Clinical trial results:
A Multi-center, Open-label, Single Arm Study to Characterize the Pharmacokinetics and Pharmacodynamics Profile of Intravenous Ferric Carboxymaltose in Pediatric Subjects 1 –17 years old with Iron Deficiency Anemia (IDA)

Summary

EudraCT number	2014-004232-19
Trial protocol	PL
Global end of trial date	22 January 2017

Results information

Result version number	v1 (current)
This version publication date	24 April 2021
First version publication date	24 April 2021
Summary attachment (see zip file)	2014-004232-19_CSR Synopsis_13Jun2017 (2014-004232-19_CSR Synopsis_13Jun2017.pdf)

Trial information

Trial identification

Sponsor protocol code	1VIT13036

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02410213
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Luitpold Pharmaceuticals, Inc
Sponsor organisation address	800 Adams Avenue, Norristown, United States, PA 19403
Public contact	Mark A. Falone, American Regent, mfalone@americanregent.com
Scientific contact	Mark A. Falone, American Regent, mfalone@americanregent.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?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	01 June 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	22 January 2017
Global end of trial reached?	Yes
Global end of trial date	22 January 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objectives of this study are to characterize the pharmacokinetics and determine appropriate dosing and safety of Ferric Carboxymaltose for the pediatric population suffering from iron deficiency (ID) with anemia.

Protection of trial subjects:

The parent(s)/guardian(s) and the minors, if appropriate for age, were informed by the Investigator about the nature of the study, along with the aims, methods, anticipated benefits, potential hazards, and discomfort that participation may have entailed. Written informed consent and assent were obtained from the parent(s)/guardian(s) and the minors, if appropriate for age. The study protocol and the informed consent form were submitted to the Independent Ethics Committee (IEC) or Institutional Review Board (IRB) for review and approval before study initiation. The study was conducted in accordance with recognized international scientific and ethical standards, including but not limited to the International Conference on Harmonization guideline for Good Clinical Practice (ICH GCP) and the original principles embodied in the Declaration of Helsinki.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	19 February 2015
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	Russian Federation: 5
Country: Number of subjects enrolled	Poland: 30
Worldwide total number of subjects	35
EEA total number of subjects	30

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	3
Children (2-11 years)	14

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

Subject disposition

Recruitment

Recruitment details:

The study was conducted at eight sites in Poland and at two sites in Russia between 19 February 2015 and 22 January 2017.

Pre-assignment

Screening details:

The screening period, starting at Day -14 and following obtainment of informed consent/assent, was of maximum 14 days to allow for all screening results to be obtained and validated.

Pre-assignment period milestones

Number of subjects started	35
Number of subjects completed	35

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Blinding implementation details:

Not applicable

Arms

Are arms mutually exclusive?	Yes
Arm title	Cohort 1

Arm description:

Subjects assigned to cohort 1 received a single dose of FCM at 7.5 mg/kg.

Arm type	Experimental
Investigational medicinal product name	Ferric Carboxymaltose
Investigational medicinal product code	FCM
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

7.5 mg/kg single dose intravenous at 100 mg/min

Arm title	Cohort 2

Arm description:

Subjects assigned to cohort 2 received a single dose of FCM at 15 mg/kg with a maximum single dose of 150 mg.

Arm type	Experimental
Investigational medicinal product name	Ferric Carboxymaltose
Investigational medicinal product code	FCM
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

15 mg/kg single dose intravenous at 100 mg/min, maximum single dose 150 mg

Number of subjects in period 1	Cohort 1	Cohort 2
Started	16	19
Completed	16	19

Baseline characteristics

Reporting groups	
Reporting group title	Cohort 1
Reporting group description:	
Subjects assigned to cohort 1 received a single dose of FCM at 7.5 mg/kg.	
Reporting group title	Cohort 2
Reporting group description:	
Subjects assigned to cohort 2 received a single dose of FCM at 15 mg/kg with a maximum single dose of 150 mg.	

Reporting group values	Cohort 1	Cohort 2	Total
Number of subjects	16	19	35
Age categorical			
Mean age of subjects assigned to cohort 1 received a single dose of FCM at 7.5 mg/kg was 9.1 years. Mean age of subjects assigned to cohort 1 received a single dose of FCM at 15 mg/kg was 10.3 years.			
Units: Subjects			
Infants and toddlers (28 days-23 months)			0
Children (2-11 years)			0
Adolescents (12-17 years)			0
Age continuous			
Units: years			
arithmetic mean	9.1	10.3	
standard deviation	± 6.13	± 5.77	-
Gender categorical			
Units: Subjects			
Female	10	9	19
Male	6	10	16

End points

End points reporting groups

Reporting group title	Cohort 1
Reporting group description:	
Subjects assigned to cohort 1 received a single dose of FCM at 7.5 mg/kg.	
Reporting group title	Cohort 2
Reporting group description:	
Subjects assigned to cohort 2 received a single dose of FCM at 15 mg/kg with a maximum single dose of 150 mg.	

Primary: Hemoglobin

End point title	Hemoglobin[1]
End point description:	
Mean increases in hemoglobin from baseline to Day 35	
End point type	Primary
End point timeframe:	
Baseline Day 35	

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: No formal hypothesis testing was planned for this study. Only descriptive, summary statistics were planned for assessment of dosing and safety.

End point values	Cohort 1	Cohort 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	19		
Units: g/dL				
arithmetic mean (standard deviation)	1.9 (± 1.38)	2.8 (± 1.15)		

Statistical analyses

No statistical analyses for this end point

Primary: Ferritin

End point title	Ferritin[2]
End point description:	
Mean increases in ferritin from baseline to Day 35	
End point type	Primary
End point timeframe:	
Baseline Day 35	

Notes:

[2] - 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: No formal hypothesis testing was planned for this study. Only descriptive, summary statistics were planned for assessment of dosing and safety.

End point values	Cohort 1	Cohort 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	19		
Units: ng/mL				
arithmetic mean (standard deviation)	35.1 (± 98.22)	52.4 (± 31.7)		

Statistical analyses

No statistical analyses for this end point

Primary: TSAT

End point title	TSAT[3]

End point description:

Mean increases in TSAT from baseline to Day 35

End point type	Primary

End point timeframe:

Baseline
Day 35

Notes:

[3] - 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: No formal hypothesis testing was planned for this study. Only descriptive, summary statistics were planned for assessment of dosing and safety.

End point values	Cohort 1	Cohort 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	19		
Units: %				
arithmetic mean (standard deviation)	9.9 (± 11.54)	13.5 (± 6.88)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: Day 0 to Day 35	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	17.0
Reporting groups	
Reporting group title	Cohort 1
Reporting group description: -	
Reporting group title	Cohort 2
Reporting group description: -	

Serious adverse events	Cohort 1	Cohort 2	
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 16 (12.50%)	0 / 19 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Infections and infestations			
Sinusitis			
subjects affected / exposed	1 / 16 (6.25%)	0 / 19 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper respiratory tract infection			
subjects affected / exposed	1 / 16 (6.25%)	0 / 19 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Cohort 1	Cohort 2	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	9 / 16 (56.25%)	12 / 19 (63.16%)	
Investigations			
Alanine aminotransferase increased			

subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	1	
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	1	
Vascular disorders			
Hot flush			
subjects affected / exposed	1 / 16 (6.25%)	0 / 19 (0.00%)	
occurrences (all)	1	0	
Hypertension			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	1	
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 16 (6.25%)	1 / 19 (5.26%)	
occurrences (all)	1	1	
Blood and lymphatic system disorders			
Lymphadenitis			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	1	
General disorders and administration site conditions			
Hyperthermia			
subjects affected / exposed	0 / 16 (0.00%)	2 / 19 (10.53%)	
occurrences (all)	0	2	
Infusion site pruritus			
subjects affected / exposed	1 / 16 (6.25%)	0 / 19 (0.00%)	
occurrences (all)	1	0	
Injection site pain			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	1	
Pyrexia			
subjects affected / exposed	2 / 16 (12.50%)	0 / 19 (0.00%)	
occurrences (all)	2	0	
Thirst			
subjects affected / exposed	1 / 16 (6.25%)	0 / 19 (0.00%)	
occurrences (all)	1	0	

Eye disorders			
Blepharospasm			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	1	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	1	
Abdominal pain upper			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	1	
Aphthous stomatitis			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	1	
Constipation			
subjects affected / exposed	1 / 16 (6.25%)	0 / 19 (0.00%)	
occurrences (all)	1	0	
Enteritis			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	1	
Gastroduodentitis			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	1	
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	1	
Haematochezia			
subjects affected / exposed	1 / 16 (6.25%)	0 / 19 (0.00%)	
occurrences (all)	1	0	
Haemorrhoidal haemorrhage			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			
Dysphonia			
subjects affected / exposed	1 / 16 (6.25%)	0 / 19 (0.00%)	
occurrences (all)	1	0	

Dyspnoea exertional			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	1	
Epistaxis			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	1	
Rhinorhoea			
subjects affected / exposed	0 / 16 (0.00%)	3 / 19 (15.79%)	
occurrences (all)	0	3	
Wheezing			
subjects affected / exposed	1 / 16 (6.25%)	1 / 19 (5.26%)	
occurrences (all)	1	1	
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	1	
Rash			
subjects affected / exposed	2 / 16 (12.50%)	1 / 19 (5.26%)	
occurrences (all)	2	1	
Rash papular			
subjects affected / exposed	1 / 16 (6.25%)	0 / 19 (0.00%)	
occurrences (all)	1	0	
Urticaria			
subjects affected / exposed	0 / 16 (0.00%)	3 / 19 (15.79%)	
occurrences (all)	0	3	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	1	
Pharyngitis			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	1	
Respiratory tract infection			
subjects affected / exposed	1 / 16 (6.25%)	0 / 19 (0.00%)	
occurrences (all)	1	0	
Sinusitis			

subjects affected / exposed	1 / 16 (6.25%)	0 / 19 (0.00%)	
occurrences (all)	1	0	
Upper respiratory tract infection			
subjects affected / exposed	1 / 16 (6.25%)	2 / 19 (10.53%)	
occurrences (all)	1	2	
Urinary tract infection			
subjects affected / exposed	1 / 16 (6.25%)	0 / 19 (0.00%)	
occurrences (all)	1	0	
Viral pharyngitis			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
29 July 2014	Amendment #1 incorporated the following changes/additions: - The sample size rationale was revised to include equal age distribution within each cohort. - Exclusion criterion #3 was revised to exclude subjects with a body mass index ≤5th percentile by age. - The study design was changed to Phase 2. - Additional wording in section 7.1 "All laboratory values at the end of the study/Day 35 that have been deemed clinical significant by the Investigator should be followed until they are back into normal range".
08 October 2014	Amendment #2 incorporated the following changes: - Exclusion criterion #4 (male or female subjects 1 year of age weighing <12 kg) was added. - Exclusion criterion #12 (significant blood loss [>100 mL] within the last 3 months or any current bleeding disorders or anticipated need for surgery that may result in significant blood loss [>100 mL]) was deleted. - The total blood volume requirement was decreased from 72 mL to 44.5 mL. - Injectafer® was replaced with FCM throughout the protocol.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported