# Clinical trial results:
# A randomized, repeat dose, open label, parallel group, multi-center study to evaluate the effect of daprodustat compared to darbepoetin alfa on forearm blood flow in participants with anemia of chronic kidney disease that are not dialysis dependent

## Summary

| | |
|---|---|
| EudraCT number | 2017-002268-42 |
| Trial protocol | GB |
| Global end of trial date | 29 May 2019 |

**Results information**

| | |
|---|---|
| Result version number | v2 (current) |
| This version publication date | 23 July 2021 |
| First version publication date | 03 June 2021 |
| Version creation reason | |

## Trial information

**Trial identification**

| | |
|---|---|
| Sponsor protocol code | 205767 |

**Additional study identifiers**

| | |
|---|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT03446612 |
| WHO universal trial number (UTN) | - |

Notes:

**Sponsors**

| | |
|---|---|
| Sponsor organisation name | GlaxoSmithKline |
| Sponsor organisation address | 980 Great West Road, Brentford, Middlesex, United Kingdom, |
| Public contact | GSK Response Center, GlaxoSmithKline, 1 8664357343, GSKClinicalSupportHD@gsk.com |
| Scientific contact | GSK Response Center, GlaxoSmithKline, 1 8664357343, GSKClinicalSupportHD@gsk.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 | 17 December 2020 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 29 May 2019 |
| Was the trial ended prematurely? | Yes |

Notes:

## General information about the trial

Main objective of the trial:

To compare the effect of daprodustat to darbepoetin alfa on endothelial function in participants with anemia of chronic kidney disease that are not dialysis dependent

Protection of trial subjects:

Not applicable

Background therapy: -

Evidence for comparator: -

| | |
|---|---|
| Actual start date of recruitment | 10 January 2019 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | No |

Notes:

## Population of trial subjects

### Subjects enrolled per country

| | |
|---|---|
| Country: Number of subjects enrolled | United Kingdom: 6 |
| Worldwide total number of subjects | 6 |
| EEA total number of subjects | 0 |

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) | 5 |
| From 65 to 84 years | 1 |
| 85 years and over | 0 |

## Subject disposition

### Recruitment

Recruitment details:

This was an open label, parallel group study that evaluated the effect of daprodustat and darbepoetin alfa on forearm blood flow (FBF) in participants with anemia of chronic kidney disease that are not dialysis dependent.

### Pre-assignment

Screening details:

Participants were enrolled in multiple centers in United Kingdom. A total of 6 participants were enrolled in the study and only 5 participants were randomized to receive study treatment.

### Period 1

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

### Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | Daprodustat |

Arm description:

Participants were randomized to receive 2 milligram (mg) daprodustat tablets once daily via oral route for a period of 41 days.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Daprodustat |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Daprodustat was available as 1 milligrams (mg), 2 mg and 4 mg oral tablets. Daprodustat was administered once daily by oral route without regard for food

| | |
|---|---|
| **Arm title** | Darbepoetin alfa |

Arm description:

Participants were randomized to receive darbepoetin alfa solution for injection, administered as a single subcutaneous injection, once every two weeks (Days 1, 14 and 28).

| | |
|---|---|
| Arm type | Active comparator |
| Investigational medicinal product name | Darbepoetin alfa |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Darbepoetin alfa was given as solution for injection for subcutaneous administration every 2 weeks

| **Number of subjects in period 1[1]** | Daprodustat | Darbepoetin alfa |
|---|---|---|
| Started | 2 | 3 |
| Completed | 2 | 2 |
| Not completed | 0 | 1 |
| Protocol defined stopping criteria | - | 1 |

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: A total of 6 participants were enrolled in the study and only 5 participants were randomized to receive study treatment.

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | Daprodustat |
| Reporting group description: | |
| Participants were randomized to receive 2 milligram (mg) daprodustat tablets once daily via oral route for a period of 41 days. | |
| Reporting group title | Darbepoetin alfa |
| Reporting group description: | |
| Participants were randomized to receive darbepoetin alfa solution for injection, administered as a single subcutaneous injection, once every two weeks (Days 1, 14 and 28). | |

| Reporting group values | Daprodustat | Darbepoetin alfa | Total |
|---|---|---|---|
| Number of subjects | 2 | 3 | 5 |
| Age categorical<br>Units: Subjects | | | |
| Adults (18-64 years) | 2 | 2 | 4 |
| From 65-84 years | 0 | 1 | 1 |
| Age Continuous<br>Units: Years | | | |
| arithmetic mean | 62.0 | 53.0 | |
| standard deviation | ± 2.83 | ± 15.72 | - |
| Sex: Female, Male<br>Units: Participants | | | |
| Female | 1 | 1 | 2 |
| Male | 1 | 2 | 3 |
| Race/Ethnicity, Customized<br>Units: Subjects | | | |
| White/Caucasian/European Heritage | 2 | 3 | 5 |

## End points

### End points reporting groups

| | |
|---|---|
| Reporting group title | Daprodustat |
| Reporting group description: | |
| Participants were randomized to receive 2 milligram (mg) daprodustat tablets once daily via oral route for a period of 41 days. | |
| Reporting group title | Darbepoetin alfa |
| Reporting group description: | |
| Participants were randomized to receive darbepoetin alfa solution for injection, administered as a single subcutaneous injection, once every two weeks (Days 1, 14 and 28). | |
| Subject analysis set title | Daprodustat, Darbepoetin alfa |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: | |
| This arm is a combination of Daprodustat and Darbepoetin alfa Arm to present difference in FBF ratio | |
| Subject analysis set title | Daprodustat, Darbepoetin alfa |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: | |
| This arm is a combination of Daprodustat and Darbepoetin alfa Arm to present difference in FBF ratio | |

### Primary: Change in FBF ratio in response to acetylcholine (Day 1 to Day 42)

| | |
|---|---|
| End point title | Change in FBF ratio in response to acetylcholine (Day 1 to Day 42)[1] |
| End point description: | |
| Venous occlusion plethysmography was used for FBF assessment. Acetylcholine was infused intra-arterially at 7.5, 15 and 30 micrograms/minute (ug/min) each for 6 minutes per infusion. FBF ratio was defined as the ratio of a participant's treatment (infused) arm value divided by the non-treatment (non-infused) arm value. The overall ratio was determined by taking the participant's Day 42 FBF ratio and dividing by the Day 1 FBF ratio. Change in FBF ratio was the difference between daprodustat and darbepoetin alfa FBF ratio. Pharmacodynamic Per-Protocol (PDPP) population included all randomized participants who provided pharmacodynamic (PD) data at Day 1 and Day 42. PDPP Population. Only those participants with data available at the specified data points were analyzed (represented by n=X in the category titles). 99999 indicates standard deviation could not be calculated as a single participant was analyzed. | |
| End point type | Primary |
| End point timeframe: | |
| Day 1 to Day 42 | |

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There are no statistical data to report

| End point values | Daprodustat, Darbepoetin alfa | | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 2 | | | |
| Units: Ratio | | | | |
| arithmetic mean (standard deviation) | | | | |
| 7.5 ug/min, n=2 | 0.6953 (± 0.12998) | | | |
| 15 ug/min, n=1 | 0.1683 (± 99999) | | | |
| 30 ug/min, n=1 | 0.3238 (± 99999) | | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change in the absolute FBF from Day 1 to Day 42 in response to acetylcholine

| End point title | Change in the absolute FBF from Day 1 to Day 42 in response to acetylcholine |
|---|---|

End point description:

Venous occlusion plethysmography was used for FBF assessment. Acetylcholine was infused intra-arterially at 7.5, 15 and 30 ug/min each for 6 minutes per infusion. Measures were made in both arms concurrently. Change in the absolute FBF from Day 1 to Day 42 in response to acetylcholine is the difference between absolute value of FBF in infused arm on Day 1 and Day 42 in response to acetylcholine. PDPP Population. Only those participants with data available at the specified data points were analyzed (represented by n=X in the category titles). 99999 indicates standard deviation could not be calculated as a single participant was analyzed.

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

End point timeframe:

Day 1 to Day 42

| End point values | Daprodustat | Darbepoetin alfa | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 2 | 2 | | |
| Units: ug/min | | | | |
| arithmetic mean (standard deviation) | | | | |
| 7.5 ug/min, n=2, 2 | 8.3180 (± 4.50592) | -6.0360 (± 3.09976) | | |
| 15 ug/min, n=1, 2 | -4.6374 (± 99999) | -8.8299 (± 9.98143) | | |
| 30 ug/min, n=1, 2 | -2.6735 (± 99999) | -4.5121 (± 5.66731) | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change in FBF ratio in response to sodium nitroprusside (Day 1 to Day 42)

| End point title | Change in FBF ratio in response to sodium nitroprusside (Day 1 to Day 42) |
|---|---|

End point description:

Venous occlusion plethysmography was used for FBF assessment. Sodium nitroprusside was infused at 3 and 10 micrograms/minute each for 6 minutes per infusion into the brachial artery of the test arm. FBF

ratio was defined as the ratio of a participant's treatment (infused) arm value divided by the non-treatment (non-infused) arm value. The overall ratio was determined by taking the participant's Day 42 FBF ratio and dividing by the Day 1 FBF ratio. Change in FBF ratio was the difference between daprodustat and darbepoetin alfa FBF ratio. PDPP Population. Only those participants with data available at the specified data points were analyzed. 99999 indicates standard deviation could not be calculated as a single participant was analyzed.

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

End point timeframe:

Day 1 to Day 42

| **End point values** | Daprodustat, Darbepoetin alfa | | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 1 | | | |
| Units: Ratio | | | | |
| arithmetic mean (standard deviation) | | | | |
| 3 ug/min<br>10 ug/min | 0.2968 (± 99999)<br>1.4425 (± 99999) | | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change in the absolute FBF from Day 1 to Day 42 in response to sodium nitroprusside

| End point title | Change in the absolute FBF from Day 1 to Day 42 in response to sodium nitroprusside |
|---|---|

End point description:

Venous occlusion plethysmography was used for FBF assessment. Sodium nitroprusside was infused at 3 and 10 ug/min each for 6 minutes per infusion into the brachial artery of the test arm. Measures were made in both arms concurrently. Change in the absolute FBF from Day 1 to Day 42 in response to sodium nitroprusside is the difference between absolute value of FBF in infused arm on Day 1 and Day 42 in response to sodium nitroprusside. PDPP Population. Only those participants with data available at the specified data points were analyzed. 99999 indicates standard deviation could not be calculated as a single participant was analyzed.

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

End point timeframe:

Day 1 to Day 42

| **End point values** | Daprodustat | Darbepoetin alfa | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 1 | 2 | | |
| Units: ug/min | | | | |
| arithmetic mean (standard deviation) | | | | |

| | | | | |
|---|---|---|---|---|
| 3 ug/min | -0.2560 (± 99999) | 0.3844 (± 0.52197) | | |
| 10 ug/min | 6.8103 (± 99999) | -0.2873 (± 1.11519) | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change in FBF ratio in response to NG-monomethyl arginine acetate (L-NMMA) (Day 1 to Day 42)

| End point title | Change in FBF ratio in response to NG-monomethyl arginine acetate (L-NMMA) (Day 1 to Day 42) |
|---|---|

End point description:

Venous occlusion plethysmography was used for FBF assessment. Effects on basal nitric oxide synthesis was assessed using L-NMMA at doses of 2 and 8 micromoles per minute (umol/min) each infused for 6 minutes into the brachial artery of the test arm. FBF ratio was defined as the ratio of a participant's treatment (infused) arm value divided by the non-treatment (non-infused) arm value. The overall ratio was determined by taking the participant's Day 42 FBF ratio and dividing by the Day 1 FBF ratio. Change in FBF ratio was the difference between daprodustat and darbepoetin alfa FBF ratio. PDPP Population. Only those participants with data available at the specified data points were analyzed. 99999 indicates standard deviation could not be calculated as a single participant was analyzed.

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

End point timeframe:

Day 1 to Day 42

| **End point values** | Daprodustat, Darbepoetin alfa | | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 1 | | | |
| Units: Ratio | | | | |
| arithmetic mean (standard deviation) | | | | |
| 2 umol/min | -0.1598 (± 99999) | | | |
| 8 umol/min | -0.3715 (± 99999) | | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change in the absolute FBF from Day 1 to Day 42 in response to L-NMMA

| End point title | Change in the absolute FBF from Day 1 to Day 42 in response to L-NMMA |
|---|---|

End point description:

Venous occlusion plethysmography was used for FBF assessment. Effects on basal nitric oxide synthesis was assessed using L-NMMA at doses of 2 and 8 umol/min each infused for 6 minutes into the brachial artery of the test arm. Measures were made in both arms concurrently. Change in the absolute FBF from

Day 1 to Day 42 in response to L-NMMA is the difference between absolute value of FBF in infused arm on Day 1 and Day 42 in response to L-NMMA. PDPP Population. Only those participants with data available at the specified data points were analyzed. 99999 indicates standard deviation could not be calculated as a single participant was analyzed.

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

End point timeframe:

Day 1 to Day 42

| **End point values** | Daprodustat | Darbepoetin alfa | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 1 | 1 | | |
| Units: umol/min | | | | |
| arithmetic mean (standard deviation) | | | | |
| 2 umol/min | 1.1508 (± 99999) | 0.3558 (± 99999) | | |
| 8 umol/min | 0.0974 (± 99999) | 0.0399 (± 99999) | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change in FBF ratio in response to acetylcholine at Day 42 versus (vs) Day 1 in participants treated with daprodustat

| End point title | Change in FBF ratio in response to acetylcholine at Day 42 versus (vs) Day 1 in participants treated with daprodustat[2] |
|---|---|

End point description:

Venous occlusion plethysmography was used for FBF assessment. Acetylcholine was infused intra-arterially at 7.5, 15 and 30 ug/min each for 6 minutes per infusion. The Day 42 ratio was calculated by taking the participants Day 42 treatment (infused) arm and dividing by the Day 42 non-treatment (control) arm value. The Day 1 ratio was calculated by taking the participants Day 1 treatment (infused) arm and dividing by the Day 1 non-treatment (control) arm value. Change in FBF ratio from Day 1 to Day 42 was determined by taking the participants Day 42 ratio and dividing by the Day 1 ratio. PDPP Population. Only those participants with data available at the specified data points were analyzed (represented by n=X in the category titles). 99999 indicates standard deviation could not be calculated as a single participant was analyzed.

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

End point timeframe:

Day 1 and Day 42

Notes:

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: There are no statistical data to report

| **End point values** | Daprodustat | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 2 | | | |
| Units: Ratio | | | | |
| arithmetic mean (standard deviation) | | | | |

| | | | | |
|---|---|---|---|---|
| 7.5 ug/min, n=2 | 0.2744 (± 0.91996) | | | |
| 15 ug/min, n=1 | -0.8503 (± 99999) | | | |
| 30 ug/min, n=1 | 0.5482 (± 99999) | | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change in FBF ratio in response to sodium nitroprusside at Day 42 vs Day 1 in participants treated with daprodustat

| End point title | Change in FBF ratio in response to sodium nitroprusside at Day 42 vs Day 1 in participants treated with daprodustat[3] |
|---|---|

End point description:

Venous occlusion plethysmography was used for FBF assessment. Sodium nitroprusside was infused at 3 and 10 ug/min each for 6 minutes per infusion into the brachial artery of the test arm. The Day 42 ratio was calculated by taking the participants Day 42 treatment (infused) arm and dividing by the Day 42 non-treatment (control) arm value. The Day 1 ratio was calculated by taking the participants Day 1 treatment (infused) arm and dividing by the Day 1 non-treatment (control) arm value. Change in FBF ratio from Day 1 to Day 42 was determined by taking the participants Day 42 ratio and dividing by the Day 1 ratio. PDPP Population. Only those participants with data available at the specified data points were analyzed. 99999 indicates standard deviation could not be calculated as a single participant was analyzed.

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

End point timeframe:

Day 1 and Day 42

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: There are no statistical data to report

| End point values | Daprodustat | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 1 | | | |
| Units: Ratio | | | | |
| arithmetic mean (standard deviation) | | | | |
| 3 ug/min | 0.1618 (± 99999) | | | |
| 10 ug/min | 3.2651 (± 99999) | | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change in FBF ratio in response to L-NMMA at Day 42 vs Day 1 in participants treated with daprodustat

| End point title | Change in FBF ratio in response to L-NMMA at Day 42 vs Day 1 in participants treated with daprodustat[4] |
|---|---|

End point description:

Venous occlusion plethysmography was used for FBF assessment. Effects on basal nitric oxide synthesis was assessed using L-NMMA at doses of 2 and 8 umol/min each infused for 6 minutes into the brachial artery of the test arm. The Day 42 ratio was calculated by taking the participants Day 42 treatment (infused) arm and dividing by the Day 42 non-treatment (control) arm value. The Day 1 ratio was calculated by taking the participants Day 1 treatment (infused) arm and dividing by the Day 1 non-treatment (control) arm value. Change in FBF ratio from Day 1 to Day 42 was determined by taking the participants Day 42 ratio and dividing by the Day 1 ratio. PDPP Population. Only those participants with data available at the specified data points were analyzed. 99999 indicates standard deviation could not be calculated as a single participant was analyzed.

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

End point timeframe:

Day 1 and Day 42

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: There are no statistical data to report

| **End point values** | Daprodustat | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 1 | | | |
| Units: Ratio | | | | |
| arithmetic mean (standard deviation) | | | | |
| 2 umol/min | -0.3896 (± 99999) | | | |
| 8 umol/min | -0.7216 (± 99999) | | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change in FBF ratio in response to acetylcholine at Day 42 vs Day 1 in participants treated with darbepoetin alfa

| End point title | Change in FBF ratio in response to acetylcholine at Day 42 vs Day 1 in participants treated with darbepoetin alfa[5] |
|---|---|

End point description:

Venous occlusion plethysmography was used for FBF assessment. Acetylcholine was infused intra-arterially at 7.5, 15 and 30 ug/min each for 6 minutes per infusion. The Day 42 ratio was calculated by taking the participants Day 42 treatment (infused) arm and dividing by the Day 42 non-treatment (control) arm value. The Day 1 ratio was calculated by taking the participants Day 1 treatment (infused) arm and dividing by the Day 1 non-treatment (control) arm value. Change in FBF ratio from Day 1 to Day 42 was determined by taking the participants Day 42 ratio and dividing by the Day 1 ratio. PDPP Population

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

End point timeframe:

Day 1 and Day 42

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: There are no statistical data to report

| End point values | Darbepoetin alfa | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 2 | | | |
| Units: Ratio | | | | |
| arithmetic mean (standard deviation) | | | | |
| 7.5 ug/min | -2.0376 (± 0.63291) | | | |
| 15 ug/min | -1.4559 (± 0.01558) | | | |
| 30 ug/min | -1.0652 (± 1.56389) | | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change in FBF ratio in response to sodium nitroprusside at Day 42 vs Day 1 in participants treated with darbepoetin alfa

| End point title | Change in FBF ratio in response to sodium nitroprusside at Day 42 vs Day 1 in participants treated with darbepoetin alfa[6] |
|---|---|

End point description:

Venous occlusion plethysmography was used for FBF assessment. Sodium nitroprusside was infused at 3 and 10 ug/min each for 6 minutes per infusion into the brachial artery of the test arm. The Day 42 ratio was calculated by taking the participants Day 42 treatment (infused) arm and dividing by the Day 42 non-treatment (control) arm value. The Day 1 ratio was calculated by taking the participants Day 1 treatment (infused) arm and dividing by the Day 1 non-treatment (control) arm value. Change in FBF ratio from Day 1 to Day 42 was determined by taking the participants Day 42 ratio and dividing by the Day 1 ratio. PDPP Population.

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

End point timeframe:

Day 1 and Day 42

Notes:

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: There are no statistical data to report

| End point values | Darbepoetin alfa | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 2 | | | |
| Units: Ratio | | | | |
| arithmetic mean (standard deviation) | | | | |
| 3 ug/min | -0.7503 (± 0.26692) | | | |
| 10 ug/min | -1.2405 (± 0.15366) | | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change in FBF ratio in response to L-NMMA at Day 42 vs Day 1 in participants treated with darbepoetin alfa

| End point title | Change in FBF ratio in response to L-NMMA at Day 42 vs Day 1 in participants treated with darbepoetin alfa[7] |
|---|---|

End point description:

Venous occlusion plethysmography was used for FBF assessment. Effects on basal nitric oxide synthesis was assessed using L-NMMA at doses of 2 and 8 umol/min each infused for 6 minutes into the brachial artery of the test arm. The Day 42 ratio was calculated by taking the participants Day 42 treatment (infused) arm and dividing by the Day 42 non-treatment (control) arm value. The Day 1 ratio was calculated by taking the participants Day 1 treatment (infused) arm and dividing by the Day 1 non-treatment (control) arm value. Change in FBF ratio from Day 1 to Day 42 was determined by taking the participants Day 42 ratio and dividing by the Day 1 ratio. PDPP Population. Only those participants with data available at the specified data points were analyzed. 99999 indicates standard deviation could not be calculated as a single participant was analyzed.

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

End point timeframe:

Day 1 and Day 42

Notes:

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: There are no statistical data to report

| **End point values** | Darbepoetin alfa | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 1 | | | |
| Units: Ratio | | | | |
| arithmetic mean (standard deviation) | | | | |
| 2 umol/min | -0.081 (± 99999) | | | |
| 8 umol/min | -0.1351 (± 99999) | | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Change in the absolute FBF in response to acetylcholine at Day 42 vs Day 1 in participants treated with daprodustat

| End point title | Change in the absolute FBF in response to acetylcholine at Day 42 vs Day 1 in participants treated with daprodustat[8] |
|---|---|

End point description:

Venous occlusion plethysmography was used for FBF assessment. Acetylcholine was infused intra-arterially at 7.5, 15 and 30 ug/min each for 6 minutes per infusion. Measures were made in both arms concurrently. Change in the absolute FBF in response to acetylcholine at Day 42 vs Day1 is the difference between absolute value of FBF in infused arm on Day 1 and Day 42 in response to acetylcholine in participants treated with daprodustat. PDPP Population. Only those participants with data available at the specified data points were analyzed (represented by n=X in the category titles). 99999 indicates standard deviation could not be calculated as a single participant was analyzed.

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

End point timeframe:

Day 1 and Day 42

Notes:

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: There are no statistical data to report

| End point values | Daprodustat | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 2 | | | |
| Units: ug/min | | | | |
| arithmetic mean (standard deviation) | | | | |
| 7.5 ug/min, n=2 | 8.3180 (± 4.50592) | | | |
| 15 ug/min, n=1 | -4.6374 (± 99999) | | | |
| 30 ug/min, n=1 | -2.6735 (± 99999) | | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change in the absolute FBF in response to sodium nitroprusside at Day 42 vs Day 1 in participants treated with daprodustat

| End point title | Change in the absolute FBF in response to sodium nitroprusside at Day 42 vs Day 1 in participants treated with daprodustat[9] |
|---|---|

End point description:

Venous occlusion plethysmography was used for FBF assessment. Sodium nitroprusside was infused at 3 and 10 ug/min each for 6 minutes per infusion into the brachial artery of the test arm. Measures were made in both arms concurrently. Change in the absolute FBF in response to sodium nitroprusside at Day 42 vs Day 1 is the difference between absolute value of FBF in infused arm on Day 1 and Day 42 in response to sodium nitroprusside in participants treated with daprodustat. PDPP Population. Only those participants with data available at the specified data points were analyzed. 99999 indicates standard deviation could not be calculated as a single participant was analyzed.

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

End point timeframe:

Day 1 and Day 42

Notes:

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: There are no statistical data to report

| End point values | Daprodustat | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 1 | | | |
| Units: ug/min | | | | |
| arithmetic mean (standard deviation) | | | | |
| 3 ug/min | -0.2560 (± 99999) | | | |
| 10 ug/min | 6.8103 (± 99999) | | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change in the absolute FBF in response to L-NMMA at Day 42 vs Day 1 in participants treated with daprodustat

| End point title | Change in the absolute FBF in response to L-NMMA at Day 42 vs Day 1 in participants treated with daprodustat[10] |
|---|---|

End point description:

Venous occlusion plethysmography was used for FBF assessment. Effects on basal nitric oxide synthesis was assessed using L-NMMA at doses of 2 and 8 umol/min each infused for 6 minutes into the brachial artery of the test arm. Measures were made in both arms concurrently. Change in the absolute FBF in response to L-NMMA at Day 42 vs Day 1 is the difference between absolute value of FBF in infused arm on Day 1 and Day 42 in response to L-NMMA in participants treated with daprodustat. PDPP Population. Only those participants with data available at the specified data points were analyzed. 99999 indicates standard deviation could not be calculated as a single participant was analyzed.

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

End point timeframe:

Day 1 and Day 42

Notes:

[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: There are no statistical data to report

| End point values | Daprodustat | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 1 | | | |
| Units: umol/min | | | | |
| arithmetic mean (standard deviation) | | | | |
| 2 umol/min | 1.1508 (± 99999) | | | |
| 8 umol/min | 0.0974 (± 99999) | | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change in the absolute FBF in response to acetylcholine at Day 42 vs Day 1 in participants treated with darbepoetin alfa

| End point title | Change in the absolute FBF in response to acetylcholine at Day 42 vs Day 1 in participants treated with darbepoetin alfa[11] |
|---|---|

End point description:

Venous occlusion plethysmography was used for FBF assessment. Acetylcholine was infused intra-arterially at 7.5, 15 and 30 ug/min each for 6 minutes per infusion. Measures were made in both arms concurrently. Change in the absolute FBF in response to acetylcholine at Day 42 vs Day1 is the difference between absolute value of FBF in infused arm on Day 1 and Day 42 in response to acetylcholine in participants treated with darbepoetin alfa. PDPP Population.

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

End point timeframe:

Day 1 and Day 42

Notes:

[11] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: There are no statistical data to report

| **End point values** | Darbepoetin alfa | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 2 | | | |
| Units: ug/min | | | | |
| arithmetic mean (standard deviation) | | | | |
| 7.5 ug/min | -6.0360 (± 3.09976) | | | |
| 15 ug/min | -8.8299 (± 9.98143) | | | |
| 30 ug/min | -4.5121 (± 5.66731) | | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change in the absolute FBF in response to sodium nitroprusside at Day 42 vs Day 1 in participants treated with darbepoetin alfa

| End point title | Change in the absolute FBF in response to sodium nitroprusside at Day 42 vs Day 1 in participants treated with darbepoetin alfa[12] |
|---|---|

End point description:

Venous occlusion plethysmography was used for FBF assessment. Sodium nitroprusside was infused at 3 and 10 ug/min each for 6 minutes per infusion into the brachial artery of the test arm. Measures were made in both arms concurrently. Change in the absolute FBF in response to sodium nitroprusside at Day 42 vs Day 1 is the difference between absolute value of FBF in infused arm on Day 1 and Day 42 in response to sodium nitroprusside in participants treated with darbepoetin alfa. PDPP Population.

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

End point timeframe:

Day 1 and Day 42

Notes:

[12] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: There are no statistical data to report

| **End point values** | Darbepoetin alfa | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 2 | | | |
| Units: ug/min | | | | |
| arithmetic mean (standard deviation) | | | | |
| 3 ug/min | 0.3844 (± 0.52197) | | | |
| 10 ug/min | -0.2873 (± 1.11519) | | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change in the absolute FBF in response to L-NMMA at Day 42 vs Day 1 in participants treated with darbepoetin alfa

| End point title | Change in the absolute FBF in response to L-NMMA at Day 42 vs Day 1 in participants treated with darbepoetin alfa[13] |
|---|---|

End point description:

Venous occlusion plethysmography was used for FBF assessment. Effects on basal nitric oxide synthesis was assessed using L-NMMA at doses of 2 and 8 umol/min each infused for 6 minutes into the brachial artery of the test arm. Measures were made in both arms concurrently. Change in the absolute FBF in response to L-NMMA at Day 42 vs Day 1 is the difference between absolute value of FBF in infused arm on Day 1 and Day 42 in response to L-NMMA in participants treated with darbepoetin alfa. PDPP Population. Only those participants with data available at the specified data points were analyzed. 99999 indicates standard deviation could not be calculated as a single participant was analyzed.

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

End point timeframe:

Day 1 and Day 42

Notes:

[13] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: There are no statistical data to report

| **End point values** | Darbepoetin alfa | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 1 | | | |
| Units: umol/min | | | | |
| arithmetic mean (standard deviation) | | | | |
| 2 umol/min | 0.3558 (± 99999) | | | |
| 8 umol/min | 0.0399 (± 99999) | | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change in Augmentation index (AIx) from Day 1 to 42

| End point title | Change in Augmentation index (AIx) from Day 1 to 42 |
|---|---|

End point description:

Pulse wave analysis (PWA) is a reproducible, noninvasive method for assessing AIx (a measure of the contribution that wave reflection makes to the arterial pressure waveform). The amplitude and timing of the reflected wave ultimately depends on the stiffness of the small (pre-resistance) vessels and large arteries, and thus, AIx provides a measure of systemic arterial stiffness. A high-fidelity micro

manometer was used to obtain accurate readings of the peripheral pressure waveforms by flattening, but not occluding, the radial artery of the dominant arm using gentle pressure. AIx was defined as the augmentation (difference between systolic peaks) expressed as a percentage of the overall pulse pressure. Data for change in AIx from Day 1 to 42 was presented. PDPP Population.

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

End point timeframe:

Day 1 to Day 42

| **End point values** | Daprodustat | Darbepoetin alfa | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 2 | 2 | | |
| Units: Percentage | | | | |
| arithmetic mean (standard deviation) | -3.000 (± 0.0000) | -4.000 (± 2.8284) | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Change in pulse wave velocity (PWV) from Day 1 to Day 42

| End point title | Change in pulse wave velocity (PWV) from Day 1 to Day 42 |
|---|---|

End point description:

PWV was assessed with a high-fidelity micro manometer which was used to obtain accurate readings of the peripheral pressure waveforms by flattening, but not occluding, the carotid and femoral arteries as the two points of measure. Data for change in PWV from Day 1 to 42 was presented. PDPP Population.

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

End point timeframe:

Day 1 to Day 42

| **End point values** | Daprodustat | Darbepoetin alfa | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 2 | 2 | | |
| Units: meters per second (m/sec) | | | | |
| arithmetic mean (standard deviation) | 2.075 (± 1.4496) | 0.100 (± 0.2828) | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Number of participants with any adverse events (AEs) and serious adverse events (SAEs)

| End point title | Number of participants with any adverse events (AEs) and serious adverse events (SAEs) |
|---|---|

End point description:

An AE is any untoward medical occurrence in a clinical study participants, temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. SAE is defined as any untoward medical occurrence that, at any dose results in death, is life-threatening, requires hospitalization or prolongation of existing hospitalization, results in disability, is a congenital anomaly/birth effect. Safety Population includes all randomized participants who received at least one dose of study treatment.

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

End point timeframe:

Up to 59 days

| **End point values** | Daprodustat | Darbepoetin alfa | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 2 | 3 | | |
| Units: Participants | | | | |
| Any AEs | 0 | 1 | | |
| Any SAEs | 0 | 0 | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Number of participants with any AE of special interest (AESI)

| End point title | Number of participants with any AE of special interest (AESI) |
|---|---|

End point description:

AESIs were identified based on non-clinical studies with daprodustat, clinical experience with recombinant human erythropoietins (rhEPOs), and current information regarding hypoxia-inducible factor (HIF)-regulated pathways in mediating hypoxia-associated pathophysiology. The AESIs for daprodustat were identified as follows: Thrombosis and/or tissue ischemia secondary to excessive erythropoiesis; Death, MI, stroke, heart failure, thromboembolic events, thrombosis of vascular access; Cardiomyopathy; Pulmonary artery hypertension; Cancer-related mortality and tumor progression and recurrence Esophageal and gastric erosions; Proliferative retinopathy, macular edema, choroidal neovascularization; Exacerbation of rheumatoid arthritis and Worsening of hypertension. Safety Population.

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

End point timeframe:

Up to 59 days

| **End point values** | Daprodustat | Darbepoetin alfa | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 2 | 3 | | |
| Units: Participants | 0 | 0 | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Number of participants discontinuing the randomized study treatment

| End point title | Number of participants discontinuing the randomized study treatment |
|---|---|

End point description:

Number of participants who discontinued the randomized study treatment were assessed. Safety Population.

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

End point timeframe:

Up to Day 42

| End point values | Daprodustat | Darbepoetin alfa | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 2 | 3 | | |
| Units: Participants | 0 | 0 | | |

### Statistical analyses

No statistical analyses for this end point

## Other pre-specified: Absolute values of diastolic blood pressure (DBP) and systolic blood pressure (SBP)

| End point title | Absolute values of diastolic blood pressure (DBP) and systolic blood pressure (SBP) |
|---|---|

End point description:

DBP and SBP were measured in a semi-supine position with a completely automated device preceded by at least 5 minutes of rest for the participant in a quiet setting without distractions. Safety Population. Only those participants with data available at the specified data points were analyzed (represented by n=X in the category titles).

| End point type | Other pre-specified |
|---|---|

End point timeframe:

Days 1, 14, 28, 42 and 59

| End point values | Daprodustat | Darbepoetin alfa | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 2 | 3 | | |
| Units: millimeters of mercury (mmHg) | | | | |
| arithmetic mean (standard deviation) | | | | |
| DBP, Day 1, n=2, 3 | 73.5 (± 13.44) | 69.3 (± 13.05) | | |
| DBP, Day 14, n=2, 3 | 67.0 (± 5.66) | 74.3 (± 13.05) | | |
| DBP, Day 28, n=2, 3 | 73.5 (± 7.78) | 79.3 (± 25.54) | | |
| DBP, Day 42, n=2, 2 | 76.0 (± 9.90) | 73.0 (± 8.49) | | |
| DBP, Day 59, n=2, 3 | 69.5 (± 9.19) | 82.7 (± 18.15) | | |
| SBP, Day 1, n=2, 3 | 144.0 (± 43.84) | 134.3 (± 18.34) | | |
| SBP, Day 14, n=2, 3 | 130.0 (± 28.28) | 127.7 (± 23.25) | | |
| SBP, Day 28, n=2, 3 | 135.5 (± 12.02) | 147.3 (± 39.63) | | |
| SBP, Day 42, n=2, 2 | 145.5 (± 33.23) | 148.0 (± 45.25) | | |
| SBP, Day 59, n=2, 3 | 135.5 (± 31.82) | 142.3 (± 29.14) | | |

## Statistical analyses

No statistical analyses for this end point

## Other pre-specified: Change from Baseline in DBP and SBP

| End point title | Change from Baseline in DBP and SBP |
|---|---|

End point description:

DBP and SBP were measured in a semi-supine position with a completely automated device preceded by at least 5 minutes of rest for the participant in a quiet setting without distractions. Baseline value (Day 1) is the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline is defined as post-dose visit value minus Baseline value. Safety Population. Only those participants with data available at the specified data points were analyzed (represented by n=X in the category titles).

| End point type | Other pre-specified |
|---|---|

End point timeframe:

Baseline (Day 1) and at Days 14, 28, 42 and 59

| End point values | Daprodustat | Darbepoetin alfa | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 2 | 3 | | |
| Units: mmHg | | | | |
| arithmetic mean (standard deviation) | | | | |
| DBP, Day 14, n=2, 3 | -6.5 (± 7.78) | 5.0 (± 0.00) | | |
| DBP, Day 28, n=2, 3 | 0.0 (± 21.21) | 10.0 (± 13.00) | | |
| DBP, Day 42, n=2, 2 | 2.5 (± 3.54) | 10.5 (± 0.71) | | |
| DBP, Day 59, n=2, 3 | -4.0 (± 4.24) | 13.3 (± 5.13) | | |

| | | | | |
|---|---|---|---|---|
| SBP, Day 14, n=2, 3 | -14.0 (± 15.56) | -6.7 (± 4.93) | | |
| SBP, Day 28, n=2, 3 | -8.5 (± 31.82) | 13.0 (± 38.43) | | |
| SBP, Day 42, n=2, 2 | 1.5 (± 10.61) | 10.5 (± 20.51) | | |
| SBP, Day 59, n=2, 3 | -8.5 (± 12.02) | 8.0 (± 24.02) | | |

### Statistical analyses

No statistical analyses for this end point

### Other pre-specified: Absolute values of electrocardiogram (ECG) mean heart rate

| End point title | Absolute values of electrocardiogram (ECG) mean heart rate |
|---|---|

End point description:

Full 12-lead ECG were recorded with the participant in a semi-supine position to measure heart rate. Safety Population. Only those participants with data available at the specified data points were analyzed (represented by n=X in the category titles).

| End point type | Other pre-specified |
|---|---|

End point timeframe:

Days 1, 42 and 59

| End point values | Daprodustat | Darbepoetin alfa | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 2 | 3 | | |
| Units: Beats per minute | | | | |
| arithmetic mean (standard deviation) | | | | |
| Day 1, n=2, 3 | 69.0 (± 2.83) | 70.0 (± 14.11) | | |
| Day 42, n=2, 2 | 61.0 (± 14.14) | 62.0 (± 9.90) | | |
| Day 59, n=2, 3 | 71.5 (± 9.19) | 73.7 (± 20.03) | | |

### Statistical analyses

No statistical analyses for this end point

### Other pre-specified: Change from Baseline in ECG mean heart rate

| End point title | Change from Baseline in ECG mean heart rate |
|---|---|

End point description:

Full 12-lead ECG were recorded with the participant in a semi-supine position to measure heart rate. Baseline value (Day 1) is the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline is defined as post-dose visit value minus Baseline value. Safety Population. Only those participants with data available at the specified data points were analyzed (represented by n=X in the category titles).

| End point type | Other pre-specified |
|---|---|

End point timeframe:

Baseline (Day 1) and at Days 42 and 59

| End point values | Daprodustat | Darbepoetin alfa | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 2 | 3 | | |
| Units: Beats per minute | | | | |
| arithmetic mean (standard deviation) | | | | |
| Day 42, n=2, 2 | -8.0 (± 11.31) | -0.5 (± 2.12) | | |
| Day 59, n=2, 3 | 2.5 (± 12.02) | 3.7 (± 9.50) | | |

## Statistical analyses

No statistical analyses for this end point

## Other pre-specified: Absolute values of ECG parameters- PR interval, QRS interval, and QT interval and QT interval corrected for heart rate using Bazett's formula (QTcB)

| End point title | Absolute values of ECG parameters- PR interval, QRS interval, and QT interval and QT interval corrected for heart rate using Bazett's formula (QTcB) |
|---|---|

End point description:

Full 12-lead ECGs were recorded with the participant in a semi-supine position to measure PR interval, QRS duration, QT interval and QTcB, calculated (machine read or manually). Safety Population. Only those participants with data available at the specified data points were analyzed (represented by n=X in the category titles).

| End point type | Other pre-specified |
|---|---|

End point timeframe:

Days 1, 42 and 59

| End point values | Daprodustat | Darbepoetin alfa | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 2 | 3 | | |
| Units: Milliseconds | | | | |
| arithmetic mean (standard deviation) | | | | |
| PR Interval, Day 1, n=2, 3 | 139.0 (± 1.41) | 181.7 (± 23.16) | | |
| PR Interval, Day 42, n=2, 2 | 146.5 (± 7.78) | 192.5 (± 10.61) | | |
| PR Interval, Day 59, n=2, 3 | 146.5 (± 2.12) | 182.0 (± 18.00) | | |
| QRS Duration, Day 1, n=2, 3 | 87.0 (± 7.07) | 94.7 (± 5.03) | | |
| QRS Duration, Day 42, n=2, 2 | 88.5 (± 9.19) | 96.5 (± 10.61) | | |
| QRS Duration, Day 59, n=2, 3 | 87.0 (± 9.90) | 95.3 (± 7.02) | | |
| QT Interval, Day 1, n=2, 3 | 395.5 (± 6.36) | 391.3 (± 14.47) | | |
| QT Interval, Day 42, n=2, 2 | 413.5 (± 20.51) | 388.0 (± 11.31) | | |

| | | | | |
|---|---|---|---|---|
| QT Interval, Day 59, n=2, 3 | 383.5 (± 44.55) | 382.3 (± 33.71) | | |
| QTcB Interval, Day 1, n=2, 3 | 424.0 (± 1.41) | 420.7 (± 31.79) | | |
| QTcB Interval, Day 42, n=2, 2 | 414.5 (± 27.58) | 393.0 (± 19.80) | | |
| QTcB Interval, Day 59, n=2, 3 | 416.5 (± 21.92) | 417.3 (± 33.32) | | |

## Statistical analyses

No statistical analyses for this end point

## Other pre-specified: Change from Baseline in ECG parameters- PR interval, QRS duration, and QT interval and QTcB

| End point title | Change from Baseline in ECG parameters- PR interval, QRS duration, and QT interval and QTcB |
|---|---|

End point description:

Full 12-lead ECGs were recorded with the participant in a semi-supine position to measure PR interval, QRS duration, QT (uncorrected) interval and QTcB, calculated (machine read or manually). Baseline value (Day 1) is the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline is defined as post-dose visit value minus Baseline value. Safety Population. Only those participants with data available at the specified data points were analyzed (represented by n=X in the category titles).

| End point type | Other pre-specified |
|---|---|

End point timeframe:

Baseline (Day 1) and at Days 42 and 59

| End point values | Daprodustat | Darbepoetin alfa | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 2 | 3 | | |
| Units: Milliseconds | | | | |
| arithmetic mean (standard deviation) | | | | |
| PR Interval, Day 42, n=2, 2 | 7.5 (± 6.36) | -2.0 (± 19.80) | | |
| PR Interval, Day 59, n=2, 3 | 7.5 (± 0.71) | 0.3 (± 16.86) | | |
| QRS Duration, Day 42, n=2, 2 | 1.5 (± 2.12) | 1.5 (± 3.54) | | |
| QRS Duration, Day 59, n=2, 3 | 0.0 (± 2.83) | 0.7 (± 2.31) | | |
| QT Interval, Day 42, n=2, 2 | 18.0 (± 14.14) | -7.0 (± 7.07) | | |
| QT Interval, Day 59, n=2, 3 | -12.0 (± 50.91) | -9.0 (± 19.67) | | |
| QTcB Interval, Day 42, n=2, 2 | -9.5 (± 26.16) | -9.5 (± 13.44) | | |
| QTcB Interval, Day 59, n=2, 3 | -7.5 (± 20.51) | -3.3 (± 8.02) | | |

## Statistical analyses

No statistical analyses for this end point

## Other pre-specified: Absolute values of the hematology parameters of platelet count, white blood cell (WBC) count (Absolute), basophils, eosinophils, lymphocytes, monocytes and neutrophils

| End point title | Absolute values of the hematology parameters of platelet count, white blood cell (WBC) count (Absolute), basophils, eosinophils, lymphocytes, monocytes and neutrophils |
|---|---|

End point description:

Blood samples were collected for the analysis of hematology parameters including platelet count, leukocytes, basophils, eosinophils, lymphocytes, monocytes and neutrophils. Safety Population. Only those participants with data available at the specified data points were analyzed (represented by n=X in the category titles).

| End point type | Other pre-specified |
|---|---|

End point timeframe:

Days 1, 42 and 59

| **End point values** | Daprodustat | Darbepoetin alfa | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 2 | 3 | | |
| Units: Giga cells per Liter | | | | |
| arithmetic mean (standard deviation) | | | | |
| Platelet count, Day 1, n=2, 3 | 199.0 (± 63.64) | 191.7 (± 68.13) | | |
| Platelet count, Day 42, n=2, 2 | 203.5 (± 57.28) | 121.5 (± 13.44) | | |
| Platelet count, Day 59, n=2, 3 | 193.0 (± 41.01) | 50.08 (± 50.08) | | |
| Leukocytes, Day 1, n=2, 3 | 5.05 (± 1.202) | 6.30 (± 2.117) | | |
| Leukocytes, Day 42, n=2, 2 | 6.05 (± 2.616) | 5.75 (± 2.051) | | |
| Leukocytes, Day 59, n=2, 3 | 5.30 (± 1.414) | 7.20 (± 2.261) | | |
| Basophils, Day 1, n=2, 3 | 0.045 (± 0.0212) | 0.057 (± 0.0503) | | |
| Basophils, Day 42, n=2, 2 | 0.045 (± 0.0212) | 0.045 (± 0.0212) | | |
| Basophils, Day 59, n=2, 3 | 0.035 (± 0.0071) | 0.050 (± 0.0400) | | |
| Eosinophils, Day 1, n=2, 3 | 0.295 (± 0.1485) | 0.230 (± 0.1353) | | |
| Eosinophils, Day 42, n=2, 2 | 0.300 (± 0.1980) | 0.175 (± 0.0778) | | |
| Eosinophils, Day 59, n=2, 3 | 0.245 (± 0.1485) | 0.220 (± 0.1311) | | |
| Lymphocytes, Day 1, n=2, 3 | 1.160 (± 0.2404) | 2.037 (± 1.4989) | | |
| Lymphocytes, Day 42, n=2, 2 | 1.275 (± 0.2616) | 1.150 (± 0.4808) | | |
| Lymphocytes, Day 59, n=2, 3 | 0.785 (± 0.3748) | 2.033 (± 1.3580) | | |
| Monocytes, Day 1, n=2, 3 | 0.400 (± 0.0566) | 0.607 (± 0.3147) | | |
| Monocytes, Day 42, n=2, 2 | 0.415 (± 0.0071) | 0.445 (± 0.2192) | | |
| Monocytes, Day 59, n=2, 3 | 0.415 (± 0.0778) | 0.563 (± 0.2574) | | |
| Neutrophils, Day 1, n=2, 3 | 3.160 (± 1.3576) | 3.387 (± 0.2053) | | |

| | | | | |
|---|---|---|---|---|
| Neutrophils, Day 42, n=2, 2 | 4.010 (± 2.6870) | 3.970 (± 2.1920) | | |
| Neutrophils, Day 59, n=2, 3 | 3.825 (± 1.0112) | 4.343 (± 1.0060) | | |

### Statistical analyses

No statistical analyses for this end point

### Other pre-specified: Change from Baseline in hematology parameters of platelet count, WBC count (Absolute), basophils, eosinophils, lymphocytes, monocytes and neutrophils

| End point title | Change from Baseline in hematology parameters of platelet count, WBC count (Absolute), basophils, eosinophils, lymphocytes, monocytes and neutrophils |
|---|---|

End point description:

Blood samples were collected for the analysis of hematology parameters including platelet count, leukocytes, basophils, eosinophils, lymphocytes, monocytes and neutrophils. Baseline value (Day 1) is the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline is defined as post-dose visit value minus Baseline value. Safety Population. Only those participants with data available at the specified data points were analyzed (represented by n=X in the category titles).

| End point type | Other pre-specified |
|---|---|

End point timeframe:

Baseline (Day 1) and at Days 42 and 59

| End point values | Daprodustat | Darbepoetin alfa | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 2 | 3 | | |
| Units: Giga cells per Liter | | | | |
| arithmetic mean (standard deviation) | | | | |
| Platelet count, Day 42, n=2, 2 | 4.5 (± 6.36) | -51.0 (± 70.71) | | |
| Platelet count, Day 59, n=2, 3 | -6.0 (± 22.63) | -26.3 (± 51.98) | | |
| Leukocytes, Day 42, n=2, 2 | 1.00 (± 1.414) | 0.65 (± 2.616) | | |
| Leukocytes, Day 59, n=2, 3 | 0.25 (± 0.212) | 0.90 (± 1.054) | | |
| Basophils, Day 42, n=2, 2 | 0.000 (± 0.0000) | 0.015 (± 0.0071) | | |
| Basophils, Day 59, n=2, 3 | -0.010 (± 0.0283) | -0.007 (± 0.0115) | | |
| Eosinophils, Day 42, n=2, 2 | 0.005 (± 0.0495) | 0.015 (± 0.0071) | | |
| Eosinophils, Day 59, n=2, 3 | -0.050 (± 0.0000) | -0.010 (± 0.0100) | | |
| Lymphocytes, Day 42, n=2, 2 | 0.115 (± 0.0212) | -0.040 (± 0.0424) | | |
| Lymphocytes, Day 59, n=2, 3 | -0.375 (± 0.6152) | -0.003 (± 0.1443) | | |
| Monocytes, Day 42, n=2, 2 | 0.015 (± 0.0636) | 0.020 (± 0.2263) | | |

| | | | | |
|---|---|---|---|---|
| Monocytes, Day 59, n=2, 3 | 0.015 (± 0.0212) | -0.043 (± 0.0586) | | |
| Neutrophils, Day 42, n=2, 2 | 0.850 (± 1.3294) | 0.670 (± 2.3900) | | |
| Neutrophils, Day 59, n=2, 3 | 0.665 (± 0.3465) | 0.957 (± 1.0929) | | |

### Statistical analyses

No statistical analyses for this end point

### Other pre-specified: Absolute values of the hematology parameter of red blood cell (RBC) count and reticulocyte count (RC)

| End point title | Absolute values of the hematology parameter of red blood cell (RBC) count and reticulocyte count (RC) |
|---|---|

End point description:

Blood samples were collected for the analysis of hematology parameters including RBC count and RC. Safety Population. Only those participants with data available at the specified data points were analyzed (represented by n=X in the category titles).

| End point type | Other pre-specified |
|---|---|

End point timeframe:

Days 1, 42 and 59

| End point values | Daprodustat | Darbepoetin alfa | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 2 | 3 | | |
| Units: Trillion cells per liter | | | | |
| arithmetic mean (standard deviation) | | | | |
| RBC, Day 1, n=2, 3 | 3.45 (± 0.354) | 3.20 (± 0.300) | | |
| RBC, Day 42, n=2, 2 | 3.30 (± 0.283) | 3.65 (± 0.071) | | |
| RBC, Day 59, n=2, 3 | 3.35 (± 0.354) | 3.63 (± 0.493) | | |
| RC, Day 1, n=2, 3 | 0.04090 (± 0.018102) | 0.06090 (± 0.038112) | | |
| RC, Day 42, n=2, 2 | 0.04610 (± 0.023052) | 0.07970 (± 0.057983) | | |
| RC, Day 59, n=2, 3 | 0.03490 (± 0.014708) | 0.04580 (± 0.049537) | | |

### Statistical analyses

No statistical analyses for this end point

### Other pre-specified: Change from Baseline in hematology parameters of RBC count and RC

| End point title | Change from Baseline in hematology parameters of RBC count and RC |
|---|---|

End point description:

Blood samples were collected for the analysis of hematology parameters including RBC count and RC. Baseline value (Day 1) is the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline is defined as post-dose visit value minus Baseline value. Safety Population. Only those participants with data available at the specified data points were analyzed (represented by n=X in the category titles).

| End point type | Other pre-specified |
|---|---|

End point timeframe:

Baseline (Day 1) and at Days 42 and 59

| **End point values** | Daprodustat | Darbepoetin alfa | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 2 | 3 | | |
| Units: Trillion cells per liter | | | | |
| arithmetic mean (standard deviation) | | | | |
| RBC, Day 42, n=2, 2 | -0.15 (± 0.071) | 0.60 (± 0.141) | | |
| RBC, Day 59, n=2, 3 | -0.10 (± 0.000) | 0.43 (± 0.252) | | |
| RC, Day 42, n=2, 2 | 0.00520 (± 0.004950) | 0.00815 (± 0.010819) | | |
| RC, Day 59, n=2, 3 | -0.00600 (± 0.003394) | -0.01510 (± 0.011467) | | |

## Statistical analyses

No statistical analyses for this end point

## Other pre-specified: Absolute values of the hematology parameters of hemoglobin and Mean Corpuscle Hemoglobin concentration (MCHC)

| End point title | Absolute values of the hematology parameters of hemoglobin and Mean Corpuscle Hemoglobin concentration (MCHC) |
|---|---|

End point description:

Blood samples were collected for the analysis of hematology parameters including hemoglobin and MCHC. Safety Population. Only those participants with data available at the specified data points were analyzed (represented by n=X in the category titles).

| End point type | Other pre-specified |
|---|---|

End point timeframe:

Days 1, 42 and 59

| **End point values** | Daprodustat | Darbepoetin alfa | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 2 | 3 | | |
| Units: Grams per deciliter | | | | |
| arithmetic mean (standard deviation) | | | | |
| Hemoglobin, Day 1, n=2, 3 | 10.60 (± 0.849) | 9.77 (± 0.586) | | |

| | | | | |
|---|---|---|---|---|
| Hemoglobin, Day 42, n=2, 2 | 10.45 (± 0.778) | 11.40 (± 0.424) | | |
| Hemoglobin, Day 59, n=2, 3 | 10.40 (± 0.849) | 11.27 (± 1.002) | | |
| MCHC, Day 1, n=2, 3 | 34.10 (± 0.000) | 34.23 (± 0.351) | | |
| MCHC, Day 42, n=2, 2 | 34.10 (± 0.141) | 33.75 (± 1.909) | | |
| MCHC, Day 59, n=2, 3 | 34.00 (± 0.141) | 34.33 (± 1.447) | | |

### Statistical analyses

No statistical analyses for this end point

### Other pre-specified: Change from Baseline in hematology parameters- Hemoglobin and MCHC

| End point title | Change from Baseline in hematology parameters- Hemoglobin and MCHC |
|---|---|

End point description:

Blood samples were collected for the analysis of hematology parameters including hemoglobin and MCHC. Baseline value (Day 1) is the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline is defined as post-dose visit value minus Baseline value. Safety Population. Only those participants with data available at the specified data points were analyzed (represented by n=X in the category titles).

| End point type | Other pre-specified |
|---|---|

End point timeframe:

Baseline (Day 1) and at Days 42 and 59

| End point values | Daprodustat | Darbepoetin alfa | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 2 | 3 | | |
| Units: Grams per deciliter | | | | |
| arithmetic mean (standard deviation) | | | | |
| Hemoglobin, Day 42, n=2, 2 | -0.15 (± 0.071) | 1.85 (± 0.212) | | |
| Hemoglobin, Day 59, n=2, 3 | -0.20 (± 0.000) | 1.50 (± 0.520) | | |
| MCHC, Day 42, n=2, 2 | 0.00 (± 0.141) | -0.65 (± 1.626) | | |
| MCHC, Day 59, n=2, 3 | -0.10 (± 0.141) | 0.10 (± 1.127) | | |

### Statistical analyses

No statistical analyses for this end point

### Other pre-specified: Absolute values of hematology parameter: hematocrit

| End point title | Absolute values of hematology parameter: hematocrit |
|---|---|

End point description:

Blood samples were collected for the analysis of hematology parameters including hematocrit. Safety Population. Only those participants with data available at the specified data points were analyzed (represented by n=X in the category titles).

| End point type | Other pre-specified |
|---|---|

End point timeframe:

Days 1, 42 and 59

| **End point values** | Daprodustat | Darbepoetin alfa | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 2 | 3 | | |
| Units: Proportion of red blood cells in blood | | | | |
| arithmetic mean (standard deviation) | | | | |
| Day 1, n=2, 3 | 0.3105 (± 0.02616) | 0.2850 (± 0.01769) | | |
| Day 42, n=2, 2 | 0.3065 (± 0.02475) | 0.3385 (± 0.00636) | | |
| Day 59, n=2, 3 | 0.3065 (± 0.02475) | 0.3277 (± 0.03412) | | |

## Statistical analyses

No statistical analyses for this end point

## Other pre-specified: Change from Baseline in hematology parameter: hematocrit

| End point title | Change from Baseline in hematology parameter: hematocrit |
|---|---|

End point description:

Blood samples were collected for the analysis of hematology parameters including hematocrit. Baseline value (Day 1) is the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline is defined as post-dose visit value minus Baseline value. Safety Population. Only those participants with data available at the specified data points were analyzed (represented by n=X in the category titles).

| End point type | Other pre-specified |
|---|---|

End point timeframe:

Baseline (Day 1) and at Days 42 and 59

| **End point values** | Daprodustat | Darbepoetin alfa | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 2 | 3 | | |
| Units: Proportion of red blood cells in blood | | | | |
| arithmetic mean (standard deviation) | | | | |
| Day 42, n=2, 2 | -0.0040 (± 0.00141) | 0.0615 (± 0.02192) | | |

| | | | | |
|---|---|---|---|---|
| Day 59, n=2, 3 | -0.0040 (± 0.00141) | 0.0427 (± 0.02212) | | |

### Statistical analyses

No statistical analyses for this end point

### Other pre-specified: Absolute values of hematology parameter of red blood cell distribution width (RDW)

| End point title | Absolute values of hematology parameter of red blood cell distribution width (RDW) |
|---|---|

End point description:

Blood samples were collected for the analysis of hematology parameters including RDW. Baseline value (Day 1) is the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Safety Population. Only those participants with data available at the specified data points were analyzed (represented by n=X in the category titles).

| End point type | Other pre-specified |
|---|---|

End point timeframe:

Days 1, 42 and 59

| End point values | Daprodustat | Darbepoetin alfa | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 2 | 3 | | |
| Units: Percentage of width | | | | |
| arithmetic mean (standard deviation) | | | | |
| Day 1, n=2, 3 | 0.3105 (± 0.02616) | 0.2850 (± 0.01769) | | |
| Day 42, n=2, 2 | 13.45 (± 0.212) | 14.00 (± 0.424) | | |
| Day 59, n=2, 3 | 13.20 (± 0.141) | 13.70 (± 0.200) | | |

### Statistical analyses

No statistical analyses for this end point

### Other pre-specified: Change from Baseline in RDW

| End point title | Change from Baseline in RDW |
|---|---|

End point description:

Blood samples were collected for the analysis of hematology parameters including RDW. Baseline value (Day 1) is the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline is defined as post-dose visit value minus Baseline value. Safety Population. Only those participants with data available at the specified data points were analyzed (represented by n=X in the category titles).

| End point type | Other pre-specified |
|---|---|

End point timeframe:

Baseline (Day 1) and at Days 42 and 59

| End point values | Daprodustat | Darbepoetin alfa | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 2 | 3 | | |
| Units: Percentage of width | | | | |
| arithmetic mean (standard deviation) | | | | |
| Day 42, n=2, 2 | 0.00 (± 0.424) | 1.15 (± 0.636) | | |
| Day 59, n=2, 3 | -0.25 (± 0.354) | 0.70 (± 0.436) | | |

## Statistical analyses

No statistical analyses for this end point

## Other pre-specified: Absolute values of the hematology parameter of mean corpuscular hemoglobin (MCH)

| End point title | Absolute values of the hematology parameter of mean corpuscular hemoglobin (MCH) |
|---|---|

End point description:

Blood samples were collected for the analysis of hematology parameters including MCH. Safety Population. Only those participants with data available at the specified data points were analyzed (represented by n=X in the category titles).

| End point type | Other pre-specified |
|---|---|

End point timeframe:

Days 1, 42 and 59

| End point values | Daprodustat | Darbepoetin alfa | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 2 | 3 | | |
| Units: Picograms | | | | |
| arithmetic mean (standard deviation) | | | | |
| Day 1, n=2, 3 | 30.95 (± 0.354) | 30.67 (± 1.457) | | |
| Day 42, n=2, 2 | 31.40 (± 0.424) | 31.40 (± 0.707) | | |
| Day 59, n=2, 3 | 31.10 (± 0.141) | 30.93 (± 1.716) | | |

## Statistical analyses

No statistical analyses for this end point

## Other pre-specified: Change from Baseline in hematology parameter of MCH

| End point title | Change from Baseline in hematology parameter of MCH |
|---|---|

End point description:

Blood samples were collected for the analysis of hematology parameters including MCH. Baseline value (Day 1) is the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline is defined as post-dose visit value minus Baseline value. Safety Population. Only those participants with data available at the specified data points were analyzed (represented by n=X in the category titles).

| End point type | Other pre-specified |
|---|---|

End point timeframe:

Baseline (Day 1) and at Days 42 and 59

| End point values | Daprodustat | Darbepoetin alfa | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 2 | 3 | | |
| Units: Picograms | | | | |
| arithmetic mean (standard deviation) | | | | |
| Day 42, n=2, 2 | 0.45 (± 0.071) | -0.10 (± 0.990) | | |
| Day 59, n=2, 3 | 0.15 (± 0.212) | 0.27 (± 0.862) | | |

### Statistical analyses

No statistical analyses for this end point

## Other pre-specified: Absolute values of the hematology parameter of mean corpuscular volume (MCV)

| End point title | Absolute values of the hematology parameter of mean corpuscular volume (MCV) |
|---|---|

End point description:

Blood samples were collected for the analysis of hematology parameters including MCV. Safety Population. Only those participants with data available at the specified data points were analyzed (represented by n=X in the category titles).

| End point type | Other pre-specified |
|---|---|

End point timeframe:

Days 1, 42 and 59

| End point values | Daprodustat | Darbepoetin alfa | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 2 | 3 | | |
| Units: Femtoliters | | | | |
| arithmetic mean (standard deviation) | | | | |
| Day 1, n=2, 3 | 91.0 (± 1.41) | 89.7 (± 3.51) | | |
| Day 42, n=2, 2 | 92.0 (± 1.41) | 93.0 (± 2.83) | | |

| | | | | |
|---|---|---|---|---|
| Day 59, n=2, 3 | 91.5 (± 0.71) | 90.0 (± 3.00) | | |

### Statistical analyses

No statistical analyses for this end point

### Other pre-specified: Change from Baseline in hematology parameter of MCV

| End point title | Change from Baseline in hematology parameter of MCV |
|---|---|

End point description:

Blood samples were collected for the analysis of hematology parameters including MCV. Baseline value (Day 1) is the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline is defined as post-dose visit value minus Baseline value. Safety Population. Only those participants with data available at the specified data points were analyzed (represented by n=X in the category titles).

| End point type | Other pre-specified |
|---|---|

End point timeframe:

Baseline (Day 1) and at Days 42 and 59

| End point values | Daprodustat | Darbepoetin alfa | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 2 | 3 | | |
| Units: Femtoliters | | | | |
| arithmetic mean (standard deviation) | | | | |
| Day 42, n=2, 2 | 1.0 (± 0.00) | 1.5 (± 0.71) | | |
| Day 59, n=2, 3 | 0.5 (± 0.71) | 0.3 (± 0.58) | | |

### Statistical analyses

No statistical analyses for this end point

### Other pre-specified: Absolute values of clinical chemistry parameters of sodium, potassium, carbon-dioxide (total), chloride, glucose and urea

| End point title | Absolute values of clinical chemistry parameters of sodium, potassium, carbon-dioxide (total), chloride, glucose and urea |
|---|---|

End point description:

Blood samples will be collected for the analysis of clinical chemistry parameters including; sodium, potassium, carbon-dioxide (total), chloride, glucose and urea. Safety Population. Only those participants with data available at the specified data points were analyzed (represented by n=X in the category titles).

| End point type | Other pre-specified |
|---|---|

End point timeframe:

Days 1, 42 and 59

| End point values | Daprodustat | Darbepoetin alfa | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 2 | 3 | | |
| Units: Millimoles per Liter | | | | |
| arithmetic mean (standard deviation) | | | | |
| Sodium, Day 1, n=2, 3 | 140.0 (± 1.41) | 136.7 (± 0.58) | | |
| Sodium, Day 42, n=2, 2 | 139.5 (± 3.54) | 135.0 (± 7.07) | | |
| Sodium, Day 59, n=2, 3 | 138.5 (± 0.71) | 136.0 (± 2.65) | | |
| Potassium, Day 1, n=2, 3 | 4.70 (± 0.141) | 5.03 (± 0.757) | | |
| Potassium, Day 42, n=2, 2 | 4.55 (± 0.495) | 5.15 (± 0.495) | | |
| Potassium, Day 59, n=2, 3 | 4.45 (± 0.071) | 4.77 (± 0.306) | | |
| Carbon-dioxide (total), Day 1, n=2, 3 | 20.5 (± 3.54) | 19.0 (± 3.46) | | |
| Carbon-dioxide (total), Day 42, n=2, 2 | 22.0 (± 1.41) | 19.0 (± 0.00) | | |
| Carbon-dioxide (total), Day 59, n=2, 3 | 22.5 (± 2.12) | 21.0 (± 2.00) | | |
| Chloride, Day 1, n=2, 3 | 108.0 (± 0.00) | 105.7 (± 5.03) | | |
| Chloride, Day 42, n=2, 2 | 108.0 (± 4.24) | 104.0 (± 9.90) | | |
| Chloride, Day 59, n=2, 3 | 108.0 (± 2.83) | 104.7 (± 3.51) | | |
| Glucose, Day 1, n=2, 3 | 7.60 (± 3.111) | 6.40 (± 4.424) | | |
| Glucose, Day 42, n=2, 2 | 6.95 (± 2.333) | 12.50 (± 12.162) | | |
| Glucose, Day 59, n=2, 3 | 7.45 (± 4.172) | 10.10 (± 7.066) | | |
| Urea, Day 1, n=2, 3 | 18.00 (± 2.828) | 16.67 (± 5.508) | | |
| Urea, Day 42, n=2, 2 | 16.75 (± 2.475) | 21.00 (± 0.707) | | |
| Urea, Day 59, n=2, 3 | 16.50 (± 0.707) | 19.33 (± 5.795) | | |

## Statistical analyses

No statistical analyses for this end point

## Other pre-specified: Change from Baseline in clinical chemistry parameter: sodium, potassium, carbon-dioxide (total), chloride, glucose and urea

| End point title | Change from Baseline in clinical chemistry parameter: sodium, potassium, carbon-dioxide (total), chloride, glucose and urea |
|---|---|

End point description:

Blood samples will be collected for the analysis of clinical chemistry parameters including; sodium, potassium, carbon-dioxide (total), chloride, glucose and urea. Baseline value (Day 1) is the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline is defined as post-dose visit value minus Baseline value. Safety Population. Only those participants with data available at the specified data points were analyzed (represented by n=X in the category titles).

| End point type | Other pre-specified |
|---|---|

End point timeframe:

Baseline (Day 1) and at Days 42 and 59

| End point values | Daprodustat | Darbepoetin alfa | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 2 | 3 | | |
| Units: Millimoles per Liter | | | | |
| arithmetic mean (standard deviation) | | | | |
| Sodium, Day 42, n=2, 2 | -0.5 (± 4.95) | -1.5 (± 6.36) | | |
| Sodium, Day 59, n=2, 3 | -1.5 (± 2.12) | -0.7 (± 2.31) | | |
| Potassium, Day 42, n=2, 2 | -0.15 (± 0.354) | -0.05 (± 0.495) | | |
| Potassium, Day 59, n=2, 3 | -0.25 (± 0.071) | -0.27 (± 0.503) | | |
| Carbon-dioxide (total), Day 42, n=2, 2 | 1.5 (± 4.95) | 1.0 (± 4.24) | | |
| Carbon-dioxide (total), Day 59, n=2, 3 | 2.0 (± 1.41) | 2.0 (± 2.00) | | |
| Chloride, Day 42, n=2, 2 | 0.0 (± 4.24) | -2.0 (± 2.83) | | |
| Chloride, Day 59, n=2, 3 | 0.0 (± 2.83) | 1.73 (± 1.73) | | |
| Glucose, Day 42, n=2, 2 | -0.65 (± 0.778) | 4.25 (± 7.849) | | |
| Glucose, Day 59, n=2, 3 | -0.15 (± 1.061) | 3.70 (± 3.477) | | |
| Urea, Day 42, n=2, 2 | -1.25 (± 5.303) | 3.00 (± 7.778) | | |
| Urea, Day 59, n=2, 3 | -1.50 (± 3.536) | 2.67 (± 2.754) | | |

## Statistical analyses

No statistical analyses for this end point

## Other pre-specified: Absolute values of clinical chemistry parameters of creatinine

| End point title | Absolute values of clinical chemistry parameters of creatinine |
|---|---|

End point description:

Blood samples will be collected for the analysis of clinical chemistry parameters including; creatinine. Safety Population. Only those participants with data available at the specified data points were analyzed (represented by n=X in the category titles).

| End point type | Other pre-specified |
|---|---|

End point timeframe:

Days 1, 42 and 59

| End point values | Daprodustat | Darbepoetin alfa | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 2 | 3 | | |
| Units: Micromoles per Liter | | | | |
| arithmetic mean (standard deviation) | | | | |

| | | | | |
|---|---|---|---|---|
| Creatinine, Day 1, n=2, 3 | 246.65 (± 9.970) | 225.40 (± 74.164) | | |
| Creatinine, Day 42, n=2, 2 | 249.75 (± 15.627) | 272.25 (± 88.742) | | |
| Creatinine, Day 59, n=2, 3 | 260.35 (± 8.132) | 245.17 (± 91.086) | | |

### Statistical analyses

No statistical analyses for this end point

### Other pre-specified: Change from Baseline in clinical chemistry parameter: creatinine

| End point title | Change from Baseline in clinical chemistry parameter: creatinine |
|---|---|

End point description:

Blood samples will be collected for the analysis of clinical chemistry parameters including; creatinine. Baseline value (Day 1) is the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline is defined as post-dose visit value minus Baseline value. Safety Population. Only those participants with data available at the specified data points were analyzed (represented by n=X in the category titles).

| End point type | Other pre-specified |
|---|---|

End point timeframe:

Baseline (Day 1) and at Days 42 and 59

| End point values | Daprodustat | Darbepoetin alfa | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 2 | 3 | | |
| Units: Micromoles per Liter | | | | |
| arithmetic mean (standard deviation) | | | | |
| Creatinine, Day 42, n=2, 2 | 3.10 (± 5.657) | 36.70 (± 13.152) | | |
| Creatinine, Day 59, n=2, 3 | 13.70 (± 18.102) | 19.77 (± 33.416) | | |

### Statistical analyses

No statistical analyses for this end point

### Other pre-specified: Absolute values of clinical chemistry parameters of bilirubin (direct/indirect and total)

| End point title | Absolute values of clinical chemistry parameters of bilirubin (direct/indirect and total) |
|---|---|

End point description:

Blood samples will be collected for the analysis of clinical chemistry parameters including; bilirubin (direct/indirect and total). Safety Population. Only those participants with data available at the specified data points were analyzed (represented by n=X in the category titles). 99999 indicates standard deviation could not be calculated as a single participant was analyzed.

| End point type | Other pre-specified |
|---|---|

End point timeframe:

Days 1, 14, 28, 42 and 59

| End point values | Daprodustat | Darbepoetin alfa | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 2 | 3 | | |
| Units: Micromoles per Liter | | | | |
| arithmetic mean (standard deviation) | | | | |
| Bilirubin total, Day 1, n=2, 3 | 5.0 (± 1.41) | 6.0 (± 0.00) | | |
| Bilirubin total, Day 14, n=2, 3 | 5.0 (± 1.41) | 7.3 (± 1.15) | | |
| Bilirubin total, Day 28, n=2, 3 | 6.0 (± 0.00) | 6.0 (± 0.00) | | |
| Bilirubin total, Day 42, n=2, 2 | 6.0 (± 0.00) | 9.0 (± 4.24) | | |
| Bilirubin total, Day 59, n=2, 3 | 5.0 (± 1.41) | 6.7 (± 1.15) | | |
| Direct Bilirubin, Day 1, n=2, 2 | 1.0 (± 1.41) | 2.0 (± 0.00) | | |
| Direct Bilirubin, Day 14, n=2, 2 | 1.0 (± 1.41) | 2.0 (± 0.00) | | |
| Direct Bilirubin, Day 28, n=2, 2 | 1.0 (± 1.41) | 2.0 (± 0.00) | | |
| Direct Bilirubin, Day 42, n=2, 1 | 2.0 (± 0.00) | 2.0 (± 99999) | | |
| Direct Bilirubin, Day 59, n=2, 2 | 2.0 (± 0.00) | 2.0 (± 0.00) | | |
| Indirect Bilirubin, Day 1, n=2, 2 | 4.0 (± 0.00) | 4.0 (± 0.00) | | |
| Indirect Bilirubin, Day 14, n=2, 2 | 4.0 (± 0.00) | 5.0 (± 1.41) | | |
| Indirect Bilirubin, Day 28, n=2, 2 | 5.0 (± 1.41) | 4.0 (± 0.00) | | |
| Indirect Bilirubin, Day 42, n=2, 1 | 4.0 (± 0.00) | 10.0 (± 99999) | | |
| Indirect Bilirubin, Day 59, n=2, 2 | 3.0 (± 1.41) | 5.0 (± 1.41) | | |

### Statistical analyses

No statistical analyses for this end point

## Other pre-specified: Change from Baseline in clinical chemistry parameter: bilirubin (direct/indirect and total)

| End point title | Change from Baseline in clinical chemistry parameter: bilirubin (direct/indirect and total) |
|---|---|

End point description:

Blood samples will be collected for the analysis of clinical chemistry parameters including; creatinine and bilirubin (direct/indirect and total). Baseline value (Day 1) is the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline is defined as post-dose visit value minus Baseline value. Safety Population. Only those participants with data available at the specified data points were analyzed (represented by n=X in the category titles). 99999 indicates standard deviation could not be calculated as a single participant was analyzed.

| End point type | Other pre-specified |
|---|---|

End point timeframe:

Baseline (Day 1) and at Days 14, 28, 42 and 59

| End point values | Daprodustat | Darbepoetin alfa | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 2 | 3 | | |
| Units: Micromoles per Liter | | | | |
| arithmetic mean (standard deviation) | | | | |
| Bilirubin total, Day 14, n=2, 3 | 0.0 (± 0.00) | 1.3 (± 1.15) | | |
| Bilirubin total, Day 28, n=2, 3 | 1.0 (± 1.41) | 0.0 (± 0.00) | | |
| Bilirubin total, Day 42, n=2, 2 | 1.0 (± 1.41) | 3.0 (± 4.24) | | |
| Bilirubin total, Day 59, n=2, 3 | 0.0 (± 0.00) | 0.7 (± 1.15) | | |
| Direct Bilirubin, Day 14, n=2, 2 | 0.0 (± 0.00) | 0.0 (± 0.00) | | |
| Direct Bilirubin, Day 28, n=2, 2 | 0.0 (± 0.00) | 0.0 (± 0.00) | | |
| Direct Bilirubin, Day 42, n=2, 1 | 1.0 (± 1.41) | 0.0 (± 99999) | | |
| Direct Bilirubin, Day 59, n=2, 2 | 1.0 (± 1.41) | 0.0 (± 0.00) | | |
| Indirect Bilirubin, Day 14, n=2, 2 | 0.0 (± 0.00) | 1.0 (± 1.41) | | |
| Indirect Bilirubin, Day 28, n=2, 2 | 1.0 (± 1.41) | 0.0 (± 0.00) | | |
| Indirect Bilirubin, Day 42, n=2, 1 | 0.0 (± 0.00) | 6.0 (± 99999) | | |
| Indirect Bilirubin, Day 59, n=2, 2 | -1.0 (± 1.41) | 1.0 (± 1.41) | | |

### Statistical analyses

No statistical analyses for this end point

### Other pre-specified: Absolute values of clinical chemistry parameters of Alanine transaminase (ALT), Alkaline Phosphatase (ALP) and Aspartate transaminase (AST)

| End point title | Absolute values of clinical chemistry parameters of Alanine transaminase (ALT), Alkaline Phosphatase (ALP) and Aspartate transaminase (AST) |
|---|---|

End point description:

Blood samples will be collected for the analysis of clinical chemistry parameters including; ALT, ALP and AST. Safety Population. Only those participants with data available at the specified data points were analyzed (represented by n=X in the category titles).

| End point type | Other pre-specified |
|---|---|

End point timeframe:

Days 1, 14, 28, 42 and 59

| End point values | Daprodustat | Darbepoetin alfa | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 2 | 3 | | |
| Units: International units per Liter | | | | |
| arithmetic mean (standard deviation) | | | | |
| ALT, Day 1, n=2, 3 | 21.0 (± 4.24) | 26.7 (± 7.02) | | |
| ALT, Day 14, n=2, 3 | 15.0 (± 4.24) | 20.3 (± 6.81) | | |
| ALT, Day 28, n=2, 3 | 15.5 (± 4.95) | 18.3 (± 8.08) | | |
| ALT, Day 42, n=2, 2 | 16.0 (± 4.24) | 22.0 (± 9.90) | | |
| ALT, Day 59, n=2, 3 | 20.5 (± 10.61) | 23.3 (± 8.08) | | |
| ALP, Day 1, n=2, 3 | 113.5 (± 61.52) | 95.0 (± 42.44) | | |

| | | | | |
|---|---|---|---|---|
| ALP, Day 14, n=2, 3 | 97.0 (± 42.43) | 91.0 (± 33.87) | | |
| ALP, Day 28, n=2, 3 | 99.5 (± 45.96) | 91.7 (± 38.40) | | |
| ALP, Day 42, n=2, 2 | 99.0 (± 39.60) | 100.5 (± 37.48) | | |
| ALP, Day 59, n=2, 3 | 108.5 (± 55.86) | 90.3 (± 29.26) | | |
| AST, Day 1, n=2, 3 | 19.5 (± 7.78) | 21.7 (± 1.53) | | |
| AST, Day 14, n=2, 3 | 16.5 (± 7.78) | 18.3 (± 3.51) | | |
| AST, Day 28, n=2, 3 | 18.0 (± 9.90) | 18.7 (± 7.09) | | |
| AST, Day 42, n=2, 2 | 17.5 (± 10.61) | 16.5 (± 4.95) | | |
| AST, Day 59, n=2, 3 | 20.5 (± 10.61) | 19.3 (± 6.03) | | |

## Statistical analyses

No statistical analyses for this end point

## Other pre-specified: Change from Baseline in clinical chemistry parameter: ALT, ALP and AST

| End point title | Change from Baseline in clinical chemistry parameter: ALT, ALP and AST |
|---|---|

End point description:

Blood samples will be collected for the analysis of clinical chemistry parameters including; ALT, ALP and AST. Baseline value (Day 1) is the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline is defined as post-dose visit value minus Baseline value. Safety Population. Only those participants with data available at the specified data points were analyzed (represented by n=X in the category titles).

| End point type | Other pre-specified |
|---|---|

End point timeframe:

Baseline (Day 1) and at Days 14, 28, 42 and 59

| **End point values** | Daprodustat | Darbepoetin alfa | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 2 | 3 | | |
| Units: International units per Liter | | | | |
| arithmetic mean (standard deviation) | | | | |
| ALT, Day 14, n=2, 3 | -6.0 (± 0.00) | -6.3 (± 1.53) | | |
| ALT, Day 28, n=2, 3 | -5.5 (± 0.71) | -8.3 (± 1.15) | | |
| ALT, Day 42, n=2, 2 | -5.0 (± 0.00) | -5.0 (± 0.00) | | |
| ALT, Day 59, n=2, 3 | -0.5 (± 6.36) | -3.3 (± 4.62) | | |
| ALP, Day 14, n=2, 3 | -16.5 (± 19.09) | -4.0 (± 12.12) | | |
| ALP, Day 28, n=2, 3 | -14.0 (± 15.56) | -3.3 (± 4.04) | | |
| ALP, Day 42, n=2, 2 | -14.5 (± 21.92) | -6.5 (± 14.85) | | |
| ALP, Day 59, n=2, 3 | -5.0 (± 5.66) | -4.7 (± 13.61) | | |
| AST, Day 14, n=2, 3 | -3.0 (± 0.00) | -3.3 (± 2.08) | | |
| AST, Day 28, n=2, 3 | -1.5 (± 2.12) | -3.0 (± 6.00) | | |
| AST, Day 42, n=2, 2 | -2.0 (± 2.83) | -5.0 (± 2.83) | | |

| | | | | |
|---|---|---|---|---|
| AST, Day 59, n=2, 3 | 1.0 (± 2.83) | -2.3 (± 5.03) | | |

## Statistical analyses

No statistical analyses for this end point

## Other pre-specified: Absolute values of clinical chemistry parameters of Albumin

| End point title | Absolute values of clinical chemistry parameters of Albumin |
|---|---|

End point description:

Blood samples will be collected for the analysis of clinical chemistry parameters including; Albumin. Safety Population. Only those participants with data available at the specified data points were analyzed (represented by n=X in the category titles).

| End point type | Other pre-specified |
|---|---|

End point timeframe:

Days 1, 14, 28, 42 and 59

| End point values | Daprodustat | Darbepoetin alfa | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 2 | 3 | | |
| Units: Grams per Liter | | | | |
| arithmetic mean (standard deviation) | | | | |
| Day 1, n=2, 3 | 37.0 (± 5.66) | 41.7 (± 2.31) | | |
| Day 14, n=2, 3 | 36.5 (± 2.12) | 40.7 (± 3.06) | | |
| Day 28, n=2, 3 | 35.5 (± 3.54) | 39.3 (± 3.21) | | |
| Day 42, n=2, 2 | 35.5 (± 3.54) | 38.5 (± 0.71) | | |
| Day 59, n=2, 3 | 36.5 (± 6.36) | 40.3 (± 1.53) | | |

## Statistical analyses

No statistical analyses for this end point

## Other pre-specified: Change from Baseline in clinical chemistry parameter: Albumin

| End point title | Change from Baseline in clinical chemistry parameter: Albumin |
|---|---|

End point description:

Blood samples will be collected for the analysis of clinical chemistry parameters including; Albumin. Baseline value (Day 1) is the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline is defined as post-dose visit value minus Baseline value. Safety Population. Only those participants with data available at the specified data points were analyzed (represented by n=X in the category titles).

| End point type | Other pre-specified |
|---|---|

End point timeframe:

Baseline (Day 1) and at Days 14, 28, 42 and 59

| End point values | Daprodustat | Darbepoetin alfa | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 2 | 3 | | |
| Units: Grams per Liter | | | | |
| arithmetic mean (standard deviation) | | | | |
| Day 14, n=2, 3 | -0.05 (± 0.354) | -0.10 (± 0.200) | | |
| Day 28, n=2, 3 | -0.15 (± 0.212) | -0.23 (± 0.321) | | |
| Day 42, n=2, 2 | -0.15 (± 0.212) | -0.25 (± 0.354) | | |
| Day 59, n=2, 3 | -0.05 (± 0.071) | -0.13 (± 0.153) | | |

## Statistical analyses

No statistical analyses for this end point

## Adverse events

| Adverse events information | |
|---|---|
| Timeframe for reporting adverse events: | |
| Non-SAEs and SAEs were collected from the start of the treatment and Up to 59 days | |
| Adverse event reporting additional description: | |
| Non-SAEs and SAEs were collected in the Safety Population which comprised of participants who received at least one dose of study treatment. | |
| Assessment type | Systematic |

| Dictionary used | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 22.0 |

| Reporting groups | |
|---|---|
| Reporting group title | Darbepoetin alfa |
| Reporting group description: | |
| Participants were randomized to receive darbepoetin alfa solution for injection, administered as a single subcutaneous injection, once every two weeks (Days 1, 14 and 28). | |
| Reporting group title | Daprodustat |
| Reporting group description: | |
| Participants were randomized to receive 2 milligram (mg) daprodustat tablets once daily via oral route for a period of 41 days. | |

| Serious adverse events | Darbepoetin alfa | Daprodustat | |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 2 (0.00%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | | | |

Frequency threshold for reporting non-serious adverse events: 0 %

| Non-serious adverse events | Darbepoetin alfa | Daprodustat | |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 0 / 2 (0.00%) | |
| Gastrointestinal disorders | | | |
| Faeces soft | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 0 / 2 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Abdominal pain upper | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 0 / 2 (0.00%) | |
| occurrences (all) | 1 | 0 | |

| | | | |
|---|---|---|---|
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 0 / 2 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Joint swelling | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 0 / 2 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Metabolism and nutrition disorders | | | |
| Gout | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 0 / 2 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Bilateral foot discomfort secondary to Gout | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 0 / 2 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Swollen right foot secondary to Gout | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 0 / 2 (0.00%) | |
| occurrences (all) | 1 | 0 | |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---|---|
| 29 January 2018 | Amendment 01: The study team was required per regulatory agencies to change the protocol to include a serum pregnancy testing at screening. During the amendment process, minor updates were made for study optimization. |

Notes:

### Interruptions (globally)

Were there any global interruptions to the trial? Yes

| Date | Interruption | Restart date |
|---|---|---|
| 29 May 2019 | Study pause due to significant protocol amendment | - |

Notes:

### Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Amendment 02: 07-AUG-2019: Study restarted but no participants recruited prior to termination date. Thus not reported due to limitations in disclosure form.

Notes: