ClinicalTrials.gov Protocol and Results Registration System (PRS) Receipt
Release Date: 06/06/2014

Grantor: CDER IND/IDE Number: 55,054 Serial Number:

Head to Head Study Against Sevelamer Hydrochloride

This study has been completed.

Sponsor:	Shire
Collaborators:	
Information provided by (Responsible Party):	Shire
ClinicalTrials.gov Identifier:	NCT00441545

Purpose

To compare the efficacy of Fosrenol (Lanthanum carbonate) and sevelamer hydrochloride in the reduction of serum phosphorus levels from baseline.

Condition	Intervention	Phase
Chronic Kidney Disease, Stage 5	Drug: Fosrenol (Lanthanum Carbonate) Drug: Sevelamer hydrochloride	Phase 3

Study Type: Interventional
Study Design: Treatment, Crossover Assignment, Open Label, Randomized, Safety/Efficacy Study
Official Title: A Prospective, Multicenter, Open-label, Randomized, Cross-over Study to Compare the Efficacy and Safety of Fosrenol® and Sevelamer Hydrochloride in Patients Receiving Hemodialysis for End Stage Renal Disease

Further study details as provided by Shire:

Primary Outcome Measure:

- Change From Baseline in Serum Phosphorus Levels at 4 Weeks [Time Frame: 4 weeks] [Designated as safety issue: No]

Secondary Outcome Measures:

- Change From Baseline in Serum Calcium Levels at 4 Weeks [Time Frame: 4 weeks] [Designated as safety issue: No]
- Levels of Intact Parathyroid Hormone (iPTH) at Baseline and 4 Weeks [Time Frame: Baseline and 4 weeks] [Designated as safety issue: No]
- Patients Achieving Kidney Disease Outcomes Quality Initiative (KDOQI) Target for Serum Phosphorous at 4 Weeks [Time Frame: 4 weeks] [Designated as safety issue: No]
  Kidney Disease Outcomes Quality Initiative (KDOQI) target for serum phosphorous is 3.5 - 5.5 mg/dL (1.13 - 1.77 mmol/L)

Enrollment: 182
Study Start Date: February 2007
Primary Completion Date: July 2008
Study Completion Date: July 2008

Arms	Assigned Interventions
Experimental: 1 Fosrenol (Lanthanum carbonate)	Drug: Fosrenol (Lanthanum Carbonate) The starting dose is a total daily dose of 2250mg of Fosrenol (Lanthanum carbonate) to a maximum dose of 3000mg daily. Chewable tablets will be administered orally with meals in 750mg and 1000mg strength tablets. Other Names: FOSRENOL
Active Comparator: 2 Sevelamer hydrochloride	Drug: Sevelamer hydrochloride The starting dose is a total daily dose of 4800mg of sevelamer hydrochloride up to a maximum of 6400 mg daily. Sevelamer hydrochloride 800mg tablets, administered orally with meals.

Detailed Description:

To compare the efficacy of Fosrenol (Lanthanum carbonate) and sevelamer hydrochloride in the reduction of serum phosphorus levels from baseline.

Eligibility

Ages Eligible for Study: 18 Years and older
Genders Eligible for Study: Both
Accepts Healthy Volunteers: No

Criteria

Inclusion Criteria:

- Adults with end stage renal disease who are receiving dialysis

Exclusion Criteria:

- Subjects with significant gastrointestinal disorders
- Subjects who are pregnant or nursing
- Subjects currently taking lanthanum carbonate, sevelamer hydrochloride, cinacalcet hydrochloride
- Subjects who are HIV positive
- Subjects with clinical significant liver disease

Contacts and Locations

Locations

United States, Arizona

DSI Renal Inc.
Mesa, Arizona, United States, 85202

AKDHC Medical Research Services, LLC
Phoenix, Arizona, United States, 85012

Southwest Kidney Institute, PLC
Tempe, Arizona, United States, 85284

Southwest Kidney Institute, PLC
Tempe, Arizona, United States, 85284
Tempe, Arizona, United States, 85284

University of Arizona Health Service Center
Tuscon, Arizona, United States, 85724

United States, Arkansas

Clinical Research Connections
Jonesboro, Arkansas, United States, 72401

United States, California

South Valley Dialysis Center
Encino, California, United States, 91316

VA Greater Los Angeles Health Care System, West LA
Los Angeles, California, United States, 90073

Apex Research of Riverside
Riverside, California, United States, 92505

North Valley Nephrology
Yuba City, California, United States, 95991

United States, Colorado

Western Nephrology & Metabolic Bone Disease, PC
Thornton, Colorado, United States, 80260

United States, Florida

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Gainesville, Florida, United States, 32608

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Pines Clinical Research

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Macon, Georgia, United States, 31217
United States, Illinois
Evanston Northwestern Hospital
Evanston, Illinois, United States, 60201
Research by Design, LLC
Evergreen Park, Illinois, United States, 60805
United States, Indiana
Nephrology Inc.
Mishawaka, Indiana, United States, 46545
United States, Louisiana
Renal Associates of Baton Rouge
Baton Rouge, Louisiana, United States, 70809
United States, Nebraska
Creighton University Medical Center
Omaha, Nebraska, United States, 68131
United States, New Jersey
Hypertension and Nephrology, Associates
Eatontown, New Jersey, United States, 07724
United States, New York
Winthrop Dialysis Center
Mineola, New York, United States, 11501
SUNY at Stony Brook NY
Stony Brook, New York, United States, 11794
United States, North Carolina
Wake Nephrology Associates
Raleigh, North Carolina, United States, 27609
Southeastern Nephrology Associates
Wilmington, North Carolina, United States, 28401
United States, Oregon
Northwest Renal Clinic
Portland, Oregon, United States, 97210
United States, South Carolina
Carolina Nephrology, PA
Greenville, South Carolina, United States, 29605
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Bad Konig, Germany, 64732
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Investigators

Principal Investigator:	Stuart Sprague, D.O.	Evanston Northwestern Hospital

More Information

FDA recall information
http://www.fda.gov/opacom/7alerts.html

FDA Medical Products Safety Alerts
http://www.fda.gov/Medwatch/SAFETY/2007/safety07.htm

FDA-approved label
http://www.fosrenol.com/pdf/FOS-00683_FosrenolPI.pdf

Synopsis of study results
http://www.clinicalstudyresults.org/documents/company-study_9571_0.pdf

Publications:
Lanthanum carbonate vs. sevelamer hydrochloride for the reduction of serum phosphorus in hemodialysis patients: a crossover study. SM Sprague, EA Ross, SD Nath, et al. Clinical Nephrology 2009;72:252-8.

Responsible Party: Shire
Study ID Numbers: SPD405-319
2006-004959-38 [EudraCT Number]
Health Authority: United States: Food and Drug Administration

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Study Results

Participant Flow

Recruitment Details	Following Washout 1, eligible subjects with serum phosphorus levels greater than or equal to 6.0mg/dL (greater than or equal to 1.94mmol/L) and calcium levels greater than or equal to 8.4mg/dL (greater than or equal to 2.10mmol/L) were randomized in a 1:1 ratio to receive either Fosrenol or sevelamer hydrochloride (HCl) for 4 weeks.
Pre-Assignment Details	The study consisted of the following phases: screening (1 week), washout 1 (2 weeks), treatment (4 weeks), Washout 2 (2 weeks), crossover treatment (4 weeks), and a 30-day follow-up

Reporting Groups

	Description
Fosrenol First	Fosrenol (Lanthanum carbonate) dosing began at 2250mg/day, administered orally as one 750mg tablet taken three times per day with meals for 1 week. After receiving this dose for 1 week, subjects received the final dose of 3000mg/day, administered orally as one 1000mg tablet three times per day with meals. Subjects were to remain on the final Fosrenol dose of 3000mg/day for 3 weeks. After washout, patients then crossover to receive Sevelamer HCl for 4 weeks (see below).
Sevelamer HCl First	Sevelamer HCl dosing began at 4800mg/day, administered orally as two 800mg tablets taken three times per day with meals for 1 week. After receiving this dose for 1 week, subjects received the final dose of 6400mg/day, administered orally as three 800mg tablets taken two times per day with meals and two 800mg tablets taken once per day with the lighter meal (i.e., a total of eight 800mg tablets per day). Subjects were to remain on the final sevelamer HCl dose of 6400mg/day for 3 weeks. After washout, patients then crossover to receive Fosrenol for 4 weeks (see above).

First Intervention

	Fosrenol First	Sevelamer HCl First
Started	95	87
Completed	77	75
Not Completed	18	12
Adverse Event	6	5
Protocol Violation	2	2
Withdrawal by Subject	3	3
Kidney transplant	1	1
Lack of Efficacy	2	0
Subject exceeded safety criteria	0	1
Subject met an exclusionary criteria	1	0
Extended hospitalization	1	0
Site error	1	0
Sponsor's request	1	0

Washout

	Fosrenol First	Sevelamer HCl First
Started	77	75
Completed	77	75
Not Completed	0	0

Second Intervention

	Fosrenol First	Sevelamer HCl First
Started	77	75
Completed	65	68
Not Completed	12	7
Adverse Event	5	2
Protocol Violation	4	1
Withdrawal by Subject	1	1

	Fosrenol First	Sevelamer HCl First
Kidney Transplant	1	1
Lack of Efficacy	0	1
Subject exceeded safety criteria	1	0
Subject moved	0	1

Baseline Characteristics

Reporting Groups

	Description
Entire Study Population	

Baseline Measures

	Entire Study Population
Number of Participants	182
Age, Categorical [units: participants]	
<=18 years	0
Between 18 and 65 years	140
>=65 years	42
Age, Continuous [units: years] Mean (Standard Deviation)	55.5 (13.10)
Gender, Male/Female [units: participants]	
Female	80
Male	102
Region of Enrollment [units: participants]	
United States	139
Puerto Rico	1
Germany	41

	Entire Study Population
United Kingdom	1

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Change From Baseline in Serum Phosphorus Levels at 4 Weeks
Measure Description	
Time Frame	4 weeks
Safety Issue?	No

Analysis Population Description

ITT population defined as subjects who were randomized, received at least one dose of investigational product, and had at least one post-dose assessment of the primary efficacy variable.

Reporting Groups

	Description
Fosrenol	Lanthanum carbonate
Sevelamer HCl	

Measured Values

	Fosrenol	Sevelamer HCl
Number of Participants Analyzed	165	161
Change From Baseline in Serum Phosphorus Levels at 4 Weeks [units: mg/dL] Least Squares Mean (Standard Error)	-1.73 (0.129)	-1.44 (0.132)

Statistical Analysis 1 for Change From Baseline in Serum Phosphorus Levels at 4 Weeks

Statistical Analysis Overview	Comparison Groups	Fosrenol, Sevelamer HCl
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.1130
	Comments	[Not specified]
	Method	ANCOVA
	Comments	[Not specified]

2. Secondary Outcome Measure:

Measure Title	Change From Baseline in Serum Calcium Levels at 4 Weeks
Measure Description	
Time Frame	4 weeks
Safety Issue?	No

Analysis Population Description

ITT

Reporting Groups

	Description
Fosrenol	Lanthanum carbonate
Sevelamer HCl	

Measured Values

	Fosrenol	Sevelamer HCl
Number of Participants Analyzed	165	161
Change From Baseline in Serum Calcium Levels at 4 Weeks [units: mg/dL] Least Squares Mean (Standard Error)	0.06 (0.045)	-0.06 (0.046)

Statistical Analysis 1 for Change From Baseline in Serum Calcium Levels at 4 Weeks

Statistical Analysis Overview	Comparison Groups	Fosrenol, Sevelamer HCl
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.0249
	Comments	[Not specified]
	Method	ANCOVA
	Comments	[Not specified]

3. Secondary Outcome Measure:

Measure Title	Levels of Intact Parathyroid Hormone (iPTH) at Baseline and 4 Weeks
Measure Description	
Time Frame	Baseline and 4 weeks
Safety Issue?	No

Analysis Population Description

ITT

Reporting Groups

	Description
Fosrenol	Lanthanum carbonate
Sevelamer HCl	

Measured Values

	Fosrenol	Sevelamer HCl
Number of Participants Analyzed	165	161
Levels of Intact Parathyroid Hormone (iPTH) at Baseline and 4 Weeks [units: pg/mL] Mean (Standard Error)		
Baseline	225.46 (11.094)	225.46 (11.094)
Endpoint	296.48 (17.412)	291.18 (16.181)

4. Secondary Outcome Measure:

Measure Title	Patients Achieving Kidney Disease Outcomes Quality Initiative (KDOQI) Target for Serum Phosphorous at 4 Weeks
Measure Description	Kidney Disease Outcomes Quality Initiative (KDOQI) target for serum phosphorous is 3.5 - 5.5 mg/dL (1.13 - 1.77 mmol/L)

Time Frame	4 weeks
Safety Issue?	No

Analysis Population Description
[Not Specified]

Reporting Groups

	Description
Fosrenol	Lanthanum carbonate
Sevelamer HCl	

Measured Values

	Fosrenol	Sevelamer HCl
Number of Participants Analyzed	165	161
Patients Achieving Kidney Disease Outcomes Quality Initiative (KDOQI) Target for Serum Phosphorous at 4 Weeks [units: Percentage of Participants]	42.7	34.6

Reported Adverse Events

Time Frame	[Not specified]
Additional Description	[Not specified]

Reporting Groups

	Description
Fosrenol	Fosrenol (Lanthanum carbonate) dosing began at 2250mg/day, administered orally as one 750mg tablet taken three times per day with meals for 1 week. After receiving this dose for 1 week, subjects received the final dose of 3000mg/day, administered orally as one 1000mg tablet three times per day with meals. Subjects were to remain on the final Fosrenol dose of 3000mg/day for 3 weeks. After washout, patients then crossover to receive Sevelamer HCl for 4 weeks (see below).

	Description
Sevelamer HCl	Sevelamer HCl dosing began at 4800mg/day, administered orally as two 800mg tablets taken three times per day with meals for 1 week. After receiving this dose for 1 week, subjects received the final dose of 6400mg/day, administered orally as three 800mg tablets taken two times per day with meals and two 800mg tablets taken once per day with the lighter meal (i.e., a total of eight 800mg tablets per day). Subjects were to remain on the final sevelamer HCl dose of 6400mg/day for 3 weeks. After washout, patients then crossover to receive Fosrenol for 4 weeks (see above).

Serious Adverse Events

	Fosrenol	Sevelamer HCl
	Affected/At Risk (%)	Affected/At Risk (%)
Total	18/170 (10.59%)	20/163 (12.27%)
Blood and lymphatic system disorders		
Anemia *	0/170 (0%)	1/163 (0.61%)
Cardiac disorders		
Congestive heart failure *	1/170 (0.59%)	2/163 (1.23%)
Coronary atery disease *	2/170 (1.18%)	2/163 (1.23%)
Myocardial infarction *	2/170 (1.18%)	2/163 (1.23%)
Unstable angina *	1/170 (0.59%)	0/163 (0%)
Ear and labyrinth disorders		
Vertigo *	0/170 (0%)	1/163 (0.61%)
Gastrointestinal disorders		
Abdominal pain *	1/170 (0.59%)	1/163 (0.61%)
General disorders		
Chest pain *	2/170 (1.18%)	0/163 (0%)
Weakness *	0/170 (0%)	2/163 (1.23%)
Infections and infestations		
Cellulitis *	1/170 (0.59%)	1/163 (0.61%)
Clostridium difficile colitis *	0/170 (0%)	2/163 (1.23%)
Cystitis *	1/170 (0.59%)	1/163 (0.61%)
Foot infection *	1/170 (0.59%)	1/163 (0.61%)

	Fosrenol	Sevelamer HCl
	Affected/At Risk (%)	Affected/At Risk (%)
Osteomyelitis *	2/170 (1.18%)	1/163 (0.61%)
Pneumonia *	3/170 (1.76%)	1/163 (0.61%)
Septic phlebitis *	1/170 (0.59%)	0/163 (0%)
Metabolism and nutrition disorders		
Hyperkalemia *	1/170 (0.59%)	1/163 (0.61%)
Hypoglycemia *	0/170 (0%)	1/163 (0.61%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)		
Breast cancer *	1/170 (0.59%)	0/163 (0%)
Nervous system disorders		
Cerebral vascular accident *	3/170 (1.76%)	0/163 (0%)
Presyncope *	0/170 (0%)	1/163 (0.61%)
Pripheral neuropathy *	1/170 (0.59%)	0/163 (0%)
Stroke *	1/170 (0.59%)	0/163 (0%)
Respiratory, thoracic and mediastinal disorders		
Dyspnoea *	0/170 (0%)	1/163 (0.61%)
Respiratory failure *	0/170 (0%)	1/163 (0.61%)
Skin and subcutaneous tissue disorders		
Extremity necrosis *	0/170 (0%)	3/163 (1.84%)
Vascular disorders		
Death *	1/170 (0.59%)	0/163 (0%)
Hypotension *	2/170 (1.18%)	0/163 (0%)

* Indicates events were collected by non-systematic methods.

Other Adverse Events
Frequency Threshold Above Which Other Adverse Events are Reported: 5%

	Fosrenol	Sevelamer HCl
	Affected/At Risk (%)	Affected/At Risk (%)
Total	31/170 (18.24%)	27/163 (16.56%)

	Fosrenol	Sevelamer HCl
	Affected/At Risk (%)	Affected/At Risk (%)
Gastrointestinal disorders		
Diarrhea *	12/170 (7.06%)	12/163 (7.36%)
Nausea *	15/170 (8.82%)	9/163 (5.52%)
Vomiting *	9/170 (5.29%)	6/163 (3.68%)

* Indicates events were collected by non-systematic methods.

Limitations and Caveats

[Not specified]

More Information

Certain Agreements:

Principal Investigators are NOT employed by the organization sponsoring the study.

There IS an agreement between the Principal Investigator and the Sponsor (or its agents) that restricts the PI's rights to discuss or publish trial results after the trial is completed.

If a multicenter publication is not submitted within twelve (12) months after conclusion, abandonment or termination of the Study at all sites, or after Sponsor confirms there shall be no multicenter Study publication, the Institution and/or such Principal Investigator may publish the results from the Institution site individually.

Results Point of Contact:

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