



Clinical trial results:

Open-label, multicenter, single arm, phase III study to collect additional safety and efficacy data with deferasirox film-coated tablets in patients completing study CICL670F2201

Summary

EudraCT number	2016-000186-23
Trial protocol	AT GR IT
Global end of trial date	23 July 2019

Results information

Result version number	v1 (current)
This version publication date	07 February 2020
First version publication date	07 February 2020

Trial information

Trial identification

Sponsor protocol code	CICL670AIC04
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02720536
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novartis Pharma AG
Sponsor organisation address	CH-4002, Basel, Switzerland,
Public contact	Study Director, Novartis Pharma AG, 41 613241111, Novartis.email@novartis.com
Scientific contact	Study Director, Novartis Pharma AG, 41 613241111, Novartis.email@novartis.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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	23 July 2019
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	23 July 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the overall safety of deferasirox FCT formulation in patients with transfusion dependent thalassemia or MDS at very low, low or intermediate risk

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	16 August 2016
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	Austria: 3
Country: Number of subjects enrolled	Greece: 10
Country: Number of subjects enrolled	Italy: 40
Worldwide total number of subjects	53
EEA total number of subjects	53

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)	3
Adults (18-64 years)	47
From 65 to 84 years	3

85 years and over	0
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Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

All patients completed study C1CL670F2201 prior to entry into this 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
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Arm description:

Treatment will be administered daily for up to 24 months. For each patient the daily dose is calculated based on the patient's actual body weight.

Arm type	Experimental
Investigational medicinal product name	Deferasirox
Investigational medicinal product code	ICL670
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Deferasirox was supplied as film-coated tablets of 90 mg, 180 mg and 360 mg dose strengths

Number of subjects in period 1	Deferasirox
Started	53
Completed	34
Not completed	19
PR- unwilling to comply with procedures	1
PR - unsatisfactory therapeutic effect	2
PR - abnormal lab value(s)	1
PR - pregnancy	2
Primary reason (PR) - subject withdrawal	11
PR - death	1
PR - adverse event	1

Baseline characteristics

Reporting groups

Reporting group title	Deferasirox
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Reporting group description:

Treatment will be administered daily for up to 24 months. For each patient the daily dose is calculated based on the patient's actual body weight.

Reporting group values	Deferasirox	Total	
Number of subjects	53	53	
Age Categorical			
Units: Participants			
<18	3	3	
≥18 - <50	46	46	
≥ 50 - <65	1	1	
≥ 65	3	3	
Sex: Female, Male			
Units:			
Female	35	35	
Male	18	18	
Race/Ethnicity, Customized			
Units: Subjects			
Caucasian	50	50	
Asian	1	1	
Other	2	2	
Main underlying disease			
Participants with myelodysplastic syndrome (MDS) and transfusion-dependent thalassemia. The very low, low or intermediate risk MDS was to be determined by the Revised International Prognostic Scoring System (IPSS-R) and IPSS-R was to be confirmed by a bone marrow examination within 6 months prior to study entry. MDS with INT risk =MDS with intermediate risk			
Units: Subjects			
MDS with very low risk as per the IPSS - R	2	2	
MDS with low risk as per the IPSS - R	1	1	
MDS with INT risk as per the IPSS - R	1	1	
Transfusion-dependent thalassemia	49	49	

End points

End points reporting groups

Reporting group title	Deferasirox
Reporting group description: Treatment will be administered daily for up to 24 months. For each patient the daily dose is calculated based on the patient's actual body weight.	
Subject analysis set title	Month 12
Subject analysis set type	Safety analysis
Subject analysis set description: Change from baseline at month 12	
Subject analysis set title	Baseline
Subject analysis set type	Full analysis
Subject analysis set description: Serum ferritin value at baseline	
Subject analysis set title	Month 6
Subject analysis set type	Full analysis
Subject analysis set description: Serum ferritin value at baseline and at month 6	
Subject analysis set title	Month 12
Subject analysis set type	Full analysis
Subject analysis set description: Serum ferritin value at baseline and at month 12	
Subject analysis set title	Baseline
Subject analysis set type	Safety analysis
Subject analysis set description: Baseline of laboratory value	
Subject analysis set title	Month 6
Subject analysis set type	Safety analysis
Subject analysis set description: Change from baseline at month 6	
Subject analysis set title	Month 6
Subject analysis set type	Safety analysis
Subject analysis set description: Change from baseline at month 6	
Subject analysis set title	Month 6
Subject analysis set type	Safety analysis
Subject analysis set description: Change from baseline at month 6	
Subject analysis set title	Month 6
Subject analysis set type	Safety analysis
Subject analysis set description: Change from baseline at month 6	
Subject analysis set title	Baseline
Subject analysis set type	Safety analysis
Subject analysis set description: Baseline of laboratory value	
Subject analysis set title	Month 12
Subject analysis set type	Safety analysis
Subject analysis set description: Change from baseline at month 12	

Primary: Overview of number of participants with adverse events

End point title	Overview of number of participants with adverse events ^[1]
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End point description:

Numbers represent counts of participants within the categories. An adverse event (AE) was defined as treatment emergent if its onset date is on or after (\geq) the first administration of study treatment within this study or events present prior to start of study treatment but increased in severity on or after (\geq) the first administration of study treatment within this study but not later than 30 days after the last study treatment in this study

End point type	Primary
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End point timeframe:

Baseline up to approximately 25 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: No analysis was done

End point values	Deferasirox			
Subject group type	Reporting group			
Number of subjects analysed	53			
Units: number of participants				
Adverse events (AEs)	52			
Treatment related AEs	20			
Severe adverse events	14			
Treatment related severe adverse events	2			
Serious adverse events (SAEs)	13			
Treatment related SAEs	0			
Fatal SAEs	1			
Treatment related fatal SAEs	0			
AEs leading to discontinuation	4			
Treatment related AEs leading to discontinuation	2			
AEs leading to dose adjust/interruption	33			
AEs requiring additional therapy	4			

Statistical analyses

No statistical analyses for this end point

Primary: Change from baseline red blood cells (RBC) (10**12/L) at Month 6 and Month 12 (Safety set)

End point title	Change from baseline red blood cells (RBC) (10**12/L) at Month 6 and Month 12 (Safety set) ^[2]
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End point description:

The change from baseline at each time point is calculated only for subjects with a value at baseline and the particular time point. Post = Post baseline, Change = Post - Baseline, Percentage relative change = $100 \times ([\text{Post} - \text{Baseline}] / \text{Baseline})$. Percentage relative change is calculated for each patient individually and then overall descriptive summary statistics is obtained for subjects with a value at baseline and the particular time point

End point type	Primary
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End point timeframe:

Baseline, 6 and 12 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: No analysis was done

End point values	Month 12	Baseline	Month 6	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	40	53	42	
Units: 10**12/L				
arithmetic mean (standard deviation)				
Baseline	3.746 (± 0.5071)	3.753 (± 0.4909)	3.733 (± 0.5016)	
Post	3.607 (± 0.5423)	999.9 (± 999.9)	3.610 (± 0.5153)	
Change	-0.139 (± 0.4330)	999.9 (± 999.9)	-0.124 (± 0.3892)	
Percentage relative change	-3.281 (± 11.7360)	999.9 (± 999.9)	-2.887 (± 10.3411)	

Statistical analyses

No statistical analyses for this end point

Primary: Change from baseline white blood cells (WBC) (10**9/L) at Month 6 and Month 12

End point title	Change from baseline white blood cells (WBC) (10**9/L) at Month 6 and Month 12 ^[3]
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End point description:

The change from baseline at each time point is calculated only for subjects with a value at baseline and the particular time point. Post = Post baseline, Change = Post - Baseline, Percentage relative change = $100 \times ([\text{Post} - \text{Baseline}] / \text{Baseline})$. Percentage relative change is calculated for each patient individually and then overall descriptive summary statistics is obtained for subjects with a value at baseline and the particular time point

End point type	Primary
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End point timeframe:

Baseline, 6 and 12 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: No analysis was done

End point values	Month 12	Baseline	Month 6	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	40	53	42	
Units: 10**9/L				
arithmetic mean (standard deviation)				
Baseline	9.100 (± 5.4667)	9.336 (± 5.1383)	9.559 (± 5.6650)	
Post	9.007 (± 4.4385)	999.9 (± 999.9)	9.090 (± 4.3712)	
Change	-0.093 (± 4.5792)	999.9 (± 999.9)	-0.469 (± 4.0727)	

Percentage relative change	9.537 (± 47.2220)	999.9 (± 999.9)	3.788 (± 33.4252)	
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Statistical analyses

No statistical analyses for this end point

Primary: Change from baseline platelets (10**9/L) at Month 6 and Month 12

End point title	Change from baseline platelets (10**9/L) at Month 6 and Month 12 ^[4]
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End point description:

The change from baseline at each time point is calculated only for subjects with a value at baseline and the particular time point. Post = Post baseline, Change = Post - Baseline, Percentage relative change = $100 \times ([\text{Post} - \text{Baseline}] / \text{Baseline})$. Percentage relative change is calculated for each patient individually and then overall descriptive summary statistics is obtained for subjects with a value at baseline and the particular time point

End point type	Primary
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End point timeframe:

Baseline, 6 and 12 months

Notes:

[4] - 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 analysis was done

End point values	Month 12	Baseline	Month 6	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	40	53	42	
Units: 10**9/L				
arithmetic mean (standard deviation)				
Baseline	339.4 (± 196.41)	330.1 (± 188.81)	336.5 (± 195.97)	
Post	361.9 (± 165.91)	999.9 (± 999.9)	344.2 (± 190.43)	
Change	22.4 (± 100.72)	999.9 (± 999.9)	7.7 (± 112.98)	
Percentage relative change	14.9 (± 27.98)	999.9 (± 999.9)	10.3 (± 40.78)	

Statistical analyses

No statistical analyses for this end point

Primary: Change from baseline serum creatinine (umol/L) at Month 6 and Month 12

End point title	Change from baseline serum creatinine (umol/L) at Month 6 and Month 12 ^[5]
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End point description:

The change from baseline at each time point is calculated only for subjects with a value at baseline and the particular time point. Post = Post baseline, Change = Post - Baseline, Percentage relative change = $100 \times ([\text{Post} - \text{Baseline}] / \text{Baseline})$. Percentage relative change is calculated for each patient

individually and then overall descriptive summary statistics is obtained for subjects with a value at baseline and the particular time point

End point type	Primary
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End point timeframe:

Baseline, 6 and 12 months

Notes:

[5] - 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 analysis was done

End point values	Month 12	Baseline	Month 6	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	40	53	43	
Units: umol/L				
arithmetic mean (standard deviation)				
Baseline	57.4 (± 16.91)	55.1 (± 16.16)	54.4 (± 16.34)	
Post	63.5 (± 16.78)	999.9 (± 999.9)	62.0 (± 16.17)	
Change	6.1 (± 11.09)	999.9 (± 999.9)	7.6 (± 9.51)	
Percentage relative change	12.7 (± 18.66)	999.9 (± 999.9)	17.1 (± 21.54)	

Statistical analyses

No statistical analyses for this end point

Primary: Change from baseline creatinine clearance (mL/min) at Month 6 and Month 12

End point title	Change from baseline creatinine clearance (mL/min) at Month 6 and Month 12 ^[6]
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End point description:

The change from baseline at each time point is calculated only for subjects with a value at baseline and the particular time point. Post = Post baseline, Change = Post - Baseline, Percentage relative change = $100 \times ([\text{Post} - \text{Baseline}] / \text{Baseline})$. Percentage relative change is calculated for each patient individually and then overall descriptive summary statistics is obtained for subjects with a value at baseline and the particular time point

End point type	Primary
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End point timeframe:

Baseline, 6 and 12 months

Notes:

[6] - 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 analysis was done

End point values	Month 12	Month 6	Baseline	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	40	41	52	
Units: mL/min				
arithmetic mean (standard deviation)				
Baseline	129.6 (± 50.30)	131.8 (± 56.98)	131.9 (± 51.32)	

Post	119.8 (± 49.34)	116.0 (± 48.71)	999.9 (± 999.9)	
Change	-9.8 (± 32.74)	-15.8 (± 35.12)	999.9 (± 999.9)	
Percentage relative change	-4.5 (± 31.37)	-7.9 (± 30.68)	999.9 (± 999.9)	

Statistical analyses

No statistical analyses for this end point

Primary: Change from baseline Alanine Aminotransferase/Serum Glutamic Pyruvic Transaminase (ALT/SGPT) (U/L) at Month 6 and Month 12

End point title	Change from baseline Alanine Aminotransferase/Serum Glutamic Pyruvic Transaminase (ALT/SGPT) (U/L) at Month 6 and Month 12 ^[7]
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End point description:

The change from baseline at each time point is calculated only for subjects with a value at baseline and the particular time point. Post = Post baseline, Change = Post - Baseline, Percentage relative change = $100 \times ([\text{Post} - \text{Baseline}] / \text{Baseline})$. Percentage relative change is calculated for each patient individually and then overall descriptive summary statistics is obtained for subjects with a value at baseline and the particular time point

End point type	Primary
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End point timeframe:

Baseline, 6 and 12 months

Notes:

[7] - 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 analysis was done

End point values	Month 12	Baseline	Month 6	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	40	53	44	
Units: U/L				
arithmetic mean (standard deviation)				
Baseline	39.5 (± 33.32)	37.4 (± 31.47)	39.4 (± 33.51)	
Post	25.9 (± 19.08)	999.9 (± 999.9)	28.9 (± 21.12)	
Change	-13.6 (± 27.44)	999.9 (± 999.9)	-10.5 (± 29.16)	
Percentage relative change	-4.3 (± 68.59)	999.9 (± 999.9)	2.8 (± 83.58)	

Statistical analyses

No statistical analyses for this end point

Primary: Change from baseline Aspartate Aminotransferase/Serum Glutamic Oxaloacetic Transaminase (AST/SGOT) (U/L) at Month 6 and Month 12

End point title	Change from baseline Aspartate Aminotransferase/Serum Glutamic Oxaloacetic Transaminase (AST/SGOT) (U/L) at
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End point description:

The change from baseline at each time point is calculated only for subjects with a value at baseline and the particular time point. Post = Post baseline, Change = Post - Baseline, Percentage relative change = $100 \times ([\text{Post} - \text{Baseline}] / \text{Baseline})$. Percentage relative change is calculated for each patient individually and then overall descriptive summary statistics is obtained for subjects with a value at baseline and the particular time point

End point type	Primary
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End point timeframe:

Baseline, 6 and 12 months

Notes:

[8] - 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 analysis was done

End point values	Baseline	Month 6	Month 12	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	53	43	39	
Units: U/L				
arithmetic mean (standard deviation)				
Baseline	30.7 (± 24.40)	32.9 (± 26.48)	33.7 (± 26.67)	
Post	999.9 (± 999.9)	27.6 (± 18.81)	25.2 (± 12.78)	
Change	999.9 (± 999.9)	-5.3 (± 21.03)	-8.5 (± 19.18)	
Percentage relative change	999.9 (± 999.9)	2.9 (± 58.91)	-6.2 (± 46.20)	

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute and relative change of serum ferritin level from baseline at month 6 and 12

End point title	Absolute and relative change of serum ferritin level from baseline at month 6 and 12
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End point description:

The change from baseline at each time point is calculated only for subjects with a value at baseline and the particular time point. Post = Post baseline, Change = Post - Baseline, Percentage relative change = $100 \times ([\text{Post} - \text{Baseline}] / \text{Baseline})$. Percentage relative change is calculated for each patient individually and then overall descriptive summary statistics is obtained for subjects with a value at baseline and the particular time point. A negative change from baseline is regarded as an improvement in this study

End point type	Secondary
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End point timeframe:

Baseline, 6 and 12 months

End point values	Baseline	Month 6	Month 12	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	53	44	36	
Units: ug/l				
arithmetic mean (standard deviation)				
Baseline	2523.51 (± 1746.087)	2614.12 (± 1781.287)	2542.76 (± 1904.087)	
Post baseline	999.9 (± 999.9)	2228.94 (± 1910.182)	1924.49 (± 1839.818)	
Absolute change from baseline	999.9 (± 999.9)	-385.18 (± 1038.789)	-618.26 (± 1054.150)	
Percentage relative change from baseline	999.9 (± 999.9)	-18.61 (± 32.969)	-29.08 (± 33.056)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were collected from first dose of study treatment until end of study treatment plus 30 days post treatment, up to maximum duration of 25 months

Adverse event reporting additional description:

Consistent with EudraCT disclosure specifications, Novartis has reported under the Serious adverse events field "number of deaths resulting from adverse events" all those deaths, resulting from serious adverse events that are deemed to be causally related to treatment by the investigator.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	22.0
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Reporting groups

Reporting group title	DFXFCT
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Reporting group description:

DFXFCT

Serious adverse events	DFXFCT		
Total subjects affected by serious adverse events			
subjects affected / exposed	13 / 53 (24.53%)		
number of deaths (all causes)	1		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Malignant melanoma			
subjects affected / exposed	1 / 53 (1.89%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Ovarian adenoma			
subjects affected / exposed	1 / 53 (1.89%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Papillary thyroid cancer			
subjects affected / exposed	1 / 53 (1.89%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Injury, poisoning and procedural complications			

Femur fracture			
subjects affected / exposed	1 / 53 (1.89%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Fracture			
subjects affected / exposed	1 / 53 (1.89%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Lumbar vertebral fracture			
subjects affected / exposed	1 / 53 (1.89%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Rib fracture			
subjects affected / exposed	1 / 53 (1.89%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Ulna fracture			
subjects affected / exposed	1 / 53 (1.89%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	1 / 53 (1.89%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Cardiac failure			
subjects affected / exposed	1 / 53 (1.89%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous			
subjects affected / exposed	1 / 53 (1.89%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		

Hepatobiliary disorders	Biliary colic			
	subjects affected / exposed	1 / 53 (1.89%)		
	occurrences causally related to treatment / all	0 / 1		
	deaths causally related to treatment / all	0 / 1		
Cholecystitis	subjects affected / exposed	1 / 53 (1.89%)		
	occurrences causally related to treatment / all	0 / 1		
	deaths causally related to treatment / all	0 / 1		
Cholestasis	subjects affected / exposed	1 / 53 (1.89%)		
	occurrences causally related to treatment / all	0 / 1		
	deaths causally related to treatment / all	0 / 1		
Hepatic failure	subjects affected / exposed	1 / 53 (1.89%)		
	occurrences causally related to treatment / all	0 / 1		
	deaths causally related to treatment / all	0 / 1		
Psychiatric disorders	Panic attack			
	subjects affected / exposed	1 / 53 (1.89%)		
	occurrences causally related to treatment / all	0 / 1		
	deaths causally related to treatment / all	0 / 1		
Renal and urinary disorders	Calculus urinary			
	subjects affected / exposed	1 / 53 (1.89%)		
	occurrences causally related to treatment / all	0 / 1		
	deaths causally related to treatment / all	0 / 1		
	Hydronephrosis			
	subjects affected / exposed	1 / 53 (1.89%)		
	occurrences causally related to treatment / all	0 / 1		
	deaths causally related to treatment / all	0 / 1		
	Renal colic			

subjects affected / exposed	1 / 53 (1.89%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Ureterolithiasis			
subjects affected / exposed	1 / 53 (1.89%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Endocrine disorders			
Goitre			
subjects affected / exposed	1 / 53 (1.89%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Infections and infestations			
Diverticulitis			
subjects affected / exposed	1 / 53 (1.89%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Lower respiratory tract infection			
subjects affected / exposed	1 / 53 (1.89%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Lymph gland infection			
subjects affected / exposed	1 / 53 (1.89%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Urosepsis			
subjects affected / exposed	1 / 53 (1.89%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Product issues			
Device failure			
subjects affected / exposed	1 / 53 (1.89%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		

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

Non-serious adverse events	DFXFCT		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	48 / 53 (90.57%)		
Investigations			
Blood creatinine increased			
subjects affected / exposed	4 / 53 (7.55%)		
occurrences (all)	4		
Urine protein/creatinine ratio increased			
subjects affected / exposed	8 / 53 (15.09%)		
occurrences (all)	19		
Vascular disorders			
Hypertension			
subjects affected / exposed	3 / 53 (5.66%)		
occurrences (all)	3		
Cardiac disorders			
Palpitations			
subjects affected / exposed	3 / 53 (5.66%)		
occurrences (all)	3		
Nervous system disorders			
Headache			
subjects affected / exposed	14 / 53 (26.42%)		
occurrences (all)	28		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	10 / 53 (18.87%)		
occurrences (all)	35		
Influenza like illness			
subjects affected / exposed	5 / 53 (9.43%)		
occurrences (all)	6		
Pyrexia			

subjects affected / exposed occurrences (all)	13 / 53 (24.53%) 21		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	10 / 53 (18.87%)		
occurrences (all)	18		
Abdominal pain upper			
subjects affected / exposed	11 / 53 (20.75%)		
occurrences (all)	14		
Constipation			
subjects affected / exposed	3 / 53 (5.66%)		
occurrences (all)	3		
Diarrhoea			
subjects affected / exposed	14 / 53 (26.42%)		
occurrences (all)	25		
Dyspepsia			
subjects affected / exposed	4 / 53 (7.55%)		
occurrences (all)	5		
Gastritis			
subjects affected / exposed	5 / 53 (9.43%)		
occurrences (all)	6		
Nausea			
subjects affected / exposed	12 / 53 (22.64%)		
occurrences (all)	14		
Vomiting			
subjects affected / exposed	12 / 53 (22.64%)		
occurrences (all)	14		
Hepatobiliary disorders			
Hypertransaminasaemia			
subjects affected / exposed	4 / 53 (7.55%)		
occurrences (all)	7		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	12 / 53 (22.64%)		
occurrences (all)	18		
Oropharyngeal pain			

subjects affected / exposed	9 / 53 (16.98%)		
occurrences (all)	16		
Productive cough			
subjects affected / exposed	3 / 53 (5.66%)		
occurrences (all)	3		
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	3 / 53 (5.66%)		
occurrences (all)	3		
Glycosuria			
subjects affected / exposed	3 / 53 (5.66%)		
occurrences (all)	4		
Proteinuria			
subjects affected / exposed	4 / 53 (7.55%)		
occurrences (all)	5		
Renal colic			
subjects affected / exposed	3 / 53 (5.66%)		
occurrences (all)	6		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	3 / 53 (5.66%)		
occurrences (all)	6		
Back pain			
subjects affected / exposed	5 / 53 (9.43%)		
occurrences (all)	13		
Musculoskeletal pain			
subjects affected / exposed	6 / 53 (11.32%)		
occurrences (all)	11		
Myalgia			
subjects affected / exposed	3 / 53 (5.66%)		
occurrences (all)	3		
Neck pain			
subjects affected / exposed	3 / 53 (5.66%)		
occurrences (all)	3		
Pain in extremity			

subjects affected / exposed	5 / 53 (9.43%)		
occurrences (all)	7		
Infections and infestations			
Ear infection			
subjects affected / exposed	4 / 53 (7.55%)		
occurrences (all)	5		
Gastroenteritis			
subjects affected / exposed	7 / 53 (13.21%)		
occurrences (all)	14		
Influenza			
subjects affected / exposed	9 / 53 (16.98%)		
occurrences (all)	11		
Nasopharyngitis			
subjects affected / exposed	3 / 53 (5.66%)		
occurrences (all)	7		
Pharyngitis			
subjects affected / exposed	7 / 53 (13.21%)		
occurrences (all)	10		
Respiratory tract infection			
subjects affected / exposed	4 / 53 (7.55%)		
occurrences (all)	5		
Rhinitis			
subjects affected / exposed	8 / 53 (15.09%)		
occurrences (all)	9		
Sinusitis			
subjects affected / exposed	3 / 53 (5.66%)		
occurrences (all)	4		
Tonsillitis			
subjects affected / exposed	5 / 53 (9.43%)		
occurrences (all)	5		
Upper respiratory tract infection			
subjects affected / exposed	4 / 53 (7.55%)		
occurrences (all)	4		
Urinary tract infection			
subjects affected / exposed	6 / 53 (11.32%)		
occurrences (all)	6		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
25 October 2017	<ul style="list-style-type: none">• The description related to study treatment duration was amended.• References to "Core and Extension" study were removed throughout the protocol.• Aligned protocol text with the Exjade prescribing information.• Corrected discrepancies on the description of the visit intervals.• Clarification was given on drug supply disposal and destruction and dosing regimen.• Corrected description for local clinical laboratory parameters collection plan.• Removed reference related to collection of pregnancy outcomes for the pregnant partners of male patients in accordance with Novartis's pregnancy guidance working group.• Clarification was given about demographic and other baseline data to be summarized descriptively in line with actual eCRF design.• Corrected description for duration of treatment exposure, actual and planned daily dose.• Clarification about the descriptive statistical analyses of the primary objective.• Updated description for supportive sensitivity analyses• Added description for secondary efficacy objective analyses• Updated description for adverse events analyses

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported