

**Clinical trial results:****A Two Part, Multi Centre, Randomized, Placebo Controlled, Double Blind Study of TRK 170 for the Treatment of Crohn's Disease****Summary**

EudraCT number	2011-000854-44
Trial protocol	SE BE NO HU NL PL CZ BG LV
Global end of trial date	15 November 2013

**Results information**

Result version number	v1 (current)
This version publication date	05 February 2016
First version publication date	05 February 2016

**Trial information****Trial identification**

Sponsor protocol code	170CDT01
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**Additional study identifiers**

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

Notes:

**Sponsors**

Sponsor organisation name	Toray Industries, Inc.
Sponsor organisation address	1-1, Nihonbashi-muromachi 2-chome, Chuo-ku, Tokyo, Japan, 103-8666
Public contact	Project leader - Anders Nilsson, TFS, +46 462801800, tfs.international@tfscro.com
Scientific contact	Project leader - Anders Nilsson, TFS, +46 462801800, tfs.international@tfscro.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	Interim
Date of interim/final analysis	15 November 2013
Is this the analysis of the primary completion data?	Yes
Primary completion date	15 November 2013
Global end of trial reached?	Yes
Global end of trial date	15 November 2013
Was the trial ended prematurely?	Yes

Notes:

## General information about the trial

Main objective of the trial:

The primary objective:

Part A

To evaluate the effect of TRK-170 on mucosal healing as measured by Crohn's Disease Endoscopic Index of Severity (CDEIS) score based on ileocolonoscopy and use this evaluation to decide which dose(s) of TRK- 170 should be used in Part B

Part B

To evaluate the efficacy of TRK-170 in patients with active CD as measured by CDAI score

After the interim analysis following completion of Part A, the decision was made not to conduct Part B

Protection of trial subjects:

Patients were given anesthetics and sedatives as premedication for the colonoscopy procedures.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	27 April 2011
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

## Population of trial subjects

### Subjects enrolled per country

Country: Number of subjects enrolled	Poland: 92
Country: Number of subjects enrolled	Sweden: 5
Country: Number of subjects enrolled	Bulgaria: 42
Country: Number of subjects enrolled	Czech Republic: 23
Country: Number of subjects enrolled	France: 4
Country: Number of subjects enrolled	Hungary: 21
Country: Number of subjects enrolled	Latvia: 9
Country: Number of subjects enrolled	Romania: 4
Country: Number of subjects enrolled	Serbia: 9
Country: Number of subjects enrolled	Ukraine: 28
Worldwide total number of subjects	237
EEA total number of subjects	200

Notes:

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**Subjects enrolled per age group**

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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)	237
From 65 to 84 years	0
85 years and over	0

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## Subject disposition

### Recruitment

Recruitment details:

Recruitment took place from 2011 to 2013.

Recruitment took place at hospitals and gastroenterology clinics in Europe.

### Pre-assignment

Screening details:

237 patients were screened of which 123 patients met the inclusion criteria and not the exclusion criteria.

### Period 1

Period 1 title	Baseline
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Investigator, Monitor, Subject, Data analyst, Carer, Assessor

Blinding implementation details:

The IP code for each patient was contained in a sealed envelope with one envelope designated for each randomized study number. No envelope was opened unless it was critical to the treatment/outcome of an AE.

All doses were administered with the same number of tablets, hence the patients were blinded both to treatment and dose.

### Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	TRK-170 12 mg

Arm description:

Dosing of TRK-170 12 mg

Arm type	Experimental
Investigational medicinal product name	TRK-170
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

12 mg oral in tablet form, twice daily for 8 weeks.

<b>Arm title</b>	TRK-170 60 mg
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Arm description:

Dosing of TRK-170 60 mg

Arm type	Experimental
Investigational medicinal product name	TRK-170
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

60 mg oral in tablet form, twice daily for 8 weeks.

<b>Arm title</b>	TRK-170 120 mg
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Arm description:

Dosing of TRK-170 120 mg

Arm type	Experimental
Investigational medicinal product name	TRK-170
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

120 mg oral in tablet form, twice daily for 8 weeks.

<b>Arm title</b>	Placebo
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Arm description:

Dosing with placebo.

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

Dosage and administration details:

Placebo, oral in tablet form, twice daily for 8 weeks.

<b>Number of subjects in period 1<sup>[1]</sup></b>	TRK-170 12 mg	TRK-170 60 mg	TRK-170 120 mg
Started	31	31	31
Completed	31	31	31

<b>Number of subjects in period 1<sup>[1]</sup></b>	Placebo
Started	30
Completed	30

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: Two subjects did not take any IMP.

## Period 2

Period 2 title	Treatment
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Blinding implementation details:

The IP code for each patient was contained in a sealed envelope with one envelope designated for each randomized study number. No envelope was to be opened unless it was critical to the treatment/outcome of an AE. All doses were to be administered with the same number of tablets, hence the patients were

blinded both to treatment and dose.

## Arms

Are arms mutually exclusive?	Yes
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<b>Arm title</b>	TRK-170 12 mg
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Arm description:

Dosing of TRK-170 12 mg

Arm type	Experimental
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Investigational medicinal product name	TRK-170
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Investigational medicinal product code	
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Other name	
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Pharmaceutical forms	Tablet
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Routes of administration	Oral use
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Dosage and administration details:

12 mg oral in tablet form, twice daily for 8 weeks.

<b>Arm title</b>	TRK-170 60 mg
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Arm description:

Dosing of TRK-170 60 mg

Arm type	Experimental
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Investigational medicinal product name	TRK-170
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Investigational medicinal product code	
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Other name	
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Pharmaceutical forms	Tablet
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Routes of administration	Oral use
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Dosage and administration details:

60 mg oral in tablet form, twice daily for 8 weeks.

<b>Arm title</b>	TRK-170 120 mg
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Arm description:

Dosing of TRK-170 120 mg

Arm type	Experimental
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Investigational medicinal product name	TRK-170
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Investigational medicinal product code	
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Other name	
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Pharmaceutical forms	Tablet
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Routes of administration	Oral use
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Dosage and administration details:

120 mg oral in tablet form, twice daily, for 8 weeks.

<b>Arm title</b>	Placebo
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Arm description:

Dosing with Placebo

Arm type	Placebo
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Investigational medicinal product name	Placebo
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Investigational medicinal product code	
----------------------------------------	--

Other name	
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Pharmaceutical forms	Tablet
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Routes of administration	Oral use
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Dosage and administration details:

Placebo oral in tablet form for 8 weeks.

<b>Number of subjects in period 2<sup>[2]</sup></b>	TRK-170 12 mg	TRK-170 60 mg	TRK-170 120 mg
Started	30	31	30
Completed	25	25	27
Not completed	5	6	3
Consent withdrawn by subject	2	2	3
disease exacerbation	-	1	-
Adverse event, non-fatal	2	2	-
violation of inclusion/exclusion criteria	-	1	-
Lost to follow-up	1	-	-

<b>Number of subjects in period 2<sup>[2]</sup></b>	Placebo
Started	30
Completed	27
Not completed	3
Consent withdrawn by subject	1
disease exacerbation	-
Adverse event, non-fatal	2
violation of inclusion/exclusion criteria	-
Lost to follow-up	-

Notes:

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

Justification: Subjects withdrew during the treatment period due to reasons specified.

## Baseline characteristics

### Reporting groups

Reporting group title	TRK-170 12 mg
Reporting group description:	
Dosing of TRK-170 12 mg	
Reporting group title	TRK-170 60 mg
Reporting group description:	
Dosing of TRK-170 60 mg	
Reporting group title	TRK-170 120 mg
Reporting group description:	
Dosing of TRK-170 120 mg	
Reporting group title	Placebo
Reporting group description:	
Dosing with placebo.	

Reporting group values	TRK-170 12 mg	TRK-170 60 mg	TRK-170 120 mg
Number of subjects	31	31	31
Age categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	31	31	31
From 65-84 years	0	0	0
85 years and over	0	0	0
Gender categorical			
Units: Subjects			
Female	13	13	14
Male	18	18	17

Reporting group values	Placebo	Total	
Number of subjects	30	123	
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)	30	123	
From 65-84 years	0	0	

85 years and over	0	0	
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Gender categorical Units: Subjects			
Female	15	55	
Male	15	68	

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### Subject analysis sets

Subject analysis set title	Safety Set
Subject analysis set type	Safety analysis

Subject analysis set description:

All randomized patients who received at least 1 dose of the study drug.

Subject analysis set title	Full Analysis Set
Subject analysis set type	Full analysis

Subject analysis set description:

All randomized patients who were diagnosed with CD, took at least 1 dose of the study drug, and had at least 1 post-baseline assessment of any efficacy data.

Reporting group values	Safety Set	Full Analysis Set	
Number of subjects	121	120	
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)	121	120	
From 65-84 years	0	0	
85 years and over	0	0	
Gender categorical Units: Subjects			
Female	54	54	
Male	67	66	

## End points

### End points reporting groups

Reporting group title	TRK-170 12 mg
Reporting group description:	
Dosing of TRK-170 12 mg	
Reporting group title	TRK-170 60 mg
Reporting group description:	
Dosing of TRK-170 60 mg	
Reporting group title	TRK-170 120 mg
Reporting group description:	
Dosing of TRK-170 120 mg	
Reporting group title	Placebo
Reporting group description:	
Dosing with placebo.	
Reporting group title	TRK-170 12 mg
Reporting group description:	
Dosing of TRK-170 12 mg	
Reporting group title	TRK-170 60 mg
Reporting group description:	
Dosing of TRK-170 60 mg	
Reporting group title	TRK-170 120 mg
Reporting group description:	
Dosing of TRK-170 120 mg	
Reporting group title	Placebo
Reporting group description:	
Dosing with Placebo	
Subject analysis set title	Safety Set
Subject analysis set type	Safety analysis
Subject analysis set description:	
All randomized patients who received at least 1 dose of the study drug.	
Subject analysis set title	Full Analysis Set
Subject analysis set type	Full analysis
Subject analysis set description:	
All randomized patients who were diagnosed with CD, took at least 1 dose of the study drug, and had at least 1 post-baseline assessment of any efficacy data.	

### Primary: CDEIS, change from baseline to end of treatment (week 8)

End point title	CDEIS, change from baseline to end of treatment (week 8)
End point description:	
CDEIS was the primary efficacy variable in Part A. The numerical change from baseline to end of treatment was analysed using analysis of covariance (ANCOVA). Model includes adjustment for baseline CDEIS.	
End point type	Primary
End point timeframe:	
Visit 2 (baseline) to Visit 6 (Week 8)	

<b>End point values</b>	TRK-170 12 mg	TRK-170 60 mg	TRK-170 120 mg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	23	21	20	24
Units: Change in CDEIS score				
arithmetic mean (standard deviation)	-1.24 (± 6.02)	-1.31 (± 4.23)	-1.73 (± 9.77)	-1.14 (± 7.73)

## Statistical analyses

<b>Statistical analysis title</b>	12mg vs placebo (FAS)
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Statistical analysis description:

ANCOVA for Change from Baseline at Week 8 in CDEIS adjusted for baseline CDIES, TRK-170 12 mg vs Placebo (FAS)

Comparison groups	TRK-170 12 mg v Placebo
Number of subjects included in analysis	47
Analysis specification	Pre-specified
Analysis type	superiority <sup>[1]</sup>
P-value	= 0.796
Method	ANCOVA

Notes:

[1] - ANCOVA for Change from Baseline at Week 8 in CDEIS adjusted for baseline CDIES, TRK-170 12 mg vs Placebo (FAS)

<b>Statistical analysis title</b>	60mg vs placebo (FAS)
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Statistical analysis description:

ANCOVA for Change from Baseline at Week 8 in CDEIS adjusted for baseline CDIES, TRK-170 60 mg vs Placebo (FAS)

Comparison groups	TRK-170 60 mg v Placebo
Number of subjects included in analysis	45
Analysis specification	Pre-specified
Analysis type	superiority <sup>[2]</sup>
P-value	= 0.917
Method	ANCOVA

Notes:

[2] - ANCOVA for Change from Baseline at Week 8 in CDEIS adjusted for baseline CDIES, TRK-170 60 mg vs Placebo (FAS)

<b>Statistical analysis title</b>	120mg vs placebo (FAS)
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Statistical analysis description:

ANCOVA for Change from Baseline at Week 8 in CDEIS adjusted for baseline CDIES, TRK-170 120 mg vs Placebo (FAS)

Comparison groups	TRK-170 120 mg v Placebo
Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	superiority <sup>[3]</sup>
P-value	= 0.311
Method	ANCOVA

Notes:

[3] - ANCOVA for Change from Baseline at Week 8 in CDEIS adjusted for baseline CDIES, TRK-170 120 mg vs Placebo (FAS)

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

All study subjects/patients were carefully monitored for the occurrence of AEs during the study period from the signing of informed consent to the completion of the follow up visit.

Adverse event reporting additional description:

The Investigator or authorized designee collected AEs with a non leading question such as "have you experienced any new health problems or worsening of existing conditions" as well as reporting events directly observed or spontaneously volunteered by patients.

Assessment type	Systematic
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### Dictionary used

Dictionary name	MedDRA
Dictionary version	16.1

### Reporting groups

Reporting group title	TRK-170 12 mg
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Reporting group description:

Dosing of TRK-170 12 mg for 8 weeks.

Reporting group title	TRK-170 60 mg
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Reporting group description:

Dosing of TRK-170 60 mg for 8 weeks.

Reporting group title	TRK-170 120 mg
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Reporting group description:

Dosing, TRK-170 120 mg for 8 weeks.

Reporting group title	Placebo
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Reporting group description:

Dosing with placebo for 8 weeks.

<b>Serious adverse events</b>	TRK-170 12 mg	TRK-170 60 mg	TRK-170 120 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 30 (6.67%)	1 / 31 (3.23%)	2 / 30 (6.67%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 30 (3.33%)	0 / 31 (0.00%)	0 / 30 (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
Crohn's disease			
subjects affected / exposed	1 / 30 (3.33%)	0 / 31 (0.00%)	0 / 30 (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

Lower gastrointestinal haemorrhage subjects affected / exposed	0 / 30 (0.00%)	0 / 31 (0.00%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
<b>Infections and infestations</b>			
Abdominal abscess subjects affected / exposed	0 / 30 (0.00%)	1 / 31 (3.23%)	0 / 30 (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

<b>Serious adverse events</b>	Placebo		
<b>Total subjects affected by serious adverse events</b>			
subjects affected / exposed	0 / 30 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
<b>Gastrointestinal disorders</b>			
Abdominal pain subjects affected / exposed	0 / 30 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Crohn's disease subjects affected / exposed	0 / 30 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Lower gastrointestinal haemorrhage subjects affected / exposed	0 / 30 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
<b>Infections and infestations</b>			
Abdominal abscess subjects affected / exposed	0 / 30 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

<b>Non-serious adverse events</b>	TRK-170 12 mg	TRK-170 60 mg	TRK-170 120 mg
Total subjects affected by non-serious adverse events subjects affected / exposed	16 / 30 (53.33%)	8 / 31 (25.81%)	11 / 30 (36.67%)
Vascular disorders Hypotension subjects affected / exposed occurrences (all)	2 / 30 (6.67%) 2	0 / 31 (0.00%) 0	0 / 30 (0.00%) 0
Nervous system disorders Headache subjects affected / exposed occurrences (all)	1 / 30 (3.33%) 1	3 / 31 (9.68%) 3	1 / 30 (3.33%) 1
General disorders and administration site conditions Pyrexia subjects affected / exposed occurrences (all)	1 / 30 (3.33%) 1	0 / 31 (0.00%) 0	0 / 30 (0.00%) 0
Gastrointestinal disorders Crohn's disease subjects affected / exposed occurrences (all)  Abdominal pain subjects affected / exposed occurrences (all)  Abdominal pain upper subjects affected / exposed occurrences (all)	3 / 30 (10.00%) 3  2 / 30 (6.67%) 3  0 / 30 (0.00%) 0	1 / 31 (3.23%) 1  0 / 31 (0.00%) 0  0 / 31 (0.00%) 0	4 / 30 (13.33%) 4  0 / 30 (0.00%) 0  0 / 30 (0.00%) 0
Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all)	2 / 30 (6.67%) 2	0 / 31 (0.00%) 0	0 / 30 (0.00%) 0

<b>Non-serious adverse events</b>	Placebo		
Total subjects affected by non-serious adverse events subjects affected / exposed	13 / 30 (43.33%)		
Vascular disorders Hypotension subjects affected / exposed occurrences (all)	0 / 30 (0.00%) 0		

Nervous system disorders Headache subjects affected / exposed occurrences (all)	0 / 30 (0.00%) 0		
General disorders and administration site conditions Pyrexia subjects affected / exposed occurrences (all)	2 / 30 (6.67%) 2		
Gastrointestinal disorders Crohn's disease subjects affected / exposed occurrences (all)  Abdominal pain subjects affected / exposed occurrences (all)  Abdominal pain upper subjects affected / exposed occurrences (all)	1 / 30 (3.33%) 1  4 / 30 (13.33%) 4  3 / 30 (10.00%) 3		
Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all)	2 / 30 (6.67%) 2		

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
11 April 2011	Incorporation of changes requested by the Swedish Medical Products Agency. Amendment took place before inclusion of patients.
20 May 2011	Clarification of language used in inclusion/exclusion criteria. Addition of a reason for withdrawal. Addition of monitoring of early neurological symptoms of any developing disorders. Amendment took place before the inclusion of any patients.
20 July 2011	Addition of vital signs assessments to Visits 3, 4, 5, and 6. Amendment took place before inclusion of any patients.
25 November 2011	To align with the tablet standards in participating countries the limit for 5-ASA was increased to 2.5 g/day. CDAI collection at Visit 2 (Day 1) and Visit 6 (Week 8) were adjusted. The amendment took place after inclusion of patients.
14 November 2013	Changes in statistical definitions. The amendment took place after inclusion of patients.

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported