Clinical trial results:
A Multi-Center, Randomized, Double-Blind, Placebo-controlled Study of Adalimumab in Japanese Subjects with Moderately to Severely Active Ulcerative Colitis

Summary

EudraCT number	2014-004559-29
Trial protocol	Outside EU/EEA
Global end of trial date	14 August 2013

Results information

Result version number	v2 (current)
This version publication date	18 May 2016
First version publication date	24 June 2015
Version creation reason	• Correction of full data set potential timestamp issues

Trial information

Trial identification

Sponsor protocol code	M10-447

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00853099
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	AbbVie
Sponsor organisation address	1 North Waukegan Road, North Chicago, IL, United States, 60064
Public contact	Global Medical Information, AbbVie, 001 800-633-9110,
Scientific contact	Morio Ozawa, AbbVie, morio.ozawa@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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	14 August 2013
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	14 August 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The purpose of this study is to assess the efficacy and safety of adalimumab in Japanese subjects with moderately to severely active ulcerative colitis (UC).

Patients are randomized 1:1:1 to receive subcutaneous injections of adalimumab at either 160/80 mg at Week 0/2 and 40 mg every other week (eow) starting at Week 4 to Week 50, 80/40 mg at Week 0/2 and 40 mg eow starting at Week 4 to Week 50, or placebo eow starting at Week 0 to Week 50 under the double-blind condition.

At or after Week 8, participants who have inadequate response during the double-blind period can switch to the rescue arm, where participants from the placebo group initially receive adalimumab 160 mg and 80 mg 2 weeks later and those from the adalimumab group receive adalimumab 40 mg initially and 2 weeks later under double-blind conditions. All participants in the rescue arm then receive 40 mg adalimumab eow until Week 50. Seven participants randomized to placebo did not receive any adalimumab.

Protection of trial subjects:

Participant and/or legal guardian (if subject < 20 years of age) read and understood information provided about the study and gave written permission.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	27 February 2009
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: 274
Worldwide total number of subjects	274
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)	0
Children (2-11 years)	0
Adolescents (12-17 years)	4
Adults (18-64 years)	249
From 65 to 84 years	21
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

The study included a screening period of 21 days.

Period 1

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

Arms

Are arms mutually exclusive?	No
Arm title	Double-blind Placebo

Arm description:

Participants received placebo subcutaneous injections every 2 weeks for 52 weeks. From Week 8, participants with an inadequate response could switch to rescue therapy, where they initially received adalimumab 160 mg, 80 mg 2 weeks later, and then 40 mg every other week. Participants who completed the 52-week double-blind period received open-label adalimumab 40 mg every other week, with the possibility to escalate to 80 mg every other week, until drug approval.

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

Dosage and administration details:

Adalimumab administered by subcutaneous injection as rescue medication

Investigational medicinal product name	placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Placebo for adalimumab administered by subcutaneous injection

Arm title	Double-blind Adalimumab 80 mg/40 mg

Arm description:

Participants received adalimumab 80 mg on Day 1, 40 mg at Week 2 and 40 mg every other week from Week 4 to Week 50, via subcutaneous injection. From Week 8, participants with an inadequate response could switch to rescue therapy, where they received adalimumab 40 mg every other week. Participants who completed the 52-week double-blind period received open-label adalimumab 40 mg every other week, with the possibility to escalate to 80 mg every other week, until drug approval.

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

Dosage and administration details:

Adalimumab administered by subcutaneous injection

Arm title	Double-blind Adalimumab 160 mg/80 mg

Arm description:

Participants received adalimumab 160 mg on Day 1, 80 mg at Week 2 and 40 mg every other week from Week 4 to Week 50, via subcutaneous injection. From Week 8, participants with an inadequate response could switch to rescue therapy, where they received adalimumab 40 mg every other week.

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

Dosage and administration details:

Adalimumab administered by subcutaneous injection

Number of subjects in period 1	Double-blind Placebo	Double-blind Adalimumab 80 mg/40 mg	Double-blind Adalimumab 160 mg/80 mg
Started	96	87	90
Treated	96	87	90
Completed Week 8	92	85	86
Completed	73	58	60
Not completed	23	29	30
Consent withdrawn by subject	2	3	-
Not Specified	-	-	1
Adverse event	7	9	13
Lack of efficacy	14	17	16

Period 2

Period 2 title	Double-blind + Open-label Periods
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Arm title	All Adalimumab

Arm description:

All participants who received at least one dose of adalimumab during the study (adalimumab treatment groups in the double-blind phase, and participants randomized to placebo who received adalimumab in the rescue phase or open-label phase).

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

Dosage and administration details:

Adalimumab administered by subcutaneous injection

Number of subjects in period 2	All Adalimumab
Started	266
Completed	119
Not completed	147
Consent withdrawn by subject	20
Not Specified	6
Adverse event	47
Lack of efficacy	74

Baseline characteristics

Reporting groups[1]	
Reporting group title	Double-blind Placebo

Reporting group description:

Participants received placebo subcutaneous injections every 2 weeks for 52 weeks. From Week 8, participants with an inadequate response could switch to rescue therapy, where they initially received adalimumab 160 mg, 80 mg 2 weeks later, and then 40 mg every other week. Participants who completed the 52-week double-blind period received open-label adalimumab 40 mg every other week, with the possibility to escalate to 80 mg every other week, until drug approval.

Reporting group title	Double-blind Adalimumab 80 mg/40 mg

Reporting group description:

Participants received adalimumab 80 mg on Day 1, 40 mg at Week 2 and 40 mg every other week from Week 4 to Week 50, via subcutaneous injection. From Week 8, participants with an inadequate response could switch to rescue therapy, where they received adalimumab 40 mg every other week. Participants who completed the 52-week double-blind period received open-label adalimumab 40 mg every other week, with the possibility to escalate to 80 mg every other week, until drug approval.

Reporting group title	Double-blind Adalimumab 160 mg/80 mg

Reporting group description:

Participants received adalimumab 160 mg on Day 1, 80 mg at Week 2 and 40 mg every other week from Week 4 to Week 50, via subcutaneous injection. From Week 8, participants with an inadequate response could switch to rescue therapy, where they received adalimumab 40 mg every other week.

Notes:

[1] - The number of subjects reported to be in the baseline period is not equal to the worldwide number of subjects enrolled in the trial. It is expected that these numbers will be the same.
Justification: 1 participant, incorrectly treated with open-label (rescue) study drug at Week 0, was excluded.

Reporting group values	Double-blind Placebo	Double-blind Adalimumab 80 mg/40 mg	Double-blind Adalimumab 160 mg/80 mg
Number of subjects	96	87	90
Age categorical Units: Subjects			
Age Continuous			
Demographic data are provided for the Full Analysis Set (FAS), which includes all patients who received at least 1 dose of study drug any time during the first 52 weeks and with at least 1 efficacy measurement after the first dose of study medication.			
Units: years			
arithmetic mean	41.3	44.4	42.5
standard deviation	± 13.56	± 15.04	± 14.56
Gender, Male/Female Units: participants			
Female	26	37	29
Male	70	50	61
Mayo score			
A composite score of ulcerative colitis disease activity calculated as the sum of 4 subscores: Stool frequency, based on the participant's diary, scored from 0 (normal number of stools) to 3 (≥5 stools than normal); Rectal bleeding, based on the participant's diary, scored from 0 (no blood) to 3 (blood only passed); Endoscopy, scored from 0 (normal or inactive disease) to 3 (severe disease, spontaneous bleeding, ulceration); and Physician's Global Assessment, scored from 0 (normal) to 3 (severe disease). The total Mayo score ranges from 0 to 12; higher scores indicate more severe disease.			
Units: scores on a scale			
arithmetic mean	8.5	8.5	8.6
standard deviation	± 1.56	± 1.42	± 1.44

Reporting group values	Total		
Number of subjects	273		
Age categorical Units: Subjects			

Age Continuous			
Demographic data are provided for the Full Analysis Set (FAS), which includes all patients who received at least 1 dose of study drug any time during the first 52 weeks and with at least 1 efficacy measurement after the first dose of study medication.			
Units: years arithmetic mean standard deviation	- 		
Gender, Male/Female Units: participants			
Female	92		
Male	181		
Mayo score			
A composite score of ulcerative colitis disease activity calculated as the sum of 4 subscores: Stool frequency, based on the participant's diary, scored from 0 (normal number of stools) to 3 (≥5 stools than normal); Rectal bleeding, based on the participant's diary, scored from 0 (no blood) to 3 (blood only passed); Endoscopy, scored from 0 (normal or inactive disease) to 3 (severe disease, spontaneous bleeding, ulceration); and Physician's Global Assessment, scored from 0 (normal) to 3 (severe disease). The total Mayo score ranges from 0 to 12; higher scores indicate more severe disease.			
Units: scores on a scale arithmetic mean standard deviation	- 		

End points

End points reporting groups

Reporting group title	Double-blind Placebo

Reporting group description:

Participants received placebo subcutaneous injections every 2 weeks for 52 weeks. From Week 8, participants with an inadequate response could switch to rescue therapy, where they initially received adalimumab 160 mg, 80 mg 2 weeks later, and then 40 mg every other week. Participants who completed the 52-week double-blind period received open-label adalimumab 40 mg every other week, with the possibility to escalate to 80 mg every other week, until drug approval.

Reporting group title	Double-blind Adalimumab 80 mg/40 mg

Reporting group description:

Participants received adalimumab 80 mg on Day 1, 40 mg at Week 2 and 40 mg every other week from Week 4 to Week 50, via subcutaneous injection. From Week 8, participants with an inadequate response could switch to rescue therapy, where they received adalimumab 40 mg every other week. Participants who completed the 52-week double-blind period received open-label adalimumab 40 mg every other week, with the possibility to escalate to 80 mg every other week, until drug approval.

Reporting group title	Double-blind Adalimumab 160 mg/80 mg

Reporting group description:

Participants received adalimumab 160 mg on Day 1, 80 mg at Week 2 and 40 mg every other week from Week 4 to Week 50, via subcutaneous injection. From Week 8, participants with an inadequate response could switch to rescue therapy, where they received adalimumab 40 mg every other week.

Reporting group title	All Adalimumab

Reporting group description:

All participants who received at least one dose of adalimumab during the study (adalimumab treatment groups in the double-blind phase, and participants randomized to placebo who received adalimumab in the rescue phase or open-label phase).

Primary: Percentage of Participants With Clinical Remission at 8 Weeks

End point title	Percentage of Participants With Clinical Remission at 8 Weeks[1]

End point description:

Clinical remission was defined as a Mayo score ≤ 2 with no individual subscore > 1. The Mayo score is a composite score of UC disease activity calculated as the sum of 4 subscores:
•Stool Frequency Subscore (SFS), based on the participant's diary, scored from 0 (normal number of stools) to 3 (5 or more stools than normal);
•Rectal Bleeding Subscore (RBS), based on the participant's diary, scored from 0 (no blood) to 3 (blood only passed);
•Endoscopy Subscore (ESS), based on colonoscopy or sigmoidoscopy , scored from 0 (normal or inactive disease) to 3 (severe disease, spontaneous bleeding, ulceration);
•Physician's Global Assessment (PGA) subscore, based on the physician's overall assessment, scored from 0 (normal) to 3 (severe disease).
The total Mayo score ranges from 0 to 12; higher scores representing more severe disease.
FAS; non-responder imputation (NRI) was used, where all missing values and values after the start of rescue treatment were considered non-remission.

End point type	Primary

End point timeframe:

Week 8

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	Double-blind Placebo	Double-blind Adalimumab 80 mg/40 mg	Double-blind Adalimumab 160 mg/80 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	96	87	90	
Units: percentage of participants				
number (not applicable)	11.5	13.8	10	

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants With Clinical Remission at 52 Weeks

End point title	Percentage of Participants With Clinical Remission at 52

End point description:

Clinical remission was defined as a Mayo score ≤ 2 with no individual subscore > 1. The Mayo score is a composite score of ulcerative colitis disease activity calculated as the sum of 4 subscores:
Stool Frequency Subscore (SFS), based on the participant's diary and scored from 0 (normal number of stools) to 3 (5 or more stools than normal);
•Rectal Bleeding Subscore (RBS), based on the participant's diary and scored from 0 (no blood) to 3 (blood only passed);
•Endoscopy Subscore (ESS), based on colonoscopy or sigmoidoscopy and scored from 0 (normal or inactive disease) to 3 (severe disease, spontaneous bleeding, ulceration);
•Physician's Global Assessment (PGA) subscore, based on the physician's overall assessment, and scored from 0 (normal) to 3 (severe disease).
The total Mayo score ranges from 0 to 12 points, with higher scores representing more severe disease.

End point type	Primary

End point timeframe:

Week 52

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Descriptive data are summarized for this end point per protocol.

End point values	Double-blind Placebo	Double-blind Adalimumab 80 mg/40 mg	Double-blind Adalimumab 160 mg/80 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	96[3]	87[4]	90[5]	
Units: percentage of participants				
number (not applicable)	7.3	26.4	20	

Notes:

[3] - FAS; NRI was used

[4] - FAS; NRI was used

[5] - FAS; NRI was used

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Clinical Remission at 8, 32, and 52 Weeks

End point title	Percentage of Participants With Clinical Remission at 8, 32, and 52 Weeks

End point description:

Clinical remission was defined as a Mayo score ≤ 2 with no individual subscore > 1. The Mayo score is a composite score of ulcerative colitis disease activity calculated as the sum of 4 subscores:
•Stool Frequency Subscore (SFS), based on the participant's diary and scored from 0 (normal number of stools) to 3 (5 or more stools than normal);
•Rectal Bleeding Subscore (RBS), based on the participant's diary and scored from 0 (no blood) to 3 (blood only passed);
•Endoscopy Subscore (ESS), based on colonoscopy or sigmoidoscopy and scores from 0 (normal or inactive disease) to 3 (severe disease, spontaneous bleeding, ulceration);•Physician's Global Assessment (PGA) subscore, based on the physician's overall assessment, and scored from 0 (normal) to 3 (severe disease).
The total Mayo score ranges from 0 to 12 points, with higher scores representing more severe disease.

End point type	Secondary

End point timeframe:

Weeks 8, 32, and 52

End point values	Double-blind Placebo	Double-blind Adalimumab 80 mg/40 mg	Double-blind Adalimumab 160 mg/80 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	96[6]	87[7]	90[8]	
Units: percentage of participants				
number (not applicable)				
Week 8	11.5	13.8	10	
Week 32	8.3	17.2	17.8	
Week 52	7.3	26.4	20	

Notes:

[6] - FAS; NRI was used

[7] - FAS; NRI was used

[8] - FAS; NRI was used

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With a Clinical Response

End point title	Percentage of Participants With a Clinical Response

End point description:

A clinical response was defined as a decrease in Mayo score of ≥ 3 points and ≥ 30% from Baseline PLUS a decrease in the Rectal Bleeding Subscore (RBS) ≥ 1 or an absolute RBS of 0 or 1.
The Mayo score is a composite score of ulcerative colitis disease activity calculated as the sum of 4 subscores:
•Stool Frequency Subscore, based on the participant's diary and scored from 0 (normal number of stools) to 3 (5 or more stools than normal);
•Rectal Bleeding Subscore, based on the participant's diary and scored from 0 (no blood) to 3 (blood only passed);
•Endoscopy Subscore, based on colonoscopy or sigmoidoscopy and scored from 0 (normal or inactive disease) to 3 (severe disease, spontaneous bleeding, ulceration);
•Physician's Global Assessment subscore, based on the physician's overall assessment, and scored from 0 (normal) to 3 (severe disease).
The total Mayo score ranges from 0 to 12 points, with higher scores representing more severe disease.

End point type	Secondary

End point timeframe:

Baseline and Weeks 8, 32, and 52

End point values	Double-blind Placebo	Double-blind Adalimumab 80 mg/40 mg	Double-blind Adalimumab 160 mg/80 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	96[9]	87[10]	90[11]	
Units: percentage of participants				
number (not applicable)				
Week 8	35.4	42.5	50	
Week 32	20.8	33.3	37.8	
Week 52	17.7	29.9	31.1	

Notes:

[9] - FAS; NRI was used

[10] - FAS; NRI was used

[11] - FAS; NRI was used

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with Mucosal Healing

End point title	Percentage of Participants with Mucosal Healing

End point description:

Mucosal healing was defined as an endoscopy subscore of ≤ 1 and was assessed using flexible sigmoidoscopy performed at Weeks 8, 32, and 52.
The endoscopy subscore ranges from zero to three as follows:
0 = Normal or inactive disease, 1 = Mild disease (erythema, decreased vascular pattern, mild friability), 2 = Moderate disease (marked erythema, absent vascular pattern, friability, erosions), 3 = Severe disease (spontaneous bleeding, ulceration).

End point type	Secondary

End point timeframe:

Weeks 8, 32, and 52

End point values	Double-blind Placebo	Double-blind Adalimumab 80 mg/40 mg	Double-blind Adalimumab 160 mg/80 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	96[12]	87[13]	90[14]	
Units: percentage of participants				
number (not applicable)				
Week 8	30.2	39.1	44.4	
Week 32	21.9	27.6	31.1	
Week 52	15.6	28.7	28.9	

Notes:

[12] - FAS; NRI was used

[13] - FAS; NRI was used

[14] - FAS; NRI was used

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Rectal Bleeding Subscore Indicative of Mild Disease (≤ 1)

End point title	Percentage of Participants With Rectal Bleeding Subscore Indicative of Mild Disease (≤ 1)

End point description:

Rectal bleeding was assessed from the participant's diary, taking the worst score from the 3 days prior to each study visit. The rectal bleeding subscore ranges from 0 to 3, according to the following scale: 0 = no blood seen, 1 = streaks of blood with stool less than half the time, 2 = obvious blood with stool most of the time, 3 = blood alone passed.

End point type	Secondary

End point timeframe:

Weeks 8, 32, and 52

End point values	Double-blind Placebo	Double-blind Adalimumab 80 mg/40 mg	Double-blind Adalimumab 160 mg/80 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	96[15]	87[16]	90[17]	
Units: percentage of participants				
number (not applicable)				
Week 8	67.7	80.5	71.1	
Week 32	28.1	40.2	43.3	
Week 52	22.9	32.2	34.4	

Notes:

[15] - FAS; NRI was used

[16] - FAS; NRI was used

[17] - FAS; NRI was used

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Physician's Global Assessment Subscore Indicative of Mild Disease (≤ 1)

End point title	Percentage of Participants With Physician's Global Assessment Subscore Indicative of Mild Disease (≤ 1)

End point description:

The Physician's Global Assessment Subscore acknowledges the three other subscores (Stool Frequency, Rectal Bleeding, and Endoscopy), the participant's daily record of abdominal discomfort and functional assessment, and other observations such as physical findings and the participant's performance status. Possible scores range from 0 to 3 as follows:
0 = Normal (other subscores are 0), 1 = Mild disease (other subscores are mostly 1), 2 = Moderate disease (other subscores are 1 to 2), 3 = Severe disease (other subscores are 2 to 3).

End point type	Secondary

End point timeframe:

Weeks 8, 32, and 52

End point values	Double-blind Placebo	Double-blind Adalimumab 80 mg/40 mg	Double-blind Adalimumab 160 mg/80 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	96[18]	87[19]	90[20]	
Units: percentage of participants				
number (not applicable)				
Week 8	44.8	47.1	61.1	
Week 32	28.1	36.8	37.8	
Week 52	19.8	29.9	34.4	

Notes:

[18] - FAS; NRI was used

[19] - FAS; NRI was used

[20] - FAS; NRI was used

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Stool Frequency Subscore Indicative of Mild Disease (≤ 1)

End point title	Percentage of Participants With Stool Frequency Subscore Indicative of Mild Disease (≤ 1)

End point description:

Stool frequency was assessed from the participant's diary, taking the worst score from the 3 days prior to each study visit. The stool frequency subscore ranges from 0 to 3, according to the following scale: 0 = Normal number of stools for this participant, 1 = 1-2 stools more than normal, 2 = 3-4 stools more than normal, 3 = 5 or more stools more than normal.

End point type	Secondary

End point timeframe:

Weeks 8, 32, and 52

End point values	Double-blind Placebo	Double-blind Adalimumab 80 mg/40 mg	Double-blind Adalimumab 160 mg/80 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	96[21]	87[22]	90[23]	
Units: percentage of participants				
number (not applicable)				
Week 8	32.3	34.5	40	
Week 32	20.8	33.3	31.1	
Week 52	13.5	28.7	28.9	

Notes:

[21] - FAS; NRI was used

[22] - FAS; NRI was used

[23] - FAS; NRI was used

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Inflammatory Bowel Disease Questionnaire (IBDQ) Responders

End point title	Percentage of Inflammatory Bowel Disease Questionnaire (IBDQ) Responders

End point description:

An inflammatory bowel disease questionnaire responder was defined as a participant with at least a 16-point increase from Baseline in total Inflammatory Bowel Disease Questionnaire (IBDQ) score. The IBDQ is a 32-item questionnaire consisting of 4 dimensions: bowel-related symptoms, systemic function, social function, and emotional status. The responses to each question within each domain range from 1 (significant impairment) to 7 (no impairment), with the total score ranging from 32 (very poor) to 224 (perfect health-related quality of life).

End point type	Secondary

End point timeframe:

Baseline and Weeks 8, 32, and 52

End point values	Double-blind Placebo	Double-blind Adalimumab 80 mg/40 mg	Double-blind Adalimumab 160 mg/80 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	96[24]	87[25]	90[26]	
Units: percentage of participants				
number (not applicable)				
Week 8	39.6	48.3	42.2	
Week 32	21.9	33.3	28.9	
Week 52	12.5	29.9	21.1	

Notes:

[24] - FAS; NRI was used

[25] - FAS; NRI was used

[26] - FAS; NRI was used

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Adverse Events up to Week 8

End point title	Number of Participants With Adverse Events up to Week 8

End point description:

An adverse event (AE) is defined as any untoward medical occurrence in a patient or clinical investigation participant administered a pharmaceutical product and which does not necessarily have a causal relationship with this treatment.
The investigator assessed the relationship of each event to the use of study drug as either probably related, possibly related, probably not related or not related.
A serious adverse event is an event that results in death, is life-threatening, requires or prolongs hospitalization, results in a congenital anomaly, persistent or significant disability/incapacity or is an important medical event that, based on medical judgment, may jeopardize the participant and may require medical or surgical intervention to prevent any of the outcomes listed above.
For more details on adverse events please see the Adverse Event section below.

End point type	Secondary

End point timeframe:

8 weeks

End point values	Double-blind Placebo	Double-blind Adalimumab 80 mg/40 mg	Double-blind Adalimumab 160 mg/80 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	96[27]	87[28]	90[29]	
Units: participants				
number (not applicable)				
Any adverse event	45	49	40	
Any AE at least possibly drug related	10	14	12	
Any serious adverse event	7	2	4	
Any AE leading to discontinuation of study drug	4	0	6	

Notes:

[27] - The Safety Analysis Set includes all participants who received at least one dose of study medication
[28] - The Safety Analysis Set includes all participants who received at least one dose of study medication
[29] - The Safety Analysis Set includes all participants who received at least one dose of study medication

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Adverse Events up to Week 52

End point title	Number of Participants With Adverse Events up to Week 52

End point description:

An adverse event (AE) is defined as any untoward medical occurrence in a patient or clinical investigation participant administered a pharmaceutical product and which does not necessarily have a causal relationship with this treatment.
The investigator assessed the relationship of each event to the use of study drug as either probably related, possibly related, probably not related or not related.
A serious adverse event is an event that results in death, is life-threatening, requires or prolongs hospitalization, results in a congenital anomaly, persistent or significant disability/incapacity or is an important medical event that, based on medical judgment, may jeopardize the participant and may require medical or surgical intervention to prevent any of the outcomes listed above.
For more details on adverse events please see the Adverse Event section below.

End point type	Secondary

End point timeframe:

52 weeks

End point values	Double-blind Placebo	Double-blind Adalimumab 80 mg/40 mg	Double-blind Adalimumab 160 mg/80 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	96[30]	87[31]	90[32]	
Units: participants				
number (not applicable)				
Any adverse event	67	68	75	
Any AE at least possibly drug related	17	23	32	
Any serious adverse event	12	14	10	

Any AE leading to discontinuation of study drug	5	5	12	

Notes:

[30] - The Safety Analysis Set includes all participants who received at least one dose of study medication
[31] - The Safety Analysis Set includes all participants who received at least one dose of study medication
[32] - The Safety Analysis Set includes all participants who received at least one dose of study medication

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Adverse Events During the Adalimumab Treatment Period

End point title	Number of Participants With Adverse Events During the Adalimumab Treatment Period

End point description:

An adverse event (AE) is defined as any untoward medical occurrence in a patient or clinical investigation participant administered a pharmaceutical product and which does not necessarily have a causal relationship with this treatment.
The investigator assessed the relationship of each event to the use of study drug as either probably related, possibly related, probably not related or not related.
A serious adverse event is an event that results in death, is life-threatening, requires or prolongs hospitalization, results in a congenital anomaly, persistent or significant disability/incapacity or is an important medical event that, based on medical judgment, may jeopardize the participant and may require medical or surgical intervention to prevent any of the outcomes listed above.
For more details on adverse events please see the Adverse Event section below.

End point type	Secondary

End point timeframe:

221 weeks

End point values	All Adalimumab			
Subject group type	Reporting group			
Number of subjects analysed	266[33]			
Units: participants				
number (not applicable)				
Any adverse event	261			
Any AE at least possibly drug related	142			
Any serious adverse event	90			
Any AE leading to discontinuation of study drug	37			

Notes:

[33] - The Safety Analysis Set includes all participants who received at least one dose of study medication

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

For the 3 randomized treatment arms, adverse events (AEs) were reported from the time of study drug administration up to Week 52 (double-blind period); for All Adalimumab, AEs were reported up to 221 weeks+70 days following discontinuation of study drug.

Adverse event reporting additional description:

Serious AEs (SAEs) were collected from the time participants signed the study-specific informed consent. For SAEs, the number of participants affected in the Double-blind Placebo arm (n=13) is reported from the final database lock, versus the number reported in Outcome Measure 11 (n=12), which was from the interim database lock.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	15.1

Reporting groups

Reporting group title	Double-blind Placebo

Reporting group description:

Participants received placebo subcutaneous injections every 2 weeks for 52 weeks. From Week 8, participants with an inadequate response could switch to rescue therapy, where they initially received adalimumab 160 mg, 80 mg 2 weeks later, and then 40 mg every other week.

Reporting group title	Double-blind Adalimumab 80 mg/40 mg

Reporting group description:

Participants received adalimumab 80 mg on Day 1, 40 mg at Week 2 and 40 mg every other week from Week 4 to Week 50, via subcutaneous injection. From Week 8, participants with an inadequate response could switch to rescue therapy, where they received adalimumab 40 mg every other week.

Reporting group title	Double-blind Adalimumab 160 mg/80 mg

Reporting group description:

Participants received adalimumab 160 mg on Day 1, 80 mg at Week 2 and 40 mg every other week from Week 4 to Week 50, via subcutaneous injection. From Week 8, participants with an inadequate response could switch to rescue therapy, where they received adalimumab 40 mg every other week.

Reporting group title	All Adalimumab

Reporting group description:

All participants who received at least one dose of adalimumab during the study (adalimumab treatment groups in the double-blind phase, and participants randomized to placebo who received adalimumab in the rescue phase or open-label phase).

Serious adverse events	Double-blind Placebo	Double-blind Adalimumab 80 mg/40 mg	Double-blind Adalimumab 160 mg/80 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	13 / 96 (13.54%)	14 / 87 (16.09%)	10 / 90 (11.11%)
number of deaths (all causes)	0	0	2
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cervix carcinoma			

subjects affected / exposed	0 / 96 (0.00%)	0 / 87 (0.00%)	0 / 90 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Breast cancer			
subjects affected / exposed	0 / 96 (0.00%)	0 / 87 (0.00%)	0 / 90 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatic carcinoma			
subjects affected / exposed	0 / 96 (0.00%)	0 / 87 (0.00%)	1 / 90 (1.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal cancer			
subjects affected / exposed	0 / 96 (0.00%)	0 / 87 (0.00%)	0 / 90 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Parathyroid tumour			
subjects affected / exposed	0 / 96 (0.00%)	1 / 87 (1.15%)	0 / 90 (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
Thyroid cancer			
subjects affected / exposed	0 / 96 (0.00%)	0 / 87 (0.00%)	0 / 90 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Uterine leiomyoma			
subjects affected / exposed	0 / 96 (0.00%)	0 / 87 (0.00%)	0 / 90 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Takayasu's arteritis			
subjects affected / exposed	0 / 96 (0.00%)	0 / 87 (0.00%)	0 / 90 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			

Immunosuppressant drug therapy			
subjects affected / exposed	0 / 96 (0.00%)	0 / 87 (0.00%)	0 / 90 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Adverse drug reaction			
subjects affected / exposed	0 / 96 (0.00%)	1 / 87 (1.15%)	0 / 90 (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
Drug intolerance			
subjects affected / exposed	0 / 96 (0.00%)	0 / 87 (0.00%)	0 / 90 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Death			
subjects affected / exposed	0 / 96 (0.00%)	0 / 87 (0.00%)	1 / 90 (1.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Fatigue			
subjects affected / exposed	0 / 96 (0.00%)	0 / 87 (0.00%)	0 / 90 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malaise			
subjects affected / exposed	0 / 96 (0.00%)	0 / 87 (0.00%)	0 / 90 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Cervical dysplasia			
subjects affected / exposed	0 / 96 (0.00%)	0 / 87 (0.00%)	0 / 90 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Depression			

subjects affected / exposed	1 / 96 (1.04%)	1 / 87 (1.15%)	0 / 90 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Drug level			
subjects affected / exposed	0 / 96 (0.00%)	1 / 87 (1.15%)	0 / 90 (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
Medical observation			
subjects affected / exposed	0 / 96 (0.00%)	0 / 87 (0.00%)	0 / 90 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Hand fracture			
subjects affected / exposed	0 / 96 (0.00%)	1 / 87 (1.15%)	0 / 90 (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
Intentional overdose			
subjects affected / exposed	0 / 96 (0.00%)	0 / 87 (0.00%)	0 / 90 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Heat illness			
subjects affected / exposed	0 / 96 (0.00%)	0 / 87 (0.00%)	0 / 90 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wound			
subjects affected / exposed	0 / 96 (0.00%)	1 / 87 (1.15%)	0 / 90 (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
Ligament injury			
subjects affected / exposed	0 / 96 (0.00%)	0 / 87 (0.00%)	0 / 90 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Cardiac disorders			
Atrial flutter			
subjects affected / exposed	0 / 96 (0.00%)	0 / 87 (0.00%)	1 / 90 (1.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Supraventricular tachycardia			
subjects affected / exposed	0 / 96 (0.00%)	0 / 87 (0.00%)	1 / 90 (1.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pericarditis			
subjects affected / exposed	0 / 96 (0.00%)	0 / 87 (0.00%)	0 / 90 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ventricular tachycardia			
subjects affected / exposed	1 / 96 (1.04%)	0 / 87 (0.00%)	0 / 90 (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
Nervous system disorders			
Cerebral haemorrhage			
subjects affected / exposed	0 / 96 (0.00%)	0 / 87 (0.00%)	0 / 90 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epilepsy			
subjects affected / exposed	0 / 96 (0.00%)	0 / 87 (0.00%)	0 / 90 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neuropathy peripheral			
subjects affected / exposed	0 / 96 (0.00%)	0 / 87 (0.00%)	0 / 90 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			
Sudden hearing loss			

subjects affected / exposed	0 / 96 (0.00%)	0 / 87 (0.00%)	0 / 90 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Diabetic retinopathy			
subjects affected / exposed	0 / 96 (0.00%)	0 / 87 (0.00%)	0 / 90 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Colitis ulcerative			
subjects affected / exposed	8 / 96 (8.33%)	5 / 87 (5.75%)	5 / 90 (5.56%)
occurrences causally related to treatment / all	0 / 8	0 / 5	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colonic polyp			
subjects affected / exposed	0 / 96 (0.00%)	1 / 87 (1.15%)	0 / 90 (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
Enterocolitis			
subjects affected / exposed	0 / 96 (0.00%)	0 / 87 (0.00%)	0 / 90 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal dysplasia			
subjects affected / exposed	0 / 96 (0.00%)	0 / 87 (0.00%)	1 / 90 (1.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal polyp			
subjects affected / exposed	0 / 96 (0.00%)	0 / 87 (0.00%)	0 / 90 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis acute			
subjects affected / exposed	0 / 96 (0.00%)	0 / 87 (0.00%)	0 / 90 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal stenosis			

subjects affected / exposed	1 / 96 (1.04%)	0 / 87 (0.00%)	0 / 90 (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
Rectal ulcer haemorrhage			
subjects affected / exposed	0 / 96 (0.00%)	0 / 87 (0.00%)	0 / 90 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Stomatitis			
subjects affected / exposed	1 / 96 (1.04%)	0 / 87 (0.00%)	0 / 90 (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
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	0 / 96 (0.00%)	0 / 87 (0.00%)	0 / 90 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis			
subjects affected / exposed	0 / 96 (0.00%)	0 / 87 (0.00%)	0 / 90 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Erythema nodosum			
subjects affected / exposed	0 / 96 (0.00%)	0 / 87 (0.00%)	0 / 90 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Calculus ureteric			
subjects affected / exposed	0 / 96 (0.00%)	0 / 87 (0.00%)	0 / 90 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nephrolithiasis			
subjects affected / exposed	0 / 96 (0.00%)	0 / 87 (0.00%)	0 / 90 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Tubulointerstitial nephritis			
subjects affected / exposed	0 / 96 (0.00%)	0 / 87 (0.00%)	0 / 90 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 96 (0.00%)	1 / 87 (1.15%)	0 / 90 (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
Joint range of motion decreased			
subjects affected / exposed	0 / 96 (0.00%)	0 / 87 (0.00%)	0 / 90 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Muscle haemorrhage			
subjects affected / exposed	0 / 96 (0.00%)	0 / 87 (0.00%)	0 / 90 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteonecrosis			
subjects affected / exposed	0 / 96 (0.00%)	0 / 87 (0.00%)	0 / 90 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Periarthritis			
subjects affected / exposed	0 / 96 (0.00%)	0 / 87 (0.00%)	0 / 90 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rotator cuff syndrome			
subjects affected / exposed	0 / 96 (0.00%)	1 / 87 (1.15%)	0 / 90 (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
Infections and infestations			
Appendicitis			
subjects affected / exposed	0 / 96 (0.00%)	0 / 87 (0.00%)	0 / 90 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Bacterial infection			
subjects affected / exposed	1 / 96 (1.04%)	0 / 87 (0.00%)	0 / 90 (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
Bronchitis			
subjects affected / exposed	0 / 96 (0.00%)	1 / 87 (1.15%)	1 / 90 (1.11%)
occurrences causally related to treatment / all	0 / 0	0 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bursitis infective			
subjects affected / exposed	0 / 96 (0.00%)	0 / 87 (0.00%)	0 / 90 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cytomegalovirus infection			
subjects affected / exposed	0 / 96 (0.00%)	0 / 87 (0.00%)	0 / 90 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enteritis infectious			
subjects affected / exposed	1 / 96 (1.04%)	0 / 87 (0.00%)	0 / 90 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Erysipelas			
subjects affected / exposed	0 / 96 (0.00%)	0 / 87 (0.00%)	0 / 90 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	0 / 96 (0.00%)	0 / 87 (0.00%)	0 / 90 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal infection			
subjects affected / exposed	0 / 96 (0.00%)	0 / 87 (0.00%)	0 / 90 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gingivitis			

subjects affected / exposed	0 / 96 (0.00%)	0 / 87 (0.00%)	1 / 90 (1.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pelvic abscess			
subjects affected / exposed	0 / 96 (0.00%)	0 / 87 (0.00%)	0 / 90 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infection			
subjects affected / exposed	0 / 96 (0.00%)	0 / 87 (0.00%)	0 / 90 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia bacterial			
subjects affected / exposed	0 / 96 (0.00%)	1 / 87 (1.15%)	1 / 90 (1.11%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 96 (0.00%)	0 / 87 (0.00%)	1 / 90 (1.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis acute			
subjects affected / exposed	0 / 96 (0.00%)	1 / 87 (1.15%)	0 / 90 (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
Pseudomembranous colitis			
subjects affected / exposed	0 / 96 (0.00%)	0 / 87 (0.00%)	0 / 90 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tuberculosis			
subjects affected / exposed	0 / 96 (0.00%)	0 / 87 (0.00%)	1 / 90 (1.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Upper respiratory tract infection			

subjects affected / exposed	0 / 96 (0.00%)	0 / 87 (0.00%)	1 / 90 (1.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 96 (1.04%)	0 / 87 (0.00%)	0 / 90 (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
Diabetes mellitus			
subjects affected / exposed	0 / 96 (0.00%)	0 / 87 (0.00%)	0 / 90 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	All Adalimumab		
Total subjects affected by serious adverse events			
subjects affected / exposed	90 / 266 (33.83%)		
number of deaths (all causes)	2		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cervix carcinoma			
subjects affected / exposed	1 / 266 (0.38%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Breast cancer			
subjects affected / exposed	1 / 266 (0.38%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Pancreatic carcinoma			
subjects affected / exposed	1 / 266 (0.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Rectal cancer			

subjects affected / exposed	3 / 266 (1.13%)		
occurrences causally related to treatment / all	1 / 3		
deaths causally related to treatment / all	0 / 0		
Parathyroid tumour			
subjects affected / exposed	1 / 266 (0.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Thyroid cancer			
subjects affected / exposed	1 / 266 (0.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Uterine leiomyoma			
subjects affected / exposed	2 / 266 (0.75%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Takayasu's arteritis			
subjects affected / exposed	1 / 266 (0.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Surgical and medical procedures			
Immunosuppressant drug therapy			
subjects affected / exposed	1 / 266 (0.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Adverse drug reaction			
subjects affected / exposed	1 / 266 (0.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Drug intolerance			
subjects affected / exposed	1 / 266 (0.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Death				
subjects affected / exposed	1 / 266 (0.38%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Fatigue				
subjects affected / exposed	1 / 266 (0.38%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Malaise				
subjects affected / exposed	2 / 266 (0.75%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
Reproductive system and breast disorders				
Cervical dysplasia				
subjects affected / exposed	1 / 266 (0.38%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Psychiatric disorders				
Depression				
subjects affected / exposed	1 / 266 (0.38%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Investigations				
Drug level				
subjects affected / exposed	1 / 266 (0.38%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Medical observation				
subjects affected / exposed	3 / 266 (1.13%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Injury, poisoning and procedural complications				
Hand fracture				

subjects affected / exposed	1 / 266 (0.38%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Intentional overdose				
subjects affected / exposed	1 / 266 (0.38%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Heat illness				
subjects affected / exposed	2 / 266 (0.75%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Wound				
subjects affected / exposed	1 / 266 (0.38%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Ligament injury				
subjects affected / exposed	1 / 266 (0.38%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cardiac disorders				
Atrial flutter				
subjects affected / exposed	1 / 266 (0.38%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Supraventricular tachycardia				
subjects affected / exposed	1 / 266 (0.38%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pericarditis				
subjects affected / exposed	1 / 266 (0.38%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Ventricular tachycardia				

subjects affected / exposed	0 / 266 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Cerebral haemorrhage			
subjects affected / exposed	1 / 266 (0.38%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Epilepsy			
subjects affected / exposed	1 / 266 (0.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Neuropathy peripheral			
subjects affected / exposed	1 / 266 (0.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Ear and labyrinth disorders			
Sudden hearing loss			
subjects affected / exposed	1 / 266 (0.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Eye disorders			
Diabetic retinopathy			
subjects affected / exposed	1 / 266 (0.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Colitis ulcerative			
subjects affected / exposed	38 / 266 (14.29%)		
occurrences causally related to treatment / all	2 / 40		
deaths causally related to treatment / all	0 / 0		
Colonic polyp			

subjects affected / exposed	3 / 266 (1.13%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Enterocolitis				
subjects affected / exposed	1 / 266 (0.38%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal dysplasia				
subjects affected / exposed	3 / 266 (1.13%)			
occurrences causally related to treatment / all	1 / 3			
deaths causally related to treatment / all	0 / 0			
Intestinal polyp				
subjects affected / exposed	1 / 266 (0.38%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pancreatitis acute				
subjects affected / exposed	1 / 266 (0.38%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Rectal stenosis				
subjects affected / exposed	1 / 266 (0.38%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Rectal ulcer haemorrhage				
subjects affected / exposed	1 / 266 (0.38%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Stomatitis				
subjects affected / exposed	0 / 266 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hepatobiliary disorders				
Cholelithiasis				

subjects affected / exposed	1 / 266 (0.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cholecystitis			
subjects affected / exposed	2 / 266 (0.75%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Erythema nodosum			
subjects affected / exposed	1 / 266 (0.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Calculus ureteric			
subjects affected / exposed	1 / 266 (0.38%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Nephrolithiasis			
subjects affected / exposed	1 / 266 (0.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Tubulointerstitial nephritis			
subjects affected / exposed	1 / 266 (0.38%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 266 (0.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Joint range of motion decreased			
subjects affected / exposed	1 / 266 (0.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Muscle haemorrhage				
subjects affected / exposed	1 / 266 (0.38%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Osteonecrosis				
subjects affected / exposed	1 / 266 (0.38%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Periarthritis				
subjects affected / exposed	1 / 266 (0.38%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Rotator cuff syndrome				
subjects affected / exposed	1 / 266 (0.38%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
Appendicitis				
subjects affected / exposed	1 / 266 (0.38%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Bacterial infection				
subjects affected / exposed	0 / 266 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bronchitis				
subjects affected / exposed	2 / 266 (0.75%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
Bursitis infective				
subjects affected / exposed	1 / 266 (0.38%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Cytomegalovirus infection				

subjects affected / exposed	1 / 266 (0.38%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Enteritis infectious			
subjects affected / exposed	2 / 266 (0.75%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Erysipelas			
subjects affected / exposed	1 / 266 (0.38%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Gastroenteritis			
subjects affected / exposed	2 / 266 (0.75%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal infection			
subjects affected / exposed	1 / 266 (0.38%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Gingivitis			
subjects affected / exposed	1 / 266 (0.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pelvic abscess			
subjects affected / exposed	1 / 266 (0.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infection			
subjects affected / exposed	1 / 266 (0.38%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonia bacterial			

subjects affected / exposed	3 / 266 (1.13%)		
occurrences causally related to treatment / all	1 / 3		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	1 / 266 (0.38%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Pyelonephritis acute			
subjects affected / exposed	2 / 266 (0.75%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Pseudomembranous colitis			
subjects affected / exposed	1 / 266 (0.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Tuberculosis			
subjects affected / exposed	1 / 266 (0.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Upper respiratory tract infection			
subjects affected / exposed	1 / 266 (0.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 266 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Diabetes mellitus			
subjects affected / exposed	2 / 266 (0.75%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Double-blind Placebo	Double-blind Adalimumab 80 mg/40 mg	Double-blind Adalimumab 160 mg/80 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	51 / 96 (53.13%)	47 / 87 (54.02%)	60 / 90 (66.67%)
Investigations			
White blood cell count decreased			
subjects affected / exposed	2 / 96 (2.08%)	3 / 87 (3.45%)	6 / 90 (6.67%)
occurrences (all)	2	3	8
Vascular disorders			
Hypertension			
subjects affected / exposed	2 / 96 (2.08%)	1 / 87 (1.15%)	1 / 90 (1.11%)
occurrences (all)	2	1	1
Nervous system disorders			
Headache			
subjects affected / exposed	6 / 96 (6.25%)	3 / 87 (3.45%)	7 / 90 (7.78%)
occurrences (all)	9	3	7
Blood and lymphatic system disorders			
Iron deficiency anaemia			
subjects affected / exposed	7 / 96 (7.29%)	4 / 87 (4.60%)	8 / 90 (8.89%)
occurrences (all)	7	4	8
General disorders and administration site conditions			
Malaise			
subjects affected / exposed	0 / 96 (0.00%)	3 / 87 (3.45%)	7 / 90 (7.78%)
occurrences (all)	0	3	7
Injection site reaction			
subjects affected / exposed	2 / 96 (2.08%)	7 / 87 (8.05%)	6 / 90 (6.67%)
occurrences (all)	2	7	7
Pyrexia			
subjects affected / exposed	4 / 96 (4.17%)	4 / 87 (4.60%)	5 / 90 (5.56%)
occurrences (all)	4	4	5
Gastrointestinal disorders			
Colitis ulcerative			
subjects affected / exposed	5 / 96 (5.21%)	2 / 87 (2.30%)	5 / 90 (5.56%)
occurrences (all)	6	2	6
Dental caries			

subjects affected / exposed	5 / 96 (5.21%)	6 / 87 (6.90%)	3 / 90 (3.33%)
occurrences (all)	5	6	3
Nausea			
subjects affected / exposed	4 / 96 (4.17%)	2 / 87 (2.30%)	5 / 90 (5.56%)
occurrences (all)	5	2	6
Stomatitis			
subjects affected / exposed	1 / 96 (1.04%)	0 / 87 (0.00%)	1 / 90 (1.11%)
occurrences (all)	1	0	1
Vomiting			
subjects affected / exposed	1 / 96 (1.04%)	0 / 87 (0.00%)	4 / 90 (4.44%)
occurrences (all)	1	0	4
Hepatobiliary disorders			
Hepatic function abnormal			
subjects affected / exposed	0 / 96 (0.00%)	1 / 87 (1.15%)	1 / 90 (1.11%)
occurrences (all)	0	1	1
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	2 / 96 (2.08%)	0 / 87 (0.00%)	2 / 90 (2.22%)
occurrences (all)	2	0	2
Upper respiratory tract inflammation			
subjects affected / exposed	4 / 96 (4.17%)	3 / 87 (3.45%)	5 / 90 (5.56%)
occurrences (all)	5	4	6
Skin and subcutaneous tissue disorders			
Eczema			
subjects affected / exposed	2 / 96 (2.08%)	4 / 87 (4.60%)	1 / 90 (1.11%)
occurrences (all)	2	4	1
Rash			
subjects affected / exposed	5 / 96 (5.21%)	4 / 87 (4.60%)	3 / 90 (3.33%)
occurrences (all)	5	5	3
Psychiatric disorders			
Insomnia			
subjects affected / exposed	2 / 96 (2.08%)	2 / 87 (2.30%)	3 / 90 (3.33%)
occurrences (all)	2	2	3
Musculoskeletal and connective tissue disorders			
Back pain			

subjects affected / exposed	3 / 96 (3.13%)	3 / 87 (3.45%)	4 / 90 (4.44%)
occurrences (all)	3	3	4
Arthralgia			
subjects affected / exposed	1 / 96 (1.04%)	5 / 87 (5.75%)	2 / 90 (2.22%)
occurrences (all)	1	6	2
Infections and infestations			
Gastroenteritis			
subjects affected / exposed	1 / 96 (1.04%)	0 / 87 (0.00%)	2 / 90 (2.22%)
occurrences (all)	1	0	2
Influenza			
subjects affected / exposed	6 / 96 (6.25%)	3 / 87 (3.45%)	4 / 90 (4.44%)
occurrences (all)	6	3	4
Nasopharyngitis			
subjects affected / exposed	21 / 96 (21.88%)	19 / 87 (21.84%)	30 / 90 (33.33%)
occurrences (all)	38	29	44
Oral herpes			
subjects affected / exposed	0 / 96 (0.00%)	1 / 87 (1.15%)	0 / 90 (0.00%)
occurrences (all)	0	1	0
Pharyngitis			
subjects affected / exposed	2 / 96 (2.08%)	1 / 87 (1.15%)	1 / 90 (1.11%)
occurrences (all)	2	1	1

Non-serious adverse events	All Adalimumab		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	235 / 266 (88.35%)		
Investigations			
White blood cell count decreased			
subjects affected / exposed	22 / 266 (8.27%)		
occurrences (all)	30		
Vascular disorders			
Hypertension			
subjects affected / exposed	15 / 266 (5.64%)		
occurrences (all)	15		
Nervous system disorders			
Headache			
subjects affected / exposed	42 / 266 (15.79%)		
occurrences (all)	62		

Blood and lymphatic system disorders			
Iron deficiency anaemia			
subjects affected / exposed	24 / 266 (9.02%)		
occurrences (all)	29		
General disorders and administration site conditions			
Malaise			
subjects affected / exposed	13 / 266 (4.89%)		
occurrences (all)	13		
Injection site reaction			
subjects affected / exposed	25 / 266 (9.40%)		
occurrences (all)	29		
Pyrexia			
subjects affected / exposed	24 / 266 (9.02%)		
occurrences (all)	28		
Gastrointestinal disorders			
Colitis ulcerative			
subjects affected / exposed	20 / 266 (7.52%)		
occurrences (all)	20		
Dental caries			
subjects affected / exposed	27 / 266 (10.15%)		
occurrences (all)	28		
Nausea			
subjects affected / exposed	26 / 266 (9.77%)		
occurrences (all)	32		
Stomatitis			
subjects affected / exposed	14 / 266 (5.26%)		
occurrences (all)	18		
Vomiting			
subjects affected / exposed	23 / 266 (8.65%)		
occurrences (all)	26		
Hepatobiliary disorders			
Hepatic function abnormal			
subjects affected / exposed	14 / 266 (5.26%)		
occurrences (all)	16		
Respiratory, thoracic and mediastinal disorders			

Oropharyngeal pain subjects affected / exposed occurrences (all)	23 / 266 (8.65%) 30		
Upper respiratory tract inflammation subjects affected / exposed occurrences (all)	27 / 266 (10.15%) 55		
Skin and subcutaneous tissue disorders Eczema subjects affected / exposed occurrences (all)	27 / 266 (10.15%) 33		
Rash subjects affected / exposed occurrences (all)	27 / 266 (10.15%) 30		
Psychiatric disorders Insomnia subjects affected / exposed occurrences (all)	23 / 266 (8.65%) 23		
Musculoskeletal and connective tissue disorders Back pain subjects affected / exposed occurrences (all)	31 / 266 (11.65%) 34		
Arthralgia subjects affected / exposed occurrences (all)	21 / 266 (7.89%) 25		
Infections and infestations Gastroenteritis subjects affected / exposed occurrences (all)	16 / 266 (6.02%) 16		
Influenza subjects affected / exposed occurrences (all)	20 / 266 (7.52%) 22		
Nasopharyngitis subjects affected / exposed occurrences (all)	162 / 266 (60.90%) 463		
Oral herpes			

subjects affected / exposed	14 / 266 (5.26%)		
occurrences (all)	14		
Pharyngitis			
subjects affected / exposed	15 / 266 (5.64%)		
occurrences (all)	19		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
20 April 2009	Clarified the concomitant usage of corticosteroids. Description change for protocol deviation due to the revision of GCP.
10 May 2011	Added the procedure to collecting Mayo score and partial Mayo score information for 5 days (from 5 days to 1 day before the evaluation date).
12 April 2012	Added tuberculosis text in the procedure on or after Week 52.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported