



Clinical trial results:

A randomized, open-label, multicenter, two arm, phase II study to evaluate treatment compliance, efficacy and safety of an improved deferasirox formulation (granules) in pediatric patients with iron overload

Summary

EudraCT number	2013-004739-55
Trial protocol	BE BG FR HU DK IT
Global end of trial date	15 January 2024

Results information

Result version number	v1
This version publication date	25 July 2024
First version publication date	25 July 2024

Trial information

Trial identification

Sponsor protocol code	CICL670F2202
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02435212
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novartis Pharmaceuticals
Sponsor organisation address	Novartis Campus, Basel, Switzerland,
Public contact	Clinical Disclosure Office, Novartis Pharma AG, 41 613241111, novartis.email@novartis.com
Scientific contact	Clinical Disclosure Office, 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	15 January 2024
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	15 January 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

- To evaluate both formulations on subject compliance, using stick pack/tablet count over 24-weeks of treatment in ICT naive subjects during Core phase.
- To evaluate the change from baseline in serum ferritin after 24-weeks of treatment for both formulations in ICT naive subjects during the Core phase.

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	21 October 2015
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: 8
Country: Number of subjects enrolled	Bulgaria: 13
Country: Number of subjects enrolled	Malaysia: 18
Country: Number of subjects enrolled	United States: 17
Country: Number of subjects enrolled	Russian Federation: 6
Country: Number of subjects enrolled	Philippines: 12
Country: Number of subjects enrolled	Thailand: 40
Country: Number of subjects enrolled	Türkiye: 18
Country: Number of subjects enrolled	Oman: 27
Country: Number of subjects enrolled	Italy: 13
Country: Number of subjects enrolled	Lebanon: 23
Country: Number of subjects enrolled	France: 9
Country: Number of subjects enrolled	Hungary: 1
Country: Number of subjects enrolled	Panama: 2
Country: Number of subjects enrolled	Tunisia: 5
Country: Number of subjects enrolled	Egypt: 6
Country: Number of subjects enrolled	India: 6

Worldwide total number of subjects	224
EEA total number of subjects	44

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)	195
Adolescents (12-17 years)	29
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

After enrollment, participants previously treated with iron chelation therapy (ICT) underwent a 5-day chelation washout period prior to the commencement of the 48-week treatment (Core phase).

Period 1

Period 1 title	Core Phase
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	DFX DT

Arm description:

Participants received deferasirox (DFX) dispersible tablets (DT) orally once daily based on body weight for 48 weeks in the Core phase. The starting dose was 20mg/kg/day which was then adjusted based on tolerability, safety and efficacy considerations. After the Core phase, participants could enter the Optional Extension phase and cross over to DFX granules administered orally once daily in the form of stick packs for up to 5 years. Participants entering the Optional Extension phase received the equivalent strength-adjusted DFX granules dose corresponding to the last DT dose in the Core phase taking dose adjustment guidelines into account.

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

Dosage and administration details:

Deferasirox DT orally once daily based on body weight for 48 weeks in the Core phase. The starting dose was 20mg/kg/day which was then adjusted based on tolerability, safety and efficacy considerations.

Arm title	DFX Granule
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Arm description:

Participants received deferasirox (DFX) granules orally once daily based on body weight in the form of stick packs for 48 weeks in the Core phase. The starting dose was 14 mg/kg/day which was then adjusted based on tolerability, safety and efficacy considerations. After the Core phase, participants could enter the Optional Extension phase and continued receiving DFX granules at the same dose as was given at the end of the Core phase taking dose adjustment guidelines into account for up to 5 years.

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

Dosage and administration details:

Deferasirox granules orally once daily based on body weight in the form of stick packs for 48 weeks in the Core phase. The starting dose was 14 mg/kg/day which was then adjusted based on tolerability, safety and efficacy considerations.

Number of subjects in period 1	DFX DT	DFX Granule
Started	112	112
Completed	87	99
Not completed	25	13
Consent withdrawn by subject	3	-
Physician decision	3	-
Recovery	1	-
Adverse event	8	5
Lost to follow-up	-	1
Withdrawal by parent/guardian	9	4
Protocol deviation	1	2
Lack of efficacy	-	1

Period 2

Period 2 title	Optional Extension Phase
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	DFX DT

Arm description:

Participants received deferasirox (DFX) dispersible tablets (DT) orally once daily based on body weight for 48 weeks in the Core phase. The starting dose was 20mg/kg/day which was then adjusted based on tolerability, safety and efficacy considerations. After the Core phase, participants could enter the Optional Extension phase and cross over to DFX granules administered orally once daily in the form of stick packs for up to 5 years. Participants entering the Optional Extension phase received the equivalent strength-adjusted DFX granules dose corresponding to the last DT dose in the Core phase taking dose adjustment guidelines into account.

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

Dosage and administration details:

On the optional extension phase, DFX granules were administered orally once daily in the form of stick packs for up to 5 years. The dose received was the equivalent strength-adjusted DFX granules dose corresponding to the last DT dose in the Core phase taking dose adjustment guidelines into account.

Arm title	DFX Granule
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Arm description:

Participants received deferasirox (DFX) granules orally once daily based on body weight in the form of stick packs for 48 weeks in the Core phase. The starting dose was 14 mg/kg/day which was then adjusted based on tolerability, safety and efficacy considerations. After the Core phase, participants could enter the Optional Extension phase and continued receiving DFX granules at the same dose as was

given at the end of the Core phase taking dose adjustment guidelines into account for up to 5 years.

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

Dosage and administration details:

On the optional extension phase, DFX granules were continued administered at the same dose as was given at the end of the Core phase taking dose adjustment guidelines into account for up to 5 years.

Number of subjects in period 2^[1]	DFX DT	DFX Granule
Started	69	77
Completed	42	46
Not completed	27	31
Adverse event, serious fatal	1	-
Physician decision	6	8
Consent withdrawn by subject	2	2
Recovery	1	1
Adverse event, non-fatal	3	9
Technical problems	2	-
Withdrawal by parent/guardian	10	7
Lack of efficacy	2	3
Protocol deviation	-	1

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: The extension phase was optional for patients who completed the core phase.

Baseline characteristics

Reporting groups

Reporting group title	DFX DT
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Reporting group description:

Participants received deferiasirox (DFX) dispersible tablets (DT) orally once daily based on body weight for 48 weeks in the Core phase. The starting dose was 20mg/kg/day which was then adjusted based on tolerability, safety and efficacy considerations. After the Core phase, participants could enter the Optional Extension phase and cross over to DFX granules administered orally once daily in the form of stick packs for up to 5 years. Participants entering the Optional Extension phase received the equivalent strength-adjusted DFX granules dose corresponding to the last DT dose in the Core phase taking dose adjustment guidelines into account.

Reporting group title	DFX Granule
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Reporting group description:

Participants received deferiasirox (DFX) granules orally once daily based on body weight in the form of stick packs for 48 weeks in the Core phase. The starting dose was 14 mg/kg/day which was then adjusted based on tolerability, safety and efficacy considerations. After the Core phase, participants could enter the Optional Extension phase and continued receiving DFX granules at the same dose as was given at the end of the Core phase taking dose adjustment guidelines into account for up to 5 years.

Reporting group values	DFX DT	DFX Granule	Total
Number of subjects	112	112	224
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	99	96	195
Adolescents (12-17 years)	13	16	29
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Age Continuous Units: years			
arithmetic mean	5.8	5.9	-
standard deviation	± 3.89	± 3.94	-
Sex/Gender, Customized Units: participants			
Female	54	56	110
Male	58	56	114
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	7	7	14
Not Hispanic or Latino	104	105	209
Unknown or Not Reported	1	0	1
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	38	44	82

Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	11	8	19
White	57	52	109
More than one race	0	0	0
Unknown or Not Reported	6	8	14

End points

End points reporting groups

Reporting group title	DFX DT
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Reporting group description:

Participants received deferasirox (DFX) dispersible tablets (DT) orally once daily based on body weight for 48 weeks in the Core phase. The starting dose was 20mg/kg/day which was then adjusted based on tolerability, safety and efficacy considerations. After the Core phase, participants could enter the Optional Extension phase and cross over to DFX granules administered orally once daily in the form of stick packs for up to 5 years. Participants entering the Optional Extension phase received the equivalent strength-adjusted DFX granules dose corresponding to the last DT dose in the Core phase taking dose adjustment guidelines into account.

Reporting group title	DFX Granule
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Reporting group description:

Participants received deferasirox (DFX) granules orally once daily based on body weight in the form of stick packs for 48 weeks in the Core phase. The starting dose was 14 mg/kg/day which was then adjusted based on tolerability, safety and efficacy considerations. After the Core phase, participants could enter the Optional Extension phase and continued receiving DFX granules at the same dose as was given at the end of the Core phase taking dose adjustment guidelines into account for up to 5 years.

Reporting group title	DFX DT
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Reporting group description:

Participants received deferasirox (DFX) dispersible tablets (DT) orally once daily based on body weight for 48 weeks in the Core phase. The starting dose was 20mg/kg/day which was then adjusted based on tolerability, safety and efficacy considerations. After the Core phase, participants could enter the Optional Extension phase and cross over to DFX granules administered orally once daily in the form of stick packs for up to 5 years. Participants entering the Optional Extension phase received the equivalent strength-adjusted DFX granules dose corresponding to the last DT dose in the Core phase taking dose adjustment guidelines into account.

Reporting group title	DFX Granule
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Reporting group description:

Participants received deferasirox (DFX) granules orally once daily based on body weight in the form of stick packs for 48 weeks in the Core phase. The starting dose was 14 mg/kg/day which was then adjusted based on tolerability, safety and efficacy considerations. After the Core phase, participants could enter the Optional Extension phase and continued receiving DFX granules at the same dose as was given at the end of the Core phase taking dose adjustment guidelines into account for up to 5 years.

Subject analysis set title	DFX DT - Core phase
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Subject analysis set type	Full analysis
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Subject analysis set description:

Participants received deferasirox (DFX) dispersible tablets (DT) orally once daily based on body weight for 48 weeks in the Core phase. The starting dose was 20mg/kg/day which was then adjusted based on tolerability, safety and efficacy considerations.

Subject analysis set title	DFX Granule - Core phase
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Subject analysis set type	Full analysis
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Subject analysis set description:

Participants received deferasirox (DFX) granules orally once daily based on body weight in the form of stick packs for 48 weeks in the Core phase. The starting dose was 14 mg/kg/day which was then adjusted based on tolerability, safety and efficacy considerations.

Subject analysis set title	DFX DT Cross-over Granule - Optional Extension Phase
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Subject analysis set type	Full analysis
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Subject analysis set description:

After the Core phase, participants could enter the Optional Extension phase and cross over to DFX granules administered orally once daily in the form of stick packs for up to 5 years. Participants entering the Optional Extension phase received the equivalent strength-adjusted DFX granules dose corresponding to the last DT dose in the Core phase taking dose adjustment guidelines into account.

Subject analysis set title	DFX Granules - Core and Optional Extension Phase
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Subject analysis set type	Full analysis
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Subject analysis set description:

Participants received deferasirox (DFX) granules orally once daily based on body weight in the form of

stick packs for 48 weeks in the Core phase. The starting dose was 14 mg/kg/day which was then adjusted based on tolerability, safety and efficacy considerations. After the Core phase, participants could enter the Optional Extension phase and continued receiving DFX granules at the same dose as was given at the end of the Core phase taking dose adjustment guidelines into account for up to 5 years.

Primary: Percentage of overall compliance using stick pack or tablet counts in iron chelation therapy (ICT)-naïve participants during the Core phase

End point title	Percentage of overall compliance using stick pack or tablet counts in iron chelation therapy (ICT)-naïve participants during the Core phase
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End point description:

Compliance was calculated as the ratio of total count consumed to total count prescribed of deferasirox granule stick packs or dispersible tablets, where total count consumed was derived from cumulative dispensed, returned and lost/wasted counts over 24 weeks of treatment and total count prescribed was derived from cumulative prescribed count over 24 weeks of treatment.

End point type	Primary
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End point timeframe:

24 weeks

End point values	DFX DT	DFX Granule		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	54	54		
Units: percentage of compliance				
arithmetic mean (confidence interval 95%)	89.45 (85.29 to 93.61)	91.78 (87.81 to 95.75)		

Statistical analyses

Statistical analysis title	Overall compliance
Comparison groups	DFX DT v DFX Granule
Number of subjects included in analysis	108
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.3598
Method	ANCOVA
Parameter estimate	Least squares mean
Point estimate	2.58
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.99
upper limit	8.15
Variability estimate	Standard error of the mean
Dispersion value	2.803

Primary: Change from Baseline in serum ferritin (SF) for both study drug

formulations in ICT naïve participants during the Core phase

End point title	Change from Baseline in serum ferritin (SF) for both study drug formulations in ICT naïve participants during the Core phase
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End point description:

The analysis included the comparison of means between the two treatment arms of change from baseline after 24 weeks of treatment in serum ferritin in pediatric ICT naïve participants with iron overload. The endpoint was assessed at Week 25 visit. The Number of Subjects Analyzed differs as stated on the category column, in case of difference from Number of subjects that started the Arm.

End point type	Primary
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End point timeframe:

From Baseline to Week 25

End point values	DFX DT	DFX Granule		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	54	54		
Units: µg/L				
arithmetic mean (confidence interval 95%)				
Baseline (n=54,54)	2063.7 (1807.17 to 2320.15)	1955.5 (1712.57 to 2198.49)		
Week 25 (n=38,44)	2216.3 (1929.59 to 2502.93)	2228.4 (2011.69 to 2445.18)		
Change from Baseline to Week 25 (n=38,44)	250.5 (-84.63 to 585.58)	340.0 (115.48 to 564.59)		

Statistical analyses

Statistical analysis title	Serum Ferritin
Comparison groups	DFX DT v DFX Granule
Number of subjects included in analysis	108
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.2546
Method	ANCOVA
Parameter estimate	Least squares mean
Point estimate	176.36
Confidence interval	
level	95 %
sides	2-sided
lower limit	-129
upper limit	481.72
Variability estimate	Standard error of the mean
Dispersion value	153.933

Secondary: Percentage of overall compliance using stick pack or tablet counts in ICT-naïve participants during the Core phase

End point title	Percentage of overall compliance using stick pack or tablet counts in ICT-naïve participants during the Core phase
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End point description:

Compliance was calculated as the ratio of total count consumed to total count prescribed of deferasirox granule stick packs or dispersible tablets over 48 weeks of treatment.

End point type	Secondary
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End point timeframe:

48 weeks

End point values	DFX DT	DFX Granule		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	54	54		
Units: percentage of compliance				
arithmetic mean (confidence interval 95%)	91.57 (87.65 to 95.49)	94.80 (91.48 to 98.13)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change Over-time in Domain Score of Modified Satisfaction with Iron Chelation Therapy (mSICT) using Patient Reported Outcomes (PRO) Questionnaires

End point title	Change Over-time in Domain Score of Modified Satisfaction with Iron Chelation Therapy (mSICT) using Patient Reported Outcomes (PRO) Questionnaires
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End point description:

Participants aged between 10 years and less than 18 years at enrollment completed PRO questionnaires by themselves. The mSICT questionnaire for PRO consisted of 3 domains: adherence, satisfaction/preference, and concerns. The adherence domain had a minimum score of 6 and maximum score of 30; a lower score for adherence indicates better adherence. Satisfaction/preference domain had a minimum score of 2 and maximum score of 10; a lower score for satisfaction/preference indicates better satisfaction/preference. Concerns domain had a minimum score of 3 and maximum score of 15; a higher score for concerns indicate fewer concerns. The Number of Subjects Analyzed differs as stated on the category column, in case of difference from Number of subjects that started the Arm.

End point type	Secondary
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End point timeframe:

At Week 2, Week 3, Week 25 and Week 48

End point values	DFX DT	DFX Granule		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	17		
Units: score on a scale				
arithmetic mean (standard deviation)				
Adherence (Week 2) (n=13,15)	9.5 (± 2.30)	7.6 (± 1.99)		

Adherence (Week 3) (n=16,17)	10.9 (± 4.95)	6.6 (± 0.79)		
Adherence (Week 25) (n=13,11)	11.9 (± 3.93)	9.2 (± 3.31)		
Adherence (Week 48) (n=13,15)	12.9 (± 4.17)	8.4 (± 2.29)		
Satisfaction/preference (Week 2) (n=13,15)	5.2 (± 2.09)	2.9 (± 1.36)		
Satisfaction/preference (Week 3) (n=16,17)	4.0 (± 1.32)	3.1 (± 1.22)		
Satisfaction/preference (Week 25) (n=13,11)	5.5 (± 2.37)	3.0 (± 1.10)		
Satisfaction/preference (Week 48) (n=13,15)	4.8 (± 2.24)	3.1 (± 0.92)		
Concerns (Week 2) (n=13,15)	13.1 (± 2.18)	14.5 (± 1.06)		
Concerns (Week 3) (n=16,17)	13.4 (± 2.10)	14.4 (± 0.80)		
Concerns (Week 25) (n=13,11)	11.5 (± 3.13)	14.5 (± 1.21)		
Concerns (Week 48) (n=13,15)	12.8 (± 2.20)	13.5 (± 2.75)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Serum Ferritin (SF) for Both Study Drug Formulations in ICT naïve Participants During the Core Phase

End point title	Change From Baseline in Serum Ferritin (SF) for Both Study Drug Formulations in ICT naïve Participants During the Core Phase
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End point description:

The analysis included the comparison of means between the two treatment arms of change from baseline after 48 weeks of treatment in serum ferritin in pediatric ICT naïve participants with iron overload.

End point type	Secondary
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End point timeframe:

From Baseline to 48 weeks

End point values	DFX DT	DFX Granule		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	54	54		
Units: µg/L				
arithmetic mean (confidence interval 95%)	305.8 (4.28 to 607.24)	317.0 (69.10 to 564.88)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Serum Ferritin (SF) for Both Study Drug Formulations in pre-treated Participants During the Core Phase

End point title	Change From Baseline in Serum Ferritin (SF) for Both Study
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End point description:

The analysis included the comparison of means between the two treatment arms of change from baseline after 24 weeks and after 48 weeks of treatment in serum ferritin in pre-treated participants. The Number of Subjects Analyzed differs as stated on the category column, in case of difference from Number of subjects that started the Arm.

End point type	Secondary
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End point timeframe:

From Baseline to 24 weeks and 48 weeks

End point values	DFX DT	DFX Granule		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	58	58		
Units: µg/L				
arithmetic mean (confidence interval 95%)				
Change from Baseline to Week 25 (n=48,52)	59.0 (-210.88 to 328.79)	150.3 (-59.43 to 360.01)		
Change from Baseline to Week 48 (n=52,50)	207.7 (-94.29 to 509.68)	215.7 (-50.47 to 481.95)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change Over-time in Domain Score of Modified Satisfaction with Iron Chelation Therapy (mSICT) using Observer Reported Outcomes (ObsRO) Questionnaire (Caregiver's perspective)

End point title	Change Over-time in Domain Score of Modified Satisfaction with Iron Chelation Therapy (mSICT) using Observer Reported Outcomes (ObsRO) Questionnaire (Caregiver's perspective)
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End point description:

The ObsRO questionnaires for participants aged between 2 years and less than 10 years were designed as observations made by caregivers such as the parent or legal guardian. The caregivers continued completing the ObsRO questionnaires even after the participant turned 10 years for consistency in responses. The mSICT questionnaire consisted of 2 domains: adherence and concerns per caregiver's perspective. The adherence domain had a minimum score of 5 and a maximum score of 25; a lower score for adherence indicates better adherence. The concerns domain had a minimum score of 1 and a maximum score of 5; a higher score for concerns indicates fewer concerns. The Number of Subjects Analyzed differs as stated on the category column, in case of difference from Number of subjects that started the Arm.

End point type	Secondary
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End point timeframe:

At Week 2, Week 3, Week 25 and Week 48

End point values	DFX DT	DFX Granule		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	73	74		
Units: score on a scale				
arithmetic mean (standard deviation)				
Adherence (Week 2) (n=68,64)	7.7 (± 2.84)	5.8 (± 1.32)		
Adherence (Week 3) (n=73,74)	7.8 (± 2.64)	5.8 (± 1.43)		
Adherence (Week 25) (n=61,53)	7.1 (± 2.35)	6.5 (± 1.69)		
Adherence (Week 48) (n=60,54)	7.5 (± 2.53)	6.8 (± 2.57)		
Concerns (Week 2) (n=68,64)	3.9 (± 1.32)	4.5 (± 0.94)		
Concerns (Week 3) (n=73,74)	4.1 (± 1.31)	4.7 (± 0.71)		
Concerns (Week 25) (n=61,53)	4.3 (± 1.00)	4.5 (± 0.89)		
Concerns (Week 48) (n=60,54)	4.0 (± 1.24)	4.6 (± 0.77)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change Over-time in Domain Score of Palatability using Patient Reported Outcomes (PRO) Questionnaires

End point title	Change Over-time in Domain Score of Palatability using Patient Reported Outcomes (PRO) Questionnaires
End point description:	The palatability questionnaire was used to measure: taste, aftertaste, whether medication was taken and how the participant perceived the amount of medication taken. This questionnaire had a minimum score of 0 and maximum score of 11; a higher score means better palatability. Participants aged between 10 years and less than 18 years at enrollment completed the PRO questionnaire by themselves. The Number of Subjects Analyzed differs as stated on the category column, in case of difference from Number of subjects that started the Arm.
End point type	Secondary
End point timeframe:	At Week 2, Week 3, Week 25 and Week 48

End point values	DFX DT	DFX Granule		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	17		
Units: score on a scale				
arithmetic mean (standard deviation)				
Week 2 (n=13,15)	8.8 (± 3.32)	10.3 (± 1.91)		
Week 3 (n=16,17)	9.6 (± 2.83)	10.9 (± 0.24)		
Week 25 (n=13,11)	9.2 (± 2.70)	10.4 (± 1.80)		
Week 48 (n=13,14)	9.4 (± 3.07)	11.0 (± 0.00)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change Over-time in Domain Score of Modified Satisfaction with Iron Chelation Therapy (mSICT) using Observer Reported Outcomes (ObsRO) Questionnaire (Child's perspective)

End point title	Change Over-time in Domain Score of Modified Satisfaction with Iron Chelation Therapy (mSICT) using Observer Reported Outcomes (ObsRO) Questionnaire (Child's perspective)
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End point description:

The ObsRO questionnaires for participants aged between 2 years and less than 10 years were designed as observations made by caregivers such as the parent or legal guardian. The caregivers continued completing the ObsRO questionnaires even after the participant turned 10 years for consistency in responses. The mSICT questionnaire is presented for 2 domains: adherence and concerns per child's perspective. The adherence domain had a minimum score of 6 and a maximum score of 30; a lower score for adherence indicates better adherence. The concerns domain had a minimum score of 2 and a maximum score of 10; a higher score for concerns indicates fewer concerns. The Number of Subjects Analyzed differs as stated on the category column, in case of difference from Number of subjects that started the Arm.

End point type	Secondary
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End point timeframe:

At Week 2, Week 3, Week 25 and Week 48

End point values	DFX DT	DFX Granule		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	73	74		
Units: score on a scale				
arithmetic mean (standard deviation)				
Adherence (Week 2) (n=68,64)	12.1 (± 4.57)	8.2 (± 2.28)		
Adherence (Week 3) (n=73,74)	11.7 (± 3.78)	8.2 (± 2.64)		
Adherence (Week 25) (n=61,53)	11.1 (± 3.82)	9.1 (± 2.64)		
Adherence (Week 48) (n=60,54)	11.3 (± 3.99)	9.1 (± 3.00)		
Concerns (Week 2) (n=68,64)	8.5 (± 2.29)	9.2 (± 1.66)		
Concerns (Week 3) (n=73,74)	8.7 (± 2.00)	8.8 (± 2.04)		
Concerns (Week 25) (n=61,53)	8.6 (± 1.94)	8.7 (± 1.85)		
Concerns (Week 48) (n=60,54)	8.8 (± 1.75)	9.0 (± 1.82)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change Over-time in Domain Score of Palatability using Observer Reported Outcomes (ObsRO) Questionnaire

End point title	Change Over-time in Domain Score of Palatability using Observer Reported Outcomes (ObsRO) Questionnaire
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End point description:

The palatability questionnaire was used to measure: taste, aftertaste, whether medication was taken and how the participant perceived the amount of medication taken. This questionnaire had a minimum score of 0 and maximum score of 11; a higher score means better palatability. The ObsRO questionnaires for participants aged between 2 years and less than 10 years were designed as observations made by caregivers such as the parent or legal guardian. The caregivers continued

completing the ObsRO questionnaires even after the participant turned 10 years for consistency in responses. The Number of Subjects Analyzed differs as stated on the category column, in case of difference from Number of subjects that started the Arm.

End point type	Secondary
End point timeframe:	
At Week 2, Week 3, Week 25 and Week 48	

End point values	DFX DT	DFX Granule		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	72	72		
Units: score on a scale				
arithmetic mean (standard deviation)				
Week 2 (n=68,62)	8.9 (± 3.13)	10.9 (± 0.90)		
Week 3 (n=72,72)	9.4 (± 2.88)	10.8 (± 0.79)		
Week 25 (n=61,52)	9.3 (± 2.83)	10.6 (± 1.73)		
Week 48 (n=60,53)	9.0 (± 3.11)	10.9 (± 0.96)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change over time in weekly dose violation rate using Compliance Patient Reported Outcomes (PRO) Questionnaire

End point title	Change over time in weekly dose violation rate using Compliance Patient Reported Outcomes (PRO) Questionnaire
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End point description:

The compliance questionnaire consisted of 2 items: 1. To assess if the medication was taken (yes/no) and 2. To record of the time when the medication was taken (with a not applicable option for participants who did not take their medication). Daily diary records were used to calculate the rate of dose violation in each study arm (doses missed completely or not taken before 12 PM). The dose violation rate was calculated as:

$[\text{Number of dose violations} / \text{Drug exposure (days)}] * 100.$

The Number of Subjects Analyzed differs as stated on the category column, in case of difference from Number of subjects that started the Arm.

End point type	Secondary
End point timeframe:	
At Week 1, Week 13, Week 25, Week 37 and Week 48	

End point values	DFX DT	DFX Granule		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	16		
Units: percentage of days with dose violations				
arithmetic mean (standard deviation)				
Week 1 (n=16,16)	26.86 (± 37.966)	26.79 (± 38.992)		

Week 13 (n=15,12)	12.78 (± 31.000)	23.41 (± 35.906)		
Week 25 (n=12,9)	13.19 (± 29.614)	25.93 (± 42.583)		
Week 37 (n=9,9)	18.89 (± 32.745)	30.16 (± 41.921)		
Week 48 (n=7,6)	2.86 (± 7.559)	52.38 (± 52.424)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change over time in weekly dose violation rate using Compliance Observer Reported Outcomes (ObsRO) Questionnaire

End point title	Change over time in weekly dose violation rate using Compliance Observer Reported Outcomes (ObsRO) Questionnaire
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End point description:

The compliance questionnaire consisted of 2 items: 1. To assess if the medication was taken (yes/no) and 2. To record the time when the medication was taken (with a not applicable option for participants who did not take their medication). Daily diary records were used to calculate the rate of dose violation in each treatment arm (doses missed completely or not taken before 12 PM). The ObsRO questionnaires for participants aged between 2 years and less than 10 years were designed as observations made by caregivers such as the parent or legal guardian. The caregivers continued completing the ObsRO questionnaires even after the participant turned 10 years for consistency in responses. The Number of Subjects Analyzed differs as stated on the category column, in case of difference from Number of subjects that started the Arm.

End point type	Secondary
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End point timeframe:

At Week 1, Week 13, Week 25, Week 37 and Week 48

End point values	DFX DT	DFX Granule		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	62	60		
Units: score on a scale				
arithmetic mean (standard deviation)				
Week 1 (n=62,60)	18.80 (± 29.912)	27.79 (± 37.577)		
Week 13 (n=60,57)	10.38 (± 27.374)	18.65 (± 35.513)		
Week 25 (n=48,53)	7.79 (± 23.025)	13.72 (± 31.813)		
Week 37 (n=54,53)	13.86 (± 31.769)	20.01 (± 37.632)		
Week 48 (n=36,34)	13.56 (± 32.211)	14.50 (± 31.123)		

Statistical analyses

No statistical analyses for this end point

Secondary: Pre-dose Concentrations of Deferasirox to Support the Assessment of Compliance

End point title	Pre-dose Concentrations of Deferasirox to Support the Assessment of Compliance
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End point description:

Pre-dose pharmacokinetic (PK) data from participants in the Pharmacokinetic Analysis Set 1 (PAS-1) were analyzed to assess variability of individual participant's compliance. A linear mixed effect power model to pre-dose samples which fulfill compliance criteria in terms of steady state (4 consecutive same doses prior to the PK sample drawn), time-windows (PK sample drawn 20 to 28 hours after previous dose) and without any vomiting episodes within the 4 hours prior to the PK sample were fitted. The model considered dose, treatment group, stratification factors and potential other factors, such as body weight as covariates. The Number of Subjects Analyzed differs as stated on the category column, in case of difference from Number of subjects that started the Arm.

End point type	Secondary
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End point timeframe:

At Weeks 1, 3, 5, 9, 13, 17, 21, 25, 29, 33, 37, 41, and 45

End point values	DFX DT	DFX Granule		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	106	105		
Units: µmol/L				
geometric mean (geometric coefficient of variation)				
Week 1 (n=95,93)	2.93 (± 369.5)	1.40 (± 235.4)		
Week 3 (n=59,73)	14.2 (± 137.0)	11.8 (± 117.1)		
Week 5 (n=69,73)	14.4 (± 115.7)	11.7 (± 127.5)		
Week 9 (n=68,74)	20.1 (± 115.8)	12.1 (± 97.1)		
Week 13 (n=63,66)	19.7 (± 124.2)	13.5 (± 107.5)		
Week 17 (n=62,56)	18.4 (± 109.4)	13.1 (± 135.3)		
Week 21 (n=64,64)	19.6 (± 120.4)	13.4 (± 163.6)		
Week 25 (n=60,62)	17.1 (± 147.2)	15.9 (± 108.6)		
Week 29 (n=63,65)	23.8 (± 111.3)	13.2 (± 156.6)		
Week 33 (n=65,69)	21.4 (± 184.0)	14.1 (± 175.6)		
Week 37 (n=62,72)	20.8 (± 137.1)	14.6 (± 135.3)		
Week 41 (n=66,71)	21.8 (± 131.6)	15.5 (± 134.7)		
Week 45 (n=63,71)	28.3 (± 141.2)	19.0 (± 117.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Adverse Events (AEs) and Serious Adverse Events (SAEs) during the Core Phase

End point title	Number of Participants with Adverse Events (AEs) and Serious Adverse Events (SAEs) during the Core Phase
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End point description:

An adverse event (AE) is any untoward medical occurrence (e.g. any unfavorable and unintended sign

[including abnormal laboratory findings], symptom or disease) in a clinical investigation participant after providing written informed consent for participation in the study.

End point type	Secondary
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End point timeframe:

From Baseline to 48 weeks

End point values	DFX DT - Core phase	DFX Granule - Core phase		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	111	110		
Units: participants				
All AEs	108	100		
All SAEs	23	27		

Statistical analyses

No statistical analyses for this end point

Secondary: Concentrations of Deferasirox Between 2 and 4 Hours Post-dose at Weeks 5 and 9

End point title	Concentrations of Deferasirox Between 2 and 4 Hours Post-dose at Weeks 5 and 9
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End point description:

Post-dose pharmacokinetic (PK) data from participants in the Pharmacokinetic Analysis Set 1 (PAS-1) were analyzed along with Pre-dose PK data. The Number of Subjects Analyzed differs as stated on the category column, in case of difference from Number of subjects that started the Arm.

End point type	Secondary
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End point timeframe:

At Week 5 and Week 9

End point values	DFX DT	DFX Granule		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	106	105		
Units: µmol/L				
geometric mean (geometric coefficient of variation)				
Week 5 (3 hour post-dose) (n=66,70)	65.2 (± 80.5)	53.2 (± 86.2)		
Week 9 (3 hour post-dose) (n=62,61)	70.4 (± 77.0)	59.8 (± 61.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Adverse Events (AEs) and Serious Adverse Events (SAEs) During the Entire Granule Period

End point title	Number of Participants With Adverse Events (AEs) and Serious Adverse Events (SAEs) During the Entire Granule Period
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End point description:

An adverse event (AE) is any untoward medical occurrence (e.g. any unfavorable and unintended sign [including abnormal laboratory findings], symptom or disease) in a clinical investigation after participant providing written informed consent for participation in the study. In the DFX Granules arm, AEs are reported since the initial randomization to the arm in the core phase and continuing in the extension phase. In the DFX cross-over arm, AEs are reported for participants since the participant crossed-over from dispersible tablet to granules in the extension phase only.

End point type	Secondary
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End point timeframe:

From Baseline to 305 weeks

End point values	DFX DT Cross-over Granule - Optional Extension Phase	DFX Granules - Core and Optional Extension Phase		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	69	110		
Units: participants				
AEs	64	106		
Suspected AEs	48	73		
SAEs	22	38		
Suspected SAEs	4	7		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Adverse Events of Special Interest (AESI) During the Entire Granule Period

End point title	Number of Participants With Adverse Events of Special Interest (AESI) During the Entire Granule Period
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End point description:

An adverse event (AE) is any untoward medical occurrence (e.g. any unfavorable and unintended sign [including abnormal laboratory findings], symptom or disease) in a clinical investigation after participant providing written informed consent for participation in the study. In the DFX Granules arm, AEs are reported since the initial randomization to the arm in the core phase and continuing in the extension phase. In the DFX cross-over arm, AEs are reported for participants since the participant crossed-over from dispersible tablet to granules in the extension phase only. AESI included active monitoring for renal toxicity; including renal failure, hepatic toxicity; including hepatic failure, and gastrointestinal hemorrhage

End point type	Secondary
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End point timeframe:

From Baseline to 305 weeks

End point values	DFX DT Cross-over Granule - Optional Extension Phase	DFX Granules - Core and Optional Extension Phase		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	69	110		
Units: participants				
Any AESI	52	79		
Gastrointestinal hemorrhages	3	4		
Hearing loss	5	5		
Lens opacities, Retinal changes and Optic neuritis	0	2		
Liver disorders - Hepatic failure	1	0		
Liver disorders - Increased liver transaminases	16	46		
Peripheral blood cytopenias	5	7		
Renal disorders - Acute renal failure	1	0		
Renal disorders - Increased serum creatinine	4	8		
Renal disorders -Proteinuria	40	49		
Renal disorders - Renal tubular disorders	4	0		
Severe Cutaneous Adverse Reactions (SCARs)	0	1		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From initial randomization up to 48 weeks (Core phase) and Up to 5 years from entering the extension phase (Optional Extension phase)

Adverse event reporting additional description:

The Safety Set consisted of all participants who received at least 1 dose of granule formulation during the core or extension phase. The participants in extension phase received granules regardless of which arm they were initially randomized. Three participants did not receive the study drug and hence were excluded from the safety set.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	26.1
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Reporting groups

Reporting group title	DFX DT Cross-over Granule - Optional Extension Phase
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Reporting group description:

After the Core phase, participants could enter the Optional Extension phase and cross over to DFX granules administered orally once daily in the form of stick packs for up to 5 years. Participants entering the Optional Extension phase received the equivalent strength-adjusted DFX granules dose corresponding to the last DT dose in the Core phase taking dose adjustment guidelines into account.

Reporting group title	DFX Granules - Optional Extension Phase
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Reporting group description:

After the Core phase, participants could enter the Optional Extension phase and continued receiving DFX granules at the same dose as was given at the end of the Core phase taking dose adjustment guidelines into account for up to 5 years.

Reporting group title	DFX Granule- Core Phase
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Reporting group description:

Participants received deferasirox (DFX) granules orally once daily based on body weight in the form of stick packs for 48 weeks in the Core phase. The starting dose was 14 mg/kg/day which was then adjusted based on tolerability, safety and efficacy considerations.

Reporting group title	DFX DT- Core Phase
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Reporting group description:

Participants received deferasirox (DFX) dispersible tablets (DT) orally once daily based on body weight for 48 weeks in the Core phase. The starting dose was 20mg/kg/day which was then adjusted based on tolerability, safety and efficacy considerations.

Serious adverse events	DFX DT Cross-over Granule - Optional Extension Phase	DFX Granules - Optional Extension Phase	DFX Granule- Core Phase
Total subjects affected by serious adverse events			
subjects affected / exposed	22 / 69 (31.88%)	20 / 77 (25.97%)	27 / 110 (24.55%)
number of deaths (all causes)	1	0	0
number of deaths resulting from adverse events	0	0	0
Vascular disorders			
Circulatory collapse			

subjects affected / exposed	1 / 69 (1.45%)	0 / 77 (0.00%)	0 / 110 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 69 (1.45%)	2 / 77 (2.60%)	4 / 110 (3.64%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oedema peripheral			
subjects affected / exposed	1 / 69 (1.45%)	0 / 77 (0.00%)	0 / 110 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sudden death			
subjects affected / exposed	1 / 69 (1.45%)	0 / 77 (0.00%)	0 / 110 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Tonsillar hypertrophy			
subjects affected / exposed	1 / 69 (1.45%)	0 / 77 (0.00%)	0 / 110 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory distress			
subjects affected / exposed	0 / 69 (0.00%)	0 / 77 (0.00%)	0 / 110 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural effusion			
subjects affected / exposed	1 / 69 (1.45%)	0 / 77 (0.00%)	0 / 110 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Obstructive sleep apnoea syndrome			
subjects affected / exposed	0 / 69 (0.00%)	1 / 77 (1.30%)	0 / 110 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Bronchial hyperreactivity			
subjects affected / exposed	0 / 69 (0.00%)	0 / 77 (0.00%)	0 / 110 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute chest syndrome			
subjects affected / exposed	1 / 69 (1.45%)	2 / 77 (2.60%)	1 / 110 (0.91%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Urine protein/creatinine ratio increased			
subjects affected / exposed	0 / 69 (0.00%)	1 / 77 (1.30%)	0 / 110 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemoglobin decreased			
subjects affected / exposed	2 / 69 (2.90%)	0 / 77 (0.00%)	0 / 110 (0.00%)
occurrences causally related to treatment / all	0 / 11	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood creatinine increased			
subjects affected / exposed	0 / 69 (0.00%)	0 / 77 (0.00%)	1 / 110 (0.91%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Ligament sprain			
subjects affected / exposed	1 / 69 (1.45%)	0 / 77 (0.00%)	0 / 110 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Foot fracture			
subjects affected / exposed	1 / 69 (1.45%)	0 / 77 (0.00%)	0 / 110 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile nonhaemolytic transfusion reaction			

subjects affected / exposed	0 / 69 (0.00%)	0 / 77 (0.00%)	1 / 110 (0.91%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Craniofacial fracture			
subjects affected / exposed	1 / 69 (1.45%)	0 / 77 (0.00%)	0 / 110 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lip injury			
subjects affected / exposed	0 / 69 (0.00%)	0 / 77 (0.00%)	1 / 110 (0.91%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Overdose			
subjects affected / exposed	1 / 69 (1.45%)	1 / 77 (1.30%)	0 / 110 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transfusion reaction			
subjects affected / exposed	0 / 69 (0.00%)	0 / 77 (0.00%)	1 / 110 (0.91%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Tension headache			
subjects affected / exposed	0 / 69 (0.00%)	1 / 77 (1.30%)	0 / 110 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Hypersplenism			
subjects affected / exposed	0 / 69 (0.00%)	1 / 77 (1.30%)	0 / 110 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anaemia			
subjects affected / exposed	0 / 69 (0.00%)	0 / 77 (0.00%)	1 / 110 (0.91%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile neutropenia			

subjects affected / exposed	0 / 69 (0.00%)	1 / 77 (1.30%)	0 / 110 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sickle cell anaemia with crisis			
subjects affected / exposed	0 / 69 (0.00%)	2 / 77 (2.60%)	3 / 110 (2.73%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lymphadenitis			
subjects affected / exposed	0 / 69 (0.00%)	0 / 77 (0.00%)	1 / 110 (0.91%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Leukocytosis			
subjects affected / exposed	0 / 69 (0.00%)	0 / 77 (0.00%)	0 / 110 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombocytopenia			
subjects affected / exposed	0 / 69 (0.00%)	1 / 77 (1.30%)	0 / 110 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Pancreatitis acute			
subjects affected / exposed	0 / 69 (0.00%)	1 / 77 (1.30%)	0 / 110 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Stress ulcer			
subjects affected / exposed	0 / 69 (0.00%)	0 / 77 (0.00%)	1 / 110 (0.91%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper gastrointestinal haemorrhage			
subjects affected / exposed	0 / 69 (0.00%)	0 / 77 (0.00%)	2 / 110 (1.82%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malpositioned teeth			

subjects affected / exposed	0 / 69 (0.00%)	0 / 77 (0.00%)	0 / 110 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal haemorrhage			
subjects affected / exposed	1 / 69 (1.45%)	0 / 77 (0.00%)	0 / 110 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastritis			
subjects affected / exposed	0 / 69 (0.00%)	1 / 77 (1.30%)	0 / 110 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Food poisoning			
subjects affected / exposed	0 / 69 (0.00%)	1 / 77 (1.30%)	0 / 110 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	1 / 69 (1.45%)	0 / 77 (0.00%)	0 / 110 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	0 / 69 (0.00%)	1 / 77 (1.30%)	0 / 110 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Jaundice cholestatic			
subjects affected / exposed	0 / 69 (0.00%)	1 / 77 (1.30%)	0 / 110 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertransaminasaemia			
subjects affected / exposed	0 / 69 (0.00%)	0 / 77 (0.00%)	0 / 110 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatitis acute			

subjects affected / exposed	0 / 69 (0.00%)	1 / 77 (1.30%)	0 / 110 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Drug-induced liver injury			
subjects affected / exposed	1 / 69 (1.45%)	0 / 77 (0.00%)	0 / 110 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholelithiasis			
subjects affected / exposed	0 / 69 (0.00%)	3 / 77 (3.90%)	0 / 110 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis			
subjects affected / exposed	0 / 69 (0.00%)	1 / 77 (1.30%)	0 / 110 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholangitis acute			
subjects affected / exposed	0 / 69 (0.00%)	1 / 77 (1.30%)	0 / 110 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bile duct stone			
subjects affected / exposed	0 / 69 (0.00%)	1 / 77 (1.30%)	0 / 110 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Urticaria			
subjects affected / exposed	1 / 69 (1.45%)	0 / 77 (0.00%)	0 / 110 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Drug reaction with eosinophilia and systemic symptoms			
subjects affected / exposed	0 / 69 (0.00%)	0 / 77 (0.00%)	1 / 110 (0.91%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			

Fanconi syndrome acquired subjects affected / exposed	3 / 69 (4.35%)	0 / 77 (0.00%)	0 / 110 (0.00%)
occurrences causally related to treatment / all	3 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 69 (1.45%)	0 / 77 (0.00%)	0 / 110 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pain in extremity			
subjects affected / exposed	0 / 69 (0.00%)	0 / 77 (0.00%)	1 / 110 (0.91%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Amoebiasis			
subjects affected / exposed	0 / 69 (0.00%)	0 / 77 (0.00%)	0 / 110 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ascariasis			
subjects affected / exposed	0 / 69 (0.00%)	0 / 77 (0.00%)	0 / 110 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	1 / 69 (1.45%)	0 / 77 (0.00%)	0 / 110 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19 pneumonia			
subjects affected / exposed	0 / 69 (0.00%)	1 / 77 (1.30%)	0 / 110 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19			
subjects affected / exposed	1 / 69 (1.45%)	0 / 77 (0.00%)	0 / 110 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Dengue fever			
subjects affected / exposed	1 / 69 (1.45%)	1 / 77 (1.30%)	2 / 110 (1.82%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis			
subjects affected / exposed	0 / 69 (0.00%)	1 / 77 (1.30%)	0 / 110 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchiolitis			
subjects affected / exposed	0 / 69 (0.00%)	0 / 77 (0.00%)	2 / 110 (1.82%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bacterial infection			
subjects affected / exposed	1 / 69 (1.45%)	0 / 77 (0.00%)	0 / 110 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atypical pneumonia			
subjects affected / exposed	0 / 69 (0.00%)	0 / 77 (0.00%)	1 / 110 (0.91%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis viral			
subjects affected / exposed	1 / 69 (1.45%)	0 / 77 (0.00%)	0 / 110 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dengue haemorrhagic fever			
subjects affected / exposed	1 / 69 (1.45%)	0 / 77 (0.00%)	0 / 110 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	4 / 69 (5.80%)	4 / 77 (5.19%)	2 / 110 (1.82%)
occurrences causally related to treatment / all	0 / 4	0 / 4	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis rotavirus			

subjects affected / exposed	0 / 69 (0.00%)	0 / 77 (0.00%)	0 / 110 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis salmonella			
subjects affected / exposed	1 / 69 (1.45%)	0 / 77 (0.00%)	0 / 110 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis viral			
subjects affected / exposed	0 / 69 (0.00%)	0 / 77 (0.00%)	1 / 110 (0.91%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza			
subjects affected / exposed	1 / 69 (1.45%)	0 / 77 (0.00%)	0 / 110 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nasopharyngitis			
subjects affected / exposed	0 / 69 (0.00%)	0 / 77 (0.00%)	0 / 110 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Otitis media acute			
subjects affected / exposed	0 / 69 (0.00%)	0 / 77 (0.00%)	1 / 110 (0.91%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Parotid abscess			
subjects affected / exposed	0 / 69 (0.00%)	0 / 77 (0.00%)	1 / 110 (0.91%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Periorbital cellulitis			
subjects affected / exposed	1 / 69 (1.45%)	0 / 77 (0.00%)	0 / 110 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pharyngitis			

subjects affected / exposed	2 / 69 (2.90%)	1 / 77 (1.30%)	0 / 110 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pharyngotonsillitis			
subjects affected / exposed	0 / 69 (0.00%)	1 / 77 (1.30%)	1 / 110 (0.91%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	1 / 69 (1.45%)	0 / 77 (0.00%)	1 / 110 (0.91%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tonsillitis			
subjects affected / exposed	2 / 69 (2.90%)	1 / 77 (1.30%)	0 / 110 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Systemic viral infection			
subjects affected / exposed	0 / 69 (0.00%)	1 / 77 (1.30%)	1 / 110 (0.91%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subcutaneous abscess			
subjects affected / exposed	1 / 69 (1.45%)	0 / 77 (0.00%)	0 / 110 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sinusitis			
subjects affected / exposed	2 / 69 (2.90%)	0 / 77 (0.00%)	0 / 110 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sinobronchitis			
subjects affected / exposed	1 / 69 (1.45%)	0 / 77 (0.00%)	0 / 110 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Shigella infection			

subjects affected / exposed	0 / 69 (0.00%)	0 / 77 (0.00%)	0 / 110 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Scarlet fever			
subjects affected / exposed	1 / 69 (1.45%)	0 / 77 (0.00%)	0 / 110 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia respiratory syncytial viral			
subjects affected / exposed	0 / 69 (0.00%)	0 / 77 (0.00%)	1 / 110 (0.91%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia bacterial			
subjects affected / exposed	0 / 69 (0.00%)	0 / 77 (0.00%)	1 / 110 (0.91%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection			
subjects affected / exposed	2 / 69 (2.90%)	2 / 77 (2.60%)	0 / 110 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 69 (0.00%)	0 / 77 (0.00%)	1 / 110 (0.91%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral infection			
subjects affected / exposed	1 / 69 (1.45%)	0 / 77 (0.00%)	0 / 110 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Varicella			
subjects affected / exposed	0 / 69 (0.00%)	1 / 77 (1.30%)	0 / 110 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			

subjects affected / exposed	1 / 69 (1.45%)	0 / 77 (0.00%)	0 / 110 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wound infection			
subjects affected / exposed	0 / 69 (0.00%)	0 / 77 (0.00%)	1 / 110 (0.91%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Lactase deficiency			
subjects affected / exposed	0 / 69 (0.00%)	0 / 77 (0.00%)	1 / 110 (0.91%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypokalaemia			
subjects affected / exposed	0 / 69 (0.00%)	2 / 77 (2.60%)	0 / 110 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Electrolyte imbalance			
subjects affected / exposed	1 / 69 (1.45%)	0 / 77 (0.00%)	0 / 110 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetic ketoacidosis			
subjects affected / exposed	1 / 69 (1.45%)	0 / 77 (0.00%)	0 / 110 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dehydration			
subjects affected / exposed	2 / 69 (2.90%)	2 / 77 (2.60%)	0 / 110 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	DFX DT- Core Phase		
Total subjects affected by serious adverse events			
subjects affected / exposed	23 / 111 (20.72%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

Vascular disorders			
Circulatory collapse			
subjects affected / exposed	0 / 111 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	4 / 111 (3.60%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Oedema peripheral			
subjects affected / exposed	0 / 111 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Sudden death			
subjects affected / exposed	0 / 111 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Tonsillar hypertrophy			
subjects affected / exposed	1 / 111 (0.90%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory distress			
subjects affected / exposed	1 / 111 (0.90%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pleural effusion			
subjects affected / exposed	0 / 111 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Obstructive sleep apnoea syndrome			

subjects affected / exposed	0 / 111 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Bronchial hyperreactivity			
subjects affected / exposed	1 / 111 (0.90%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Acute chest syndrome			
subjects affected / exposed	0 / 111 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Investigations			
Urine protein/creatinine ratio increased			
subjects affected / exposed	0 / 111 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Haemoglobin decreased			
subjects affected / exposed	1 / 111 (0.90%)		
occurrences causally related to treatment / all	0 / 10		
deaths causally related to treatment / all	0 / 0		
Blood creatinine increased			
subjects affected / exposed	0 / 111 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Ligament sprain			
subjects affected / exposed	0 / 111 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Foot fracture			
subjects affected / exposed	0 / 111 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Febrile nonhaemolytic transfusion reaction			
subjects affected / exposed	0 / 111 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Craniofacial fracture			
subjects affected / exposed	0 / 111 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Lip injury			
subjects affected / exposed	0 / 111 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Overdose			
subjects affected / exposed	0 / 111 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Transfusion reaction			
subjects affected / exposed	0 / 111 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Tension headache			
subjects affected / exposed	0 / 111 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Hypersplenism			
subjects affected / exposed	1 / 111 (0.90%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Anaemia			
subjects affected / exposed	2 / 111 (1.80%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		

Febrile neutropenia			
subjects affected / exposed	0 / 111 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Sickle cell anaemia with crisis			
subjects affected / exposed	5 / 111 (4.50%)		
occurrences causally related to treatment / all	0 / 12		
deaths causally related to treatment / all	0 / 0		
Lymphadenitis			
subjects affected / exposed	1 / 111 (0.90%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Leukocytosis			
subjects affected / exposed	1 / 111 (0.90%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Thrombocytopenia			
subjects affected / exposed	0 / 111 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Pancreatitis acute			
subjects affected / exposed	0 / 111 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Stress ulcer			
subjects affected / exposed	0 / 111 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Upper gastrointestinal haemorrhage			
subjects affected / exposed	0 / 111 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Malpositioned teeth			

subjects affected / exposed	1 / 111 (0.90%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 111 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastritis			
subjects affected / exposed	1 / 111 (0.90%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Food poisoning			
subjects affected / exposed	0 / 111 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vomiting			
subjects affected / exposed	0 / 111 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Diarrhoea			
subjects affected / exposed	0 / 111 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Jaundice cholestatic			
subjects affected / exposed	0 / 111 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypertransaminasaemia			
subjects affected / exposed	1 / 111 (0.90%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatitis acute			

subjects affected / exposed	0 / 111 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Drug-induced liver injury			
subjects affected / exposed	0 / 111 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cholelithiasis			
subjects affected / exposed	1 / 111 (0.90%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cholecystitis			
subjects affected / exposed	0 / 111 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cholangitis acute			
subjects affected / exposed	0 / 111 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Bile duct stone			
subjects affected / exposed	0 / 111 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Urticaria			
subjects affected / exposed	0 / 111 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Drug reaction with eosinophilia and systemic symptoms			
subjects affected / exposed	0 / 111 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			

Fanconi syndrome acquired subjects affected / exposed	1 / 111 (0.90%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 111 (0.90%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pain in extremity			
subjects affected / exposed	0 / 111 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Amoebiasis			
subjects affected / exposed	1 / 111 (0.90%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Ascariasis			
subjects affected / exposed	1 / 111 (0.90%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cellulitis			
subjects affected / exposed	0 / 111 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
COVID-19 pneumonia			
subjects affected / exposed	0 / 111 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
COVID-19			
subjects affected / exposed	0 / 111 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Dengue fever				
subjects affected / exposed	1 / 111 (0.90%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Bronchitis				
subjects affected / exposed	3 / 111 (2.70%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Bronchiolitis				
subjects affected / exposed	0 / 111 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bacterial infection				
subjects affected / exposed	0 / 111 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Atypical pneumonia				
subjects affected / exposed	0 / 111 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bronchitis viral				
subjects affected / exposed	0 / 111 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Dengue haemorrhagic fever				
subjects affected / exposed	0 / 111 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastroenteritis				
subjects affected / exposed	0 / 111 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastroenteritis rotavirus				

subjects affected / exposed	1 / 111 (0.90%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastroenteritis salmonella			
subjects affected / exposed	0 / 111 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastroenteritis viral			
subjects affected / exposed	1 / 111 (0.90%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Influenza			
subjects affected / exposed	2 / 111 (1.80%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Nasopharyngitis			
subjects affected / exposed	1 / 111 (0.90%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Otitis media acute			
subjects affected / exposed	1 / 111 (0.90%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Parotid abscess			
subjects affected / exposed	0 / 111 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Periorbital cellulitis			
subjects affected / exposed	0 / 111 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pharyngitis			

subjects affected / exposed	0 / 111 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pharyngotonsillitis			
subjects affected / exposed	0 / 111 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	3 / 111 (2.70%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Tonsillitis			
subjects affected / exposed	2 / 111 (1.80%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Systemic viral infection			
subjects affected / exposed	0 / 111 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Subcutaneous abscess			
subjects affected / exposed	0 / 111 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Sinusitis			
subjects affected / exposed	0 / 111 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Sinobronchitis			
subjects affected / exposed	0 / 111 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Shigella infection			

subjects affected / exposed	1 / 111 (0.90%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Scarlet fever			
subjects affected / exposed	0 / 111 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pneumonia respiratory syncytial viral			
subjects affected / exposed	0 / 111 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pneumonia bacterial			
subjects affected / exposed	0 / 111 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Upper respiratory tract infection			
subjects affected / exposed	0 / 111 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 111 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Viral infection			
subjects affected / exposed	2 / 111 (1.80%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Varicella			
subjects affected / exposed	0 / 111 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Urinary tract infection			

subjects affected / exposed	0 / 111 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Wound infection			
subjects affected / exposed	0 / 111 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Lactase deficiency			
subjects affected / exposed	0 / 111 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypokalaemia			
subjects affected / exposed	0 / 111 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Electrolyte imbalance			
subjects affected / exposed	0 / 111 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Diabetic ketoacidosis			
subjects affected / exposed	0 / 111 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Dehydration			
subjects affected / exposed	1 / 111 (0.90%)		
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	DFX DT Cross-over Granule - Optional Extension Phase	DFX Granules - Optional Extension Phase	DFX Granule- Core Phase
Total subjects affected by non-serious adverse events subjects affected / exposed	63 / 69 (91.30%)	63 / 77 (81.82%)	97 / 110 (88.18%)
Investigations			
Blood bilirubin increased subjects affected / exposed	4 / 69 (5.80%)	5 / 77 (6.49%)	3 / 110 (2.73%)
occurrences (all)	5	7	4
Blood creatinine increased subjects affected / exposed	3 / 69 (4.35%)	6 / 77 (7.79%)	0 / 110 (0.00%)
occurrences (all)	9	10	0
Transaminases increased subjects affected / exposed	2 / 69 (2.90%)	8 / 77 (10.39%)	9 / 110 (8.18%)
occurrences (all)	2	18	15
Urine protein/creatinine ratio increased subjects affected / exposed	36 / 69 (52.17%)	28 / 77 (36.36%)	27 / 110 (24.55%)
occurrences (all)	103	92	48
Alanine aminotransferase increased subjects affected / exposed	11 / 69 (15.94%)	11 / 77 (14.29%)	20 / 110 (18.18%)
occurrences (all)	13	24	29
Bilirubin conjugated increased subjects affected / exposed	2 / 69 (2.90%)	3 / 77 (3.90%)	12 / 110 (10.91%)
occurrences (all)	3	3	29
Aspartate aminotransferase increased subjects affected / exposed	8 / 69 (11.59%)	7 / 77 (9.09%)	12 / 110 (10.91%)
occurrences (all)	8	16	13
Nervous system disorders			
Headache subjects affected / exposed	5 / 69 (7.25%)	2 / 77 (2.60%)	9 / 110 (8.18%)
occurrences (all)	7	2	9
General disorders and administration site conditions			
Pyrexia subjects affected / exposed	15 / 69 (21.74%)	16 / 77 (20.78%)	26 / 110 (23.64%)
occurrences (all)	20	21	35
Gastrointestinal disorders			

Abdominal pain upper subjects affected / exposed occurrences (all)	3 / 69 (4.35%) 4	4 / 77 (5.19%) 5	4 / 110 (3.64%) 5
Abdominal pain subjects affected / exposed occurrences (all)	4 / 69 (5.80%) 5	0 / 77 (0.00%) 0	12 / 110 (10.91%) 16
Constipation subjects affected / exposed occurrences (all)	4 / 69 (5.80%) 4	0 / 77 (0.00%) 0	2 / 110 (1.82%) 2
Dental caries subjects affected / exposed occurrences (all)	3 / 69 (4.35%) 4	2 / 77 (2.60%) 3	5 / 110 (4.55%) 5
Diarrhoea subjects affected / exposed occurrences (all)	7 / 69 (10.14%) 10	6 / 77 (7.79%) 7	9 / 110 (8.18%) 15
Gastritis subjects affected / exposed occurrences (all)	4 / 69 (5.80%) 4	4 / 77 (5.19%) 5	1 / 110 (0.91%) 1
Vomiting subjects affected / exposed occurrences (all)	9 / 69 (13.04%) 13	4 / 77 (5.19%) 5	9 / 110 (8.18%) 14
Nausea subjects affected / exposed occurrences (all)	3 / 69 (4.35%) 3	1 / 77 (1.30%) 1	4 / 110 (3.64%) 4
Respiratory, thoracic and mediastinal disorders			
Cough subjects affected / exposed occurrences (all)	14 / 69 (20.29%) 18	9 / 77 (11.69%) 18	15 / 110 (13.64%) 17
Rhinorrhoea subjects affected / exposed occurrences (all)	4 / 69 (5.80%) 4	6 / 77 (7.79%) 11	7 / 110 (6.36%) 7
Rhinitis allergic subjects affected / exposed occurrences (all)	3 / 69 (4.35%) 4	5 / 77 (6.49%) 5	5 / 110 (4.55%) 6
Oropharyngeal pain			

subjects affected / exposed occurrences (all)	3 / 69 (4.35%) 3	2 / 77 (2.60%) 2	8 / 110 (7.27%) 9
Epistaxis subjects affected / exposed occurrences (all)	4 / 69 (5.80%) 6	0 / 77 (0.00%) 0	3 / 110 (2.73%) 3
Skin and subcutaneous tissue disorders Rash subjects affected / exposed occurrences (all)	2 / 69 (2.90%) 2	4 / 77 (5.19%) 4	6 / 110 (5.45%) 6
Renal and urinary disorders Proteinuria subjects affected / exposed occurrences (all)	4 / 69 (5.80%) 19	9 / 77 (11.69%) 62	9 / 110 (8.18%) 16
Infections and infestations Gastroenteritis subjects affected / exposed occurrences (all)	5 / 69 (7.25%) 8	6 / 77 (7.79%) 9	5 / 110 (4.55%) 5
Rhinitis subjects affected / exposed occurrences (all)	3 / 69 (4.35%) 10	1 / 77 (1.30%) 1	9 / 110 (8.18%) 12
Pharyngitis subjects affected / exposed occurrences (all)	12 / 69 (17.39%) 16	7 / 77 (9.09%) 9	11 / 110 (10.00%) 12
Nasopharyngitis subjects affected / exposed occurrences (all)	14 / 69 (20.29%) 36	11 / 77 (14.29%) 24	11 / 110 (10.00%) 14
Influenza subjects affected / exposed occurrences (all)	2 / 69 (2.90%) 2	7 / 77 (9.09%) 7	5 / 110 (4.55%) 5
COVID-19 subjects affected / exposed occurrences (all)	8 / 69 (11.59%) 9	9 / 77 (11.69%) 9	0 / 110 (0.00%) 0
Bronchitis subjects affected / exposed occurrences (all)	4 / 69 (5.80%) 5	3 / 77 (3.90%) 3	3 / 110 (2.73%) 5
Systemic viral infection			

subjects affected / exposed occurrences (all)	1 / 69 (1.45%) 1	4 / 77 (5.19%) 4	0 / 110 (0.00%) 0
Tonsillitis subjects affected / exposed occurrences (all)	5 / 69 (7.25%) 7	3 / 77 (3.90%) 3	7 / 110 (6.36%) 8
Upper respiratory tract infection subjects affected / exposed occurrences (all)	23 / 69 (33.33%) 58	24 / 77 (31.17%) 44	31 / 110 (28.18%) 42
Urinary tract infection subjects affected / exposed occurrences (all)	6 / 69 (8.70%) 8	6 / 77 (7.79%) 18	3 / 110 (2.73%) 3

Non-serious adverse events	DFX DT- Core Phase		
Total subjects affected by non-serious adverse events subjects affected / exposed	104 / 111 (93.69%)		
Investigations			
Blood bilirubin increased subjects affected / exposed occurrences (all)	4 / 111 (3.60%) 7		
Blood creatinine increased subjects affected / exposed occurrences (all)	3 / 111 (2.70%) 3		
Transaminases increased subjects affected / exposed occurrences (all)	7 / 111 (6.31%) 10		
Urine protein/creatinine ratio increased subjects affected / exposed occurrences (all)	39 / 111 (35.14%) 69		
Alanine aminotransferase increased subjects affected / exposed occurrences (all)	15 / 111 (13.51%) 26		
Bilirubin conjugated increased subjects affected / exposed occurrences (all)	16 / 111 (14.41%) 35		
Aspartate aminotransferase increased			

subjects affected / exposed occurrences (all)	11 / 111 (9.91%) 19		
Nervous system disorders Headache subjects affected / exposed occurrences (all)	8 / 111 (7.21%) 10		
General disorders and administration site conditions Pyrexia subjects affected / exposed occurrences (all)	24 / 111 (21.62%) 39		
Gastrointestinal disorders Abdominal pain upper subjects affected / exposed occurrences (all)	4 / 111 (3.60%) 4		
Abdominal pain subjects affected / exposed occurrences (all)	4 / 111 (3.60%) 6		
Constipation subjects affected / exposed occurrences (all)	5 / 111 (4.50%) 6		
Dental caries subjects affected / exposed occurrences (all)	7 / 111 (6.31%) 7		
Diarrhoea subjects affected / exposed occurrences (all)	14 / 111 (12.61%) 15		
Gastritis subjects affected / exposed occurrences (all)	0 / 111 (0.00%) 0		
Vomiting subjects affected / exposed occurrences (all)	15 / 111 (13.51%) 20		
Nausea subjects affected / exposed occurrences (all)	8 / 111 (7.21%) 9		
Respiratory, thoracic and mediastinal disorders			

Cough subjects affected / exposed occurrences (all)	12 / 111 (10.81%) 14		
Rhinorrhoea subjects affected / exposed occurrences (all)	4 / 111 (3.60%) 4		
Rhinitis allergic subjects affected / exposed occurrences (all)	0 / 111 (0.00%) 0		
Oropharyngeal pain subjects affected / exposed occurrences (all)	1 / 111 (0.90%) 1		
Epistaxis subjects affected / exposed occurrences (all)	1 / 111 (0.90%) 1		
Skin and subcutaneous tissue disorders Rash subjects affected / exposed occurrences (all)	7 / 111 (6.31%) 8		
Renal and urinary disorders Proteinuria subjects affected / exposed occurrences (all)	8 / 111 (7.21%) 16		
Infections and infestations Gastroenteritis subjects affected / exposed occurrences (all)	8 / 111 (7.21%) 10		
Rhinitis subjects affected / exposed occurrences (all)	3 / 111 (2.70%) 3		
Pharyngitis subjects affected / exposed occurrences (all)	3 / 111 (2.70%) 4		
Nasopharyngitis subjects affected / exposed occurrences (all)	12 / 111 (10.81%) 13		
Influenza			

subjects affected / exposed	4 / 111 (3.60%)		
occurrences (all)	6		
COVID-19			
subjects affected / exposed	0 / 111 (0.00%)		
occurrences (all)	0		
Bronchitis			
subjects affected / exposed	4 / 111 (3.60%)		
occurrences (all)	5		
Systemic viral infection			
subjects affected / exposed	0 / 111 (0.00%)		
occurrences (all)	0		
Tonsillitis			
subjects affected / exposed	2 / 111 (1.80%)		
occurrences (all)	2		
Upper respiratory tract infection			
subjects affected / exposed	34 / 111 (30.63%)		
occurrences (all)	51		
Urinary tract infection			
subjects affected / exposed	2 / 111 (1.80%)		
occurrences (all)	2		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
01 December 2015	The main changes of this amendment was: 1. Expand the study population by revising the inclusion criteria; 2. Modify the secondary objectives; 3. In order to optimize the patient safety and the toxicity monitoring, eligibility criteria and the management guidelines for cardiac and hepatic toxicity have been revised; 4. modified dose modification rules for hepatic toxicity management guidelines; 5. Clarification to the concomitant medications and contraception; 6. Statistical methods and data analysis section has been updated.
15 June 2016	The purpose of this amendment was: 1. To allow the sites in Egypt to use a local laboratory instead of central laboratory for the analysis of safety required in this trial and to exempt patients' enrolled in Egypt from the collection of PK samples. This exemption is granted to Egypt due to national restriction on export of any biological samples out of Egypt. 2. To clarify the inclusion criteria #2 for France concerning children aged from 2 to 6 years old as per Exjade prescribing information.
24 August 2016	The purpose of this amendment was: 1. To add an optional extension phase to the existing study. 2. To sharpen the clarification of the eligibility criteria related to renal criteria in order to promote better Investigator understanding, leading to better adherence and improved renal safety. 3. To provide the investigators with further clarified dose modification guidance for renal monitoring with regards to creatinine clearance, increased serum creatinine and proteinuria. Clear guidance on how to reinstate treatment after required dose interruption has also been included in order to improve patient safety.
15 June 2017	The purpose of this amendment was to include an interim analysis, allow for paper PRO completion, and clarify various points to improve site understanding and consistency in implementation of the protocol.
06 December 2017	The purpose of this amendment was to modify the assessment timepoint for the primary analysis (currently change from baseline for serum ferritin and compliance after 48 weeks of treatment), and to reduce the sample size for the chelation naive patients, following recent interaction with Health Authorities. The eligibility criteria for the extension phase have been modified.
24 June 2021	The main purpose of this amendment was to introduce the requirement for central collection and assessment of photographs from ocular examinations (lens photographs and wide angle fundus photographs) collected during the study by a Novartis designated imaging Contract Research Organization (CRO). This change is in response to a Health Authority request to submit CALYPSO ophthalmic data (for up to 2 years of follow up) to support the ocular safety evaluation of deferasirox.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

