Clinical trial results:
A single-center, randomized, single-blind study in parallel groups to evaluate the efficacy and safety of a new intravenous iron HES preparation as compared to intravenous iron dextran (Cosmofer) in anemic patients

Summary

EudraCT number	2009-014351-72
Trial protocol	AT SK
Global end of trial date	09 August 2011

Results information

Result version number	v1 (current)
This version publication date	18 August 2016
First version publication date	18 August 2016
Summary attachment (see zip file)	Synopsis SWB0109 (Synopsis SWB0109.pdf)

Trial information

Trial identification

Sponsor protocol code	SWB0109

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Serumwerk Bernburg AG
Sponsor organisation address	Hallesche Landstrasse 105b, Bernburg, Germany, 06406
Public contact	Susanne Manhart, Serumwerk Bernburg AG, +49 3471860180, smanhart@serumwerk.de
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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	12 May 2011
Is this the analysis of the primary completion data?	Yes
Primary completion date	12 May 2011
Global end of trial reached?	Yes
Global end of trial date	09 August 2011
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Compare efficacy and safety of iron-HES vs Cosmofer (iron dextran)

Protection of trial subjects:

The protocol was approved by local ethics committees and competent authorities. The trial was conducted in accordance with good clinical practice and the Declaration of Helsinki. Informed consent was obtained in writing Prior to any trial related activities.

Background therapy: -

Evidence for comparator:

Cosmofer (iron dextran) was chosen as comparator based on the biochemical and pharmacological similarity of HES and dextran as carrier of the iron molecule. CosmoFer® is indicated for the treatment of iron deficiency in the following indications:
• When oral iron preparations cannot be used, e.g. due to intolerance, or in case of demonstrated lack of effect of oral iron therapy
• Where there is a clinical need to deliver iron rapidly to iron stores.
The diagnosis of iron deficiency must be based on appropriate laboratory tests (e.g. Serum ferritin, serum iron, transferrin saturation and hypochromic red cells).

Actual start date of recruitment	29 January 2010
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Slovakia: 20
Country: Number of subjects enrolled	Austria: 34
Worldwide total number of subjects	54
EEA total number of subjects	54

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)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	27
From 65 to 84 years	27
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Subjects were screened in the period January 2010 to May 2011. The trial took place at one site in Austria and one site in Slovakia.

Pre-assignment

Screening details:

Anemic CKD patients were recruited and screened for inclusion and exclusion criteria. No study specific procedure was done prior written informed consent was obtained.

Period 1

Period 1 title	overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Single blind
Roles blinded	Subject

Blinding implementation details:

This is a single blind study which is justified as the main variables of this study are laboratory tests and the fact that only a single medication application was investigated.

Arms

Are arms mutually exclusive?	Yes
Arm title	Feramyl

Arm description:

One single iron dosage was infused as specified in the reference medications's SPC (Cosmofer):
After the application of the test dose an one hour Observation period for rare anaphylactic reactions was scheduled according to the Cosmofer SPC. Thereafter - provided no adverse reaction was observed - one single full dose was applied as intravenous Infusion over about four hours.

Arm type	Experimental
Investigational medicinal product name	Feramyl 50mg/ml Ampoules
Investigational medicinal product code	Feramyl
Other name	iron HES
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous drip use

Dosage and administration details:

The doses were selected individually after obtaining necessary parameters and calculation using using the formulae for patients suffering from anemia according to the SPC of Cosmofer. After the application of the test dose and one hour observation period one single full dose was applied as intravenous infusion over about four hours.

Arm title	Cosmofer

Arm description:

One single iron dosage was infused as specified in the SPC of Cosmofer:
After the application of the test dose an one hour observation period for rare anaphylactic reactions was scheduled according to the Cosmofer SPC. Thereafter - provided no adverse reaction was observed - one single full dose was applied as intravenous Infusion over about four hours.

Arm type	Active comparator
Investigational medicinal product name	Cosmofer 50mg/ml ampoules
Investigational medicinal product code	Cosmofer
Other name	iron dextran
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous drip use

Dosage and administration details:

The doses were selected individually after obtaining necessary parameters and calculation using using the formulae for patients suffering from anemia according to the SPC of Cosmofer. After the application of the test dose and one hour observation period one single full dose was applied as intravenous infusion over about four hours.

Number of subjects in period 1	Feramyl	Cosmofer
Started	27	27
Completed	26	26
Not completed	1	1
serious adverse event	-	1
Protocol deviation	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Feramyl
Reporting group description:	
One single iron dosage was infused as specified in the reference medications's SPC (Cosmofer): After the application of the test dose an one hour Observation period for rare anaphylactic reactions was scheduled according to the Cosmofer SPC. Thereafter - provided no adverse reaction was observed - one single full dose was applied as intravenous Infusion over about four hours.	
Reporting group title	Cosmofer
Reporting group description:	
One single iron dosage was infused as specified in the SPC of Cosmofer: After the application of the test dose an one hour observation period for rare anaphylactic reactions was scheduled according to the Cosmofer SPC. Thereafter - provided no adverse reaction was observed - one single full dose was applied as intravenous Infusion over about four hours.	

Reporting group values	Feramyl	Cosmofer	Total
Number of subjects	27	27	54
Age categorical			
Units: Subjects			
In utero			0
Preterm newborn infants (gestational age < 37 wks)			0
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)			0
From 65-84 years			0
85 years and over			0
Age continuous			
Units: years			
arithmetic mean	60.73	63.09	
standard deviation	± 14.19	± 9.89	-
Gender categorical			
Units: Subjects			
Female	11	12	23
Male	16	15	31
hemoglobin			
Hemoglobin at baseline of the ITT population			
Units: g/dl			
arithmetic mean	11.29	11.11	
standard deviation	± 0.95	± 1.08	-
Hematocrit			
Hematocrit at baseline of the ITT population			
Units: percent			
arithmetic mean	34.5	34.11	
standard deviation	± 2.92	± 3.13	-
TSAT			

Transferrin Saturation at baseline of the ITT population			
Units: percent			
arithmetic mean	19.55	19.24	
standard deviation	± 9.871	± 7.32	-
SF			
Serum Ferritin (ITT Population)			
Units: µg/L			
arithmetic mean	79.48	102.5	
standard deviation	± 71.46	± 112.1	-

End points

End points reporting groups

Reporting group title	Feramyl

Reporting group description:

One single iron dosage was infused as specified in the reference medications's SPC (Cosmofer):
After the application of the test dose an one hour Observation period for rare anaphylactic reactions was scheduled according to the Cosmofer SPC. Thereafter - provided no adverse reaction was observed - one single full dose was applied as intravenous Infusion over about four hours.

Reporting group title	Cosmofer

Reporting group description:

One single iron dosage was infused as specified in the SPC of Cosmofer:
After the application of the test dose an one hour observation period for rare anaphylactic reactions was scheduled according to the Cosmofer SPC. Thereafter - provided no adverse reaction was observed - one single full dose was applied as intravenous Infusion over about four hours.

Primary: hemoglobin

End point title	hemoglobin

End point description:

Primary endpoint was the hemoglobin Level at day 7.

End point type	Primary

End point timeframe:

hemoglobin at day 7

End point values	Feramyl	Cosmofer		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	26	26		
Units: g/dl				
arithmetic mean (standard deviation)				
hemoglobin	11.61 (± 0.92)	11.5 (± 1.23)		

Statistical analyses

Statistical analysis title	Analysis of the primary variable

Statistical analysis description:

Analysis of the primary variable was performed based on the absolute values of hemoglobin at day 7 using the observed cases technique. The Primary endpoint was tested for equivalence of the ratio average hemoglobin of the test medication vs the reference medication. This is the only confirmatory evaluation of the study data.

Comparison groups	Feramyl v Cosmofer

Number of subjects included in analysis	52
Analysis specification	Pre-specified
Analysis type	equivalence[1]
P-value	< 0.7128 [2]
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)
Point estimate	1.0097
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.9581
upper limit	1.0641

Notes:

[1] - The results of the analysis according to Fieller's theorem show an average ratio Feramyl/Cosmofer at day of 101% with a 95%-CI ranging from 96% to 106%.
[2] - non-significant

Secondary: Hematocrit (HCT)

End point title	Hematocrit (HCT)

End point description:

Hematocrit at day 7 of the PP population. The secondary endpoints for efficacy were the items of the iron Status (HCT, TSAT, SF) at day 7.

End point type	Secondary

End point timeframe:

time points of assessment: at baseline, at 30 min after infusion, at day 7

End point values	Feramyl	Cosmofer		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	26	26		
Units: percent				
arithmetic mean (standard deviation)				
HCT	35.13 (± 2.66)	35.11 (± 3.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: Transferrin saturation (TSAT)

End point title	Transferrin saturation (TSAT)

End point description:

TSAT at day 7 of the PP population. The secondary endpoints for efficacy were the items of the iron status (HCT, TSAT, SF) at day 7.

End point type	Secondary

End point timeframe:

time points of assessment: at baseline, at 30 min after infusion, at day 7

End point values	Feramyl	Cosmofer		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	26	26		
Units: percent				
arithmetic mean (standard deviation)				
TSAT	35.347 (± 14.484)	43.424 (± 17.907)		

Statistical analyses

No statistical analyses for this end point

Secondary: Serum ferritin (SF)

End point title	Serum ferritin (SF)

End point description:

SF at day 7 of the PP population. The secondary endpoints for efficacy were the items of the iron Status (HCT, TSAT, SF) at day 7

End point type	Secondary

End point timeframe:

time points of assessment: at baseline, at 30 min after infusion, at day 7

End point values	Feramyl	Cosmofer		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	26	26		
Units: µg/L				
arithmetic mean (standard deviation)				
SF	512.1 (± 159.11)	601.93 (± 235.78)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

January 2010 - May 2011

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	12

Reporting groups

Reporting group title	Feramyl
Reporting group description: -	
Reporting group title	Cosmofer
Reporting group description: -	

Serious adverse events	Feramyl	Cosmofer	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 27 (0.00%)	2 / 27 (7.41%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Immune system disorders			
Anaphylactoid reaction	Additional description: The Patient developed the SAE after administration of the test dose within a few minutes. The Situation was not reported life-threatening and teh Patient recovered completely in a few days.		
subjects affected / exposed	0 / 27 (0.00%)	1 / 27 (3.70%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
urinary retention and infection	Additional description: The Patient had a two years history of recurrent Problems in the urinary tract and developed 5 days after the full dose of cosmofer urinary symptoms. A hospitalization was necessary for treatment of the urinary retention and infection.		
subjects affected / exposed	0 / 27 (0.00%)	1 / 27 (3.70%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 1 %

Non-serious adverse events	Feramyl	Cosmofer	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 27 (14.81%)	3 / 27 (11.11%)	
Cardiac disorders			
Bradycardia	Additional description: very short bradycardia and vertigo		
subjects affected / exposed	1 / 27 (3.70%)	0 / 27 (0.00%)	
occurrences (all)	1	0	
Nervous system disorders			
Cephalea			
subjects affected / exposed	0 / 27 (0.00%)	2 / 27 (7.41%)	
occurrences (all)	0	2	
General disorders and administration site conditions			
arm pain	Additional description: mild pain in the arm		
subjects affected / exposed	0 / 27 (0.00%)	1 / 27 (3.70%)	
occurrences (all)	0	1	
nocturnal sweat			
subjects affected / exposed	0 / 27 (0.00%)	1 / 27 (3.70%)	
occurrences (all)	0	1	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 27 (0.00%)	1 / 27 (3.70%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea	Additional description: mild dyspnoea		
subjects affected / exposed	0 / 27 (0.00%)	1 / 27 (3.70%)	
occurrences (all)	0	1	
Skin and subcutaneous tissue disorders			
Eczema	Additional description: mild eczema in teh Region of the interphalangeal limb of finger V		
subjects affected / exposed	1 / 27 (3.70%)	0 / 27 (0.00%)	
occurrences (all)	1	0	
skin coloration	Additional description: The Patient got accidentally some amount of the infusion paravenously into the subcutis of his right forearm within the first 30 min.		
subjects affected / exposed	1 / 27 (3.70%)	0 / 27 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal and connective tissue disorders			
Pain in extremity	Additional description: mild pain in the chest and the shoulder		

subjects affected / exposed	0 / 27 (0.00%)	1 / 27 (3.70%)	
occurrences (all)	0	1	
Hip pain	Additional description: pain in the left hip Joint 3 days after infusion		
subjects affected / exposed	1 / 27 (3.70%)	0 / 27 (0.00%)	
occurrences (all)	1	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
02 February 2010	to change the the inclusion criteria "age" from 30 years to 18 years to include more patients
11 May 2010	to allow inpatients
07 September 2010	The Submission of the protocol (Version 2) for Centre 2 - which was identical and included the two amendments of Centre 1 - was accepted by the UNB (University of Bratislava) ethics committee at 7th of September 2010. Also the State Institute for Drug Control (SIDC) of the Republic of Slovakia accepted the protocol at 12th of October 2010.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported