

**Clinical trial results:**

An Open Label, Parallel Group, Multi-centre, Phase III Study to Assess the Efficacy and Safety of D961H for the Maintenance Therapy Following Initial Treatment in Japanese Paediatric Patients with Reflux Esophagitis and for the Prevention of Recurrence of Gastric Ulcer or Duodenal Ulcer in Japanese Paediatric Patients Treated with Non-steroidal Anti-inflammatory Drugs or Low-dose Aspirin

Summary

EudraCT number	2018-000213-20
Trial protocol	Outside EU/EEA
Global end of trial date	10 May 2023

Results information

Result version number	v1 (current)
This version publication date	07 July 2023
First version publication date	07 July 2023

Trial information**Trial identification**

Sponsor protocol code	D961WC00001
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Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Biometrics & Real World Analytics Department, AstraZeneca Japan
Sponsor organisation address	Grand Front Osaka Tower B. 3-1, Ofuka-cho, Kita-ku, Osaka, Japan, 530-0011
Public contact	Masahiro Nii/Japan project statistician, Biometrics & Real World Analytics Department, AstraZeneca Japan, 81 7022748322, masahiro.nii@astrazeneca.com
Scientific contact	Masahiro Nii/Japan project statistician, Biometrics & Real World Analytics Department, AstraZeneca Japan, 81 7022748322, 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	10 April 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	10 April 2023
Global end of trial reached?	Yes
Global end of trial date	10 May 2023
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

There were two primary objectives in this study.

One of the primary objectives was to assess the efficacy and safety of once-daily oral administration of D961H for the maintenance of RE healing in Japanese paediatric patients aged 1 to 14 years that have symptomatically healed RE (defined as no more than mild RE-related symptoms) and if EGD is done, no visible mucosal breaks observed. The other was to assess the efficacy and safety of once-daily oral administration of D961H for the prevention of GU/DU recurrence in Japanese paediatric patients aged 1 to 14 years treated with long term NSAIDs/LDA therapy.

Protection of trial subjects:

Nothing special

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	24 July 2018
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: 49
Worldwide total number of subjects	49
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)	10
Children (2-11 years)	26
Adolescents (12-17 years)	13

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

Subject disposition

Recruitment

Recruitment details:

First subject enrolled on 24 July 2018 Last subject last visit on 27 December 2022. This study was conducted at a total of 17 sites in Japan.

Pre-assignment

Screening details:

Out of 53 enrolled subjects, 49 subjects were registered and 4 subjects were not registered. The reasons of no registration were 'Screening Failure at screening visit' (3 subjects) and 'Prematurely discontinued initial healing therapy period' (1 subject in Group 2).

Pre-assignment period milestones

Number of subjects started	49
Number of subjects completed	49

Period 1

Period 1 title	Overall Study (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:

Maintenance of healing for reflux esophagitis, Initial healing phase (8 weeks), D961H 10 mg once-daily; Maintenance phase (24 or 44 weeks), D961H 10 mg once-daily, Body weight<20 kg

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

Dosage and administration details:

10 mg once daily

Arm title	Group 2
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Arm description:

Maintenance of healing for reflux esophagitis, Initial healing phase (8 weeks), D961H 20 mg once-daily; Maintenance phase (24 or 44 weeks) starts with D961H 10 mg once-daily and may be increased to 20 mg once-daily based on investigator's discretion, Body weight≥20 kg

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

Dosage and administration details:

10 mg or 20 mg once daily

Arm title	Group 3
Arm description: Prevention of recurrence for gastric ulcer and/or duodenal ulcer, D961H 10 mg once-daily (32 or 52 weeks), Body weight<20 kg	
Arm type	Experimental
Investigational medicinal product name	D961H
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard, Granules for oral solution in sachet
Routes of administration	Oral use
Dosage and administration details: 10 mg once daily	
Arm title	Group 4
Arm description: Prevention of recurrence for gastric and/or duodenal ulcer, D961H starts with 10 mg once-daily, and may be increased to 20 mg once-daily based on investigator's discretion (32 or 52 weeks), Body weight>=20 kg	
Arm type	Experimental
Investigational medicinal product name	D961H
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard, Granules for oral solution in sachet
Routes of administration	Oral use
Dosage and administration details: 10 mg or 20 mg once daily	

Number of subjects in period 1	Group 1	Group 2	Group 3
Started	7	20	9
Completed	6	18	9
Not completed	1	2	0
Physician decision	1	1	-
Consent withdrawn by subject	-	-	-
Protocol deviation	-	1	-

Number of subjects in period 1	Group 4
Started	13
Completed	12
Not completed	1
Physician decision	-
Consent withdrawn by subject	1
Protocol deviation	-

Baseline characteristics

Reporting groups

Reporting group title	Group 1
Reporting group description:	
Maintenance of healing for reflux esophagitis, Initial healing phase (8 weeks), D961H 10 mg once-daily; Maintenance phase (24 or 44 weeks), D961H 10 mg once-daily, Body weight<20 kg	
Reporting group title	Group 2
Reporting group description:	
Maintenance of healing for reflux esophagitis, Initial healing phase (8 weeks), D961H 20 mg once-daily; Maintenance phase (24 or 44 weeks) starts with D961H 10 mg once-daily and may be increased to 20 mg once-daily based on investigator's discretion, Body weight>=20 kg	
Reporting group title	Group 3
Reporting group description:	
Prevention of recurrence for gastric ulcer and/or duodenal ulcer, D961H 10 mg once-daily (32 or 52 weeks), Body weight<20 kg	
Reporting group title	Group 4
Reporting group description:	
Prevention of recurrence for gastric and/or duodenal ulcer, D961H starts with 10 mg once-daily, and may be increased to 20 mg once-daily based on investigator's discretion (32 or 52 weeks), Body weight>=20 kg	

Reporting group values	Group 1	Group 2	Group 3
Number of subjects	7	20	9
Age Categorical			
Units: Participants			
<=3 years	4	0	2
4-5 years	1	0	3
6-7 years	2	2	3
8-9 years	0	7	1
10-11 years	0	4	0
12-14 years	0	7	0
Age Continuous			
Units: Years			
arithmetic mean	3.7	10.4	5.2
standard deviation	± 1.7	± 2.2	± 2.1
Sex: Female, Male			
Units: Participants			
Female	0	6	5
Male	7	14	4
Race (NIH/OMB)			
Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	7	20	9
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	0
White	0	0	0
More than one race	0	0	0
Unknown or Not Reported	0	0	0

Reporting group values	Group 4	Total	
Number of subjects	13	49	
Age Categorical Units: Participants			
<=3 years	0	6	
4-5 years	0	4	
6-7 years	1	8	
8-9 years	1	9	
10-11 years	5	9	
12-14 years	6	13	
Age Continuous Units: Years			
arithmetic mean	11.3		
standard deviation	± 2.4	-	
Sex: Female, Male Units: Participants			
Female	7	18	
Male	6	31	
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	
Asian	13	49	
Native Hawaiian or Other Pacific Islander	0	0	
Black or African American	0	0	
White	0	0	
More than one race	0	0	
Unknown or Not Reported	0	0	

End points

End points reporting groups

Reporting group title	Group 1
Reporting group description: Maintenance of healing for reflux esophagitis, Initial healing phase (8 weeks), D961H 10 mg once-daily; Maintenance phase (24 or 44 weeks), D961H 10 mg once-daily, Body weight<20 kg	
Reporting group title	Group 2
Reporting group description: Maintenance of healing for reflux esophagitis, Initial healing phase (8 weeks), D961H 20 mg once-daily; Maintenance phase (24 or 44 weeks) starts with D961H 10 mg once-daily and may be increased to 20 mg once-daily based on investigator's discretion, Body weight≥20 kg	
Reporting group title	Group 3
Reporting group description: Prevention of recurrence for gastric ulcer and/or duodenal ulcer, D961H 10 mg once-daily (32 or 52 weeks), Body weight<20 kg	
Reporting group title	Group 4
Reporting group description: Prevention of recurrence for gastric and/or duodenal ulcer, D961H starts with 10 mg once-daily, and may be increased to 20 mg once-daily based on investigator's discretion (32 or 52 weeks), Body weight≥20 kg	

Primary: Presence/absence of reflux esophagitis relapse from Week 8 to Week 32

End point title	Presence/absence of reflux esophagitis relapse from Week 8 to Week 32 ^{[1][2]}
End point description: Maintenance therapy for healed reflux esophagitis study part: Presence/absence of reflux esophagitis relapse from 8 to 32 weeks for all participants by assessment of the composite endpoint (reflux esophagitis -related symptoms or optional esophagogastroduodenoscopy findings) during the maintenance therapy.	
End point type	Primary
End point timeframe: 8 to 32 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: There was no plan to compare the endpoint between the arms. The objective of this study was to evaluate the number of participants with presence of reflux esophagitis in each arm.

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: There was no plan to compare the endpoint between the arms. The objective of this study was to evaluate the number of participants with presence of reflux esophagitis in each arm.

End point values	Group 1	Group 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7	19		
Units: Participants				
Presence of reflux esophagitis relapse	0	1		
Absence of reflux esophagitis relapse	7	18		

Statistical analyses

No statistical analyses for this end point

Primary: Presence/absence of gastric ulcer or duodenal ulcer recurrence from Week 0 to Week 32

End point title	Presence/absence of gastric ulcer or duodenal ulcer recurrence from Week 0 to Week 32 ^[3] ^[4]
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End point description:

Prevention of gastric ulcer or duodenal ulcer recurrence associated with long term non-steroidal anti-inflammatory drugs or low-dose aspirin therapy study part:

Presence/absence of gastric ulcer or duodenal ulcer recurrence from 0 to 32 weeks for all participants by assessment of the composite endpoint (gastric ulcer or duodenal ulcer-related symptoms or optional esophagogastroduodenoscopy findings) during the prevention therapy.

End point type	Primary
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End point timeframe:

0 to 32 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: There was no plan to compare the endpoint between the arms. The objective of this study was to evaluate the number of participants with presence of GU/DU recurrence in each arm.

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This endpoint was applied only for Group 3 and Group 4.

End point values	Group 3	Group 4		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	13		
Units: Participants				
Presence of GU or DU recurrence	1	0		
Absence of GU or DU recurrence	8	13		

Statistical analyses

No statistical analyses for this end point

Primary: Adverse events during reflux esophagitis maintenance therapy from Week 8 to Week 32

End point title	Adverse events during reflux esophagitis maintenance therapy from Week 8 to Week 32 ^[5] ^[6]
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End point description:

Maintenance therapy for healed reflux esophagitis study part:

Safety from 8 to 32 weeks for all participants. Number of participants with any adverse event during the period.

End point type	Primary
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End point timeframe:

8 to 32 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: There was no plan to compare the endpoint between the arms. The objective of this study was to evaluate the number of participants with any adverse events in each arm.

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was applied only for Group 1 and Group 2.

End point values	Group 1	Group 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7	20		
Units: Participants				
Participants with any adverse event	7	16		

Statistical analyses

No statistical analyses for this end point

Primary: Adverse events during gastric ulcer or duodenal ulcer recurrence prevention therapy from Week 0 to Week 32

End point title	Adverse events during gastric ulcer or duodenal ulcer recurrence prevention therapy from Week 0 to Week 32 ^[7] ^[8]
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End point description:

Prevention of gastric ulcer or duodenal ulcer recurrence associated with long term non-steroidal anti-inflammatory drugs or low-dose aspirin therapy study part:
Safety from 0 to 32 weeks for all participants. Number of participants with any adverse event during the period.

End point type	Primary
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End point timeframe:

0 to 32 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: There was no plan to compare the endpoint between the arms. The objective of this study was to evaluate the number of participants with any adverse events in each arm.

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was applied only for Group 3 and Group 4.

End point values	Group 3	Group 4		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	13		
Units: Participants				
Participants with any adverse event	8	11		

Statistical analyses

No statistical analyses for this end point

Secondary: Presence/absence of reflux esophagitis relapse from Week 8 to Week 52

End point title	Presence/absence of reflux esophagitis relapse from Week 8 to Week 52 ^[9]
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End point description:

Presence/absence of reflux esophagitis relapse from 8 to 52 weeks for participants who continued the study treatment after Week 32 by assessment of the composite endpoint (reflux esophagitis-related symptoms or optional esophagogastroduodenoscopy findings) during the maintenance therapy.

End point type Secondary

End point timeframe:

8 to 52 weeks

Notes:

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: This endpoint was applied only for Group 1 and Group 2.

End point values	Group 1	Group 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	16		
Units: Participants				
Presence of reflux esophagitis relapse	1	4		
Absence of reflux esophagitis relapse	5	12		

Statistical analyses

No statistical analyses for this end point

Secondary: Presence/absence of gastric ulcer or duodenal ulcer recurrence from Week 0 to Week 52

End point title Presence/absence of gastric ulcer or duodenal ulcer recurrence from Week 0 to Week 52^[10]

End point description:

Presence/absence of gastric ulcer or duodenal ulcer recurrence from 0 to 52 weeks for participants who continued the study treatment after Week 32 by assessment of the composite endpoint (gastric ulcer or duodenal ulcer-related symptoms or optional esophagogastroduodenoscopy findings) during the prevention therapy.

End point type Secondary

End point timeframe:

0 to 52 weeks

Notes:

[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This endpoint was applied only for Group 3 and Group 4.

End point values	Group 3	Group 4		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	7		
Units: Participants				
Presence of GU or DU recurrence	1	0		
Absence of GU or DU recurrence	5	7		

Statistical analyses

No statistical analyses for this end point

Secondary: Adverse events during reflux esophagitis maintenance therapy from Week 8 to Week 52

End point title	Adverse events during reflux esophagitis maintenance therapy from Week 8 to Week 52 ^[11]
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End point description:

Maintenance therapy for healed reflux esophagitis study part:

Safety from 8 to 52 weeks for participants who continued the study treatment after Week 32. Number of participants with any adverse event during the period

End point type	Secondary
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End point timeframe:

8 to 52 weeks

Notes:

[11] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This endpoint was applied only for Group 1 and Group 2.

End point values	Group 1	Group 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	16		
Units: Participants				
Participants with any adverse event	6	15		

Statistical analyses

No statistical analyses for this end point

Secondary: Adverse events during gastric ulcer or duodenal ulcer recurrence prevention therapy from Week 0 to Week 52

End point title	Adverse events during gastric ulcer or duodenal ulcer recurrence prevention therapy from Week 0 to Week 52 ^[12]
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End point description:

Prevention of gastric ulcer or duodenal ulcer recurrence associated with long term non-steroidal anti-inflammatory drugs or low-dose aspirin therapy study part:

Safety from 0 to 52 weeks for participants who continued the study treatment after Week 32. Number of participants with any adverse event

End point type	Secondary
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End point timeframe:

0 to 52 weeks

Notes:

[12] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This endpoint was applied only for Group 3 and Group 4.

End point values	Group 3	Group 4		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	7		
Units: Participants				
Participants with any adverse event	6	6		

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 52 weeks or withdrawal. Other adverse events were collected from the start of investigational drug administration to 52 weeks or withdrawal.

Adverse event reporting additional description:

For Group 1 and 2, only adverse events that occurred after the start of the maintenance therapy, that is, Week 8 were summarized. For Group 3 and 4, all adverse events that occurred after the start of the prevention therapy period were summarized.

Assessment type	Non-systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	25.1
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Reporting groups

Reporting group title	Group 1
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Reporting group description:

Maintenance of healing for reflux esophagitis, Initial healing phase (8 weeks), D961H 10 mg once-daily; Maintenance phase (24 or 44 weeks), D961H 10 mg once-daily, Body weight<20 kg

Reporting group title	Group 4
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Reporting group description:

Prevention of recurrence for gastric and/or duodenal ulcer, D961H starts with 10 mg once-daily, and may be increased to 20 mg once-daily based on investigator's discretion (32 or 52 weeks), Body weight≥20 kg

Reporting group title	Group 3
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Reporting group description:

Prevention of recurrence for gastric ulcer and/or duodenal ulcer, D961H 10 mg once-daily (32 or 52 weeks), Body weight<20 kg

Reporting group title	Group 2
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Reporting group description:

Maintenance of healing for reflux esophagitis, Initial healing phase (8 weeks), D961H 20 mg once-daily; Maintenance phase (24 or 44 weeks) starts with D961H 10 mg once-daily and may be increased to 20 mg once-daily based on investigator's discretion, Body weight≥20 kg

Serious adverse events	Group 1	Group 4	Group 3
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 7 (0.00%)	2 / 13 (15.38%)	3 / 9 (33.33%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Vascular disorders			
Polyarteritis nodosa			
subjects affected / exposed	0 / 7 (0.00%)	1 / 13 (7.69%)	0 / 9 (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
Congenital, familial and genetic disorders			

Pulmonary artery atresia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 13 (0.00%)	1 / 9 (11.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Cyclic vomiting syndrome			
subjects affected / exposed	0 / 7 (0.00%)	0 / 13 (0.00%)	1 / 9 (11.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Skin ulcer			
subjects affected / exposed	0 / 7 (0.00%)	1 / 13 (7.69%)	0 / 9 (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
Musculoskeletal and connective tissue disorders			
Chronic recurrent multifocal osteomyelitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 13 (0.00%)	1 / 9 (11.11%)
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			
Campylobacter gastroenteritis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 13 (0.00%)	1 / 9 (11.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Otitis media acute			
subjects affected / exposed	0 / 7 (0.00%)	1 / 13 (7.69%)	0 / 9 (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
Serious adverse events	Group 2		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 20 (5.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			

Vascular disorders Polyarteritis nodosa subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 20 (0.00%)		
	0 / 0		
	0 / 0		
Congenital, familial and genetic disorders Pulmonary artery atresia subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 20 (0.00%)		
	0 / 0		
	0 / 0		
Gastrointestinal disorders Cyclic vomiting syndrome subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 20 (0.00%)		
	0 / 0		
	0 / 0		
Skin and subcutaneous tissue disorders Skin ulcer subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 20 (0.00%)		
	0 / 0		
	0 / 0		
Musculoskeletal and connective tissue disorders Chronic recurrent multifocal osteomyelitis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 20 (0.00%)		
	0 / 0		
	0 / 0		
Infections and infestations Campylobacter gastroenteritis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all Otitis media acute subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	1 / 20 (5.00%)		
	0 / 1		
	0 / 0		
	0 / 20 (0.00%)		
	0 / 0		
	0 / 0		

Frequency threshold for reporting non-serious adverse events: 3 %

Non-serious adverse events	Group 1	Group 4	Group 3
Total subjects affected by non-serious adverse events			
subjects affected / exposed	7 / 7 (100.00%)	11 / 13 (84.62%)	9 / 9 (100.00%)
Vascular disorders			
Haematoma			
subjects affected / exposed	1 / 7 (14.29%)	0 / 13 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 7 (14.29%)	0 / 13 (0.00%)	2 / 9 (22.22%)
occurrences (all)	1	0	2
Peripheral swelling			
subjects affected / exposed	0 / 7 (0.00%)	0 / 13 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	0 / 7 (0.00%)	1 / 13 (7.69%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Food allergy			
subjects affected / exposed	0 / 7 (0.00%)	0 / 13 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Drug hypersensitivity			
subjects affected / exposed	0 / 7 (0.00%)	1 / 13 (7.69%)	0 / 9 (0.00%)
occurrences (all)	0	13	0
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 7 (0.00%)	0 / 13 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Bronchitis chronic			

subjects affected / exposed	0 / 7 (0.00%)	1 / 13 (7.69%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Upper respiratory tract inflammation			
subjects affected / exposed	0 / 7 (0.00%)	1 / 13 (7.69%)	0 / 9 (0.00%)
occurrences (all)	0	2	0
Rhinitis allergic			
subjects affected / exposed	0 / 7 (0.00%)	0 / 13 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Oropharyngeal pain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 13 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Cough			
subjects affected / exposed	0 / 7 (0.00%)	0 / 13 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	2
Psychiatric disorders			
Insomnia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 13 (7.69%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Agitation			
subjects affected / exposed	0 / 7 (0.00%)	0 / 13 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Restlessness			
subjects affected / exposed	0 / 7 (0.00%)	1 / 13 (7.69%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Investigations			
Hepatic enzyme increased			
subjects affected / exposed	0 / 7 (0.00%)	1 / 13 (7.69%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 7 (0.00%)	0 / 13 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Fall			
subjects affected / exposed	0 / 7 (0.00%)	1 / 13 (7.69%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Heat stroke			

subjects affected / exposed	0 / 7 (0.00%)	1 / 13 (7.69%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Traumatic haematoma			
subjects affected / exposed	0 / 7 (0.00%)	1 / 13 (7.69%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Wound			
subjects affected / exposed	1 / 7 (14.29%)	0 / 13 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Spinal compression fracture			
subjects affected / exposed	0 / 7 (0.00%)	1 / 13 (7.69%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Nail injury			
subjects affected / exposed	0 / 7 (0.00%)	0 / 13 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Ligament sprain			
subjects affected / exposed	1 / 7 (14.29%)	0 / 13 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Thermal burn			
subjects affected / exposed	2 / 7 (28.57%)	0 / 13 (0.00%)	0 / 9 (0.00%)
occurrences (all)	2	0	0
Nervous system disorders			
Migraine			
subjects affected / exposed	0 / 7 (0.00%)	1 / 13 (7.69%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Orthostatic intolerance			
subjects affected / exposed	0 / 7 (0.00%)	1 / 13 (7.69%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Somnolence			
subjects affected / exposed	0 / 7 (0.00%)	0 / 13 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Headache			
subjects affected / exposed	0 / 7 (0.00%)	0 / 13 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Iron deficiency anaemia			

subjects affected / exposed	0 / 7 (0.00%)	1 / 13 (7.69%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Neutropenia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 13 (7.69%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Ear and labyrinth disorders			
Motion sickness			
subjects affected / exposed	1 / 7 (14.29%)	0 / 13 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Eye disorders			
Accommodation disorder			
subjects affected / exposed	0 / 7 (0.00%)	1 / 13 (7.69%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Conjunctivitis allergic			
subjects affected / exposed	0 / 7 (0.00%)	1 / 13 (7.69%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal disorders			
Chronic gastritis			
subjects affected / exposed	0 / 7 (0.00%)	1 / 13 (7.69%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Abdominal distension			
subjects affected / exposed	1 / 7 (14.29%)	0 / 13 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Abdominal pain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 13 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Acetonaemic vomiting			
subjects affected / exposed	0 / 7 (0.00%)	0 / 13 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Enterocolitis			
subjects affected / exposed	1 / 7 (14.29%)	0 / 13 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Diarrhoea			
subjects affected / exposed	0 / 7 (0.00%)	0 / 13 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Dental caries			

subjects affected / exposed	0 / 7 (0.00%)	1 / 13 (7.69%)	1 / 9 (11.11%)
occurrences (all)	0	1	1
Constipation			
subjects affected / exposed	1 / 7 (14.29%)	0 / 13 (0.00%)	1 / 9 (11.11%)
occurrences (all)	1	0	1
Colitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 13 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Eosinophilic oesophagitis			
subjects affected / exposed	1 / 7 (14.29%)	0 / 13 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Irritable bowel syndrome			
subjects affected / exposed	0 / 7 (0.00%)	0 / 13 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Vomiting			
subjects affected / exposed	1 / 7 (14.29%)	1 / 13 (7.69%)	2 / 9 (22.22%)
occurrences (all)	1	3	2
Stomatitis			
subjects affected / exposed	0 / 7 (0.00%)	1 / 13 (7.69%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Malpositioned teeth			
subjects affected / exposed	0 / 7 (0.00%)	0 / 13 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Skin and subcutaneous tissue disorders			
Dermatitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 13 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Acne			
subjects affected / exposed	0 / 7 (0.00%)	0 / 13 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Ingrowing nail			
subjects affected / exposed	0 / 7 (0.00%)	1 / 13 (7.69%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Miliaria			
subjects affected / exposed	0 / 7 (0.00%)	0 / 13 (0.00%)	2 / 9 (22.22%)
occurrences (all)	0	0	2

Rash			
subjects affected / exposed	0 / 7 (0.00%)	0 / 13 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Urticaria			
subjects affected / exposed	0 / 7 (0.00%)	1 / 13 (7.69%)	2 / 9 (22.22%)
occurrences (all)	0	1	2
Dry skin			
subjects affected / exposed	0 / 7 (0.00%)	1 / 13 (7.69%)	1 / 9 (11.11%)
occurrences (all)	0	1	1
Musculoskeletal and connective tissue disorders			
Chronic recurrent multifocal osteomyelitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 13 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Back pain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 13 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Arthralgia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 13 (7.69%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Ankylosing spondylitis			
subjects affected / exposed	0 / 7 (0.00%)	1 / 13 (7.69%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Myalgia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 13 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Mixed connective tissue disease			
subjects affected / exposed	0 / 7 (0.00%)	1 / 13 (7.69%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Osteoporosis			
subjects affected / exposed	0 / 7 (0.00%)	1 / 13 (7.69%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Rheumatoid nodule			
subjects affected / exposed	0 / 7 (0.00%)	1 / 13 (7.69%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Infections and infestations			

Conjunctivitis			
subjects affected / exposed	1 / 7 (14.29%)	0 / 13 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Bronchitis mycoplasmal			
subjects affected / exposed	0 / 7 (0.00%)	0 / 13 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Bronchitis			
subjects affected / exposed	2 / 7 (28.57%)	0 / 13 (0.00%)	1 / 9 (11.11%)
occurrences (all)	6	0	1
Acute haemorrhagic conjunctivitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 13 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Cystitis			
subjects affected / exposed	0 / 7 (0.00%)	1 / 13 (7.69%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Herpangina			
subjects affected / exposed	0 / 7 (0.00%)	0 / 13 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Herpes zoster			
subjects affected / exposed	0 / 7 (0.00%)	1 / 13 (7.69%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Dermatitis infected			
subjects affected / exposed	0 / 7 (0.00%)	0 / 13 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Erythema infectiosum			
subjects affected / exposed	1 / 7 (14.29%)	0 / 13 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Gastroenteritis			
subjects affected / exposed	1 / 7 (14.29%)	0 / 13 (0.00%)	3 / 9 (33.33%)
occurrences (all)	1	0	4
Hand-foot-and-mouth disease			
subjects affected / exposed	0 / 7 (0.00%)	0 / 13 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	6 / 7 (85.71%)	4 / 13 (30.77%)	2 / 9 (22.22%)
occurrences (all)	12	16	9

Molluscum contagiosum			
subjects affected / exposed	1 / 7 (14.29%)	0 / 13 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Influenza			
subjects affected / exposed	2 / 7 (28.57%)	3 / 13 (23.08%)	0 / 9 (0.00%)
occurrences (all)	2	3	0
Hordeolum			
subjects affected / exposed	0 / 7 (0.00%)	0 / 13 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Pneumonia mycoplasmal			
subjects affected / exposed	0 / 7 (0.00%)	0 / 13 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Otitis media acute			
subjects affected / exposed	0 / 7 (0.00%)	0 / 13 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Paronychia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 13 (7.69%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Pharyngitis			
subjects affected / exposed	3 / 7 (42.86%)	3 / 13 (23.08%)	2 / 9 (22.22%)
occurrences (all)	6	3	6
Otitis media			
subjects affected / exposed	0 / 7 (0.00%)	0 / 13 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Skin candida			
subjects affected / exposed	0 / 7 (0.00%)	0 / 13 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Skin bacterial infection			
subjects affected / exposed	0 / 7 (0.00%)	1 / 13 (7.69%)	0 / 9 (0.00%)
occurrences (all)	0	2	0
Sinusitis			
subjects affected / exposed	1 / 7 (14.29%)	0 / 13 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Respiratory syncytial virus infection			
subjects affected / exposed	0 / 7 (0.00%)	0 / 13 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1

Skin infection			
subjects affected / exposed	0 / 7 (0.00%)	0 / 13 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Viral infection			
subjects affected / exposed	0 / 7 (0.00%)	1 / 13 (7.69%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Varicella			
subjects affected / exposed	1 / 7 (14.29%)	0 / 13 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Upper respiratory tract infection			
subjects affected / exposed	0 / 7 (0.00%)	1 / 13 (7.69%)	2 / 9 (22.22%)
occurrences (all)	0	1	2
Tonsillitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 13 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Streptococcal infection			
subjects affected / exposed	0 / 7 (0.00%)	0 / 13 (0.00%)	2 / 9 (22.22%)
occurrences (all)	0	0	2
Metabolism and nutrition disorders			
Vitamin K deficiency			
subjects affected / exposed	0 / 7 (0.00%)	0 / 13 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Zinc deficiency			
subjects affected / exposed	0 / 7 (0.00%)	0 / 13 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Group 2		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	17 / 20 (85.00%)		
Vascular disorders			
Haematoma			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences (all)	0		
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		

Peripheral swelling subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1		
Immune system disorders Seasonal allergy subjects affected / exposed occurrences (all)	2 / 20 (10.00%) 2		
Food allergy subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1		
Drug hypersensitivity subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0		
Respiratory, thoracic and mediastinal disorders Asthma subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1		
Bronchitis chronic subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0		
Upper respiratory tract inflammation subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 5		
Rhinitis allergic subjects affected / exposed occurrences (all)	2 / 20 (10.00%) 2		
Oropharyngeal pain subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1		
Cough subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0		
Psychiatric disorders Insomnia subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0		

Agitation subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1		
Restlessness subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0		
Investigations Hepatic enzyme increased subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0		
Injury, poisoning and procedural complications Contusion subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1		
Fall subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0		
Heat stroke subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0		
Traumatic haematoma subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0		
Wound subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0		
Spinal compression fracture subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0		
Nail injury subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1		
Ligament sprain subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1		
Thermal burn			

subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0		
Nervous system disorders			
Migraine			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences (all)	0		
Orthostatic intolerance			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Somnolence			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Headache			
subjects affected / exposed	3 / 20 (15.00%)		
occurrences (all)	7		
Blood and lymphatic system disorders			
Iron deficiency anaemia			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences (all)	0		
Neutropenia			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences (all)	0		
Ear and labyrinth disorders			
Motion sickness			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences (all)	0		
Eye disorders			
Accommodation disorder			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences (all)	0		
Conjunctivitis allergic			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders			
Chronic gastritis			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		

Abdominal distension			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences (all)	0		
Abdominal pain			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Acetonaemic vomiting			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Enterocolitis			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences (all)	0		
Diarrhoea			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Dental caries			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences (all)	0		
Constipation			
subjects affected / exposed	5 / 20 (25.00%)		
occurrences (all)	5		
Colitis			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Eosinophilic oesophagitis			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences (all)	0		
Irritable bowel syndrome			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Vomiting			
subjects affected / exposed	2 / 20 (10.00%)		
occurrences (all)	2		
Stomatitis			
subjects affected / exposed	2 / 20 (10.00%)		
occurrences (all)	2		

Malpositioned teeth subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0		
Skin and subcutaneous tissue disorders			
Dermatitis subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1		
Acne subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1		
Ingrowing nail subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0		
Miliaria subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0		
Rash subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0		
Urticaria subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 2		
Dry skin subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0		
Musculoskeletal and connective tissue disorders			
Chronic recurrent multifocal osteomyelitis subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0		
Back pain subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1		
Arthralgia subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0		
Ankylosing spondylitis			

subjects affected / exposed	0 / 20 (0.00%)		
occurrences (all)	0		
Myalgia			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Mixed connective tissue disease			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences (all)	0		
Osteoporosis			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences (all)	0		
Rheumatoid nodule			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences (all)	0		
Infections and infestations			
Conjunctivitis			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Bronchitis mycoplasmal			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences (all)	0		
Bronchitis			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences (all)	0		
Acute haemorrhagic conjunctivitis			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences (all)	0		
Cystitis			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences (all)	0		
Herpangina			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences (all)	0		
Herpes zoster			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences (all)	0		

Dermatitis infected			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Erythema infectiosum			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences (all)	0		
Gastroenteritis			
subjects affected / exposed	5 / 20 (25.00%)		
occurrences (all)	5		
Hand-foot-and-mouth disease			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Nasopharyngitis			
subjects affected / exposed	5 / 20 (25.00%)		
occurrences (all)	10		
Molluscum contagiosum			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences (all)	0		
Influenza			
subjects affected / exposed	2 / 20 (10.00%)		
occurrences (all)	2		
Hordeolum			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences (all)	0		
Pneumonia mycoplasmal			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Otitis media acute			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences (all)	0		
Paronychia			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences (all)	0		
Pharyngitis			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences (all)	0		

Otitis media			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Skin candida			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Skin bacterial infection			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences (all)	0		
Sinusitis			
subjects affected / exposed	2 / 20 (10.00%)		
occurrences (all)	3		
Respiratory syncytial virus infection			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences (all)	0		
Skin infection			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Viral infection			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences (all)	0		
Varicella			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Upper respiratory tract infection			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	3		
Tonsillitis			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Streptococcal infection			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Metabolism and nutrition disorders			
Vitamin K deficiency			

subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Zinc deficiency			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

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

Notes: