Clinical trial results:
Single-arm, Companion Study to Myelodysplastic Syndrome (MDS) 20090160 Using Darbepoetin alfa for the Treatment of Anaemic Subjects With Myelodysplastic Syndrome

Summary

EudraCT number	2013-000727-13
Trial protocol	BE
Global end of trial date	20 March 2017

Results information

Result version number	v1 (current)
This version publication date	02 March 2018
First version publication date	02 March 2018

Trial information

Trial identification

Sponsor protocol code	20130113

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02175277
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Amgen Inc.
Sponsor organisation address	One Amgen Center Drive, Thousand Oaks, CA, United States, 91320
Public contact	IHQ Medical Info-Clinical Trials, Amgen (EUROPE) GmbH, MedInfoInternational@amgen.com
Scientific contact	IHQ Medical Info-Clinical Trials, Amgen (EUROPE) GmbH, MedInfoInternational@amgen.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	20 March 2017
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	20 March 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study was to provide required access of investigational product (darbepoetin alfa) beyond the end of the active treatment period (EOATP) of the darbepoetin alfa MDS 20090160 study for subjects who had continued demonstration of benefit from darbepoetin alfa treatment and to describe the safety of longer-term use in this patient population.

Protection of trial subjects:

This study was conducted in accordance with International Council for Harmonisation (ICH) Good Clinical Practice (GCP) regulations/guidelines.
All subjects provided written informed consent before undergoing any study-related procedures, including screening procedures.
The study protocol, amendments, and the informed consent form (ICF) were reviewed by the Institutional Review Boards (IRBs) and Independent Ethics Committees (IECs). No subjects were recruited into the study and no investigational product (IP) was shipped until the IRB/IEC gave written approval of the protocol and ICF and Amgen received copies of these approvals.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	12 June 2014
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	Belgium: 9
Worldwide total number of subjects	9
EEA total number of subjects	9

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)	1
From 65 to 84 years	8
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This study was conducted at 5 centers in Belgium from 12 June 2014 (first subject enrolled) to 20 March 2017 (last subject completed study).

Pre-assignment

Screening details:

This study enrolled participants who completed the active treatment period of the phase 3 Study 20090160 (2013-000727-13).

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	Darbepoetin alfa

Arm description:

Participants received darbepoetin alfa for up to 73 weeks or until progression to acute myeloid leukemia (AML), whichever occurred first.

Arm type	Experimental
Investigational medicinal product name	Darbepoetin alfa
Investigational medicinal product code	
Other name	Aranesp®
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

The first dose of darbepoetin alfa was the same as that administered at the last dosing visit of the active treatment period in Study 20090160. Doses could be increased up to a maximum of 500 µg every two weeks (Q2W).

Number of subjects in period 1	Darbepoetin alfa
Started	9
Completed	8
Not completed	1
Protocol-specified criteria	1

Baseline characteristics

Reporting groups	
Reporting group title	Overall Study

Reporting group description: -

Reporting group values	Overall Study	Total	
Number of subjects	9	9	
Age Categorical Units: Subjects			
Adults (18-64 years)	1	1	
From 65-84 years	8	8	
85 years and over	0	0	
Age Continuous Units: years			
arithmetic mean	71.3		
standard deviation	± 7.9	-	
Gender Categorical Units: Subjects			
Female	3	3	
Male	6	6	
Race Units: Subjects			
White	9	9	
Ethnicity Units: Subjects			
Hispanic/Latino	1	1	
Not Hispanic/Latino	8	8	

End points

End points reporting groups

Reporting group title	Darbepoetin alfa

Reporting group description:

Participants received darbepoetin alfa for up to 73 weeks or until progression to acute myeloid leukemia (AML), whichever occurred first.

Primary: Number of Participants with Treatment-emergent Adverse Events

End point title	Number of Participants with Treatment-emergent Adverse Events[1]

End point description:

Adverse events (AEs) were graded for severity according to the Common Terminology Criteria for Adverse Events (CTCAE), version 4.0, where Grade 1 indicates a mild AE, Grade 2 indicates a moderate AE, Grade 3 indicates severe or medically significant but not immediately life-threatening and Grade 4 indicates life-threatening consequences; urgent intervention indicated.
A serious adverse event was defined as an adverse event that met at least one of the following serious criteria:
• fatal
• life threatening
• required in-patient hospitalization or prolongation of existing hospitalization
• resulted in persistent or significant disability/incapacity
• congenital anomaly/birth defect
• other medically important serious event
The investigator assessed whether each adverse events was related to darbepoetin alfa.

End point type	Primary

End point timeframe:

From first dose of darbepoetin alfa to 30 days after last dose; the maximum treatment duration was 73 weeks.

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: All study results were descriptive, with no inferential testing.

End point values	Darbepoetin alfa			
Subject group type	Reporting group			
Number of subjects analysed	9			
Units: participants				
All adverse events	9			
Adverse events ≥ grade 2	8			
Adverse events ≥ grade 3	2			
Adverse events ≥ grade 4	0			
Serious adverse events	3			
AEs leading to discontinuation of darbepoetin alfa	1			
Fatal adverse events	0			
Treatment-related adverse events	0			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From first dose of darbepoetin alfa to 30 days after last dose; the maximum treatment duration was 73 weeks.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	19.1

Reporting groups

Reporting group title	Darbepoetin alfa

Reporting group description:

Participants received darbepoetin alfa for up to 73 weeks or until progression to acute myeloid leukemia (AML), whichever occurred first.

Serious adverse events	Darbepoetin alfa		
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 9 (33.33%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Nervous system disorders			
Ischaemic stroke			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Eye disorders			
Macular fibrosis			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Darbepoetin alfa		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	9 / 9 (100.00%)		
Vascular disorders			
Haematoma			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Hypotension			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	2		
Fatigue			
subjects affected / exposed	4 / 9 (44.44%)		
occurrences (all)	10		
Injection site haematoma			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Malaise			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Pyrexia			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	3 / 9 (33.33%)		
occurrences (all)	4		
Dysphonia			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Dyspnoea			

subjects affected / exposed occurrences (all) Dyspnoea exertional subjects affected / exposed occurrences (all) Epistaxis subjects affected / exposed occurrences (all) Oropharyngeal pain subjects affected / exposed occurrences (all) Rhinorrhoea subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 1 4 / 9 (44.44%) 8 1 / 9 (11.11%) 2 3 / 9 (33.33%) 4 1 / 9 (11.11%) 1		
Psychiatric disorders Depression subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 1		
Investigations Blood creatinine increased subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 1		
Injury, poisoning and procedural complications Contusion subjects affected / exposed occurrences (all) Fall subjects affected / exposed occurrences (all) Upper limb fracture subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 2 1 / 9 (11.11%) 1 1 / 9 (11.11%) 1		
Cardiac disorders Palpitations subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 1		

Nervous system disorders			
Dizziness			
subjects affected / exposed	2 / 9 (22.22%)		
occurrences (all)	3		
Headache			
subjects affected / exposed	2 / 9 (22.22%)		
occurrences (all)	2		
Restless legs syndrome			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	2 / 9 (22.22%)		
occurrences (all)	2		
Neutropenia			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Eye disorders			
Chalazion			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Visual acuity reduced			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	3 / 9 (33.33%)		
occurrences (all)	3		
Abdominal pain upper			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	3		
Abdominal pain			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Aphthous ulcer			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	2		

Diarrhoea subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 1			
Dry mouth subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 1			
Haematochezia subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 2			
Inguinal hernia subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 1			
Nausea subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 1			
Vomiting subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 2			
Skin and subcutaneous tissue disorders				
Erythema subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 1			
Pruritus subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 1			
Rash subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 1			
Rash generalised subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 1			
Skin discomfort subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 1			
Urticaria				

subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	2		
Renal and urinary disorders			
Nocturia			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Bone pain			
subjects affected / exposed	2 / 9 (22.22%)		
occurrences (all)	2		
Hypercreatinaemia			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Muscle spasms			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	2		
Musculoskeletal chest pain			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Pain in extremity			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Infections and infestations			
Bronchitis			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Gingivitis			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Herpes simplex			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Influenza			

subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Nasopharyngitis			
subjects affected / exposed	2 / 9 (22.22%)		
occurrences (all)	2		
Oral fungal infection			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Pharyngitis			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Sinusitis			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Upper respiratory tract infection			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Urinary tract infection			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	2		

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