



## Clinical trial results: Efficacy and Safety of Fumaric Acid Esters (Fumaderm®) in the Treatment of Patients with Cutaneous Lupus Erythematosus: A Mono- Centre, Open-Label, Prospective Pilot Study

### Summary

EudraCT number	2010-023645-29
Trial protocol	DE
Global end of trial date	12 February 2014

### Results information

Result version number	v1 (current)
This version publication date	11 January 2022
First version publication date	11 January 2022

### Trial information

#### Trial identification

Sponsor protocol code	UKM 10_0020
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#### Additional study identifiers

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

Notes:

### Sponsors

Sponsor organisation name	Universitätsklinikum Münster
Sponsor organisation address	Albert-Schweitzer-Campus 1, Münster, Germany, 48149
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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	24 October 2013
Is this the analysis of the primary completion data?	Yes
Primary completion date	24 October 2013
Global end of trial reached?	Yes
Global end of trial date	12 February 2014
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

The main objective of the trial was to evaluate the therapeutic effect of fumaric acid esters (Fumaderm®) in the treatment of Cutaneous Lupus Erythematosus (CLE) with respect to proportion of responders based on the Revised Cutaneous Lupus Disease Area and Severity Index (RCLASI) activity score for skin lesions at baseline and after 24 weeks of treatment or at the latest assessment for patients who withdrew prematurely (Last Observation Carried Forward, LOCF).

Protection of trial subjects:

The study was conducted in accordance with the Declaration of Helsinki and the ICH Guidelines in Good Clinical Practice. The study was not started before the competent ethics committee had given a favorable opinion. Written informed consent was obtained from all patients and the study was only conducted as approved by the Ethics committee and the competent authority. Amendments were only implemented after approval.

Background therapy:

Throughout the trial, daily use of sunscreen (sun protection factor, SPF $\geq$ 50) was recommended to all patients. The management of CLE could also involve the use of topical medications, such as topical steroids, or systemic rescue medications, such as antimalarials.

Evidence for comparator: -

Actual start date of recruitment	11 July 2011
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	1 Months
Independent data monitoring committee (IDMC) involvement?	No

Notes:

## Population of trial subjects

### Subjects enrolled per country

Country: Number of subjects enrolled	Germany: 11
Worldwide total number of subjects	11
EEA total number of subjects	11

Notes:

### Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0

Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	11
From 65 to 84 years	0
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details:

Patients were recruited in the Department of Dermatology at the University of Muenster in Germany. The recruitment period was from July 2011 to October 2013.

### Pre-assignment

Screening details:

11 patients with a clinically and histologically confirmed diagnosis of CLE refractory to topical corticosteroids were included in the study.

### Period 1

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

### Arms

<b>Arm title</b>	Fumaric acid ester
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Arm description:

Patients who received study treatment with fumaric acid ester (Fumaderm®).

Arm type	Experimental
Investigational medicinal product name	Fumaderm®
Investigational medicinal product code	
Other name	Fumaric acid ester
Pharmaceutical forms	Gastro-resistant tablet
Routes of administration	Oral use

Dosage and administration details:

Patients were treated for 24 weeks with fumaric acid ester (Fumaderm®). Study treatment was started with one tablet of Fumaderm® initial (30mg dimethylfumarate and 75mg monoethylfumarate salts) per day and was stepwise increased weekly (during nine weeks) up to six tablets Fumaderm® (120 mg dimethylfumarate and 95 mg monoethylfumarate salts) per day. In case of side effects, the dose was adapted to the highest tolerable level.

<b>Number of subjects in period 1</b>	Fumaric acid ester
Started	11
Completed	11

## Baseline characteristics

### Reporting groups

Reporting group title	Treatment period
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Reporting group description: -

Reporting group values	Treatment period	Total	
Number of subjects	11	11	
Age categorical			
Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	11	11	
From 65-84 years	0	0	
85 years and over	0	0	
Gender categorical			
Units: Subjects			
Female	7	7	
Male	4	4	

## End points

### End points reporting groups

Reporting group title	Fumaric acid ester
Reporting group description: Patients who received study treatment with fumaric acid ester (Fumaderm®).	
Subject analysis set title	Week 0
Subject analysis set type	Intention-to-treat
Subject analysis set description: Patients treated with fumaric acid ester who were examined before starting therapy (week 0).	
Subject analysis set title	Week 12
Subject analysis set type	Intention-to-treat
Subject analysis set description: Patients treated with fumaric acid ester who were examined during therapy (week 12).	
Subject analysis set title	Week 24
Subject analysis set type	Intention-to-treat
Subject analysis set description: Patients treated with fumaric acid ester who were examined during therapy (week 24).	
Subject analysis set title	Week 28
Subject analysis set type	Intention-to-treat
Subject analysis set description: Patients treated with fumaric acid ester who were examined 4 weeks after end of study treatment (week 28, Follow up).	

### Primary: RCLASI activity score for skin lesions

End point title	RCLASI activity score for skin lesions
End point description: Efficacy of fumaric acid ester on disease severity as evaluated by RCLASI activity score for skin lesions.	
End point type	Primary
End point timeframe: Week 0, 12, 24 and 28	

End point values	Week 0	Week 12	Week 24	Week 28
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	11	9	11	11
Units: Activity score				
arithmetic mean (standard deviation)	14.8 (± 6.7)	9.4 (± 5.2)	9.5 (± 6.1)	9.9 (± 4.2)

### Statistical analyses

Statistical analysis title	RCLASI activity score skin lesions - week 0 vs 12
Statistical analysis description: As this study was an exploratory study, all inferential statistics were exploratory (hypotheses generating), not confirmatory, and were interpreted accordingly; i.e. p values are interpreted as a metric weight of evidence against the respective null hypothesis of no effect/ no difference. No adjustment for multiple testing was performed.	

Comparison groups	Week 0 v Week 12
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.002 <sup>[1]</sup>
Method	t-test for paired data

Notes:

[1] - The inferential analyses were carried out by means of student's t-tests for paired data.

<b>Statistical analysis title</b>	RCLASI activity score skin lesions - week 0 vs 24
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Statistical analysis description:

As this study was an exploratory study, all inferential statistics were exploratory (hypotheses generating), not confirmatory, and were interpreted accordingly; i.e. p values are interpreted as a metric weight of evidence against the respective null hypothesis of no effect/ no difference. No adjustment for multiple testing was performed.

Comparison groups	Week 0 v Week 24
Number of subjects included in analysis	22
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.009 <sup>[2]</sup>
Method	t-test for paired data

Notes:

[2] - The inferential analyses were carried out by means of student's t-tests for paired data.

<b>Statistical analysis title</b>	RCLASI activity score skin lesions - week 0 vs 28
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Statistical analysis description:

As this study was an exploratory study, all inferential statistics were exploratory (hypotheses generating), not confirmatory, and were interpreted accordingly; i.e. p values are interpreted as a metric weight of evidence against the respective null hypothesis of no effect/ no difference. No adjustment for multiple testing was performed.

Comparison groups	Week 0 v Week 28
Number of subjects included in analysis	22
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.01 <sup>[3]</sup>
Method	t-test for paired data

Notes:

[3] - The inferential analyses were carried out by means of student's t-tests for paired data.

### Secondary: RCLASI activity score total

End point title	RCLASI activity score total
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End point description:

Efficacy of fumaric acid ester on disease severity as evaluated by total RCLASI activity score.

End point type	Secondary
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End point timeframe:

Week 0, 12, 24 and 28

End point values	Week 0	Week 12	Week 24	Week 28
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	11	9	11	11
Units: Activity score				
arithmetic mean (standard deviation)	15.5 (± 5.3)	9.9 (± 4.9)	10.1 (± 6.6)	10.5 (± 4.6)

## Statistical analyses

<b>Statistical analysis title</b>	RCLASI activity score total - week 0 vs week 12
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Statistical analysis description:

As this study was an exploratory study, all inferential statistics were exploratory (hypotheses generating), not confirmatory, and were interpreted accordingly; i.e. p values are interpreted as a metric weight of evidence against the respective null hypothesis of no effect/ no difference. No adjustment for multiple testing was performed.

Comparison groups	Week 0 v Week 12
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.002 [4]
Method	t-test for paired data

Notes:

[4] - The inferential analyses were carried out by means of student's t-tests for paired data.

<b>Statistical analysis title</b>	RCLASI activity score total - week 0 vs week 24
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Statistical analysis description:

As this study was an exploratory study, all inferential statistics were exploratory (hypotheses generating), not confirmatory, and were interpreted accordingly; i.e. p values are interpreted as a metric weight of evidence against the respective null hypothesis of no effect/ no difference. No adjustment for multiple testing was performed.

Comparison groups	Week 0 v Week 24
Number of subjects included in analysis	22
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.009 [5]
Method	t-test for paired data

Notes:

[5] - The inferential analyses were carried out by means of student's t-tests for paired data.

<b>Statistical analysis title</b>	RCLASI activity score total - week 0 vs week 28
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Statistical analysis description:

As this study was an exploratory study, all inferential statistics were exploratory (hypotheses generating), not confirmatory, and were interpreted accordingly; i.e. p values are interpreted as a metric weight of evidence against the respective null hypothesis of no effect/ no difference. No adjustment for multiple testing was performed.

Comparison groups	Week 0 v Week 28
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Number of subjects included in analysis	22
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.01 [6]
Method	t-test for paired data

Notes:

[6] - The inferential analyses were carried out by means of student's t-tests for paired data.

### Secondary: RCLASI damage score total

End point title	RCLASI damage score total
End point description:	Efficacy of fumaric acid ester on disease severity as evaluated by total RCLASI damage score.
End point type	Secondary
End point timeframe:	Week 0, 12, 24 and 28

End point values	Week 0	Week 12	Week 24	Week 28
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	11	9	11	11
Units: Activity score				
arithmetic mean (standard deviation)	5.7 (± 2.9)	4.4 (± 1.7)	4.9 (± 3.6)	4.2 (± 3.7)

### Statistical analyses

<b>Statistical analysis title</b>	RCLASI damage score total - week 0 vs week 12
Statistical analysis description:	As this study was an exploratory study, all inferential statistics were exploratory (hypotheses generating), not confirmatory, and were interpreted accordingly; i.e. p values are interpreted as a metric weight of evidence against the respective null hypothesis of no effect/ no difference. No adjustment for multiple testing was performed.
Comparison groups	Week 0 v Week 12
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3 [7]
Method	t-test for paired data

Notes:

[7] - The inferential analyses were carried out by means of student's t-tests for paired data.

<b>Statistical analysis title</b>	RCLASI damage score total - week 0 vs week 24
Statistical analysis description:	As this study was an exploratory study, all inferential statistics were exploratory (hypotheses generating), not confirmatory, and were interpreted accordingly; i.e. p values are interpreted as a metric weight of evidence against the respective null hypothesis of no effect/ no difference. No adjustment for multiple testing was performed.
Comparison groups	Week 0 v Week 24

Number of subjects included in analysis	22
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3 [8]
Method	t-test for paired data

Notes:

[8] - The inferential analyses were carried out by means of student's t-tests for paired data.

<b>Statistical analysis title</b>	RCLASI damage score total - week 0 vs week 28
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Statistical analysis description:

As this study was an exploratory study, all inferential statistics were exploratory (hypotheses generating), not confirmatory, and were interpreted accordingly; i.e. p values are interpreted as a metric weight of evidence against the respective null hypothesis of no effect/ no difference. No adjustment for multiple testing was performed.

Comparison groups	Week 0 v Week 28
Number of subjects included in analysis	22
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.07 [9]
Method	t-test for paired data

Notes:

[9] - The inferential analyses were carried out by means of student's t-tests for paired data.

### Secondary: VAS score for itch

End point title	VAS score for itch
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End point description:

Efficacy of fumaric acid ester on disease severity as evaluated by patient assessment score VAS (Visual Analogue Scale) for itch.

End point type	Secondary
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End point timeframe:

Week 0, 12 and 24

End point values	Week 0	Week 12	Week 24	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	10	9	11	
Units: VAS score				
arithmetic mean (standard deviation)	5.0 (± 3.2)	2.1 (± 1.8)	3.3 (± 2.7)	

### Statistical analyses

<b>Statistical analysis title</b>	VAS score for itch - week 0 vs week 12
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Statistical analysis description:

As this study was an exploratory study, all inferential statistics were exploratory (hypotheses generating), not confirmatory, and were interpreted accordingly; i.e. p values are interpreted as a metric weight of evidence against the respective null hypothesis of no effect/ no difference. No adjustment for multiple testing was performed.

Comparison groups	Week 0 v Week 12
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Number of subjects included in analysis	19
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.03 <sup>[10]</sup>
Method	t-test for paired data

Notes:

[10] - The inferential analyses were carried out by means of student's t-tests for paired data.

<b>Statistical analysis title</b>	VAS score for itch - week 0 vs week 24
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Statistical analysis description:

As this study was an exploratory study, all inferential statistics were exploratory (hypotheses generating), not confirmatory, and were interpreted accordingly; i.e. p values are interpreted as a metric weight of evidence against the respective null hypothesis of no effect/ no difference. No adjustment for multiple testing was performed.

Comparison groups	Week 0 v Week 24
Number of subjects included in analysis	21
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.06 <sup>[11]</sup>
Method	t-test for paired data

Notes:

[11] - The inferential analyses were carried out by means of student's t-tests for paired data.

### Secondary: VAS score for pain

End point title	VAS score for pain
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End point description:

Efficacy of fumaric acid ester on disease severity as evaluated by patient assessment score VAS for pain.

End point type	Secondary
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End point timeframe:

Week 0, 12 and 24

End point values	Week 0	Week 12	Week 24	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	10	9	11	
Units: VAS score				
arithmetic mean (standard deviation)	3.4 (± 3.4)	2.0 (± 2.7)	2.4 (± 2.2)	

### Statistical analyses

<b>Statistical analysis title</b>	VAS score for pain - week 0 vs week 12
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Statistical analysis description:

As this study was an exploratory study, all inferential statistics were exploratory (hypotheses generating), not confirmatory, and were interpreted accordingly; i.e. p values are interpreted as a metric weight of evidence against the respective null hypothesis of no effect/ no difference. No adjustment for multiple testing was performed.

Comparison groups	Week 0 v Week 12
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Number of subjects included in analysis	19
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.05
Method	t-test for paired data

<b>Statistical analysis title</b>	VAS score for pain - week 0 vs week 24
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Statistical analysis description:

As this study was an exploratory study, all inferential statistics were exploratory (hypotheses generating), not confirmatory, and were interpreted accordingly; i.e. p values are interpreted as a metric weight of evidence against the respective null hypothesis of no effect/ no difference. No adjustment for multiple testing was performed.

Comparison groups	Week 0 v Week 24
Number of subjects included in analysis	21
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4
Method	t-test for paired data

## Secondary: PAGI Score

End point title	PAGI Score
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End point description:

Efficacy of fumaric acid ester on disease severity as evaluated by patient assessment score PAGI (Patient Assessment of Global Improvement).

End point type	Secondary
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End point timeframe:

Week 0, 12 and 24

End point values	Week 0	Week 12	Week 24	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	11	9	10	
Units: PAGI score				
arithmetic mean (standard deviation)	-0.6 (± 0.7)	1.4 (± 0.7)	1.3 (± 0.8)	

## Statistical analyses

<b>Statistical analysis title</b>	PAGI score - week 0 vs week 12
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Statistical analysis description:

As this study was an exploratory study, all inferential statistics were exploratory (hypotheses generating), not confirmatory, and were interpreted accordingly; i.e. p values are interpreted as a metric weight of evidence against the respective null hypothesis of no effect/ no difference. No adjustment for multiple testing was performed.

Comparison groups	Week 0 v Week 12
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Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0003 <sup>[12]</sup>
Method	t-test for paired data

Notes:

[12] - The inferential analyses were carried out by means of student's t-tests for paired data.

<b>Statistical analysis title</b>	PAGI score - week 0 vs week 24
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Statistical analysis description:

As this study was an exploratory study, all inferential statistics were exploratory (hypotheses generating), not confirmatory, and were interpreted accordingly; i.e. p values are interpreted as a metric weight of evidence against the respective null hypothesis of no effect/ no difference. No adjustment for multiple testing was performed.

Comparison groups	Week 0 v Week 24
Number of subjects included in analysis	21
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0007 <sup>[13]</sup>
Method	t-test for paired data

Notes:

[13] - The inferential analyses were carried out by means of student's t-tests for paired data.

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Adverse events were recorded from the time of informed consent until the final study visit.

Assessment type	Systematic
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	16.1
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### Reporting groups

Reporting group title	Safety group
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Reporting group description:

Patients who received at least one dose of fumaric acid ester (Fumaderm®).

Serious adverse events	Safety group		
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 11 (18.18%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
General disorders and administration site conditions			
Medical device pain			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Intervertebral disc protrusion			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Safety group		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	11 / 11 (100.00%)		
Investigations			

Transaminases increased subjects affected / exposed occurrences (all)	1 / 11 (9.09%) 1		
Vascular disorders Flushing subjects affected / exposed occurrences (all)	4 / 11 (36.36%) 5		
Hypertension subjects affected / exposed occurrences (all)	1 / 11 (9.09%) 1		
Cardiac disorders Palpitations subjects affected / exposed occurrences (all)	2 / 11 (18.18%) 2		
Nervous system disorders Dizziness subjects affected / exposed occurrences (all)	1 / 11 (9.09%) 1		
Headache subjects affected / exposed occurrences (all)	3 / 11 (27.27%) 6		
Gastrointestinal disorders Abdominal pain subjects affected / exposed occurrences (all)	5 / 11 (45.45%) 7		
Abdominal pain upper subjects affected / exposed occurrences (all)	1 / 11 (9.09%) 1		
Constipation subjects affected / exposed occurrences (all)	1 / 11 (9.09%) 2		
Diarrhoea subjects affected / exposed occurrences (all)	4 / 11 (36.36%) 8		
Flatulence subjects affected / exposed occurrences (all)	1 / 11 (9.09%) 1		

Gastrointestinal pain subjects affected / exposed occurrences (all)	1 / 11 (9.09%) 2		
Nausea subjects affected / exposed occurrences (all)	1 / 11 (9.09%) 1		
Vomiting subjects affected / exposed occurrences (all)	1 / 11 (9.09%) 1		
Skin and subcutaneous tissue disorders			
Pruritus subjects affected / exposed occurrences (all)	1 / 11 (9.09%) 1		
Psoriasis subjects affected / exposed occurrences (all)	1 / 11 (9.09%) 1		
Rash papular subjects affected / exposed occurrences (all)	1 / 11 (9.09%) 1		
Skin exfoliation subjects affected / exposed occurrences (all)	1 / 11 (9.09%) 1		
Musculoskeletal and connective tissue disorders			
Intervertebral disc protrusion subjects affected / exposed occurrences (all)	1 / 11 (9.09%) 1		
Infections and infestations			
Bronchitis bacterial subjects affected / exposed occurrences (all)	1 / 11 (9.09%) 1		
Ear infection subjects affected / exposed occurrences (all)	2 / 11 (18.18%) 2		
Erysipelas subjects affected / exposed occurrences (all)	1 / 11 (9.09%) 1		

Gastrointestinal infection subjects affected / exposed occurrences (all)	1 / 11 (9.09%) 1		
Helicobacter infection subjects affected / exposed occurrences (all)	1 / 11 (9.09%) 1		
Nasopharyngitis subjects affected / exposed occurrences (all)	4 / 11 (36.36%) 4		
Sinusitis subjects affected / exposed occurrences (all)	2 / 11 (18.18%) 2		
Tonsillitis subjects affected / exposed occurrences (all)	1 / 11 (9.09%) 1		
Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all)	1 / 11 (9.09%) 1		

## **More information**

### **Substantial protocol amendments (globally)**

Were there any global substantial amendments to the protocol? No

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### **Interruptions (globally)**

Were there any global interruptions to the trial? No

### **Limitations and caveats**

None reported

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### **Online references**

<http://www.ncbi.nlm.nih.gov/pubmed/27147621>