17 to Week 20) before receiving monotherapy with SC infusions of pegcetacoplan 1080 mg twice-weekly or every 3 days up to the end of the open-label period (Week 48). | |
| Subject analysis set title | Open-label Run-in Period: Crossover to Pegcetacoplan |
| Subject analysis set type | Full analysis |
| Subject analysis set description: Subjects in the open-label run-in period received pegcetacoplan 1080 mg twice-weekly in addition to eculizumab for 4 weeks (Week 17 to Week 20). | |

Primary: Least Squares (LS) Mean Change From Baseline to Week 16 in Hemoglobin (Hb) Level During the RCP

| | |
|-----------------|---|
| End point title | Least Squares (LS) Mean Change From Baseline to Week 16 in Hemoglobin (Hb) Level During the RCP |
|-----------------|---|

End point description:

Baseline was the average of measurements recorded before taking the first dose of pegcetacoplan, which included local and central laboratory values during the screening period. Analysis excluded data before the RCP and was censored for transfusions. The ITT set included all randomized subjects.

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

End point timeframe:

Baseline and Week 16

| End point values | RCP: Pegcetacoplan | RCP: Eculizumab | | |
|-------------------------------------|-----------------------|----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 41 | 39 | | |
| Units: g/dL | | | | |
| least squares mean (standard error) | 2.37 (\pm 0.363) | -1.47 (\pm 0.666) | | |

Statistical analyses

| | |
|----------------------------|---------------------------------|
| Statistical analysis title | Pegcetacoplan Versus Eculizumab |
|----------------------------|---------------------------------|

Statistical analysis description:

The primary endpoint analysis was a between-treatment-group comparison using a mixed effect model for repeated measures (MMRM). The difference between pegcetacoplan and eculizumab LS mean Hb changes from Baseline at Week 16 was calculated along with its 2-sided 95% confidence interval (CI) and associated P-value from the MMRM model for the ITT set, censored for transfusions.

| | |
|---|--------------------------------------|
| Comparison groups | RCP: Pegcetacoplan v RCP: Eculizumab |
| Number of subjects included in analysis | 80 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[1] |
| P-value | < 0.0001 |
| Method | MMRM |
| Parameter estimate | LS mean difference |
| Point estimate | 3.84 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 2.33 |
| upper limit | 5.34 |

Notes:

[1] - Superiority was tested at the 5% level. MMRM includes treatment + baseline value + analysis visit + strata + analysis visit \times treatment, where strata is the combination of randomization stratification factors.

Secondary: Percentage of Subjects Who Did Not Require a Transfusion (Transfusion Avoidance) During the RCP

| | |
|-----------------|---|
| End point title | Percentage of Subjects Who Did Not Require a Transfusion (Transfusion Avoidance) During the RCP |
|-----------------|---|

End point description:

Subjects who experienced more than 1 transfusion during the RCP are only counted once. Subjects who did not have a transfusion but withdrew before Week 16 were considered as having a transfusion in the analysis of transfusion avoidance. The ITT set included all randomized subjects.

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

End point timeframe:

Day 1 to Week 16

| End point values | RCP: Pegcetacoplan | RCP: Eculizumab | | |
|-------------------------------|-----------------------|--------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 41 | 39 | | |
| Units: Percentage of subjects | | | | |
| number (not applicable) | 85.4 | 15.4 | | |

Statistical analyses

| | |
|----------------------------|---------------------------------|
| Statistical analysis title | Pegcetacoplan Versus Eculizumab |
|----------------------------|---------------------------------|

Statistical analysis description:

Analysis was based on prespecified non-inferiority margins (NIM) and non-inferiority was achieved if the lower confidence limit or upper confidence limit of the 95% CI of the treatment difference met the prespecified NIM of -20%. Stratified Cochran-Mantel Haenszel (CMH) chi-square test was used for treatment comparison and the 95% CI for difference in percentage between treatments is constructed using the stratified (Miettinen-Nurminen) method.

| | |
|-------------------|--------------------------------------|
| Comparison groups | RCP: Pegcetacoplan v RCP: Eculizumab |
|-------------------|--------------------------------------|

| | |
|---|----|
| Number of subjects included in analysis | 80 |
|---|----|

| | |
|------------------------|---------------|
| Analysis specification | Pre-specified |
|------------------------|---------------|

| | |
|---------------|--------------------------------|
| Analysis type | non-inferiority ^[2] |
|---------------|--------------------------------|

| | |
|---------|----------|
| P-value | < 0.0001 |
|---------|----------|

| | |
|--------|--------------------|
| Method | Miettinen-Nurminen |
|--------|--------------------|

| | |
|--------------------|----------------------|
| Parameter estimate | Risk difference (RD) |
|--------------------|----------------------|

| | |
|----------------|--------|
| Point estimate | 0.6253 |
|----------------|--------|

Confidence interval

| | |
|-------|------|
| level | 95 % |
|-------|------|

| | |
|-------|---------|
| sides | 2-sided |
|-------|---------|

| | |
|-------------|-------|
| lower limit | 0.483 |
|-------------|-------|

| | |
|-------------|--------|
| upper limit | 0.7677 |
|-------------|--------|

Notes:

[2] - Non-inferiority was tested at the 2.5% level.

Secondary: LS Mean Change From Baseline to Week 16 in Absolute Reticulocyte Count (ARC) During the RCP

| | |
|-----------------|---|
| End point title | LS Mean Change From Baseline to Week 16 in Absolute Reticulocyte Count (ARC) During the RCP |
|-----------------|---|

End point description:

Baseline was the average of available measurements recorded from central laboratory before taking the first dose of pegcetacoplan. Analysis excluded data before the RCP and was censored for transfusions. The ITT set included all randomized subjects.

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

End point timeframe:
Baseline and Week 16

| End point values | RCP: Pegcetacoplan | RCP: Eculizumab | | |
|---|-----------------------|---------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 41 | 39 | | |
| Units: 10 ⁹ cells/ liter (L) | | | | |
| least squares mean (standard error) | -135.82 (± 6.543) | 27.79 (± 11.859) | | |

Statistical analyses

| Statistical analysis title | Pegcetacoplan Versus Eculizumab |
|---|--------------------------------------|
| Statistical analysis description: | |
| Analysis was based on prespecified NIM and non-inferiority was achieved if the lower confidence limit or upper confidence limit of the 95% CI of the treatment difference met the prespecified NIM of 10. | |
| Comparison groups | RCP: Pegcetacoplan v RCP: Eculizumab |
| Number of subjects included in analysis | 80 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[3] |
| P-value | < 0.0001 |
| Method | MMRM |
| Parameter estimate | LS mean difference |
| Point estimate | -163.61 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -189.91 |
| upper limit | -137.3 |

Notes:

[3] - Non-inferiority was tested at the 2.5% level. MMRM includes treatment + baseline value + analysis visit + strata + analysis visit × treatment, where strata is the combination of randomization stratification factors.

Secondary: LS Mean Change From Baseline to Week 16 in Lactate Dehydrogenase (LDH) Level During the RCP

| | |
|---|---|
| End point title | LS Mean Change From Baseline to Week 16 in Lactate Dehydrogenase (LDH) Level During the RCP |
| End point description: | |
| Baseline was the average of available measurements recorded from central laboratory before taking the first dose of pegcetacoplan. Analysis excluded data before the RCP and was censored for transfusions. The ITT set included all randomized subjects. | |
| End point type | Secondary |
| End point timeframe: | |
| Baseline and Week 16 | |

| End point values | RCP: Pegcetacoplan | RCP: Eculizumab | | |
|-------------------------------------|---------------------------|---------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 41 | 39 | | |
| Units: Units (U)/L | | | | |
| least squares mean (standard error) | -14.76 (\pm 42.708) | -10.12 (\pm 71.025) | | |

Statistical analyses

| Statistical analysis title | Pegcetacoplan Versus Eculizumab |
|---|--------------------------------------|
| Statistical analysis description: | |
| Analysis was based on prespecified NIM and non-inferiority was achieved if the lower confidence limit or upper confidence limit of the 95% CI of the treatment difference met the prespecified NIM of 20. | |
| Comparison groups | RCP: Pegcetacoplan v RCP: Eculizumab |
| Number of subjects included in analysis | 80 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[4] |
| P-value | = 0.9557 |
| Method | MMRM |
| Parameter estimate | LS mean difference |
| Point estimate | -4.63 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -181.3 |
| upper limit | 172.04 |

Notes:

[4] - Non-inferiority was tested at the 2.5% level. MMRM includes treatment + baseline value + analysis visit + strata + analysis visit \times treatment, where strata is the combination of randomization stratification factors.

Secondary: LS Mean Change From Baseline to Week 16 in Functional Assessment of Chronic Illness Therapy (FACIT) - Fatigue Scale Score During the RCP

| | |
|-----------------|--|
| End point title | LS Mean Change From Baseline to Week 16 in Functional Assessment of Chronic Illness Therapy (FACIT) - Fatigue Scale Score During the RCP |
|-----------------|--|

End point description:

The FACIT-fatigue scale version 4 is a 13-item Likert scaled instrument where the subject was presented with 13 statements and asked to indicate their response as it applied to the past 7 days. The 5 possible responses were 'Not at all' (0), 'A little bit' (1), 'Somewhat' (2), 'Quite a bit' (3) and 'Very much' (4). With 13 statements the total score had a range of 0 to 52. A higher score corresponds to a higher quality of life (QoL). Baseline was the last available, nonmissing observation before taking the first dose of pegcetacoplan. Data collected after transfusion is excluded from analysis. The ITT set included all randomized subjects.

| | |
|----------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Baseline and Week 16 | |

| End point values | RCP: Pegcetacoplan | RCP: Eculizumab | | |
|-------------------------------------|-----------------------|----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 41 | 39 | | |
| Units: Score on a scale | | | | |
| least squares mean (standard error) | 9.22 (\pm 1.607) | -2.65 (\pm 2.821) | | |

Statistical analyses

| Statistical analysis title | Pegcetacoplan Versus Eculizumab |
|----------------------------|---------------------------------|
|----------------------------|---------------------------------|

Statistical analysis description:

Non-inferiority was not assessed because of the prespecified hierarchical testing. Analysis was a between-treatment-group comparison using an MMRM. The difference between pegcetacoplan and eculizumab LS mean changes from Baseline at Week 16 was calculated along with its 2-sided 95% CI and associated P-value from the MMRM model for the ITT set, censored for transfusions.

| | |
|---|--------------------------------------|
| Comparison groups | RCP: Pegcetacoplan v RCP: Eculizumab |
| Number of subjects included in analysis | 80 |
| Analysis specification | Pre-specified |
| Analysis type | other ^[5] |
| P-value | = 0.0005 |
| Method | MMRM |
| Parameter estimate | LS mean difference |
| Point estimate | 11.87 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 5.49 |
| upper limit | 18.25 |

Notes:

[5] - MRMM includes treatment + baseline value + analysis visit + strata + analysis visit \times treatment, where strata is the combination of randomization stratification factors.

Secondary: Percentage of Subjects Who Achieved a Hb Response in the Absence of Transfusions at Week 16

| | |
|-----------------|---|
| End point title | Percentage of Subjects Who Achieved a Hb Response in the Absence of Transfusions at Week 16 |
|-----------------|---|

End point description:

Hb response was defined as an increase of at least 1 g/dL in Hb from Baseline at Week 16. Baseline was the average of measurements recorded before taking the first dose of pegcetacoplan, which included local and central laboratory values during the screening period. Analysis excluded data before the RCP and was censored for transfusions. The ITT set included all randomized subjects.

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

End point timeframe:

Baseline and Week 16

| End point values | RCP: Pegcetacoplan | RCP: Eculizumab | | |
|-------------------------------|-----------------------|--------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 41 | 39 | | |
| Units: Percentage of subjects | | | | |
| number (not applicable) | 75.6 | 0.0 | | |

Statistical analyses

| Statistical analysis title | Pegcetacoplan Versus Eculizumab |
|--|--------------------------------------|
| Statistical analysis description: | |
| Stratified CMH chi-square test was used for treatment comparison and the 95% CI for difference in percentage between treatments is constructed using the stratified Miettinen-Nurminen method. | |
| Comparison groups | RCP: Pegcetacoplan v RCP: Eculizumab |
| Number of subjects included in analysis | 80 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | Difference in percentage] |
| Point estimate | 0.6745 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.5452 |
| upper limit | 0.8039 |

Secondary: Percentage of Subjects Who Achieved Reticulocyte Normalization in the Absence of Transfusions at Week 16

| End point title | Percentage of Subjects Who Achieved Reticulocyte Normalization in the Absence of Transfusions at Week 16 |
|---|--|
| End point description: | |
| Reticulocyte normalization was defined as the ARC being below the upper limit of the gender-specific normal range at Week 16, censored for transfusions. Subjects who received a transfusion between Day 1 and Week 16 or withdrew without providing efficacy data at Week 16 were classified as nonresponders. The ITT set includes all randomized subjects. | |
| End point type | Secondary |
| End point timeframe: | |
| Week 16 | |

| End point values | RCP: Pegcetacoplan | RCP: Eculizumab | | |
|-------------------------------|-----------------------|--------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 41 | 39 | | |
| Units: Percentage of subjects | | | | |
| number (not applicable) | 78.0 | 2.6 | | |

Statistical analyses

| | |
|---|--------------------------------------|
| Statistical analysis title | Pegcetacoplan Versus Eculizumab |
| Statistical analysis description: Stratified CMH chi-square test was used for treatment comparison and the 95% CI for difference in percentage between treatments is constructed using the stratified Miettinen-Nurminen method. | |
| Comparison groups | RCP: Pegcetacoplan v RCP: Eculizumab |
| Number of subjects included in analysis | 80 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | Difference in percentage |
| Point estimate | 0.6639 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.5309 |
| upper limit | 0.7968 |

Secondary: Percentage of Subjects Who Achieved Hb Normalization in the Absence of Transfusions at Week 16

| | |
|--|--|
| End point title | Percentage of Subjects Who Achieved Hb Normalization in the Absence of Transfusions at Week 16 |
| End point description: Hb normalization was defined as the Hb level being above the lower limit of the normal range at Week 16, censored for transfusions. Subjects who received a transfusion between Day 1 and Week 16 or withdrew without providing efficacy data at Week 16 are classified as nonnormalization. The ITT set included all randomized subjects. | |
| End point type | Secondary |
| End point timeframe: Week 16 | |

| End point values | RCP: Pegcetacoplan | RCP: Eculizumab | | |
|-------------------------------|-----------------------|--------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 41 | 39 | | |
| Units: Percentage of subjects | | | | |
| number (not applicable) | 34.1 | 0.0 | | |

Statistical analyses

| | |
|---|--------------------------------------|
| Statistical analysis title | Pegcetacoplan Versus Eculizumab |
| Statistical analysis description: Stratified CMH chi-square test was used for treatment comparison and the 95% CI for difference in percentage between treatments is constructed using the stratified Miettinen-Nurminen method. | |
| Comparison groups | RCP: Pegcetacoplan v RCP: Eculizumab |
| Number of subjects included in analysis | 80 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | Difference in percentage |
| Point estimate | 0.3043 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.1493 |
| upper limit | 0.4593 |

Secondary: LS Mean Change From Baseline to Week 16 in Indirect Bilirubin Level During the RCP

| | |
|---|--|
| End point title | LS Mean Change From Baseline to Week 16 in Indirect Bilirubin Level During the RCP |
| End point description: Baseline was the average of available measurements recorded from central laboratory before taking the first dose of pegcetacoplan. Analysis excluded data before the RCP and was censored for transfusions. The ITT set included all randomized subjects. | |
| End point type | Secondary |
| End point timeframe: Baseline and Week 16 | |

| End point values | RCP: Pegcetacoplan | RCP: Eculizumab | | |
|-------------------------------------|-----------------------|--------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 41 | 39 | | |
| Units: Micromole (μmol)/L | | | | |
| least squares mean (standard error) | -17.78 (± 2.727) | 4.15 (± 4.477) | | |

Statistical analyses

| | |
|--|--------------------------------------|
| Statistical analysis title | Pegcetacoplan Versus Eculizumab |
| Statistical analysis description: Analysis was a between-treatment-group comparison using an MMRM. The difference between pegcetacoplan and eculizumab LS mean changes from Baseline at Week 16 was calculated along with its 2-sided 95% CI and associated P-value from the MMRM model for the ITT set, censored for transfusions. | |
| Comparison groups | RCP: Pegcetacoplan v RCP: Eculizumab |

| | |
|---|----------------------|
| Number of subjects included in analysis | 80 |
| Analysis specification | Pre-specified |
| Analysis type | other ^[6] |
| P-value | = 0.0002 |
| Method | MMRM |
| Parameter estimate | LS mean difference |
| Point estimate | -21.93 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -32.49 |
| upper limit | -11.36 |

Notes:

[6] - MMRM includes treatment + baseline value + analysis visit + strata + analysis visit × treatment, where strata is the combination of randomization stratification factors.

Secondary: LS Mean Change From Baseline to Week 16 in Haptoglobin Level During the RCP

| | |
|-----------------|---|
| End point title | LS Mean Change From Baseline to Week 16 in Haptoglobin Level During the RCP |
|-----------------|---|

End point description:

Baseline was the average of available measurements recorded from central laboratory before taking the first dose of pegcetacoplan. Analysis excluded data before the RCP and was censored for transfusions. The ITT set included all randomized subjects.

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

End point timeframe:

Baseline and Week 16

| End point values | RCP: Pegcetacoplan | RCP: Eculizumab | | |
|-------------------------------------|-----------------------|--------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 41 | 39 | | |
| Units: g/L | | | | |
| least squares mean (standard error) | -0.02 (± 0.033) | 0.12 (± 0.063) | | |

Statistical analyses

| | |
|----------------------------|---------------------------------|
| Statistical analysis title | Pegcetacoplan Versus Eculizumab |
|----------------------------|---------------------------------|

Statistical analysis description:

Analysis was a between-treatment-group comparison using an MMRM. The difference between pegcetacoplan and eculizumab LS mean changes from Baseline at Week 16 was calculated along with its 2-sided 95% CI and associated P-value from the MMRM model for the ITT set, censored for transfusions.

| | |
|-------------------|--------------------------------------|
| Comparison groups | RCP: Pegcetacoplan v RCP: Eculizumab |
|-------------------|--------------------------------------|

| | |
|---|----------------------|
| Number of subjects included in analysis | 80 |
| Analysis specification | Pre-specified |
| Analysis type | other ^[7] |
| P-value | = 0.0369 |
| Method | MMRM |
| Parameter estimate | LS mean difference |
| Point estimate | -0.14 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.28 |
| upper limit | -0.01 |

Notes:

[7] - MMRM includes treatment + baseline value + analysis visit + strata + analysis visit × treatment, where strata is the combination of randomization stratification factors.

Secondary: LS Mean Change From Baseline to Week 16 in Linear Analog Scale Assessment (LASA) Scores During the RCP

| | |
|-----------------|--|
| End point title | LS Mean Change From Baseline to Week 16 in Linear Analog Scale Assessment (LASA) Scores During the RCP |
|-----------------|--|

End point description:

The LASA consists of 3 items, where the respondents were asked to rate their perceived level of functioning. Specific domains included activity level, ability to carry out daily activities, and an item for overall QoL. Their level of functioning was reported on a 0 to 100 scale with 0 indicates "As low as could be" and 100 indicates "As high as could be". The combined score ranged from 0 to 300, with higher scores corresponding to a higher QoL. The ITT set included all randomized subjects.

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

End point timeframe:

Baseline and Week 16

| End point values | RCP: Pegcetacoplan | RCP: Eculizumab | | |
|-------------------------------------|-----------------------|---------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 41 | 39 | | |
| Units: Score on a scale | | | | |
| least squares mean (standard error) | 49.38 (± 10.189) | -9.72 (± 18.988) | | |

Statistical analyses

| | |
|----------------------------|---------------------------------|
| Statistical analysis title | Pegcetacoplan Versus Eculizumab |
|----------------------------|---------------------------------|

Statistical analysis description:

Analysis was a between-treatment-group comparison using an MMRM. The difference between pegcetacoplan and eculizumab LS mean changes from Baseline at Week 16 was calculated along with its 2-sided 95% CI and associated P-value from the MMRM model for the ITT set, censored for transfusions.

| | |
|-------------------|--------------------------------------|
| Comparison groups | RCP: Pegcetacoplan v RCP: Eculizumab |
|-------------------|--------------------------------------|

| | |
|---|----------------------|
| Number of subjects included in analysis | 80 |
| Analysis specification | Pre-specified |
| Analysis type | other ^[8] |
| P-value | = 0.0069 |
| Method | MMRM |
| Parameter estimate | LS mean difference |
| Point estimate | 59.1 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 16.88 |
| upper limit | 101.32 |

Notes:

[8] - MMRM includes treatment + baseline value + analysis visit + strata + analysis visit × treatment, where strata is the combination of randomization stratification factors.

Secondary: LS Mean Change From Baseline to Week 16 in European Organisation for Research and Treatment of Cancer (EORTC) Quality of Life Questionnaire - Core 30 Scale (QLQ-C30) Scores During the RCP

| | |
|-----------------|---|
| End point title | LS Mean Change From Baseline to Week 16 in European Organisation for Research and Treatment of Cancer (EORTC) Quality of Life Questionnaire - Core 30 Scale (QLQ-C30) Scores During the RCP |
|-----------------|---|

End point description:

The EORTC QLQ-C30 questionnaire (version 3.0) consists of 30 questions comprised of both multi-item scales and single-item measures to assess overall QoL in subjects. Questions are designated by functional scales, symptom scales, and global subject QoL/overall perceived health status. For the first 28 questions the 4 possible responses are 'Not at all' (1), 'A little' (2), 'Quite a bit' (3) and 'Very much' (4). For the remaining 2 questions the response is requested on a 7-point scale from 1 ('Very poor') to 7 ('Excellent'). The raw scale scores were linear transformed, producing scale scores that ranged from 0% to 100%. A high scale score represents a higher response level. Hence for the functional scales and the global health status a higher score indicates a better QoL, whilst for the symptom scale scores this is implied by a lower score. The ITT set included all randomized subjects.

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

End point timeframe:

Baseline and Week 16

| End point values | RCP: Pegcetacoplan | RCP: Eculizumab | | |
|---|-----------------------|--------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 41 | 39 | | |
| Units: Score on a scale | | | | |
| least squares mean (standard error) | | | | |
| Global Health Status/QoL | 15.91 (± 3.635) | -2.71 (± 8.515) | | |
| Functional Scales - Physical functioning | 16.92 (± 2.081) | 4.06 (± 3.605) | | |
| Functional Scales - Role functioning | 15.39 (± 3.930) | -9.04 (± 6.954) | | |
| Functional Scales - Emotional functioning | 7.98 (± 3.366) | 3.86 (± 7.237) | | |
| Functional Scales - Cognitive functioning | 5.76 (± 3.258) | -3.80 (± 6.420) | | |
| Functional Scales - Social functioning | 15.08 (± 2.946) | 3.82 (± 6.349) | | |

| | | | | |
|---|------------------|-----------------|--|--|
| Symptom Scales - Fatigue | -22.93 (± 3.321) | -2.18 (± 6.644) | | |
| Symptom Scales - Nausea and vomiting | -0.34 (± 1.632) | -0.33 (± 3.876) | | |
| Symptom Scales - Pain | -0.74 (± 4.323) | 2.01 (± 7.841) | | |
| Symptom Scales - Dyspnoea | -20.12 (± 3.488) | -5.55 (± 7.019) | | |
| Symptom Scales - Insomnia | -9.18 (± 3.955) | -9.50 (± 7.090) | | |
| Symptom Scales - Appetite loss | -3.76 (± 3.357) | 4.19 (± 7.009) | | |
| Symptom Scales - Constipation | 2.98 (± 3.248) | 1.19 (± 8.129) | | |
| Symptom Scales - Diarrhoea | 0.31 (± 3.711) | 1.68 (± 8.204) | | |
| Symptom Scales - Financial difficulties | -6.82 (± 3.853) | 0.58 (± 6.297) | | |

Statistical analyses

| Statistical analysis title | Global Health Status/QoL |
|---|--------------------------------------|
| Statistical analysis description: | |
| Analysis was a between-treatment-group comparison using an MMRM. The difference between pegcetacoplan and eculizumab LS mean changes from Baseline at Week 16 was calculated along with its 2-sided 95% CI and associated P-value from the MMRM model for the ITT set, censored for transfusions. | |
| Comparison groups | RCP: Pegcetacoplan v RCP: Eculizumab |
| Number of subjects included in analysis | 80 |
| Analysis specification | Pre-specified |
| Analysis type | other ^[9] |
| P-value | = 0.0486 |
| Method | MMRM |
| Parameter estimate | LS mean difference |
| Point estimate | 18.62 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.12 |
| upper limit | 37.13 |

Notes:

[9] - MRMM includes treatment + baseline value + analysis visit + strata + analysis visit × treatment, where strata is the combination of randomization stratification factors.

| Statistical analysis title | Functional Scales - Physical functioning |
|---|--|
| Statistical analysis description: | |
| Analysis was a between-treatment-group comparison using an MMRM. The difference between pegcetacoplan and eculizumab LS mean changes from Baseline at Week 16 was calculated along with its 2-sided 95% CI and associated P-value from the MMRM model for the ITT set, censored for transfusions. | |
| Comparison groups | RCP: Pegcetacoplan v RCP: Eculizumab |

| | |
|---|-----------------------|
| Number of subjects included in analysis | 80 |
| Analysis specification | Pre-specified |
| Analysis type | other ^[10] |
| P-value | = 0.0023 |
| Method | MMRM |
| Parameter estimate | LS mean difference |
| Point estimate | 12.86 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 4.86 |
| upper limit | 20.86 |

Notes:

[10] - MMRM includes treatment + baseline value + analysis visit + strata + analysis visit × treatment, where strata is the combination of randomization stratification factors.

| | |
|-----------------------------------|--------------------------------------|
| Statistical analysis title | Functional Scales - Role functioning |
|-----------------------------------|--------------------------------------|

Statistical analysis description:

Analysis was a between-treatment-group comparison using an MMRM. The difference between pegcetacoplan and eculizumab LS mean changes from Baseline at Week 16 was calculated along with its 2-sided 95% CI and associated P-value from the MMRM model for the ITT set, censored for transfusions.

| | |
|---|--------------------------------------|
| Comparison groups | RCP: Eculizumab v RCP: Pegcetacoplan |
| Number of subjects included in analysis | 80 |
| Analysis specification | Pre-specified |
| Analysis type | other ^[11] |
| P-value | = 0.0027 |
| Method | MMRM |
| Parameter estimate | LS mean difference |
| Point estimate | 24.43 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 8.84 |
| upper limit | 40.01 |

Notes:

[11] - MMRM includes treatment + baseline value + analysis visit + strata + analysis visit × treatment, where strata is the combination of randomization stratification factors.

| | |
|-----------------------------------|---|
| Statistical analysis title | Functional Scales - Emotional functioning |
|-----------------------------------|---|

Statistical analysis description:

Analysis was a between-treatment-group comparison using an MMRM. The difference between pegcetacoplan and eculizumab LS mean changes from Baseline at Week 16 was calculated along with its 2-sided 95% CI and associated P-value from the MMRM model for the ITT set, censored for transfusions.

| | |
|---|--------------------------------------|
| Comparison groups | RCP: Pegcetacoplan v RCP: Eculizumab |
| Number of subjects included in analysis | 80 |
| Analysis specification | Pre-specified |
| Analysis type | other ^[12] |
| P-value | = 0.6013 |
| Method | MMRM |
| Parameter estimate | LS mean difference |
| Point estimate | 4.11 |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -11.58 |
| upper limit | 19.8 |

Notes:

[12] - MRMM includes treatment + baseline value + analysis visit + strata + analysis visit × treatment, where strata is the combination of randomization stratification factors.

| | |
|-----------------------------------|---|
| Statistical analysis title | Functional Scales - Cognitive functioning |
|-----------------------------------|---|

Statistical analysis description:

Analysis was a between-treatment-group comparison using an MMRM. The difference between pegcetacoplan and eculizumab LS mean changes from Baseline at Week 16 was calculated along with its 2-sided 95% CI and associated P-value from the MMRM model for the ITT set, censored for transfusions.

| | |
|---|--------------------------------------|
| Comparison groups | RCP: Pegcetacoplan v RCP: Eculizumab |
| Number of subjects included in analysis | 80 |
| Analysis specification | Pre-specified |
| Analysis type | other ^[13] |
| P-value | = 0.1792 |
| Method | MMRM |
| Parameter estimate | LS mean difference |
| Point estimate | 9.56 |

Confidence interval

| | |
|-------------|---------|
| level | 95 % |
| sides | 2-sided |
| lower limit | -4.52 |
| upper limit | 23.64 |

Notes:

[13] - MRMM includes treatment + baseline value + analysis visit + strata + analysis visit × treatment, where strata is the combination of randomization stratification factors.

| | |
|-----------------------------------|--|
| Statistical analysis title | Functional Scales - Social functioning |
|-----------------------------------|--|

Statistical analysis description:

Analysis was a between-treatment-group comparison using an MMRM. The difference between pegcetacoplan and eculizumab LS mean changes from Baseline at Week 16 was calculated along with its 2-sided 95% CI and associated P-value from the MMRM model for the ITT set, censored for transfusions.

| | |
|---|--------------------------------------|
| Comparison groups | RCP: Pegcetacoplan v RCP: Eculizumab |
| Number of subjects included in analysis | 80 |
| Analysis specification | Pre-specified |
| Analysis type | other ^[14] |
| P-value | = 0.1039 |
| Method | MMRM |
| Parameter estimate | LS mean difference |
| Point estimate | 11.27 |

Confidence interval

| | |
|-------------|---------|
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.38 |
| upper limit | 24.92 |

Notes:

[14] - MRMM includes treatment + baseline value + analysis visit + strata + analysis visit × treatment, where strata is the combination of randomization stratification factors.

| | |
|-----------------------------------|--------------------------|
| Statistical analysis title | Symptom Scales - Fatigue |
|-----------------------------------|--------------------------|

Statistical analysis description:

Analysis was a between-treatment-group comparison using an MMRM. The difference between pegcetacoplan and eculizumab LS mean changes from Baseline at Week 16 was calculated along with its 2-sided 95% CI and associated P-value from the MMRM model for the ITT set, censored for transfusions.

| | |
|---|--------------------------------------|
| Comparison groups | RCP: Pegcetacoplan v RCP: Eculizumab |
| Number of subjects included in analysis | 80 |
| Analysis specification | Pre-specified |
| Analysis type | other ^[15] |
| P-value | = 0.0062 |
| Method | MMRM |
| Parameter estimate | LS mean difference |
| Point estimate | -20.74 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -35.29 |
| upper limit | -6.19 |

Notes:

[15] - MRMM includes treatment + baseline value + analysis visit + strata + analysis visit × treatment, where strata is the combination of randomization stratification factors.

| | |
|-----------------------------------|--------------------------------------|
| Statistical analysis title | Symptom Scales - Nausea and vomiting |
|-----------------------------------|--------------------------------------|

Statistical analysis description:

Analysis was a between-treatment-group comparison using an MMRM. The difference between pegcetacoplan and eculizumab LS mean changes from Baseline at Week 16 was calculated along with its 2-sided 95% CI and associated P-value from the MMRM model for the ITT set, censored for transfusions.

| | |
|---|--------------------------------------|
| Comparison groups | RCP: Pegcetacoplan v RCP: Eculizumab |
| Number of subjects included in analysis | 80 |
| Analysis specification | Pre-specified |
| Analysis type | other ^[16] |
| P-value | = 0.9975 |
| Method | MMRM |
| Parameter estimate | LS mean difference |
| Point estimate | -0.01 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -8.38 |
| upper limit | 8.35 |

Notes:

[16] - MRMM includes treatment + baseline value + analysis visit + strata + analysis visit × treatment, where strata is the combination of randomization stratification factors.

| | |
|-----------------------------------|-----------------------|
| Statistical analysis title | Symptom Scales - Pain |
|-----------------------------------|-----------------------|

Statistical analysis description:

Analysis was a between-treatment-group comparison using an MMRM. The difference between pegcetacoplan and eculizumab LS mean changes from Baseline at Week 16 was calculated along with its 2-sided 95% CI and associated P-value from the MMRM model for the ITT set, censored for transfusions.

| | |
|-------------------|--------------------------------------|
| Comparison groups | RCP: Pegcetacoplan v RCP: Eculizumab |
|-------------------|--------------------------------------|

| | |
|---|-----------------------|
| Number of subjects included in analysis | 80 |
| Analysis specification | Pre-specified |
| Analysis type | other ^[17] |
| P-value | = 0.7554 |
| Method | MMRM |
| Parameter estimate | LS mean difference |
| Point estimate | -2.76 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -20.36 |
| upper limit | 14.85 |

Notes:

[17] - MMRM includes treatment + baseline value + analysis visit + strata + analysis visit × treatment, where strata is the combination of randomization stratification factors.

| | |
|-----------------------------------|---------------------------|
| Statistical analysis title | Symptom Scales - Dyspnoea |
|-----------------------------------|---------------------------|

Statistical analysis description:

Analysis was a between-treatment-group comparison using an MMRM. The difference between pegcetacoplan and eculizumab LS mean changes from Baseline at Week 16 was calculated along with its 2-sided 95% CI and associated P-value from the MMRM model for the ITT set, censored for transfusions.

| | |
|---|--------------------------------------|
| Comparison groups | RCP: Pegcetacoplan v RCP: Eculizumab |
| Number of subjects included in analysis | 80 |
| Analysis specification | Pre-specified |
| Analysis type | other ^[18] |
| P-value | = 0.062 |
| Method | MMRM |
| Parameter estimate | LS mean difference |
| Point estimate | -14.57 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -29.9 |
| upper limit | 0.76 |

Notes:

[18] - MMRM includes treatment + baseline value + analysis visit + strata + analysis visit × treatment, where strata is the combination of randomization stratification factors.

| | |
|-----------------------------------|---------------------------|
| Statistical analysis title | Symptom Scales - Insomnia |
|-----------------------------------|---------------------------|

Statistical analysis description:

Analysis was a between-treatment-group comparison using an MMRM. The difference between pegcetacoplan and eculizumab LS mean changes from Baseline at Week 16 was calculated along with its 2-sided 95% CI and associated P-value from the MMRM model for the ITT set, censored for transfusions.

| | |
|---|--------------------------------------|
| Comparison groups | RCP: Pegcetacoplan v RCP: Eculizumab |
| Number of subjects included in analysis | 80 |
| Analysis specification | Pre-specified |
| Analysis type | other ^[19] |
| P-value | = 0.9686 |
| Method | MMRM |
| Parameter estimate | LS mean difference |
| Point estimate | 0.32 |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -15.67 |
| upper limit | 16.3 |

Notes:

[19] - MRMM includes treatment + baseline value + analysis visit + strata + analysis visit × treatment, where strata is the combination of randomization stratification factors.

| | |
|-----------------------------------|--------------------------------|
| Statistical analysis title | Symptom Scales - Appetite loss |
|-----------------------------------|--------------------------------|

Statistical analysis description:

Analysis was a between-treatment-group comparison using an MMRM. The difference between pegcetacoplan and eculizumab LS mean changes from Baseline at Week 16 was calculated along with its 2-sided 95% CI and associated P-value from the MMRM model for the ITT set, censored for transfusions.

| | |
|---|--------------------------------------|
| Comparison groups | RCP: Pegcetacoplan v RCP: Eculizumab |
| Number of subjects included in analysis | 80 |
| Analysis specification | Pre-specified |
| Analysis type | other ^[20] |
| P-value | = 0.3002 |
| Method | MMRM |
| Parameter estimate | LS mean difference |
| Point estimate | -7.95 |

Confidence interval

| | |
|-------------|---------|
| level | 95 % |
| sides | 2-sided |
| lower limit | -23.23 |
| upper limit | 7.33 |

Notes:

[20] - MRMM includes treatment + baseline value + analysis visit + strata + analysis visit × treatment, where strata is the combination of randomization stratification factors.

| | |
|-----------------------------------|-------------------------------|
| Statistical analysis title | Symptom Scales - Constipation |
|-----------------------------------|-------------------------------|

Statistical analysis description:

Analysis was a between-treatment-group comparison using an MMRM. The difference between pegcetacoplan and eculizumab LS mean changes from Baseline at Week 16 was calculated along with its 2-sided 95% CI and associated P-value from the MMRM model for the ITT set, censored for transfusions.

| | |
|---|--------------------------------------|
| Comparison groups | RCP: Pegcetacoplan v RCP: Eculizumab |
| Number of subjects included in analysis | 80 |
| Analysis specification | Pre-specified |
| Analysis type | other ^[21] |
| P-value | = 0.8374 |
| Method | MMRM |
| Parameter estimate | LS mean difference |
| Point estimate | 1.79 |

Confidence interval

| | |
|-------------|---------|
| level | 95 % |
| sides | 2-sided |
| lower limit | -15.7 |
| upper limit | 19.29 |

Notes:

[21] - MRMM includes treatment + baseline value + analysis visit + strata + analysis visit × treatment, where strata is the combination of randomization stratification factors.

| | |
|-----------------------------------|----------------------------|
| Statistical analysis title | Symptom Scales - Diarrhoea |
|-----------------------------------|----------------------------|

Statistical analysis description:

Analysis was a between-treatment-group comparison using an MMRM. The difference between pegcetacoplan and eculizumab LS mean changes from Baseline at Week 16 was calculated along with its 2-sided 95% CI and associated P-value from the MMRM model for the ITT set, censored for transfusions.

| | |
|---|--------------------------------------|
| Comparison groups | RCP: Pegcetacoplan v RCP: Eculizumab |
| Number of subjects included in analysis | 80 |
| Analysis specification | Pre-specified |
| Analysis type | other ^[22] |
| P-value | = 0.8775 |
| Method | MMRM |
| Parameter estimate | LS mean difference |
| Point estimate | -1.38 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -19.28 |
| upper limit | 16.52 |

Notes:

[22] - MRMM includes treatment + baseline value + analysis visit + strata + analysis visit × treatment, where strata is the combination of randomization stratification factors.

| | |
|-----------------------------------|---|
| Statistical analysis title | Symptom Scales - Financial difficulties |
|-----------------------------------|---|

Statistical analysis description:

Analysis was a between-treatment-group comparison using an MMRM. The difference between pegcetacoplan and eculizumab LS mean changes from Baseline at Week 16 was calculated along with its 2-sided 95% CI and associated P-value from the MMRM model for the ITT set, censored for transfusions.

| | |
|---|--------------------------------------|
| Comparison groups | RCP: Pegcetacoplan v RCP: Eculizumab |
| Number of subjects included in analysis | 80 |
| Analysis specification | Pre-specified |
| Analysis type | other ^[23] |
| P-value | = 0.3066 |
| Method | MMRM |
| Parameter estimate | LS mean difference |
| Point estimate | -7.4 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -21.76 |
| upper limit | 6.95 |

Notes:

[23] - MRMM includes treatment + baseline value + analysis visit + strata + analysis visit × treatment, where strata is the combination of randomization stratification factors.

Secondary: Total Number of PRBC Units Transfused During the RCP

| | |
|-----------------|--|
| End point title | Total Number of PRBC Units Transfused During the RCP |
|-----------------|--|

End point description:

Subjects who withdrew during the RCP before Week 16 will have their number of units of PRBC estimated from the duration they were in the study. The ITT set included all randomized subjects.

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

End point timeframe:

Day 1 to Week 16

| End point values | RCP: Pegcetacoplan | RCP: Eculizumab | | |
|-----------------------------|-----------------------|--------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 41 | 39 | | |
| Units: PRBC Units | | | | |
| number (not applicable) | 26 | 198 | | |

Statistical analyses

| | |
|--|--------------------------------------|
| Statistical analysis title | Pegcetacoplan versus Eculizumab |
| Statistical analysis description: | |
| Wilcoxon rank-sum test P-value for the comparison between treatments is based on median using stratified non-parametric analysis. The 95% CI is constructed using Hodges-Lehmann Estimation of Location Shift. | |
| Comparison groups | RCP: Pegcetacoplan v RCP: Eculizumab |
| Number of subjects included in analysis | 80 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | < 0.0001 |
| Method | Wilcoxon rank-sum test |
| Parameter estimate | Median difference (final values) |
| Point estimate | 3 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 2 |
| upper limit | 4 |

Secondary: Mean Change From Baseline to Week 48 in Hb Level During the Treatment Period

| | |
|---|--|
| End point title | Mean Change From Baseline to Week 48 in Hb Level During the Treatment Period |
| End point description: | |
| Baseline was the average of measurements recorded before taking the first dose of pegcetacoplan, which included local and central laboratory values during the screening period. Analysis excluded data before the RCP and was censored for transfusions. The ITT set included all randomized subjects. | |
| End point type | Secondary |
| End point timeframe: | |
| Baseline and Week 48 | |

| End point values | Treatment Period: Pegcetacoplan | Treatment Period: Eculizumab | | |
|--------------------------------------|------------------------------------|---------------------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 33 | 30 | | |
| Units: g/dL | | | | |
| arithmetic mean (standard deviation) | 2.47 (± 1.72) | 2.93 (± 2.09) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Week 17 to Week 48 in Hb Level During the Open-label Period

| | |
|-----------------|--|
| End point title | Mean Change From Week 17 to Week 48 in Hb Level During the Open-label Period |
|-----------------|--|

End point description:

Baseline was the average of measurements recorded before taking the first dose of pegcetacoplan, which included local and central laboratory values during the screening period. Analysis excluded data before the RCP and was censored for transfusions. The ITT set included all randomized subjects.

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

End point timeframe:

Week 17 and Week 48

| End point values | Open-label Period: Continue Pegcetacoplan | Open-label Period: Crossover to Pegcetacoplan | | |
|--------------------------------------|---|---|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 33 | 29 | | |
| Units: g/dL | | | | |
| arithmetic mean (standard deviation) | -0.16 (± 1.154) | 2.89 (± 2.078) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Baseline to Week 48 in ARC During the Treatment Period

| | |
|-----------------|---|
| End point title | Mean Change From Baseline to Week 48 in ARC During the Treatment Period |
|-----------------|---|

End point description:

Baseline was the average of available measurements recorded from central laboratory before taking the first dose of pegcetacoplan. Analysis excluded data before the RCP and was censored for transfusions. The ITT set included all randomized subjects.

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

End point timeframe:
Baseline and Week 48

| End point values | Treatment Period: Pegcetacoplan | Treatment Period: Eculizumab | | |
|--------------------------------------|------------------------------------|---------------------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 31 | 29 | | |
| Units: 10 ⁹ cells/L | | | | |
| arithmetic mean (standard deviation) | -135.64 (± 67.90) | -128.22 (± 59.60) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Week 17 to Week 48 in ARC During the Open-label Period

| | |
|-----------------|---|
| End point title | Mean Change From Week 17 to Week 48 in ARC During the Open-label Period |
|-----------------|---|

End point description:

Baseline was the average of available measurements recorded from central laboratory before taking the first dose of pegcetacoplan. Analysis excluded data before the RCP and was censored for transfusions. The ITT set included all randomized subjects.

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

End point timeframe:

Week 17 and Week 48

| End point values | Open-label Period: Continue Pegcetacoplan | Open-label Period: Crossover to Pegcetacoplan | | |
|--------------------------------------|--|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 31 | 29 | | |
| Units: 10 ⁹ cells/L | | | | |
| arithmetic mean (standard deviation) | -6.50 (± 26.471) | -121.15 (± 70.969) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Baseline to Week 48 in LDH Level During the Treatment Period

| | |
|---|---|
| End point title | Mean Change From Baseline to Week 48 in LDH Level During the Treatment Period |
| End point description: Baseline was the average of available measurements recorded from central laboratory before taking the first dose of pegcetacoplan. Analysis excluded data before the RCP and was censored for transfusions. The ITT set included all randomized subjects. | |
| End point type | Secondary |
| End point timeframe: Baseline and Week 48 | |

| End point values | Treatment Period: Pegcetacoplan | Treatment Period: Eculizumab | | |
|--------------------------------------|------------------------------------|---------------------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 33 | 30 | | |
| Units: U/L | | | | |
| arithmetic mean (standard deviation) | -41.53 (\pm 153.68) | -105.27 (\pm 315.59) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Week 17 to Week 48 in LDH Level During the Open-label Period

| | |
|---|---|
| End point title | Mean Change From Week 17 to Week 48 in LDH Level During the Open-label Period |
| End point description: Baseline was the average of available measurements recorded from central laboratory before taking the first dose of pegcetacoplan. Analysis excluded data before the RCP and was censored for transfusions. The ITT set included all randomized subjects. | |
| End point type | Secondary |
| End point timeframe: Week 17 and Week 48 | |

| End point values | Open-label Period: Continue Pegcetacoplan | Open-label Period: Crossover to Pegcetacoplan | | |
|--------------------------------------|--|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 33 | 28 | | |
| Units: U/L | | | | |
| arithmetic mean (standard deviation) | 8.03 (\pm 129.285) | -46.84 (\pm 292.607) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Baseline to Week 48 in FACIT-fatigue Scale Score During the Treatment Period

| | |
|-----------------|---|
| End point title | Mean Change From Baseline to Week 48 in FACIT-fatigue Scale Score During the Treatment Period |
|-----------------|---|

End point description:

The FACIT-fatigue scale version 4 is a 13-item Likert scaled instrument where the subject was presented with 13 statements and asked to indicate their response as it applied to the past 7 days. The 5 possible responses were 'Not at all' (0), 'A little bit' (1), 'Somewhat' (2), 'Quite a bit' (3) and 'Very much' (4). With 13 statements the total score had a range of 0 to 52. A higher score corresponds to a higher QoL. Baseline was the last available, nonmissing observation before taking the first dose of pegcetacoplan. Data collected after transfusion is excluded from analysis. The ITT set included all randomized subjects.

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

End point timeframe:

Baseline and Week 48

| End point values | Treatment Period: Pegcetacoplan | Treatment Period: Eculizumab | | |
|--------------------------------------|------------------------------------|---------------------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 30 | 29 | | |
| Units: Score on a scale | | | | |
| arithmetic mean (standard deviation) | 10.14 (± 9.06) | 9.62 (± 10.34) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Week 17 to Week 48 in FACIT-fatigue Scale Score During the Open-label Period

| | |
|-----------------|---|
| End point title | Mean Change From Week 17 to Week 48 in FACIT-fatigue Scale Score During the Open-label Period |
|-----------------|---|

End point description:

The FACIT-fatigue scale is a 13 item Likert scaled instrument where the subject was presented with 13 statements and asked to indicate their response as it applied to the past 7 days. The 5 possible responses were 'Not at all' (0), 'A little bit' (1), 'Somewhat' (2), 'Quite a bit' (3) and 'Very much' (4). With 13 statements the total score had a range of 0 to 52. Higher score corresponds to a higher QoL. The ITT set included all randomized subjects.

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

End point timeframe:

Week 17 and Week 48

| End point values | Open-label Period: Continue Pegcetacoplan | Open-label Period: Crossover to Pegcetacoplan | | |
|--------------------------------------|--|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 30 | 26 | | |
| Units: Score on a scale | | | | |
| arithmetic mean (standard deviation) | 1.28 (\pm 7.805) | 10.19 (\pm 10.973) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Baseline to Week 48 in LASA Scores During the Treatment Period

| | |
|-----------------|---|
| End point title | Mean Change From Baseline to Week 48 in LASA Scores During the Treatment Period |
|-----------------|---|

End point description:

The LASA consists of 3 items, where the respondents were asked to rate their perceived level of functioning. Specific domains included activity level, ability to carry out daily activities, and an item for overall QoL. Their level of functioning was reported on a 0 to 100 scale with 0 indicates "As low as could be" and 100 indicates "As high as could be". The combined score ranged from 0 to 300, with higher scores corresponding to a higher QoL. The ITT set included all randomized subjects.

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

End point timeframe:

Baseline and Week 48

| End point values | Treatment Period: Pegcetacoplan | Treatment Period: Eculizumab | | |
|--------------------------------------|------------------------------------|---------------------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 29 | 29 | | |
| Units: Score on a scale | | | | |
| arithmetic mean (standard deviation) | 58.66 (\pm 51.16) | 56.52 (\pm 65.55) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Week 17 to Week 48 in LASA Scores During the Open-label Period

| | |
|-----------------|---|
| End point title | Mean Change From Week 17 to Week 48 in LASA Scores During the Open-label Period |
|-----------------|---|

End point description:

The FACIT-fatigue scale is a 13 item Likert scaled instrument where the subject was presented with 13 statements and asked to indicate their response as it applied to the past 7 days. The 5 possible responses were 'Not at all' (0), 'A little bit' (1), 'Somewhat' (2), 'Quite a bit' (3) and 'Very much' (4).

With 13 statements the total score had a range of 0 to 52. Higher score corresponds to a higher QoL. The ITT set included all randomized subjects.

| | |
|----------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Week 17 and Week 48 | |

| End point values | Open-label Period: Continue Pegcetacoplan | Open-label Period: Crossover to Pegcetacoplan | | |
|--------------------------------------|---|---|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 30 | 26 | | |
| Units: Score on a scale | | | | |
| arithmetic mean (standard deviation) | 13.13 (± 46.296) | 62.92 (± 60.053) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Baseline to Week 48 in QLQ-C30 Scores During the Treatment Period

| | |
|-----------------|--|
| End point title | Mean Change From Baseline to Week 48 in QLQ-C30 Scores During the Treatment Period |
|-----------------|--|

End point description:

The EORTC QLQ-C30 questionnaire (version 3.0) consists of 30 questions comprised of both multi-item scales and single-item measures to assess overall QoL in subjects. Questions are designated by functional scales, symptom scales, and global subject QoL/overall perceived health status. For the first 28 questions the 4 possible responses are 'Not at all' (1), 'A little' (2), 'Quite a bit' (3) and 'Very much' (4). For the remaining 2 questions the response is requested on a 7-point scale from 1 ('Very poor') to 7 ('Excellent'). The raw scale scores were linear transformed, producing scale scores that ranged from 0% to 100%. A high scale score represents a higher response level. Hence for the functional scales and the global health status a higher score indicates a better QoL, whilst for the symptom scale scores this is implied by a lower score. The ITT set included all randomized subjects.

| | |
|----------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Baseline and Week 48 | |

| End point values | Treatment Period: Pegcetacoplan | Treatment Period: Eculizumab | | |
|--|---------------------------------|------------------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 30 | 28 | | |
| Units: Score on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Global Health Status/QoL | 18.89 (± 17.635) | 13.99 (± 22.912) | | |
| Functional Scales - Physical functioning | 15.33 (± 15.278) | 10.80 (± 17.765) | | |

| | | | | |
|---|-------------------|-------------------|--|--|
| Functional Scales - Role functioning | 16.67 (± 27.334) | 20.11 (± 27.595) | | |
| Functional Scales - Emotional functioning | 10.28 (± 18.657) | 5.36 (± 17.005) | | |
| Functional Scales - Cognitive functioning | 7.78 (± 23.462) | 0.00 (± 18.703) | | |
| Functional Scales - Social functioning | 16.11 (± 24.166) | 14.88 (± 22.379) | | |
| Symptom Scales - Fatigue | -21.48 (± 26.733) | -23.75 (± 29.506) | | |
| Symptom Scales - Nausea and vomiting | -2.22 (± 11.357) | 0.00 (± 4.454) | | |
| Symptom Scales - Pain | 0.56 (± 27.849) | 3.45 (± 20.596) | | |
| Symptom Scales - Dyspnoea | -17.78 (± 29.985) | -27.59 (± 33.415) | | |
| Symptom Scales - Insomnia | -6.67 (± 25.371) | 0.00 (± 28.172) | | |
| Symptom Scales - Appetite loss | -7.78 (± 14.339) | -3.45 (± 22.440) | | |
| Symptom Scales - Constipation | -1.11 (± 22.289) | -2.38 (± 8.742) | | |
| Symptom Scales - Diarrhoea | 1.11 (± 29.664) | 5.95 (± 15.853) | | |
| Symptom Scales - Financial difficulties | -15.56 (± 24.343) | -8.33 (± 19.510) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Week 17 to Week 48 in QLQ-C30 Scores During the Open-label Period

| | |
|--|--|
| End point title | Mean Change From Week 17 to Week 48 in QLQ-C30 Scores During the Open-label Period |
| End point description: | |
| <p>The EORTC QLQ-C30 questionnaire (version 3.0) consists of 30 questions comprised of both multi-item scales and single-item measures to assess overall QoL in subjects. Questions are designated by functional scales, symptom scales, and global subject QoL/overall perceived health status. For the first 28 questions the 4 possible responses are 'Not at all' (1), 'A little' (2), 'Quite a bit' (3) and 'Very much' (4). For the remaining 2 questions the response is requested on a 7-point scale from 1 ('Very poor') to 7 ('Excellent'). The raw scale scores were linear transformed, producing scale scores that ranged from 0% to 100%. A high scale score represents a higher response level. Hence for the functional scales and the global health status a higher score indicates a better QoL, whilst for the symptom scale scores this is implied by a lower score. The ITT set included all randomized subjects.</p> | |
| End point type | Secondary |
| End point timeframe: | |
| Week 17 and Week 48 | |

| End point values | Open-label Period: Continue Pegcetacoplan | Open-label Period: Crossover to Pegcetacoplan | | |
|--|--|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 30 | 26 | | |
| Units: Score on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Global Health Status/QoL | 7.22 (± 19.664) | 23.08 (± 22.149) | | |
| Functional Scales - Physical functioning | 0.89 (± 10.168) | 11.03 (± 17.173) | | |
| Functional Scales - Role functioning | 5.00 (± 20.599) | 19.87 (± 22.617) | | |
| Functional Scales - Emotional functioning | -2.22 (± 27.328) | 1.92 (± 13.806) | | |
| Functional Scales - Cognitive functioning | -2.78 (± 16.999) | 2.56 (± 24.355) | | |
| Functional Scales - Social functioning | 3.89 (± 18.919) | 12.18 (± 23.361) | | |
| Symptom Scales - Fatigue | -2.96 (± 20.824) | -23.08 (± 28.790) | | |
| Symptom Scales - Nausea and vomiting | -2.22 (± 5.762) | -4.49 (± 12.072) | | |
| Symptom Scales - Pain | -2.78 (± 23.195) | -5.77 (± 21.051) | | |
| Symptom Scales - Dyspnoea | 3.33 (± 25.295) | -19.23 (± 28.555) | | |
| Symptom Scales - Insomnia | 8.89 (± 23.050) | -5.13 (± 27.797) | | |
| Symptom Scales - Appetite loss | -8.89 (± 26.164) | -5.13 (± 22.494) | | |
| Symptom Scales - Constipation | -1.11 (± 20.498) | -1.28 (± 11.473) | | |
| Symptom Scales - Diarrhoea | -4.44 (± 28.679) | 3.85 (± 27.206) | | |
| Symptom Scales - Financial difficulties | -2.22 (± 12.172) | -2.56 (± 16.119) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Total Number of PRBC Units Transfused During the Open-Label Period

| | |
|-----------------|--|
| End point title | Total Number of PRBC Units Transfused During the Open-Label Period |
|-----------------|--|

End point description:

Number of units of PRBC transfused to subjects in the open-label period are reported. The ITT set included all randomized subjects.

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

End point timeframe:

Week 17 to Week 48

| End point values | Open-label Period: Continue Pegcetacoplan | Open-label Period: Crossover to Pegcetacoplan | Open-label Run-in Period: Crossover to Pegcetacoplan | |
|-----------------------------|--|--|---|--|
| Subject group type | Reporting group | Reporting group | Subject analysis set | |
| Number of subjects analysed | 38 | 39 | 38 | |
| Units: PRBC Units | | | | |
| number (not applicable) | 68 | 110 | 14 | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Day -28 to Week 54, a maximum of approximately 58 weeks

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

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 20.0 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|--|
| Reporting group title | Run-in Periods: Pegcetacoplan + Eculizumab |
|-----------------------|--|

Reporting group description:

During the 4-week run-in period (Day -28 to ≤Day 1) all subjects received twice-weekly SC doses of pegcetacoplan 1080 mg in addition to their current dosage of eculizumab treatment. During the 4-week open-label run-in period (Week 17 to Week 20) subjects randomized to receive monotherapy with their pre-screening stable dose of eculizumab via intravenous infusion every 2 weeks during the RCP also received twice-weekly SC doses of pegcetacoplan 1080 mg.

| | |
|-----------------------|----------------------------------|
| Reporting group title | Open-label Period: Pegcetacoplan |
|-----------------------|----------------------------------|

Reporting group description:

The subjects who were randomized to receive monotherapy with SC infusions of pegcetacoplan 1080 mg twice-weekly or every 3 days during the RCP continued to receive monotherapy with pegcetacoplan until the end of the open-label period (Week 17 to Week 48). Subjects randomized to receive monotherapy with their pre-screening stable dose of eculizumab via intravenous infusion every 2 weeks during the RCP received monotherapy with SC infusions of pegcetacoplan 1080 mg twice-weekly or every 3 days after the open-label run-in period, up to the end of the open-label period (Week 20 to Week 48).

| | |
|-----------------------|-----------------|
| Reporting group title | RCP: Eculizumab |
|-----------------------|-----------------|

Reporting group description:

Subjects randomized to receive monotherapy with their pre-screening stable dose of eculizumab via intravenous infusion every 2 weeks during the RCP.

| | |
|-----------------------|--------------------|
| Reporting group title | RCP: Pegcetacoplan |
|-----------------------|--------------------|

Reporting group description:

Subjects randomized to receive monotherapy with SC infusions of pegcetacoplan 1080 mg twice-weekly or every 3 days during the RCP.

| Serious adverse events | Run-in Periods: Pegcetacoplan + Eculizumab | Open-label Period: Pegcetacoplan | RCP: Eculizumab |
|---|--|-------------------------------------|-----------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 4 / 80 (5.00%) | 18 / 77 (23.38%) | 5 / 39 (12.82%) |
| number of deaths (all causes) | 0 | 1 | 0 |
| number of deaths resulting from adverse events | 0 | 1 | 0 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Acute myeloid leukaemia | | | |
| subjects affected / exposed | 0 / 80 (0.00%) | 1 / 77 (1.30%) | 0 / 39 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diffuse large B-cell lymphoma | | | |

| | | | |
|--|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 80 (0.00%) | 1 / 77 (1.30%) | 0 / 39 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vascular disorders | | | |
| Deep vein thrombosis | | | |
| subjects affected / exposed | 0 / 80 (0.00%) | 1 / 77 (1.30%) | 0 / 39 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| General disorders and administration site conditions | | | |
| Pyrexia | | | |
| subjects affected / exposed | 0 / 80 (0.00%) | 0 / 77 (0.00%) | 0 / 39 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hyperthermia | | | |
| subjects affected / exposed | 0 / 80 (0.00%) | 0 / 77 (0.00%) | 1 / 39 (2.56%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Immune system disorders | | | |
| Allergy to immunoglobulin therapy | | | |
| subjects affected / exposed | 0 / 80 (0.00%) | 1 / 77 (1.30%) | 0 / 39 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Reproductive system and breast disorders | | | |
| Ovarian cyst | | | |
| subjects affected / exposed | 0 / 80 (0.00%) | 1 / 77 (1.30%) | 0 / 39 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Dyspnoea | | | |
| subjects affected / exposed | 0 / 80 (0.00%) | 0 / 77 (0.00%) | 0 / 39 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Epistaxis | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 80 (0.00%) | 1 / 77 (1.30%) | 0 / 39 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypersensitivity pneumonitis | | | |
| subjects affected / exposed | 0 / 80 (0.00%) | 1 / 77 (1.30%) | 0 / 39 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac disorders | | | |
| Atrial fibrillation | | | |
| subjects affected / exposed | 0 / 80 (0.00%) | 0 / 77 (0.00%) | 0 / 39 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nervous system disorders | | | |
| Facial paralysis | | | |
| subjects affected / exposed | 0 / 80 (0.00%) | 0 / 77 (0.00%) | 0 / 39 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Blood and lymphatic system disorders | | | |
| Haemolysis | | | |
| subjects affected / exposed | 1 / 80 (1.25%) | 5 / 77 (6.49%) | 1 / 39 (2.56%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 5 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cytopenia | | | |
| subjects affected / exposed | 0 / 80 (0.00%) | 1 / 77 (1.30%) | 0 / 39 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Haemolytic anaemia | | | |
| subjects affected / exposed | 0 / 80 (0.00%) | 1 / 77 (1.30%) | 1 / 39 (2.56%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Thrombocytopenia | | | |
| subjects affected / exposed | 0 / 80 (0.00%) | 1 / 77 (1.30%) | 0 / 39 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|----------------|----------------|----------------|
| Anaemia | | | |
| subjects affected / exposed | 0 / 80 (0.00%) | 0 / 77 (0.00%) | 2 / 39 (5.13%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal disorders | | | |
| Abdominal pain | | | |
| subjects affected / exposed | 0 / 80 (0.00%) | 1 / 77 (1.30%) | 1 / 39 (2.56%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Intestinal ischaemia | | | |
| subjects affected / exposed | 0 / 80 (0.00%) | 1 / 77 (1.30%) | 0 / 39 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Oedematous pancreatitis | | | |
| subjects affected / exposed | 0 / 80 (0.00%) | 1 / 77 (1.30%) | 0 / 39 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Small intestinal obstruction | | | |
| subjects affected / exposed | 0 / 80 (0.00%) | 1 / 77 (1.30%) | 0 / 39 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatobiliary disorders | | | |
| Cholelithiasis | | | |
| subjects affected / exposed | 0 / 80 (0.00%) | 1 / 77 (1.30%) | 0 / 39 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatocellular injury | | | |
| subjects affected / exposed | 0 / 80 (0.00%) | 0 / 77 (0.00%) | 1 / 39 (2.56%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hyperbilirubinaemia | | | |
| subjects affected / exposed | 0 / 80 (0.00%) | 0 / 77 (0.00%) | 1 / 39 (2.56%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|----------------|----------------|----------------|
| Jaundice | | | |
| subjects affected / exposed | 0 / 80 (0.00%) | 0 / 77 (0.00%) | 1 / 39 (2.56%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal and urinary disorders | | | |
| Acute kidney injury | | | |
| subjects affected / exposed | 0 / 80 (0.00%) | 1 / 77 (1.30%) | 0 / 39 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Haematoma muscle | | | |
| subjects affected / exposed | 0 / 80 (0.00%) | 1 / 77 (1.30%) | 0 / 39 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| COVID-19 | | | |
| subjects affected / exposed | 0 / 80 (0.00%) | 1 / 77 (1.30%) | 0 / 39 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| Gastroenteritis | | | |
| subjects affected / exposed | 0 / 80 (0.00%) | 2 / 77 (2.60%) | 0 / 39 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bacterial infection | | | |
| subjects affected / exposed | 0 / 80 (0.00%) | 0 / 77 (0.00%) | 0 / 39 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Biliary sepsis | | | |
| subjects affected / exposed | 0 / 80 (0.00%) | 1 / 77 (1.30%) | 0 / 39 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diverticulitis | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 80 (0.00%) | 1 / 77 (1.30%) | 0 / 39 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Post procedural sepsis | | | |
| subjects affected / exposed | 0 / 80 (0.00%) | 1 / 77 (1.30%) | 0 / 39 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Sepsis | | | |
| subjects affected / exposed | 2 / 80 (2.50%) | 1 / 77 (1.30%) | 0 / 39 (0.00%) |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 0 / 80 (0.00%) | 1 / 77 (1.30%) | 0 / 39 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nasopharyngitis | | | |
| subjects affected / exposed | 1 / 80 (1.25%) | 0 / 77 (0.00%) | 0 / 39 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| Serious adverse events | RCP: Pegcetacoplan | | |
|---|--------------------|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 7 / 41 (17.07%) | | |
| number of deaths (all causes) | 0 | | |
| number of deaths resulting from adverse events | 0 | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Acute myeloid leukaemia | | | |
| subjects affected / exposed | 0 / 41 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Diffuse large B-cell lymphoma | | | |
| subjects affected / exposed | 0 / 41 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

| | | | |
|--|----------------|--|--|
| Vascular disorders | | | |
| Deep vein thrombosis | | | |
| subjects affected / exposed | 0 / 41 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| General disorders and administration site conditions | | | |
| Pyrexia | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hyperthermia | | | |
| subjects affected / exposed | 0 / 41 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Immune system disorders | | | |
| Allergy to immunoglobulin therapy | | | |
| subjects affected / exposed | 0 / 41 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Reproductive system and breast disorders | | | |
| Ovarian cyst | | | |
| subjects affected / exposed | 0 / 41 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Dyspnoea | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Epistaxis | | | |
| subjects affected / exposed | 0 / 41 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hypersensitivity pneumonitis | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 0 / 41 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cardiac disorders | | | |
| Atrial fibrillation | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Nervous system disorders | | | |
| Facial paralysis | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Blood and lymphatic system disorders | | | |
| Haemolysis | | | |
| subjects affected / exposed | 2 / 41 (4.88%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cytopenia | | | |
| subjects affected / exposed | 0 / 41 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Haemolytic anaemia | | | |
| subjects affected / exposed | 0 / 41 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Thrombocytopenia | | | |
| subjects affected / exposed | 0 / 41 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Anaemia | | | |
| subjects affected / exposed | 0 / 41 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

| | | | |
|---|----------------|--|--|
| Gastrointestinal disorders | | | |
| Abdominal pain | | | |
| subjects affected / exposed | 0 / 41 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Intestinal ischaemia | | | |
| subjects affected / exposed | 0 / 41 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Oedematous pancreatitis | | | |
| subjects affected / exposed | 0 / 41 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Small intestinal obstruction | | | |
| subjects affected / exposed | 0 / 41 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hepatobiliary disorders | | | |
| Cholelithiasis | | | |
| subjects affected / exposed | 0 / 41 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hepatocellular injury | | | |
| subjects affected / exposed | 0 / 41 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hyperbilirubinaemia | | | |
| subjects affected / exposed | 0 / 41 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Jaundice | | | |
| subjects affected / exposed | 0 / 41 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

| | | | |
|---|----------------|--|--|
| Renal and urinary disorders | | | |
| Acute kidney injury | | | |
| subjects affected / exposed | 0 / 41 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Musculoskeletal and connective tissue disorders | | | |
| Haematoma muscle | | | |
| subjects affected / exposed | 0 / 41 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Infections and infestations | | | |
| COVID-19 | | | |
| subjects affected / exposed | 0 / 41 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastroenteritis | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Bacterial infection | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Biliary sepsis | | | |
| subjects affected / exposed | 0 / 41 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Diverticulitis | | | |
| subjects affected / exposed | 0 / 41 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Post procedural sepsis | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 0 / 41 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Sepsis | | | |
| subjects affected / exposed | 0 / 41 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 0 / 41 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 0 / 41 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

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

| Non-serious adverse events | Run-in Periods: Pegcetacoplan + Eculizumab | Open-label Period: Pegcetacoplan | RCP: Eculizumab |
|---|--|-------------------------------------|------------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 71 / 80 (88.75%) | 71 / 77 (92.21%) | 36 / 39 (92.31%) |
| Vascular disorders | | | |
| Hypertension | | | |
| subjects affected / exposed | 0 / 80 (0.00%) | 3 / 77 (3.90%) | 1 / 39 (2.56%) |
| occurrences (all) | 0 | 4 | 1 |
| General disorders and administration site conditions | | | |
| Injection site erythema | | | |
| subjects affected / exposed | 33 / 80 (41.25%) | 9 / 77 (11.69%) | 0 / 39 (0.00%) |
| occurrences (all) | 75 | 127 | 0 |
| Fatigue | | | |
| subjects affected / exposed | 5 / 80 (6.25%) | 8 / 77 (10.39%) | 6 / 39 (15.38%) |
| occurrences (all) | 5 | 11 | 7 |
| Pyrexia | | | |

| | | | |
|---|------------------------|----------------------|----------------------|
| subjects affected / exposed occurrences (all) | 6 / 80 (7.50%) 6 | 6 / 77 (7.79%) 9 | 1 / 39 (2.56%) 1 |
| Injection site pruritus subjects affected / exposed occurrences (all) | 12 / 80 (15.00%) 14 | 5 / 77 (6.49%) 7 | 0 / 39 (0.00%) 0 |
| Asthenia subjects affected / exposed occurrences (all) | 1 / 80 (1.25%) 1 | 4 / 77 (5.19%) 4 | 5 / 39 (12.82%) 7 |
| Injection site bruising subjects affected / exposed occurrences (all) | 2 / 80 (2.50%) 3 | 3 / 77 (3.90%) 7 | 0 / 39 (0.00%) 0 |
| Injection site induration subjects affected / exposed occurrences (all) | 5 / 80 (6.25%) 12 | 5 / 77 (6.49%) 27 | 0 / 39 (0.00%) 0 |
| Injection site reaction subjects affected / exposed occurrences (all) | 8 / 80 (10.00%) 26 | 2 / 77 (2.60%) 8 | 0 / 39 (0.00%) 0 |
| Injection site swelling subjects affected / exposed occurrences (all) | 10 / 80 (12.50%) 18 | 1 / 77 (1.30%) 4 | 0 / 39 (0.00%) 0 |
| Injection site pain subjects affected / exposed occurrences (all) | 6 / 80 (7.50%) 13 | 4 / 77 (5.19%) 68 | 0 / 39 (0.00%) 0 |
| Vaccination site pain subjects affected / exposed occurrences (all) | 3 / 80 (3.75%) 3 | 0 / 77 (0.00%) 0 | 2 / 39 (5.13%) 2 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough subjects affected / exposed occurrences (all) | 2 / 80 (2.50%) 2 | 9 / 77 (11.69%) 9 | 1 / 39 (2.56%) 1 |
| Oropharyngeal pain subjects affected / exposed occurrences (all) | 0 / 80 (0.00%) 0 | 6 / 77 (7.79%) 7 | 3 / 39 (7.69%) 3 |
| Dyspnoea | | | |

| | | | |
|--|---------------------|---------------------|---------------------|
| subjects affected / exposed occurrences (all) | 4 / 80 (5.00%) 4 | 2 / 77 (2.60%) 2 | 3 / 39 (7.69%) 4 |
| Psychiatric disorders | | | |
| Anxiety | | | |
| subjects affected / exposed | 2 / 80 (2.50%) | 4 / 77 (5.19%) | 2 / 39 (5.13%) |
| occurrences (all) | 2 | 5 | 2 |
| Insomnia | | | |
| subjects affected / exposed | 0 / 80 (0.00%) | 1 / 77 (1.30%) | 2 / 39 (5.13%) |
| occurrences (all) | 0 | 1 | 2 |
| Injury, poisoning and procedural complications | | | |
| Vaccination complication | | | |
| subjects affected / exposed | 2 / 80 (2.50%) | 2 / 77 (2.60%) | 0 / 39 (0.00%) |
| occurrences (all) | 3 | 2 | 0 |
| Contusion | | | |
| subjects affected / exposed | 3 / 80 (3.75%) | 4 / 77 (5.19%) | 0 / 39 (0.00%) |
| occurrences (all) | 3 | 4 | 0 |
| Cardiac disorders | | | |
| Palpitations | | | |
| subjects affected / exposed | 1 / 80 (1.25%) | 1 / 77 (1.30%) | 2 / 39 (5.13%) |
| occurrences (all) | 2 | 1 | 2 |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 10 / 80 (12.50%) | 8 / 77 (10.39%) | 9 / 39 (23.08%) |
| occurrences (all) | 12 | 13 | 10 |
| Dizziness | | | |
| subjects affected / exposed | 3 / 80 (3.75%) | 3 / 77 (3.90%) | 5 / 39 (12.82%) |
| occurrences (all) | 3 | 3 | 5 |
| Lethargy | | | |
| subjects affected / exposed | 0 / 80 (0.00%) | 0 / 77 (0.00%) | 2 / 39 (5.13%) |
| occurrences (all) | 0 | 0 | 2 |
| Blood and lymphatic system disorders | | | |
| Haemolysis | | | |
| subjects affected / exposed | 1 / 80 (1.25%) | 13 / 77 (16.88%) | 9 / 39 (23.08%) |
| occurrences (all) | 1 | 14 | 14 |
| Thrombocytopenia | | | |

| | | | |
|--|------------------|------------------|-----------------|
| subjects affected / exposed | 2 / 80 (2.50%) | 3 / 77 (3.90%) | 0 / 39 (0.00%) |
| occurrences (all) | 2 | 5 | 0 |
| Anaemia | | | |
| subjects affected / exposed | 1 / 80 (1.25%) | 2 / 77 (2.60%) | 5 / 39 (12.82%) |
| occurrences (all) | 1 | 2 | 5 |
| Gastrointestinal disorders | | | |
| Diarrhoea | | | |
| subjects affected / exposed | 10 / 80 (12.50%) | 11 / 77 (14.29%) | 2 / 39 (5.13%) |
| occurrences (all) | 11 | 15 | 2 |
| Abdominal pain | | | |
| subjects affected / exposed | 2 / 80 (2.50%) | 3 / 77 (3.90%) | 3 / 39 (7.69%) |
| occurrences (all) | 2 | 3 | 3 |
| Abdominal distension | | | |
| subjects affected / exposed | 1 / 80 (1.25%) | 4 / 77 (5.19%) | 1 / 39 (2.56%) |
| occurrences (all) | 1 | 4 | 1 |
| Nausea | | | |
| subjects affected / exposed | 7 / 80 (8.75%) | 2 / 77 (2.60%) | 2 / 39 (5.13%) |
| occurrences (all) | 8 | 4 | 2 |
| Vomiting | | | |
| subjects affected / exposed | 1 / 80 (1.25%) | 3 / 77 (3.90%) | 4 / 39 (10.26%) |
| occurrences (all) | 1 | 3 | 4 |
| Abdominal discomfort | | | |
| subjects affected / exposed | 2 / 80 (2.50%) | 0 / 77 (0.00%) | 2 / 39 (5.13%) |
| occurrences (all) | 2 | 0 | 2 |
| Constipation | | | |
| subjects affected / exposed | 1 / 80 (1.25%) | 2 / 77 (2.60%) | 3 / 39 (7.69%) |
| occurrences (all) | 1 | 2 | 3 |
| Hepatobiliary disorders | | | |
| Hyperbilirubinaemia | | | |
| subjects affected / exposed | 0 / 80 (0.00%) | 3 / 77 (3.90%) | 2 / 39 (5.13%) |
| occurrences (all) | 0 | 3 | 2 |
| Skin and subcutaneous tissue disorders | | | |
| Erythema | | | |
| subjects affected / exposed | 0 / 80 (0.00%) | 3 / 77 (3.90%) | 0 / 39 (0.00%) |
| occurrences (all) | 0 | 3 | 0 |
| Renal and urinary disorders | | | |

| | | | |
|---|---------------------|------------------------|----------------------|
| Acute kidney injury subjects affected / exposed occurrences (all) | 0 / 80 (0.00%) 0 | 4 / 77 (5.19%) 4 | 0 / 39 (0.00%) 0 |
| Chromaturia subjects affected / exposed occurrences (all) | 3 / 80 (3.75%) 3 | 2 / 77 (2.60%) 2 | 2 / 39 (5.13%) 3 |
| Haemoglobinuria subjects affected / exposed occurrences (all) | 0 / 80 (0.00%) 0 | 1 / 77 (1.30%) 1 | 2 / 39 (5.13%) 2 |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia subjects affected / exposed occurrences (all) | 2 / 80 (2.50%) 2 | 6 / 77 (7.79%) 7 | 2 / 39 (5.13%) 2 |
| Pain in extremity subjects affected / exposed occurrences (all) | 3 / 80 (3.75%) 3 | 5 / 77 (6.49%) 6 | 2 / 39 (5.13%) 2 |
| Back pain subjects affected / exposed occurrences (all) | 3 / 80 (3.75%) 3 | 2 / 77 (2.60%) 2 | 4 / 39 (10.26%) 4 |
| Myalgia subjects affected / exposed occurrences (all) | 3 / 80 (3.75%) 3 | 4 / 77 (5.19%) 4 | 1 / 39 (2.56%) 3 |
| Infections and infestations | | | |
| Nasopharyngitis subjects affected / exposed occurrences (all) | 4 / 80 (5.00%) 5 | 12 / 77 (15.58%) 13 | 2 / 39 (5.13%) 2 |
| Upper respiratory tract infection subjects affected / exposed occurrences (all) | 0 / 80 (0.00%) 0 | 7 / 77 (9.09%) 8 | 1 / 39 (2.56%) 1 |
| Urinary tract infection subjects affected / exposed occurrences (all) | 1 / 80 (1.25%) 1 | 7 / 77 (9.09%) 7 | 2 / 39 (5.13%) 2 |
| Oral herpes subjects affected / exposed occurrences (all) | 1 / 80 (1.25%) 1 | 6 / 77 (7.79%) 7 | 0 / 39 (0.00%) 0 |
| Sinusitis | | | |

| | | | |
|--|---------------------|---------------------|---------------------|
| subjects affected / exposed occurrences (all) | 1 / 80 (1.25%) 1 | 3 / 77 (3.90%) 3 | 2 / 39 (5.13%) 2 |
| Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all) | 0 / 80 (0.00%) 0 | 2 / 77 (2.60%) 2 | 2 / 39 (5.13%) 2 |

| | | | |
|---|---|--|--|
| Non-serious adverse events | RCP: Pegcetacoplan | | |
| Total subjects affected by non-serious adverse events subjects affected / exposed | 36 / 41 (87.80%) | | |
| Vascular disorders Hypertension subjects affected / exposed occurrences (all) | 3 / 41 (7.32%) 3 | | |
| General disorders and administration site conditions Injection site erythema subjects affected / exposed occurrences (all) Fatigue subjects affected / exposed occurrences (all) Pyrexia subjects affected / exposed occurrences (all) Injection site pruritus subjects affected / exposed occurrences (all) Asthenia subjects affected / exposed occurrences (all) Injection site bruising subjects affected / exposed occurrences (all) Injection site induration subjects affected / exposed occurrences (all) Injection site reaction | 7 / 41 (17.07%) 44 2 / 41 (4.88%) 2 1 / 41 (2.44%) 1 1 / 41 (2.44%) 1 3 / 41 (7.32%) 3 2 / 41 (4.88%) 2 3 / 41 (7.32%) 8 | | |

| | | | |
|--|--|--|--|
| <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>4 / 41 (9.76%)</p> <p>56</p> | | | |
| <p>Injection site swelling</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>4 / 41 (9.76%)</p> <p>6</p> | | | |
| <p>Injection site pain</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>1 / 41 (2.44%)</p> <p>9</p> | | | |
| <p>Vaccination site pain</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>0 / 41 (0.00%)</p> <p>0</p> | | | |
| <p>Respiratory, thoracic and mediastinal disorders</p> <p>Cough</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>1 / 41 (2.44%)</p> <p>1</p> <p>Oropharyngeal pain</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>0 / 41 (0.00%)</p> <p>0</p> <p>Dyspnoea</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>1 / 41 (2.44%)</p> <p>1</p> | | | |
| <p>Psychiatric disorders</p> <p>Anxiety</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>1 / 41 (2.44%)</p> <p>1</p> <p>Insomnia</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>0 / 41 (0.00%)</p> <p>0</p> | | | |
| <p>Injury, poisoning and procedural complications</p> <p>Vaccination complication</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>2 / 41 (4.88%)</p> <p>2</p> <p>Contusion</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>1 / 41 (2.44%)</p> <p>1</p> | | | |
| Cardiac disorders | | | |

| | | | |
|---|---|--|--|
| Palpitations subjects affected / exposed occurrences (all) | 0 / 41 (0.00%) 0 | | |
| Nervous system disorders Headache subjects affected / exposed occurrences (all) Dizziness subjects affected / exposed occurrences (all) Lethargy subjects affected / exposed occurrences (all) | 2 / 41 (4.88%) 2 1 / 41 (2.44%) 1 0 / 41 (0.00%) 0 | | |
| Blood and lymphatic system disorders Haemolysis subjects affected / exposed occurrences (all) Thrombocytopenia subjects affected / exposed occurrences (all) Anaemia subjects affected / exposed occurrences (all) | 4 / 41 (9.76%) 4 2 / 41 (4.88%) 2 0 / 41 (0.00%) 0 | | |
| Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all) Abdominal pain subjects affected / exposed occurrences (all) Abdominal distension subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all) Vomiting | 9 / 41 (21.95%) 9 4 / 41 (9.76%) 4 0 / 41 (0.00%) 0 2 / 41 (4.88%) 2 | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 0 / 41 (0.00%) | | |
| occurrences (all) | 0 | | |
| Abdominal discomfort | | | |
| subjects affected / exposed | 2 / 41 (4.88%) | | |
| occurrences (all) | 2 | | |
| Constipation | | | |
| subjects affected / exposed | 0 / 41 (0.00%) | | |
| occurrences (all) | 0 | | |
| Hepatobiliary disorders | | | |
| Hyperbilirubinaemia | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 1 | | |
| Skin and subcutaneous tissue disorders | | | |
| Erythema | | | |
| subjects affected / exposed | 2 / 41 (4.88%) | | |
| occurrences (all) | 2 | | |
| Renal and urinary disorders | | | |
| Acute kidney injury | | | |
| subjects affected / exposed | 0 / 41 (0.00%) | | |
| occurrences (all) | 0 | | |
| Chromaturia | | | |
| subjects affected / exposed | 0 / 41 (0.00%) | | |
| occurrences (all) | 0 | | |
| Haemoglobinuria | | | |
| subjects affected / exposed | 0 / 41 (0.00%) | | |
| occurrences (all) | 0 | | |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 2 / 41 (4.88%) | | |
| occurrences (all) | 2 | | |
| Pain in extremity | | | |
| subjects affected / exposed | 2 / 41 (4.88%) | | |
| occurrences (all) | 5 | | |
| Back pain | | | |
| subjects affected / exposed | 3 / 41 (7.32%) | | |
| occurrences (all) | 4 | | |

| | | | |
|---|---------------------|--|--|
| Myalgia subjects affected / exposed occurrences (all) | 1 / 41 (2.44%) 1 | | |
| Infections and infestations | | | |
| Nasopharyngitis subjects affected / exposed occurrences (all) | 3 / 41 (7.32%) 3 | | |
| Upper respiratory tract infection subjects affected / exposed occurrences (all) | 1 / 41 (2.44%) 1 | | |
| Urinary tract infection subjects affected / exposed occurrences (all) | 0 / 41 (0.00%) 0 | | |
| Oral herpes subjects affected / exposed occurrences (all) | 2 / 41 (4.88%) 2 | | |
| Sinusitis subjects affected / exposed occurrences (all) | 1 / 41 (2.44%) 1 | | |
| Metabolism and nutrition disorders | | | |
| Decreased appetite subjects affected / exposed occurrences (all) | 0 / 41 (0.00%) 0 | | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|------------------|--|
| 21 August 2018 | <p>Protocol amendment 1 included the following changes:</p> <ul style="list-style-type: none">- Allowed subjects to proceed to Visit 2 at any time (rather than waiting at least 2 weeks) after confirmation of study eligibility.- Clarified the appropriate 6-hour postdose pharmacokinetics sample window: ± 30 minutes.- End of trial was defined as follows: The end of the trial is defined as when the last subject either completes their Week 48 visit and enrolls in the long-term safety extension (LTSE) study, or, should a subject elect not to enter the LTSE study, when the last subject completes their exit visit at Week 60.- Clarified that during the 4-week run-in period (Week - 4 to Day -1), Visit 5 (Day 1), and through the course of the study, pegcetacoplan administration and study visits should be conducted and scheduled independently of each subject's regular eculizumab administration schedule.- Inclusion Criterion #13: added to require that subjects have a body mass index (BMI) ≤ 40 in order to qualify for study entry.- Inclusion Criterion #5: updated eligibility of ARC $> 1.0 \times$ upper limit of normal (ULN) at screening visit (from previous requirement of $> 1.5 \times$ ULN).- LDH isoenzymes and erythropoietin were added to the serum chemistry panel. |
| 13 December 2018 | <p>Protocol amendment 2 included the following changes:</p> <ul style="list-style-type: none">- Screening window extended to up to 8 weeks (Week - 12)- Clarified that use of silica reagents in coagulation panels was to be avoided.- Added emphasis that subjects should be instructed to take pegcetacoplan treatment as prescribed and should contact the investigator immediately for guidance in the event of any missed doses.- Allowed administration of eculizumab at home.- Clarified that there was no requirement for eculizumab to be administered on the day of a study visit.- Clarified that subjects administer pegcetacoplan at the study site through the run-in period and on Day 1. After that, every effort should be made to ensure that the subject's pegcetacoplan dosing schedule aligned with study visit days. If not possible, dosing should occur according to the dosing schedule and not the visit schedule, as there was no requirement for subjects to administer pegcetacoplan at the study site.- Noted that if a screening visit was more than 28 days before dosing, the hematology panel should be repeated. |
| 08 February 2019 | <p>Protocol amendment 3 included the following changes:</p> <ul style="list-style-type: none">- Re-arranged secondary endpoints into key secondary and secondary endpoints. The classification of "tertiary endpoints" was removed and former tertiary endpoints were reclassified as secondary endpoints. The duration of when the endpoint was being assessed was specified within some endpoint descriptions for clarity.- Modified randomization stratification factors as follows:<ol style="list-style-type: none">1. Number of PRBC transfusions within the 12 months prior to Day -28 (< 4; ≥ 4)2. Platelet count at screening ($< 100,000$; $\geq 100,000$).- The study diagram and descriptions of the study were modified to remove references to the wash-out period.- Modified Inclusion Criterion #13: excluded subjects with Class 2 or greater obesity (subjects with a BMI ≥ 35.0 kg/m²). |

| | |
|----------------|--|
| 16 August 2019 | <p>Protocol amendment 4 included the following changes:</p> <ul style="list-style-type: none"> - Clarified <i>S. pneumoniae</i> vaccination requirements. - Clarified that during the screening period (from up to Week -12 to Week -4), clinical laboratory tests (eg, hematology, coagulation, serum chemistry, flow cytometry, urinalysis) could be repeated with written approval from the sponsor (including the assigned medical monitor), with no requirement to designate the subject as a screen failure. - Dose adjustment was updated to mandate dose escalation to 1080 mg every third day upon the first instance of LDH $>2 \times$ ULN, rather than requiring LDH to be elevated on 2 consecutive occasions at least 1 week apart. - Clarified subject transfusion history collection requirements. |
| 06 May 2020 | <p>As a result of the COVID-19 global pandemic, Apellis issued an Urgent Safety Measure to safeguard the rights, welfare, and safety of APL2-302 study subjects and investigative site staff.</p> <p>Protocol amendment 5 included the following changes:</p> <ul style="list-style-type: none"> - Added clarifying language to indicate that a dose adjustment can occur for subjects receiving pegcetacoplan monotherapy if LDH is $>2 \times$ ULN "on 1 occasion." - Terminology updated to reflect current language regarding antidrug antibody assessments, pegcetacoplan peptide antibodies, or anti-pegcetacoplan antibodies. - The "Unknown" category of relationship between adverse events and serious adverse events to study treatment was removed. - Severity of events definitions were updated. - Appendix 6 added to reflect changes made as a result of the COVID-19 pandemic. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported