



Clinical trial results:

A phase II, multi-center, single-arm, prospective study to evaluate the safety and efficacy of deferasirox in beta-thalassemia major patients after hematopoietic stem cell transplantation

Summary

EudraCT number	2016-001561-88
Trial protocol	Outside EU/EEA
Global end of trial date	21 October 2015

Results information

Result version number	v1 (current)
This version publication date	25 June 2016
First version publication date	25 June 2016

Trial information

Trial identification

Sponsor protocol code	CICL670ATR04
-----------------------	--------------

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01610297
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novartis
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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	21 October 2015
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	21 October 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the present study was to determine the safety; incidence, type and severity of adverse events including renal, hepatic, biochemistry and hematologic parameters of deferasirox in the treatment of iron overload after HSCT in patients with beta-thalassemia major in 12 months period

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 September 2013
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	Turkey: 27
Worldwide total number of subjects	27
EEA total number of subjects	0

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)	20
Adolescents (12-17 years)	7
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

The patients received oral deferasirox at an initial dose of 10 mg/kg/day and dose escalation was allowed up to 20 mg/kg daily for 12 months or until the serum ferritin level was below 500 µg/L. Dose titration was allowed in 3 months periods by 5 mg/kg/day at the discretion of the investigator

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	ICL670
-----------	--------

Arm description:

Oral dose of ICL670 at 10 mg/kg daily

Arm type	Experimental
Investigational medicinal product name	Deferasinox
Investigational medicinal product code	ICL670
Other name	
Pharmaceutical forms	Dispersible tablet
Routes of administration	Oral use

Dosage and administration details:

deferasirox (ICL670) 10 mg/kg, oral, daily

Number of subjects in period 1	ICL670
Started	27
Completed	26
Not completed	1
Lost to follow-up	1

Baseline characteristics

Reporting groups

Reporting group title	ICL670
-----------------------	--------

Reporting group description:

Oral dose of ICL670 at 10 mg/kg daily

Reporting group values	ICL670	Total	
Number of subjects	27	27	
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)	20	20	
Adolescents (12-17 years)	7	7	
Adults (18-64 years)	0	0	
From 65-84 years	0	0	
85 years and over	0	0	
Age Continuous			
Units: years			
arithmetic mean	9.07		
standard deviation	± 3.81	-	
Gender, Male/Female			
Units: Participants			
Female	8	8	
Male	19	19	

End points

End points reporting groups

Reporting group title	ICL670
Reporting group description:	
Oral dose of ICL670 at 10 mg/kg daily	

Primary: Number of Participants with Adverse Events, Serious Adverse Events and Deaths as a measure of Safety and Tolerability

End point title	Number of Participants with Adverse Events, Serious Adverse Events and Deaths as a measure of Safety and Tolerability ^[1]
-----------------	--

End point description:

To determine the safety; incidence, type and severity of adverse events including renal, hepatic, biochemistry and hematologic parameters of deferasirox in the treatment of iron overload after HSCT in patients with beta-thalassemia major in 12 months period. No statistical analysis was planned for this primary outcome. The Safety Set (SS) includes all included patients who were included in the study.

End point type	Primary
----------------	---------

End point timeframe:

12 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: There was no planned analysis for this safety endpoint.

End point values	ICL670			
Subject group type	Reporting group			
Number of subjects analysed	27			
Units: Participants				
Adverse events	25			
Serious adverse events	3			
Death	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Change in serum ferritin level

End point title	Change in serum ferritin level
-----------------	--------------------------------

End point description:

Friedman test and Wilcoxon Signed Rank test were conducted to test whether there is a significant change in the serum ferritin level. The Full Analysis Set (FAS) comprises all patients in whom study treatment has been started and received at least one dose.

End point type	Secondary
----------------	-----------

End point timeframe:

Baseline, 12 Months

End point values	ICL670			
Subject group type	Reporting group			
Number of subjects analysed	27			
Units: ng/mL				
arithmetic mean (standard deviation)				
Baseline	1766.81 (\pm 599.64)			
Month 12	903.56 (\pm 596.62)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change in the further parameters of iron overload (cardiac iron concentration by MR examination)

End point title	Change in the further parameters of iron overload (cardiac iron concentration by MR examination)
-----------------	--

End point description:

Friedman test and Wilcoxon Signed Rank test were conducted to test whether there is a significant change in the T2*MRI (Cardiac MRI). The Full Analysis Set (FAS) comprises all patients in whom study treatment has been started and received at least one dose.

End point type	Secondary
End point timeframe:	
Baseline, 12 month	

End point values	ICL670			
Subject group type	Reporting group			
Number of subjects analysed	27			
Units: T2*MRI				
arithmetic mean (standard deviation)				
Baseline Cardiac MRI(n= 27)	26.48 (\pm 7.49)			
Week 52 Cardiac MRI (n=24)	28.25 (\pm 5.53)			

Statistical analyses

No statistical analyses for this end point

Secondary: The percentage of patients reaching serum ferritin levels lower than 500 µg/L

End point title	The percentage of patients reaching serum ferritin levels lower than 500 µg/L
End point description: Friedman test and Wilcoxon Signed Rank test were conducted to test whether there is a significant change in the serum ferritin level. The Full Analysis Set (FAS) comprises all patients in whom study treatment has been started and received at least one dose.	
End point type	Secondary
End point timeframe: Week 28 and Week 52	

End point values	ICL670			
Subject group type	Reporting group			
Number of subjects analysed	27			
Units: Patients				
number (not applicable)				
Week 28	7.7			
Week 52	33.3			

Statistical analyses

No statistical analyses for this end point

Secondary: Change in the further parameters of iron overload (liver iron concentration by Magnetic resonance imaging (MRI examination))

End point title	Change in the further parameters of iron overload (liver iron concentration by Magnetic resonance imaging (MRI examination))
End point description: Friedman test and Wilcoxon Signed Rank test were conducted to test whether there is a significant change in the R2*MRI (Liver MRI).	
End point type	Secondary
End point timeframe: Baseline, 12 Months	

End point values	ICL670			
Subject group type	Reporting group			
Number of subjects analysed	27			
Units: mg\g dry weight				
arithmetic mean (standard deviation)				
Baseline Liver MRI (n=27)	12.07 (± 9.42)			
Week 52 Liver MRI (n=25)	4.62 (± 2.85)			

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 are reported in this record from First Patient First Treatment until Last Patient Last Visit.

Assessment type	Systematic
-----------------	------------

Dictionary used

Dictionary name	MedDRA
-----------------	--------

Dictionary version	18.0
--------------------	------

Reporting groups

Reporting group title	ICL670
-----------------------	--------

Reporting group description:

Oral dose of ICL670 at 10 mg/kg daily

Serious adverse events	ICL670		
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 27 (11.11%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Investigations			
Neutrophil count decreased			
subjects affected / exposed	2 / 27 (7.41%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Alanine aminotransferase increased			
subjects affected / exposed	1 / 27 (3.70%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 27 (3.70%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Surgical and medical procedures			
Office visit			

subjects affected / exposed	1 / 27 (3.70%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Influenza like illness			
subjects affected / exposed	1 / 27 (3.70%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Hepatitis B			
subjects affected / exposed	1 / 27 (3.70%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	ICL670		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	23 / 27 (85.19%)		
Investigations			
Aspartate aminotransferase increased			
subjects affected / exposed	6 / 27 (22.22%)		
occurrences (all)	1		
White blood cell count decreased			
subjects affected / exposed	2 / 27 (7.41%)		
occurrences (all)	1		
Alanine aminotransferase increased			
subjects affected / exposed	7 / 27 (25.93%)		
occurrences (all)	1		
Blood and lymphatic system disorders			
Anemia			
subjects affected / exposed	7 / 27 (25.93%)		
occurrences (all)	1		
General disorders and administration site conditions			

Pyrexia subjects affected / exposed occurrences (all)	7 / 27 (25.93%) 1		
Influenza like illness subjects affected / exposed occurrences (all)	2 / 27 (7.41%) 1		
Immune system disorders Hypersensitivity subjects affected / exposed occurrences (all)	2 / 27 (7.41%) 1		
Gastrointestinal disorders Diarrhea subjects affected / exposed occurrences (all)	3 / 27 (11.11%) 1		
Vomiting subjects affected / exposed occurrences (all)	3 / 27 (11.11%) 1		
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)	7 / 27 (25.93%) 1		
Influenza subjects affected / exposed occurrences (all)	5 / 27 (18.52%) 1		
Upper respiratory tract infection subjects affected / exposed occurrences (all)	2 / 27 (7.41%) 1		
Rhinorrhea subjects affected / exposed occurrences (all)	2 / 27 (7.41%) 1		
Skin and subcutaneous tissue disorders Eczema subjects affected / exposed occurrences (all)	2 / 27 (7.41%) 1		
Infections and infestations			

Pharyngitis			
subjects affected / exposed	6 / 27 (22.22%)		
occurrences (all)	1		
Haemophilus infection			
subjects affected / exposed	2 / 27 (7.41%)		
occurrences (all)	1		
Herpes zoster			
subjects affected / exposed	2 / 27 (7.41%)		
occurrences (all)	1		
Infection			
subjects affected / exposed	2 / 27 (7.41%)		
occurrences (all)	1		
Sinusitis			
subjects affected / exposed	2 / 27 (7.41%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported