



## Clinical trial results:

### A Multi-Center, Randomized, Double-blind, Placebo-controlled Study of Adalimumab for the Induction of Clinical Remission in Japanese Subjects With Crohn's Disease

#### Summary

EudraCT number	2014-004560-38
Trial protocol	Outside EU/EEA
Global end of trial date	25 December 2007

#### Results information

Result version number	v1 (current)
This version publication date	20 April 2016
First version publication date	07 June 2015

#### Trial information

##### Trial identification

Sponsor protocol code	M04-729
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##### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00445939
WHO universal trial number (UTN)	-

Notes:

#### Sponsors

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

Notes:

#### Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	Yes

Notes:

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**Results analysis stage**

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Analysis stage	Final
Date of interim/final analysis	25 December 2007
Is this the analysis of the primary completion data?	No

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Global end of trial reached?	Yes
Global end of trial date	25 December 2007
Was the trial ended prematurely?	No

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Notes:

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**General information about the trial**

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Main objective of the trial:

The purpose of this study is to demonstrate the efficacy and safety of adalimumab for the induction of clinical remission in Japanese subjects with Crohn's disease.

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Protection of trial subjects:

Subject and/or legal guardian read and understood the information provided about the study and gave written permission.

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Background therapy: -

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Evidence for comparator: -

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Actual start date of recruitment	01 February 2007
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

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Notes:

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**Population of trial subjects**

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**Subjects enrolled per country**

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Country: Number of subjects enrolled	Japan: 90
Worldwide total number of subjects	90
EEA total number of subjects	0

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Notes:

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**Subjects enrolled per age group**

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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)	3
Adults (18-64 years)	87
From 65 to 84 years	0
85 years and over	0

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## Subject disposition

### Recruitment

Recruitment details:

Subjects with moderate to severe Crohn's Disease (Crohn's Disease Activity Index [CDAI]  $\geq 220$  and  $\leq 450$ ) were enrolled into study. The period from the first dose of study drug to the evaluation at Week 4 is Period A. The period from the study drug injection at Week 4 to the evaluation at Week 8 is Period B.

### Pre-assignment

Screening details:

All subjects were evaluated at Week 4. If responders (CDAI decrease  $\geq 70$  points compared to Baseline), rolled over to a maintenance study. If non-responders (CDAI decrease of  $< 70$  points compared to Baseline), continued in study and received: adalimumab 160/80 mg + 40/40 mg, or adalimumab 80/40 mg + 40/40 mg or placebo + adalimumab 160/80 mg.

### Period 1

Period 1 title	Period A - Week 0 - Week 4
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Carer, Assessor

### Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	Period A - Adalimumab 160 mg/80 mg

Arm description:

Adalimumab 160 mg at Week 0, 80 mg at Week 2

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:

160 mg at Week 0, 80 mg at Week 2

<b>Arm title</b>	Period A - Adalimumab 80 mg/40 mg
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Arm description:

Adalimumab 80 mg at Week 0, 40 mg at Week 2

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:

80 mg at Week 0, 40 mg at Week 2

<b>Arm title</b>	Period A - Placebo
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Arm description:

Placebo at Week 0, placebo at Week 2

Arm type	Placebo
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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: Placebo at Week 0 and Week 2	

Number of subjects in period 1	Period A - Adalimumab 160 mg/80 mg	Period A - Adalimumab 80 mg/40 mg	Period A - Placebo
Started	33	34	23
Completed	32	32	23
Not completed	1	2	0
Adverse event	1	2	-

## Period 2

Period 2 title	Period B - Week 4 - Week 8
Is this the baseline period?	No
Allocation method	Non-randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Carer, Assessor

## Arms

Are arms mutually exclusive?	Yes
Arm title	Period B - Adalimumab 160 mg/80 mg

### Arm description:

Non-responders continued after 4 weeks, placebo at Week 0 and Week 2 (Period A), adalimumab 160 mg at Week 4, 80 mg at Week 6 (Period B)

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:

160 mg at Week 4, 80 mg at Week 6

Arm title	Period B - Adalimumab 40 mg /40 mg
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### Arm description:

Non-responders continued after 4 weeks, adalimumab 160 at Week 0, 80 mg at Week 2 or adalimumab 80 mg at Week 0, 40 mg at Week 2 (Period A), 40 mg at Week 4, 40 mg at Week 6 (Period B)

Arm type	Experimental
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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:

40 mg at Week 4, 40 mg at Week 6

<b>Number of subjects in period 2<sup>[1]</sup></b>	Period B - Adalimumab 160 mg/80 mg	Period B - Adalimumab 40 mg /40 mg
Started	16	21
Completed	14	20
Not completed	2	1
Adverse event	2	1

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: All subjects were evaluated at Week 4; responders were rolled over into a maintenance study (Adalimumab 160 mg/80 mg, n=23; Adalimumab 80 mg/40 mg, n=20; and Placebo, n=7). Non-responders continued after 4 weeks; previous 16 placebo subjects allocated to 160/80 mg group in Period 2; previous 160/80 (n=9) and 80/40 mg (n=12) subjects allocated to the 40/40 group in Period 2.

## Baseline characteristics

### Reporting groups

Reporting group title	Period A - Adalimumab 160 mg/80 mg
Reporting group description: Adalimumab 160 mg at Week 0, 80 mg at Week 2	
Reporting group title	Period A - Adalimumab 80 mg/40 mg
Reporting group description: Adalimumab 80 mg at Week 0, 40 mg at Week 2	
Reporting group title	Period A - Placebo
Reporting group description: Placebo at Week 0, placebo at Week 2	

Reporting group values	Period A - Adalimumab 160 mg/80 mg	Period A - Adalimumab 80 mg/40 mg	Period A - Placebo
Number of subjects	33	34	23
Age categorical Units: Subjects			

Age continuous Units: years arithmetic mean standard deviation	32 ± 9.6	30.6 ± 9.26	30.4 ± 6.93
Gender categorical			
Gender, Male/Female who received first dose of study drug			
Units: Subjects			
Female	13	18	7
Male	20	16	16

Reporting group values	Total		
Number of subjects	90		
Age categorical Units: Subjects			

Age continuous Units: years arithmetic mean standard deviation	-		
Gender categorical			
Gender, Male/Female who received first dose of study drug			
Units: Subjects			
Female	38		
Male	52		

## End points

### End points reporting groups

Reporting group title	Period A - Adalimumab 160 mg/80 mg
Reporting group description: Adalimumab 160 mg at Week 0, 80 mg at Week 2	
Reporting group title	Period A - Adalimumab 80 mg/40 mg
Reporting group description: Adalimumab 80 mg at Week 0, 40 mg at Week 2	
Reporting group title	Period A - Placebo
Reporting group description: Placebo at Week 0, placebo at Week 2	
Reporting group title	Period B - Adalimumab 160 mg/80 mg
Reporting group description: Non-responders continued after 4 weeks, placebo at Week 0 and Week 2 (Period A), adalimumab 160 mg at Week 4, 80 mg at Week 6 (Period B)	
Reporting group title	Period B - Adalimumab 40 mg /40 mg
Reporting group description: Non-responders continued after 4 weeks, adalimumab 160 at Week 0, 80 mg at Week 2 or adalimumab 80 mg at Week 0, 40 mg at Week 2 (Period A), 40 mg at Week 4, 40 mg at Week 6 (Period B)	
Subject analysis set title	Adalimumab 160 mg/80 mg + 40/40 mg
Subject analysis set type	Full analysis
Subject analysis set description: Adalimumab 160 mg at Week 0, 80 mg at Week 2, 40 mg at Week 4, and 40 mg at Week 6	
Subject analysis set title	Adalimumab 80 mg/40 mg + 40/40 mg
Subject analysis set type	Full analysis
Subject analysis set description: Adalimumab 80 mg at Week 0, 40 mg at Week 2, 40 mg at Week 4, and 40 mg at Week 6	
Subject analysis set title	Placebo + Adalimumab 160/80 mg
Subject analysis set type	Full analysis
Subject analysis set description: Placebo at Week 0, placebo at Week 2, adalimumab 160 mg at Week 4, and adalimumab 80 mg at Week 6	

### Primary: Number of Subjects With a Clinical Remission (Crohn's Disease Activity Index [CDAI] < 150) at Week 4

End point title	Number of Subjects With a Clinical Remission (Crohn's Disease Activity Index [CDAI] < 150) at Week 4 <sup>[1]</sup>
End point description: CDAI is used to quantify the symptoms of patients with Crohn's Disease. A score below 150 indicates remission and a score above 450 indicates severe disease. Comparison of the number of subjects with a clinical remission (CDAI < 150) in the adalimumab 160 mg (Week 0)/ 80 mg (Week 2) and adalimumab 80 mg (Week 0)/ 40 mg (Week 2) groups at Week 4. The primary analysis will be performed on the full analysis set (FAS: randomized subjects who received at least one dose of study drug) using the non-responder imputation (NRI) for missing remission observations.	
End point type	Primary
End point timeframe: 4 weeks	

#### 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 were summarized for this end point per protocol.

End point values	Period A - Adalimumab 160 mg/80 mg	Period A - Adalimumab 80 mg/40 mg	Period A - Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	33	34	23	
Units: participants	11	6	3	

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of Subjects With Clinical Remission (CDAI < 150) at Week 2

End point title	Number of Subjects With Clinical Remission (CDAI < 150) at Week 2
End point description: Number of subjects in each treatment group in clinical remission (CDAI < 150) in the FAS using NRI at Week 2. CDAI is used to quantify the symptoms of patients with Crohn's Disease. A score below 150 indicates remission and a score above 450 indicates severe disease.	
End point type	Secondary
End point timeframe: Week 2	

End point values	Period A - Adalimumab 160 mg/80 mg	Period A - Adalimumab 80 mg/40 mg	Period A - Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	33	34	23	
Units: Participants	6	5	1	

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of Subjects With Clinical Response (CR-70 and CR-100) in Period A

End point title	Number of Subjects With Clinical Response (CR-70 and CR-100) in Period A
End point description: The number of subjects in each treatment group with a CR-70 (CDAI decrease of $\geq 70$ compared to Baseline) and CR-100 (CDAI decrease of $\geq 100$ compared to Baseline) at Week 2 and Week 4. CDAI is used to quantify the symptoms of patients with Crohn's Disease. A score below 150 indicates remission and a score above 450 indicates severe disease. Subjects in the FAS are included in the analysis.	
End point type	Secondary
End point timeframe: Week 2 and Week 4	



End point values	Period A - Adalimumab 160 mg/80 mg	Period A - Adalimumab 80 mg/40 mg	Period A - Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	33	34	23	
Units: Participants				
CR-70 at Week 2	15	17	4	
CR-70 at Week 4	23	20	7	
CR-100 at Week 2	10	11	2	
CR-100 at Week 4	15	17	4	

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Subjects With Clinical Response (CR-70 and CR-100) in Period B

End point title	Number of Subjects With Clinical Response (CR-70 and CR-100) in Period B
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End point description:

The Number of subjects in each treatment group with a CR-70 (CDAI decrease of  $\geq 70$  compared to Baseline) and CR-100 (CDAI decrease of  $\geq 100$  compared to Baseline) in subjects who were non-responders at Week 4 at Week 6 and Week 8. CDAI is used to quantify the symptoms of patients with Crohn's Disease. A score below 150 indicates remission and a score above 450 indicates severe disease. Full analysis set - subjects rated as non-responders (did not attain CDAI reduction  $\geq 70$ ) in the evaluation of CR-70 and CR-100 at Week 4. For Week 6 and Week 8, descriptive statistics were performed only for non-responders at Week 4 in the three treatment groups: adalimumab 160/80 mg + 40/40 mg, adalimumab 80/40 mg + 40/40 mg, and placebo + 160/80 mg.

End point type	Secondary
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End point timeframe:

Week 6 and Week 8

End point values	Adalimumab 160 mg/80 mg + 40/40 mg	Adalimumab 80 mg/40 mg + 40/40 mg	Placebo + Adalimumab 160/80 mg	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	9	12	16	
Units: Participants				
CR-70 at Week 6	1	4	9	
CR-70 at Week 8	3	5	12	
CR-100 at Week 6	0	1	3	
CR-100 at Week 8	0	2	7	

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of Subjects With Clinical Remission (CDAI <150) at Week 6 and Week 8

End point title	Number of Subjects With Clinical Remission (CDAI <150) at Week 6 and Week 8
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End point description:

The number of subjects with clinical remission (CDAI < 150) in the subjects who were non-responders at Week 4 calculated with NRI at Week 6 and Week 8. CDAI is used to quantify the symptoms of patients with Crohn's Disease. A score below 150 indicates remission and a score above 450 indicates severe disease.

Subjects who were rated as non-responders (CDAI reduction < 70) in the evaluation of clinical remission (CDAI < 150) at Week 4. For Week 6 and Week 8, descriptive statistics were performed only for non-responders at Week 4 in the three treatment groups: adalimumab 160/80 mg + 40/40 mg, adalimumab 80/40 mg + 40/40 mg, and placebo + adalimumab 160/80 mg.

End point type	Secondary
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End point timeframe:

Week 6 and Week 8

End point values	Adalimumab 160 mg/80 mg + 40/40 mg	Adalimumab 80 mg/40 mg + 40/40 mg	Placebo + Adalimumab 160/80 mg	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	33	34	23	
Units: Participants				
Clinical Remission at Week 6	0	1	2	
Clinical Remission at Week 8	0	1	2	

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Treatment-emergent adverse events were collected from time of study drug administration to 70 days after last dose of study drug.

Assessment type	Non-systematic
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	9.1
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### Reporting groups

Reporting group title	Adalimumab 160 mg/80 mg
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Reporting group description:

Adalimumab 160 mg at Week 0, 80 mg at Week 2

Reporting group title	Adalimumab 80 mg/40 mg
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Reporting group description:

Adalimumab 80 mg at Week 0, 40 mg at Week 2

Reporting group title	Placebo
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Reporting group description:

Placebo at Week 0, placebo at Week 2

Reporting group title	Adalimumab 160 mg/80 mg + 40/40 mg
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Reporting group description:

Adalimumab 160 mg at Week 0, 80 mg at Week 2, 40 mg at Week 4, 40 mg at Week 6

Reporting group title	Adalimumab 80/40 mg + 40/40 mg
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Reporting group description:

Adalimumab 80 mg at Week 0, 40 mg at Week 2, 40 mg at Week 4, 40 mg at Week 6

Reporting group title	Placebo + Adalimumab 160/80 mg
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Reporting group description:

Placebo at Week 0, Placebo at Week 2, 160 mg at Week 4, 80 mg at Week 6

Serious adverse events	Adalimumab 160 mg/80 mg	Adalimumab 80 mg/40 mg	Placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 33 (3.03%)	3 / 34 (8.82%)	2 / 23 (8.70%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Investigations			
C-reactive protein increased (at investigator's discretion)			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 33 (0.00%)	1 / 34 (2.94%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			

Crohn's disease			
subjects affected / exposed	0 / 33 (0.00%)	2 / 34 (5.88%)	2 / 23 (8.70%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subileus			
subjects affected / exposed	0 / 33 (0.00%)	1 / 34 (2.94%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Epididymitis			
subjects affected / exposed	1 / 33 (3.03%)	0 / 34 (0.00%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Abdominal abscess			
subjects affected / exposed	0 / 33 (0.00%)	1 / 34 (2.94%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
<b>Serious adverse events</b>	Adalimumab 160 mg/80 mg + 40/40 mg	Adalimumab 80/40 mg + 40/40 mg	Placebo + Adalimumab 160/80 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 9 (11.11%)	1 / 12 (8.33%)	0 / 16 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Investigations			
C-reactive protein increased (at investigator's discretion)			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 9 (0.00%)	0 / 12 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Crohn's disease			

subjects affected / exposed	1 / 9 (11.11%)	1 / 12 (8.33%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subileus			
subjects affected / exposed	0 / 9 (0.00%)	0 / 12 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Epididymitis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 12 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Abdominal abscess			
subjects affected / exposed	0 / 9 (0.00%)	0 / 12 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

<b>Non-serious adverse events</b>	Adalimumab 160 mg/80 mg	Adalimumab 80 mg/40 mg	Placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	13 / 33 (39.39%)	15 / 34 (44.12%)	8 / 23 (34.78%)
General disorders and administration site conditions			
Adverse drug reaction			
subjects affected / exposed	1 / 33 (3.03%)	1 / 34 (2.94%)	1 / 23 (4.35%)
occurrences (all)	1	1	1
Application site swelling			
subjects affected / exposed	0 / 33 (0.00%)	0 / 34 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Chest pain			
subjects affected / exposed	0 / 33 (0.00%)	0 / 34 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Feeling abnormal			

subjects affected / exposed occurrences (all)	0 / 33 (0.00%) 0	0 / 34 (0.00%) 0	0 / 23 (0.00%) 0
Injection site erythema subjects affected / exposed occurrences (all)	2 / 33 (6.06%) 2	0 / 34 (0.00%) 0	0 / 23 (0.00%) 0
Injection site pain subjects affected / exposed occurrences (all)	1 / 33 (3.03%) 1	2 / 34 (5.88%) 2	0 / 23 (0.00%) 0
Injection site reaction subjects affected / exposed occurrences (all)	1 / 33 (3.03%) 1	3 / 34 (8.82%) 3	2 / 23 (8.70%) 2
Instillation site pain subjects affected / exposed occurrences (all)	0 / 33 (0.00%) 0	0 / 34 (0.00%) 0	0 / 23 (0.00%) 0
Malaise subjects affected / exposed occurrences (all)	0 / 33 (0.00%) 0	3 / 34 (8.82%) 3	0 / 23 (0.00%) 0
Pyrexia subjects affected / exposed occurrences (all)	1 / 33 (3.03%) 1	2 / 34 (5.88%) 2	0 / 23 (0.00%) 0
Immune system disorders Hypersensitivity subjects affected / exposed occurrences (all)	0 / 33 (0.00%) 0	0 / 34 (0.00%) 0	0 / 23 (0.00%) 0
Respiratory, thoracic and mediastinal disorders Rhinorrhoea subjects affected / exposed occurrences (all)	0 / 33 (0.00%) 0	3 / 34 (8.82%) 3	0 / 23 (0.00%) 0
Investigations Antinuclear antibody increased (at investigator's discretion) alternative assessment type: Systematic subjects affected / exposed occurrences (all)	0 / 33 (0.00%) 0	1 / 34 (2.94%) 1	0 / 23 (0.00%) 0
Blood albumin decreased (at investigator's discretion) alternative assessment type: Systematic			

subjects affected / exposed occurrences (all)	0 / 33 (0.00%) 0	0 / 34 (0.00%) 0	0 / 23 (0.00%) 0
Blood creatine phosphokinase increased (at investigator's discretion) alternative assessment type: Systematic subjects affected / exposed occurrences (all)	0 / 33 (0.00%) 0	1 / 34 (2.94%) 1	0 / 23 (0.00%) 0
Blood glucose increased (at investigator's discretion) alternative assessment type: Systematic subjects affected / exposed occurrences (all)	2 / 33 (6.06%) 2	0 / 34 (0.00%) 0	0 / 23 (0.00%) 0
Injury, poisoning and procedural complications Thermal burn subjects affected / exposed occurrences (all)	0 / 33 (0.00%) 0	0 / 34 (0.00%) 0	0 / 23 (0.00%) 0
Nervous system disorders Headache subjects affected / exposed occurrences (all)	3 / 33 (9.09%) 3	0 / 34 (0.00%) 0	1 / 23 (4.35%) 1
Blood and lymphatic system disorders Anaemia alternative assessment type: Systematic subjects affected / exposed occurrences (all)  Iron deficiency anaemia alternative assessment type: Systematic subjects affected / exposed occurrences (all)	0 / 33 (0.00%) 0  1 / 33 (3.03%) 1	0 / 34 (0.00%) 0  1 / 34 (2.94%) 1	0 / 23 (0.00%) 0  0 / 23 (0.00%) 0
Gastrointestinal disorders Abdominal distension subjects affected / exposed occurrences (all)  Abdominal pain subjects affected / exposed occurrences (all)	2 / 33 (6.06%) 2  0 / 33 (0.00%) 0	0 / 34 (0.00%) 0  0 / 34 (0.00%) 0	0 / 23 (0.00%) 0  1 / 23 (4.35%) 1

Constipation subjects affected / exposed occurrences (all)	2 / 33 (6.06%) 2	0 / 34 (0.00%) 0	1 / 23 (4.35%) 1
Diarrhoea subjects affected / exposed occurrences (all)	0 / 33 (0.00%) 0	0 / 34 (0.00%) 0	1 / 23 (4.35%) 1
Haemorrhoids subjects affected / exposed occurrences (all)	0 / 33 (0.00%) 0	0 / 34 (0.00%) 0	0 / 23 (0.00%) 0
Intestinal obstruction subjects affected / exposed occurrences (all)	0 / 33 (0.00%) 0	0 / 34 (0.00%) 0	0 / 23 (0.00%) 0
Nausea subjects affected / exposed occurrences (all)	1 / 33 (3.03%) 1	1 / 34 (2.94%) 1	3 / 23 (13.04%) 3
Vomiting subjects affected / exposed occurrences (all)	2 / 33 (6.06%) 2	0 / 34 (0.00%) 0	1 / 23 (4.35%) 1
Hepatobiliary disorders Hepatic function abnormal alternative assessment type: Systematic subjects affected / exposed occurrences (all)	1 / 33 (3.03%) 1	2 / 34 (5.88%) 2	0 / 23 (0.00%) 0
Skin and subcutaneous tissue disorders Alopecia subjects affected / exposed occurrences (all)	0 / 33 (0.00%) 0	0 / 34 (0.00%) 0	0 / 23 (0.00%) 0
Dry skin subjects affected / exposed occurrences (all)	0 / 33 (0.00%) 0	0 / 34 (0.00%) 0	0 / 23 (0.00%) 0
Rash subjects affected / exposed occurrences (all)	2 / 33 (6.06%) 2	0 / 34 (0.00%) 0	1 / 23 (4.35%) 1
Musculoskeletal and connective tissue disorders Back pain			



subjects affected / exposed occurrences (all)	0 / 33 (0.00%) 0	0 / 34 (0.00%) 0	0 / 23 (0.00%) 0
Infections and infestations			
Herpes simplex subjects affected / exposed occurrences (all)	0 / 33 (0.00%) 0	0 / 34 (0.00%) 0	0 / 23 (0.00%) 0
Nasopharyngitis subjects affected / exposed occurrences (all)	0 / 33 (0.00%) 0	1 / 34 (2.94%) 1	0 / 23 (0.00%) 0
Tonsillitis subjects affected / exposed occurrences (all)	0 / 33 (0.00%) 0	0 / 34 (0.00%) 0	0 / 23 (0.00%) 0
Upper respiratory tract infection subjects affected / exposed occurrences (all)	3 / 33 (9.09%) 3	1 / 34 (2.94%) 1	1 / 23 (4.35%) 1
Urinary tract infection subjects affected / exposed occurrences (all)	0 / 33 (0.00%) 0	0 / 34 (0.00%) 0	0 / 23 (0.00%) 0
Metabolism and nutrition disorders			
Glucose tolerance impaired (at investigator's discretion) subjects affected / exposed occurrences (all)	0 / 33 (0.00%) 0	0 / 34 (0.00%) 0	0 / 23 (0.00%) 0
Hypoglycaemia alternative assessment type: Systematic subjects affected / exposed occurrences (all)	0 / 33 (0.00%) 0	0 / 34 (0.00%) 0	0 / 23 (0.00%) 0

<b>Non-serious adverse events</b>	Adalimumab 160 mg/80 mg + 40/40 mg	Adalimumab 80/40 mg + 40/40 mg	Placebo + Adalimumab 160/80 mg
Total subjects affected by non-serious adverse events subjects affected / exposed	5 / 9 (55.56%)	9 / 12 (75.00%)	8 / 16 (50.00%)
General disorders and administration site conditions			
Adverse drug reaction subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 1	0 / 12 (0.00%) 0	0 / 16 (0.00%) 0
Application site swelling			

subjects affected / exposed	1 / 9 (11.11%)	0 / 12 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Chest pain			
subjects affected / exposed	1 / 9 (11.11%)	0 / 12 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Feeling abnormal			
subjects affected / exposed	1 / 9 (11.11%)	0 / 12 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Injection site erythema			
subjects affected / exposed	0 / 9 (0.00%)	0 / 12 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Injection site pain			
subjects affected / exposed	0 / 9 (0.00%)	0 / 12 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Injection site reaction			
subjects affected / exposed	0 / 9 (0.00%)	1 / 12 (8.33%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Instillation site pain			
subjects affected / exposed	1 / 9 (11.11%)	0 / 12 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Malaise			
subjects affected / exposed	0 / 9 (0.00%)	0 / 12 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Pyrexia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 12 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	0 / 9 (0.00%)	1 / 12 (8.33%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Respiratory, thoracic and mediastinal disorders			
Rhinorrhoea			
subjects affected / exposed	0 / 9 (0.00%)	0 / 12 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Investigations			

Antinuclear antibody increased (at investigator's discretion) alternative assessment type: Systematic subjects affected / exposed occurrences (all)	0 / 9 (0.00%) 0	1 / 12 (8.33%) 1	0 / 16 (0.00%) 0
Blood albumin decreased (at investigator's discretion) alternative assessment type: Systematic subjects affected / exposed occurrences (all)	0 / 9 (0.00%) 0	1 / 12 (8.33%) 1	0 / 16 (0.00%) 0
Blood creatine phosphokinase increased (at investigator's discretion) alternative assessment type: Systematic subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 1	0 / 12 (0.00%) 0	0 / 16 (0.00%) 0
Blood glucose increased (at investigator's discretion) alternative assessment type: Systematic subjects affected / exposed occurrences (all)	0 / 9 (0.00%) 0	0 / 12 (0.00%) 0	0 / 16 (0.00%) 0
Injury, poisoning and procedural complications Thermal burn subjects affected / exposed occurrences (all)	0 / 9 (0.00%) 0	1 / 12 (8.33%) 1	0 / 16 (0.00%) 0
Nervous system disorders Headache subjects affected / exposed occurrences (all)	0 / 9 (0.00%) 0	2 / 12 (16.67%) 2	1 / 16 (6.25%) 1
Blood and lymphatic system disorders Anaemia alternative assessment type: Systematic subjects affected / exposed occurrences (all)  Iron deficiency anaemia alternative assessment type: Systematic subjects affected / exposed occurrences (all)	0 / 9 (0.00%) 0  1 / 9 (11.11%) 1	1 / 12 (8.33%) 1  0 / 12 (0.00%) 0	0 / 16 (0.00%) 0  1 / 16 (6.25%) 1

Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	0 / 9 (0.00%)	1 / 12 (8.33%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Abdominal pain			
subjects affected / exposed	0 / 9 (0.00%)	1 / 12 (8.33%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Constipation			
subjects affected / exposed	0 / 9 (0.00%)	0 / 12 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Diarrhoea			
subjects affected / exposed	0 / 9 (0.00%)	1 / 12 (8.33%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Haemorrhoids			
subjects affected / exposed	0 / 9 (0.00%)	0 / 12 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Intestinal obstruction			
subjects affected / exposed	0 / 9 (0.00%)	0 / 12 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Nausea			
subjects affected / exposed	0 / 9 (0.00%)	0 / 12 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Vomiting			
subjects affected / exposed	0 / 9 (0.00%)	0 / 12 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Hepatobiliary disorders			
Hepatic function abnormal			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 9 (0.00%)	0 / 12 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	0 / 9 (0.00%)	1 / 12 (8.33%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Dry skin			

subjects affected / exposed occurrences (all)	0 / 9 (0.00%) 0	0 / 12 (0.00%) 0	1 / 16 (6.25%) 1
Rash subjects affected / exposed occurrences (all)	0 / 9 (0.00%) 0	0 / 12 (0.00%) 0	0 / 16 (0.00%) 0
Musculoskeletal and connective tissue disorders Back pain subjects affected / exposed occurrences (all)	0 / 9 (0.00%) 0	0 / 12 (0.00%) 0	1 / 16 (6.25%) 1
Infections and infestations Herpes simplex subjects affected / exposed occurrences (all)	0 / 9 (0.00%) 0	0 / 12 (0.00%) 0	1 / 16 (6.25%) 1
Nasopharyngitis subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 1	1 / 12 (8.33%) 1	3 / 16 (18.75%) 3
Tonsillitis subjects affected / exposed occurrences (all)	0 / 9 (0.00%) 0	1 / 12 (8.33%) 1	0 / 16 (0.00%) 0
Upper respiratory tract infection subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 1	0 / 12 (0.00%) 0	0 / 16 (0.00%) 0
Urinary tract infection subjects affected / exposed occurrences (all)	0 / 9 (0.00%) 0	0 / 12 (0.00%) 0	1 / 16 (6.25%) 1
Metabolism and nutrition disorders Glucose tolerance impaired (at investigator's discretion) subjects affected / exposed occurrences (all)	0 / 9 (0.00%) 0	1 / 12 (8.33%) 1	0 / 16 (0.00%) 0
Hypoglycaemia alternative assessment type: Systematic subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 1	0 / 12 (0.00%) 0	0 / 16 (0.00%) 0

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
20 March 2007	To add the severity of Crohn's disease history in original case report form.

Notes:

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### 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.

Small population, therefore no statistical tests were performed.
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Notes: