Clinical trial results:
A single-arm, open-label study of the palatability and tolerability of Exjade taken with meals, with different liquids or crushed and added to food

Due to EudraCT system limitations, which EMA is aware of, data using 999 as data points in this record are not an accurate representation of the clinical trial results. Please use https://www.novctrd.com/CtrdWeb/home.novfor complete trial results.

Summary

EudraCT number	2011-004217-17
Trial protocol	Outside EU/EEA
Global end of trial date	31 August 2010

Results information

Result version number	v1 (current)
This version publication date	06 July 2018
First version publication date	06 July 2018

Trial information

Trial identification

Sponsor protocol code	CICL670AUS32

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00845871
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)	EMEA-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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	31 August 2010
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	31 August 2010
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of the study was to evaluate the palatability of deferasirox with alternative methods of administration over three months of assessment.

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	13 May 2009
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: 65
Worldwide total number of subjects	65
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)	15
Adolescents (12-17 years)	17

Adults (18-64 years)	23
From 65 to 84 years	10
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted at 23 centres in United States.

Pre-assignment

Screening details:

A total of 82 subjects were screened, out of which 65 subjects were enrolled into the study.

Period 1

Period 1 title	Run-in period
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Blinding implementation details:

The study was open label, hence no blinding was performed.

Arms

Arm title	Deferasirox (Run-in period)

Arm description:

Subjects were administered with deferasirox starting dose of 20 milligram/kilogram/day (mg/kg/day), daily 30 minutes before meal.

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

Dosage and administration details:

Subjects were administered with deferasirox starting dose of 20 mg/kg orally on daily basis with meal.

Number of subjects in period 1	Deferasirox (Run-in period)
Started	65
Completed	65

Period 2

Period 2 title	Overall period
Is this the baseline period?	Yes[1]
Allocation method	Not applicable
Blinding used	Not blinded

Blinding implementation details:

The study was open label, hence no blinding was performed.

Arms

Arm title	Deferasirox (Assessment period)

Arm description:

Subjects were administered daily with deferasirox at a minimum starting dose of 20 mg/kg/day along with different food and liquids consistently for 12 weeks of assessment period. For subjects receiving > 30 mg/kg/day, a maximum of 40 mg/kg/day was allowed.

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

Dosage and administration details:

Subjects were administered daily with deferasirox starting dose of 20 mg/kg orally to a maximum dose of 40 mg/kg/day.

Notes:

[1] - Period 1 is not the baseline period. It is expected that period 1 will be the baseline period.

Justification: The study design comprised of a run-in period prior randomization of subjects into the assessment period. The assessment period was considered as baseline period.

Number of subjects in period 2	Deferasirox (Assessment period)
Started	65
Completed	58
Not completed	7
Abnormal laboratory value(s)	1
Consent withdrawn by subject	3
Adverse event, non-fatal	2
'Abnormal test procedure result(s) '	1

Baseline characteristics

Reporting groups	
Reporting group title	Overall period
Reporting group description:	
All enrolled subjects were analysed regardless of any treatment received or not.	

Reporting group values	Overall period	Total	
Number of subjects	65	65	
Age categorical Units: Subjects			
Children (2-11 years)	15	15	
Adolescents (12-17 years)	17	17	
Adults (18-64 years)	23	23	
From 65-84 years	10	10	
Age continuous Units: years			
arithmetic mean	27		
standard deviation	± 22.88	-	
Gender categorical Units: Subjects			
Female	27	27	
Male	38	38	

End points

End points reporting groups

Reporting group title	Deferasirox (Run-in period)
Reporting group description:	
Subjects were administered with deferasirox starting dose of 20 milligram/kilogram/day (mg/kg/day), daily 30 minutes before meal.	
Reporting group title	Deferasirox (Assessment period)
Reporting group description:	
Subjects were administered daily with deferasirox at a minimum starting dose of 20 mg/kg/day along with different food and liquids consistently for 12 weeks of assessment period. For subjects receiving > 30 mg/kg/day, a maximum of 40 mg/kg/day was allowed.	
Subject analysis set title	Breakfast (Deferasirox with soft food)
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Subjects received crushed deferasirox added to soft food at breakfast	
Subject analysis set title	Breakfast (Deferasirox with liquid)
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Subjects received deferasirox dispersed in a beverage of choice (non-carbonated, non-alcoholic liquid) at breakfast.	
Subject analysis set title	Dinner (Deferasirox with soft food)
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Subjects received crushed deferasirox added to a soft food at dinner.	
Subject analysis set title	Dinner (Deferasirox with liquid)
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Subjects received deferasirox dispersed in a beverage of choice (a non-carbonated, non-alcoholic liquid) at dinner.	
Subject analysis set title	No meal (Deferasirox with liquid)
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Subjects received deferasirox dispersed in a beverage of choice (non-carbonated, non-alcoholic liquid) with no meal.	
Subject analysis set title	No meal (Deferasirox with soft food)
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Subjects received crushed deferasirox added to a soft food with no meal.	

Primary: Subjective assessment of deferasirox formulation palatability based on Facial Hedonic Scale at Week 8 and Week 12

End point title	Subjective assessment of deferasirox formulation palatability based on Facial Hedonic Scale at Week 8 and Week 12[1]
End point description:	
Palatability was assessed by subjects based on a five-point Facial Hedonic scale defined as: dislike extremely; somewhat dislike; neither like or dislike; somewhat like; like extremely for the meal and method of administration. For subjects under 5 years of age, the scale was completed by parent or caregiver. The primary analysis was performed in the Intent to treat (ITT) population defined as all subjects enrolled regardless of any treatment received or not.	
End point type	Primary
End point timeframe:	
Week 8 and Week 12	

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: Only descriptive summary statistics was planned for this outcome measure.

End point values	Breakfast (Deferasirox with soft food)	Breakfast (Deferasirox with liquid)	Dinner (Deferasirox with soft food)	Dinner (Deferasirox with liquid)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	20	18	14	17
Units: Percentage of subjects				
number (not applicable)				
Week 8, Dislike extremely (n=10,7,3,7,17,7)	10	0	0	0
Week 8, Somewhat dislike (n=10,7,3,7,17,7)	0	28.6	0	14.3
Week 8, Neither like or dislike (n=10,7,3,7,17,7)	20	28.6	33.3	28.6
Week 8, Somewhat like (n=10,7,3,7,17,7)	30	0	0	28.6
Week 8, Like extremely (n=10,7,3,7,17,7)	40	42.9	66.7	28.6
Week 12, Dislike extremely (n=6,4,3,3,23,10)	0	0	0	0
Week 12, Somewhat dislike (n=6,4,3,3,23,10)	0	25	0	0
Week 12, Neither like or dislike (n=6,4,3,3,23,10)	16.7	25	0	33.3
Week 12, Somewhat like (n=6,4,3,3,23,10)	33.3	0	66.7	33.3
Week 12, Like extremely (n=6,4,3,3,23,10)	50	50	33.3	33.3

End point values	No meal (Deferasirox with liquid)	No meal (Deferasirox with soft food)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	39	30		
Units: Percentage of subjects				
number (not applicable)				
Week 8, Dislike extremely (n=10,7,3,7,17,7)	0	0		
Week 8, Somewhat dislike (n=10,7,3,7,17,7)	5.9	14.3		
Week 8, Neither like or dislike (n=10,7,3,7,17,7)	29.4	28.6		
Week 8, Somewhat like (n=10,7,3,7,17,7)	17.6	42.9		
Week 8, Like extremely (n=10,7,3,7,17,7)	47.1	14.3		
Week 12, Dislike extremely (n=6,4,3,3,23,10)	4.3	0		
Week 12, Somewhat dislike (n=6,4,3,3,23,10)	4.3	10		
Week 12, Neither like or dislike (n=6,4,3,3,23,10)	56.5	50		

Week 12, Somewhat like (n=6,4,3,3,23,10)	8.7	10		
Week 12, Like extremely (n=6,4,3,3,23,10)	26.1	30		

Statistical analyses

No statistical analyses for this end point

Primary: Subjective assessment of deferasirox formulation palatability based on Facial Hedonic Scale at Week 1 to Week 4

End point title	Subjective assessment of deferasirox formulation palatability based on Facial Hedonic Scale at Week 1 to Week 4[2]

End point description:

Palatability was assessed by subjects based on a five-point Facial Hedonic scale defined as: dislike extremely; somewhat dislike; neither like or dislike; somewhat like; like extremely for the meal and method of administration. For subjects under 5 years of age, the scale was completed by parent or caregiver. The primary analysis was performed in the ITT population.

End point type	Primary

End point timeframe:

Week 1, Week 2, Week 3 and Week 4

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: Only descriptive summary statistics was planned for this outcome measure.

End point values	Deferasirox (Run-in period)			
Subject group type	Reporting group			
Number of subjects analysed	65			
Units: Percentage of subjects				
number (not applicable)				
Week 1, Dislike extremely (n= 54)	14.8			
Week 1, Somewhat dislike (n= 54)	22.2			
Week 1, Neither like or dislike (n= 54)	20.4			
Week 1, Somewhat like (n= 54)	24.1			
Week 1, Like extremely (n= 54)	18.5			
Week 2, Dislike extremely (n= 55)	16.4			
Week 2, Somewhat dislike (n= 55)	20			
Week 2, Neither like or dislike (n= 55)	23.6			
Week 2, Somewhat like (n= 55)	23.6			
Week 2, Like extremely (n= 55)	16.4			
Week 3, Dislike extremely (n= 51)	15.7			
Week 3, Somewhat dislike (n= 51)	25.5			
Week 3, Neither like or dislike (n= 51)	23.5			
Week 3, Somewhat like (n= 51)	17.6			
Week 3, Like extremely (n= 51)	17.6			
Week 4, Dislike extremely (n= 43)	11.6			
Week 4, Somewhat dislike (n= 43)	20.9			
Week 4, Neither like or dislike (n= 43)	30.2			
Week 4, Somewhat like (n= 43)	18.6			
Week 4, Like extremely (n= 43)	18.6			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage change from Week 4 in trough plasma concentration of deferasirox to Week 8, Week 12 and Week 16

End point title	Percentage change from Week 4 in trough plasma concentration of deferasirox to Week 8, Week 12 and Week 16

End point description:

Blood samples were drawn at every visit as close as possible to 24 hours post dose from each subject participating in the study and trough plasma concentrations were estimated. The analysis was performed in the ITT population.

End point type	Secondary

End point timeframe:

Pre-dose (0), 1 hour, 2 hour, 4 hour and 6 hour (Post-dose)

End point values	Deferasirox (Assessment period)			
Subject group type	Reporting group			
Number of subjects analysed	65			
Units: Percentage change in median				
number (not applicable)				
Week 8, Deferasirox 20 mg/kg (n= 11)	83.8			
Week 12, Deferasirox 20 mg/kg (n= 8)	238.9			
Week 16, Deferasirox 20 mg/kg (n= 12)	40.5			
Week 8, Deferasirox 30 mg/kg (n= 8)	-30.4			
Week 12, Deferasirox 30 mg/kg (n= 9)	18.5			
Week 16, Deferasirox 30 mg/kg (n= 9)	88.3			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with adverse events (AEs), serious adverse events (SAEs), permanent discontinuation and temporary interruption

End point title	Number of subjects with adverse events (AEs), serious adverse events (SAEs), permanent discontinuation and temporary interruption

End point description:

Adverse events (AEs) were defined as any unfavourable 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

(SAEs) were defined as 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 judgement of investigators represent significant hazards. Subjects who had permanently terminated from the treatment or kept the treatment on hold/deviated from protocol due to adverse event were defined as subjects with permanent discontinuation and temporary interruption, respectively. The analysis was performed in the Safety Set (SAF) population, defined as all subjects who received at least one dose of study medication.

End point type	Secondary

End point timeframe:

Day 1 up to Week 16

End point values	Deferasirox (Run-in period)	Breakfast (Deferasirox with soft food)	Breakfast (Deferasirox with liquid)	Dinner (Deferasirox with soft food)
Subject group type	Reporting group	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	62	20	18	14
Units: Number of subjects				
AEs	390	10	6	6
SAEs	5	5	0	1
AEs leading to permanent discontinuation	0	2	0	0
AEs leading to temporary interruption	4	2	1	0

End point values	Dinner (Deferasirox with liquid)	No meal (Deferasirox with liquid)	No meal (Deferasirox with soft food)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	17	39	30	
Units: Number of subjects				
AEs	6	24	11	
SAEs	1	6	0	
AEs leading to permanent discontinuation	0	0	1	
AEs leading to temporary interruption	0	2	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of gastro-intestinal side effects of deferasirox

End point title	Duration of gastro-intestinal side effects of deferasirox

End point description:

Gastrointestinal tolerability was assessed in subjects who experienced stomach ache, nausea, vomiting, and diarrhoea. Duration of an event was determined by taking each subject's maximum weekly duration of that event. The analysis was performed in the SAF population. Here, the value 99999.9 in the mean and standard deviation field represents not available estimable data when the subject analysed was 0 and 1, respectively.

End point type	Secondary

End point timeframe:

Week 1 up to Week 16

End point values	Breakfast (Deferasirox with soft food)	Breakfast (Deferasirox with liquid)	Dinner (Deferasirox with soft food)	Dinner (Deferasirox with liquid)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	20	18	14	17
Units: Days				
arithmetic mean (standard deviation)				
Stomach ache (n= 5, 5, 7, 4, 11, 11)	3.2 (± 2.17)	3.6 (± 3.13)	2.3 (± 1.5)	2.7 (± 1.38)
Nausea (n= 2, 2, 1, 3, 8, 5)	1.5 (± 0.71)	2 (± 0)	1.3 (± 0.58)	5 (± 99999.9)
Vomiting (n= 1, 2, 1, 1, 5, 5,)	2 (± 99999.9)	2 (± 0)	1 (± 99999.9)	5 (± 9999.9)
Diarrhoea (n= 3, 4, 3, 0, 9, 10)	4.7 (± 2.52)	3.5 (± 2.38)	99999.9 (± 99999.9)	2.7 (± 0.58)

End point values	No meal (Deferasirox with liquid)	No meal (Deferasirox with soft food)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	39	30		
Units: Days				
arithmetic mean (standard deviation)				
Stomach ache (n= 5, 5, 7, 4, 11, 11)	2.5 (± 1.86)	3.1 (± 2.21)		
Nausea (n= 2, 2, 1, 3, 8, 5)	2.5 (± 2.07)	3.4 (± 1.67)		
Vomiting (n= 1, 2, 1, 1, 5, 5,)	2 (± 1.73)	1.4 (± 0.89)		
Diarrhoea (n= 3, 4, 3, 0, 9, 10)	3.7 (± 2.45)	2.9 (± 1.85)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with gastro-intestinal side effects of deferasirox

End point title	Number of subjects with gastro-intestinal side effects of deferasirox

End point description:

Gastrointestinal tolerability was assessed in subjects who experienced stomach ache, nausea, vomiting, and diarrhoea. Occurence rate of stomach ache, nausea, vomiting and diarrhoea was determined. The assessment was done for the frequency and duration of the gastrointestinal side effect in subject. The analysis was performed in the SAF population.

End point type	Secondary

End point timeframe:

Week 1 up to Week 16

End point values	Breakfast (Deferasirox with soft food)	Breakfast (Deferasirox with liquid)	Dinner (Deferasirox with soft food)	Dinner (Deferasirox with liquid)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	20	18	14	17
Units: Number of subjects				
Stomach ache	6	6	4	7
Nausea	2	2	3	1
Vomiting	1	2	1	1
Diarrhoea	3	4	0	3

End point values	No meal (Deferasirox with liquid)	No meal (Deferasirox with soft food)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	39	30		
Units: Number of subjects				
Stomach ache	13	11		
Nausea	9	6		
Vomiting	5	5		
Diarrhoea	9	10		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in serum ferritin at Week 16

End point title	Change from baseline in serum ferritin at Week 16

End point description:

Ferritin protein stores iron and provides overall iron levels. Higher ferritin in blood showed higher iron content. Fluctuations from normal serum ferritin levels (500 ng/mL) observed at two consecutive visits led to dose adjustment of deferasirox. The analysis was performed in the ITT population. The 'n' signifies those subjects evaluable for this measure at specified time points for each group respectively.

End point type	Secondary

End point timeframe:

Baseline up to Week 16 (End of study)

End point values	Deferasirox (Assessment period)			
Subject group type	Reporting group			
Number of subjects analysed	65			
Units: Nanogram/mlillilitre				
arithmetic mean (standard deviation)				
Age 2 to < 10 years (n= 10)	-198.1 (± 653.11)			

Age 10 to < 60 years (n= 44) Age ≥ 60 years (n= 10)	38.3 (± 859.45) -593 (± 1683.39)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Serious Adverse Events are monitored from date of First Subject First Visit (FSFV) until Last Subject Last Visit (LSLV). All other adverse events are monitored from First Subject First Treatment until Last Subject Last Visit.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	12.0

Reporting groups

Reporting group title	Deferasirox

Reporting group description:

Subjects were administered daily with deferasirox at a minimum starting dose of 20 mg/kg/day along with different food and liquids consistently for 12 weeks of assessment period. For subjects receiving > 30 mg/kg/day, a maximum of 40 mg/kg/day was allowed.

Serious adverse events	Deferasirox		
Total subjects affected by serious adverse events			
subjects affected / exposed	15 / 65 (23.08%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Congenital, familial and genetic disorders			
Sickle cell anaemia with crisis			
subjects affected / exposed	8 / 65 (12.31%)		
occurrences causally related to treatment / all	0 / 10		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Hypotension			
subjects affected / exposed	1 / 65 (1.54%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Catheter related complication			
subjects affected / exposed	1 / 65 (1.54%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pyrexia			

subjects affected / exposed	3 / 65 (4.62%)		
occurrences causally related to treatment / all	1 / 3		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Acute chest syndrome			
subjects affected / exposed	1 / 65 (1.54%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Pancreatitis acute			
subjects affected / exposed	1 / 65 (1.54%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	1 / 65 (1.54%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Pneumonia			
subjects affected / exposed	1 / 65 (1.54%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Sepsis			
subjects affected / exposed	2 / 65 (3.08%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Perirectal abscess			
subjects affected / exposed	1 / 65 (1.54%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Influenza			

subjects affected / exposed	1 / 65 (1.54%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Viral infection			
subjects affected / exposed	1 / 65 (1.54%)		
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	Deferasirox		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	47 / 65 (72.31%)		
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	4 / 65 (6.15%)		
occurrences (all)	5		
Nervous system disorders			
Headache			
subjects affected / exposed	7 / 65 (10.77%)		
occurrences (all)	11		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	8 / 65 (12.31%)		
occurrences (all)	9		
Pyrexia			
subjects affected / exposed	15 / 65 (23.08%)		
occurrences (all)	18		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	8 / 65 (12.31%)		
occurrences (all)	14		
Abdominal pain upper			
subjects affected / exposed	8 / 65 (12.31%)		
occurrences (all)	10		
Vomiting			

subjects affected / exposed	10 / 65 (15.38%)		
occurrences (all)	10		
Nausea			
subjects affected / exposed	15 / 65 (23.08%)		
occurrences (all)	16		
Diarrhoea			
subjects affected / exposed	20 / 65 (30.77%)		
occurrences (all)	24		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	6 / 65 (9.23%)		
occurrences (all)	7		
Oropharyngeal pain			
subjects affected / exposed	5 / 65 (7.69%)		
occurrences (all)	5		
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	4 / 65 (6.15%)		
occurrences (all)	4		
Pain in extremity			
subjects affected / exposed	5 / 65 (7.69%)		
occurrences (all)	6		
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	8 / 65 (12.31%)		
occurrences (all)	11		
Metabolism and nutrition disorders			
Anorexia			
subjects affected / exposed	4 / 65 (6.15%)		
occurrences (all)	4		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
04 March 2009	Assessment schedule and inclusion/exclusion criteria, modified diarrhoea algorithm, and revised timing of PK assessments and pregnancy tests were updated.
03 September 2009	New safety recommendations were incorporated.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Due to EudraCT system limitations, which EMA is aware of, data using 999 as data points in this record are not an accurate representation of the clinical trial results. Please use https://www.novctrd.com/CtrdWeb/home.novfor complete trial results.

Notes: