Clinical trial results:
Multicentric, parallel, controlled, randomized, single blind clinical evaluation of a new low sodium peritoneal dialysis solution on patients with hypertension treated with continous ambulatory or automated peritoneal dialysis.

Summary

EudraCT number	2007-005365-35
Trial protocol	SE DE FR DK GB
Global end of trial date	14 October 2014

Results information

Result version number	v1 (current)
This version publication date	11 March 2022
First version publication date	11 March 2022
Summary attachment (see zip file)	Davies_PDI_2020_PDOne_Study (Davies_PDI_2020_PDOne_Study.pdf)

Trial information

Trial identification

Sponsor protocol code	1449

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00794326
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Fresenius Medical Care Deutschland GmbH
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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?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	25 April 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	14 October 2014
Global end of trial reached?	Yes
Global end of trial date	14 October 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The trial was performed to investigate the effect of a once-daily dwell with a glucose-compensated low-Na solution in hypertensive peritoneal dialysis (PD) patients
(Test product PDsol 12, an isotonic low Na solution (Na 112 mM, glucose concentration 2%, 340 mOsm/L); Reference product Selutrio 40, Na 133 mM, isotonic 1.5% glucose solution, 356 mOsm/L). The objective was to demonstrate superiority of the low-Na solution over a standard solution regarding the lowering of blood pressure (BP).

Protection of trial subjects:

The treatment with PDsol 12 was safe and well tolerated when compared to standard treatment. The profile of TEAE findings was generally consistent with the PD population represented in this study (e.g. complications such as peritonitis which are common for subjects on PD therapy), the nature of the underlying disease, and the expected safety profile of PDsol 12.

Background therapy:

Peritoneal dialysis

Evidence for comparator: -	
Actual start date of recruitment	20 October 2008
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	Sweden: 46
Country: Number of subjects enrolled	United Kingdom: 40
Country: Number of subjects enrolled	Denmark: 5
Country: Number of subjects enrolled	France: 34
Country: Number of subjects enrolled	Germany: 33
Worldwide total number of subjects	158
EEA total number of subjects	118

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37	0

wk	
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	95
From 65 to 84 years	63
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The patients to be included in this clinical study are suffering from chronic renal failure and are treated with peritoneal dialysis. These patients shall meet the inclusion and exclusion criteria defined for this study. 158 CAPD/ APD eligible and randomized patients were recruited according to the statistical hypothesis.

Pre-assignment

Screening details:

Run-in phase 4 weeks: The study will start with a run-in period (around 4-weeks) for both medical and practical reasons: if after inclusion visit a change is decided in PD dose 4 weeks is a reasonable duration to allow stabilization on new prescription.

Period 1

Period 1 title	Run-in-phase
Is this the baseline period?	No
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Arm title	Run-in-phase

Arm description:

Run-in phase 4 weeks: The study will start with a run-in period (around 4-weeks) during which the patients' eligibility for participation was confirmed. They were stabilised on their currently prescribed standard dialysis treatment regimen.

Arm type	Active comparator
Investigational medicinal product name	Selutrio 40
Investigational medicinal product code	
Other name	Gambrosol Trio 40
Pharmaceutical forms	Intraperitoneal solution
Routes of administration	Intraperitoneal use

Dosage and administration details:

1 daytime dwell time during 4 ± 1 hours

Number of subjects in period 1	Run-in-phase
Started	158
Completed	128
Not completed	30
not known	3
In-/ exclusion criteria not fulfilled	5
Ineligibility after ABPM results	3
No reason for termination documented	16
Patient PD treatment not stable	3

Period 2

Period 2 title	Efficacy period - Safety analysis set
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Single blind
Roles blinded	Investigator[1]

Blinding implementation details:

The study was single-blinded since the identity of study medication could be easily recognized by the investigator based on subjects' laboratory data during the study. Both IMPs (i.e. test- and reference products) were manufactured to look the same and differed only by the name/code indicated on the label (i.e. PDsol 12/1 and PDsol 12/2).

Arms

Are arms mutually exclusive?	Yes
Arm title	PDsol 12 group

Arm description:

1 bag PDsol 12 (1 daytime dwell time during 4 ± 1 hours)
Treatment with study medication started on the day after visit T0 and lasted 6 months. The standard Na, isotonic glucose bag was to be replaced for one daytime dwell time during 4 ± 1 hours by PDsol 12 for subjects assigned to low Na treatment (i.e. PDsol 12 group).

Arm type	Experimental
Investigational medicinal product name	PDsol 12
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Intraperitoneal solution
Routes of administration	Intraperitoneal use

Dosage and administration details:

1 bag PDsol 12 (1 daytime dwell time during 4 ± 1 hours)

Arm title	Selutrio 40 group

Arm description:

1 bag Selutrio 40 (1 daytime dwell time during 4 ± 1 hours)
Treatment with study medication started on the day after visit T0 and lasted 6 months. The standard Na, isotonic glucose bag was to be replaced for one daytime dwell time during 4 ± 1 hours by Selutrio 40 for subjects assigned to treatment with the reference product (Selutrio 40 group).

Arm type	Active comparator
Investigational medicinal product name	Selutrio 40
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Intraperitoneal solution
Routes of administration	Intraperitoneal use

Dosage and administration details:

1 daytime dwell time during 4 ± 1 hours

Notes:

[1] - The roles blinded appear inconsistent with a simple blinded trial.

Justification: The study was single-blinded since the identity of study medication could be easily recognized by the investigator based on subjects' laboratory data during the study.

Number of subjects in period 2	PDsol 12 group	Selutrio 40 group
Started	63	65
Completed	60	63
Not completed	3	2
Adverse event, non-fatal	3	2

Period 3

Period 3 title	Safety period - Full analysis set (FAS)
Is this the baseline period?	Yes[2]
Allocation method	Randomised - controlled
Blinding used	Single blind
Roles blinded	Investigator[3]

Blinding implementation details:

The study was single-blinded since the identity of study medication could be easily recognized by the investigator based on subjects' laboratory data during the study. Both IMPs (i.e. test- and reference products) were manufactured to look the same and differed only by the name/code indicated on the label (i.e. PDsol 12/1 and PDsol 12/2).

Arms

Are arms mutually exclusive?	Yes
Arm title	PDsol 12 group

Arm description:

1 bag PDsol 12 (1 daytime dwell time during 4 ± 1 hours)
Treatment with study medication started on the day after visit T0 and lasted 6 months. The standard Na, isotonic glucose bag was to be replaced for one daytime dwell time during 4 ± 1 hours by PDsol 12 for subjects assigned to low Na treatment (i.e. PDsol 12 group).

Arm type	Experimental
Investigational medicinal product name	PDsol 12
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Intraperitoneal solution
Routes of administration	Intraperitoneal use

Dosage and administration details:

1 bag PDsol 12 (1 daytime dwell time during 4 ± 1 hours)

Arm title	Selutrio 40 group

Arm description:

1 bag Solutio 40 (1 daytime dwell time during 4 ± 1 hours)
Treatment with study medication started on the day after visit T0 and lasted 6 months. The standard Na, isotonic glucose bag was to be replaced for one daytime dwell time during 4 ± 1 hours by Selutrio 40 for subjects assigned to treatment with the reference product (Selutrio 40 group).

Arm type	Active comparator
Investigational medicinal product name	Selutrio 40
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Intraperitoneal solution
Routes of administration	Intraperitoneal use

Dosage and administration details:

1 daytime dwell time during 4 ± 1 hours

Notes:

[2] - Period 1 is not the baseline period. It is expected that period 1 will be the baseline period.

Justification: The presentation of baseline characteristics are based on the Full Analysis Set. The Full Analysis Set (FAS) will consist of all randomized patients after a four-week run-in period.

[3] - The roles blinded appear inconsistent with a simple blinded trial.

Justification: The study was single-blinded since the identity of study medication could be easily recognized by the investigator based on subjects' laboratory data during the study.

Number of subjects in period 3[4]	PDsol 12 group	Selutrio 40 group
Started	60	63
Completed	45	43
Not completed	15	20
Transfer to hemodialysis	2	2
Adverse event, serious fatal	-	1
Consent withdrawn by subject	1	4
• Stop of PD for 6 weeks due to hernia repair	1	-
Adverse event, non-fatal	5	6
Kidney/renal transplantation	1	3
Poor compliance	-	1
Atrial fibrillation	-	1
Adequate PD therapy was no longer possible	1	-
Patient condition no longer requires trial	4	-
subject's condition no longer required study treat	-	2

Notes:

[4] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: All baseline characteristics were analyzed for the Full analysis set (FAS). All 123 subjects who attended T0 and received at least one bag of study medication were included in the FAS.

Period 4

Period 4 title	Follow up period
Is this the baseline period?	No
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Arm title	Follow up

Arm description:

Follow up for 2 months after completion of study treatment according to site routine (for all subjects to monitor BP and antihypertensive and/or diuretic medication after stopping the use of study medication and enable control of possible BP increase).

Arm type	Active comparator
Investigational medicinal product name	PDsol 12
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Intraperitoneal solution
Routes of administration	Intraperitoneal use

Dosage and administration details:

1 bag PDsol 12 (1 daytime dwell time during 4 ± 1 hours)

Number of subjects in period 4	Follow up
Started	88
Completed	88

Baseline characteristics

Reporting groups	
Reporting group title	PDsol 12 group
Reporting group description:	
1 bag PDsol 12 (1 daytime dwell time during 4 ± 1 hours) Treatment with study medication started on the day after visit T0 and lasted 6 months. The standard Na, isotonic glucose bag was to be replaced for one daytime dwell time during 4 ± 1 hours by PDsol 12 for subjects assigned to low Na treatment (i.e. PDsol 12 group).	

Reporting group title	Selutrio 40 group
Reporting group description:	
1 bag Solutio 40 (1 daytime dwell time during 4 ± 1 hours) Treatment with study medication started on the day after visit T0 and lasted 6 months. The standard Na, isotonic glucose bag was to be replaced for one daytime dwell time during 4 ± 1 hours by Selutrio 40 for subjects assigned to treatment with the reference product (Selutrio 40 group).	

Reporting group values	PDsol 12 group	Selutrio 40 group	Total
Number of subjects	60	63	123
Age categorical Units: Subjects			
Adults 18 years and more	60	63	123
Age continuous Units: years			
median	61.0	55.0	
full range (min-max)	31 to 84	23 to 83	-
Gender categorical Units: Subjects			
Female	14	18	32
Male	46	45	91
Dry weight Units: kg			
median	81.8	76.7	
full range (min-max)	42 to 128	42 to 102	-
Height Units: cm			
median	174.0	172.0	
full range (min-max)	150 to 190	152 to 186	-
Residual renal function Units: mL/min/1.73 m2			
arithmetic mean	5.0	4.9	
standard deviation	± 3.27	± 3.61	-
24-h Total creatinine clearance Units: mL/min/1.73 m2			
arithmetic mean	13.2	7.9	
standard deviation	± 15.5	± 6.6	-
Total weekly Kt/V			
parameter for dialysis adequacy			
Units: no unit			
arithmetic mean	2.3	2.3	
standard deviation	± 0.62	± 0.53	-

End points

End points reporting groups

Reporting group title	Run-in-phase

Reporting group description:

Run-in phase 4 weeks: The study will start with a run-in period (around 4-weeks) during which the patients' eligibility for participation was confirmed. They were stabilised on their currently prescribed standard dialysis treatment regimen.

Reporting group title	PDsol 12 group

Reporting group description:

1 bag PDsol 12 (1 daytime dwell time during 4 ± 1 hours)
Treatment with study medication started on the day after visit T0 and lasted 6 months. The standard Na, isotonic glucose bag was to be replaced for one daytime dwell time during 4 ± 1 hours by PDsol 12 for subjects assigned to low Na treatment (i.e. PDsol 12 group).

Reporting group title	Selutrio 40 group

Reporting group description:

1 bag Selutrio 40 (1 daytime dwell time during 4 ± 1 hours)
Treatment with study medication started on the day after visit T0 and lasted 6 months. The standard Na, isotonic glucose bag was to be replaced for one daytime dwell time during 4 ± 1 hours by Selutrio 40 for subjects assigned to treatment with the reference product (Selutrio 40 group).

Reporting group title	PDsol 12 group

Reporting group description:

1 bag PDsol 12 (1 daytime dwell time during 4 ± 1 hours)
Treatment with study medication started on the day after visit T0 and lasted 6 months. The standard Na, isotonic glucose bag was to be replaced for one daytime dwell time during 4 ± 1 hours by PDsol 12 for subjects assigned to low Na treatment (i.e. PDsol 12 group).

Reporting group title	Selutrio 40 group

Reporting group description:

1 bag Solutio 40 (1 daytime dwell time during 4 ± 1 hours)
Treatment with study medication started on the day after visit T0 and lasted 6 months. The standard Na, isotonic glucose bag was to be replaced for one daytime dwell time during 4 ± 1 hours by Selutrio 40 for subjects assigned to treatment with the reference product (Selutrio 40 group).

Reporting group title	Follow up

Reporting group description:

Follow up for 2 months after completion of study treatment according to site routine (for all subjects to monitor BP and antihypertensive and/or diuretic medication after stopping the use of study medication and enable control of possible BP increase).

Primary: Responder rate

End point title	Responder rate

End point description:

Responders are defined as having experienced at least one of the following response criteria:
a. Improvement of arterial hypertension by a decrease of 6 mmHg or more on the mean 24h SBP, measured from ABPM (T2-Baseline) in patients without antihypertensive medication modification.
b. Documented occurrence of hypotension requiring a medical action (decrease of antihypertensive drug medication) during the efficacy period (visit T0 through T2) confirmed by the DSMB.
The primary endpoint will be analysed with the Cochran-Mantel-Haenszel test stratified for the 24h AMBP SBP stratification variable.
Superiority of the new formulation over standard-Na solution could not be confirmed statistically ($p = 0.512$). Our sensitivity analysis in which patients with missing response data were counted as either responders or nonresponders, as well as the analysis in the PPS ($p = 0.296$), led to the same conclusion.

End point type	Primary

End point timeframe:

study phase
Mean 24h SBP will be calculated as the arithmetic mean value of all available observations for the 24h observation period.

End point values	PDsol 12 group	Selutrio 40 group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	60	63		
Units: numbers				
Subjets with valid data	58	55		
Total responders	20	16		
Response defined by (a) Mean 24-h systolic blood p	11	16		
Response defined by (b) Fall in blood pressure req	9	0		

Statistical analyses

Statistical analysis title	Primary endpoint
Comparison groups	Selutrio 40 group v PDsol 12 group
Number of subjects included in analysis	123
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.05
Method	Cochran-Mantel-Haenszel

Secondary: Serial BP measurements during the 8-week efficacy period

End point title	Serial BP measurements during the 8-week efficacy period

End point description:

Secondary outcomes for Blood pressure (BP) included 24-h ABPM of daytime and night-time SBP and DBP and office BP measurements

End point type	Secondary

End point timeframe:

Serial BP measurements during the 8-week efficacy period (Full analysis set (FAS))

End point values	PDsol 12 group	Selutrio 40 group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	60[1]	63[2]		
Units: mmHg				
arithmetic mean (standard deviation)				
24-h ABPM SBP (mmHg)	-2.3 (± 15.9)	-1.2 (± 14.5)		
24-h ABMP DBP (mmHg)	-1.0 (± 10.3)	-1.0 (± 8.6)		
24-h ABPM SBP (mmHg) day	-1.9 (± 15.5)	-1.7 (± 15.1)		
24-h ABMP DBP (mmHg) day	-0.7 (± 10.4)	-1.3 (± 9.4)		
24-h ABPM SBP (mmHg) night	-3.5 (± 16.1)	0.6 (± 15.0)		
24-h ABMP DBP (mmHg) night	-2.1 (± 11.2)	0.3 (± 7.9)		
Office SBP (mmHg	-5.0 (± 16.7)	-3.3 (± 15.9)		
Office DBP (mmHg	-1.8 (± 8.7)	-0.6 (± 12.8)		
Self-measured SBP (mmHg)	-5.6 (± 14.6)	3.6 (± 13.3)		
Self-measured DBP (mmHg)	-3.2 (± 8.3)	1.7 (± 9.4)		

Notes:

[1] - Full analysis set (FAS)

[2] - Full analysis set (FAS)

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

AEs were analyzed in safety analysis set (SAF) timeframe 6 months

Adverse event reporting additional description:

- Listening of most frequently reported treatment-emergent AEs (occurrence in ≥3% of subjects in total) from beginning of study treatment to end of study by SOC and PT (SAF)
- Listing of treatment-emergent SAEs (occurrence in ≥2 subjects in either treatment group) by SOC and PT (SAF)

TEAE or serious TEAE (TESAE) were defined as any AE or SAE.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.0

Reporting groups

Reporting group title	Safety analysis set

Reporting group description:

The safety analysis set will consist of all randomized subjects that received any amount of study medication.

Reporting group title	PDsol 12

Reporting group description: -

Reporting group title	Selutrio 40

Reporting group description: -

Serious adverse events	Safety analysis set	PDsol 12	Selutrio 40
Total subjects affected by serious adverse events			
subjects affected / exposed	35 / 128 (27.34%)	16 / 63 (25.40%)	19 / 65 (29.23%)
number of deaths (all causes)	2	1	1
number of deaths resulting from adverse events	2	1	1
Vascular disorders			
Hypotension			
subjects affected / exposed	3 / 128 (2.34%)	3 / 63 (4.76%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
General disorders and administration site conditions			
subjects affected / exposed	4 / 128 (3.13%)	1 / 63 (1.59%)	3 / 65 (4.62%)
occurrences causally related to treatment / all	0 / 4	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sudden death			

subjects affected / exposed	1 / 128 (0.78%)	0 / 63 (0.00%)	1 / 65 (1.54%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	2 / 128 (1.56%)	0 / 63 (0.00%)	2 / 65 (3.08%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 12
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Pulmonary oedema			
subjects affected / exposed	3 / 128 (2.34%)	0 / 63 (0.00%)	3 / 65 (4.62%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Peritonitis			
subjects affected / exposed	8 / 128 (6.25%)	4 / 63 (6.35%)	4 / 65 (6.15%)
occurrences causally related to treatment / all	0 / 8	0 / 4	0 / 6
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peritonitis bacterial			
subjects affected / exposed	3 / 128 (2.34%)	1 / 63 (1.59%)	2 / 65 (3.08%)
occurrences causally related to treatment / all	0 / 3	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Septic shock			
subjects affected / exposed	1 / 128 (0.78%)	1 / 63 (1.59%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Metabolism and nutrition disorders			
Metabolism and nutrition disorders			
subjects affected / exposed	3 / 128 (2.34%)	1 / 63 (1.59%)	2 / 65 (3.08%)
occurrences causally related to treatment / all	0 / 3	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 3 %

Non-serious adverse events	Safety analysis set	PDsol 12	Selutrio 40
Total subjects affected by non-serious adverse events			
subjects affected / exposed	114 / 128 (89.06%)	50 / 63 (79.37%)	49 / 65 (75.38%)
Vascular disorders			
Hypotension			
subjects affected / exposed	28 / 128 (21.88%)	17 / 63 (26.98%)	11 / 65 (16.92%)
occurrences (all)	28	17	11
Hypertension			
subjects affected / exposed	10 / 128 (7.81%)	4 / 63 (6.35%)	6 / 65 (9.23%)
occurrences (all)	10	4	6
General disorders and administration site conditions			
Oedema peripheral			
subjects affected / exposed	8 / 128 (6.25%)	2 / 63 (3.17%)	6 / 65 (9.23%)
occurrences (all)	8	2	6
Asthenia			
subjects affected / exposed	2 / 128 (1.56%)	2 / 63 (3.17%)	0 / 65 (0.00%)
occurrences (all)	2	2	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	5 / 128 (3.91%)	0 / 63 (0.00%)	5 / 65 (7.69%)
occurrences (all)	5	0	5
Investigations			
Investigations			
subjects affected / exposed	5 / 128 (3.91%)	2 / 63 (3.17%)	3 / 65 (4.62%)
occurrences (all)	5	2	4
Injury, poisoning and procedural complications			
Injury, poisoning and procedural complications			
subjects affected / exposed	4 / 128 (3.13%)	2 / 63 (3.17%)	2 / 65 (3.08%)
occurrences (all)	4	2	2
Nervous system disorders			
Dizziness			
subjects affected / exposed	10 / 128 (7.81%)	7 / 63 (11.11%)	3 / 65 (4.62%)
occurrences (all)	10	7	3
Headache			
subjects affected / exposed	5 / 128 (3.91%)	2 / 63 (3.17%)	3 / 65 (4.62%)
occurrences (all)	5	2	3

Ear and labyrinth disorders			
Ear and labyrinth disorders			
subjects affected / exposed	4 / 128 (3.13%)	1 / 63 (1.59%)	3 / 65 (4.62%)
occurrences (all)	4	1	3
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	7 / 128 (5.47%)	1 / 63 (1.59%)	6 / 65 (9.23%)
occurrences (all)	7	1	6
Diarrhoea			
subjects affected / exposed	4 / 128 (3.13%)	1 / 63 (1.59%)	3 / 65 (4.62%)
occurrences (all)	4	1	3
Abdominal pain			
subjects affected / exposed	5 / 128 (3.91%)	1 / 63 (1.59%)	4 / 65 (6.15%)
occurrences (all)	5	1	4
Skin and subcutaneous tissue disorders			
Skin and subcutaneous tissue disorders			
subjects affected / exposed	8 / 128 (6.25%)	7 / 63 (11.11%)	1 / 65 (1.54%)
occurrences (all)	8	7	1
Renal and urinary disorders			
Renal and urinary disorders			
subjects affected / exposed	4 / 128 (3.13%)	2 / 63 (3.17%)	2 / 65 (3.08%)
occurrences (all)	4	2	2
Endocrine disorders			
Endocrine disorders			
subjects affected / exposed	4 / 128 (3.13%)	2 / 63 (3.17%)	2 / 65 (3.08%)
occurrences (all)	4	2	2
Musculoskeletal and connective tissue disorders			
Muscle spasms			
subjects affected / exposed	4 / 128 (3.13%)	3 / 63 (4.76%)	1 / 65 (1.54%)
occurrences (all)	4	3	1
Infections and infestations			
Peritonitis			
subjects affected / exposed	17 / 128 (13.28%)	8 / 63 (12.70%)	9 / 65 (13.85%)
occurrences (all)	25	9	12
Bronchitis			
subjects affected / exposed	5 / 128 (3.91%)	3 / 63 (4.76%)	2 / 65 (3.08%)
occurrences (all)	5	3	2

Peritonitis bacterial subjects affected / exposed occurrences (all)	3 / 128 (2.34%) 3	1 / 63 (1.59%) 1	2 / 65 (3.08%) 2
Metabolism and nutrition disorders Hyperkalaemia subjects affected / exposed occurrences (all)	4 / 128 (3.13%) 4	2 / 63 (3.17%) 2	2 / 65 (3.08%) 2
Hyponatraemia subjects affected / exposed occurrences (all)	4 / 128 (3.13%) 4	3 / 63 (4.76%) 3	1 / 65 (1.54%) 1

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
16 June 2009	1st amendment of CSP version 3.0: • Modification/ Deletion of exclusion criteria
24 June 2009	2nd amendment of CSP version 3.0: implemented in the amended CSP version 4.0 • Study flowchart was included as an integrated part of the amended protocol • Corrections in the statistical section of the protocol
22 October 2009	The 3rd amendment of CSP version 3.0: implemented in the amended CSP version 5.0 • Change in sponsor's name and address due to acquisition of the PD business of Gambro AB by the Fresenius Medical Care Deutschland GmbH, dated 27-DEC-2010 • Prolongation of study duration until December 2013 • Modification of one inclusion criterion and one exclusion criterion
04 June 2012	1st amendment of CSP version 6.0: • Deletion of one exclusion criterion
05 December 2013	2nd amendment of CSP version 6.0: • Prolongation of recruitment until 31-DEC-2014 • Update of study site number and countries (UK was added) • Replacement of the IMP name "Gambrosol trio 40" with the new name "Gambrosol trio 40/Selutrio 40" given the planned removal of "Gambro" from all product names as of Q1/2014
22 August 2014	3rd amendment of CSP version 6.0: • Correction of primary objective • Change in one secondary efficacy variable • Clarification of DSMB function and responsibilities • Involvement of a CRO for data entry/data management processes

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/32425111