Clinical trial results:
An Open-Label Multicenter Study to Evaluate the Impact of Adalimumab on Quality of Life, Health Care Utilization and Costs of Ulcerative Colitis Subjects in the Usual Clinical Practice Setting

Summary

EudraCT number	2011-002411-29
Trial protocol	SE ES GB DE BE DK GR PT AT IE IT FI CZ SK PL
Global end of trial date	28 May 2015

Results information

Result version number	v1 (current)
This version publication date	07 May 2016
First version publication date	07 May 2016

Trial information

Trial identification

Sponsor protocol code	M13-045

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01550965
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	AbbVie Deutschland GmbH & Co. KG
Sponsor organisation address	Abbott House, Vanwall Business Park, Vanwall Road, Maidenhead, Berkshire, United Kingdom, SL6 4XE
Public contact	Global Medical Information, AbbVie, 001 800-633-9110,
Scientific contact	John Medich, AbbVie, john.medich@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	28 May 2015
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	28 May 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

This study evaluated the quality of life (QOL) and economic impact of adalimumab treatment in subjects with ulcerative colitis (UC).

Protection of trial subjects:

All subjects entering the study had to sign an informed consent that was explained to them and questions encouraged.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	24 May 2012
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	Poland: 24
Country: Number of subjects enrolled	Portugal: 4
Country: Number of subjects enrolled	Slovakia: 10
Country: Number of subjects enrolled	Spain: 24
Country: Number of subjects enrolled	Sweden: 2
Country: Number of subjects enrolled	United Kingdom: 90
Country: Number of subjects enrolled	Austria: 5
Country: Number of subjects enrolled	Belgium: 29
Country: Number of subjects enrolled	Czech Republic: 3
Country: Number of subjects enrolled	Denmark: 11
Country: Number of subjects enrolled	France: 31
Country: Number of subjects enrolled	Germany: 14
Country: Number of subjects enrolled	Greece: 8
Country: Number of subjects enrolled	Ireland: 14
Country: Number of subjects enrolled	Italy: 49
Country: Number of subjects enrolled	Canada: 53
Country: Number of subjects enrolled	Israel: 27
Country: Number of subjects enrolled	Russian Federation: 50
Country: Number of subjects enrolled	Switzerland: 3
Country: Number of subjects enrolled	Turkey: 12

Worldwide total number of subjects	463
EEA total number of subjects	318

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)	432
From 65 to 84 years	31
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 463 subjects were enrolled: 461 in the intent to treat (ITT) population were analyzed for efficacy (excluding 2 due to lack of post-baseline measurement data); 463 were analyzed for safety (subjects who had received at least one dose of study drug).

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	Subjects Receiving Adalimumab

Arm description:

Adults with active UC who had failed conventional therapy received Adalimumab 160 mg at Baseline Visit, 80 mg at Week 2 Visit, and 40 mg every other week (EOW) starting at Week 4. Non-responders to adalimumab were to be discontinued from treatment at Week 8. After Week 8, dose escalation to 40 mg weekly was allowed for flare or nonresponse.

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

Dosage and administration details:

Adalimumab pre-filled syringe, administered by subcutaneous injection.

Number of subjects in period 1	Subjects Receiving Adalimumab
Started	463
Completed	353
Not completed	110
Consent withdrawn by subject	10
Adverse Event	26
Not Specified	13
Lost to follow-up	2
Lack of efficacy	59

Baseline characteristics

Reporting groups	
Reporting group title	Overall Study

Reporting group description: -

Reporting group values	Overall Study	Total	
Number of subjects	463	463	
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	41.8		
standard deviation	± 13.72	-	
Gender categorical Units: Subjects			
Female	207	207	
Male	256	256	

End points

End points reporting groups

Reporting group title	Subjects Receiving Adalimumab

Reporting group description:

Adults with active UC who had failed conventional therapy received Adalimumab 160 mg at Baseline Visit, 80 mg at Week 2 Visit, and 40 mg every other week (EOW) starting at Week 4. Non-responders to adalimumab were to be discontinued from treatment at Week 8. After Week 8, dose escalation to 40 mg weekly was allowed for flare or nonresponse.

Primary: Mean Change From Baseline in Short Inflammatory Bowel Disease Questionnaire (SIBDQ): Total Score

End point title	Mean Change From Baseline in Short Inflammatory Bowel Disease Questionnaire (SIBDQ): Total Score[1]

End point description:

The SIBDQ is a disease-specific health-related quality of life (HRQOL) questionnaire, able to detect and define meaningful clinical changes in inflammatory bowel disease (IBD) subjects by measuring physical, social and emotional status. The SIBDQ consists of 10 questions; each question is scored on a scale from 1 (poor QOL) to 7 (optimum QOL). A higher score indicates a better health-related quality of life. Total scores range from 10 (poor QoL) to 70 (good QoL).

End point type	Primary

End point timeframe:

Week 0 (baseline) and Week 26

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: Hypothesis testing for the first ranked primary outcome was performed in a hierarchical order using the two-sided paired t-test for mean change equal to zero. The mean difference (95% CI) from baseline to week 26 was 17.40 (16.08 to 18.73) (P<0.001).

End point values	Subjects Receiving Adalimumab			
Subject group type	Reporting group			
Number of subjects analysed	460[2]			
Units: units on a scale				
arithmetic mean (standard deviation)	17.4 (± 14.48)			

Notes:

[2] - All subjects in the ITT population with evaluable data.

Statistical analyses

No statistical analyses for this end point

Primary: Mean Change From the 6 Months Prior to Treatment With Adalimumab to the 6 Months After Beginning Treatment With Adalimumab in Costs of UC-related Medical Care Excluding Adalimumab Costs

End point title	Mean Change From the 6 Months Prior to Treatment With Adalimumab to the 6 Months After Beginning Treatment With Adalimumab in Costs of UC-related Medical Care Excluding Adalimumab Costs[3]

End point description:

Medical care costs included, but were not limited to: surgical procedures, hospitalizations, bed days in

hospital, unscheduled physician consultations, emergency room visits, unscheduled examination appointments, radiology appointments, endoscopy appointments and medications.

End point type	Primary

End point timeframe:

6 months prior to treatment start (Week 0 [baseline]) and 6 months after treatment start (total 12 months)

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: Hypothesis testing for the second ranked primary outcome was performed in a hierarchical order using the two-sided paired t-test for mean change equal to zero. The mean difference (95% CI) from 6 months prior to treatment start (Week 0 [baseline]) and 6 months after treatment start (total 12 months) was -1383.81 (-1586.36 to -1181.26) (P<0.001).

End point values	Subjects Receiving Adalimumab			
Subject group type	Reporting group			
Number of subjects analysed	461[4]			
Units: Pound Sterling (GBP)				
arithmetic mean (standard deviation)	-1383.8 (± 2213.06)			

Notes:

[4] - All subjects in the ITT population with evaluable data.

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From the 6 Months Prior to Treatment With Adalimumab to the 6 Months After Beginning Treatment With Adalimumab in Total All-cause Direct Health Care Costs (Excluding Adalimumab Costs)

End point title	Mean Change From the 6 Months Prior to Treatment With Adalimumab to the 6 Months After Beginning Treatment With Adalimumab in Total All-cause Direct Health Care Costs (Excluding Adalimumab Costs)

End point description:

Medical care costs included, but were not limited to: surgical procedures, hospitalizations, bed days in hospital, unscheduled physician consultations, emergency room visits, unscheduled examination appointments, radiology appointments, endoscopy appointments and medications.

End point type	Secondary

End point timeframe:

6 months prior to treatment start (Week 0 [baseline]) and 6 months after treatment start (total 12 months)

End point values	Subjects Receiving Adalimumab			
Subject group type	Reporting group			
Number of subjects analysed	461[5]			
Units: Pound Sterling (GBP)				
arithmetic mean (standard deviation)	-1297.8 (± 2888.89)			

Notes:

[5] - All subjects in the ITT population with evaluable data.

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From the 6 Months Prior to Treatment With Adalimumab to the 6 Months After Beginning Treatment With Adalimumab in UC-related Direct and Indirect Health Care Costs

End point title	Mean Change From the 6 Months Prior to Treatment With Adalimumab to the 6 Months After Beginning Treatment With Adalimumab in UC-related Direct and Indirect Health Care Costs

End point description:

UC-related direct and indirect health care costs included, but were not limited to: surgical procedures, hospitalizations, bed days in hospital, unscheduled physician consultations, emergency room visits, unscheduled examination appointments, radiology appointments, endoscopy appointments, medications and indirect costs based on WPAI.

End point type	Secondary

End point timeframe:

6 months prior to treatment start (Week 0 [baseline]) and 6 months after treatment start (total 12 months)

End point values	Subjects Receiving Adalimumab			
Subject group type	Reporting group			
Number of subjects analysed	461[6]			
Units: Pound Sterling (GBP)				
arithmetic mean (standard deviation)	-4308.3 (± 7394.75)			

Notes:

[6] - All subjects in the ITT population with evaluable data.

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From the 6 Months Prior to Treatment With Adalimumab to the 6 Months After Beginning Treatment With Adalimumab in UC-related and All-cause Hospitalization

End point title	Mean Change From the 6 Months Prior to Treatment With Adalimumab to the 6 Months After Beginning Treatment With Adalimumab in UC-related and All-cause Hospitalization

End point description:

Hospitalization was defined as number of bed days in hospital as determined from the health care utilization information.

End point type	Secondary

End point timeframe:

6 months prior to treatment start (Week 0 [baseline]) and 6 months after treatment start (total 12 months)

End point values	Subjects Receiving Adalimumab			
Subject group type	Reporting group			
Number of subjects analysed	158[7]			
Units: Days				
arithmetic mean (standard deviation)	-7.3 (± 16.06)			

Notes:

[7] - All subjects in the ITT population with evaluable data.

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Baseline in Subject's Satisfaction Using Treatment Satisfaction Questionnaire for Medication (TSQM)

End point title	Mean Change From Baseline in Subject's Satisfaction Using Treatment Satisfaction Questionnaire for Medication (TSQM)

End point description:

TSQM is a questionnaire to be completed by the subjects to determine their satisfaction of the medications for ulcerative colitis including the study drug. The TSQM is a 14-item subject-rated scale that evaluates the effectiveness, side effects, convenience, and global satisfaction of the medication over the past 2-3 weeks. Each question is scored from 1 (worst) to 7 points (best); total scores range from 0 to 100 (higher score indicates better satisfaction). N = subjects with evaluable baseline and post-baseline data.

End point type	Secondary

End point timeframe:

Week 0 (baseline) and Week 26

End point values	Subjects Receiving Adalimumab			
Subject group type	Reporting group			
Number of subjects analysed	449[8]			
Units: Units on a scale				
arithmetic mean (standard deviation)				
Effectiveness (N=452)	24.4 (± 31.09)			
Side Effects (N=449)	18.9 (± 38.06)			
Convenience (N=451)	6.2 (± 24.87)			
Global Satisfaction (N=449)	22.6 (± 32.84)			

Notes:

[8] - All subjects in the ITT population with evaluable data.

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From the 6 Months Prior to Treatment With Adalimumab to the 6 Months After Beginning Treatment With Adalimumab in UC-related Outpatient Utilization, Including Emergency Department Visits, Unscheduled Consultation, Exam Procedures

End point title	Mean Change From the 6 Months Prior to Treatment With Adalimumab to the 6 Months After Beginning Treatment With Adalimumab in UC-related Outpatient Utilization, Including Emergency Department Visits, Unscheduled Consultation, Exam Procedures

End point description:

UC-related outpatient utilization was determined from the health care utilization information. Outpatient utilization was the number of procedures/surgeries performed during outpatient visits. Subjects without any outpatient utilization were excluded.

End point type	Secondary

End point timeframe:

6 months prior to treatment start (Week 0 [baseline]) and 6 months after treatment start (total 12 months)

End point values	Subjects Receiving Adalimumab			
Subject group type	Reporting group			
Number of subjects analysed	453[9]			
Units: Procedures/ Surgeries				
arithmetic mean (standard deviation)				
Overall	-4.8 (± 6.25)			
During emergency department visits	0 (± 1.09)			
During primary care doctor visits	-0.9 (± 2.82)			

Notes:

[9] - All subjects in the ITT population with evaluable data.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Absence of Blood in Stool

End point title	Percentage of Subjects With Absence of Blood in Stool

End point description:

Subjects with absence of blood in stool were reported.

End point type	Secondary

End point timeframe:

Week 26

End point values	Subjects Receiving Adalimumab			
Subject group type	Reporting group			
Number of subjects analysed	461[10]			
Units: Percentage of Participants				
number (not applicable)	56.6			

Notes:

[10] - All subjects in the ITT population with evaluable data.

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Baseline in Short Inflammatory Bowel Disease Questionnaire (SIBDQ): Total Score Over Time

End point title	Mean Change From Baseline in Short Inflammatory Bowel Disease Questionnaire (SIBDQ): Total Score Over Time

End point description:

The SIBDQ is a disease-specific health-related quality of life (HRQoL) questionnaire, used to detect changes in inflammatory bowel disease (IBD) subjects by measuring physical, social and emotional status. The SIBDQ consists of 10 questions, each question is scored on a scale from 1 (poor QoL) to 7 (good QoL). A higher score indicates a better health-related quality of life. Total scores range from 10 (poor QoL) to 70 (good QoL). Efficacy assessments were not specified at week 18; missing data at week 18 were imputed using last observation carried forward (LOCF). N = subjects with evaluable baseline and post-baseline data.

End point type	Secondary

End point timeframe:

Week 0 (baseline), Week 2, Week 8, Week 18, and Week 26

End point values	Subjects Receiving Adalimumab			
Subject group type	Reporting group			
Number of subjects analysed	460[11]			
Units: Units on a scale				
arithmetic mean (standard deviation)				
Week 2 (N=457)	11.1 (± 9.81)			
Week 8 (N=459)	15.4 (± 12.83)			
Week 18 (N=459)	14.8 (± 13.06)			
Week 26 (N=460)	17.4 (± 14.48)			

Notes:

[11] - All subjects in the ITT population with evaluable data.

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Baseline in Physician's Global Assessment (PGA)

End point title	Mean Change From Baseline in Physician's Global Assessment (PGA)

End point description:

The Physician's Global Assessment was used to measure the subject's disease activity. The physician considered the subject's reported information such as number of stools, rectal bleeding, abdominal discomfort, and functional assessment during the previous day prior to the visit, and other observations such as physical findings, and the subject's performance status at the time of the visit. Based on the above information the investigator made an overall assessment of subject's current severity of UC using the ordinal scale from 0 (normal) to 3 (severe disease). Efficacy assessments were not specified at week 18; missing data at week 18 were imputed using last observation carried forward (LOCF).

End point type	Secondary

End point timeframe:

Week 0 (baseline), Week 2, Week 8, Week 18, and Week 26

End point values	Subjects Receiving Adalimumab			
Subject group type	Reporting group			
Number of subjects analysed	461[12]			
Units: Units on a scale				
arithmetic mean (standard deviation)				
Week 2	-0.6 (± 0.69)			
Week 8	-1.1 (± 0.85)			
Week 18	-0.9 (± 0.95)			
Week 26	-1.1 (± 0.97)			

Notes:

[12] - All subjects in the ITT population with evaluable data.

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Baseline in Total Simple Clinical Colitis Activity Index (SCCAI)

End point title	Mean Change From Baseline in Total Simple Clinical Colitis Activity Index (SCCAI)

End point description:

The SCCAI measures disease activity as assessed by the investigator and includes the following 6 items: bowel frequency (day), bowel frequency (night), urgency of defecation, blood in stool, general well-being and extra colonic features. The score ranges from 0 (best) to 19 points (worst). Efficacy assessments were not specified at week 18; missing data at week 18 were imputed using last observation carried forward (LOCF).

End point type	Secondary

End point timeframe:

Week 0 (baseline), Week 2, Week 8, Week 18, and Week 26

End point values	Subjects Receiving Adalimumab			
Subject group type	Reporting group			
Number of subjects analysed	461[13]			
Units: Units on a scale				
arithmetic mean (standard deviation)				
Week 2	-3.2 (± 2.55)			
Week 8	-4.1 (± 3.33)			
Week 18	-3 (± 3.79)			
Week 26	-4.1 (± 3.88)			

Notes:

[13] - All subjects in the ITT population with evaluable data.

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Baseline in European Quality of Life – 5 Dimensions – 5 Level (EQ-5D-5L) Total Score

End point title	Mean Change From Baseline in European Quality of Life – 5 Dimensions – 5 Level (EQ-5D-5L) Total Score

End point description:

EQ-5D-5L Total Score provides a descriptive profile of health status. It comprises of 5 dimensions of health (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression) to describe the subject's current health state. Each dimension comprises 5 levels with corresponding numeric scores ranging from 1 (no problems) through 5 (extreme problems). A unique EQ-5D-5L health state was defined by combining the numeric level scores for each of the 5 dimensions and the total score ranges from -0.594 to 1, with higher scores representing a better health state. An increase in the EQ-5D-5L total score indicates improvement. Efficacy assessments were not specified at week 18; missing data at week 18 were imputed using last observation carried forward (LOCF). N = subjects with evaluable baseline and post-baseline data.

End point type	Secondary

End point timeframe:

Week 0 (baseline), Week 2, Week 8, Week 18, and Week 26

End point values	Subjects Receiving Adalimumab			
Subject group type	Reporting group			
Number of subjects analysed	454[14]			
Units: Units on a scale				
arithmetic mean (standard deviation)				
Week 2 (N=452)	0.1 (± 0.18)			
Week 8 (N=454)	0.1 (± 0.21)			
Week 18 (N=454)	0.1 (± 0.22)			
Week 26 (N=454)	0.1 (± 0.23)			

Notes:

[14] - All subjects in the ITT population with evaluable data.

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Baseline in Work Productivity and Activity Impairment Questionnaire: Specific Health Problem (WPAI-SHP): Percentage of Work Time Missed

End point title	Mean Change From Baseline in Work Productivity and Activity Impairment Questionnaire: Specific Health Problem (WPAI-SHP): Percentage of Work Time Missed

End point description:

WPAI-SHP is a questionnaire used to assess the effect of the subject's health problems on their ability to work and perform regular activities. A higher score indicates an increased impairment. A positive value of change indicates an increased impairment of work productivity and the limitation of activities of daily life, while a negative value indicates an improvement. The percentage of work time missed data was applicable to employed subjects only. Efficacy assessments were not specified at week 18; missing data at week 18 were imputed using last observation carried forward (LOCF). N = subjects with evaluable baseline and post-baseline data.

End point type	Secondary

End point timeframe:

Week 0 (baseline), Week 2, Week 8, Week 18, and Week 26

End point values	Subjects Receiving Adalimumab			
Subject group type	Reporting group			
Number of subjects analysed	227[15]			
Units: Percentage of work time missed				
arithmetic mean (standard deviation)				
Week 2 (N=214)	-8.6 (± 25.55)			
Week 8 (N=227)	-12.2 (± 30.97)			
Week 18 (N=225)	-11.6 (± 32.04)			
Week 26 (N=223)	-11.4 (± 30.85)			

Notes:

[15] - All subjects in the ITT population with evaluable data.

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Baseline in Work Productivity and Activity Impairment Questionnaire: Specific Health Problem (WPAI-SHP): Percentage of Impairment While Working

End point title	Mean Change From Baseline in Work Productivity and Activity Impairment Questionnaire: Specific Health Problem (WPAI-SHP): Percentage of Impairment While Working

End point description:

WPAI-SHP is a questionnaire used to assess the effect of the subject's health problems on their ability to work and perform regular activities. A higher score indicates an increased impairment. A positive value of change indicates an increased impairment of work productivity and the limitation of activities of daily life, while a negative value indicates an improvement. The percentage of impairment while working data was applicable to employed subjects only. Efficacy assessments were not specified at week 18; missing data at week 18 were imputed using last observation carried forward (LOCF). N = subjects with evaluable baseline and post-baseline data.

End point type	Secondary

End point timeframe:

Week 0 (baseline), Week 2, Week 8, Week 18, and Week 26

End point values	Subjects Receiving Adalimumab			
Subject group type	Reporting group			
Number of subjects analysed	234[16]			
Units: Percentage of impairment while working				
arithmetic mean (standard deviation)				
Week 2 (N=221)	-16.6 (± 25.94)			
Week 8 (N=234)	-22.9 (± 30.91)			
Week 18 (N=232)	-21.7 (± 30.98)			
Week 26 (N=229)	-24.5 (± 29.78)			

Notes:

[16] - All subjects in the ITT population with evaluable data.

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Baseline in Work Productivity and Activity Impairment Questionnaire: Specific Health Problem (WPAI-SHP): Overall Work Impairment Percentage

End point title	Mean Change From Baseline in Work Productivity and Activity Impairment Questionnaire: Specific Health Problem (WPAI-SHP): Overall Work Impairment Percentage

End point description:

WPAI-SHP is a questionnaire used to assess the effect of the subject's health problems on their ability to work and perform regular activities. A higher score indicates an increased impairment. A positive value of change indicates an increased impairment of work productivity and the limitation of activities of daily life, while a negative value indicates an improvement. The overall work impairment data was applicable to employed subjects only. Efficacy assessments were not specified at week 18; missing data at week 18 were imputed using last observation carried forward (LOCF). N = subjects with evaluable baseline and post-baseline data.

End point type	Secondary

End point timeframe:

Week 0 (baseline), Week 2, Week 8, Week 18, and Week 26

End point values	Subjects Receiving Adalimumab			
Subject group type	Reporting group			
Number of subjects analysed	225[17]			
Units: Percentage of overall work impairment				
arithmetic mean (standard deviation)				
Week 2 (N= 211)	-18.3 (± 27.72)			
Week 8 (N= 225)	-26.5 (± 34.56)			
Week 18 (N= 223)	-25.3 (± 35.1)			
Week 26 (N= 221)	-29.2 (± 32.32)			

Notes:

[17] - All subjects in the ITT population with evaluable data.

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Baseline in Work Productivity and Activity Impairment Questionnaire: Specific Health Problem (WPAI-SHP): Percentage of Activity Impairment

End point title	Mean Change From Baseline in Work Productivity and Activity Impairment Questionnaire: Specific Health Problem (WPAI-SHP): Percentage of Activity Impairment

End point description:

WPAI-SHP is a questionnaire used to assess the effect of the subject's health problems on their ability to work and perform regular activities. A higher score indicates an increased impairment. A positive value of change indicates an increased impairment of work productivity and the limitation of activities of daily life, while a negative value indicates an improvement. Efficacy assessments were not specified at week 18; missing data at week 18 were imputed using last observation carried forward (LOCF). N = subjects with evaluable baseline and post-baseline data.

End point type	Secondary

End point timeframe:

Week 0 (baseline), Week 2, Week 8, Week 18, and Week 26

End point values	Subjects Receiving Adalimumab			
Subject group type	Reporting group			
Number of subjects analysed	446[18]			
Units: Percentage of activity impairment				
arithmetic mean (standard deviation)				
Week 2 (N=435)	-18.2 (± 24.55)			
Week 8 (N=446)	-25.4 (± 30.84)			
Week 18 (N=446)	-24.4 (± 31.35)			
Week 26 (N-446)	-27.2 (± 32.83)			

Notes:
[18] - All subjects in the ITT population with evaluable data.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse Events were collected from the time of study drug administration to 70 days after last dose of study drug (up to 36 weeks).

Adverse event reporting additional description:

Serious Adverse Events were also collected from the time that informed consent was obtained until 70 days after last dose (up to 39 weeks).

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.1

Reporting groups

Reporting group title	Subjects Receiving Adalimumab

Reporting group description:

Adults with active UC who had failed conventional therapy received Adalimumab 160 mg at Baseline Visit, 80 mg at Week 2 Visit, and 40 mg every other week (EOW) starting at Week 4. Non-responders to Adalimumab were to be discontinued from treatment at Week 8. After Week 8, dose escalation to 40 mg weekly was allowed for flare or non-response.

Serious adverse events	Subjects Receiving Adalimumab		
Total subjects affected by serious adverse events			
subjects affected / exposed	67 / 463 (14.47%)		
number of deaths (all causes)	1		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Malignant melanoma of eyelid			
subjects affected / exposed	1 / 463 (0.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Prostate cancer			
subjects affected / exposed	1 / 463 (0.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Testicular seminoma (pure)			
subjects affected / exposed	1 / 463 (0.22%)		
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 / 463 (0.43%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Pregnancy, puerperium and perinatal conditions			
Foetal death			
subjects affected / exposed	1 / 463 (0.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Foetal distress syndrome			
subjects affected / exposed	1 / 463 (0.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Accidental death			
subjects affected / exposed	1 / 463 (0.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Asthenia			
subjects affected / exposed	1 / 463 (0.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Depression			
subjects affected / exposed	1 / 463 (0.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Ankle fracture			
subjects affected / exposed	1 / 463 (0.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumothorax traumatic			

subjects affected / exposed	1 / 463 (0.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Silent myocardial infarction			
subjects affected / exposed	1 / 463 (0.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Cerebral haemorrhage			
subjects affected / exposed	1 / 463 (0.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Dizziness			
subjects affected / exposed	1 / 463 (0.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Intracranial venous sinus thrombosis			
subjects affected / exposed	1 / 463 (0.22%)		
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	2 / 463 (0.43%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Pancytopenia			
subjects affected / exposed	1 / 463 (0.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Thrombocytopenia			
subjects affected / exposed	1 / 463 (0.22%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

Gastrointestinal disorders			
Abdominal pain lower			
subjects affected / exposed	1 / 463 (0.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Colitis ulcerative			
subjects affected / exposed	41 / 463 (8.86%)		
occurrences causally related to treatment / all	1 / 46		
deaths causally related to treatment / all	0 / 0		
Diarrhoea			
subjects affected / exposed	1 / 463 (0.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal haemorrhage			
subjects affected / exposed	1 / 463 (0.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Megacolon			
subjects affected / exposed	1 / 463 (0.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Dermatosis			
subjects affected / exposed	1 / 463 (0.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pruritus generalised			
subjects affected / exposed	1 / 463 (0.22%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Endocrine disorders			
Hyperthyroidism			

subjects affected / exposed	1 / 463 (0.22%)		
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	1 / 463 (0.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Osteitis			
subjects affected / exposed	1 / 463 (0.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Appendicitis			
subjects affected / exposed	1 / 463 (0.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cellulitis			
subjects affected / exposed	1 / 463 (0.22%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Cytomegalovirus infection			
subjects affected / exposed	1 / 463 (0.22%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Gastroenteritis			
subjects affected / exposed	1 / 463 (0.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Herpes zoster			
subjects affected / exposed	1 / 463 (0.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Osteomyelitis			
subjects affected / exposed	1 / 463 (0.22%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Otitis media			
subjects affected / exposed	1 / 463 (0.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pyelonephritis			
subjects affected / exposed	1 / 463 (0.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Rectal abscess			
subjects affected / exposed	1 / 463 (0.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Sinusitis			
subjects affected / exposed	1 / 463 (0.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Wound sepsis			
subjects affected / exposed	1 / 463 (0.22%)		
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	Subjects Receiving Adalimumab		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	178 / 463 (38.44%)		
Nervous system disorders			
Headache			
subjects affected / exposed	60 / 463 (12.96%)		
occurrences (all)	112		

Gastrointestinal disorders Colitis ulcerative subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all)	 61 / 463 (13.17%) 72 29 / 463 (6.26%) 34		
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) Oropharyngeal pain subjects affected / exposed occurrences (all)	 27 / 463 (5.83%) 30 25 / 463 (5.40%) 27		
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all)	 33 / 463 (7.13%) 34		
Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all)	 37 / 463 (7.99%) 46		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
19 September 2011	The purpose of this amendment was to add visit windows, extend the Screening period to allow for receipt of test results, add enrollment fulfillment statement, and clarified description of study design and study drug discontinuation; inclusion and exclusion criteria were updated; corrected efficacy variable description, revised the secondary variables to accurately define the secondary endpoints, and deleted ECG and CXR from safety variables; updated statistical analyses of efficacy, statistical analyses of safety, and other analyses with corrected and consolidated description of the analyses; and updated recording of previous medications to within 6 months prior to Week 0 (baseline) and provided direction on concomitant medication recording.
05 April 2012	The purpose of this amendment was to add week 18 visit and the week 18 study window; added the criterion for non-response at week 8 per country requirements; changed the starting week for dose escalation to be consistent with the proposed label; changed the age requirements to ensure that the subjects were at least 18 years old at the time the informed consent was signed; and exclusion criteria were clarified, added and revised.
28 February 2013	The purpose of the amendment was to change the effectiveness endpoint "Mean Change From the 6 Months Prior to Treatment With Adalimumab to the 6 Months After Beginning Treatment With Adalimumab in Costs of UC-related Medical Care Excluding Adalimumab Costs" from a secondary effectiveness endpoint to the second ranked primary effectiveness endpoint; revised the number of subjects to be enrolled in the study due to recalculation of sample size based on change of primary effectiveness endpoints and increased the number of sites in order to facilitate enrollment; extended the screening period for initiation of prophylactic anti-TB therapy and for repeat screening procedure(s) or laboratory test(s); and removed the wording of previous treatment with an anti-TNF agent including infliximab as an exclusion criterion and modified to indicate that the study design would enroll approximately 30% of anti-TNF experienced subjects.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported