



Clinical trial results:

A 2-Week, Randomized, Placebo-Controlled, Fixed Dose Period Followed by a 6-Month, Single-Arm, Open-Label, Dose Titration Period Study to Investigate the Efficacy and Safety of Sevelamer Carbonate in Hyperphosphatemic Pediatric Patients with Chronic Kidney Disease Summary

EudraCT number	2011-002329-23
Trial protocol	LT PL
Global end of trial date	16 June 2015

Results information

Result version number	v1 (current)
This version publication date	19 June 2016
First version publication date	19 June 2016

Trial information

Trial identification

Sponsor protocol code	SVCARB07609
-----------------------	-------------

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01574326
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Genzyme Corporation
Sponsor organisation address	500 Kendall Street, Cambridge, United States, 02142
Public contact	Trial Transparency Team, Sanofi aventis recherche & développement, Contact-US@sanofi.com
Scientific contact	Trial Transparency Team, Sanofi aventis recherche & développement, Contact-US@sanofi.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	28 July 2015
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	16 June 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

In hyperphosphatemic pediatric subjects with chronic kidney disease (CKD) to:

- Evaluate the safety and tolerability of sevelamer carbonate
- Evaluate the efficacy of sevelamer carbonate on the control of serum phosphorus

Protection of trial subjects:

The study was conducted by investigators experienced in the treatment of pediatric subjects. The parent(s) or guardian(s) as well as the children were fully informed of all pertinent aspects of the clinical trial as well as the possibility to discontinue at any time. In addition to the consent form for the parent(s)/guardian(s), an assent form in child-appropriate language was provided and explained to the child. Repeated invasive procedures were minimized. The number of blood samples as well as the amount of blood drawn were adjusted according to age and weight. A topical anesthesia may have been used to minimize distress and discomfort.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	11 May 2012
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: 8
Country: Number of subjects enrolled	Germany: 2
Country: Number of subjects enrolled	Lithuania: 2
Country: Number of subjects enrolled	United States: 89
Worldwide total number of subjects	101
EEA total number of subjects	12

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	0

months)	
Children (2-11 years)	20
Adolescents (12-17 years)	73
Adults (18-64 years)	8
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted at 29 centres in 4 countries. A total of 128 subjects were screened between 11 May 2012 and 14 November 2014. Of whom, 101 subjects were randomized and 27 were screen failures.

Pre-assignment

Screening details:

Subjects were stratified in (1:1) by screening body surface area (≥ 1.2 vs < 1.2 m²) & qualifying serum phosphorus (≥ 7.0 vs < 7.0 mg/dL), to receive either sevelamer carbonate or placebo during 2-week fixed dose period (FDP). Following FDP, subjects entered 26-week dose titration period (DTP), during which all subjects received sevelamer carbonate.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	FDP-placebo for sevelamer carbonate, DTP-sevelamer carbonate

Arm description:

Subjects received placebo for sevelamer carbonate for 2 weeks in FDP and thereafter these subjects received sevelamer carbonate for 26 weeks in DTP. In DTP the dose of sevelamer carbonate could be titrated up/down [titrations were based on screening body surface area (BSA) category].

Arm type	Placebo
Investigational medicinal product name	Placebo in FDP period only
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet, Powder for oral suspension
Routes of administration	Oral use

Dosage and administration details:

Placebo matched to sevelamer carbonate 3 times a day (TID) for 2 weeks in FDP: 0.4 g TID for BSA < 0.75 m² or 0.8 g TID for BSA ≥ 0.75 - < 1.2 m² as powder for oral suspension (POS) & 1.6g TID for BSA ≥ 1.2 m² as POS/tablets depending upon subject's preference. If a child ate < 3 meals/snacks/day, dose was only to be given with meals/snacks, eg, if BSA ≥ 0.75 - < 1.2 m² & 2 meals/snacks /day that subject took 0.8 g BID with meals. In DTP these subjects received sevelamer carbonate. Starting dose was based on screening BSA & same as prescribed in FDP. Dose was titrated up/down every 2 weeks for 6 weeks & then every 4 weeks, to achieve a serum phosphorus level within age appropriate normal values, or up to maximum dose as per Investigator's opinion. Dose titrations were based on BSA category: 0.2 g TID for BSA < 0.75 m², 0.4 g TID for BSA ≥ 0.75 - < 1.2 m² & 0.8 g TID for BSA ≥ 1.2 m² [smaller titrations were permitted based on Investigator's judgment, but could not be < 0.2 g TID with meals/snacks].

Arm title	FDP-sevelamer carbonate, DTP-sevelamer carbonate
------------------	--

Arm description:

Subjects received sevelamer carbonate 0.4 g TID or 0.8 g TID or 1.6 g TID (based on screening BSA category for 2 weeks in FDP and thereafter these subjects continued to receive sevelamer carbonate in DTP. In DTP dose could be titrated up/down every 2 weeks for 6 weeks and then every 4 weeks to achieve a serum phosphorus level within the age appropriate normal values or, up to maximum dose as per Investigator's opinion. Dose titrations were based on BSA category: by 0.2 g TID for BSA < 0.75 m², 0.4 g TID for BSA ≥ 0.75 - < 1.2 m² and 0.8 g TID for BSA ≥ 1.2 m² [smaller titrations were permitted based on Investigator's judgment, but could not be < 0.2 g TID with meals/snacks].

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

Investigational medicinal product name	Sevelamer carbonate
Investigational medicinal product code	GZ419831
Other name	Renvela ®
Pharmaceutical forms	Powder for oral suspension, Tablet
Routes of administration	Oral use

Dosage and administration details:

Sevelamer carbonate TID for 2 weeks in FDP: 0.4 g TID for BSA <0.75 m² or 0.8 g TID for BSA ≥0.75-<1.2 m² as POS & 1.6 g TID for BSA ≥1.2 m² either as POS or as tablets depending upon subject's preference. If a child ate <3 meals/snacks/day, dose was only to be given with meals/snacks. For eg. if BSA was ≥0.75-<1.2 m² & 2 meals/snacks/day that subject took 0.8 g BID with meals. In DTP these subjects continued to receive sevelamer carbonate. Starting dose in DTP was based on screening BSA & same as dose prescribed during FDP. Dose could be titrated up/down every 2 weeks for 6 weeks & then every 4 weeks, to achieve a serum phosphorus level within age appropriate normal values, or until, maximum dose as per Investigator's opinion. Dose titrations were based on BSA category: by 0.2 g TID for BSA <0.75 m², 0.4 g TID for BSA ≥0.75-<1.2 m² & 0.8 g TID for BSA ≥1.2 m² [smaller titrations were permitted based on Investigator's judgment, but could not be <0.2 g TID with meals/snacks].

Number of subjects in period 1	FDP-placebo for sevelamer carbonate, DTP-sevelamer carbonate	FDP-sevelamer carbonate, DTP-sevelamer carbonate
Started	51	50
Treated	51	49
Completed	35	31
Not completed	16	19
Physician decision	5	3
Adverse Event	1	3
Other: Mainly kidney transplant	8	8
Randomized but not treated	-	1
Withdrawal by Subject	2	4

Baseline characteristics

Reporting groups

Reporting group title	FDP-placebo for sevelamer carbonate, DTP-sevelamer carbonate
-----------------------	--

Reporting group description:

Subjects received placebo for sevelamer carbonate for 2 weeks in FDP and thereafter these subjects received sevelamer carbonate for 26 weeks in DTP. In DTP the dose of sevelamer carbonate could be titrated up/down [titrations were based on screening body surface area (BSA) category].

Reporting group title	FDP-sevelamer carbonate, DTP-sevelamer carbonate
-----------------------	--

Reporting group description:

Subjects received sevelamer carbonate 0.4 g TID or 0.8 g TID or 1.6 g TID (based on screening BSA category for 2 weeks in FDP and thereafter these subjects continued to receive sevelamer carbonate in DTP. In DTP dose could be titrated up/down every 2 weeks for 6 weeks and then every 4 weeks to achieve a serum phosphorus level within the age appropriate normal values or, up to maximum dose as per Investigator's opinion. Dose titrations were based on BSA category: by 0.2 g TID for BSA <0.75 m², 0.4 g TID for BSA ≥0.75 - <1.2 m² and 0.8 g TID for BSA ≥1.2 m² [smaller titrations were permitted based on Investigator's judgment, but could not be < 0.2 g TID with meals/snacks].

Reporting group values	FDP-placebo for sevelamer carbonate, DTP-sevelamer carbonate	FDP-sevelamer carbonate, DTP-sevelamer carbonate	Total
Number of subjects	51	50	101
Age categorical			
Units: Subjects			

Age continuous			
Age continuous is reported here for safety set: N= 51 and N=49 for 'FDP-placebo for sevelamer carbonate, DTP-sevelamer carbonate' and 'FDP-sevelamer carbonate, DTP-sevelamer carbonate' arms respectively.			
Units: years			
arithmetic mean	14.3	13.9	
standard deviation	± 3.11	± 2.75	-
Gender categorical			
Units: Subjects			
Female	18	19	37
Male	33	31	64

End points

End points reporting groups

Reporting group title	FDP-placebo for sevelamer carbonate, DTP-sevelamer carbonate
-----------------------	--

Reporting group description:

Subjects received placebo for sevelamer carbonate for 2 weeks in FDP and thereafter these subjects received sevelamer carbonate for 26 weeks in DTP. In DTP the dose of sevelamer carbonate could be titrated up/down [titrations were based on screening body surface area (BSA) category].

Reporting group title	FDP-sevelamer carbonate, DTP-sevelamer carbonate
-----------------------	--

Reporting group description:

Subjects received sevelamer carbonate 0.4 g TID or 0.8 g TID or 1.6 g TID (based on screening BSA category for 2 weeks in FDP and thereafter these subjects continued to receive sevelamer carbonate in DTP. In DTP dose could be titrated up/down every 2 weeks for 6 weeks and then every 4 weeks to achieve a serum phosphorus level within the age appropriate normal values or, up to maximum dose as per Investigator's opinion. Dose titrations were based on BSA category: by 0.2 g TID for BSA <0.75 m², 0.4 g TID for BSA ≥0.75 - <1.2 m² and 0.8 g TID for BSA ≥1.2 m² [smaller titrations were permitted based on Investigator's judgment, but could not be < 0.2 g TID with meals/snacks].

Subject analysis set title	FDP- placebo for sevelamer carbonate; DTP- sevelamer carbonate
----------------------------	--

Subject analysis set type	Per protocol
---------------------------	--------------

Subject analysis set description:

Subjects received placebo for sevelamer carbonate for first 2 weeks in FDP. Thereafter subjects received sevelamer carbonate for 26 weeks in DTP.

Subject analysis set title	FDP - sevelamer carbonate, DTP - sevelamer carbonate
----------------------------	--

Subject analysis set type	Per protocol
---------------------------	--------------

Subject analysis set description:

Subjects received sevelamer carbonate 0.4 g TID or 0.8 g TID or 1.6 g TID (based on the screening BSA category) for 2 weeks in FDP. Thereafter subjects continued to receive sevelamer carbonate for 26 weeks in DTP (based on the screening BSA category).

Subject analysis set title	FDP -placebo for sevelamer carbonate
----------------------------	--------------------------------------

Subject analysis set type	Per protocol
---------------------------	--------------

Subject analysis set description:

Subjects received placebo for sevelamer carbonate for first 2 weeks in FDP.

Subject analysis set title	FDP - sevelamer carbonate
----------------------------	---------------------------

Subject analysis set type	Per protocol
---------------------------	--------------

Subject analysis set description:

Subjects received sevelamer carbonate 0.4 g TID or 0.8 g TID or 1.6 g TID (based on the screening BSA category) for 2 weeks in FDP.

Primary: Change from Baseline (Week 0) to Week 2 in Serum Phosphorus

End point title	Change from Baseline (Week 0) to Week 2 in Serum Phosphorus
-----------------	---

End point description:

Analysis was performed on full analysis set for the fixed dose period (FAS-FDP) and included all treated subjects with a baseline phosphorus value and at least 1 post-baseline phosphorus assessment after the first dose of study drug and on or before Week 2. FAS-FDP subjects were analyzed according to their randomized treatment. A confirmatory analysis was conducted using the per protocol set for the fixed dose period (PPS-FDP).

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

End point timeframe:

Baseline, Week 2

End point values	FDP -placebo for sevelamer carbonate	FDP - sevelamer carbonate		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	49	48		
Units: mg/dL				
arithmetic mean (standard deviation)				
At Baseline	7.2 (± 1.841)	7.2 (± 2.09)		
At Week 2	7.24 (± 2.029)	6.34 (± 1.306)		
Change from Baseline to Week 2	0.04 (± 1.478)	-0.87 (± 1.649)		

Statistical analyses

Statistical analysis title	Sevelamer Carbonate vs Placebo
Statistical analysis description:	
Primary efficacy endpoint, change from baseline to Week 2 in serum phosphorus, was compared between treatment groups using analysis of covariance (ANCOVA) with baseline phosphorus and screening BSA as covariates and fixed effect for treatment. No center effect was included in the model. The estimate of the treatment difference (Sevelamer Carbonate - Placebo) and its 95% CI were presented. Significance was to be declared if the p-value was ≤0.05.	
Comparison groups	FDP -placebo for sevelamer carbonate v FDP - sevelamer carbonate
Number of subjects included in analysis	97
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.001
Method	ANCOVA
Parameter estimate	Least Square (LS) mean difference
Point estimate	-0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.44
upper limit	-0.37

Primary: Treatment – Emergent Adverse Events (AE)

End point title	Treatment – Emergent Adverse Events (AE) ^[1]
End point description:	
A serious adverse event (SAE) was an AE resulting in any of the following outcomes or deemed significant for any other reason: death; initial or prolonged inpatient hospitalization; life-threatening experience (immediate risk of dying); persistent or significant disability/incapacity; congenital anomaly/birth defect. AEs - from the time of signing the informed consent through the end of the study for all subjects. SAEs occurring during the 15 days following study completion or early termination were also to be collected. Analysis was performed on safety set, which included all enrolled subjects who received at least 1 dose of study drug. Subjects were analyzed according to actual received treatment.	
End point type	Primary
End point timeframe:	
Up to 32 Weeks [up to 4 weeks washout period, 2 weeks FDP and 26 weeks DTP]	

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 data reported is qualitative, hence, no statistical analysis is provided.

End point values	FDP-placebo for sevelamer carbonate, DTP-sevelamer carbonate	FDP-sevelamer carbonate, DTP-sevelamer carbonate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	51	49		
Units: subjects				
Any AE: FDP	20	19		
AE related: FDP	3	2		
Any SAE: FDP	1	4		
SAE related: FDP	0	0		
Any AE Leading to Study Drug Discontinuation: FDP	1	1		
Any AE: DTP	42	35		
AE related: DTP	9	4		
Any SAE: DTP	14	17		
SAE related: DTP	2	2		
Any AE Leading to Study Drug Discontinuation: DTP	0	3		
Death	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline (Week 0) to Week 28/Early Termination in Serum Phosphorus

End point title	Change from Baseline (Week 0) to Week 28/Early Termination in Serum Phosphorus
-----------------	--

End point description:

Analysis was performed on full analysis set for the dose titration period (FAS-DTP) and included all treated subjects with a baseline phosphorus value and at least 1 post-baseline phosphorus assessment after Week 2. FAS-DTP subjects were analysed according to their randomized treatment.

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

End point timeframe:

Baseline, Week 28/Early Termination

End point values	FDP-placebo for sevelamer carbonate, DTP-sevelamer carbonate	FDP-sevelamer carbonate, DTP-sevelamer carbonate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	49	46		
Units: mg/dL				

arithmetic mean (standard deviation)				
At Baseline (Week 0)	7.05 (± 1.797)	7.28 (± 2.103)		
At Week 28 / Early Termination	5.92 (± 1.612)	6.04 (± 1.878)		
Change from Baseline to Week 28/Early Termination	-1.13 (± 2.061)	-1.23 (± 2.206)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All AEs were collected from signature of informed consent form up to final visit regardless of seriousness or relationship to investigational product. SAEs occurring during 15 days following study completion or early termination were also to be collected.

Adverse event reporting additional description:

Reported adverse events are treatment-emergent adverse events (includes non-serious adverse events and serious adverse events as applicable) that is AE that developed/worsened during the 'on treatment period' (from the first dose of study drug up to end of study period). Analysis was performed on safety set.

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

Dictionary used

Dictionary name	MedDRA
Dictionary version	18

Reporting groups

Reporting group title	FDP - Placebo
-----------------------	---------------

Reporting group description:

Subjects exposed to placebo (for sevelamer carbonate) for first 2 weeks in FDP (median exposure of 15 days).

Reporting group title	FDP - Sevelamer carbonate
-----------------------	---------------------------

Reporting group description:

Subjects exposed to sevelamer carbonate 0.4 g TID or 0.8 g TID or 1.6 g TID (based on the screening BSA category) for first 2 weeks in FDP (median exposure of 15 days).

Reporting group title	DTP - Sevelamer carbonate
-----------------------	---------------------------

Reporting group description:

Subjects who received placebo and subjects who received sevelamer carbonate in FDP received sevelamer carbonate for 26 weeks in DTP (median exposure of 183.5 days in subjects who were on sevelamer carbonate in FDP and 183 days in subjects who were on placebo FDP).

Serious adverse events	FDP - Placebo	FDP - Sevelamer carbonate	DTP - Sevelamer carbonate
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 51 (1.96%)	4 / 49 (8.16%)	31 / 100 (31.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 51 (0.00%)	2 / 49 (4.08%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertensive Crisis			

subjects affected / exposed	0 / 51 (0.00%)	0 / 49 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypotension			
subjects affected / exposed	0 / 51 (0.00%)	0 / 49 (0.00%)	2 / 100 (2.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Orthostatic Hypotension			
subjects affected / exposed	0 / 51 (0.00%)	0 / 49 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vena Cava Thrombosis			
subjects affected / exposed	0 / 51 (0.00%)	0 / 49 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Device Dislocation			
subjects affected / exposed	0 / 51 (0.00%)	0 / 49 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device Malfunction			
subjects affected / exposed	0 / 51 (0.00%)	0 / 49 (0.00%)	2 / 100 (2.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device Occlusion			
subjects affected / exposed	0 / 51 (0.00%)	1 / 49 (2.04%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Extravasation			
subjects affected / exposed	0 / 51 (0.00%)	0 / 49 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fatigue			

subjects affected / exposed	0 / 51 (0.00%)	0 / 49 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Non-Cardiac Chest Pain			
subjects affected / exposed	0 / 51 (0.00%)	0 / 49 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	0 / 51 (0.00%)	0 / 49 (0.00%)	3 / 100 (3.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Anti-Neutrophil Cytoplasmic Antibody Positive Vasculitis			
subjects affected / exposed	0 / 51 (0.00%)	0 / 49 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Kidney Transplant Rejection			
subjects affected / exposed	0 / 51 (0.00%)	0 / 49 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Acute Respiratory Failure			
subjects affected / exposed	0 / 51 (0.00%)	0 / 49 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea			
subjects affected / exposed	0 / 51 (0.00%)	0 / 49 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoxia			
subjects affected / exposed	0 / 51 (0.00%)	0 / 49 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Pulmonary Embolism			
subjects affected / exposed	0 / 51 (0.00%)	0 / 49 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Mental Status Changes			
subjects affected / exposed	0 / 51 (0.00%)	0 / 49 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Blood Creatinine Increased			
subjects affected / exposed	0 / 51 (0.00%)	0 / 49 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Arteriovenous Fistula Site Complication			
subjects affected / exposed	0 / 51 (0.00%)	0 / 49 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arteriovenous Fistula Thrombosis			
subjects affected / exposed	0 / 51 (0.00%)	0 / 49 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Laceration			
subjects affected / exposed	0 / 51 (0.00%)	0 / 49 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post Procedural Constipation			
subjects affected / exposed	0 / 51 (0.00%)	0 / 49 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Shunt Occlusion			

subjects affected / exposed	0 / 51 (0.00%)	0 / 49 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Hypoxic-Ischaemic Encephalopathy			
subjects affected / exposed	0 / 51 (0.00%)	0 / 49 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 51 (0.00%)	0 / 49 (0.00%)	2 / 100 (2.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal Pain			
subjects affected / exposed	0 / 51 (0.00%)	0 / 49 (0.00%)	3 / 100 (3.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Constipation			
subjects affected / exposed	0 / 51 (0.00%)	0 / 49 (0.00%)	2 / 100 (2.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	0 / 51 (0.00%)	0 / 49 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastritis			
subjects affected / exposed	0 / 51 (0.00%)	0 / 49 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	0 / 51 (0.00%)	0 / 49 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Renal and urinary disorders			
Focal Segmental Glomerulosclerosis			
subjects affected / exposed	0 / 51 (0.00%)	0 / 49 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oliguria			
subjects affected / exposed	0 / 51 (0.00%)	0 / 49 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal Failure			
subjects affected / exposed	0 / 51 (0.00%)	0 / 49 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal Impairment			
subjects affected / exposed	0 / 51 (0.00%)	0 / 49 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 51 (0.00%)	0 / 49 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Flank Pain			
subjects affected / exposed	0 / 51 (0.00%)	0 / 49 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Bacteraemia			
subjects affected / exposed	0 / 51 (0.00%)	0 / 49 (0.00%)	2 / 100 (2.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Catheter Site Infection			

subjects affected / exposed	0 / 51 (0.00%)	0 / 49 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fungal Peritonitis			
subjects affected / exposed	0 / 51 (0.00%)	0 / 49 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis Viral			
subjects affected / exposed	1 / 51 (1.96%)	0 / 49 (0.00%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pelvic Inflammatory Disease			
subjects affected / exposed	0 / 51 (0.00%)	0 / 49 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peritonitis			
subjects affected / exposed	0 / 51 (0.00%)	1 / 49 (2.04%)	2 / 100 (2.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peritonitis Bacterial			
subjects affected / exposed	0 / 51 (0.00%)	0 / 49 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pharyngitis			
subjects affected / exposed	0 / 51 (0.00%)	0 / 49 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 51 (0.00%)	0 / 49 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Septic Shock			

subjects affected / exposed	0 / 51 (0.00%)	0 / 49 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper Respiratory Tract Infection			
subjects affected / exposed	0 / 51 (0.00%)	0 / 49 (0.00%)	2 / 100 (2.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary Tract Infection			
subjects affected / exposed	0 / 51 (0.00%)	0 / 49 (0.00%)	2 / 100 (2.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urosepsis			
subjects affected / exposed	0 / 51 (0.00%)	0 / 49 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vaginitis Chlamydial			
subjects affected / exposed	0 / 51 (0.00%)	0 / 49 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Varicella Zoster Virus Infection			
subjects affected / exposed	0 / 51 (0.00%)	0 / 49 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral Infection			
subjects affected / exposed	0 / 51 (0.00%)	0 / 49 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Fluid Overload			
subjects affected / exposed	0 / 51 (0.00%)	0 / 49 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperkalaemia			

subjects affected / exposed	0 / 51 (0.00%)	1 / 49 (2.04%)	2 / 100 (2.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperphosphataemia			
subjects affected / exposed	0 / 51 (0.00%)	0 / 49 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypocalcaemia			
subjects affected / exposed	0 / 51 (0.00%)	0 / 49 (0.00%)	2 / 100 (2.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	FDP - Placebo	FDP - Sevelamer carbonate	DTP - Sevelamer carbonate
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 51 (11.76%)	7 / 49 (14.29%)	57 / 100 (57.00%)
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 51 (0.00%)	1 / 49 (2.04%)	7 / 100 (7.00%)
occurrences (all)	0	1	10
Hypotension			
subjects affected / exposed	1 / 51 (1.96%)	0 / 49 (0.00%)	8 / 100 (8.00%)
occurrences (all)	1	0	12
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 51 (0.00%)	1 / 49 (2.04%)	7 / 100 (7.00%)
occurrences (all)	0	1	8
Headache			
subjects affected / exposed	2 / 51 (3.92%)	2 / 49 (4.08%)	17 / 100 (17.00%)
occurrences (all)	2	2	19
General disorders and administration site conditions			
Catheter Site Pain			
subjects affected / exposed	0 / 51 (0.00%)	0 / 49 (0.00%)	6 / 100 (6.00%)
occurrences (all)	0	0	6

Pyrexia subjects affected / exposed occurrences (all)	0 / 51 (0.00%) 0	1 / 49 (2.04%) 1	16 / 100 (16.00%) 21
Immune system disorders Seasonal Allergy subjects affected / exposed occurrences (all)	0 / 51 (0.00%) 0	0 / 49 (0.00%) 0	6 / 100 (6.00%) 6
Gastrointestinal disorders Abdominal Pain subjects affected / exposed occurrences (all)	0 / 51 (0.00%) 0	1 / 49 (2.04%) 1	13 / 100 (13.00%) 18
Abdominal Pain Upper subjects affected / exposed occurrences (all)	2 / 51 (3.92%) 2	0 / 49 (0.00%) 0	9 / 100 (9.00%) 13
Diarrhoea subjects affected / exposed occurrences (all)	0 / 51 (0.00%) 0	1 / 49 (2.04%) 1	8 / 100 (8.00%) 10
Nausea subjects affected / exposed occurrences (all)	2 / 51 (3.92%) 2	0 / 49 (0.00%) 0	15 / 100 (15.00%) 21
Vomiting subjects affected / exposed occurrences (all)	3 / 51 (5.88%) 4	0 / 49 (0.00%) 0	19 / 100 (19.00%) 28
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)	0 / 51 (0.00%) 0	0 / 49 (0.00%) 0	7 / 100 (7.00%) 10
Musculoskeletal and connective tissue disorders Pain In Extremity subjects affected / exposed occurrences (all)	0 / 51 (0.00%) 0	1 / 49 (2.04%) 1	8 / 100 (8.00%) 8
Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all)	0 / 51 (0.00%) 0	0 / 49 (0.00%) 0	6 / 100 (6.00%) 7
Upper Respiratory Tract Infection			

subjects affected / exposed	0 / 51 (0.00%)	0 / 49 (0.00%)	10 / 100 (10.00%)
occurrences (all)	0	0	10

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
03 November 2011	<ul style="list-style-type: none">- Added an exclusion criterion to clarify that subjects with non-renal causes of hyperphosphatemia are not eligible.- Added re-screening due to the difficulty in enrolling pediatric subjects.- Clarified that if a child eats less than 3 meals/snacks per day, sevelamer carbonate or placebo should only be given with meals/snacks and not on an empty stomach.- Clarified that subjects who require a dose of less than 0.2 g TID with meals/snacks will be discontinued from treatment and withdrawn from the study.- Clarified that the drug preparation instructions apply to both sevelamer carbonate and placebo.- Clarified the collection and reporting of adverse events.- Clarified that subjects who become pregnant will be withdrawn from the study.- Clarified that stored samples that are not collected will not be a protocol deviation.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported