

**Clinical trial results:****A Multicenter, Open-Label Study to Evaluate the Long Term Efficacy, Safety, and Tolerability of Repeated Administration of Adalimumab in Subjects With Crohn's Disease****Summary**

EudraCT number	2013-004034-15
Trial protocol	HU GB DE ES CZ IT SK DK AT BE FR
Global end of trial date	03 November 2017

**Results information**

Result version number	v1 (current)
This version publication date	31 October 2018
First version publication date	31 October 2018

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

Sponsor protocol code	M14-347
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**Additional study identifiers**

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02185014
WHO universal trial number (UTN)	-

Notes:

**Sponsors**

Sponsor organisation name	AbbVie Deutschland GmbH & Co. KG
Sponsor organisation address	AbbVie House, Vanwall Business Park, Vanwall Road, Maidenhead, Berkshire, United Kingdom, SL6-4UB
Public contact	Global Medical Services, AbbVie, 001 800-633-9110,
Scientific contact	Anne Robinson, AbbVie, anne.robinson@abbvie.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	03 November 2017
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	03 November 2017
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

The purpose of this study is to evaluate the long term efficacy, safety, and tolerability of repeated administration of adalimumab in subjects with Crohn's disease.

Protection of trial subjects:

Subject and/or his or her representative read and understood the information provided about the study and gave written permission.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	12 August 2014
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

## Population of trial subjects

### Subjects enrolled per country

Country: Number of subjects enrolled	Austria: 6
Country: Number of subjects enrolled	Belgium: 3
Country: Number of subjects enrolled	Canada: 46
Country: Number of subjects enrolled	Czech Republic: 27
Country: Number of subjects enrolled	Denmark: 4
Country: Number of subjects enrolled	France: 6
Country: Number of subjects enrolled	Germany: 9
Country: Number of subjects enrolled	Hungary: 2
Country: Number of subjects enrolled	Israel: 7
Country: Number of subjects enrolled	Italy: 12
Country: Number of subjects enrolled	Netherlands: 12
Country: Number of subjects enrolled	Poland: 22
Country: Number of subjects enrolled	Slovakia: 1
Country: Number of subjects enrolled	Switzerland: 5
Country: Number of subjects enrolled	Ukraine: 8
Country: Number of subjects enrolled	United Kingdom: 6
Country: Number of subjects enrolled	United States: 76
Worldwide total number of subjects	252
EEA total number of subjects	110

Notes:

<b>Subjects enrolled per age group</b>	
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)	245
From 65 to 84 years	7
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

Subjects who completed Study M14-115 (NCT02185014) were eligible to enroll in this study.

### Period 1

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

### Arms

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

Participants received open-label adalimumab 40 mg by subcutaneous injection every other week for 40 weeks.

Arm type	Experimental
Investigational medicinal product name	Adalimumab
Investigational medicinal product code	
Other name	Humira, ABT-D2E7
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Adalimumab pre-filled syringe, administered by subcutaneous injection

<b>Number of subjects in period 1</b>	Adalimumab
Started	252
Completed	198
Not completed	54
Requires Alternative/Prohibited Therapy	5
Not Specified	4
Adverse event	18
Subject Noncompliance	1
Withdrew consent	8
Lost to follow-up	4
Lack of efficacy	14

## Baseline characteristics

### Reporting groups

Reporting group title	Adalimumab
Reporting group description:	
Participants received open-label adalimumab 40 mg by subcutaneous injection every other week for 40 weeks.	

Reporting group values	Adalimumab	Total	
Number of subjects	252	252	
Age categorical			
Units: Subjects			
Age continuous			
Baseline characteristics from lead-in study M14-115			
Units: years			
arithmetic mean	37.5		
standard deviation	± 12.71	-	
Gender categorical			
Baseline characteristics from lead-in study M14-115			
Units: Subjects			
Female	139	139	
Male	113	113	
Ethnicity (NIH/OMB)			
Baseline characteristics from lead-in study M14-115			
Units: Subjects			
Hispanic or Latino	7	7	
Not Hispanic or Latino	0	0	
Unknown or Not Reported	245	245	
Race (NIH/OMB)			
Baseline characteristics from lead-in study M14-115			
Units: Subjects			
American Indian or Alaska Native	0	0	
Asian	10	10	
Native Hawaiian or Other Pacific Islander	0	0	
Black or African American	12	12	
White	229	229	
More than one race	1	1	
Unknown or Not Reported	0	0	
Simplified endoscopic score for crohn's disease (SES-CD) Total Score			
The SES-CD evaluates 4 endoscopic variables in 5 segments assessed during ileocolonoscopy. The SES-CD total score is the sum of the 4 endoscopic variable scores and range from 0 to 56, where higher scores indicate more severe disease. Baseline characteristics from lead-in study M14-115.			
Units: units on a scale			
arithmetic mean	14.2		
standard deviation	± 6.74	-	

## End points

### End points reporting groups

Reporting group title	Adalimumab
Reporting group description:	
Participants received open-label adalimumab 40 mg by subcutaneous injection every other week for 40 weeks.	

### Primary: Percentage of participants with endoscopic improvement at week 40 in Participants with endoscopic improvement at Week 0

End point title	Percentage of participants with endoscopic improvement at week 40 in Participants with endoscopic improvement at Week 0 <sup>[1]</sup>
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#### End point description:

Endoscopic improvement defined as a simple endoscopic score for Crohn's Disease (SES-CD) score of  $\leq 4$  and at least a 2-point reduction compared with Study M14-115 (NCT02185014) Baseline and no subscore greater than 1 in any individual endoscopic variable. The SES-CD evaluates 4 endoscopic variables (ulcer size ranging from 0 [none] to 3 [very large]; ulcerated surface ranging from 0 [none] to 3 [ $>30\%$ ]; affected surface ranging from 0 [none] to 3 [ $>75\%$ ], and narrowing ranging from 0 [none] to 3 [cannot be passed]) in 5 segments assessed during ileocolonoscopy (ileum, right colon, transverse colon, sigmoid and left colon, and rectum). The score for each endoscopic variable is the sum of values obtained for each segment and range from 0 to 15 where higher scores indicate more severe disease. The Total Score is the sum of the 4 endoscopic variable scores and range from 0 to 56, where higher scores indicate more severe disease. Nonresponder imputation (NRI) was used for missing data.

End point type	Primary
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#### End point timeframe:

Week 40

#### 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: Descriptive data are summarized for this end point per protocol.

End point values	Adalimumab			
Subject group type	Reporting group			
Number of subjects analysed	76 <sup>[2]</sup>			
Units: percentage of participants				
number (confidence interval 95%)	31.6 (21.1 to 42.0)			

#### Notes:

[2] - All subjects with endoscopic improvement at Week 0 in Study M14-347 (end of lead-in Study M14-115)

### Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Treatment-emergent adverse events (TEAEs) and serious adverse events (TESAEs) were collected from first dose of study drug until 70 days after the last dose of study drug (up to 48 weeks).

Assessment type	Systematic
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	21.0
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### Reporting groups

Reporting group title	Adalimumab
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Reporting group description:

Participants received open-label adalimumab 40 mg by subcutaneous injection every other week for 40 weeks.

<b>Serious adverse events</b>	Adalimumab		
Total subjects affected by serious adverse events			
subjects affected / exposed	27 / 252 (10.71%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
POST PROCEDURAL HAEMORRHAGE			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
HEADACHE			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
NON-CARDIAC CHEST PAIN			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
ABDOMINAL PAIN UPPER			

subjects affected / exposed	1 / 252 (0.40%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>CROHN'S DISEASE</b>			
subjects affected / exposed	14 / 252 (5.56%)		
occurrences causally related to treatment / all	0 / 16		
deaths causally related to treatment / all	0 / 0		
<b>ILEAL STENOSIS</b>			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>INTESTINAL OBSTRUCTION</b>			
subjects affected / exposed	3 / 252 (1.19%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
<b>SMALL INTESTINAL OBSTRUCTION</b>			
subjects affected / exposed	4 / 252 (1.59%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
<b>Renal and urinary disorders</b>			
<b>NEPHROLITHIASIS</b>			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Musculoskeletal and connective tissue disorders</b>			
<b>INTERVERTEBRAL DISC PROTRUSION</b>			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Infections and infestations</b>			
<b>ANAL ABSCESS</b>			

subjects affected / exposed	3 / 252 (1.19%)		
occurrences causally related to treatment / all	1 / 3		
deaths causally related to treatment / all	0 / 0		

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

<b>Non-serious adverse events</b>	Adalimumab		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	65 / 252 (25.79%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
ACROCHORDON			
subjects affected / exposed	2 / 252 (0.79%)		
occurrences (all)	2		
GASTROINTESTINAL TRACT ADENOMA			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	1		
UTERINE LEIOMYOMA			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	1		
Vascular disorders			
FLUSHING			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	1		
HOT FLUSH			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	1		
HYPERTENSION			
subjects affected / exposed	3 / 252 (1.19%)		
occurrences (all)	4		
PERIPHERAL VENOUS DISEASE			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	3		
General disorders and administration site conditions			

CHEST PAIN			
subjects affected / exposed	2 / 252 (0.79%)		
occurrences (all)	2		
DRUG INTOLERANCE			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	1		
HYPERTHERMIA			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	1		
FATIGUE			
subjects affected / exposed	2 / 252 (0.79%)		
occurrences (all)	2		
INFLUENZA LIKE ILLNESS			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	1		
INJECTION SITE BRUISING			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	1		
INJECTION SITE PAIN			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	1		
INJECTION SITE PRURITUS			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	1		
INJECTION SITE REACTION			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	2		
NON-CARDIAC CHEST PAIN			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	1		
OEDEMA PERIPHERAL			
subjects affected / exposed	2 / 252 (0.79%)		
occurrences (all)	2		
PAIN			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	1		

PERIPHERAL SWELLING subjects affected / exposed occurrences (all)	1 / 252 (0.40%) 1		
POLYP subjects affected / exposed occurrences (all)	1 / 252 (0.40%) 1		
PYREXIA subjects affected / exposed occurrences (all)	7 / 252 (2.78%) 7		
Immune system disorders DRUG HYPERSENSITIVITY subjects affected / exposed occurrences (all)	1 / 252 (0.40%) 1		
SEASONAL ALLERGY subjects affected / exposed occurrences (all)	1 / 252 (0.40%) 1		
Reproductive system and breast disorders BREAST CYST subjects affected / exposed occurrences (all)	1 / 252 (0.40%) 1		
CERVICAL DYSPLASIA subjects affected / exposed occurrences (all)	1 / 252 (0.40%) 1		
DYSMENORRHOEA subjects affected / exposed occurrences (all)	1 / 252 (0.40%) 1		
DYSPAREUNIA subjects affected / exposed occurrences (all)	1 / 252 (0.40%) 1		
PROSTATITIS subjects affected / exposed occurrences (all)	1 / 252 (0.40%) 1		
VAGINAL HAEMORRHAGE subjects affected / exposed occurrences (all)	1 / 252 (0.40%) 1		
VAGINAL DISCHARGE			

subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	1		
VULVOVAGINAL DRYNESS			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
COUGH			
subjects affected / exposed	6 / 252 (2.38%)		
occurrences (all)	8		
NASAL ULCER			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	1		
EPISTAXIS			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	1		
OROPHARYNGEAL PAIN			
subjects affected / exposed	2 / 252 (0.79%)		
occurrences (all)	3		
PARANASAL SINUS HYPERSECRETION			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	1		
RHINITIS ALLERGIC			
subjects affected / exposed	2 / 252 (0.79%)		
occurrences (all)	2		
RHINORRHOEA			
subjects affected / exposed	2 / 252 (0.79%)		
occurrences (all)	2		
SINUS CONGESTION			
subjects affected / exposed	2 / 252 (0.79%)		
occurrences (all)	2		
SINUS PAIN			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	1		
TONSILLAR HYPERTROPHY			

subjects affected / exposed occurrences (all)	1 / 252 (0.40%) 1		
Psychiatric disorders			
ACUTE STRESS DISORDER subjects affected / exposed occurrences (all)	1 / 252 (0.40%) 1		
ANXIETY subjects affected / exposed occurrences (all)	4 / 252 (1.59%) 4		
BIPOLAR DISORDER subjects affected / exposed occurrences (all)	1 / 252 (0.40%) 1		
DEPRESSION subjects affected / exposed occurrences (all)	4 / 252 (1.59%) 4		
INSOMNIA subjects affected / exposed occurrences (all)	4 / 252 (1.59%) 4		
MOOD SWINGS subjects affected / exposed occurrences (all)	1 / 252 (0.40%) 1		
NIGHTMARE subjects affected / exposed occurrences (all)	1 / 252 (0.40%) 1		
RESTLESSNESS subjects affected / exposed occurrences (all)	1 / 252 (0.40%) 1		
SLEEP DISORDER subjects affected / exposed occurrences (all)	1 / 252 (0.40%) 1		
Investigations			
BLOOD BILIRUBIN INCREASED subjects affected / exposed occurrences (all)	1 / 252 (0.40%) 1		
ALANINE AMINOTRANSFERASE INCREASED			

subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	1		
<b>BLOOD CHOLESTEROL INCREASED</b>			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	1		
<b>BLOOD CREATININE INCREASED</b>			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	1		
<b>BLOOD TRIGLYCERIDES INCREASED</b>			
subjects affected / exposed	4 / 252 (1.59%)		
occurrences (all)	7		
<b>BLOOD URINE PRESENT</b>			
subjects affected / exposed	3 / 252 (1.19%)		
occurrences (all)	4		
<b>C-REACTIVE PROTEIN INCREASED</b>			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	1		
<b>CLOSTRIDIUM TEST POSITIVE</b>			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	1		
<b>LIVER FUNCTION TEST INCREASED</b>			
subjects affected / exposed	2 / 252 (0.79%)		
occurrences (all)	2		
<b>NEUTROPHIL COUNT INCREASED</b>			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	1		
<b>NITRITE URINE PRESENT</b>			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	1		
<b>PROTEIN URINE PRESENT</b>			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	3		
<b>RED BLOOD CELLS URINE</b>			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	1		
<b>RED BLOOD CELLS URINE POSITIVE</b>			

subjects affected / exposed occurrences (all)	1 / 252 (0.40%) 2		
WEIGHT DECREASED subjects affected / exposed occurrences (all)	1 / 252 (0.40%) 1		
WHITE BLOOD CELL COUNT INCREASED subjects affected / exposed occurrences (all)	2 / 252 (0.79%) 2		
Injury, poisoning and procedural complications			
ARTHROPOD STING subjects affected / exposed occurrences (all)	1 / 252 (0.40%) 1		
CONTUSION subjects affected / exposed occurrences (all)	1 / 252 (0.40%) 1		
CORNEAL ABRASION subjects affected / exposed occurrences (all)	1 / 252 (0.40%) 1		
LIMB INJURY subjects affected / exposed occurrences (all)	1 / 252 (0.40%) 1		
POST PROCEDURAL DIARRHOEA subjects affected / exposed occurrences (all)	1 / 252 (0.40%) 1		
POST PROCEDURAL HAEMORRHAGE subjects affected / exposed occurrences (all)	1 / 252 (0.40%) 1		
POST-TRAUMATIC NECK SYNDROME subjects affected / exposed occurrences (all)	1 / 252 (0.40%) 1		
PROCEDURAL HAEMORRHAGE subjects affected / exposed occurrences (all)	1 / 252 (0.40%) 1		
RIB FRACTURE			

subjects affected / exposed occurrences (all)	1 / 252 (0.40%) 1		
ROAD TRAFFIC ACCIDENT subjects affected / exposed occurrences (all)	1 / 252 (0.40%) 1		
TOOTH FRACTURE subjects affected / exposed occurrences (all)	1 / 252 (0.40%) 1		
Cardiac disorders PALPITATIONS subjects affected / exposed occurrences (all)	2 / 252 (0.79%) 2		
Nervous system disorders BURNING SENSATION subjects affected / exposed occurrences (all)	1 / 252 (0.40%) 1		
DIZZINESS subjects affected / exposed occurrences (all)	2 / 252 (0.79%) 2		
HEADACHE subjects affected / exposed occurrences (all)	12 / 252 (4.76%) 24		
HYPOAESTHESIA subjects affected / exposed occurrences (all)	1 / 252 (0.40%) 1		
LETHARGY subjects affected / exposed occurrences (all)	1 / 252 (0.40%) 1		
MIGRAINE subjects affected / exposed occurrences (all)	2 / 252 (0.79%) 2		
PARAESTHESIA subjects affected / exposed occurrences (all)	2 / 252 (0.79%) 2		
SCIATICA			

<p>subjects affected / exposed occurrences (all)</p> <p>SPINAL CLAUDICATION subjects affected / exposed occurrences (all)</p> <p>SYNCOPE subjects affected / exposed occurrences (all)</p>	<p>1 / 252 (0.40%) 1</p> <p>1 / 252 (0.40%) 1</p> <p>1 / 252 (0.40%) 1</p>		
<p>Blood and lymphatic system disorders</p> <p>ANAEMIA subjects affected / exposed occurrences (all)</p> <p>IRON DEFICIENCY ANAEMIA subjects affected / exposed occurrences (all)</p> <p>LEUKOPENIA subjects affected / exposed occurrences (all)</p> <p>LYMPHADENOPATHY subjects affected / exposed occurrences (all)</p>	<p>3 / 252 (1.19%) 3</p> <p>2 / 252 (0.79%) 2</p> <p>3 / 252 (1.19%) 3</p> <p>1 / 252 (0.40%) 1</p>		
<p>Eye disorders</p> <p>CATARACT subjects affected / exposed occurrences (all)</p> <p>KERATITIS subjects affected / exposed occurrences (all)</p> <p>VISION BLURRED subjects affected / exposed occurrences (all)</p>	<p>1 / 252 (0.40%) 1</p> <p>1 / 252 (0.40%) 1</p> <p>1 / 252 (0.40%) 1</p>		
<p>Gastrointestinal disorders</p> <p>ABDOMINAL DISTENSION subjects affected / exposed occurrences (all)</p> <p>ABDOMINAL MASS</p>	<p>2 / 252 (0.79%) 2</p>		

subjects affected / exposed	3 / 252 (1.19%)		
occurrences (all)	3		
<b>ABDOMINAL PAIN</b>			
subjects affected / exposed	12 / 252 (4.76%)		
occurrences (all)	13		
<b>ABDOMINAL PAIN LOWER</b>			
subjects affected / exposed	3 / 252 (1.19%)		
occurrences (all)	3		
<b>ABDOMINAL PAIN UPPER</b>			
subjects affected / exposed	6 / 252 (2.38%)		
occurrences (all)	6		
<b>ABDOMINAL RIGIDITY</b>			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	1		
<b>ABDOMINAL TENDERNESS</b>			
subjects affected / exposed	2 / 252 (0.79%)		
occurrences (all)	2		
<b>ANAL FISSURE</b>			
subjects affected / exposed	7 / 252 (2.78%)		
occurrences (all)	8		
<b>ANAL FISTULA</b>			
subjects affected / exposed	3 / 252 (1.19%)		
occurrences (all)	6		
<b>ANAL STENOSIS</b>			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	1		
<b>ANAL ULCER</b>			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	1		
<b>ANORECTAL DISCOMFORT</b>			
subjects affected / exposed	2 / 252 (0.79%)		
occurrences (all)	2		
<b>ANORECTAL DISORDER</b>			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	1		
<b>CHEILITIS</b>			

subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	1		
<b>CONSTIPATION</b>			
subjects affected / exposed	6 / 252 (2.38%)		
occurrences (all)	6		
<b>CROHN'S DISEASE</b>			
subjects affected / exposed	46 / 252 (18.25%)		
occurrences (all)	59		
<b>DENTAL CARIES</b>			
subjects affected / exposed	2 / 252 (0.79%)		
occurrences (all)	2		
<b>DIARRHOEA</b>			
subjects affected / exposed	7 / 252 (2.78%)		
occurrences (all)	7		
<b>DRY MOUTH</b>			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	1		
<b>DYSPEPSIA</b>			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	1		
<b>FLATULENCE</b>			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	1		
<b>FREQUENT BOWEL MOVEMENTS</b>			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	1		
<b>GASTROESOPHAGEAL REFLUX DISEASE</b>			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	1		
<b>HAEMATOCHYZIA</b>			
subjects affected / exposed	2 / 252 (0.79%)		
occurrences (all)	2		
<b>HAEMORRHOIDS</b>			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	1		

HIATUS HERNIA			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	1		
ILEAL STENOSIS			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	2		
INTESTINAL OBSTRUCTION			
subjects affected / exposed	4 / 252 (1.59%)		
occurrences (all)	4		
INTESTINAL STENOSIS			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	1		
IRRITABLE BOWEL SYNDROME			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	1		
LARGE INTESTINE POLYP			
subjects affected / exposed	2 / 252 (0.79%)		
occurrences (all)	2		
MOUTH ULCERATION			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	1		
MUCOUS STOOLS			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	1		
NAUSEA			
subjects affected / exposed	15 / 252 (5.95%)		
occurrences (all)	21		
PROCTALGIA			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	1		
RECTAL DISCHARGE			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	1		
RECTAL HAEMORRHAGE			
subjects affected / exposed	2 / 252 (0.79%)		
occurrences (all)	3		

SMALL INTESTINAL OBSTRUCTION subjects affected / exposed occurrences (all)	6 / 252 (2.38%) 6		
TONGUE DRY subjects affected / exposed occurrences (all)	1 / 252 (0.40%) 1		
TOOTHACHE subjects affected / exposed occurrences (all)	3 / 252 (1.19%) 3		
VOMITING subjects affected / exposed occurrences (all)	11 / 252 (4.37%) 12		
Hepatobiliary disorders CHOLELITHIASIS subjects affected / exposed occurrences (all)	1 / 252 (0.40%) 1		
HEPATIC STEATOSIS subjects affected / exposed occurrences (all)	1 / 252 (0.40%) 1		
HYPERTRANSAMINASAEMIA subjects affected / exposed occurrences (all)	1 / 252 (0.40%) 1		
Skin and subcutaneous tissue disorders ACNE subjects affected / exposed occurrences (all)	5 / 252 (1.98%) 5		
ALOPECIA subjects affected / exposed occurrences (all)	1 / 252 (0.40%) 1		
ANGIOEDEMA subjects affected / exposed occurrences (all)	1 / 252 (0.40%) 1		
DERMATITIS subjects affected / exposed occurrences (all)	5 / 252 (1.98%) 5		
DERMATITIS ALLERGIC			

subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	1		
<b>DERMATITIS CONTACT</b>			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	1		
<b>DRY SKIN</b>			
subjects affected / exposed	3 / 252 (1.19%)		
occurrences (all)	3		
<b>ECZEMA</b>			
subjects affected / exposed	2 / 252 (0.79%)		
occurrences (all)	2		
<b>ERYTHEMA</b>			
subjects affected / exposed	2 / 252 (0.79%)		
occurrences (all)	2		
<b>MILIARIA</b>			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	1		
<b>PAPULE</b>			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	1		
<b>PRURITUS</b>			
subjects affected / exposed	4 / 252 (1.59%)		
occurrences (all)	7		
<b>PRURITUS GENERALISED</b>			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	2		
<b>PSORIASIS</b>			
subjects affected / exposed	3 / 252 (1.19%)		
occurrences (all)	4		
<b>RASH</b>			
subjects affected / exposed	6 / 252 (2.38%)		
occurrences (all)	6		
<b>RASH GENERALISED</b>			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	1		
<b>RASH MACULAR</b>			

subjects affected / exposed occurrences (all)	1 / 252 (0.40%) 1		
<b>RASH PRURITIC</b> subjects affected / exposed occurrences (all)	1 / 252 (0.40%) 1		
<b>SKIN EXFOLIATION</b> subjects affected / exposed occurrences (all)	1 / 252 (0.40%) 1		
<b>SKIN LESION</b> subjects affected / exposed occurrences (all)	1 / 252 (0.40%) 1		
<b>URTICARIA</b> subjects affected / exposed occurrences (all)	1 / 252 (0.40%) 1		
<b>Renal and urinary disorders</b>			
<b>INCONTINENCE</b> subjects affected / exposed occurrences (all)	1 / 252 (0.40%) 1		
<b>NEPHROLITHIASIS</b> subjects affected / exposed occurrences (all)	2 / 252 (0.79%) 2		
<b>POLLAKIURIA</b> subjects affected / exposed occurrences (all)	1 / 252 (0.40%) 1		
<b>RENAL COLIC</b> subjects affected / exposed occurrences (all)	2 / 252 (0.79%) 2		
<b>Endocrine disorders</b>			
<b>THYROID DISORDER</b> subjects affected / exposed occurrences (all)	1 / 252 (0.40%) 1		
<b>Musculoskeletal and connective tissue disorders</b>			
<b>ARTHRALGIA</b> subjects affected / exposed occurrences (all)	18 / 252 (7.14%) 20		
<b>ARTHRITIS</b>			

subjects affected / exposed	4 / 252 (1.59%)		
occurrences (all)	4		
<b>ARTHROPATHY</b>			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	1		
<b>BACK PAIN</b>			
subjects affected / exposed	11 / 252 (4.37%)		
occurrences (all)	12		
<b>BURSITIS</b>			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	1		
<b>FISTULA DISCHARGE</b>			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	1		
<b>INTERVERTEBRAL DISC PROTRUSION</b>			
subjects affected / exposed	3 / 252 (1.19%)		
occurrences (all)	4		
<b>LUMBAR SPINAL STENOSIS</b>			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	1		
<b>MUSCLE SPASMS</b>			
subjects affected / exposed	2 / 252 (0.79%)		
occurrences (all)	2		
<b>MUSCULOSKELETAL PAIN</b>			
subjects affected / exposed	3 / 252 (1.19%)		
occurrences (all)	3		
<b>MUSCULOSKELETAL STIFFNESS</b>			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	1		
<b>PAIN IN EXTREMITY</b>			
subjects affected / exposed	6 / 252 (2.38%)		
occurrences (all)	7		
<b>ROTATOR CUFF SYNDROME</b>			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	1		

TENDONITIS			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	1		
<b>Infections and infestations</b>			
<b>ABSCCESS</b>			
subjects affected / exposed	2 / 252 (0.79%)		
occurrences (all)	2		
<b>ACUTE SINUSITIS</b>			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	1		
<b>ANAL ABSCCESS</b>			
subjects affected / exposed	9 / 252 (3.57%)		
occurrences (all)	10		
<b>BACTERIAL VAGINOSIS</b>			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	1		
<b>BACTERIAL VULVOVAGINITIS</b>			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	1		
<b>BRONCHITIS</b>			
subjects affected / exposed	4 / 252 (1.59%)		
occurrences (all)	5		
<b>CELLULITIS</b>			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	1		
<b>CONJUNCTIVITIS</b>			
subjects affected / exposed	3 / 252 (1.19%)		
occurrences (all)	4		
<b>CYSTITIS</b>			
subjects affected / exposed	4 / 252 (1.59%)		
occurrences (all)	4		
<b>EAR INFECTION</b>			
subjects affected / exposed	4 / 252 (1.59%)		
occurrences (all)	4		
<b>ECZEMA INFECTED</b>			

subjects affected / exposed	2 / 252 (0.79%)		
occurrences (all)	2		
<b>EPIDIDYMITIS</b>			
subjects affected / exposed	2 / 252 (0.79%)		
occurrences (all)	2		
<b>FUNGAL INFECTION</b>			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	1		
<b>GASTROENTERITIS</b>			
subjects affected / exposed	2 / 252 (0.79%)		
occurrences (all)	2		
<b>GASTROINTESTINAL INFECTION</b>			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	1		
<b>GINGIVITIS</b>			
subjects affected / exposed	3 / 252 (1.19%)		
occurrences (all)	3		
<b>HERPES SIMPLEX</b>			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	1		
<b>HERPES ZOSTER</b>			
subjects affected / exposed	3 / 252 (1.19%)		
occurrences (all)	3		
<b>HORDEOLUM</b>			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	1		
<b>INFLUENZA</b>			
subjects affected / exposed	4 / 252 (1.59%)		
occurrences (all)	4		
<b>LOCALISED INFECTION</b>			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	1		
<b>LOWER RESPIRATORY TRACT INFECTION</b>			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	1		

NASOPHARYNGITIS			
subjects affected / exposed	9 / 252 (3.57%)		
occurrences (all)	10		
ONYCHOMYCOSIS			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	1		
ORAL CANDIDIASIS			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	2		
ORAL HERPES			
subjects affected / exposed	4 / 252 (1.59%)		
occurrences (all)	4		
OTITIS EXTERNA			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	1		
PERIODONTITIS			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	1		
PHARYNGITIS			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	1		
PHARYNGITIS STREPTOCOCCAL			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	1		
PULPITIS DENTAL			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	1		
RESPIRATORY TRACT INFECTION			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	1		
RESPIRATORY TRACT INFECTION VIRAL			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	1		
RHINITIS			

subjects affected / exposed occurrences (all)	3 / 252 (1.19%) 3		
<b>SINUSITIS</b>			
subjects affected / exposed occurrences (all)	2 / 252 (0.79%) 2		
<b>SUBCUTANEOUS ABSCESS</b>			
subjects affected / exposed occurrences (all)	3 / 252 (1.19%) 3		
<b>TONSILLITIS</b>			
subjects affected / exposed occurrences (all)	2 / 252 (0.79%) 2		
<b>TOOTH ABSCESS</b>			
subjects affected / exposed occurrences (all)	2 / 252 (0.79%) 2		
<b>TOOTH INFECTION</b>			
subjects affected / exposed occurrences (all)	2 / 252 (0.79%) 2		
<b>UPPER RESPIRATORY TRACT INFECTION</b>			
subjects affected / exposed occurrences (all)	13 / 252 (5.16%) 13		
<b>URINARY TRACT INFECTION</b>			
subjects affected / exposed occurrences (all)	9 / 252 (3.57%) 9		
<b>VIRAL INFECTION</b>			
subjects affected / exposed occurrences (all)	1 / 252 (0.40%) 1		
<b>VULVOVAGINAL MYCOTIC INFECTION</b>			
subjects affected / exposed occurrences (all)	3 / 252 (1.19%) 4		
<b>WOUND INFECTION</b>			
subjects affected / exposed occurrences (all)	1 / 252 (0.40%) 1		
Metabolism and nutrition disorders			

DECREASED APPETITE			
subjects affected / exposed	2 / 252 (0.79%)		
occurrences (all)	2		
FOLATE DEFICIENCY			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	1		
FOOD INTOLERANCE			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	1		
GOUT			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	1		
HYPOVITAMINOSIS			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	1		
IRON DEFICIENCY			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	1		
VITAMIN B12 DEFICIENCY			
subjects affected / exposed	3 / 252 (1.19%)		
occurrences (all)	3		
VITAMIN D DEFICIENCY			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	1		

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
13 May 2014	The main purpose of this study was to update Crohn's disease flare and inadequate response criteria, update de-escalation and re-escalation criteria, clarify corticosteroid use, clarify inclusion criteria (contraception) and exclusion criteria (tuberculosis), and clarify endpoints and analyses.
04 December 2014	The main purpose of this study was to update the definition of inadequate response and first week when subjects are allowed to dose-escalate and clarify study procedures, including procedures required at unscheduled visit .

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported