



## Clinical trial results:

### An Open-Label, Single-Arm, Multicenter Study to Ascertain the Optimal Starting Dose of MIRCERA® Given Subcutaneously for the Maintenance Treatment of Anemia in Pediatric Patients With Chronic Kidney Disease on Dialysis or Not Yet on Dialysis.

#### Summary

|                          |                   |
|--------------------------|-------------------|
| EudraCT number           | 2016-004779-39    |
| Trial protocol           | ES LT HU FR PL IT |
| Global end of trial date | 19 July 2021      |

#### Results information

|                                |                  |
|--------------------------------|------------------|
| Result version number          | v1 (current)     |
| This version publication date  | 04 February 2022 |
| First version publication date | 04 February 2022 |

#### Trial information

##### Trial identification

|                       |         |
|-----------------------|---------|
| Sponsor protocol code | NH19708 |
|-----------------------|---------|

##### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT03552393 |
| WHO universal trial number (UTN)   | -           |

Notes:

#### Sponsors

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

Notes:

#### Paediatric regulatory details

|  |                     |
|--|---------------------|
| Is trial part of an agreed paediatric investigation plan (PIP)       | Yes                 |
| EMA paediatric investigation plan number(s)                          | EMA-000172-PIP01-07 |
| Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial? | No                  |
| Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial? | Yes                 |

Notes:

## Results analysis stage

|  |              |
|--|--------------|
| Analysis stage                                       | Final        |
| Date of interim/final analysis                       | 19 July 2021 |
| Is this the analysis of the primary completion data? | No           |
| Global end of trial reached?                         | Yes          |
| Global end of trial date                             | 19 July 2021 |
| Was the trial ended prematurely?                     | No           |

Notes:

## General information about the trial

Main objective of the trial:

The main objective of this trial was to ascertain the starting dose of Mircera given subcutaneously (SC) in pediatric participants with chronic kidney disease (CKD) on dialysis or not yet on dialysis when switching from stable SC maintenance treatment with epoetin alfa, epoetin beta, or darbepoetin alfa.

Protection of trial subjects:

A signed Informed Consent Form (ICF) was obtained for all study subjects: written informed consent from the parent/legal guardian was required and written informed consent or assent from the child, where appropriate, was obtained.

Background therapy: -

Evidence for comparator: -

|   |                |
|---|----------------|
| Actual start date of recruitment                          | 03 August 2018 |
| 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 | Spain: 4         |
| Country: Number of subjects enrolled | France: 5        |
| Country: Number of subjects enrolled | Hungary: 5       |
| Country: Number of subjects enrolled | Italy: 4         |
| Country: Number of subjects enrolled | Lithuania: 2     |
| Country: Number of subjects enrolled | Poland: 11       |
| Country: Number of subjects enrolled | United States: 9 |
| Worldwide total number of subjects   | 40               |
| EEA total number of subjects         | 31               |

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)  | 4 |

|                           |    |
|---------------------------|----|
| Children (2-11 years)     | 19 |
| Adolescents (12-17 years) | 17 |
| Adults (18-64 years)      | 0  |
| From 65 to 84 years       | 0  |
| 85 years and over         | 0  |

## Subject disposition

### Recruitment

Recruitment details:

The core study was 23 weeks and consisted of three periods: screening (3 weeks), dose titration (16 weeks) and evaluation (4 weeks). Participants completing the 20 weeks of treatment with hemoglobin (Hb) within +/- 1g/dL of their baseline and within the target range of 10-12 g/dL were eligible to enter an optional 24-week safety extension period.

### Pre-assignment

Screening details:

Forty pediatric participants (ages 3 months to 17 years) with a diagnosis of anemia due to chronic kidney disease (CKD) who may or may not have been on dialysis at the time of study start were switched from stable subcutaneous (SC) maintenance treatment with epoetin alfa/beta or darbepoetin to methoxy polyethylene glycol-epoetin beta (Mircera).

### Period 1

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

### Arms

|           |         |
|-----------|---------|
| Arm title | Mircera |
|-----------|---------|

Arm description:

Mircera was administered subcutaneously once every 4 weeks.

|  |  |
|--|--|
| Arm type                               | Experimental                             |
| Investigational medicinal product name | Methoxy Polyethylene Glycol-Epoetin Beta |
| Investigational medicinal product code | RO0503821                                |
| Other name                             | MIRCERA                                  |
| Pharmaceutical forms                   | Solution for injection                   |
| Routes of administration               | Subcutaneous use                         |

Dosage and administration details:

Mircera was administered subcutaneously once every 4 weeks

| Number of subjects in period 1 | Mircera |
|--------------------------------|---------|
| Started                        | 40      |
| Completed                      | 38      |
| Not completed                  | 2       |
| Kidney Transplant              | 1       |
| Prohibited Medication          | 1       |

## Baseline characteristics

### Reporting groups

|                       |                |
|-----------------------|----------------|
| Reporting group title | Overall Period |
|-----------------------|----------------|

Reporting group description: -

| Reporting group values                   | Overall Period | Total |  |
|--|----------------|-------|--|
| Number of subjects                       | 40             | 40    |  |
| Age categorical                          |                |       |  |
| Units: subjects                          |                |       |  |
| Infants and toddlers (28 days-23 months) | 4              | 4     |  |
| Children (2-11 years)                    | 19             | 19    |  |
| Adolescents (12-17 years)                | 17             | 17    |  |
| Age Continuous                           |                |       |  |
| Units: years                             |                |       |  |
| arithmetic mean                          | 10.32          |       |  |
| standard deviation                       | ± 5.69         | -     |  |
| Sex: Female, Male                        |                |       |  |
| Units: subjects                          |                |       |  |
| Female                                   | 17             | 17    |  |
| Male                                     | 23             | 23    |  |

## End points

### End points reporting groups

|   |         |
|---|---------|
| Reporting group title                                       | Mircera |
| Reporting group description:                                |         |
| Mircera was administered subcutaneously once every 4 weeks. |         |

### Primary: Change in Hemoglobin (Hb) Concentration Between the Baseline and the Evaluation Period for Each Patient

|                 |  |
|-----------------|--|
| End point title | Change in Hemoglobin (Hb) Concentration Between the Baseline and the Evaluation Period for Each Patient <sup>[1]</sup> |
|-----------------|--|

End point description:

The Hb change from baseline was calculated on a per-participant basis, using an area under the curve (AUC) approach to calculate an individual's average for both the baseline and evaluation periods and taking the difference. The baseline period was defined as the time between the day of first study dose and the previous 35 days. The evaluation period was defined as the period between Week 17 and Week 21 inclusive. ITT population included all participants enrolled in the study. Number analyzed is the number of participants with Hb concentration assessment at specified time points.

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

End point timeframe:

Baseline up to Week 21

Notes:

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

Justification: No formal statistical testing was planned to be performed for the primary endpoint.

| End point values                     | Mircera         |  |  |  |
|--------------------------------------|-----------------|--|--|--|
| Subject group type                   | Reporting group |  |  |  |
| Number of subjects analysed          | 38              |  |  |  |
| Units: g/dL                          |                 |  |  |  |
| arithmetic mean (standard deviation) |                 |  |  |  |
| Baseline                             | 11.05 (± 0.51)  |  |  |  |
| Change at Evaluation Period          | 0.48 (± 1.03)   |  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of Participants With an Average Hb Concentration During the Evaluation Period Within ± 1 g/dL of Their Baseline Hb and Above, Within or Below the Range of 10-12 g/dL

|                 |  |
|-----------------|--|
| End point title | Number of Participants With an Average Hb Concentration During the Evaluation Period Within ± 1 g/dL of Their Baseline Hb and Above, Within or Below the Range of 10-12 g/dL |
|-----------------|--|

End point description:

Number of participants with an average Hb concentration during the evaluation period within ± 1 g/dL of their baseline Hb is reported as well as the number of participants with an average Hb concentration above, within or below the range of 10-12 g/dL. The evaluation period was defined as the period between Week 17 and Week 21 inclusive. ITT population included all participants enrolled in the study. Hb values within 21 days after blood transfusion(s) were excluded from analysis.

|                       |           |
|-----------------------|-----------|
| End point type        | Secondary |
| End point timeframe:  |           |
| Week 17 up to Week 21 |           |

| End point values                              | Mircera         |  |  |  |
|---|-----------------|--|--|--|
| Subject group type                            | Reporting group |  |  |  |
| Number of subjects analysed                   | 38              |  |  |  |
| Units: participants                           |                 |  |  |  |
| Hb Above 1 g/dL of Baseline                   | 15              |  |  |  |
| Hb Maintained Within $\pm$ 1 g/dL of Baseline | 19              |  |  |  |
| Hb Below 1 g/dL of Baseline                   | 4               |  |  |  |
| Hb Above 12 g/dL                              | 12              |  |  |  |
| Hb Maintained Within 10-12 g/dL               | 24              |  |  |  |
| Hb Below 10 g/dL                              | 2               |  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Mean Hb Values and Change from Baseline

|  |   |
|--|---|
| End point title  | Mean Hb Values and Change from Baseline |
| End point description:   |   |
| The mean Hb concentration over time and the mean change in Hb from baseline over time are presented. ITT population included all participants enrolled in the study. Here 'n' signifies the number of participants evaluable at specified time-points. |   |
| End point type   | Secondary                               |
| End point timeframe:   |   |
| Baseline, Weeks 3, 5, 9, 13, 17,19, 21, 25, 29, 33, 37, 41, 45   |   |

| End point values                     | Mircera             |  |  |  |
|--------------------------------------|---------------------|--|--|--|
| Subject group type                   | Reporting group     |  |  |  |
| Number of subjects analysed          | 40                  |  |  |  |
| Units: g/dL                          |                     |  |  |  |
| arithmetic mean (standard deviation) |                     |  |  |  |
| Baseline (n=40)                      | 11.02 ( $\pm$ 0.53) |  |  |  |
| Week 3 (n=40)                        | 11.69 ( $\pm$ 0.97) |  |  |  |
| Change at Week 3 (n=40)              | 0.67 ( $\pm$ 0.74)  |  |  |  |
| Week 5 (n=40)                        | 11.21 ( $\pm$ 1.02) |  |  |  |
| Change at Week 5 (n=40)              | 0.19 ( $\pm$ 0.94)  |  |  |  |
| Week 9 (n=39)                        | 11.68 ( $\pm$ 1.42) |  |  |  |
| Change at Week 9 (n=39)              | 0.64 ( $\pm$ 1.21)  |  |  |  |
| Week 13 (n=38)                       | 11.56 ( $\pm$ 1.17) |  |  |  |
| Change at Week 13 (n=38)             | 0.51 ( $\pm$ 1.10)  |  |  |  |

|                          |                |  |  |  |
|--------------------------|----------------|--|--|--|
| Week 17 (n=37)           | 11.46 (± 1.33) |  |  |  |
| Change at Week 17 (n=37) | 0.42 (± 1.39)  |  |  |  |
| Week 19 (n=37)           | 11.81 (± 1.11) |  |  |  |
| Change at Week 19 (n=37) | 0.77 (± 1.14)  |  |  |  |
| Week 21 (n=38)           | 11.10 (± 0.91) |  |  |  |
| Change at Week 21 (n=38) | 0.05 (± 0.99)  |  |  |  |
| Week 25 (n=25)           | 11.29 (± 1.04) |  |  |  |
| Change at Week 25 (n=25) | 0.21 (± 1.12)  |  |  |  |
| Week 29 (n=23)           | 11.22 (± 1.18) |  |  |  |
| Change at Week 29 (n=23) | 0.15 (± 1.11)  |  |  |  |
| Week 33 (n=24)           | 11.09 (± 1.11) |  |  |  |
| Change at Week 33 (n=24) | 0.02 (± 1.24)  |  |  |  |
| Week 37 (n=24)           | 11.04 (± 0.77) |  |  |  |
| Change at Week 37 (n=24) | -0.03 (± 0.90) |  |  |  |
| Week 41 (n=22)           | 10.83 (± 0.83) |  |  |  |
| Change at Week 41 (n=22) | -0.22 (± 1.03) |  |  |  |
| Week 45 (n=21)           | 10.68 (± 1.02) |  |  |  |
| Change at Week 45 (n=21) | -0.35 (± 1.13) |  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change in Mircera Dose Over Time

|  |                                  |
|--|----------------------------------|
| End point title  | Change in Mircera Dose Over Time |
| End point description:   |                                  |
| A dose change was defined as a change in the administered dose strength compared to the preceding dose. Safety population included all participants who received at least one dose of study drug regardless of whether they withdrew prematurely or not. Here 'n' signifies number of participants evaluable at specified time points. |                                  |
| End point type   | Secondary                        |
| End point timeframe:   |                                  |
| Week 1 to Week 17  |                                  |

| End point values              | Mircera               |  |  |  |
|-------------------------------|-----------------------|--|--|--|
| Subject group type            | Reporting group       |  |  |  |
| Number of subjects analysed   | 40                    |  |  |  |
| Units: micrograms (µg)        |                       |  |  |  |
| median (full range (min-max)) |                       |  |  |  |
| Week 1 (n=40)                 | 75.00 (15.0 to 360.0) |  |  |  |
| Week 5 (n=39)                 | 75.00 (15.0 to 360.0) |  |  |  |
| Change at Week 5 (n=39)       | 0.00 (-50.0 to 75.0)  |  |  |  |
| Week 9 (n=39)                 | 50.00 (0.0 to 360.0)  |  |  |  |



|                          |                          |  |  |  |
|--------------------------|--------------------------|--|--|--|
| Change at Week 9 (n=39)  | 0.00 (-250.0 to 190.0)   |  |  |  |
| Week 13 (n=38)           | 50.00 (0.0 to 360.0)     |  |  |  |
| Change at Week 13 (n=38) | -25.00 (-120.0 to 210.0) |  |  |  |
| Week 17 (n=38)           | 50.00 (0.0 to 250.0)     |  |  |  |
| Change at Week 17 (n=38) | -20.00 (-250.0 to 120.0) |  |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Ratio of Mircera Starting Dose (Week 1) to the Dose at Week 17

|  |  |
|--|--|
| End point title  | Ratio of Mircera Starting Dose (Week 1) to the Dose at Week 17 |
| End point description:<br>The ratio of Mircera dose was calculated as the median (min-max) ratio of starting dose (Week 1) to the dose at Week 17. Participants who withdrew before Week 17 or who were not administered a Mircera dose at Week 17 visit due to the applicable dose adjustment rules were excluded from the ratio computation. |  |
| End point type   | Secondary  |
| End point timeframe:<br>Week 1, Week 17  |  |

| End point values              | Mircera           |  |  |  |
|-------------------------------|-------------------|--|--|--|
| Subject group type            | Reporting group   |  |  |  |
| Number of subjects analysed   | 33                |  |  |  |
| Units: ratio                  |                   |  |  |  |
| median (full range (min-max)) | 1.44 (0.2 to 3.8) |  |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of Participants With Adverse Events by Severity as Assessed by Highest World Health Organization (WHO) Toxicity Grade

|  |  |
|--|--|
| End point title  | Number of Participants With Adverse Events by Severity as Assessed by Highest World Health Organization (WHO) Toxicity Grade |
| End point description:<br>An adverse event is any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product, any new disease, or exacerbation of existing disease (a worsening in the character, frequency, or severity of a known condition), recurrence of an intermittent |  |

medical condition or any deterioration in a laboratory value or other clinical test. Safety population included all participants who received at least one dose of study drug regardless of whether they withdrew prematurely or not.

|                        |           |
|------------------------|-----------|
| End point type         | Secondary |
| End point timeframe:   |           |
| Baseline up to Week 45 |           |

|                             |                 |  |  |  |
|-----------------------------|-----------------|--|--|--|
| <b>End point values</b>     | Mircera         |  |  |  |
| Subject group type          | Reporting group |  |  |  |
| Number of subjects analysed | 40              |  |  |  |
| Units: participants         |                 |  |  |  |
| Grade 1-2                   | 25              |  |  |  |
| Grade 3-4                   | 8               |  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Bioavailability (F) of Mircera in Pediatric Participants Based on Population PK Model

|                 |   |
|-----------------|---|
| End point title | Bioavailability (F) of Mircera in Pediatric Participants Based on Population PK Model |
|-----------------|---|

End point description:

Bioavailability (F) is defined as the percentage of the administered drug, that reaches the systemic circulation. A population PK model was developed for Mircera that adequately describes pediatric data: a 1-compartment model with first order absorption and elimination processes.

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

End point timeframe:

Pre-dose at Week 1, 9, 17; post-dose at Week 3 and Week 19 and additional sample taken between 24 hours and 5 days at participant's convenience

|                             |                 |  |  |  |
|-----------------------------|-----------------|--|--|--|
| <b>End point values</b>     | Mircera         |  |  |  |
| Subject group type          | Reporting group |  |  |  |
| Number of subjects analysed | 40              |  |  |  |
| Units: percentage           |                 |  |  |  |
| number (not applicable)     | 67              |  |  |  |

### Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Up to Week 45

Adverse event reporting additional description:

Safety population included all participants who received at least one dose of study drug regardless of whether they withdrew prematurely or not.

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

### Dictionary used

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

|                    |    |
|--------------------|----|
| Dictionary version | 22 |
|--------------------|----|

### Reporting groups

|                       |         |
|-----------------------|---------|
| Reporting group title | Mircera |
|-----------------------|---------|

Reporting group description:

Mircera was administered subcutaneously once every 4 weeks.

| Serious adverse events                               | Mircera          |  |  |
|--|------------------|--|--|
| Total subjects affected by serious adverse events    |                  |  |  |
| subjects affected / exposed                          | 13 / 40 (32.50%) |  |  |
| number of deaths (all causes)                        | 0                |  |  |
| number of deaths resulting from adverse events       | 0                |  |  |
| Injury, poisoning and procedural complications       |                  |  |  |
| Anaemia postoperative                                |                  |  |  |
| subjects affected / exposed                          | 2 / 40 (5.00%)   |  |  |
| occurrences causally related to treatment / all      | 0 / 2            |  |  |
| deaths causally related to treatment / all           | 0 / 0            |  |  |
| Congenital, familial and genetic disorders           |                  |  |  |
| Hydrocele  |                  |  |  |
| subjects affected / exposed                          | 1 / 40 (2.50%)   |  |  |
| occurrences causally related to treatment / all      | 0 / 1            |  |  |
| deaths causally related to treatment / all           | 0 / 0            |  |  |
| Vascular disorders                                   |                  |  |  |
| Hypotension  |                  |  |  |
| subjects affected / exposed                          | 2 / 40 (5.00%)   |  |  |
| occurrences causally related to treatment / all      | 0 / 2            |  |  |
| deaths causally related to treatment / all           | 0 / 0            |  |  |
| General disorders and administration site conditions |                  |  |  |

|   |                |  |  |
|---|----------------|--|--|
| Device related thrombosis                       |                |  |  |
| subjects affected / exposed                     | 1 / 40 (2.50%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Gastrointestinal disorders                      |                |  |  |
| Diarrhoea                                       |                |  |  |
| subjects affected / exposed                     | 1 / 40 (2.50%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Vomiting  |                |  |  |
| subjects affected / exposed                     | 1 / 40 (2.50%) |  |  |
| occurrences causally related to treatment / all | 0 / 2          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Respiratory, thoracic and mediastinal disorders |                |  |  |
| Hypoxia   |                |  |  |
| subjects affected / exposed                     | 1 / 40 (2.50%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Musculoskeletal and connective tissue disorders |                |  |  |
| Back pain                                       |                |  |  |
| subjects affected / exposed                     | 1 / 40 (2.50%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Infections and infestations                     |                |  |  |
| Appendicitis                                    |                |  |  |
| subjects affected / exposed                     | 1 / 40 (2.50%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Device related infection                        |                |  |  |
| subjects affected / exposed                     | 1 / 40 (2.50%) |  |  |
| occurrences causally related to treatment / all | 0 / 2          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Enterovirus infection                           |                |  |  |

|   |                |  |  |  |
|---|----------------|--|--|--|
| subjects affected / exposed                     | 1 / 40 (2.50%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Gastroenteritis                                 |                |  |  |  |
| subjects affected / exposed                     | 1 / 40 (2.50%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Peritonitis                                     |                |  |  |  |
| subjects affected / exposed                     | 3 / 40 (7.50%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 3          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Pharyngotonsillitis                             |                |  |  |  |
| subjects affected / exposed                     | 1 / 40 (2.50%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Pneumonia                                       |                |  |  |  |
| subjects affected / exposed                     | 1 / 40 (2.50%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Respiratory syncytial virus bronchiolitis       |                |  |  |  |
| subjects affected / exposed                     | 1 / 40 (2.50%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Pyelonephritis                                  |                |  |  |  |
| subjects affected / exposed                     | 1 / 40 (2.50%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Rhinovirus infection                            |                |  |  |  |
| subjects affected / exposed                     | 1 / 40 (2.50%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Upper respiratory tract infection               |                |  |  |  |

|   |                |  |  |
|---|----------------|--|--|
| subjects affected / exposed                     | 1 / 40 (2.50%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Viral infection                                 |                |  |  |
| subjects affected / exposed                     | 1 / 40 (2.50%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Product issues                                  |                |  |  |
| Device malfunction                              |                |  |  |
| subjects affected / exposed                     | 1 / 40 (2.50%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |

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

| <b>Non-serious adverse events</b>                     | Mircera          |  |  |
|---|------------------|--|--|
| Total subjects affected by non-serious adverse events |                  |  |  |
| subjects affected / exposed                           | 28 / 40 (70.00%) |  |  |
| Injury, poisoning and procedural complications        |                  |  |  |
| Accidental overdose                                   |                  |  |  |
| subjects affected / exposed                           | 5 / 40 (12.50%)  |  |  |
| occurrences (all)                                     | 5                |  |  |
| Vascular disorders                                    |                  |  |  |
| Hypertension  |                  |  |  |
| subjects affected / exposed                           | 2 / 40 (5.00%)   |  |  |
| occurrences (all)                                     | 3                |  |  |
| Hypotension   |                  |  |  |
| subjects affected / exposed                           | 2 / 40 (5.00%)   |  |  |
| occurrences (all)                                     | 3                |  |  |
| Nervous system disorders                              |                  |  |  |
| Headache  |                  |  |  |
| subjects affected / exposed                           | 3 / 40 (7.50%)   |  |  |
| occurrences (all)                                     | 6                |  |  |
| Blood and lymphatic system disorders                  |                  |  |  |

|  |   |  |  |
|--|---|--|--|
| Anaemia<br>subjects affected / exposed<br>occurrences (all)  | 2 / 40 (5.00%)<br>2                             |  |  |
| General disorders and administration site conditions<br>Injection site pain<br>subjects affected / exposed<br>occurrences (all)<br><br>Pyrexia<br>subjects affected / exposed<br>occurrences (all) | 2 / 40 (5.00%)<br>2<br><br>5 / 40 (12.50%)<br>5 |  |  |
| Gastrointestinal disorders<br>Abdominal pain<br>subjects affected / exposed<br>occurrences (all)<br><br>Diarrhoea<br>subjects affected / exposed<br>occurrences (all)                              | 3 / 40 (7.50%)<br>3<br><br>3 / 40 (7.50%)<br>4  |  |  |
| Respiratory, thoracic and mediastinal disorders<br>Rhinorrhoea<br>subjects affected / exposed<br>occurrences (all)<br><br>Oropharyngeal pain<br>subjects affected / exposed<br>occurrences (all)   | 2 / 40 (5.00%)<br>3<br><br>3 / 40 (7.50%)<br>3  |  |  |
| Renal and urinary disorders<br>Haematuria<br>subjects affected / exposed<br>occurrences (all)  | 2 / 40 (5.00%)<br>2                             |  |  |
| Musculoskeletal and connective tissue disorders<br>Muscle spasms<br>subjects affected / exposed<br>occurrences (all)   | 2 / 40 (5.00%)<br>2                             |  |  |
| Infections and infestations<br>Conjunctivitis<br>subjects affected / exposed<br>occurrences (all)  | 3 / 40 (7.50%)<br>3                             |  |  |

|                                    |                 |  |  |
|------------------------------------|-----------------|--|--|
| Gastroenteritis                    |                 |  |  |
| subjects affected / exposed        | 2 / 40 (5.00%)  |  |  |
| occurrences (all)                  | 2               |  |  |
| Bronchitis                         |                 |  |  |
| subjects affected / exposed        | 2 / 40 (5.00%)  |  |  |
| occurrences (all)                  | 2               |  |  |
| Nasopharyngitis                    |                 |  |  |
| subjects affected / exposed        | 2 / 40 (5.00%)  |  |  |
| occurrences (all)                  | 2               |  |  |
| Rhinitis                           |                 |  |  |
| subjects affected / exposed        | 3 / 40 (7.50%)  |  |  |
| occurrences (all)                  | 3               |  |  |
| Pharyngitis                        |                 |  |  |
| subjects affected / exposed        | 2 / 40 (5.00%)  |  |  |
| occurrences (all)                  | 3               |  |  |
| Upper respiratory tract infection  |                 |  |  |
| subjects affected / exposed        | 6 / 40 (15.00%) |  |  |
| occurrences (all)                  | 6               |  |  |
| Urinary tract infection            |                 |  |  |
| subjects affected / exposed        | 2 / 40 (5.00%)  |  |  |
| occurrences (all)                  | 2               |  |  |
| Metabolism and nutrition disorders |                 |  |  |
| Hyperkalaemia                      |                 |  |  |
| subjects affected / exposed        | 2 / 40 (5.00%)  |  |  |
| occurrences (all)                  | 2               |  |  |
| Hyperphosphataemia                 |                 |  |  |
| subjects affected / exposed        | 2 / 40 (5.00%)  |  |  |
| occurrences (all)                  | 2               |  |  |



## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date             | Amendment   |
|------------------|---|
| 19 January 2018  | <ul style="list-style-type: none"><li>- An additional time point for immunogenicity sampling was added at Week 9 (Visit 6 [V6]).</li><li>- An additional blood sample should be stored for an anti-PEG antibody determination after the assay has been developed in those participants where loss of efficacy was observed.</li></ul>   |
| 11 July 2018     | <ul style="list-style-type: none"><li>- Lab assessments required for calculating transferrin saturation (TSAT) were clarified. TSAT calculation with either serum transferrin or total iron-binding capacity was added.</li><li>- Blood sampling volume limits were added to ensure the safety of the participants in the study in accordance with the ethical considerations for clinical trials on medicinal products conducted with a pediatric population as published by the Directorate- General for Health and Food Safety.</li><li>- To further strengthen safety monitoring for special situations that may or may not result in an adverse event, instructions regarding the reporting of accidental overdose or medication error were added.</li><li>- The grading scale for assessment of severity of adverse events was revised to use the universally accepted and current World Health Organization toxicity scale.</li><li>- Requirements for the reporting of injection reactions were added.</li><li>- Reporting requirements for medical device complaints were added. In accordance with the Kidney Disease Outcomes Quality Initiative guidelines, Kt/V assessments for PD patients was reduced to one assessment every 6 months. Kt/V assessments at V3, V6 and V13 were removed.</li></ul> |
| 07 December 2018 | <ul style="list-style-type: none"><li>- Requirements for scheduling the screening visits and the approximate length of the screening period were clarified.</li><li>- Exclusion Criteria were amended to exclude participants who have undergone a kidney transplant with use of immunosuppressive therapies known to exacerbate anemia, as inclusion of these participants would add a bias to the studied patient population.</li><li>- Mircera Dose Adjustments, were amended to clarify the dose adjustment rules for Mircera.</li></ul>  |

Notes:

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported