



## Clinical trial results:

### An Open-label, Randomised, Active-controlled, Parallel Group, Multicentre, Phase 3 Study to Investigate the Safety and Efficacy of PA21 (Velporo®) and Calcium Acetate (Phoslyra®) in Paediatric and Adolescent CKD Patients with Hyperphosphataemia

#### Summary

|                          |                  |
|--------------------------|------------------|
| EudraCT number           | 2015-004155-43   |
| Trial protocol           | LT DE PL FR      |
| Global end of trial date | 21 February 2019 |

#### Results information

|                                |                |
|--------------------------------|----------------|
| Result version number          | v1 (current)   |
| This version publication date  | 21 August 2019 |
| First version publication date | 21 August 2019 |

#### Trial information

##### Trial identification

|                       |              |
|-----------------------|--------------|
| Sponsor protocol code | PA-CL-PED-01 |
|-----------------------|--------------|

##### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT02688764 |
| WHO universal trial number (UTN)   | -           |

Notes:

#### Sponsors

|                              |   |
|------------------------------|---|
| Sponsor organisation name    | Vifor Fresenius Medical Care Renal Pharma France  |
| Sponsor organisation address | 100-101 Terrasse Boieldieu, Tour Franklin La Défense 8, Paris La Défense Cedex, France, 92042 |
| Public contact               | Medical Information, Vifor (International) Inc, medinfo@viforpharma.com                       |
| Scientific contact           | Medical Information, Vifor (International) Inc, medinfo@viforpharma.com                       |

Notes:

#### Paediatric regulatory details

|  |                     |
|--|---------------------|
| Is trial part of an agreed paediatric investigation plan (PIP)       | Yes                 |
| EMA paediatric investigation plan number(s)                          | EMA-001061-PIP01-10 |
| 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                       | 10 May 2019      |
| Is this the analysis of the primary completion data? | Yes              |
| Primary completion date                              | 21 February 2019 |
| Global end of trial reached?                         | Yes              |
| Global end of trial date                             | 21 February 2019 |
| Was the trial ended prematurely?                     | Yes              |

Notes:

## General information about the trial

Main objective of the trial:

To evaluate the efficacy of PA21 (Velphoro®) in reducing serum phosphorus levels in paediatric and adolescent subjects with CKD (Chronic Kidney Disease) at the end of Stage 1.

Protection of trial subjects:

The study was conducted in accordance with the principles of the Declaration of Helsinki including amendments in force up to and including the time the study was conducted.

The study was conducted in compliance with the International Council for Harmonisation (ICH) E6 Guideline for Good Clinical Practice (GCP), Committee for Proprietary Medicinal Products Guideline (CPMP/ICH/135/95), compliant with the European Union Clinical Trial Directive (Directive 2001/20/EC) and/or the Code of Federal Regulations (CFR) for informed consent and protection of patient rights (21 CFR, Parts 50 and 56), and in accordance with US Food and Drug Administration (FDA) regulations.

Study subjects had phosphorus and calcium levels monitored at frequent intervals (weekly during the washout stage of the study). The dose was adjusted at regular intervals to optimise serum phosphorus levels. Stopping rules were in place to ensure withdrawal of subjects whose phosphorus or calcium levels were not controlled within required limits. In addition, the study had an external Data and Safety Monitoring Board (DSMB).

Background therapy: -

Evidence for comparator: -

|   |             |
|---|-------------|
| Actual start date of recruitment                          | 26 May 2016 |
| Long term follow-up planned                               | No          |
| Independent data monitoring committee (IDMC) involvement? | Yes         |

Notes:

## Population of trial subjects

### Subjects enrolled per country

|                                      |                       |
|--------------------------------------|-----------------------|
| Country: Number of subjects enrolled | Poland: 6             |
| Country: Number of subjects enrolled | Romania: 9            |
| Country: Number of subjects enrolled | France: 6             |
| Country: Number of subjects enrolled | Germany: 6            |
| Country: Number of subjects enrolled | Lithuania: 3          |
| Country: Number of subjects enrolled | United States: 53     |
| Country: Number of subjects enrolled | Russian Federation: 2 |
| Worldwide total number of subjects   | 85                    |
| EEA total number of subjects         | 30                    |

Notes:

| <b>Subjects enrolled per age group</b>    |    |
|---|----|
| 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)                     | 29 |
| Adolescents (12-17 years)                 | 55 |
| Adults (18-64 years)                      | 1  |
| From 65 to 84 years                       | 0  |
| 85 years and over                         | 0  |

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

No study related assessments were performed until signed/dated informed consent had been provided for the subject.

The study consisted of a screening period of up to 4 weeks and a washout period of up to 3 weeks for subjects previously taking phosphate binders before randomisation. A total of 120 subjects were screened, of whom 85 were randomized.

### Period 1

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

### Arms

|                              |                  |
|------------------------------|------------------|
| Are arms mutually exclusive? | Yes              |
| <b>Arm title</b>             | PA21 (Velphoro®) |

Arm description: -

|  |   |
|--|---|
| Arm type                               | Experimental                                |
| Investigational medicinal product name | PA21 (Velphoro®)                            |
| Investigational medicinal product code |   |
| Other name                             |   |
| Pharmaceutical forms                   | Chewable tablet, Powder for oral suspension |
| Routes of administration               | Oral use                                    |

Dosage and administration details:

Formulations:

PA21 (Velphoro®), chewable tablets 500 mg and 250 mg iron

PA21 (Velphoro®), powder for oral suspension 500 mg, 250 mg and 125 mg iron

Stage 1 (Open-Label Dose Titration; up to 10 weeks): starting dose based on the participant's age. Dose was increased or decreased as required for efficacy (to achieve age specific target serum phosphorus level), provided a subject had been receiving that dose for a minimum of 2 weeks, and for safety/tolerability reasons at any time.

Stage 2 (Open-Label Safety Extension, 24 week safety extension): dose received at the end of Stage 1, unless a dose change is required. Dose modifications were to follow the same guidelines used in Stage 1.

|                  |                             |
|------------------|-----------------------------|
| <b>Arm title</b> | Calcium Acetate (Phoslyra®) |
|------------------|-----------------------------|

Arm description: -

|  |                             |
|--|-----------------------------|
| Arm type                               | Active comparator           |
| Investigational medicinal product name | Calcium Acetate (Phoslyra®) |
| Investigational medicinal product code |                             |
| Other name                             |                             |
| Pharmaceutical forms                   | Oral solution               |
| Routes of administration               | Oral use                    |

Dosage and administration details:

Formulation:

Calcium Acetate (Phoslyra®) - Oral Solution: 667 mg calcium acetate per 5 mL equivalent to 169 mg (8.45 mEq) calcium.

Stage 1 (Open-Label Dose Titration; up to 10 weeks): starting dose based on the participant's weight or, if considered more appropriate by the Investigator, at an equivalent dose of their previous phosphate

binder (PB), calcium-based or sevelamer. Dose was increased or decreased as required for efficacy (to achieve age specific target serum phosphorus level), provided a subject had been receiving that dose for a minimum of 2 weeks, and for safety/tolerability reasons at any time.

Stage 2 (Open-Label Safety Extension, 24 week safety extension): dose received at the end of Stage 1, unless a dose change is required. Dose modifications were to follow the same guidelines used in Stage 1.

| <b>Number of subjects in period 1</b>             | <b>PA21 (Velphoro®)</b> | <b>Calcium Acetate (Phoslyra®)</b> |
|---|-------------------------|------------------------------------|
| Started   | 66                      | 19                                 |
| Treated in Stage 1                                | 66                      | 19                                 |
| Treated in Stage 2                                | 43                      | 8                                  |
| Completed   | 26                      | 2                                  |
| Not completed                                     | 40                      | 17                                 |
| Non-compliance/Physician decision/Withd. subject  | 1                       | 1                                  |
| Withdrawal by parent                              | 3                       | -                                  |
| AE/Physician decision                             | 1                       | -                                  |
| AE/Withdrawal by subject                          | 1                       | -                                  |
| AE/Non-compliance with study drug                 | 1                       | -                                  |
| Non-compliance/Withdrawal by subject              | -                       | 2                                  |
| AE/Withdrawal by parent/Withdrawal by subject     | 1                       | 1                                  |
| Adverse event                                     | 3                       | 3                                  |
| AE/Non-compliance with study drug/Withd. parent   | -                       | 1                                  |
| Lack of efficacy/Physician decision               | -                       | 1                                  |
| AE/Kidney transplant                              | 1                       | -                                  |
| Non-compliance with study drug/Physician decision | 2                       | -                                  |
| Other   | 4                       | 1                                  |
| Non-compliance with study drug                    | 4                       | -                                  |
| AE/Other  | -                       | 1                                  |
| AE/Withdrawal by parent                           | 3                       | -                                  |
| AE/Lack of efficacy                               | 1                       | -                                  |
| Other/Withdrawal by parent                        | 1                       | -                                  |
| Kidney transplant                                 | 10                      | 4                                  |
| Lack of efficacy                                  | 3                       | 2                                  |

## Baseline characteristics

### Reporting groups

|                                |                             |
|--------------------------------|-----------------------------|
| Reporting group title          | PA21 (Velphoro®)            |
| Reporting group description: - |                             |
| Reporting group title          | Calcium Acetate (Phoslyra®) |
| Reporting group description: - |                             |

| Reporting group values                             | PA21 (Velphoro®) | Calcium Acetate (Phoslyra®) | Total |
|--|------------------|-----------------------------|-------|
| Number of subjects                                 | 66               | 19                          | 85    |
| Age categorical                                    |                  |                             |       |
| Units: Subjects                                    |                  |                             |       |
| In utero   | 0                | 0                           | 0     |
| Preterm newborn infants (gestational age < 37 wks) | 0                | 0                           | 0     |
| Newborns (0-27 days)                               | 0                | 0                           | 0     |
| Infants and toddlers (28 days-23 months)           | 0                | 0                           | 0     |
| Children (2-11 years)                              | 23               | 6                           | 29    |
| Adolescents (12-17 years)                          | 42               | 13                          | 55    |
| Adults (18-64 years)                               | 1                | 0                           | 1     |
| From 65-84 years                                   | 0                | 0                           | 0     |
| 85 years and over                                  | 0                | 0                           | 0     |
| Age continuous                                     |                  |                             |       |
| Units: years                                       |                  |                             |       |
| arithmetic mean                                    | 12.2             | 12.6                        |       |
| standard deviation                                 | ± 4.07           | ± 3.73                      | -     |
| Gender categorical                                 |                  |                             |       |
| Units: Subjects                                    |                  |                             |       |
| Female   | 34               | 13                          | 47    |
| Male   | 32               | 6                           | 38    |

### Subject analysis sets

|                            |                        |
|----------------------------|------------------------|
| Subject analysis set title | PA21 (Velphoro®) - FAS |
| Subject analysis set type  | Full analysis          |

Subject analysis set description:

Full Analysis Set (FAS) Population: all subjects randomised to treatment at Stage 1 who received at least 1 dose of randomised treatment and who had at least 1 post-baseline assessment of the efficacy endpoint (serum phosphorus level), analysed according to treatment randomised.

|                            |                                   |
|----------------------------|-----------------------------------|
| Subject analysis set title | Calcium Acetate (Phoslyra®) - FAS |
| Subject analysis set type  | Full analysis                     |

Subject analysis set description:

Full Analysis Set (FAS) Population: all subjects randomised to treatment at Stage 1 who received at least 1 dose of randomised treatment and who had at least 1 post-baseline assessment of the efficacy endpoint (serum phosphorus level), analysed according to treatment randomised.

| <b>Reporting group values</b>                      | PA21 (Velphoro®) - FAS | Calcium Acetate (Phoslyra®) - FAS |  |
|--|------------------------|-----------------------------------|--|
| Number of subjects                                 | 65                     | 15                                |  |
| Age categorical<br>Units: Subjects                 |                        |                                   |  |
| In utero   | 0                      | 0                                 |  |
| Preterm newborn infants (gestational age < 37 wks) | 0                      | 0                                 |  |
| Newborns (0-27 days)                               | 0                      | 0                                 |  |
| Infants and toddlers (28 days-23 months)           | 0                      | 0                                 |  |
| Children (2-11 years)                              | 23                     | 5                                 |  |
| Adolescents (12-17 years)                          | 41                     | 10                                |  |
| Adults (18-64 years)                               | 1                      | 0                                 |  |
| From 65-84 years                                   | 0                      | 0                                 |  |
| 85 years and over                                  | 0                      | 0                                 |  |
| Age continuous<br>Units: years                     |                        |                                   |  |
| arithmetic mean                                    | 12.1                   | 12.3                              |  |
| standard deviation                                 | ± 4.10                 | ± 3.96                            |  |
| Gender categorical<br>Units: Subjects              |                        |                                   |  |
| Female   | 34                     | 10                                |  |
| Male   | 31                     | 5                                 |  |

## End points

### End points reporting groups

|                                |                             |
|--------------------------------|-----------------------------|
| Reporting group title          | PA21 (Velphoro®)            |
| Reporting group description: - |                             |
| Reporting group title          | Calcium Acetate (Phoslyra®) |
| Reporting group description: - |                             |
| Subject analysis set title     | PA21 (Velphoro®) - FAS      |
| Subject analysis set type      | Full analysis               |

Subject analysis set description:

Full Analysis Set (FAS) Population: all subjects randomised to treatment at Stage 1 who received at least 1 dose of randomised treatment and who had at least 1 post-baseline assessment of the efficacy endpoint (serum phosphorus level), analysed according to treatment randomised.

|                            |                                   |
|----------------------------|-----------------------------------|
| Subject analysis set title | Calcium Acetate (Phoslyra®) - FAS |
| Subject analysis set type  | Full analysis                     |

Subject analysis set description:

Full Analysis Set (FAS) Population: all subjects randomised to treatment at Stage 1 who received at least 1 dose of randomised treatment and who had at least 1 post-baseline assessment of the efficacy endpoint (serum phosphorus level), analysed according to treatment randomised.

### Primary: Change in Serum Phosphorus Level From Baseline to the End of Stage 1 in the PA21 Group

|                 |   |
|-----------------|---|
| End point title | Change in Serum Phosphorus Level From Baseline to the End of Stage 1 in the PA21 Group <sup>[1]</sup> |
|-----------------|---|

End point description:

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

End point timeframe:

From Baseline to the End of Stage 1 (up to 10 weeks after treatment start date)

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: The primary endpoint is defined in just one arm of the study, therefore no statistical analysis can be included on this section.

|                                     |                        |  |  |  |
|-------------------------------------|------------------------|--|--|--|
| <b>End point values</b>             | PA21 (Velphoro®) - FAS |  |  |  |
| Subject group type                  | Subject analysis set   |  |  |  |
| Number of subjects analysed         | 65                     |  |  |  |
| Units: mmol/L                       |                        |  |  |  |
| least squares mean (standard error) | -0.120 (± 0.081)       |  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Change in Serum Phosphorus Level From Baseline to the End of Stage 1 in the Phoslyra Group

|   |  |
|---|--|
| End point title   | Change in Serum Phosphorus Level From Baseline to the End of Stage 1 in the Phoslyra Group |
| End point description:  |  |
| End point type  | Secondary  |
| End point timeframe:  |  |
| From Baseline to the End of Stage 1 (up to 10 weeks after treatment start date) |  |

|                                     |                                   |  |  |  |
|-------------------------------------|-----------------------------------|--|--|--|
| <b>End point values</b>             | Calcium Acetate (Phoslyra®) - FAS |  |  |  |
| Subject group type                  | Subject analysis set              |  |  |  |
| Number of subjects analysed         | 15                                |  |  |  |
| Units: mmol/L                       |                                   |  |  |  |
| least squares mean (standard error) | -0.615 ( $\pm$ 0.320)             |  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of Participants With Serum Phosphorus Level Within the Age Related Normal Range in Each Stage

|   |  |
|---|--|
| End point title   | Percentage of Participants With Serum Phosphorus Level Within the Age Related Normal Range in Each Stage |
| End point description:  |  |
| Participants With Serum Phosphorus Level Within the Age Related Normal Range in Each Stage  |  |
| End point type  | Secondary  |
| End point timeframe:  |  |
| Baseline, end of stage 1 (up to 10 weeks after treatment start date) and end of stage 2 (up to 34 weeks after treatment start date) |  |

|                                      |                        |                                   |  |  |
|--------------------------------------|------------------------|-----------------------------------|--|--|
| <b>End point values</b>              | PA21 (Velphoro®) - FAS | Calcium Acetate (Phoslyra®) - FAS |  |  |
| Subject group type                   | Subject analysis set   | Subject analysis set              |  |  |
| Number of subjects analysed          |                        |                                   |  |  |
| Units: Participants                  |                        |                                   |  |  |
| Baseline - Below normal range        | 1                      | 1                                 |  |  |
| Baseline - Within normal range       | 24                     | 5                                 |  |  |
| Baseline - Above normal range        | 40                     | 9                                 |  |  |
| End of Stage 1 - Below normal range  | 1                      | 1                                 |  |  |
| End of Stage 1 - Within normal range | 39                     | 6                                 |  |  |
| End of Stage 1 - Above normal range  | 24                     | 8                                 |  |  |
| End of Stage 2 - Below normal range  | 1                      | 0                                 |  |  |

|                                      |    |   |  |  |
|--------------------------------------|----|---|--|--|
| End of Stage 2 - Within normal range | 23 | 2 |  |  |
| End of Stage 2 - Above normal range  | 16 | 6 |  |  |

## Statistical analyses

No statistical analyses for this end point

## Post-hoc: Change in Serum Phosphorus Level From Baseline to End of Stage 1 in PA21 Group, by Age Group

|                        |  |
|------------------------|--|
| End point title        | Change in Serum Phosphorus Level From Baseline to End of Stage 1 in PA21 Group, by Age Group |
| End point description: | No subjects were 0 - <2 years old at randomisation.  |
| End point type         | Post-hoc   |
| End point timeframe:   | From Baseline to End of Stage 1 (up to 10 weeks after treatment start date)                  |

| End point values                    | PA21<br>(Velporo®) -<br>FAS |  |  |  |
|-------------------------------------|-----------------------------|--|--|--|
| Subject group type                  | Subject analysis set        |  |  |  |
| Number of subjects analysed         | 65                          |  |  |  |
| Units: mmol/L                       |                             |  |  |  |
| least squares mean (standard error) |                             |  |  |  |
| >=2 years to <6 years               | -0.078 (±<br>0.123)         |  |  |  |
| >=6 years to <12 years              | -0.200 (±<br>0.158)         |  |  |  |
| >=12 years to <=18 years            | -0.149 (±<br>0.062)         |  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Post-hoc: Change in Serum Phosphorus Level From Baseline to End of Stage 1 in PA21 Group, by Serum Phosphorus Level at Baseline

|                        |   |
|------------------------|---|
| End point title        | Change in Serum Phosphorus Level From Baseline to End of Stage 1 in PA21 Group, by Serum Phosphorus Level at Baseline |
| End point description: | The levels of Serum Phosphorus (SP) considered at baseline are those above vs within/below Age Related Normal Range   |
| End point type         | Post-hoc  |
| End point timeframe:   | From Baseline to End of Stage 1 (up to 10 weeks after treatment start date)   |

|                                      |                              |  |  |  |
|--------------------------------------|------------------------------|--|--|--|
| <b>End point values</b>              | PA21<br>(Velphoro®) -<br>FAS |  |  |  |
| Subject group type                   | Subject analysis set         |  |  |  |
| Number of subjects analysed          | 65                           |  |  |  |
| Units: mmol/L                        |                              |  |  |  |
| least squares mean (standard error)  |                              |  |  |  |
| SP above Age Related Normal Range    | -0.282 (±<br>0.096)          |  |  |  |
| SP below/within Related Normal Range | 0.082 (±<br>0.146)           |  |  |  |

### Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Through study completion, up to 34 weeks after treatment start date

|                 |                |
|-----------------|----------------|
| Assessment type | Non-systematic |
|-----------------|----------------|

### Dictionary used

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

|                    |      |
|--------------------|------|
| Dictionary version | 19.1 |
|--------------------|------|

### Reporting groups

|                       |                  |
|-----------------------|------------------|
| Reporting group title | PA21 (Velphoro®) |
|-----------------------|------------------|

Reporting group description: -

|                       |                             |
|-----------------------|-----------------------------|
| Reporting group title | Calcium Acetate (Phoslyra®) |
|-----------------------|-----------------------------|

Reporting group description: -

| Serious adverse events                            | PA21 (Velphoro®) | Calcium Acetate (Phoslyra®) |  |
|---|------------------|-----------------------------|--|
| Total subjects affected by serious adverse events |                  |                             |  |
| subjects affected / exposed                       | 18 / 66 (27.27%) | 3 / 19 (15.79%)             |  |
| number of deaths (all causes)                     | 0                | 0                           |  |
| number of deaths resulting from adverse events    | 0                | 0                           |  |
| Vascular disorders                                |                  |                             |  |
| Hypertension                                      |                  |                             |  |
| subjects affected / exposed                       | 5 / 66 (7.58%)   | 0 / 19 (0.00%)              |  |
| occurrences causally related to treatment / all   | 1 / 6            | 0 / 0                       |  |
| deaths causally related to treatment / all        | 0 / 0            | 0 / 0                       |  |
| Hypotension                                       |                  |                             |  |
| subjects affected / exposed                       | 1 / 66 (1.52%)   | 0 / 19 (0.00%)              |  |
| occurrences causally related to treatment / all   | 0 / 1            | 0 / 0                       |  |
| deaths causally related to treatment / all        | 0 / 0            | 0 / 0                       |  |
| Vena cava thrombosis                              |                  |                             |  |
| subjects affected / exposed                       | 1 / 66 (1.52%)   | 0 / 19 (0.00%)              |  |
| occurrences causally related to treatment / all   | 1 / 1            | 0 / 0                       |  |
| deaths causally related to treatment / all        | 0 / 0            | 0 / 0                       |  |
| Venous thrombosis                                 |                  |                             |  |
| subjects affected / exposed                       | 1 / 66 (1.52%)   | 0 / 19 (0.00%)              |  |
| occurrences causally related to treatment / all   | 0 / 1            | 0 / 0                       |  |
| deaths causally related to treatment / all        | 0 / 0            | 0 / 0                       |  |

|   |                |                |  |
|---|----------------|----------------|--|
| Malignant hypertension<br>subjects affected / exposed   | 0 / 66 (0.00%) | 1 / 19 (5.26%) |  |
| occurrences causally related to<br>treatment / all      | 0 / 0          | 0 / 1          |  |
| deaths causally related to<br>treatment / all           | 0 / 0          | 0 / 0          |  |
| General disorders and administration<br>site conditions |                |                |  |
| Catheter site haematoma<br>subjects affected / exposed  | 1 / 66 (1.52%) | 0 / 19 (0.00%) |  |
| occurrences causally related to<br>treatment / all      | 0 / 1          | 0 / 0          |  |
| deaths causally related to<br>treatment / all           | 0 / 0          | 0 / 0          |  |
| Oedema peripheral<br>subjects affected / exposed        | 1 / 66 (1.52%) | 0 / 19 (0.00%) |  |
| occurrences causally related to<br>treatment / all      | 0 / 1          | 0 / 0          |  |
| deaths causally related to<br>treatment / all           | 0 / 0          | 0 / 0          |  |
| Puncture site reaction<br>subjects affected / exposed   | 1 / 66 (1.52%) | 0 / 19 (0.00%) |  |
| occurrences causally related to<br>treatment / all      | 0 / 1          | 0 / 0          |  |
| deaths causally related to<br>treatment / all           | 0 / 0          | 0 / 0          |  |
| Pyrexia<br>subjects affected / exposed                  | 0 / 66 (0.00%) | 1 / 19 (5.26%) |  |
| occurrences causally related to<br>treatment / all      | 0 / 0          | 0 / 1          |  |
| deaths causally related to<br>treatment / all           | 0 / 0          | 0 / 0          |  |
| Respiratory, thoracic and mediastinal<br>disorders      |                |                |  |
| Lung disorder<br>subjects affected / exposed            | 1 / 66 (1.52%) | 0 / 19 (0.00%) |  |
| occurrences causally related to<br>treatment / all      | 0 / 1          | 0 / 0          |  |
| deaths causally related to<br>treatment / all           | 0 / 0          | 0 / 0          |  |
| Product issues  |                |                |  |
| Device malfunction<br>subjects affected / exposed       | 2 / 66 (3.03%) | 0 / 19 (0.00%) |  |
| occurrences causally related to<br>treatment / all      | 0 / 3          | 0 / 0          |  |
| deaths causally related to<br>treatment / all           | 0 / 0          | 0 / 0          |  |
| Device extrusion  |                |                |  |

|   |                |                |  |
|---|----------------|----------------|--|
| subjects affected / exposed                     | 1 / 66 (1.52%) | 0 / 19 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Device occlusion                                |                |                |  |
| subjects affected / exposed                     | 0 / 66 (0.00%) | 1 / 19 (5.26%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 2          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Investigations                                  |                |                |  |
| Weight increased                                |                |                |  |
| subjects affected / exposed                     | 2 / 66 (3.03%) | 0 / 19 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Blood creatinine increased                      |                |                |  |
| subjects affected / exposed                     | 1 / 66 (1.52%) | 0 / 19 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Blood pressure increased                        |                |                |  |
| subjects affected / exposed                     | 1 / 66 (1.52%) | 0 / 19 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Glomerular filtration rate decreased            |                |                |  |
| subjects affected / exposed                     | 1 / 66 (1.52%) | 0 / 19 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Weight decreased                                |                |                |  |
| subjects affected / exposed                     | 0 / 66 (0.00%) | 1 / 19 (5.26%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Injury, poisoning and procedural complications  |                |                |  |
| Arteriovenous fistula site complication         |                |                |  |
| subjects affected / exposed                     | 1 / 66 (1.52%) | 0 / 19 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |

|   |                |                |  |
|---|----------------|----------------|--|
| Arteriovenous fistula site haematoma            |                |                |  |
| subjects affected / exposed                     | 1 / 66 (1.52%) | 0 / 19 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Arteriovenous fistula thrombosis                |                |                |  |
| subjects affected / exposed                     | 1 / 66 (1.52%) | 0 / 19 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Cardiac disorders                               |                |                |  |
| Bradycardia                                     |                |                |  |
| subjects affected / exposed                     | 1 / 66 (1.52%) | 0 / 19 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Cardiac tamponade                               |                |                |  |
| subjects affected / exposed                     | 1 / 66 (1.52%) | 0 / 19 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Nervous system disorders                        |                |                |  |
| Benign intracranial hypertension                |                |                |  |
| subjects affected / exposed                     | 1 / 66 (1.52%) | 0 / 19 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Eye disorders                                   |                |                |  |
| Papilloedema                                    |                |                |  |
| subjects affected / exposed                     | 1 / 66 (1.52%) | 0 / 19 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Gastrointestinal disorders                      |                |                |  |
| Gastritis                                       |                |                |  |
| subjects affected / exposed                     | 1 / 66 (1.52%) | 0 / 19 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Ileus   |                |                |  |

|   |                |                |  |
|---|----------------|----------------|--|
| subjects affected / exposed                     | 1 / 66 (1.52%) | 0 / 19 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Small intestinal obstruction                    |                |                |  |
| subjects affected / exposed                     | 1 / 66 (1.52%) | 0 / 19 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Small intestinal perforation                    |                |                |  |
| subjects affected / exposed                     | 0 / 66 (0.00%) | 1 / 19 (5.26%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Vomiting  |                |                |  |
| subjects affected / exposed                     | 0 / 66 (0.00%) | 1 / 19 (5.26%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Renal and urinary disorders                     |                |                |  |
| Azotaemia                                       |                |                |  |
| subjects affected / exposed                     | 1 / 66 (1.52%) | 0 / 19 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| End stage renal disease                         |                |                |  |
| subjects affected / exposed                     | 1 / 66 (1.52%) | 0 / 19 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Hydronephrosis                                  |                |                |  |
| subjects affected / exposed                     | 1 / 66 (1.52%) | 0 / 19 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Infections and infestations                     |                |                |  |
| Device related sepsis                           |                |                |  |
| subjects affected / exposed                     | 1 / 66 (1.52%) | 0 / 19 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Sepsis  |                |                |  |

|   |                |                |  |
|---|----------------|----------------|--|
| subjects affected / exposed                     | 1 / 66 (1.52%) | 0 / 19 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Superinfection                                  |                |                |  |
| subjects affected / exposed                     | 1 / 66 (1.52%) | 0 / 19 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Tonsillitis streptococcal                       |                |                |  |
| subjects affected / exposed                     | 1 / 66 (1.52%) | 0 / 19 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Metabolism and nutrition disorders              |                |                |  |
| Fluid overload                                  |                |                |  |
| subjects affected / exposed                     | 2 / 66 (3.03%) | 0 / 19 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Decreased appetite                              |                |                |  |
| subjects affected / exposed                     | 1 / 66 (1.52%) | 0 / 19 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Dehydration                                     |                |                |  |
| subjects affected / exposed                     | 0 / 66 (0.00%) | 1 / 19 (5.26%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Electrolyte imbalance                           |                |                |  |
| subjects affected / exposed                     | 0 / 66 (0.00%) | 1 / 19 (5.26%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |

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

| <b>Non-serious adverse events</b>                     | PA21 (Velphoro®) | Calcium Acetate (Phoslyra®) |  |
|---|------------------|-----------------------------|--|
| Total subjects affected by non-serious adverse events |                  |                             |  |
| subjects affected / exposed                           | 45 / 66 (68.18%) | 14 / 19 (73.68%)            |  |
| Investigations  |                  |                             |  |
| Blood lactate dehydrogenase increased                 |                  |                             |  |
| subjects affected / exposed                           | 0 / 66 (0.00%)   | 1 / 19 (5.26%)              |  |
| occurrences (all)                                     | 0                | 1                           |  |
| Blood phosphorus increased                            |                  |                             |  |
| subjects affected / exposed                           | 0 / 66 (0.00%)   | 1 / 19 (5.26%)              |  |
| occurrences (all)                                     | 0                | 1                           |  |
| Liver function test increased                         |                  |                             |  |
| subjects affected / exposed                           | 0 / 66 (0.00%)   | 1 / 19 (5.26%)              |  |
| occurrences (all)                                     | 0                | 1                           |  |
| Nervous system disorders                              |                  |                             |  |
| Headache  |                  |                             |  |
| subjects affected / exposed                           | 2 / 66 (3.03%)   | 1 / 19 (5.26%)              |  |
| occurrences (all)                                     | 2                | 1                           |  |
| Dizziness   |                  |                             |  |
| subjects affected / exposed                           | 0 / 66 (0.00%)   | 1 / 19 (5.26%)              |  |
| occurrences (all)                                     | 0                | 1                           |  |
| General disorders and administration site conditions  |                  |                             |  |
| Pyrexia   |                  |                             |  |
| subjects affected / exposed                           | 3 / 66 (4.55%)   | 1 / 19 (5.26%)              |  |
| occurrences (all)                                     | 3                | 1                           |  |
| Catheter site haemorrhage                             |                  |                             |  |
| subjects affected / exposed                           | 0 / 66 (0.00%)   | 1 / 19 (5.26%)              |  |
| occurrences (all)                                     | 0                | 1                           |  |
| Ear and labyrinth disorders                           |                  |                             |  |
| Otorrhoea   |                  |                             |  |
| subjects affected / exposed                           | 0 / 66 (0.00%)   | 1 / 19 (5.26%)              |  |
| occurrences (all)                                     | 0                | 1                           |  |
| Gastrointestinal disorders                            |                  |                             |  |
| Diarrhoea   |                  |                             |  |
| subjects affected / exposed                           | 12 / 66 (18.18%) | 0 / 19 (0.00%)              |  |
| occurrences (all)                                     | 14               | 0                           |  |
| Nausea  |                  |                             |  |

|  |                       |                      |  |
|--|-----------------------|----------------------|--|
| subjects affected / exposed<br>occurrences (all)   | 8 / 66 (12.12%)<br>10 | 2 / 19 (10.53%)<br>2 |  |
| Vomiting<br>subjects affected / exposed<br>occurrences (all)   | 6 / 66 (9.09%)<br>6   | 2 / 19 (10.53%)<br>3 |  |
| Constipation<br>subjects affected / exposed<br>occurrences (all)   | 4 / 66 (6.06%)<br>4   | 1 / 19 (5.26%)<br>1  |  |
| Abdominal pain<br>subjects affected / exposed<br>occurrences (all)   | 3 / 66 (4.55%)<br>3   | 1 / 19 (5.26%)<br>1  |  |
| Abdominal pain upper<br>subjects affected / exposed<br>occurrences (all)   | 2 / 66 (3.03%)<br>2   | 1 / 19 (5.26%)<br>1  |  |
| Reproductive system and breast disorders<br>Amenorrhoea<br>subjects affected / exposed<br>occurrences (all)                | 0 / 66 (0.00%)<br>0   | 1 / 19 (5.26%)<br>1  |  |
| Respiratory, thoracic and mediastinal disorders<br>Cough<br>subjects affected / exposed<br>occurrences (all)               | 1 / 66 (1.52%)<br>1   | 2 / 19 (10.53%)<br>2 |  |
| Sinus congestion<br>subjects affected / exposed<br>occurrences (all)   | 0 / 66 (0.00%)<br>0   | 1 / 19 (5.26%)<br>2  |  |
| Skin and subcutaneous tissue disorders<br>Excessive granulation tissue<br>subjects affected / exposed<br>occurrences (all) | 0 / 66 (0.00%)<br>0   | 1 / 19 (5.26%)<br>1  |  |
| Pruritus<br>subjects affected / exposed<br>occurrences (all)   | 0 / 66 (0.00%)<br>0   | 1 / 19 (5.26%)<br>1  |  |
| Rash<br>subjects affected / exposed<br>occurrences (all)   | 0 / 66 (0.00%)<br>0   | 1 / 19 (5.26%)<br>2  |  |
| Renal and urinary disorders  |                       |                      |  |

|                                   |                |                 |  |
|-----------------------------------|----------------|-----------------|--|
| Dysuria                           |                |                 |  |
| subjects affected / exposed       | 1 / 66 (1.52%) | 1 / 19 (5.26%)  |  |
| occurrences (all)                 | 1              | 1               |  |
| Haematuria                        |                |                 |  |
| subjects affected / exposed       | 0 / 66 (0.00%) | 1 / 19 (5.26%)  |  |
| occurrences (all)                 | 0              | 1               |  |
| Endocrine disorders               |                |                 |  |
| Hyperparathyroidism               |                |                 |  |
| subjects affected / exposed       | 2 / 66 (3.03%) | 1 / 19 (5.26%)  |  |
| occurrences (all)                 | 3              | 1               |  |
| Hyperparathyroidism secondary     |                |                 |  |
| subjects affected / exposed       | 1 / 66 (1.52%) | 1 / 19 (5.26%)  |  |
| occurrences (all)                 | 2              | 1               |  |
| Infections and infestations       |                |                 |  |
| Urinary tract infection           |                |                 |  |
| subjects affected / exposed       | 3 / 66 (4.55%) | 2 / 19 (10.53%) |  |
| occurrences (all)                 | 5              | 3               |  |
| Upper respiratory tract infection |                |                 |  |
| subjects affected / exposed       | 2 / 66 (3.03%) | 1 / 19 (5.26%)  |  |
| occurrences (all)                 | 2              | 2               |  |
| Gastroenteritis                   |                |                 |  |
| subjects affected / exposed       | 1 / 66 (1.52%) | 1 / 19 (5.26%)  |  |
| occurrences (all)                 | 1              | 1               |  |
| Pharyngitis                       |                |                 |  |
| subjects affected / exposed       | 1 / 66 (1.52%) | 1 / 19 (5.26%)  |  |
| occurrences (all)                 | 1              | 1               |  |
| Clostridium difficile colitis     |                |                 |  |
| subjects affected / exposed       | 0 / 66 (0.00%) | 1 / 19 (5.26%)  |  |
| occurrences (all)                 | 0              | 1               |  |
| Clostridium difficile infection   |                |                 |  |
| subjects affected / exposed       | 0 / 66 (0.00%) | 1 / 19 (5.26%)  |  |
| occurrences (all)                 | 0              | 1               |  |
| Conjunctivitis                    |                |                 |  |
| subjects affected / exposed       | 0 / 66 (0.00%) | 1 / 19 (5.26%)  |  |
| occurrences (all)                 | 0              | 1               |  |
| Cystitis                          |                |                 |  |

|   |                     |                      |  |
|---|---------------------|----------------------|--|
| subjects affected / exposed<br>occurrences (all)  | 0 / 66 (0.00%)<br>0 | 1 / 19 (5.26%)<br>1  |  |
| Hand-foot-and-mouth disease<br>subjects affected / exposed<br>occurrences (all)           | 0 / 66 (0.00%)<br>0 | 1 / 19 (5.26%)<br>1  |  |
| Respiratory syncytial virus infection<br>subjects affected / exposed<br>occurrences (all) | 0 / 66 (0.00%)<br>0 | 1 / 19 (5.26%)<br>1  |  |
| Staphylococcal bacteraemia<br>subjects affected / exposed<br>occurrences (all)            | 0 / 66 (0.00%)<br>0 | 1 / 19 (5.26%)<br>1  |  |
| Metabolism and nutrition disorders  |                     |                      |  |
| Hyperphosphataemia<br>subjects affected / exposed<br>occurrences (all)                    | 3 / 66 (4.55%)<br>3 | 3 / 19 (15.79%)<br>3 |  |
| Hyperkalaemia<br>subjects affected / exposed<br>occurrences (all)                         | 2 / 66 (3.03%)<br>3 | 1 / 19 (5.26%)<br>1  |  |
| Hypophosphataemia<br>subjects affected / exposed<br>occurrences (all)                     | 0 / 66 (0.00%)<br>0 | 1 / 19 (5.26%)<br>1  |  |
| Iron deficiency<br>subjects affected / exposed<br>occurrences (all)                       | 0 / 66 (0.00%)<br>0 | 1 / 19 (5.26%)<br>1  |  |
| Metabolic acidosis<br>subjects affected / exposed<br>occurrences (all)                    | 0 / 66 (0.00%)<br>0 | 1 / 19 (5.26%)<br>1  |  |
| Hypercalcaemia<br>subjects affected / exposed<br>occurrences (all)                        | 4 / 66 (6.06%)<br>4 | 4 / 19 (21.05%)<br>4 |  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

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

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| The study was prematurely ended as a result of the modification of study requirements, as agreed with the US Food and Drug Administration (FDA) and the European Medicines Agency (EMA). |
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Notes: