Clinical trial results:
A phase IIa, randomised, double-blind, placebo-controlled, parallel-arm, multicenter study to evaluate the efficacy and safety of tralokinumab (CAT-354), a recombinant human monoclonal antibody directed against interleukin-13 (IL-13), as add-on therapy, on clinical response in patients with active, moderate-to-severe, ulcerative colitis

Summary

EudraCT number	2011-004812-40
Trial protocol	DE NL CZ IT GB
Global end of trial date	19 July 2013

Results information

Result version number	v1 (current)
This version publication date	02 October 2016
First version publication date	02 October 2016

Trial information

Trial identification

Sponsor protocol code	D2211C00001

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01482884
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	AstraZeneca R&D Mölndal
Sponsor organisation address	Pepparedsleden 1, Mölndal, Sweden, S-431 83
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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	19 July 2013
Is this the analysis of the primary completion data?	Yes
Primary completion date	26 June 2013
Global end of trial reached?	Yes
Global end of trial date	19 July 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Clinical response at week 8 based on Mayo score
Clinical response was measured as a decrease in Mayo score of ≥3 points from baseline, decrease in the total Mayo score from baseline ≥30 percentage and a decrease in the sub score for rectal bleeding ≥1 or absolute sub score for rectal bleeding of 0 or 1 point. Mayo score is sum of four sub-scores: stool frequency, rectal bleeding, endoscopy findings and the physician's global assessment. The total Mayo score ranges from 0-12, with higher scores indicating a more severe disease.

Protection of trial subjects:

No specific measures where put in place to protect trials subjects. Anti-pain treatment was based on local practice.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	26 March 2012
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	3 Months
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Czech Republic: 19
Country: Number of subjects enrolled	France: 34
Country: Number of subjects enrolled	Germany: 23
Country: Number of subjects enrolled	Italy: 21
Country: Number of subjects enrolled	Poland: 36
Country: Number of subjects enrolled	United Kingdom: 14
Worldwide total number of subjects	147
EEA total number of subjects	147

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)	143
From 65 to 84 years	4
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

147/111 patients were enrolled/randomized from 31 centres in 6 European countries. The first patient was enrolled on 26 March 2012, and the last patient completed the study on 24 June 2013.

Pre-assignment

Screening details:

Participants were enrolled for a period of 3 weeks.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Tralokinumab

Arm description:

Tralokinumab 300 mg was administered during study as two subcutaneous 150 mg injections every 2 weeks for 12 weeks starting from Visit 2.

Arm type	Experimental
Investigational medicinal product name	Tralokinumab
Investigational medicinal product code	CAT-354
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

300 mg

Arm title	Placebo

Arm description:

Placebo was administered during study as two subcutaneous injections every 2 weeks for 12 weeks starting from Visit 2.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

300 mg

Number of subjects in period 1[1]	Tralokinumab	Placebo
Started	56	55
Completed	43	37
Not completed	13	18
Consent withdrawn by subject	8	13
Medical decision due to lack of efficacy	-	1
Adverse event, non-fatal	2	1
Lost to follow-up	2	2
Protocol deviation	1	-
Lack of efficacy	-	1

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: 147 patients were enrolled from 31 centres in 6 European countries. The first patient was enrolled on 26 March 2012, and the last patient completed the study on 24 June 2013. Out of 147 enrolled patients, 36 did not meet the eligibility criteria and 1 was randomized but not treated. Therefore 111 patients were randomized in total.

Baseline characteristics

Reporting groups	
Reporting group title	Tralokinumab
Reporting group description:	
Tralokinumab 300 mg was administered during study as two subcutaneous 150 mg injections every 2 weeks for 12 weeks starting from Visit 2.	
Reporting group title	Placebo
Reporting group description:	
Placebo was administered during study as two subcutaneous injections every 2 weeks for 12 weeks starting from Visit 2.	

Reporting group values	Tralokinumab	Placebo	Total
Number of subjects	56	55	111
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	56	54	110
From 65-84 years	0	1	1
85 years and over	0	0	0
Age Continuous | Units: Years			
arithmetic mean	42.2	40.8	
standard deviation	± 11.54	± 13.26	-
Gender, Male/Female Units: Participants			
Female	29	29	58
Male	27	26	53
Race/Ethnicity, Customized Units: Subjects			
Asian	2	0	2
White	54	54	108
Other	0	1	1
Race/Ethnicity, Customized Units: Subjects			
Hispanic or Latino	2	2	4
Asian (Other than Chinese And Japanese)	2	0	2
Not Applicable	35	40	75
Other	17	13	30
Study Specific Characteristic			
Yes: if participants had received a glucocorticosteroid treatment prior to baseline and the outcome of that treatment was no improvement. No: If the outcome of the treatment was improvement or missing. Unknown: If the outcome of the treatment was unknown.			

Units: Subjects			
Yes	3	8	11
No	53	46	99
Unknown	0	1	1
Study Specific Characteristic |			
Units: Years			
arithmetic mean	9.22	7.78	
standard deviation	± 8.523	± 8.664	-
Study Specific Characteristic |			
Mayo score at baseline			
Units: Scores on scale			
arithmetic mean	8.36	8.33	
full range (min-max)	5 to 11	6 to 11	-
Study Specific Characteristic |			
Partial Mayo score at baseline			
Units: Scores on scale			
arithmetic mean	5.91	5.85	
full range (min-max)	3 to 8	3 to 8	-

Subject analysis sets

Subject analysis set title	The full analysis set consist of all randomised participants
Subject analysis set type	Full analysis

Subject analysis set description:

The full analysis set consist of all randomised participants

Reporting group values	The full analysis set consist of all randomised participants		
Number of subjects	111		
Age categorical			
Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	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)	110		
From 65-84 years	1		
85 years and over	0		
Age Continuous |			
Units: Years			
arithmetic mean	41.5		
standard deviation	± 12.39		
Gender, Male/Female			
Units: Participants			
Female	58		
Male	53		

Race/Ethnicity, Customized Units: Subjects			
Asian	2		
White	108		
Other	1		
Race/Ethnicity, Customized Units: Subjects			
Hispanic or Latino	4		
Asian (Other than Chinese And Japanese)	2		
Not Applicable	75		
Other	30		
Study Specific Characteristic			
Yes: if participants had received a glucocorticosteroid treatment prior to baseline and the outcome of that treatment was no improvement. No: If the outcome of the treatment was improvement or missing. Unknown: If the outcome of the treatment was unknown.			
Units: Subjects			
Yes	11		
No	99		
Unknown	1		
Study Specific Characteristic | Units: Years			
arithmetic mean	8.51		
standard deviation	± 8.585		
Study Specific Characteristic |			
Mayo score at baseline			
Units: Scores on scale			
arithmetic mean	8.34		
full range (min-max)	5 to 11		
Study Specific Characteristic |			
Partial Mayo score at baseline			
Units: Scores on scale			
arithmetic mean	5.88		
full range (min-max)	3 to 8		

End points

End points reporting groups

Reporting group title	Tralokinumab
Reporting group description:	
Tralokinumab 300 mg was administered during study as two subcutaneous 150 mg injections every 2 weeks for 12 weeks starting from Visit 2.	
Reporting group title	Placebo
Reporting group description:	
Placebo was administered during study as two subcutaneous injections every 2 weeks for 12 weeks starting from Visit 2.	
Subject analysis set title	The full analysis set consist of all randomised participants
Subject analysis set type	Full analysis
Subject analysis set description:	
The full analysis set consist of all randomised participants	

Primary: Clinical response at week 8 based on Mayo score

End point title	Clinical response at week 8 based on Mayo score
End point description:	
Clinical response was measured as a decrease in Mayo score of ≥3 points from baseline, decrease in the total Mayo score from baseline ≥30 percentage and a decrease in the sub score for rectal bleeding ≥1 or absolute sub score for rectal bleeding of 0 or 1 point. Mayo score is sum of four sub-scores: stool frequency, rectal bleeding, endoscopy findings and the physician's global assessment. The total Mayo score ranges from 0-12, with higher scores indicating a more severe disease.	
End point type	Primary
End point timeframe:	
Eight week treatment period	

End point values	Tralokinumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	56	55		
Units: Percentage of responders				
number (not applicable)	37.5	32.7		

Statistical analyses

Statistical analysis title	Cochran-Mantel-Haenszel (CMH) chi-square test
Statistical analysis description:	
The null hypothesis is that the proportion of participants responding on tralokinumab is less than or equal to the proportion of participants responding on placebo.	
Comparison groups	Tralokinumab v Placebo

Number of subjects included in analysis	111
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4062 [1]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	4.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-13
upper limit	22.5
Variability estimate	Standard error of the mean
Dispersion value	0.0905

Notes:

[1] - Glucocorticosteroid-refractory status as stratification factor

Secondary: Change in Mayo score from baseline to Week 8

End point title	Change in Mayo score from baseline to Week 8

End point description:

Mayo score is sum of four sub-scores: stool frequency, rectal bleeding, endoscopy findings and the physician's global assessment. The total Mayo score ranges from 0-12, with higher scores indicating a more severe disease. Change from baseline: Mayo score at week 8 minus the Mayo score at baseline.

End point type	Secondary

End point timeframe:

Eight week treatment period

End point values	Tralokinumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	45	42		
Units: Score on scale				
least squares mean (standard error)	-2.41 (± 0.58)	-1.92 (± 0.56)		

Statistical analyses

Statistical analysis title	ANCOVA Analysis of Covariance
Comparison groups	Tralokinumab v Placebo
Number of subjects included in analysis	87
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.3937
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.49

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.63
upper limit	0.65
Variability estimate	Standard error of the mean
Dispersion value	0.57

Secondary: Mucosal healing at week 8 based on Mayo score

End point title	Mucosal healing at week 8 based on Mayo score
End point description:	
Improvement of the endoscopy sub score (from the Mayo score) from 3 or 2 to 0 or 1 point, or from 1 to 0 points.	
End point type	Secondary
End point timeframe:	
Eight week treatment period	

End point values	Tralokinumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	56	55		
Units: Percentage of participants				
number (not applicable)	32.1	20		

Statistical analyses

Statistical analysis title	Cochran-Mantel-Haenszel (CMH) chi-square test
Comparison groups	Tralokinumab v Placebo
Number of subjects included in analysis	111
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.1043 [2]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	12.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4
upper limit	28.3
Variability estimate	Standard error of the mean
Dispersion value	0.0825

Notes:

[2] - Glucocorticosteroid-refractory status as stratification factor

Secondary: Clinical remission at week 8 based on Mayo score

End point title	Clinical remission at week 8 based on Mayo score

End point description:

Participants were classified as in remission if Mayo score of ≤2 with no individual sub score exceeding 1 point. Mayo score is sum of four sub-scores: stool frequency, rectal bleeding, endoscopy findings and the physician's global assessment. The total Mayo score ranges from 0-12, with higher scores indicating a more severe disease.

End point type	Secondary

End point timeframe:

Eight week treatment period

End point values	Tralokinumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	56	55		
Units: Percentage of participants				
number (not applicable)	17.9	5.5		

Statistical analyses

Statistical analysis title	Cochran-Mantel-Haenszel (CMH) chi-square test
Comparison groups	Tralokinumab v Placebo
Number of subjects included in analysis	111
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0326 [3]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	12.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.7
upper limit	24.1
Variability estimate	Standard error of the mean
Dispersion value	0.0596

Notes:

[3] - Glucocorticosteroid-refractory status as stratification factor

Secondary: Change from baseline in partial Mayo score

End point title	Change from baseline in partial Mayo score

End point description:

The partial Mayo score is the sum of the three sub-score areas: stool frequency, rectal bleeding, and the physician's global assessment.The partial Mayo score ranges from 0-9, with higher scores indicating a

more severe disease. Change from baseline: Mayo score at each post-baseline timepoint (week 4, 8, 12, 16, 20, and 24) minus the Mayo score at baseline.

End point type	Secondary

End point timeframe:

From baseline to Week 4, 8, 12, 16, 20, and 24.

End point values	Tralokinumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	56	55		
Units: Score on scale				
arithmetic mean (full range (min-max))				
Week 4	-1.8 (-8 to 3)	-0.8 (-6 to 4)		
Week 8	-2.4 (-6 to 3)	-1.7 (-6 to 1)		
Week 12	-2.7 (-7 to 3)	-2.6 (-8 to 4)		
Week 16	-2.6 (-7 to 3)	-3.3 (-7 to 2)		
Week 20	-3 (-7 to 2)	-3.6 (-8 to 1)		
Week 24	-3 (-7 to 3)	-3.6 (-7 to 1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in modified Riley score

End point title	Change from baseline in modified Riley score

End point description:

Modified Riley score is biopsy grade which range from 0-5; where 0: Normal mucosa, 1: Infiltration of lymphocytes and plasma cells in the lamina propria, 2: Infiltration of neutrophils and eosinophils in the lamina propria, 3: Infiltration of neutrophils in the epithelium, 4: Crypt destruction, 5: Erosion and/or ulceration.

End point type	Secondary

End point timeframe:

Eight week treatment period

End point values	Tralokinumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	37	35		
Units: Grade on scale				
least squares mean (standard error)	-0.49 (± 0.23)	-0.74 (± 0.24)		

Statistical analyses

Statistical analysis title	ANCOVA Analysis of Covariance
Comparison groups	Tralokinumab v Placebo
Number of subjects included in analysis	72
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.449
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	0.25
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.41
upper limit	0.91
Variability estimate	Standard error of the mean
Dispersion value	0.33

Secondary: Change from baseline in C - reactive protein

End point title	Change from baseline in C - reactive protein

End point description:

End point type	Secondary

End point timeframe:

From baseline to Week 4, 8, 12, 16, 20, and 24.

End point values	Tralokinumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	56	55		
Units: mg/L				
arithmetic mean (full range (min-max))				
Week 4	-2.755 (-33 to 25)	0.51 (-12 to 32)		
Week 8	-1.089 (-29 to 29)	0.637 (-43 to 46)		
Week 12	-2.795 (-46 to 63)	-1.974 (-61 to 43)		
Week 16	-3.49 (-53 to 19)	0.638 (-61 to 97)		
Week 20	-4.094 (-52 to 43)	-1.467 (-62 to 31)		
Week 24	-2.754 (-36 to 25)	-1.915 (-59 to 36)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in Albumin

End point title	Change from baseline in Albumin

End point description:

End point type	Secondary

End point timeframe:

From baseline to Week 4, 8, 12, 16, 20, and 24.

End point values	Tralokinumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	56	55		
Units: g/L				
arithmetic mean (full range (min-max))				
Week 4	0 (-8 to 5)	-0.7 (-7 to 6)		
Week 8	0.8 (-7 to 8)	-0.2 (-8 to 5)		
Week 12	0.3 (-9 to 5)	-0.4 (-8 to 5)		
Week 16	0.5 (-10 to 12)	0.4 (-7 to 7)		
Week 20	1.1 (-4 to 7)	0.1 (-6 to 9)		
Week 24	1.2 (-4 to 8)	0.2 (-6 to 8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in Calprotectin

End point title	Change from baseline in Calprotectin

End point description:

End point type	Secondary

End point timeframe:

From baseline to Week 4, 8, 12, 16, 20, and 24.

End point values	Tralokinumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	56	55		
Units: ug/g				
arithmetic mean (full range (min-max))				
Week 4	69.45 (-1068 to 931)	198.8 (-1315 to 4188)		
Week 8	86.47 (-894.2 to 912)	-250.52 (-4005 to 4505)		

Week 12	-39.19 (-1109 to 841)	50.31 (-1234 to 4811)		
Week 16	-75.1 (-1008 to 1056)	-338.76 (-3857 to 1138)		
Week 20	32.55 (-1155 to 4669)	-402.81 (-3835 to 794)		
Week 24	-136.78 (-1120 to 617)	-267.58 (-1172 to 824)		

Statistical analyses

No statistical analyses for this end point

Secondary: Serum concentration of Tralokinumab

End point title	Serum concentration of Tralokinumab

End point description:

End point type	Secondary

End point timeframe:

Pre-dose sampling at baseline, Week 4, 8, 12, 16, 20, and 24.

End point values	Tralokinumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	55	0[4]		
Units: ug/ml				
arithmetic mean (full range (min-max))				
pre-dose at baseline	0 (0 to 0)	(to)		
Week 4	37.9 (12.2 to 92.2)	(to)		
Week 8	50.2 (5.83 to 116)	(to)		
Week 12	48.2 (0.781 to 109)	(to)		
Week 16	27.2 (0.369 to 82.7)	(to)		
Week 20	9.32 (0.527 to 36.9)	(to)		
Week 24	3.66 (0 to 18)	(to)		

Notes:

[4] - Serum concentration is not reported for placebo patients therefore no data available.

Statistical analyses

No statistical analyses for this end point

Secondary: Immunogenicity

End point title	Immunogenicity

End point description:

Incidence of anti-drug antibodies (ADA) to tralokinumab in serum.

End point type	Secondary

End point timeframe:

Pre-dose sampling at baseline, Week 8, 12, 16, and 24.

End point values	Tralokinumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	55	55		
Units: participants				
pre-dose at baseline	0	1		
Week 8	0	1		
Week 12	0	1		
Week 16	0	1		
Week 24	0	0		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

24 Weeks

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	16.0

Reporting groups

Reporting group title	Placebo

Reporting group description:

Placebo was administered during study as two subcutaneous injections every 2 weeks for 12 weeks starting from Visit 2.

Reporting group title	Tralokinumab 300 mg

Reporting group description:

Tralokinumab 300 mg was administered during study as two subcutaneous 150 mg injections every 2 weeks for 12 weeks starting from Visit 2.

Serious adverse events	Placebo	Tralokinumab 300 mg	
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 55 (10.91%)	7 / 55 (12.73%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Nervous system disorders			
CEREBROVASCULAR ACCIDENT			
subjects affected / exposed	1 / 55 (1.82%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
ANAEMIA			
subjects affected / exposed	1 / 55 (1.82%)	1 / 55 (1.82%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
GENERAL PHYSICAL HEALTH DETERIORATION			
subjects affected / exposed	1 / 55 (1.82%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Immune system disorders			
SERUM SICKNESS			
subjects affected / exposed	0 / 55 (0.00%)	1 / 55 (1.82%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
COLITIS ULCERATIVE			
subjects affected / exposed	5 / 55 (9.09%)	5 / 55 (9.09%)	
occurrences causally related to treatment / all	1 / 6	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 2 %

Non-serious adverse events	Placebo	Tralokinumab 300 mg	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	37 / 55 (67.27%)	41 / 55 (74.55%)	
Investigations			
WEIGHT DECREASED			
subjects affected / exposed	0 / 55 (0.00%)	3 / 55 (5.45%)	
occurrences (all)	0	3	
Cardiac disorders			
TACHYCARDIA			
subjects affected / exposed	2 / 55 (3.64%)	2 / 55 (3.64%)	
occurrences (all)	2	2	
Nervous system disorders			
HEADACHE			
subjects affected / exposed	12 / 55 (21.82%)	10 / 55 (18.18%)	
occurrences (all)	22	35	
DIZZINESS			
subjects affected / exposed	2 / 55 (3.64%)	2 / 55 (3.64%)	
occurrences (all)	2	2	
Blood and lymphatic system disorders			
ANAEMIA			
subjects affected / exposed	1 / 55 (1.82%)	3 / 55 (5.45%)	
occurrences (all)	1	3	
General disorders and administration site conditions			

ASTHENIA			
subjects affected / exposed	5 / 55 (9.09%)	5 / 55 (9.09%)	
occurrences (all)	6	5	
FATIGUE			
subjects affected / exposed	2 / 55 (3.64%)	3 / 55 (5.45%)	
occurrences (all)	2	3	
INJECTION SITE ERYTHEMA			
subjects affected / exposed	0 / 55 (0.00%)	3 / 55 (5.45%)	
occurrences (all)	0	10	
INJECTION SITE REACTION			
subjects affected / exposed	0 / 55 (0.00%)	3 / 55 (5.45%)	
occurrences (all)	0	3	
PYREXIA			
subjects affected / exposed	4 / 55 (7.27%)	6 / 55 (10.91%)	
occurrences (all)	4	7	
INFLUENZA LIKE ILLNESS			
subjects affected / exposed	2 / 55 (3.64%)	0 / 55 (0.00%)	
occurrences (all)	3	0	
Gastrointestinal disorders			
ABDOMINAL PAIN			
subjects affected / exposed	6 / 55 (10.91%)	7 / 55 (12.73%)	
occurrences (all)	9	13	
COLITIS ULCERATIVE			
subjects affected / exposed	10 / 55 (18.18%)	11 / 55 (20.00%)	
occurrences (all)	12	13	
HAEMORRHOIDS			
subjects affected / exposed	1 / 55 (1.82%)	3 / 55 (5.45%)	
occurrences (all)	1	3	
TOOTHACHE			
subjects affected / exposed	1 / 55 (1.82%)	3 / 55 (5.45%)	
occurrences (all)	1	3	
ABDOMINAL DISCOMFORT			
subjects affected / exposed	0 / 55 (0.00%)	2 / 55 (3.64%)	
occurrences (all)	0	2	
ABDOMINAL TENDERNESS			

subjects affected / exposed	1 / 55 (1.82%)	2 / 55 (3.64%)	
occurrences (all)	1	2	
DIARRHOEA			
subjects affected / exposed	0 / 55 (0.00%)	2 / 55 (3.64%)	
occurrences (all)	0	2	
DYSPEPSIA			
subjects affected / exposed	2 / 55 (3.64%)	2 / 55 (3.64%)	
occurrences (all)	2	2	
NAUSEA			
subjects affected / exposed	2 / 55 (3.64%)	2 / 55 (3.64%)	
occurrences (all)	2	10	
VOMITING			
subjects affected / exposed	2 / 55 (3.64%)	2 / 55 (3.64%)	
occurrences (all)	2	3	
Respiratory, thoracic and mediastinal disorders			
DYSPNOEA			
subjects affected / exposed	0 / 55 (0.00%)	3 / 55 (5.45%)	
occurrences (all)	0	3	
OROPHARYNGEAL PAIN			
subjects affected / exposed	2 / 55 (3.64%)	4 / 55 (7.27%)	
occurrences (all)	2	5	
COUGH			
subjects affected / exposed	2 / 55 (3.64%)	2 / 55 (3.64%)	
occurrences (all)	2	2	
Skin and subcutaneous tissue disorders			
ALOPECIA			
subjects affected / exposed	2 / 55 (3.64%)	3 / 55 (5.45%)	
occurrences (all)	2	4	
Musculoskeletal and connective tissue disorders			
ARTHRALGIA			
subjects affected / exposed	7 / 55 (12.73%)	3 / 55 (5.45%)	
occurrences (all)	7	3	
BACK PAIN			
subjects affected / exposed	4 / 55 (7.27%)	3 / 55 (5.45%)	
occurrences (all)	5	5	
MUSCLE SPASMS			

subjects affected / exposed	2 / 55 (3.64%)	0 / 55 (0.00%)	
occurrences (all)	2	0	
MYALGIA			
subjects affected / exposed	2 / 55 (3.64%)	1 / 55 (1.82%)	
occurrences (all)	2	1	
PAIN IN EXTREMITY			
subjects affected / exposed	2 / 55 (3.64%)	1 / 55 (1.82%)	
occurrences (all)	2	1	
Infections and infestations			
INFLUENZA			
subjects affected / exposed	4 / 55 (7.27%)	2 / 55 (3.64%)	
occurrences (all)	5	2	
NASOPHARYNGITIS			
subjects affected / exposed	5 / 55 (9.09%)	3 / 55 (5.45%)	
occurrences (all)	6	3	
PHARYNGITIS			
subjects affected / exposed	2 / 55 (3.64%)	2 / 55 (3.64%)	
occurrences (all)	3	2	
SINUSITIS			
subjects affected / exposed	2 / 55 (3.64%)	1 / 55 (1.82%)	
occurrences (all)	2	1	
Metabolism and nutrition disorders			
DECREASED APPETITE			
subjects affected / exposed	0 / 55 (0.00%)	3 / 55 (5.45%)	
occurrences (all)	0	3	
VITAMIN D DEFICIENCY			
subjects affected / exposed	2 / 55 (3.64%)	0 / 55 (0.00%)	
occurrences (all)	2	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
18 July 2012	The number of sites increased. The enrollment period prolonged from 12 days to 21 days. Upper age limit extended to allow patients between 65 and 75 years. The required wash-out period after anti-TNF-α treatment was shortened from 12 to 8 weeks.
22 November 2012	Change in text in the Section 5.4.1 of the CSP, revised text states that "the data related to the primary variable were to be collected for analysis by the designated unblinded sponsor staff or delegates after completion of Visit 6 of all the patients".

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported