Clinical trial results:
A Multicenter, Open-Label Study of the Human Anti-TNF Monoclonal Antibody Adalimumab to Evaluate the Long Term Safety and Tolerability of Repeated Administration of Adalimumab in Subjects With Ulcerative Colitis

Summary

EudraCT number	2007-004157-28
Trial protocol	BE ES DE HU AT SK CZ FR IT NL PT SE
Global end of trial date	23 December 2016

Results information

Result version number	v1 (current)
This version publication date	07 December 2017
First version publication date	07 December 2017

Trial information

Trial identification

Sponsor protocol code	M10-223

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00573794
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	Andreas Lazar, MD, AbbVie, andreas.lazar@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	23 December 2016
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	23 December 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the long-term safety and maintenance of response of adalimumab in subjects with ulcerative colitis who participated in and successfully completed Study M06-826 (EudraCT number 2006-002781-20) or Study M06-827 (EudraCT number 2006-002782-40).

Protection of trial subjects:

Subject read and understood the information provided about the study and gave written permission.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	28 November 2007
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	Netherlands: 2
Country: Number of subjects enrolled	Poland: 28
Country: Number of subjects enrolled	Slovakia: 58
Country: Number of subjects enrolled	Spain: 3
Country: Number of subjects enrolled	Sweden: 3
Country: Number of subjects enrolled	Austria: 17
Country: Number of subjects enrolled	Belgium: 27
Country: Number of subjects enrolled	Czech Republic: 82
Country: Number of subjects enrolled	France: 14
Country: Number of subjects enrolled	Germany: 41
Country: Number of subjects enrolled	Hungary: 38
Country: Number of subjects enrolled	Italy: 9
Country: Number of subjects enrolled	Australia: 13
Country: Number of subjects enrolled	Canada: 78
Country: Number of subjects enrolled	New Zealand: 1
Country: Number of subjects enrolled	Switzerland: 9
Country: Number of subjects enrolled	United States: 166
Country: Number of subjects enrolled	Israel: 3
Worldwide total number of subjects	592
EEA total number of subjects	322

Notes:

Subjects enrolled per age group	
In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	567
From 65 to 84 years	25
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 592 subjects were randomized and received at least 1 dose of study drug (safety population); 7 subjects enrolled at 3 noncompliant sites were excluded from the analyses (Intent-to-treat 1 [ITT-1] population; N=585).

Period 1

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

Arms

Arm title	Adalimumab 40 mg EOW/EW

Arm description:

Open-label adalimumab 40 mg every other week (EOW) or every week (EW). Participants who entered from an open-label cohort continued their previous dosing regimen of adalimumab EOW or EW; participants who entered from a double-blind cohort received adalimumab EOW.

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

Dosage and administration details:

adalimumab prefilled syringes administered as subcutaneous injection EW or EOW

Number of subjects in period 1[1]	Adalimumab 40 mg EOW/EW
Started	585
Completed	255
Not completed	330
Protocol violation	6
Not Specified	46
Adverse event	81
Withdrew consent	90
Lost to follow-up	13
Lack of efficacy	94

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: ITT-1 population: All subjects who received ≥1 dose of study drug excluding 7 subjects at noncompliant sites.

Baseline characteristics

Reporting groups	
Reporting group title	Adalimumab 40 mg EOW/EW
Reporting group description:	
Open-label adalimumab 40 mg every other week (EOW) or every week (EW). Participants who entered from an open-label cohort continued their previous dosing regimen of adalimumab EOW or EW; participants who entered from a double-blind cohort received adalimumab EOW.	

Reporting group values	Adalimumab 40 mg EOW/EW	Total	
Number of subjects	585	585	
Age categorical Units: Subjects			

Age continuous			
ITT-1 population: All subjects who received ≥1 dose of study drug excluding 7 subjects at noncompliant sites.			
Units: years			
arithmetic mean	41.6		
standard deviation	± 12.85	-	
Gender categorical			
ITT-1 population: All subjects who received ≥1 dose of study drug excluding 7 subjects at noncompliant sites.			
Units: Subjects			
Female	214	214	
Male	371	371	

End points

End points reporting groups

Reporting group title	Adalimumab 40 mg EOW/EW

Reporting group description:

Open-label adalimumab 40 mg every other week (EOW) or every week (EW). Participants who entered from an open-label cohort continued their previous dosing regimen of adalimumab EOW or EW; participants who entered from a double-blind cohort received adalimumab EOW.

Primary: Partial Mayo Score: Change From Baseline Over Time

End point title	Partial Mayo Score: Change From Baseline Over Time[1]

End point description:

The Partial Mayo score (Mayo score without endoscopy) ranges from 0 (normal or inactive disease) to 9 (severe disease) and is calculated as the sum of 3 subscores (stool frequency, rectal bleeding and physician's global assessment [PGA]), each of which ranges from 0 (normal) to 3 (severe disease). A negative change in Partial Mayo score indicates improvement. N=number of subjects with evaluable data at given time point.

End point type	Primary

End point timeframe:

Baseline (Week 0), Weeks 48, 96, 144, 192, 240, 292, 340, 388

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 40 mg EOW/EW			
Subject group type	Reporting group			
Number of subjects analysed	584[2]			
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline (N=584)	2.5 (± 2.02)			
Change from Baseline to Week 48 (N=512)	-0.2 (± 2.04)			
Change from Baseline to Week 96 (N=432)	-0.4 (± 1.78)			
Change from Baseline to Week 144 (N=371)	-0.5 (± 2.06)			
Change from Baseline to Week 192 (N=292)	-0.6 (± 1.84)			
Change from Baseline to Week 240 (N=179)	-0.8 (± 1.79)			
Change from Baseline to Week 292 (N=73)	-0.7 (± 2.05)			
Change from Baseline to Week 340 (N=23)	-1.0 (± 1.97)			
Change from Baseline to Week 388 (N=3)	-2.0 (± 1.00)			

Notes:

[2] - Participants in ITT-1 population with both Baseline and visit values.

Statistical analyses

No statistical analyses for this end point

Primary: Mayo Score: Change From Baseline Over Time

End point title	Mayo Score: Change From Baseline Over Time[3]

End point description:

The Mayo score ranges from 0 (normal or inactive disease) to 12 (severe disease) and is calculated as the sum of 3 subscores (stool frequency, rectal bleeding, endoscopy, and physician's global assessment [PGA]), each of which ranges from 0 (normal) to 3 (severe disease). A negative change in Mayo score indicates improvement.N=number of subjects with evaluable data at given time point.

End point type	Primary

End point timeframe:

Baseline (Week 0), Weeks 48, 96, 144, 192, 240, 292, 340, 388

Notes:

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

End point values	Adalimumab 40 mg EOW/EW			
Subject group type	Reporting group			
Number of subjects analysed	583[4]			
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline (N=583)	3.5 (± 2.72)			
Change from Baseline to Week 48 (N=493)	-0.3 (± 2.64)			
Change from Baseline to Week 96 (N=422)	-0.5 (± 2.49)			
Change from Baseline to Week 144 (N=360)	-0.8 (± 2.73)			
Change from Baseline to Week 192 (N=277)	-0.8 (± 2.52)			
Change from Baseline to Week 240 (N=168)	-1.0 (± 2.40)			
Change from Baseline to Week 292 (N=72)	-0.9 (± 2.84)			
Change from Baseline to Week 340 (N=23)	-1.3 (± 2.87)			
Change from Baseline to Week 388 (N=3)	-2.0 (± 1.73)			

Notes:

[4] - Participants in ITT-1 population with both Baseline and visit values.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Remission Per Partial Mayo Score Over Time

End point title	Percentage of Participants With Remission Per Partial Mayo Score Over Time

End point description:

The Partial Mayo score (Mayo score without endoscopy) ranges from 0 (normal or inactive disease) to 9 (severe disease) and is calculated as the sum of 3 subscores (stool frequency, rectal bleeding and physician's global assessment [PGA]), each of which ranges from 0 (normal) to 3 (severe disease). Remission was defined as Partial Mayo score ≤ 2 with no subscore > 1. N=number of subjects with

evaluable data at given time point.

End point type	Secondary

End point timeframe:

Baseline (Week 0), Weeks 48, 96, 144, 192, 240, 292, 340, 388

End point values	Adalimumab 40 mg EOW/EW			
Subject group type	Reporting group			
Number of subjects analysed	585[5]			
Units: percentage of participants				
number (not applicable)				
Baseline (N=584)	52.4			
Change from Baseline to Week 48 (N=513)	61.2			
Change from Baseline to Week 96 (N=433)	69.3			
Change from Baseline to Week 144 (N=372)	75.0			
Change from Baseline to Week 192 (N=293)	74.7			
Change from Baseline to Week 240 (N=180)	77.2			
Change from Baseline to Week 292 (N=73)	76.7			
Change from Baseline to Week 340 (N=23)	73.9			
Change from Baseline to Week 388 (N=3)	100			

Notes:

[5] - Participants in ITT-1 population with evaluable data at given timepoint.

Statistical analyses

No statistical analyses for this end point

Secondary: Mayo Endoscopy Subscore: Change From Baseline Over Time

End point title	Mayo Endoscopy Subscore: Change From Baseline Over Time

End point description:

The Mayo Endoscopy subscore ranges from 0 (normal) to 3 (severe disease). A negative change in Mayo Endoscopy subscore indicates improvement. N=number of subjects with evaluable data at given time point.

End point type	Secondary

End point timeframe:

Baseline (Week 0), Weeks 48, 96, 144, 192, 240, 292, 340, 388

End point values	Adalimumab 40 mg EOW/EW			
Subject group type	Reporting group			
Number of subjects analysed	583[6]			
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline (N=583)	1.1 (± 0.94)			
Change from Baseline to Week 48 (N=493)	-0.1 (± 0.95)			
Change from Baseline to Week 96 (N=422)	-0.1 (± 1.02)			
Change from Baseline to Week 144 (N=360)	-0.2 (± 0.93)			
Change from Baseline to Week 192 (N=277)	-0.3 (± 0.98)			
Change from Baseline to Week 240 (N=168)	-0.3 (± 0.97)			
Change from Baseline to Week 292 (N=72)	-0.3 (± 1.03)			
Change from Baseline to Week 340 (N=23)	-0.3 (± 1.18)			
Change from Baseline to Week 388 (N=3)	0.0 (± 1.00)			

Notes:

[6] - Participants in ITT-1 population with both Baseline and visit values.

Statistical analyses

No statistical analyses for this end point

Secondary: Mayo Rectal Bleeding Subscore: Change From Baseline Over Time

End point title	Mayo Rectal Bleeding Subscore: Change From Baseline Over Time

End point description:

The Mayo Rectal Bleeding subscore ranges from 0 (normal) to 3 (severe disease). A negative change in Mayo Rectal Bleeding subscore indicates improvement. N=number of subjects with evaluable data at given time point.

End point type	Secondary

End point timeframe:

Baseline (Week 0), Weeks 48, 96, 144, 192, 240, 292, 340, 388

End point values	Adalimumab 40 mg EOW/EW			
Subject group type	Reporting group			
Number of subjects analysed	584[7]			
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline (N=584)	0.4 (± 0.68)			
Change from Baseline to Week 48 (N=512)	-0.1 (± 0.73)			
Change from Baseline to Week 96 (N=432)	-0.0 (± 0.63)			

Change from Baseline to Week 144 (N=371)	-0.1 (± 0.74)			
Change from Baseline to Week 192 (N=292)	-0.1 (± 0.69)			
Change from Baseline to Week 240 (N=179)	-0.2 (± 0.63)			
Change from Baseline to Week 292 (N=73)	-0.2 (± 0.76)			
Change from Baseline to Week 340 (N=23)	-0.2 (± 0.80)			
Change from Baseline to Week 388 (N=3)	-1.0 (± 1.00)			

Notes:

[7] - Participants in ITT-1 population with both Baseline and visit values.

Statistical analyses

No statistical analyses for this end point

Secondary: Mayo Physician's Global Assessment of Disease Severity Subscore: Change From Baseline Over Time

End point title	Mayo Physician's Global Assessment of Disease Severity Subscore: Change From Baseline Over Time

End point description:

The Mayo Physician's Global Assessment of Disease Severity subscore ranges from 0 (normal) to 3 (severe disease). A negative change in Mayo Physician's Global Assessment of Disease Severity subscore indicates improvement. N=number of subjects with evaluable data at given time point.

End point type	Secondary

End point timeframe:

Baseline (Week 0), Weeks 48, 96, 144, 192, 240, 292, 340, 388

End point values	Adalimumab 40 mg EOW/EW			
Subject group type	Reporting group			
Number of subjects analysed	584[8]			
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline (N=584)	0.8 (± 0.81)			
Change from Baseline to Week 48 (N=512)	-0.1 (± 0.89)			
Change from Baseline to Week 96 (N=432)	-0.2 (± 0.84)			
Change from Baseline to Week 144 (N=371)	-0.2 (± 0.89)			
Change from Baseline to Week 192 (N=292)	-0.2 (± 0.82)			
Change from Baseline to Week 240 (N=179)	-0.3 (± 0.82)			
Change from Baseline to Week 292 (N=73)	-0.2 (± 0.79)			
Change from Baseline to Week 340 (N=23)	-0.3 (± 0.88)			
Change from Baseline to Week 388 (N=3)	-0.7 (± 0.58)			

Notes:

[8] - Participants in ITT-1 population with both Baseline and visit values.

Statistical analyses

No statistical analyses for this end point

Secondary: Mayo Stool Frequency Subscore: Change From Baseline Over Time

End point title	Mayo Stool Frequency Subscore: Change From Baseline Over Time

End point description:

The Mayo Stool Frequency subscore ranges from 0 (normal) to 3 (severe disease). A negative change in Mayo Stool Frequency subscore indicates improvement. N=number of subjects with evaluable data at given time point.

End point type	Secondary

End point timeframe:

Baseline (Week 0), Weeks 48, 96, 144, 192, 240, 292, 340, 388

End point values	Adalimumab 40 mg EOW/EW			
Subject group type	Reporting group			
Number of subjects analysed	584[9]			
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline (N=584)	1.3 (± 1.01)			
Change from Baseline to Week 48 (N=512)	-0.1 (± 0.89)			
Change from Baseline to Week 96 (N=432)	-0.2 (± 0.84)			
Change from Baseline to Week 144 (N=371)	-0.2 (± 0.89)			
Change from Baseline to Week 192 (N=292)	-0.2 (± 0.82)			
Change from Baseline to Week 240 (N=179)	-0.3 (± 0.86)			
Change from Baseline to Week 292 (N=73)	-0.3 (± 1.00)			
Change from Baseline to Week 340 (N=23)	-0.5 (± 0.99)			
Change from Baseline to Week 388 (N=3)	-0.3 (± 0.58)			

Notes:

[9] - Participants in ITT-1 population with both Baseline and visit values.

Statistical analyses

No statistical analyses for this end point

Secondary: Inflammatory Bowel Disease Questionnaire (IBDQ): Change From

Baseline Over Time

End point title	Inflammatory Bowel Disease Questionnaire (IBDQ): Change From Baseline Over Time

End point description:

The IBDQ is a 32-item questionnaire that assesses how the subject felt during the 2 weeks before the measurement time point. Questions are related to symptoms the subject might have had as a result of UC, how the subject felt in general, how the subject's mood was, and social and work problems the subject might have that resulted from UC. An increase in IBDQ score indicates less impact of UC on the subject's life. The responses to each question 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). N=number of subjects with evaluable data at given time point.

End point type	Secondary

End point timeframe:

Baseline (Week 0), Weeks 48, 96, 144, 192, 240, 292, 340, 388

End point values	Adalimumab 40 mg EOW/EW			
Subject group type	Reporting group			
Number of subjects analysed	572[10]			
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline (N=572)	176.0 (± 34.45)			
Change from Baseline to Week 48 (N=485)	2.1 (± 28.91)			
Change from Baseline to Week 96 (N=412)	4.7 (± 28.73)			
Change from Baseline to Week 144 (N=355)	5.2 (± 30.64)			
Change from Baseline to Week 192 (N=279)	7.6 (± 28.66)			
Change from Baseline to Week 240 (N=174)	11.2 (± 25.98)			
Change from Baseline to Week 292 (N=70)	14.8 (± 27.36)			
Change from Baseline to Week 340 (N=23)	14.6 (± 28.12)			
Change from Baseline to Week 388 (N=3)	11.0 (± 12.53)			

Notes:

[10] - Participants in ITT-1 population with both Baseline and visit values.

Statistical analyses

No statistical analyses for this end point

Secondary: 36-Item Short Form Health Survey Version 2 (SF-36) Mental Component Score: Change From Baseline Over Time

End point title	36-Item Short Form Health Survey Version 2 (SF-36) Mental Component Score: Change From Baseline Over Time

End point description:

The SF-36 is a health-related survey that assesses participant's quality of life and consists of 36 questions covering 8 health domains: physical functioning, bodily pain, role limitations due to physical problems and emotional problems, general health, mental health, social functioning, vitality, and 2 component scores (mental [MCS] and physical [PCS]). MCS consisted of social functioning, vitality,

mental health, and role-emotional scales. PCS consisted of physical functioning, bodily pain, role-physical, and general health scales. Each domain is scored by summing the individual items and transforming the scores into a 0 (poorest health) to 100 (best health) scale with higher scores indicating better health status or functioning. N=number of subjects with evaluable data at given time point.

End point type	Secondary

End point timeframe:

Baseline (Week 0), Weeks 48, 96, 144, 192, 240, 292, 340, 388

End point values	Adalimumab 40 mg EOW/EW			
Subject group type	Reporting group			
Number of subjects analysed	575[11]			
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline (N=575)	47.1 (± 10.16)			
Change from Baseline to Week 48 (N=498)	-0.7 (± 9.61)			
Change from Baseline to Week 96 (N=423)	0.3 (± 9.64)			
Change from Baseline to Week 144 (N=360)	0.0 (± 9.52)			
Change from Baseline to Week 192 (N=286)	0.1 (± 9.41)			
Change from Baseline to Week 240 (N=178)	0.7 (± 7.86)			
Change from Baseline to Week 292 (N=71)	1.8 (± 8.13)			
Change from Baseline to Week 340 (N=23)	1.8 (± 6.81)			
Change from Baseline to Week 388 (N=3)	-7.3 (± 5.58)			

Notes:

[11] - Participants in ITT-1 population with both Baseline and visit values.

Statistical analyses

No statistical analyses for this end point

Secondary: 36-Item Short Form Health Survey Version 2 (SF-36) Physical Component Score: Change From Baseline Over Time

End point title	36-Item Short Form Health Survey Version 2 (SF-36) Physical Component Score: Change From Baseline Over Time

End point description:

The SF-36 is a health-related survey that assesses participant's quality of life and consists of 36 questions covering 8 health domains: physical functioning, bodily pain, role limitations due to physical problems and emotional problems, general health, mental health, social functioning, vitality, and 2 component scores (mental [MCS] and physical [PCS]). MCS consisted of social functioning, vitality, mental health, and role-emotional scales. PCS consisted of physical functioning, bodily pain, role-physical, and general health scales. Each domain is scored by summing the individual items and transforming the scores into a 0 (poorest health) to 100 (best health) scale with higher scores indicating better health status or functioning. N=number of subjects with evaluable data at given time point.

End point type	Secondary

End point timeframe:

Baseline (Week 0), Weeks 48, 96, 144, 192, 240, 292, 340, 388

End point values	Adalimumab 40 mg EOW/EW			
Subject group type	Reporting group			
Number of subjects analysed	575[12]			
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline (N=575)	49.3 (± 8.06)			
Change from Baseline to Week 48 (N=498)	0.7 (± 6.98)			
Change from Baseline to Week 96 (N=423)	1.2 (± 6.26)			
Change from Baseline to Week 144 (N=360)	1.1 (± 7.08)			
Change from Baseline to Week 192 (N=286)	1.3 (± 7.46)			
Change from Baseline to Week 240 (N=178)	2.2 (± 6.23)			
Change from Baseline to Week 292 (N=71)	2.5 (± 7.03)			
Change from Baseline to Week 340 (N=23)	3.0 (± 8.71)			
Change from Baseline to Week 388 (N=3)	8.4 (± 2.00)			

Notes:

[12] - Participants in ITT-1 population with both Baseline and visit values.

Statistical analyses

No statistical analyses for this end point

Secondary: Work Productivity and Activity Impairment: General Health Version 2.0 (WPAI:GH) Work Time Missed Because of Ulcerative Colitis: Change From Baseline Over Time

End point title	Work Productivity and Activity Impairment: General Health Version 2.0 (WPAI:GH) Work Time Missed Because of Ulcerative Colitis: Change From Baseline Over Time

End point description:

The WPAI:GH questionnaire was used to assess work and activity impairment due to symptoms of ulcerative colitis in the last 7 days. The self-administered questionnaire measures the effect of the subject's health problems on work and daily activities in the previous week, specifically, the number of hours missed from work due to health problems, how much the subject's health problems affected work productivity, and how much the subject's health problems affected regular activities. Low scores indicate little or no impact of health problems on work and activities, and a negative change in the WPAI score indicates improvement. N=number of subjects with evaluable data at given time point.

End point type	Secondary

End point timeframe:

Baseline (Week 0), Weeks 48, 96, 144, 192, 240, 292, 340, 388

End point values	Adalimumab 40 mg EOW/EW			
Subject group type	Reporting group			
Number of subjects analysed	375[13]			
Units: percent of work time missed				
arithmetic mean (standard deviation)				
Baseline (N=375)	4.5 (± 15.42)			
Change from Baseline to Week 48 (N=294)	1.6 (± 24.04)			
Change from Baseline to Week 96 (N=245)	-0.2 (± 18.41)			
Change from Baseline to Week 144 (N=213)	0.9 (± 20.19)			
Change from Baseline to Week 192 (N=170)	0.2 (± 19.05)			
Change from Baseline to Week 240 (N=109)	-1.1 (± 17.21)			
Change from Baseline to Week 292 (N=47)	8.2 (± 30.65)			
Change from Baseline to Week 340 (N=16)	6.4 (± 24.96)			
Change from Baseline to Week 388 (N=2)	0.0 (± 0.00)			

Notes:

[13] - Participants in ITT-1 population with both Baseline and visit values.

Statistical analyses

No statistical analyses for this end point

Secondary: WPAI:GH Impairment While Working: Change From Baseline Over Time

End point title	WPAI:GH Impairment While Working: Change From Baseline Over Time

End point description:

The WPAI:GH questionnaire was used to assess work and activity impairment due to symptoms of ulcerative colitis in the last 7 days. The self-administered questionnaire measures the effect of the subject's health problems on work and daily activities in the previous week, specifically, the number of hours missed from work due to health problems, how much the subject's health problems affected work productivity, and how much the subject's health problems affected regular activities. Low scores indicate little or no impact of health problems on work and activities, and a negative change in the WPAI score indicates improvement. N=number of subjects with evaluable data at given time point.

End point type	Secondary

End point timeframe:

Baseline (Week 0), Weeks 48, 96, 144, 192, 240, 292, 340, 388

End point values	Adalimumab 40 mg EOW/EW			
Subject group type	Reporting group			
Number of subjects analysed	388[14]			
Units: percent of work time impaired				
arithmetic mean (standard deviation)				
Baseline (N=388)	16.7 (± 20.73)			
Change from Baseline to Week 48 (N=315)	1.1 (± 22.45)			

Change from Baseline to Week 96 (N=262)	-1.9 (± 20.86)			
Change from Baseline to Week 144 (N=233)	-0.2 (± 24.11)			
Change from Baseline to Week 192 (N=177)	-2.9 (± 24.04)			
Change from Baseline to Week 240 (N=119)	-4.0 (± 21.40)			
Change from Baseline to Week 292 (N=52)	-3.8 (± 25.45)			
Change from Baseline to Week 340 (N=16)	-13.8 (± 26.04)			
Change from Baseline to Week 388 (N=2)	-15.0 (± 21.21)			

Notes:

[14] - Participants in ITT-1 population with both Baseline and visit values.

Statistical analyses

No statistical analyses for this end point

Secondary: WPAI:GH Overall Work Impairment: Change From Baseline Over Time

End point title	WPAI:GH Overall Work Impairment: Change From Baseline Over Time

End point description:

The WPAI:GH questionnaire was used to assess work and activity impairment due to symptoms of ulcerative colitis in the last 7 days. The self-administered questionnaire measures the effect of the subject's health problems on work and daily activities in the previous week, specifically, the number of hours missed from work due to health problems, how much the subject's health problems affected work productivity, and how much the subject's health problems affected regular activities. Low scores indicate little or no impact of health problems on work and activities, and a negative change in the WPAI score indicates improvement.

End point type	Secondary

End point timeframe:

Baseline (Week 0), Weeks 48, 96, 144, 192, 240, 292, 340, 388

End point values	Adalimumab 40 mg EOW/EW			
Subject group type	Reporting group			
Number of subjects analysed	373[15]			
Units: percent of overall work impairment				
arithmetic mean (standard deviation)				
Baseline (N=373)	20.1 (± 24.30)			
Change from Baseline to Week 48 (N=294)	1.2 (± 28.15)			
Change from Baseline to Week 96 (N=244)	-2.7 (± 24.99)			
Change from Baseline to Week 144 (N=212)	-0.8 (± 28.05)			
Change from Baseline to Week 192 (N=168)	-2.6 (± 26.69)			
Change from Baseline to Week 240 (N=109)	-5.0 (± 24.1)			

Change from Baseline to Week 292 (N=47)	1.4 (± 35.53)			
Change from Baseline to Week 340 (N=16)	-7.3 (± 12.05)			
Change from Baseline to Week 388 (N=2)	-15.0 (± 21.21)			

Notes:

[15] - Participants in ITT-1 population with both Baseline and visit values.

Statistical analyses

No statistical analyses for this end point

Secondary: WPAI:GH Activity Impairment: Change From Baseline Over Time

End point title	WPAI:GH Activity Impairment: Change From Baseline Over Time

End point description:

The WPAI:GH questionnaire was used to assess work and activity impairment due to symptoms of ulcerative colitis in the last 7 days. The self-administered questionnaire measures the effect of the subject's health problems on work and daily activities in the previous week, specifically, the number of hours missed from work due to health problems, how much the subject's health problems affected work productivity, and how much the subject's health problems affected regular activities. Low scores indicate little or no impact of health problems on work and activities, and a negative change in the WPAI score indicates improvement.N=number of subjects with evaluable data at given time point.

End point type	Secondary

End point timeframe:

Baseline (Week 0), Weeks 48, 96, 144, 192, 240, 292, 340, 388

End point values	Adalimumab 40 mg EOW/EW			
Subject group type	Reporting group			
Number of subjects analysed	550[16]			
Units: percent activity impaired				
arithmetic mean (standard deviation)				
Baseline (N=550)	21.4 (± 24.00)			
Change from Baseline to Week 48 (N=479)	1.1 (± 24.14)			
Change from Baseline to Week 96 (N=405)	-1.6 (± 21.80)			
Change from Baseline to Week 144 (N=351)	-0.7 (± 23.65)			
Change from Baseline to Week 192 (N=267)	-2.1 (± 20.91)			
Change from Baseline to Week 240 (N=171)	-3.4 (± 18.63)			
Change from Baseline to Week 292 (N=68)	-1.5 (± 19.79)			
Change from Baseline to Week 340 (N=23)	-9.6 (± 11.86)			
Change from Baseline to Week 388 (N=3)	-16.7 (± 15.28)			

Notes:

[16] - Participants in ITT-1 population with both Baseline and visit values.

Statistical analyses

No statistical analyses for this end point

Secondary: Colectomy Rate

End point title	Colectomy Rate

End point description:

The colectomy rates were estimated using Kaplan-Meier methodology based on the time to first colectomy.

End point type	Secondary

End point timeframe:

5 years

End point values	Adalimumab 40 mg EOW/EW			
Subject group type	Reporting group			
Number of subjects analysed	585[17]			
Units: percentage of participants				
number (not applicable)	3.88			

Notes:

[17] - ITT-1 population

Statistical analyses

No statistical analyses for this end point

Secondary: Health Care Resource Utilization (HCRU): Cumulative Number of Unscheduled Utilizations

End point title	Health Care Resource Utilization (HCRU): Cumulative Number of Unscheduled Utilizations

End point description:

The HCRU assesses the frequency of unscheduled outpatient visits, emergency room visits, or hospitalizations due to ulcerative colitis since the last visit. The cumulative number of unscheduled utilizations over the course of the study is presented.

End point type	Secondary

End point timeframe:

5 years

End point values	Adalimumab 40 mg EOW/EW			
Subject group type	Reporting group			
Number of subjects analysed	585[18]			
Units: cumulative number of utilizations				
number (not applicable)				
Physician	561			
Emergency Room	43			
Hospital Admission	65			
Days in Hospital	435			

Notes:
[18] - ITT-1 population

Statistical analyses

No statistical analyses for this end point

Secondary: Hematology: Mean Change From Baseline to Final Values in Hemoglobin

End point title	Hematology: Mean Change From Baseline to Final Values in Hemoglobin

End point description:

Blood samples for laboratory tests were performed at each study visit after questionnaires and vital sign determinations.

End point type	Secondary

End point timeframe:

Up to 5 years

End point values	Adalimumab 40 mg EOW/EW			
Subject group type	Reporting group			
Number of subjects analysed	575[19]			
Units: g/L				
arithmetic mean (standard deviation)	-0.1 (± 16.02)			

Notes:
[19] - Participants in the safety analysis set with both Baseline and visit values.

Statistical analyses

No statistical analyses for this end point

Secondary: Hematology: Mean Change From Baseline to Final Values in Hematocrit

End point title	Hematology: Mean Change From Baseline to Final Values in Hematocrit

End point description:

Blood samples for laboratory tests were performed at each study visit after questionnaires and vital sign determinations.

End point type	Secondary

End point timeframe:

Up to 5 years

End point values	Adalimumab 40 mg EOW/EW			
Subject group type	Reporting group			
Number of subjects analysed	575[20]			
Units: Percentage of red blood cells				
arithmetic mean (standard deviation)	0.013 (± 0.0472)			

Notes:

[20] - Participants in the safety analysis set with both Baseline and visit values.

Statistical analyses

No statistical analyses for this end point

Secondary: Hematology: Mean Change From Baseline to Final Values in Red Blood Cell Count, Platelet Count, White Blood Cell Count, Neutrophils, Lymphocytes, Monocytes, Eosinophils, and Basophils

End point title	Hematology: Mean Change From Baseline to Final Values in Red Blood Cell Count, Platelet Count, White Blood Cell Count, Neutrophils, Lymphocytes, Monocytes, Eosinophils, and Basophils

End point description:

Blood samples for laboratory tests were performed at each study visit after questionnaires and vital sign determinations.

End point type	Secondary

End point timeframe:

Up to 5 years

End point values	Adalimumab 40 mg EOW/EW			
Subject group type	Reporting group			
Number of subjects analysed	575[21]			
Units: cells x 100^9/L				
arithmetic mean (standard deviation)				
Red blood cell count (N=575)	0.03 (± 0.416)			
Platelet count (N=572)	-10.5 (± 96.98)			
White blood cell count (N=575)	0.41 (± 2.704)			
Neutrophils (N=572)	0.164 (± 2.4225)			
Lymphocytes (N=572)	0.155 (± 0.8270)			
Monocytes (N=572)	0.051 (± 0.2203)			
Eosinophils (N=572)	0.002 (± 0.1602)			
Basophils (N=572)	0.009 (± 0.0586)			

Notes:

[21] - Participants in the safety analysis set with both Baseline and visit values.

Statistical analyses

No statistical analyses for this end point

Secondary: Clinical Chemistry: Mean Change From Baseline to Final Values in Alanine Aminotransferase, Aspartate Aminotransferase, and Alkaline Phosphatase

End point title	Clinical Chemistry: Mean Change From Baseline to Final Values in Alanine Aminotransferase, Aspartate Aminotransferase, and Alkaline Phosphatase

End point description:

Blood samples for laboratory tests were performed at each study visit after questionnaires and vital sign determinations.

End point type	Secondary

End point timeframe:

Up to 5 years

End point values	Adalimumab 40 mg EOW/EW			
Subject group type	Reporting group			
Number of subjects analysed	581[22]			
Units: U/L				
arithmetic mean (standard deviation)				
Alanine aminotransferase (N=579)	3.7 (± 22.03)			
Aspartate aminotransferase (N=579)	2.6 (± 28.13)			
Alkaline phosphatase (N=581)	-0.2 (± 34.65)			

Notes:

[22] - Participants in the safety analysis set with both Baseline and visit values.

Statistical analyses

No statistical analyses for this end point

Secondary: Clinical Chemistry: Mean Change From Baseline to Final Values in Total Bilirubin, Creatinine, and Uric Acid

End point title	Clinical Chemistry: Mean Change From Baseline to Final Values in Total Bilirubin, Creatinine, and Uric Acid

End point description:

Blood samples for laboratory tests were performed at each study visit after questionnaires and vital sign determinations.

End point type	Secondary

End point timeframe:

Up to 5 years

End point values	Adalimumab 40 mg EOW/EW			
Subject group type	Reporting group			
Number of subjects analysed	581[23]			
Units: µmol/L				
arithmetic mean (standard deviation)				
Total bilirubin	-1.0 (± 5.35)			
Creatinine	2.4 (± 13.18)			
Uric acid	7.6 (± 65.52)			

Notes:

[23] - Participants in ITT-1 population with both Baseline and visit values.

Statistical analyses

No statistical analyses for this end point

Secondary: Clinical Chemistry: Mean Change From Baseline to Final Values in Blood Urea Nitrogen, Inorganic Phosphate, Calcium, Sodium, Potassium, Glucose, Cholesterol, and Triglycerides

End point title	Clinical Chemistry: Mean Change From Baseline to Final Values in Blood Urea Nitrogen, Inorganic Phosphate, Calcium, Sodium, Potassium, Glucose, Cholesterol, and Triglycerides

End point description:

Blood samples for laboratory tests were performed at each study visit after questionnaires and vital sign determinations.

End point type	Secondary

End point timeframe:

Up to 5 years

End point values	Adalimumab 40 mg EOW/EW			
Subject group type	Reporting group			
Number of subjects analysed	581[24]			
Units: mmol/L				
arithmetic mean (standard deviation)				
Blood urea nitrogen	0.32 (± 1.409)			
Inorganic phosphate	-0.003 (± 0.2312)			
Calcium	-0.012 (± 0.1185)			
Sodium	-0.0 (± 2.49)			
Potassium	0.07 (± 0.424)			
Glucose	0.05 (± 1.334)			
Cholesterol	-0.025 (± 0.8853)			
Triglycerides	0.178 (± 1.2800)			

Notes:

[24] - Participants in the safety analysis set with both Baseline and visit values.

Statistical analyses

No statistical analyses for this end point

Secondary: Clinical Chemistry: Mean Change From Baseline to Final Values in Albumin and Total Protein

End point title	Clinical Chemistry: Mean Change From Baseline to Final Values in Albumin and Total Protein

End point description:

Blood samples for laboratory tests were performed at each study visit after questionnaires and vital sign determinations.

End point type	Secondary

End point timeframe:

Up to 5 years

End point values	Adalimumab 40 mg EOW/EW			
Subject group type	Reporting group			
Number of subjects analysed	581[25]			
Units: g/L				
arithmetic mean (standard deviation)				
Albumin	-0.4 (± 3.85)			
Total protein	0.7 (± 18.99)			

Notes:

[25] - Participants in the safety analysis set with both Baseline and visit values.

Statistical analyses

No statistical analyses for this end point

Secondary: Clinical Chemistry: Mean Change From Baseline to Final Values in High-sensitivity C-reactive Protein

End point title	Clinical Chemistry: Mean Change From Baseline to Final Values in High-sensitivity C-reactive Protein

End point description:

Blood samples for laboratory tests were performed at each study visit after questionnaires and vital sign determinations.

End point type	Secondary

End point timeframe:

Up to 5 years

End point values	Adalimumab 40 mg EOW/EW			
Subject group type	Reporting group			
Number of subjects analysed	575[26]			
Units: mg/L				
arithmetic mean (standard deviation)	0.382 (± 15.1489)			

Notes:
[26] - Participants in the safety analysis set with both Baseline and visit values.

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 398 weeks).

Adverse event reporting additional description:

TEAEs and TESAEs are defined as any adverse event or serious adverse event with onset or worsening from the time that the first dose of adalimumab is administered until 5 half-lives (70 days) have elapsed following discontinuation of adalimumab administration. TEAEs were collected whether elicited or spontaneously reported by the participant.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	19.1

Reporting groups

Reporting group title	Adalimumab 40 mg EOW/EW

Reporting group description:

Open-label adalimumab 40 mg every other week (EOW) or every week (EW). Participants who entered from an open-label cohort continued their previous dosing regimen of adalimumab EOW or EW; participants who entered from a double-blind cohort received adalimumab EOW.

Serious adverse events	Adalimumab 40 mg EOW/EW		
Total subjects affected by serious adverse events			
subjects affected / exposed	158 / 592 (26.69%)		
number of deaths (all causes)	3		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma of colon			
subjects affected / exposed	1 / 592 (0.17%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
B-cell lymphoma			
subjects affected / exposed	3 / 592 (0.51%)		
occurrences causally related to treatment / all	3 / 3		
deaths causally related to treatment / all	0 / 0		
Bladder cancer			
subjects affected / exposed	1 / 592 (0.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Bladder transitional cell carcinoma				
subjects affected / exposed	1 / 592 (0.17%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cervix carcinoma stage 0				
subjects affected / exposed	1 / 592 (0.17%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Endometrial cancer				
subjects affected / exposed	1 / 592 (0.17%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gallbladder adenocarcinoma				
subjects affected / exposed	1 / 592 (0.17%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Malignant melanoma				
subjects affected / exposed	2 / 592 (0.34%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
Pancreatic neoplasm				
subjects affected / exposed	1 / 592 (0.17%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Prostate cancer				
subjects affected / exposed	2 / 592 (0.34%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Squamous cell carcinoma of skin				
subjects affected / exposed	1 / 592 (0.17%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Uterine leiomyoma				

subjects affected / exposed	3 / 592 (0.51%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	1 / 592 (0.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Haemorrhagic infarction			
subjects affected / exposed	1 / 592 (0.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Surgical and medical procedures			
Abortion induced			
subjects affected / exposed	2 / 592 (0.34%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous			
subjects affected / exposed	2 / 592 (0.34%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Drug intolerance			
subjects affected / exposed	1 / 592 (0.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Dysplasia			
subjects affected / exposed	1 / 592 (0.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Multimorbidity			

subjects affected / exposed	1 / 592 (0.17%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Non-cardiac chest pain				
subjects affected / exposed	1 / 592 (0.17%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Polyp				
subjects affected / exposed	1 / 592 (0.17%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pyrexia				
subjects affected / exposed	1 / 592 (0.17%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Systemic inflammatory response syndrome				
subjects affected / exposed	1 / 592 (0.17%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Reproductive system and breast disorders				
Menorrhagia				
subjects affected / exposed	2 / 592 (0.34%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Ovarian cyst				
subjects affected / exposed	1 / 592 (0.17%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Prostatism				
subjects affected / exposed	1 / 592 (0.17%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Prostatitis				

subjects affected / exposed	1 / 592 (0.17%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Uterine cyst				
subjects affected / exposed	1 / 592 (0.17%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
Allergic respiratory symptom				
subjects affected / exposed	1 / 592 (0.17%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Atelectasis				
subjects affected / exposed	1 / 592 (0.17%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Bronchiectasis				
subjects affected / exposed	1 / 592 (0.17%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Nasal obstruction				
subjects affected / exposed	1 / 592 (0.17%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Nasal septum deviation				
subjects affected / exposed	1 / 592 (0.17%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pulmonary embolism				
subjects affected / exposed	1 / 592 (0.17%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Sleep apnoea syndrome				

subjects affected / exposed	1 / 592 (0.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Bipolar disorder			
subjects affected / exposed	1 / 592 (0.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Psychotic behaviour			
subjects affected / exposed	1 / 592 (0.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Suicide attempt			
subjects affected / exposed	1 / 592 (0.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Investigations			
False positive tuberculosis test			
subjects affected / exposed	1 / 592 (0.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Weight decreased			
subjects affected / exposed	1 / 592 (0.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Animal bite			
subjects affected / exposed	1 / 592 (0.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Head injury			
subjects affected / exposed	1 / 592 (0.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Hip fracture			
subjects affected / exposed	1 / 592 (0.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Joint dislocation			
subjects affected / exposed	1 / 592 (0.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Joint injury			
subjects affected / exposed	1 / 592 (0.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Meniscus injury			
subjects affected / exposed	1 / 592 (0.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Rib fracture			
subjects affected / exposed	1 / 592 (0.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Road traffic accident			
subjects affected / exposed	1 / 592 (0.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Tendon rupture			
subjects affected / exposed	1 / 592 (0.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Tibia fracture			
subjects affected / exposed	1 / 592 (0.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Congenital, familial and genetic disorders			

Hypertrophic cardiomyopathy				
subjects affected / exposed	1 / 592 (0.17%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Confusional state				
subjects affected / exposed	1 / 592 (0.17%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cardiac disorders				
Aortic valve stenosis				
subjects affected / exposed	1 / 592 (0.17%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Atrial fibrillation				
subjects affected / exposed	1 / 592 (0.17%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cardio-respiratory arrest				
subjects affected / exposed	1 / 592 (0.17%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	1 / 1			
Cardiogenic shock				
subjects affected / exposed	1 / 592 (0.17%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Coronary artery disease				
subjects affected / exposed	2 / 592 (0.34%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Left ventricular dysfunction				
subjects affected / exposed	1 / 592 (0.17%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Right ventricular failure				

subjects affected / exposed	1 / 592 (0.17%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Tachycardia				
subjects affected / exposed	1 / 592 (0.17%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Nervous system disorders				
Autonomic nervous system imbalance				
subjects affected / exposed	1 / 592 (0.17%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Carotid artery stenosis				
subjects affected / exposed	1 / 592 (0.17%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Carpal tunnel syndrome				
subjects affected / exposed	1 / 592 (0.17%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Demyelination				
subjects affected / exposed	1 / 592 (0.17%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Generalised tonic-clonic seizure				
subjects affected / exposed	1 / 592 (0.17%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Ischaemic stroke				
subjects affected / exposed	1 / 592 (0.17%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Multiple sclerosis				

subjects affected / exposed	1 / 592 (0.17%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Nerve compression			
subjects affected / exposed	1 / 592 (0.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	6 / 592 (1.01%)		
occurrences causally related to treatment / all	0 / 10		
deaths causally related to treatment / all	0 / 0		
Iron deficiency anaemia			
subjects affected / exposed	1 / 592 (0.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Lymphadenopathy mediastinal			
subjects affected / exposed	1 / 592 (0.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Eye disorders			
Optic ischaemic neuropathy			
subjects affected / exposed	1 / 592 (0.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	2 / 592 (0.34%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Anal fistula			
subjects affected / exposed	1 / 592 (0.17%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		

Colitis			
subjects affected / exposed	3 / 592 (0.51%)		
occurrences causally related to treatment / all	1 / 3		
deaths causally related to treatment / all	0 / 0		
Colitis ulcerative			
subjects affected / exposed	34 / 592 (5.74%)		
occurrences causally related to treatment / all	2 / 39		
deaths causally related to treatment / all	0 / 0		
Colon dysplasia			
subjects affected / exposed	1 / 592 (0.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Crohn's disease			
subjects affected / exposed	1 / 592 (0.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal dysplasia			
subjects affected / exposed	1 / 592 (0.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal haemorrhage			
subjects affected / exposed	1 / 592 (0.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 592 (0.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Ileus			
subjects affected / exposed	1 / 592 (0.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Inguinal hernia			

subjects affected / exposed	1 / 592 (0.17%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Large intestinal stenosis				
subjects affected / exposed	1 / 592 (0.17%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Large intestine perforation				
subjects affected / exposed	2 / 592 (0.34%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Large intestine polyp				
subjects affected / exposed	2 / 592 (0.34%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Nausea				
subjects affected / exposed	1 / 592 (0.17%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumoperitoneum				
subjects affected / exposed	1 / 592 (0.17%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pseudopolyposis				
subjects affected / exposed	2 / 592 (0.34%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
Rectal haemorrhage				
subjects affected / exposed	2 / 592 (0.34%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Rectal perforation				

subjects affected / exposed	1 / 592 (0.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Rectal polyp			
subjects affected / exposed	1 / 592 (0.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Small intestinal obstruction			
subjects affected / exposed	1 / 592 (0.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Umbilical hernia			
subjects affected / exposed	1 / 592 (0.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	2 / 592 (0.34%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Hepatic cirrhosis			
subjects affected / exposed	1 / 592 (0.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Portal hypertension			
subjects affected / exposed	1 / 592 (0.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Erythema multiforme			
subjects affected / exposed	1 / 592 (0.17%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Erythema nodosum			

subjects affected / exposed	2 / 592 (0.34%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Henoch-Schonlein purpura			
subjects affected / exposed	1 / 592 (0.17%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	1 / 592 (0.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Ureterolithiasis			
subjects affected / exposed	1 / 592 (0.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Urinary incontinence			
subjects affected / exposed	1 / 592 (0.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Endocrine disorders			
Adrenal haemorrhage			
subjects affected / exposed	1 / 592 (0.17%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Goitre			
subjects affected / exposed	1 / 592 (0.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	2 / 592 (0.34%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		

Back pain			
subjects affected / exposed	1 / 592 (0.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cervical spinal stenosis			
subjects affected / exposed	1 / 592 (0.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Dupuytren's contracture			
subjects affected / exposed	1 / 592 (0.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Intervertebral disc protrusion			
subjects affected / exposed	3 / 592 (0.51%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Joint swelling			
subjects affected / exposed	1 / 592 (0.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Lupus-like syndrome			
subjects affected / exposed	1 / 592 (0.17%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Osteoarthritis			
subjects affected / exposed	5 / 592 (0.84%)		
occurrences causally related to treatment / all	0 / 8		
deaths causally related to treatment / all	0 / 0		
Osteonecrosis			
subjects affected / exposed	1 / 592 (0.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Osteoporosis			

subjects affected / exposed	1 / 592 (0.17%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Osteoporotic fracture				
subjects affected / exposed	1 / 592 (0.17%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pain in extremity				
subjects affected / exposed	1 / 592 (0.17%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Rotator cuff syndrome				
subjects affected / exposed	1 / 592 (0.17%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Sympathetic posterior cervical syndrome				
subjects affected / exposed	1 / 592 (0.17%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
Abdominal abscess				
subjects affected / exposed	2 / 592 (0.34%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
Abscess of salivary gland				
subjects affected / exposed	1 / 592 (0.17%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Anal abscess				
subjects affected / exposed	3 / 592 (0.51%)			
occurrences causally related to treatment / all	3 / 4			
deaths causally related to treatment / all	0 / 0			
Appendicitis				

subjects affected / exposed	5 / 592 (0.84%)		
occurrences causally related to treatment / all	0 / 5		
deaths causally related to treatment / all	0 / 0		
Appendicitis perforated			
subjects affected / exposed	1 / 592 (0.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Chronic sinusitis			
subjects affected / exposed	1 / 592 (0.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Clostridium difficile immunisation			
subjects affected / exposed	1 / 592 (0.17%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Colonic abscess			
subjects affected / exposed	1 / 592 (0.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Device related infection			
subjects affected / exposed	1 / 592 (0.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Diarrhoea infectious			
subjects affected / exposed	1 / 592 (0.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Diverticulitis			
subjects affected / exposed	1 / 592 (0.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Herpes zoster			

subjects affected / exposed	2 / 592 (0.34%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Herpes zoster meningitis			
subjects affected / exposed	1 / 592 (0.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infection			
subjects affected / exposed	2 / 592 (0.34%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Injection site abscess			
subjects affected / exposed	1 / 592 (0.17%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Injection site cellulitis			
subjects affected / exposed	1 / 592 (0.17%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Lung abscess			
subjects affected / exposed	1 / 592 (0.17%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Orchitis			
subjects affected / exposed	1 / 592 (0.17%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Peritonitis			
subjects affected / exposed	1 / 592 (0.17%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonia			

subjects affected / exposed	11 / 592 (1.86%)			
occurrences causally related to treatment / all	10 / 13			
deaths causally related to treatment / all	0 / 0			
Pneumonia bacterial				
subjects affected / exposed	1 / 592 (0.17%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Postoperative wound infection				
subjects affected / exposed	1 / 592 (0.17%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pulmonary tuberculosis				
subjects affected / exposed	1 / 592 (0.17%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Pyelonephritis				
subjects affected / exposed	2 / 592 (0.34%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
Pyelonephritis acute				
subjects affected / exposed	1 / 592 (0.17%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory tract infection				
subjects affected / exposed	1 / 592 (0.17%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Sinusitis				
subjects affected / exposed	2 / 592 (0.34%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Staphylococcal infection				

subjects affected / exposed	1 / 592 (0.17%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Subcutaneous abscess			
subjects affected / exposed	2 / 592 (0.34%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Urinary tract infection			
subjects affected / exposed	1 / 592 (0.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Hypokalaemia			
subjects affected / exposed	1 / 592 (0.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hyponatraemia			
subjects affected / exposed	1 / 592 (0.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Bursitis			
subjects affected / exposed	1 / 592 (0.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Adalimumab 40 mg EOW/EW		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	391 / 592 (66.05%)		
Vascular disorders			
Hypertension			
subjects affected / exposed	37 / 592 (6.25%)		
occurrences (all)	41		

Nervous system disorders Headache subjects affected / exposed occurrences (all)	 46 / 592 (7.77%) 66		
General disorders and administration site conditions Fatigue subjects affected / exposed occurrences (all)	 35 / 592 (5.91%) 40		
Gastrointestinal disorders Abdominal pain subjects affected / exposed occurrences (all) Colitis ulcerative subjects affected / exposed occurrences (all) Diarrhoea subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all)	 38 / 592 (6.42%) 52 180 / 592 (30.41%) 279 46 / 592 (7.77%) 62 34 / 592 (5.74%) 41		
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) Oropharyngeal pain subjects affected / exposed occurrences (all)	 41 / 592 (6.93%) 46 33 / 592 (5.57%) 36		
Skin and subcutaneous tissue disorders Rash subjects affected / exposed occurrences (all)	 42 / 592 (7.09%) 47		
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all)	 62 / 592 (10.47%) 88		

Back pain			
subjects affected / exposed	40 / 592 (6.76%)		
occurrences (all)	51		
Infections and infestations			
Bronchitis			
subjects affected / exposed	40 / 592 (6.76%)		
occurrences (all)	53		
Influenza			
subjects affected / exposed	42 / 592 (7.09%)		
occurrences (all)	50		
Sinusitis			
subjects affected / exposed	53 / 592 (8.95%)		
occurrences (all)	81		
Upper respiratory tract infection			
subjects affected / exposed	58 / 592 (9.80%)		
occurrences (all)	91		
Viral upper respiratory tract infection			
subjects affected / exposed	115 / 592 (19.43%)		
occurrences (all)	198		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
23 November 2011	The main purpose of this amendment was to add regular tuberculosis (TB) testing and to add language regarding physical examination to align with physicians' usual clinical practice methods.
14 March 2012	The main purpose of this amendment was to allow the option of dose de-escalation by reducing dose frequency; add blood sample collections for adalimumab concentration and anti-adalimumab antibody (AAA) assays to be used for long-term PK data; add local laboratory use if QuantiFERON-TB Gold test or equivalent is used; and extended the duration of the study to 292 weeks
17 December 2013	The main purpose of this amendment was to extend the duration of the study to 388 weeks; include additional anti-tumor necrosis factor (anti-TNF) information; and clarify chest x-ray, pregnancy information, toxicity management, and protocol deviations.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

Efficacy data after Week 292 should be interpreted with caution because less than 10% of subjects were under observation beyond Week 292.

Notes: