



Clinical trial results:

A randomized, open-label, single center, phase I, cross-over study to evaluate the pharmacokinetic comparability of deferasirox new tablet formulation with the reference dispersible formulation in healthy adult subjects

Summary

EudraCT number	2016-000248-32
Trial protocol	Outside EU/EEA
Global end of trial date	27 September 2012

Results information

Result version number	v1 (current)
This version publication date	26 July 2018
First version publication date	26 July 2018

Trial information

Trial identification

Sponsor protocol code	CICL670F2102
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
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)	Yes
EMA paediatric investigation plan number(s)	EMA-001103-PIP01-10
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	27 September 2012
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	27 September 2012
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of the trial was to evaluate the pharmacokinetic (PK) comparability of deferasirox with a reduced dosage strength of the new oral film coated tablet vs. the reference marketed dispersible tablets in healthy subjects under fasted conditions.

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	19 July 2012
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	United States: 44
Worldwide total number of subjects	44
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)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	44
From 65 to 84 years	0

85 years and over	0
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Subject disposition

Recruitment

Recruitment details:

The study was conducted at a single center in United States.

Pre-assignment

Screening details:

Of the 44 subjects enrolled, only 34 subjects were randomized and treated. Remaining 10 subjects were not randomized, received only iron-supplementation and discontinued due to following reasons:

Administrative problem (7), Subject withdrawn consent (2), Lost to follow-up (1).

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Deferasirox (Film coated then dispersible tablets)

Arm description:

Subjects were initially administered with 3*360 milligrams (mg) film coated tablets of deferasirox for a total dose of 1080 mg, followed by 3*500 mg dispersible tablets of deferasirox for a total of 1500 mg. Subjects received deferasirox with a glass of water (240 milliliter (mL) in the morning after an overnight fast (last meal or snack taken at least 10 hours (hr) earlier) and at least 1 hr before breakfast. After ingestion of dispersible tablets, the glass was rinsed with an additional 40 mL of water and administered to the subject. A washout period of 8 days was maintained between two treatments.

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

Dosage and administration details:

Subjects were orally administered with 3*360 mg deferasirox film coated tablet followed by 3*500 mg deferasirox dispersible tablet in morning after an overnight fast (last meal or snack taken at least 10 hrs earlier) and at least 1 hr before breakfast. A washout period of 8 day was maintained between two treatments.

Arm title	Deferasirox (Dispersible then film coated tablets)
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Arm description:

Subjects were initially administered with 3*500 mg dispersible tablets of deferasirox for a total of 1500 mg followed by 3*360 mg film coated tablets of deferasirox for a total dose of 1080 mg. Subjects received deferasirox with a glass of water (240 mL in the morning after an overnight fast (last meal or snack taken at least 10 hr earlier) and at least 1 hr before breakfast. After ingestion of dispersible tablets, the glass was rinsed with an additional 40 mL of water and administered to the subject. A washout period of 8 day was maintained between two treatments.

Arm type	Experimental
Investigational medicinal product name	Deferasirox
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Dosage and administration details:

Subjects were orally administered with 3*500 mg deferasirox dispersible tablet followed by 3*360 mg deferasirox film coated tablet in morning after an overnight fast (last meal or snack taken at least 10 hr

earlier) and at least 1 hr before breakfast. A washout period of 8 day was maintained between two treatments.

Number of subjects in period 1^[1]	Deferasirox (Film coated then dispersible tablets)	Deferasirox (Dispersible then film coated tablets)
Started	17	17
Completed	16	16
Not completed	1	1
Consent withdrawn by subject	-	1
Administrative Problems	1	-

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled as out of 44 subjects, only 34 subjects were randomized and treated in the trial.

Baseline characteristics

Reporting groups

Reporting group title	Deferasirox (Film coated then dispersible tablets)
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Reporting group description:

Subjects were initially administered with 3*360 milligrams (mg) film coated tablets of deferasirox for a total dose of 1080 mg, followed by 3*500 mg dispersible tablets of deferasirox for a total of 1500 mg. Subjects received deferasirox with a glass of water (240 milliliter (mL) in the morning after an overnight fast (last meal or snack taken at least 10 hours (hr) earlier) and at least 1 hr before breakfast. After ingestion of dispersible tablets, the glass was rinsed with an additional 40 mL of water and administered to the subject. A washout period of 8 days was maintained between two treatments.

Reporting group title	Deferasirox (Dispersible then film coated tablets)
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Reporting group description:

Subjects were initially administered with 3*500 mg dispersible tablets of deferasirox for a total of 1500 mg followed by 3*360 mg film coated tablets of deferasirox for a total dose of 1080 mg. Subjects received deferasirox with a glass of water (240 mL in the morning after an overnight fast (last meal or snack taken at least 10 hr earlier) and at least 1 hr before breakfast. After ingestion of dispersible tablets, the glass was rinsed with an additional 40 mL of water and administered to the subject. A washout period of 8 day was maintained between two treatments.

Reporting group values	Deferasirox (Film coated then dispersible tablets)	Deferasirox (Dispersible then film coated tablets)	Total
Number of subjects	17	17	34
Age categorical Units: Subjects			
Adults (18-55 years)	17	17	34
Age continuous Units: years arithmetic mean standard deviation	35.53 ± 12.841	36.71 ± 11.351	-
Gender categorical Units: Subjects			
Female	5	5	10
Male	12	12	24

End points

End points reporting groups

Reporting group title	Deferasirox (Film coated then dispersible tablets)
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Reporting group description:

Subjects were initially administered with 3*360 milligrams (mg) film coated tablets of deferasirox for a total dose of 1080 mg, followed by 3*500 mg dispersible tablets of deferasirox for a total of 1500 mg. Subjects received deferasirox with a glass of water (240 milliliter (mL) in the morning after an overnight fast (last meal or snack taken at least 10 hours (hr) earlier) and at least 1 hr before breakfast. After ingestion of dispersible tablets, the glass was rinsed with an additional 40 mL of water and administered to the subject. A washout period of 8 days was maintained between two treatments.

Reporting group title	Deferasirox (Dispersible then film coated tablets)
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Reporting group description:

Subjects were initially administered with 3*500 mg dispersible tablets of deferasirox for a total of 1500 mg followed by 3*360 mg film coated tablets of deferasirox for a total dose of 1080 mg. Subjects received deferasirox with a glass of water (240 mL in the morning after an overnight fast (last meal or snack taken at least 10 hr earlier) and at least 1 hr before breakfast. After ingestion of dispersible tablets, the glass was rinsed with an additional 40 mL of water and administered to the subject. A washout period of 8 day was maintained between two treatments.

Subject analysis set title	Deferasirox (Film coated tablet)
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Subject analysis set type	Sub-group analysis
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Subject analysis set description:

All subjects who were administered with a total dose of 3*360 mg (1080 mg) deferasirox as film coated tablets with a glass of water (240 mL in the morning after an overnight fast (last meal or snack taken at least 10 hr earlier) and at least 1 hr before breakfast. The subjects were analysed based on PK analysis set (PAS) defined as all safety subjects (subjects who received at least one dose of investigational product) who completed both treatment periods and provided evaluable PK.

Subject analysis set title	Deferasirox (Dispersible tablet)
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Subject analysis set type	Sub-group analysis
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Subject analysis set description:

All subjects who were administered with a total dose of 3*500 mg (1500 mg) deferasirox as dispersible tablets with a glass of water (240 mL in the morning after an overnight fast (last meal or snack taken at least 10 hr earlier) and at least 1 hr before breakfast. After ingestion of dispersible tablets, the glass was rinsed with an additional 40 mL of water and administered to the subject. The analysis was performed on PAS population.

Subject analysis set title	Iron Supplement
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Subject analysis set type	Safety analysis
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Subject analysis set description:

Subjects were daily administered with iron supplement (ferrous sulfate) 325 mg oral tablet as supportive treatment for 8 days prior to deferasirox treatment. A washout period of 6 days was maintained between supportive and deferasirox treatment. The subjects were analysed based on safety set defined as all randomized subjects who received at least one dose of investigational product (deferasirox or iron supplement).

Primary: Area under the concentration-time curve from time zero to the last measurable concentration (AUClast) of deferasirox

End point title	Area under the concentration-time curve from time zero to the last measurable concentration (AUClast) of deferasirox
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End point description:

AUClast was defined as the area under the concentration-time curve from time zero to the last measurable concentration sampling time micromole (μmol)*hr /Litre (L). The AUClast was derived based on the non-compartmental methods using Phoenix WinNonlin version 6.2. The analysis was performed in PAS population.

End point type	Primary
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End point timeframe:

Pre-dose, 0.5, 1, 1.5, 2, 3, 4, 6, 8, 12, 24, 36, 48, and 72 hr post-dose

End point values	Deferasirox (Film coated tablet)	Deferasirox (Dispersible tablet)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	32	32		
Units: $\mu\text{mol}\cdot\text{hr}/\text{L}$				
geometric mean (geometric coefficient of variation)	1273.78 ($\pm$ 39.22)	1270.79 ($\pm$ 49.7)		

Statistical analyses

Statistical analysis title	AUClast of deferasirox
Statistical analysis description:	
Geometric mean ratio of AUClast for deferasirox (film-coated tablet and dispersible tablet) was evaluated. The total number of subjects analysed in this endpoint were 32 but as this is a cross-over study the subjects analysed below are featuring as 64 as the number of subjects adds up on selecting the two arms that are being compared [Deferasirox Film coated tablet (N=32) and Deferasirox Dispersible tablet (N=32)].	
Comparison groups	Deferasirox (Dispersible tablet) v Deferasirox (Film coated tablet)
Number of subjects included in analysis	64
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Geometric Mean Ratio
Point estimate	1
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.932
upper limit	1.078

Primary: Area under the plasma concentration-time curve from time zero to infinity (AUCinf) of deferasirox

End point title	Area under the plasma concentration-time curve from time zero to infinity (AUCinf) of deferasirox
End point description:	
AUCinf was defined as the area under the plasma concentration-time curve from time zero to infinity ($\mu\text{mol}\cdot\text{hr}/\text{L}$). The AUCinf was derived based on the non-compartmental methods using Phoenix WinNonlin version 6.2. The analysis was performed in PAS population.	
End point type	Primary
End point timeframe:	
Pre-dose, 0.5, 1, 1.5, 2, 3, 4, 6, 8, 12, 24, 36, 48, and 72 hr post-dose	

End point values	Deferasirox (Film coated tablet)	Deferasirox (Dispersible tablet)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	32	32		
Units: $\mu\text{mol}\cdot\text{hr}/\text{L}$				
geometric mean (geometric coefficient of variation)	1307.04 ($\pm$ 39.15)	1327.01 ($\pm$ 50.29)		

Statistical analyses

Statistical analysis title	AUCinf of deferasirox
Statistical analysis description:	
Geometric mean ratio of AUCinf for deferasirox (film-coated tablet and dispersible tablet) was evaluated. The total number of subjects analysed in this endpoint were 32 but as this is a cross-over study the subjects analysed below are featuring as 64 as the number of subjects adds up on selecting the two arms that are being compared [Deferasirox Film coated tablet (N=32) and Deferasirox Dispersible tablet (N=32)].	
Comparison groups	Deferasirox (Film coated tablet) v Deferasirox (Dispersible tablet)
Number of subjects included in analysis	64
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Geometric Ratio
Point estimate	0.98
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.916
upper limit	1.059

Primary: Maximum (peak) observed plasma concentration after a single-dose administration (Cmax) of deferasirox

End point title	Maximum (peak) observed plasma concentration after a single-dose administration (Cmax) of deferasirox
End point description:	
Cmax was defined as the maximum (peak) observed plasma concentration after a single-dose administration ($\mu\text{mol}/\text{L}$). The Cmax was derived based on the non-compartmental methods using Phoenix WinNonlin version 6.2. The analysis was performed in PAS population.	
End point type	Primary
End point timeframe:	
Pre-dose, 0.5, 1, 1.5, 2, 3, 4, 6, 8, 12, 24, 36, 48, and 72 hr post-dose	

End point values	Deferasirox (Film coated tablet)	Deferasirox (Dispersible tablet)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	32	32		
Units: µmol/L				
geometric mean (geometric coefficient of variation)	105.83 (± 27.54)	81.54 (± 33.35)		

Statistical analyses

Statistical analysis title	Cmax of deferasirox
Statistical analysis description:	
Geometric mean ratio of Cmax for deferasirox (film-coated tablet and dispersible tablet) was evaluated. The total number of subjects analysed in this endpoint were 32 but as this is a cross-over study the subjects analysed below are featuring as 64 as the number of subjects adds up on selecting the two arms that are being compared [Deferasirox Film coated tablet (N=32) and Deferasirox Dispersible tablet (N=32)].	
Comparison groups	Deferasirox (Film coated tablet) v Deferasirox (Dispersible tablet)
Number of subjects included in analysis	64
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Geometric Ratio
Point estimate	1.3
Confidence interval	
level	90 %
sides	2-sided
lower limit	1.203
upper limit	1.4

Secondary: Time to reach maximum (peak) plasma concentration after a single-dose administration (Tmax) of deferasirox

End point title	Time to reach maximum (peak) plasma concentration after a single-dose administration (Tmax) of deferasirox
End point description:	
Tmax was defined as the time to reach maximum (peak) plasma concentration after a single-dose administration (hr). The Tmax was derived based on the non-compartmental methods using Phoenix WinNonlin version 6.2. The analysis was performed in PAS population.	
End point type	Secondary
End point timeframe:	
Pre-dose, 0.5, 1, 1.5, 2, 3, 4, 6, 8, 12, 24, 36, 48, and 72 hr post-dose	

End point values	Deferasirox (Film coated tablet)	Deferasirox (Dispersible tablet)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	32	32		
Units: hr				
median (full range (min-max))	2 (1.5 to 6.03)	3 (1 to 8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Elimination half-life with the terminal slope (lambda_z) of a semi-logarithmic concentration-time curve (T1/2) of deferasirox

End point title	Elimination half-life with the terminal slope (lambda_z) of a semi-logarithmic concentration-time curve (T1/2) of deferasirox
End point description: T1/2 was defined as the elimination half-life with the terminal slope (i.e. lambda_z) of a semi-logarithmic concentration-time curve (hr). The T1/2 was derived based on the non-compartmental methods using Phoenix WinNonlin version 6.2. The analysis was performed in PAS population.	
End point type	Secondary
End point timeframe: Pre-dose, 0.5, 1, 1.5, 2, 3, 4, 6, 8, 12, 24, 36, 48, and 72 hr post-dose	

End point values	Deferasirox (Film coated tablet)	Deferasirox (Dispersible tablet)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	32	32		
Units: hr				
geometric mean (geometric coefficient of variation)	12.48 (± 30.69)	15.64 (± 29.47)		

Statistical analyses

No statistical analyses for this end point

Secondary: Terminal slope of the elimination phase (Lambda_z) of deferasirox

End point title	Terminal slope of the elimination phase (Lambda_z) of deferasirox
End point description: Lambda_z was defined as the terminal slope of elimination phase (1/hr). The Lambda_z was derived based on the non-compartmental methods using Phoenix WinNonlin version 6.2. The analysis was performed in PAS population.	
End point type	Secondary
End point timeframe: Pre-dose, 0.5, 1, 1.5, 2, 3, 4, 6, 8, 12, 24, 36, 48, and 72 hr post-dose	

End point values	Deferasirox (Film coated tablet)	Deferasirox (Dispersible tablet)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	32	32		
Units: 1/hr				
geometric mean (geometric coefficient of variation)	0.06 (± 30.7)	0.04 (± 29.45)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with Adverse events (AEs), Serious adverse events (SAEs), Discontinued due to AEs and who died

End point title	Number of subjects with Adverse events (AEs), Serious adverse events (SAEs), Discontinued due to AEs and who died
End point description:	
AEs are defined as any unfavorable and unintended diagnosis, symptom, sign (including an abnormal laboratory finding), syndrome or disease which either occurs during study, having been absent at baseline, or, if present at baseline, appears to worsen. Serious adverse events are any untoward medical occurrences that result in death, are life threatening, require (or prolong) hospitalisation, cause persistent or significant disability/incapacity, result in congenital anomalies or birth defects, or are other conditions which in judgment of investigators represent significant hazards. The analysis was performed on safety set population.	
End point type	Secondary
End point timeframe:	
From Day 1 up to Day 43	

End point values	Deferasirox (Film coated tablet)	Deferasirox (Dispersible tablet)	Iron Supplement	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	32	32	34	
Units: Subjects				
AEs	11	6	3	
SAEs	0	0	0	
Deaths	0	0	0	
AEs leading to discontinuation	0	0	0	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

AEs were collected from First Subject First Visit (FSFV) until Last Subject Last Visit (LSLV). All AEs reported in this record were from date of First Subject First Treatment until LSLV.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	15.0
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Reporting groups

Reporting group title	Deferasirox (Film coated tablet)
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Reporting group description:

All subjects who received a total dose of 3*360 mg (1080 mg) deferasirox as film coated tablets with a glass of water (240 mL in the morning after an overnight fast (last meal or snack taken at least 10 hr earlier) and at least 1 hr before breakfast during the study.

Reporting group title	Deferasirox (Dispersible tablet)
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Reporting group description:

All subjects who received a total dose of 3*500 mg (1500 mg) deferasirox as dispersible tablets with a glass of water (240 mL in the morning after an overnight fast (last meal or snack taken at least 10 hr earlier) and at least 1 hr before breakfast during the study.

Reporting group title	Iron supplement
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Reporting group description:

All subjects who received iron supplement (ferrous sulfate) 325 mg oral tablet as supportive treatment for 8 days prior to deferasirox treatment during the study.

Reporting group title	All Subjects
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Reporting group description:

All Subjects who received at least one dose of study treatment.

Serious adverse events	Deferasirox (Film coated tablet)	Deferasirox (Dispersible tablet)	Iron supplement
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	0 / 34 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

Serious adverse events	All Subjects		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 34 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

Non-serious adverse events	Deferasirox (Film coated tablet)	Deferasirox (Dispersible tablet)	Iron supplement
Total subjects affected by non-serious adverse events subjects affected / exposed	11 / 32 (34.38%)	6 / 32 (18.75%)	3 / 34 (8.82%)
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 32 (3.13%)	0 / 32 (0.00%)	0 / 34 (0.00%)
occurrences (all)	1	0	0
Headache			
subjects affected / exposed	1 / 32 (3.13%)	2 / 32 (6.25%)	0 / 34 (0.00%)
occurrences (all)	1	2	0
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	1 / 32 (3.13%)	0 / 32 (0.00%)	0 / 34 (0.00%)
occurrences (all)	1	0	0
Pain			
subjects affected / exposed	0 / 32 (0.00%)	1 / 32 (3.13%)	0 / 34 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	1 / 32 (3.13%)	0 / 32 (0.00%)	0 / 34 (0.00%)
occurrences (all)	1	0	0
Abnormal faeces			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	1 / 34 (2.94%)
occurrences (all)	0	0	1
Diarrhoea			
subjects affected / exposed	7 / 32 (21.88%)	3 / 32 (9.38%)	0 / 34 (0.00%)
occurrences (all)	7	3	0
Dyspepsia			
subjects affected / exposed	1 / 32 (3.13%)	1 / 32 (3.13%)	0 / 34 (0.00%)
occurrences (all)	1	1	0
Faeces discoloured			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	1 / 34 (2.94%)
occurrences (all)	0	0	1
Infrequent bowel movements			

subjects affected / exposed occurrences (all)	1 / 32 (3.13%) 1	0 / 32 (0.00%) 0	0 / 34 (0.00%) 0
Reproductive system and breast disorders Menstruation irregular subjects affected / exposed occurrences (all)	1 / 32 (3.13%) 1	0 / 32 (0.00%) 0	0 / 34 (0.00%) 0
Skin and subcutaneous tissue disorders Erythema subjects affected / exposed occurrences (all)	0 / 32 (0.00%) 0	0 / 32 (0.00%) 0	1 / 34 (2.94%) 1
Papule subjects affected / exposed occurrences (all)	0 / 32 (0.00%) 0	1 / 32 (3.13%) 1	0 / 34 (0.00%) 0
Pruritus subjects affected / exposed occurrences (all)	0 / 32 (0.00%) 0	0 / 32 (0.00%) 0	1 / 34 (2.94%) 1

Non-serious adverse events	All Subjects		
Total subjects affected by non-serious adverse events subjects affected / exposed	15 / 34 (44.12%)		
Nervous system disorders Dizziness subjects affected / exposed occurrences (all)	1 / 34 (2.94%) 1		
Headache subjects affected / exposed occurrences (all)	3 / 34 (8.82%) 3		
General disorders and administration site conditions Fatigue subjects affected / exposed occurrences (all)	1 / 34 (2.94%) 1		
Pain subjects affected / exposed occurrences (all)	1 / 34 (2.94%) 1		
Gastrointestinal disorders			

Abdominal distension subjects affected / exposed occurrences (all)	1 / 34 (2.94%) 1		
Abnormal faeces subjects affected / exposed occurrences (all)	1 / 34 (2.94%) 1		
Diarrhoea subjects affected / exposed occurrences (all)	8 / 34 (23.53%) 10		
Dyspepsia subjects affected / exposed occurrences (all)	2 / 34 (5.88%) 2		
Faeces discoloured subjects affected / exposed occurrences (all)	1 / 34 (2.94%) 1		
Infrequent bowel movements subjects affected / exposed occurrences (all)	1 / 34 (2.94%) 1		
Reproductive system and breast disorders Menstruation irregular subjects affected / exposed occurrences (all)	1 / 34 (2.94%) 1		
Skin and subcutaneous tissue disorders Erythema subjects affected / exposed occurrences (all) Papule subjects affected / exposed occurrences (all) Pruritus subjects affected / exposed occurrences (all)	1 / 34 (2.94%) 1 1 / 34 (2.94%) 1 1 / 34 (2.94%) 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