Clinical trial results:
A multicenter open label phase II study to evaluate the safety and efficacy of deferasirox in combination with deferoxamine followed by transitioning to deferasirox monotherapy in -thalassemia patients with severe cardiac iron overload

Summary

EudraCT number	2009-018091-34
Trial protocol	GR
Global end of trial date	06 June 2014

Results information

Result version number	v2
This version publication date	09 May 2019
First version publication date	07 August 2015
Version creation reason	• New data added to full data set Additional Analysis added.

Trial information

Trial identification

Sponsor protocol code	CICL670AGR02

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01459718
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novartis Pharma AG
Sponsor organisation address	CH-4002, Basel, Switzerland,
Public contact	Clinical Disclosure Office, Novartis Pharma AG, 41 613241111,
Scientific contact	Clinical Disclosure Office, Novartis Pharma AG, 41 613241111,

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	06 June 2014
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	06 June 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy of the intensive treatment with deferasirox taken per os once daily (20-40 mg/kg/day) plus the subcutaneous infusion of DFO (40 mg/kg/day) for 3-4 days per week in patients with severe cardiac iron-overload (4ms ≤ MRI T2* Heart ≤ 10 ms) over a period of 24 months of study treatment.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and the International Conference on Harmonization (ICH) Good Clinical Practice (GCP) guidelines. All the local regulatory requirements pertinent to safety of trial subjects were also followed during the conduct of the trial.

Background therapy: -	
Evidence for comparator: -	
Actual start date of recruitment	19 January 2011
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	Greece: 13
Worldwide total number of subjects	13
EEA total number of subjects	13

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)	13
From 65 to 84 years	0

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

In this open-label, single arm study, 31 participants were screened (1 participant was screened twice with 2 screening numbers; therefore, enrollment number = 32). Of these screened participants, 13 participants were randomized.

Pre-assignment

Screening details:

This was an open-label, single arm study.

Period 1

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

Arms

Arm title	Deferasirox / Deferasirox + Deferoxamine (DFO)

Arm description:

During Phase A, the induction treatment at entry, participants received Deferasirox -DFO combination. During Phase B, when participants transitioned to less intensive chelation therapy, participants received Deferasirox monotherapy.

Arm type	Experimental
Investigational medicinal product name	Defasirox
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Defasirox: 20-40 mg/kg/day orally, once daily

Investigational medicinal product name	Deferoxamine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

40 mg/kg/day subcutaneous (sc) infusion, 3-4 days per week

Number of subjects in period 1	Deferasirox / Deferasirox + Deferoxamine (DFO)
Started	13
Safety Analysis Set	13
Completed	10
Not completed	3
Physician decision	1
Adverse event, non-fatal	1

Lost to follow-up	1

Baseline characteristics

Reporting groups

Reporting group title	Deferasirox / Deferasirox + Deferoxamine (DFO)

Reporting group description:

During Phase A, the induction treatment at entry, participants received Deferasirox -DFO combination. During Phase B, when participants transitioned to less intensive chelation therapy, participants received Deferasirox monotherapy.

Reporting group values	Deferasirox / Deferasirox + Deferoxamine (DFO)	Total	
Number of subjects	13	13	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	13	13	
From 65-84 years	0	0	
85 years and over	0	0	
Age Continuous | Units: Years			
arithmetic mean	32.7		
standard deviation	± 4	-	
Gender, Male/Female Units: Participants			
Female	8	8	
Male	5	5	

End points

End points reporting groups

Reporting group title	Deferasirox / Deferasirox + Deferoxamine (DFO)

Reporting group description:

During Phase A, the induction treatment at entry, participants received Deferasirox -DFO combination. During Phase B, when participants transitioned to less intensive chelation therapy, participants received Deferasirox monotherapy.

Primary: Number of subjects achieving a complete response (CR)

End point title	Number of subjects achieving a complete response (CR)[1]

End point description:

Complete Response is defined as subjects that stop intensive deferasirox -DFO treatment, at any time point during the 24 months of study, based on an improvement in the cardiac Magnetic Resonance Imaging T2 star technique (MRI T2*) value being >10ms, and continue to be treated with deferasirox monotherapy without any further need for reverting back to intensive iron chelation treatment during the 24 months of study. The analysis was performed in 'Full analysis set' population defined as all subjects who entered in the study with at least a valid post-baseline assessment of the primary efficacy variable.

End point type	Primary

End point timeframe:

24 months

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: Statistical analyses was not planned for this endpoint.

End point values	Deferasirox / Deferasirox + Deferoxamine (DFO)			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: Subjects	4			

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects achieving a partial response (PR)

End point title	Number of subjects achieving a partial response (PR)[2]

End point description:

Partial Response is defined as subjects that stop intensive deferasirox -DFO treatment at any time point during the 24 months study and transition to receive deferasirox monotherapy, but due to a deterioration in cardiac MRI T2* to a value < 10 ms revert back to intensive deferasirox -DFO iron chelation therapy during the 24 months of study. The analysis was performed in 'Full analysis set' population defined as all subjects who entered in the study with at least a valid post-baseline assessment of the primary efficacy variable.

End point type	Primary

End point timeframe:

24 months

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: Statistical analyses was not planned for this endpoint.

End point values	Deferasirox / Deferasirox + Deferoxamine (DFO)			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: Subjects	0			

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with stable disease (SD)

End point title	Number of subjects with stable disease (SD)[3]

End point description:

Stable Disease is defined as those subjects that never achieved an improvement in the cardiac MRI T2* to values >10ms during the 24 months of study. The analysis was performed in 'Full analysis set' population defined as all subjects who entered in the study with at least a valid post-baseline assessment of the primary efficacy variable.

End point type	Primary

End point timeframe:

24 months

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: Statistical analyses was not planned for this endpoint.

End point values	Deferasirox / Deferasirox + Deferoxamine (DFO)			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: Subjects	8			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in cardiac iron overload of subjects in intensive iron chelation therapy consisting of deferasirox-DFO and after transition to deferasirox monotherapy

End point title	Change from baseline in cardiac iron overload of subjects in intensive iron chelation therapy consisting of deferasirox-DFO and after transition to deferasirox monotherapy

End point description:

Cardiac iron overload was determined by cardiac MRI T2*. Cardiac iron overload also was measured by the monthly velocity of heart MRI T2*. The analysis was performed in 'Full analysis set' population defined as all subjects who entered in the study with at least a valid post-baseline assessment of the primary efficacy variable. Here 'n' number analyzed signifies number of subjects evaluable at each time point.

End point type	Secondary

End point timeframe:

screening, 6, 12, 18, 24 months

End point values	Deferasirox / Deferasirox + Deferoxamine (DFO)			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: Milliseconds				
arithmetic mean (standard deviation)				
6 Months (n=12)	0.1 (± 1.4)			
12 Months (n=10)	0.7 (± 1.9)			
18 Months (n=11)	1.3 (± 2.4)			
24 Months (n=10)	2.4 (± 3.9)			

Statistical analyses

No statistical analyses for this end point

Secondary: Time to response

End point title	Time to response

End point description:

Time to response was defined as the time from baseline when the participant had severe cardiac iron overload to the time when the participant achieved mild/moderate cardiac overload (T2*>10 ms).

End point type	Secondary

End point timeframe:

24 months

End point values	Deferasirox / Deferasirox + Deferoxamine (DFO)			
Subject group type	Reporting group			
Number of subjects analysed	0[4]			
Units: Not Applicable				
number (not applicable)				

Notes:

[4] - Study was terminated early. Efficacy was not powered for analysis due to low enrollment.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in liver iron concentration (LIC)

End point title	Change from baseline in liver iron concentration (LIC)

End point description:

Change from baseline in LIC was determined by change in liver MRI T2*. The analysis was performed in 'Full analysis set' population defined as all subjects who entered in the study with at least a valid post-baseline assessment of the primary efficacy variable. Here 'n' number analyzed signifies number of subjects evaluable at each time point.

End point type	Secondary

End point timeframe:

Baseline, 6, 12, 18, 24 months

End point values	Deferasirox / Deferasirox + Deferoxamine (DFO)			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: mg of iron/gram of dry weight of liver				
arithmetic mean (standard deviation)				
6 Months (n=12)	-5 (± 7.7)			
12 Months (n=10)	-10.3 (± 9.2)			
18 Months (n=11)	-10.2 (± 10.7)			
24 Months (n=10)	-12.4 (± 10.1)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in serum ferritin levels and LIC

End point title	Change from baseline in serum ferritin levels and LIC

End point description:

Change from baseline was evaluated by the observed changes at 6, 12, 18, 24 months.

End point type	Secondary

End point timeframe:

baseline, 6, 12, 18, 24 months

End point values	Deferasirox / Deferasirox + Deferoxamine (DFO)			
Subject group type	Reporting group			
Number of subjects analysed	0[5]			
Units: Not Applicable				
number (not applicable)				

Notes:

[5] - Study was terminated early. Efficacy was not powered for analysis due to low enrollment.

Statistical analyses

No statistical analyses for this end point

Secondary: Left Ventricular Ejection Fraction (LVEF)

End point title	Left Ventricular Ejection Fraction (LVEF)

End point description:

LVEF % was measured by cardiac magnetic resonance (CMR). The analysis was performed in 'Full analysis set' population defined as all subjects who entered in the study with at least a valid post-baseline assessment of the primary efficacy variable. Here 'n' number analyzed signifies number of subjects evaluable at each time point.

End point type	Secondary

End point timeframe:

6, 12, 18, 24 months

End point values	Deferasirox / Deferasirox + Deferoxamine (DFO)			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: Percentage				
arithmetic mean (standard deviation)				
Baseline (n=12)	65 (± 4.4)			
6 Months (n=12)	65.4 (± 5)			
12 Months (n=10)	64.8 (± 4.6)			
18 Months (n=11)	65.1 (± 4.8)			
24 Months (n=10)	66.2 (± 4.6)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events are collected from First Patient First Visit (FPFV) until Last Patient Last Visit (LPLV). All adverse events reported in this record are from date of First Patient First Treatment until Last Patient Last Visit

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.1

Reporting groups

Reporting group title	Deferasirox

Reporting group description:

Deferasirox

Serious adverse events	Deferasirox		
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 13 (38.46%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Cardiac disorders			
Sinus tachycardia			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac discomfort			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Surgical and medical procedures			
Lithotripsy			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Haemolysis			

subjects affected / exposed	1 / 13 (7.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Fatigue			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Pyrexia			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Abdominal pain			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastritis			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

Vomiting				
subjects affected / exposed	1 / 13 (7.69%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pancreatitis acute				
subjects affected / exposed	1 / 13 (7.69%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Rectal haemorrhage				
subjects affected / exposed	1 / 13 (7.69%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
Dyspnoea				
subjects affected / exposed	1 / 13 (7.69%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Renal and urinary disorders				
Renal colic				
subjects affected / exposed	2 / 13 (15.38%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Nephrolithiasis				
subjects affected / exposed	1 / 13 (7.69%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
Sepsis				
subjects affected / exposed	1 / 13 (7.69%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Urinary tract infection				

subjects affected / exposed	1 / 13 (7.69%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Deferasirox		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	12 / 13 (92.31%)		
Surgical and medical procedures			
Tooth extraction			
subjects affected / exposed	2 / 13 (15.38%)		
occurrences (all)	2		
Wisdom teeth removal			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Tooth repair			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
General disorders and administration site conditions			
Discomfort			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Chest pain			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Fatigue			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Gait disturbance			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Malaise			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	2		
Pyrexia			

subjects affected / exposed	4 / 13 (30.77%)		
occurrences (all)	8		
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Hypersensitivity			
subjects affected / exposed	2 / 13 (15.38%)		
occurrences (all)	2		
Reproductive system and breast disorders			
Dysmenorrhoea			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	7		
Genital burning sensation			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Menstrual disorder			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
Catarrh			
subjects affected / exposed	3 / 13 (23.08%)		
occurrences (all)	5		
Respiratory distress			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Cough			
subjects affected / exposed	4 / 13 (30.77%)		
occurrences (all)	4		
Dysphonia			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Paranasal sinus discomfort			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Rhinitis allergic			

subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Investigations			
Blood pressure increased			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Injury, poisoning and procedural complications			
Muscle contusion			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Arthropod bite			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Atrial fibrillation			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Sinus tachycardia			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Nervous system disorders			
Facial neuralgia			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Dizziness			
subjects affected / exposed	2 / 13 (15.38%)		
occurrences (all)	2		
Headache			
subjects affected / exposed	4 / 13 (30.77%)		
occurrences (all)	24		
Sciatica			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	3		

Hypotonia subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1		
Presyncope subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1		
Syncope subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 2		
Blood and lymphatic system disorders Thrombocytosis subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1		
Ear and labyrinth disorders Hypoacusis subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1		
Ear pain subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1		
Tinnitus subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1		
Gastrointestinal disorders Abdominal discomfort subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1		
Abdominal distension subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1		
Abdominal pain subjects affected / exposed occurrences (all)	3 / 13 (23.08%) 5		
Diarrhoea subjects affected / exposed occurrences (all)	6 / 13 (46.15%) 16		
Abdominal pain lower			

subjects affected / exposed occurrences (all)	2 / 13 (15.38%) 2		
Abdominal pain upper subjects affected / exposed occurrences (all)	2 / 13 (15.38%) 4		
Constipation subjects affected / exposed occurrences (all)	2 / 13 (15.38%) 3		
Gastrointestinal disorder subjects affected / exposed occurrences (all)	3 / 13 (23.08%) 3		
Nausea subjects affected / exposed occurrences (all)	2 / 13 (15.38%) 3		
Gastric disorder subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1		
Toothache subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1		
Vomiting subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1		
Skin and subcutaneous tissue disorders Photosensitivity reaction subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1		
Endocrine disorders Hyperthyroidism subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1		
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all)	5 / 13 (38.46%) 5		
Back pain			

subjects affected / exposed	3 / 13 (23.08%)		
occurrences (all)	5		
Musculoskeletal pain			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	2		
Bone pain			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Myalgia			
subjects affected / exposed	2 / 13 (15.38%)		
occurrences (all)	2		
Infections and infestations			
Gastroenteritis			
subjects affected / exposed	2 / 13 (15.38%)		
occurrences (all)	3		
Ear infection			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Bronchitis			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Abscess			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Nasopharyngitis			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Respiratory tract infection			
subjects affected / exposed	2 / 13 (15.38%)		
occurrences (all)	2		
Rhinitis			
subjects affected / exposed	2 / 13 (15.38%)		
occurrences (all)	2		
Viral upper respiratory tract infection			
subjects affected / exposed	2 / 13 (15.38%)		
occurrences (all)	2		

Viral infection subjects affected / exposed occurrences (all)	2 / 13 (15.38%) 3		
Upper respiratory tract infection subjects affected / exposed occurrences (all)	3 / 13 (23.08%) 4		
Tooth abscess subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
26 May 2011	Amendment 1 introduced the following changes: amendment in the Table Contents; amendment in the Sections of Study Rationale, Inclusion/Exclusion Criteria, Primary Objectives, Study Design, Treatment Arms, regarding the range values of cardiac T2*; administrative changes in section of patient treatment; amendment in the Template of Visit Schedule and assessments for the correction of any administrative issues; administrative changes in the Sections of Physical Examination, Weight and Vital Signs for Administrative changes in the Pharmacokinetic Analysis section; administrative changes in chapter for Independent Data Monitoring Board role; administrative changes in the chapter of Database Management and Quality Control; amendment in section Interim Analysis Administrative changes in chapter regarding the SSC has being modified; amendment in the Appendix referring to cardiac and liver MRI for better determination and clarification of the measurements and evaluation method; and numbering of protocol Templates and Diagrams had been updated.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported