Clinical trial results:
An Open-label, Randomised, Active-controlled, Parallel Group, Multicentre, Phase 3 Study to Investigate the Safety and Efficacy of PA21 (Velphoro®) 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)	EMEA-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:

Subjects enrolled per age group	
In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	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
Arm title	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.

Arm title	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.

Number of subjects in period 1	PA21 (Velphoro®)	Calcium Acetate (Phoslyra®)
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.

Reporting group values	PA21 (Velphoro®) - FAS	Calcium Acetate (Phoslyra®) - FAS	
Number of subjects	65	15	
Age categorical 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 Units: years			
arithmetic mean	12.1	12.3	
standard deviation	± 4.10	± 3.96	
Gender categorical 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[1]

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.

End point values	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)

End point values	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 (± 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)

End point values	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 (Velphoro®) - 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 (± 0.123)			
>=6 years to <12 years	-0.200 (± 0.158)			
>=12 years to <=18 years	-0.149 (± 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)

End point values	PA21 (Velphoro®) - 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 (± 0.096)			
SP below/within Related Normal Range	0.082 (± 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			
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	
General disorders and administration site conditions			
Catheter 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	
Oedema peripheral			
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	
Puncture site reaction			
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	
Pyrexia			
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	
Respiratory, thoracic and mediastinal disorders			
Lung disorder			
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	
Product issues			
Device malfunction			
subjects affected / exposed	2 / 66 (3.03%)	0 / 19 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to 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 %

Non-serious adverse events	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	8 / 66 (12.12%)	2 / 19 (10.53%)	
occurrences (all)	10	2	
Vomiting			
subjects affected / exposed	6 / 66 (9.09%)	2 / 19 (10.53%)	
occurrences (all)	6	3	
Constipation			
subjects affected / exposed	4 / 66 (6.06%)	1 / 19 (5.26%)	
occurrences (all)	4	1	
Abdominal pain			
subjects affected / exposed	3 / 66 (4.55%)	1 / 19 (5.26%)	
occurrences (all)	3	1	
Abdominal pain upper			
subjects affected / exposed	2 / 66 (3.03%)	1 / 19 (5.26%)	
occurrences (all)	2	1	
Reproductive system and breast disorders			
Amenorrhoea			
subjects affected / exposed	0 / 66 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 66 (1.52%)	2 / 19 (10.53%)	
occurrences (all)	1	2	
Sinus congestion			
subjects affected / exposed	0 / 66 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	2	
Skin and subcutaneous tissue disorders			
Excessive granulation tissue			
subjects affected / exposed	0 / 66 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	1	
Pruritus			
subjects affected / exposed	0 / 66 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	1	
Rash			
subjects affected / exposed	0 / 66 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	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	0 / 66 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	1	
Hand-foot-and-mouth disease			
subjects affected / exposed	0 / 66 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	1	
Respiratory syncytial virus infection			
subjects affected / exposed	0 / 66 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	1	
Staphylococcal bacteraemia			
subjects affected / exposed	0 / 66 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	1	
Metabolism and nutrition disorders			
Hyperphosphataemia			
subjects affected / exposed	3 / 66 (4.55%)	3 / 19 (15.79%)	
occurrences (all)	3	3	
Hyperkalaemia			
subjects affected / exposed	2 / 66 (3.03%)	1 / 19 (5.26%)	
occurrences (all)	3	1	
Hypophosphataemia			
subjects affected / exposed	0 / 66 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	1	
Iron deficiency			
subjects affected / exposed	0 / 66 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	1	
Metabolic acidosis			
subjects affected / exposed	0 / 66 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	1	
Hypercalcaemia			
subjects affected / exposed	4 / 66 (6.06%)	4 / 19 (21.05%)	
occurrences (all)	4	4	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

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.

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).

Notes: