



Clinical trial results:

An Open-label, parallel-group, multi-centre, phase I/III study to assess the safety, pharmacokinetics, pharmacodynamics and efficacy of repeated once-daily oral administration of D961H 10 mg and D961H 20 mg in Japanese paediatric patients 1 to 14 years old with gastrointestinal acid related diseases

Summary

EudraCT number	2016-003775-22
Trial protocol	Outside EU/EEA
Global end of trial date	25 August 2016

Results information

Result version number	v1 (current)
This version publication date	08 December 2016
First version publication date	08 December 2016

Trial information

Trial identification

Sponsor protocol code	D961TC00002
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Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	AstraZeneca Japan
Sponsor organisation address	Grand Front Osaka Tower B. 3-1, Ofuka-cho, Kita-ku, Osaka, Japan, 530-0011
Public contact	Yu Shimizuishi, Clinical operation departmnet, 81 677114669, Yu.Shimizuishi@astrazeneca.com
Scientific contact	Masahiro Nii, Biometrics Department, 81 677114571, Masahiro.Nii@astrazeneca.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	16 June 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	09 June 2016
Global end of trial reached?	Yes
Global end of trial date	25 August 2016
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study was to assess the safety and tolerability of repeated once-daily oral administration of D961H 10 mg and D961H 20 mg by the assessment of adverse events, laboratory variables and vital signs in Japanese paediatric patients aged 1 to 14 years old who either had a diagnosis of or were suspected to have gastric ulcer, duodenal ulcer, Anastomotic ulcer, non-erosive reflux disease, reflux esophagitis or Zollinger-Ellison syndrome.

Protection of trial subjects:

Nothing special

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	24 June 2014
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Japan: 50
Worldwide total number of subjects	50
EEA total number of subjects	0

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	2
Children (2-11 years)	28
Adolescents (12-17 years)	20
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The patients were enrolled from 20 sites in Japan from 24 June 2014 to 4 April 2016. Of the 55 patients screened for the study, 50 patients were eligible for the participation and were registered into the study.

Pre-assignment

Screening details:

55 patients were screened. Out of the 55 screened patients, 5 patients were not registered into the study because they did not meet inclusion/exclusion criteria.

Pre-assignment period milestones

Number of subjects started	50
Number of subjects completed	50

Period 1

Period 1 title	8 week treatment (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Blinding implementation details:

This study was open.

Arms

Are arms mutually exclusive?	Yes
Arm title	Group 1

Arm description:

D961H sachet 10 mg

Age: 1-11 years and Weight <20 kg

Arm type	Experimental
Investigational medicinal product name	D961H
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Granules for oral solution in sachet
Routes of administration	Oral use

Dosage and administration details:

sachet 10 mg once daily

Arm title	Group 2
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Arm description:

D961H capsule 10 mg

Age: 1-11 years and Weight ≥20 kg

Arm type	Experimental
Investigational medicinal product name	D961H
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

10 mg once daily

Arm title	Group 3
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Arm description: D961H capsule 20 mg Age: 1-11 years and Weight: >=20 kg	
Arm type	Experimental
Investigational medicinal product name	D961H
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use
Dosage and administration details: 20 mg once daily	
Arm title	Group 4
Arm description: D961H capsule 10 mg Age: 12-14 years and Weight: >=20 kg	
Arm type	Experimental
Investigational medicinal product name	D961H
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use
Dosage and administration details: 10 mg once daily	
Arm title	Group 5
Arm description: D961H capsule 20 mg Age: 12-14 years and Weight: >=20 kg	
Arm type	Experimental
Investigational medicinal product name	D961H
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use
Dosage and administration details: 20 mg once daily	

Number of subjects in period 1	Group 1	Group 2	Group 3
Started	10	10	10
Completed	9	10	9
Not completed	1	0	1
Consent withdrawn by subject	1	-	-
Adverse event, non-fatal	-	-	1

Number of subjects in period 1	Group 4	Group 5
Started	10	10
Completed	9	10
Not completed	1	0
Consent withdrawn by subject	1	-

Adverse event, non-fatal	-	-
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Baseline characteristics

Reporting groups

Reporting group title	Group 1
Reporting group description:	
D961H sachet 10 mg	
Age: 1-11 years and Weight <20 kg	
Reporting group title	Group 2
Reporting group description:	
D961H capsule 10 mg	
Age: 1-11 years and Weight ≥20 kg	
Reporting group title	Group 3
Reporting group description:	
D961H capsule 20 mg Age: 1-11 years and Weight: ≥20 kg	
Reporting group title	Group 4
Reporting group description:	
D961H capsule 10 mg Age: 12-14 years and Weight: ≥20 kg	
Reporting group title	Group 5
Reporting group description:	
D961H capsule 20 mg Age: 12-14 years and Weight: ≥20 kg	

Reporting group values	Group 1	Group 2	Group 3
Number of subjects	10	10	10
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)	2	0	0
Children (2-11 years)	8	10	10
Adolescents (12-17 years)	0	0	0
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	3.6	8.9	8.4
standard deviation	± 2.2	± 0.7	± 1.8
Gender Categorical			
Units: Subjects			
Female	5	6	2
Male	5	4	8

Reporting group values	Group 4	Group 5	Total
Number of subjects	10	10	50
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	2
Children (2-11 years)	0	0	28
Adolescents (12-17 years)	10	10	20
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	13.4	13.1	
standard deviation	± 0.7	± 0.9	-
Gender Categorical			
Units: Subjects			
Female	7	6	26
Male	3	4	24

End points

End points reporting groups

Reporting group title	Group 1
Reporting group description: D961H sachet 10 mg Age: 1-11 years and Weight <20 kg	
Reporting group title	Group 2
Reporting group description: D961H capsule 10 mg Age: 1-11 years and Weight ≥20 kg	
Reporting group title	Group 3
Reporting group description: D961H capsule 20 mg Age: 1-11 years and Weight: ≥20 kg	
Reporting group title	Group 4
Reporting group description: D961H capsule 10 mg Age: 12-14 years and Weight: ≥20 kg	
Reporting group title	Group 5
Reporting group description: D961H capsule 20 mg Age: 12-14 years and Weight: ≥20 kg	

Primary: Disappearance of heartburn at Week 8 by patient diaries

End point title	Disappearance of heartburn at Week 8 by patient diaries ^[1]
End point description: The disappearance of heartburn was assessed by the intensity of the symptom at Week 8. Patients who recognized disappearance of heartburn were defined as those who selected "Mild", "Moderate", or "Severe" to the question about the intensity in the patient diary at pre-dose and had the maximum intensity of "None" at Week 8.	
End point type	Primary
End point timeframe: 8 weeks	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: The objective of this study is to evaluate the safety and efficacy of D961H 10 mg and 20 mg for Japanese pediatric patients with upper gastrointestinal disease, not to compare the two dosages of D961H 10 mg and 20 mg. Therefore, no formal statistical analyses were performed and only descriptive statistical analyses were used. No appropriate information for the statistical analyses sections was available in this study.

End point values	Group 1	Group 2	Group 3	Group 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2	3	1	1
Units: Participants	2	0	0	1

End point values	Group 5			
Subject group type	Reporting group			
Number of subjects analysed	4			

Units: Participants	3			
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Statistical analyses

No statistical analyses for this end point

Primary: Disappearance of epigastric pain at Week 8 by patient diaries

End point title	Disappearance of epigastric pain at Week 8 by patient diaries ^[2]
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End point description:

The disappearance of epigastric pain was assessed by the intensity of the symptom at Week 8. Patients who recognized disappearance of epigastric pain were defined as those who selected "Mild", "Moderate", or "Severe" to the question about the intensity in the patient diary at pre-dose and had the maximum intensity of "None" at Week 8.

End point type	Primary
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End point timeframe:

8 weeks

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: The objective of this study is to evaluate the safety and efficacy of D961H 10 mg and 20 mg for Japanese pediatric patients with upper gastrointestinal disease, not to compare the two dosages of D961H 10 mg and 20 mg. Therefore, no formal statistical analyses were performed and only descriptive statistical analyses were used. No appropriate information for the statistical analyses sections was available in this study.

End point values	Group 1	Group 2	Group 3	Group 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2	6	5	4
Units: Participants	2	3	5	1

End point values	Group 5			
Subject group type	Reporting group			
Number of subjects analysed	7			
Units: Participants	3			

Statistical analyses

No statistical analyses for this end point

Primary: Disappearance of upper abdominal discomfort at Week 8 by patient diaries

End point title	Disappearance of upper abdominal discomfort at Week 8 by patient diaries ^[3]
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End point description:

The disappearance of upper abdominal discomfort was assessed by the intensity of the symptom at

Week 8. Patients who recognized disappearance of upper abdominal discomfort were defined as those who selected "Mild", "Moderate", or "Severe" to the question about the intensity in the patient diary at pre-dose and had the maximum intensity of "None" at Week 8.

End point type	Primary
End point timeframe:	
8 weeks	

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: The objective of this study is to evaluate the safety and efficacy of D961H 10 mg and 20 mg for Japanese pediatric patients with upper gastrointestinal disease, not to compare the two dosages of D961H 10 mg and 20 mg. Therefore, no formal statistical analyses were performed and only descriptive statistical analyses were used. No appropriate information for the statistical analyses sections was available in this study.

End point values	Group 1	Group 2	Group 3	Group 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	6	4	4
Units: Participants	3	2	4	2

End point values	Group 5			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: Participants	2			

Statistical analyses

No statistical analyses for this end point

Primary: Disappearance of regurgitation at Week 8 by patient diaries

End point title	Disappearance of regurgitation at Week 8 by patient diaries ^[4]
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End point description:

The disappearance of regurgitation was assessed by the intensity of the symptom at Week 8. Patients who recognized disappearance of regurgitation were defined as those who selected "Mild", "Moderate", or "Severe" to the question about the intensity in the patient diary at pre-dose and had the maximum intensity of "None" at Week 8.

End point type	Primary
End point timeframe:	
8 weeks	

Notes:

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: The objective of this study is to evaluate the safety and efficacy of D961H 10 mg and 20 mg for Japanese pediatric patients with upper gastrointestinal disease, not to compare the two dosages of D961H 10 mg and 20 mg. Therefore, no formal statistical analyses were performed and only descriptive statistical analyses were used. No appropriate information for the statistical analyses sections was available in this study.

End point values	Group 1	Group 2	Group 3	Group 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	3	5	3
Units: Participants	3	2	3	2

End point values	Group 5			
Subject group type	Reporting group			
Number of subjects analysed	4			
Units: Participants	4			

Statistical analyses

No statistical analyses for this end point

Primary: Aggravation of heartburn at Week 8 by patient diaries

End point title	Aggravation of heartburn at Week 8 by patient diaries ^[5]
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End point description:

The aggravation of heartburn was assessed by the intensity of the symptom at Week 8. Patients who recognized aggravation of heartburn were defined as those who selected "None" to the question about the intensity in the patient diary at pre-dose and had the maximum intensity of "Mild", "Moderate" or "Severe" at Week 8.

End point type	Primary
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End point timeframe:

8 weeks

Notes:

[5] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: The objective of this study is to evaluate the safety and efficacy of D961H 10 mg and 20 mg for Japanese pediatric patients with upper gastrointestinal disease, not to compare the two dosages of D961H 10 mg and 20 mg. Therefore, no formal statistical analyses were performed and only descriptive statistical analyses were used. No appropriate information for the statistical analyses sections was available in this study.

End point values	Group 1	Group 2	Group 3	Group 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	7	8	8
Units: Participants	0	0	0	0

End point values	Group 5			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: Participants	0			

Statistical analyses

No statistical analyses for this end point

Primary: Aggravation of epigastric pain at Week 8 by patient diaries

End point title	Aggravation of epigastric pain at Week 8 by patient diaries ^[6]
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End point description:

The aggravation of epigastric pain was assessed by the intensity of the symptom at Week 8. Patients who recognized aggravation of epigastric pain were defined as those who selected "None" to the question about the intensity in the patient diary at pre-dose and had the maximum intensity of "Mild", "Moderate" or "Severe" at Week 8.

End point type	Primary
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End point timeframe:

8 weeks

Notes:

[6] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: The objective of this study is to evaluate the safety and efficacy of D961H 10 mg and 20 mg for Japanese pediatric patients with upper gastrointestinal disease, not to compare the two dosages of D961H 10 mg and 20 mg. Therefore, no formal statistical analyses were performed and only descriptive statistical analyses were used. No appropriate information for the statistical analyses sections was available in this study.

End point values	Group 1	Group 2	Group 3	Group 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	4	4	5
Units: Participants	0	0	1	1

End point values	Group 5			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: Participants	1			

Statistical analyses

No statistical analyses for this end point

Primary: Aggravation of upper abdominal discomfort at Week 8 by patient diaries

End point title	Aggravation of upper abdominal discomfort at Week 8 by patient diaries ^[7]
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End point description:

The aggravation of upper abdominal discomfort was assessed by the intensity of the symptom at Week

8. Patients who recognized aggravation of upper abdominal discomfort were defined as those who selected "None" to the question about the intensity in the patient diary at pre-dose and had the maximum intensity of "Mild", "Moderate" or "Severe" at Week 8.

End point type	Primary
End point timeframe:	
8 weeks	

Notes:

[7] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: The objective of this study is to evaluate the safety and efficacy of D961H 10 mg and 20 mg for Japanese pediatric patients with upper gastrointestinal disease, not to compare the two dosages of D961H 10 mg and 20 mg. Therefore, no formal statistical analyses were performed and only descriptive statistical analyses were used. No appropriate information for the statistical analyses sections was available in this study.

End point values	Group 1	Group 2	Group 3	Group 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	4	5	5
Units: Participants	0	0	2	1

End point values	Group 5			
Subject group type	Reporting group			
Number of subjects analysed	4			
Units: Participants	0			

Statistical analyses

No statistical analyses for this end point

Primary: Aggravation of regurgitation at Week 8 by patient diaries

End point title	Aggravation of regurgitation at Week 8 by patient diaries ^[8]
End point description:	
The aggravation of regurgitation was assessed by the intensity of the symptom at Week 8. Patients who recognized aggravation of regurgitation were defined as those who selected "None" to the question about the intensity in the patient diary at pre-dose and had the maximum intensity of "Mild", "Moderate" or "Severe" at Week 8.	
End point type	Primary
End point timeframe:	
8 weeks	

Notes:

[8] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: The objective of this study is to evaluate the safety and efficacy of D961H 10 mg and 20 mg for Japanese pediatric patients with upper gastrointestinal disease, not to compare the two dosages of D961H 10 mg and 20 mg. Therefore, no formal statistical analyses were performed and only descriptive statistical analyses were used. No appropriate information for the statistical analyses sections was available in this study.

End point values	Group 1	Group 2	Group 3	Group 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	7	4	6
Units: Participants	2	0	1	0

End point values	Group 5			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: Participants	0			

Statistical analyses

No statistical analyses for this end point

Primary: Disappearance of heartburn at Week 8 by investigators

End point title	Disappearance of heartburn at Week 8 by investigators ^[9]
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End point description:

The investigators assessed the presence/absence and the intensity of heartburn at baseline and Week 8 based on questioning the patients or patients' guardians and the patient diary. Patients who recognized disappearance of heartburn were defined as those who had a heartburn at pre-dose and did not have the corresponding symptoms at Week 8 judged by investigators.

End point type	Primary
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End point timeframe:

8 weeks

Notes:

[9] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: The objective of this study is to evaluate the safety and efficacy of D961H 10 mg and 20 mg for Japanese pediatric patients with upper gastrointestinal disease, not to compare the two dosages of D961H 10 mg and 20 mg. Therefore, no formal statistical analyses were performed and only descriptive statistical analyses were used. No appropriate information for the statistical analyses sections was available in this study.

End point values	Group 1	Group 2	Group 3	Group 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2	2	0 ^[10]	2
Units: Participants	2	1		2

Notes:

[10] - No patient had the corresponding symptom at pre-dose.

End point values	Group 5			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: Participants	2			

Statistical analyses

No statistical analyses for this end point

Primary: Disappearance of epigastric pain at Week 8 by investigators

End point title	Disappearance of epigastric pain at Week 8 by investigators ^[11]
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End point description:

The investigators assessed the presence/absence and the intensity of epigastric pain at baseline and Week 8 based on questioning the patients or patients' guardians and the patient diary. Patients who recognized disappearance of epigastric pain were defined as those who had an epigastric pain at predose and did not have the corresponding symptoms at Week 8 judged by investigators.

End point type	Primary
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End point timeframe:

8 weeks

Notes:

[11] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: The objective of this study is to evaluate the safety and efficacy of D961H 10 mg and 20 mg for Japanese pediatric patients with upper gastrointestinal disease, not to compare the two dosages of D961H 10 mg and 20 mg. Therefore, no formal statistical analyses were performed and only descriptive statistical analyses were used. No appropriate information for the statistical analyses sections was available in this study.

End point values	Group 1	Group 2	Group 3	Group 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2	6	4	7
Units: Participants	2	5	4	2

End point values	Group 5			
Subject group type	Reporting group			
Number of subjects analysed	9			
Units: Participants	6			

Statistical analyses

No statistical analyses for this end point

Primary: Disappearance of upper abdominal discomfort at Week 8 by investigators

End point title	Disappearance of upper abdominal discomfort at Week 8 by investigators ^[12]
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End point description:

The investigators assessed the presence/absence and the intensity of upper abdominal discomfort at baseline and Week 8 based on questioning the patients or patients' guardians and the patient diary. Patients who recognized disappearance of upper abdominal discomfort were defined as those who had an upper abdominal discomfort at pre-dose and did not have the corresponding symptoms at Week 8 judged by investigators.

End point type	Primary
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End point timeframe:

8 weeks

Notes:

[12] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: The objective of this study is to evaluate the safety and efficacy of D961H 10 mg and 20 mg for Japanese pediatric patients with upper gastrointestinal disease, not to compare the two dosages of D961H 10 mg and 20 mg. Therefore, no formal statistical analyses were performed and only descriptive statistical analyses were used. No appropriate information for the statistical analyses sections was available in this study.

End point values	Group 1	Group 2	Group 3	Group 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	6	5	7
Units: Participants	3	5	4	4

End point values	Group 5			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: Participants	3			

Statistical analyses

No statistical analyses for this end point

Primary: Disappearance of regurgitation at Week 8 by investigators

End point title	Disappearance of regurgitation at Week 8 by investigators ^[13]
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End point description:

The investigators assessed the presence/absence and the intensity of regurgitation at baseline and Week 8 based on questioning the patients or patients' guardians and the patient diary. Patients who recognized disappearance of regurgitation were defined as those who had a regurgitation at pre-dose and did not have the corresponding symptoms at Week 8 judged by investigators.

End point type	Primary
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End point timeframe:

8 weeks

Notes:

[13] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: The objective of this study is to evaluate the safety and efficacy of D961H 10 mg and 20 mg for Japanese pediatric patients with upper gastrointestinal disease, not to compare the two dosages of D961H 10 mg and 20 mg. Therefore, no formal statistical analyses were performed and only descriptive statistical analyses were used. No appropriate information for the statistical analyses sections was available in this study.

End point values	Group 1	Group 2	Group 3	Group 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	1	5	1
Units: Participants	3	0	3	1

End point values	Group 5			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: Participants	3			

Statistical analyses

No statistical analyses for this end point

Primary: Aggravation of heartburn at Week 8 by investigators

End point title	Aggravation of heartburn at Week 8 by investigators ^[14]
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End point description:

The investigators assessed the presence/absence and the intensity of heartburn at baseline and Week 8 based on questioning the patients or patients' guardians and the patient diary. Patients who recognized aggravation of heartburn were defined as those who had no heartburn at pre-dose and did have any of the corresponding symptoms at Week 8 judged by investigators.

End point type	Primary
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End point timeframe:

8 weeks

Notes:

[14] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: The objective of this study is to evaluate the safety and efficacy of D961H 10 mg and 20 mg for Japanese pediatric patients with upper gastrointestinal disease, not to compare the two dosages of D961H 10 mg and 20 mg. Therefore, no formal statistical analyses were performed and only descriptive statistical analyses were used. No appropriate information for the statistical analyses sections was available in this study.

End point values	Group 1	Group 2	Group 3	Group 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	8	9	7
Units: Participants	0	0	0	1

End point values	Group 5			
Subject group type	Reporting group			
Number of subjects analysed	7			
Units: Participants	0			

Statistical analyses

No statistical analyses for this end point

Primary: Aggravation of epigastric pain at Week 8 by investigators

End point title	Aggravation of epigastric pain at Week 8 by investigators ^[15]
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End point description:

The investigators assessed the presence/absence and the intensity of epigastric pain at baseline and Week 8 based on questioning the patients or patients' guardians and the patient diary. Patients who recognized aggravation of epigastric pain were defined as those who had no epigastric pain at pre-dose and did have any of the corresponding symptoms at Week 8 judged by investigators.

End point type	Primary
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End point timeframe:

8 weeks

Notes:

[15] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: The objective of this study is to evaluate the safety and efficacy of D961H 10 mg and 20 mg for Japanese pediatric patients with upper gastrointestinal disease, not to compare the two dosages of D961H 10 mg and 20 mg. Therefore, no formal statistical analyses were performed and only descriptive statistical analyses were used. No appropriate information for the statistical analyses sections was available in this study.

End point values	Group 1	Group 2	Group 3	Group 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	4	5	2
Units: Participants	0	0	0	0

End point values	Group 5			
Subject group type	Reporting group			
Number of subjects analysed	1			
Units: Participants	0			

Statistical analyses

No statistical analyses for this end point

Primary: Aggravation of upper abdominal discomfort at Week 8 by investigators

End point title	Aggravation of upper abdominal discomfort at Week 8 by investigators ^[16]
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End point description:

The investigators assessed the presence/absence and the intensity of upper abdominal discomfort at

baseline and Week 8 based on questioning the patients or patients' guardians and the patient diary. Patients who recognized aggravation of upper abdominal discomfort were defined as those who had no upper abdominal discomfort at pre-dose and did have any of the corresponding symptoms at Week 8 judged by investigators.

End point type	Primary
End point timeframe:	
8 weeks	

Notes:

[16] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: The objective of this study is to evaluate the safety and efficacy of D961H 10 mg and 20 mg for Japanese pediatric patients with upper gastrointestinal disease, not to compare the two dosages of D961H 10 mg and 20 mg. Therefore, no formal statistical analyses were performed and only descriptive statistical analyses were used. No appropriate information for the statistical analyses sections was available in this study.

End point values	Group 1	Group 2	Group 3	Group 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	4	4	2
Units: Participants	0	0	0	1

End point values	Group 5			
Subject group type	Reporting group			
Number of subjects analysed	4			
Units: Participants	0			

Statistical analyses

No statistical analyses for this end point

Primary: Aggravation of regurgitation at Week 8 by investigators

End point title	Aggravation of regurgitation at Week 8 by investigators ^[17]
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End point description:

The investigators assessed the presence/absence and the intensity of regurgitation at baseline and Week 8 based on questioning the patients or patients' guardians and the patient diary. Patients who recognized aggravation of regurgitation were defined as those who had no regurgitation at pre-dose and did have any of the corresponding symptoms at Week 8 judged by investigators.

End point type	Primary
End point timeframe:	
8 weeks	

Notes:

[17] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: The objective of this study is to evaluate the safety and efficacy of D961H 10 mg and 20 mg for Japanese pediatric patients with upper gastrointestinal disease, not to compare the two dosages of D961H 10 mg and 20 mg. Therefore, no formal statistical analyses were performed and only descriptive statistical analyses were used. No appropriate information for the statistical analyses sections was available in this study.

End point values	Group 1	Group 2	Group 3	Group 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	9	4	8
Units: Participants	0	0	1	0

End point values	Group 5			
Subject group type	Reporting group			
Number of subjects analysed	7			
Units: Participants	1			

Statistical analyses

No statistical analyses for this end point

Secondary: AUCtau of esomeprazole after at least 5 days of repeated dose

End point title	AUCtau of esomeprazole after at least 5 days of repeated dose
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End point description:

End point type	Secondary
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End point timeframe:

After at least 5 days of repeated dose

End point values	Group 1	Group 2	Group 3	Group 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	9	10	9
Units: $\mu\text{mol}\cdot\text{h}/\text{L}$				
arithmetic mean (standard deviation)	7.04 (\pm 3.05)	3.52 (\pm 2.35)	11.05 (\pm 5.11)	2.38 (\pm 1.74)

End point values	Group 5			
Subject group type	Reporting group			
Number of subjects analysed	10			
Units: $\mu\text{mol}\cdot\text{h}/\text{L}$				
arithmetic mean (standard deviation)	5.82 (\pm 1.85)			

Statistical analyses

No statistical analyses for this end point

Secondary: AUC0-t of esomeprazole after at least 5 days of repeated dose

End point title	AUC0-t of esomeprazole after at least 5 days of repeated dose
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End point description:

End point type	Secondary
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End point timeframe:

After at least 5 days of repeated dose

End point values	Group 1	Group 2	Group 3	Group 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9	10	10	9
Units: $\mu\text{mol}\cdot\text{h}/\text{L}$				
arithmetic mean (standard deviation)	5.53 (\pm 3.69)	3.09 (\pm 2.34)	10.41 (\pm 4.55)	1.99 (\pm 1.3)

End point values	Group 5			
Subject group type	Reporting group			
Number of subjects analysed	10			
Units: $\mu\text{mol}\cdot\text{h}/\text{L}$				
arithmetic mean (standard deviation)	5.45 (\pm 1.78)			

Statistical analyses

No statistical analyses for this end point

Secondary: Cmax of esomeprazole after at least 5 days of repeated dose

End point title	Cmax of esomeprazole after at least 5 days of repeated dose
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End point description:

End point type	Secondary
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End point timeframe:

After at least 5 days of repeated dose

End point values	Group 1	Group 2	Group 3	Group 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9	10	10	9
Units: $\mu\text{mol}/\text{L}$				
arithmetic mean (standard deviation)	3.42 (\pm 2.09)	2.09 (\pm 1.53)	5.91 (\pm 2.19)	1.09 (\pm 0.57)

End point values	Group 5			
Subject group type	Reporting group			
Number of subjects analysed	10			
Units: µmol/L				
arithmetic mean (standard deviation)	3.13 (± 1.36)			

Statistical analyses

No statistical analyses for this end point

Secondary: tmax of esomeprazole after at least 5 days of repeated dose

End point title	tmax of esomeprazole after at least 5 days of repeated dose
End point description:	
End point type	Secondary
End point timeframe:	
After at least 5 days of repeated dose	

End point values	Group 1	Group 2	Group 3	Group 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9	10	10	9
Units: hour				
median (full range (min-max))	1.58 (1.03 to 5.92)	1.52 (0.92 to 6)	1.47 (0.93 to 1.52)	1.57 (0.93 to 2.95)

End point values	Group 5			
Subject group type	Reporting group			
Number of subjects analysed	10			
Units: hour				
median (full range (min-max))	1.75 (0.95 to 3)			

Statistical analyses

No statistical analyses for this end point

Secondary: thalf of esomeprazole after at least 5 days of repeated dose

End point title	half of esomeprazole after at least 5 days of repeated dose
End point description:	
End point type	Secondary
End point timeframe:	
After at least 5 days of repeated dose	

End point values	Group 1	Group 2	Group 3	Group 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	9	10	9
Units: hour				
arithmetic mean (standard deviation)	0.8 (± 0.18)	0.97 (± 0.55)	1.08 (± 0.44)	1.37 (± 0.88)

End point values	Group 5			
Subject group type	Reporting group			
Number of subjects analysed	10			
Units: hour				
arithmetic mean (standard deviation)	1.06 (± 0.25)			

Statistical analyses

No statistical analyses for this end point

Secondary: CL/F (Apparent total clearance) of esomeprazole after at least 5 days of repeated dose

End point title	CL/F (Apparent total clearance) of esomeprazole after at least 5 days of repeated dose
End point description:	
End point type	Secondary
End point timeframe:	
After at least 5 days of repeated dose	

End point values	Group 1	Group 2	Group 3	Group 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	9	10	9
Units: L/h				
arithmetic mean (standard deviation)	4.74 (± 1.92)	12.44 (± 8.9)	6.44 (± 3.37)	23.33 (± 24.93)

End point values	Group 5			
Subject group type	Reporting group			
Number of subjects analysed	10			
Units: L/h				
arithmetic mean (standard deviation)	10.94 (\pm 3.64)			

Statistical analyses

No statistical analyses for this end point

Secondary: Vz/F (Apparent volume of distribution) of esomeprazole after at least 5 days of repeated dose

End point title	Vz/F (Apparent volume of distribution) of esomeprazole after at least 5 days of repeated dose
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End point description:

End point type	Secondary
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End point timeframe:

After at least 5 days of repeated dose

End point values	Group 1	Group 2	Group 3	Group 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	9	10	9
Units: Liter				
arithmetic mean (standard deviation)	5.1 (\pm 1.24)	16.56 (\pm 16.21)	9.21 (\pm 4)	44.73 (\pm 72.03)

End point values	Group 5			
Subject group type	Reporting group			
Number of subjects analysed	10			
Units: Liter				
arithmetic mean (standard deviation)	15.9 (\pm 4.42)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Serious adverse events were collected from the date of signing of informed consent to 8 weeks or withdrawal. Other adverse events were collected from the start of investigational drug administration to 8 weeks or withdrawal.

Adverse event reporting additional description:

Serious adverse events were collected from the date of signing of informed consent to 8 weeks or withdrawal. Other adverse events were collected from the start of investigational drug administration to 8 weeks or withdrawal.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	19.0
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Reporting groups

Reporting group title	Group 1
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Reporting group description:

D961H sachet 10 mg

Age: 1-11 years and Weight <20 kg

Reporting group title	Group 3
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Reporting group description:

D961H capsule 20 mg Age: 1-11 years and Weight: ≥20 kg

Reporting group title	Group 2
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Reporting group description:

D961H capsule 10 mg

Age: 1-11 years and Weight ≥20 kg

Reporting group title	Group 4
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Reporting group description:

D961H capsule 10 mg Age: 12-14 years and Weight: ≥20 kg

Reporting group title	Group 5
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Reporting group description:

D961H capsule 20 mg Age: 12-14 years and Weight: ≥20 kg

Serious adverse events	Group 1	Group 3	Group 2
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 10 (20.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 10 (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
Gastrointestinal disorders			

Irritable bowel syndrome			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 10 (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
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 10 (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

Serious adverse events	Group 4	Group 5	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Irritable bowel syndrome			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Group 1	Group 3	Group 2
Total subjects affected by non-serious adverse events subjects affected / exposed	8 / 10 (80.00%)	5 / 10 (50.00%)	8 / 10 (80.00%)
Injury, poisoning and procedural complications Arthropod sting subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1	0 / 10 (0.00%) 0	0 / 10 (0.00%) 0
Nervous system disorders Headache subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 10 (0.00%) 0	2 / 10 (20.00%) 2
Blood and lymphatic system disorders Iron deficiency anaemia subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 10 (0.00%) 0	0 / 10 (0.00%) 0
General disorders and administration site conditions Oedema peripheral subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 10 (0.00%) 0	0 / 10 (0.00%) 0
Immune system disorders Seasonal allergy subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 10 (0.00%) 0	1 / 10 (10.00%) 1
Eye disorders Hordeolum subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	1 / 10 (10.00%) 1	0 / 10 (0.00%) 0
Gastrointestinal disorders Abdominal pain subjects affected / exposed occurrences (all) Anal fissure subjects affected / exposed occurrences (all) Dental caries subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0 0 / 10 (0.00%) 0 0 / 10 (0.00%) 0	1 / 10 (10.00%) 1 0 / 10 (0.00%) 0 1 / 10 (10.00%) 1	0 / 10 (0.00%) 0 1 / 10 (10.00%) 1 0 / 10 (0.00%) 0

Diarrhoea			
subjects affected / exposed	1 / 10 (10.00%)	2 / 10 (20.00%)	0 / 10 (0.00%)
occurrences (all)	1	2	0
Gingival pain			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Haemorrhoidal haemorrhage			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Stomatitis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Vomiting			
subjects affected / exposed	2 / 10 (20.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	2	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Upper respiratory tract inflammation			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Skin and subcutaneous tissue disorders			
Photosensitivity reaction			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Bronchitis			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Gastroenteritis			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0

Gastroenteritis viral			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Influenza			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Mumps			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Nasopharyngitis			
subjects affected / exposed	1 / 10 (10.00%)	2 / 10 (20.00%)	4 / 10 (40.00%)
occurrences (all)	1	3	7
Otitis media			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Paronychia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Pharyngitis			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Pneumonia			
subjects affected / exposed	2 / 10 (20.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	2	0	0
Streptococcal infection			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Upper respiratory tract infection			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	1	0	1
Varicella			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Vulvovaginal candidiasis			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0

Non-serious adverse events	Group 4	Group 5	
Total subjects affected by non-serious adverse events subjects affected / exposed	5 / 10 (50.00%)	6 / 10 (60.00%)	
Injury, poisoning and procedural complications Arthropod sting subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 10 (0.00%) 0	
Nervous system disorders Headache subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	2 / 10 (20.00%) 2	
Blood and lymphatic system disorders Iron deficiency anaemia subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	1 / 10 (10.00%) 1	
General disorders and administration site conditions Oedema peripheral subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	1 / 10 (10.00%) 1	
Immune system disorders Seasonal allergy subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 10 (0.00%) 0	
Eye disorders Hordeolum subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 10 (0.00%) 0	
Gastrointestinal disorders Abdominal pain subjects affected / exposed occurrences (all) Anal fissure subjects affected / exposed occurrences (all) Dental caries	0 / 10 (0.00%) 0 0 / 10 (0.00%) 0	1 / 10 (10.00%) 1 0 / 10 (0.00%) 0	

subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	
occurrences (all)	0	0	
Diarrhoea			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Gingival pain			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Haemorrhoidal haemorrhage			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Nausea			
subjects affected / exposed	0 / 10 (0.00%)	2 / 10 (20.00%)	
occurrences (all)	0	3	
Stomatitis			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Vomiting			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	
occurrences (all)	0	0	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	
occurrences (all)	0	0	
Upper respiratory tract inflammation			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Skin and subcutaneous tissue disorders			
Photosensitivity reaction			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	
occurrences (all)	0	0	
Gastroenteritis			

subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	1
Gastroenteritis viral		
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	1	0
Influenza		
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0
Mumps		
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0
Nasopharyngitis		
subjects affected / exposed	1 / 10 (10.00%)	3 / 10 (30.00%)
occurrences (all)	1	3
Otitis media		
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0
Paronychia		
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0
Pharyngitis		
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0
Pneumonia		
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0
Streptococcal infection		
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0
Upper respiratory tract infection		
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	1	0
Varicella		
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0
Vulvovaginal candidiasis		

subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	
occurrences (all)	0	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported