Clinical trial results:
Phase III Study of D9421-C 9 mg in Patients With Active Crohn's Disease in Japan

Summary

EudraCT number	2014-004132-20
Trial protocol	Outside EU/EEA
Global end of trial date	16 January 2015

Results information

Result version number	v1 (current)
This version publication date	15 September 2016
First version publication date	15 September 2016

Trial information

Trial identification

Sponsor protocol code	D9423C00001

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01514240
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Biometrics Department, Science Affairs Division, R&D, AstraZeneca Japan
Sponsor organisation address	Grand Front Osaka Tower B, 3-11, Ofukacho, Kitaku, Osaka, Japan, 530-0011
Public contact	Masahiro Nii, Biometrics Department, Science Affairs Division, R&D, AstraZeneca Japan, 46 6-7711-4571, Masahiro.Nii@astrazeneca.com
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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	20 October 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	20 October 2014
Global end of trial reached?	Yes
Global end of trial date	16 January 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of this study was to evaluate the clinical efficacy of D9421-C 9 mg once daily compared to Mesalazine 1 g three times a day to patients with mild to moderate active Crohn's disease affecting ileum, ileocecal region and/or ascending colon as defined by a score of 180-400 on the Crohn's Disease Activity Index (CDAI) by assessment of the remission after 8-week treatment defined by a CDAI score of ≤ 150.

Protection of trial subjects:

If patients had any AE at the end of treatment, the AEs were followed by Investeigators until the investigators judged it was unnecessary to follow the AE.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	08 February 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	Japan: 112
Worldwide total number of subjects	112
EEA total number of subjects	0

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	1
Adults (18-64 years)	109
From 65 to 84 years	2
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

First patient enrolled on 08 February 2012. Last subject last visit on 08 September 2014.

Pre-assignment

Screening details:

Out of 123 enrolled subjects, 112 subjects were randomised and 11 subjects were not randomised. The reasons of no randomisation were 'Eligibility criteria not met' (9 subjects) and 'Adverse event' (2 subjects).

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	D9421-C 9mg + Mesalazine placebo

Arm description:

Patients randomised to D9421-C 9 mg took 3 capsules of D9421-C capsule 3 mg once daily before breakfast and 4 tablets of Mesalazine tablets placebo three times a day after each meal for 8 weeks.

Arm type	Experimental
Investigational medicinal product name	D9421-C
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

9 mg once daily

Arm title	Mesalazine 3g + D9421-C placebo

Arm description:

Patients randomised to Mesalazine 3 g took 3 capsules of D9421-C capsule placebo once daily before breakfast and 4 tablets of Mesalazine tablets 250 mg three times a day after each meal for 8 weeks.

Arm type	Active comparator
Investigational medicinal product name	Mesalazine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

1g three times a day

Number of subjects in period 1	D9421-C 9mg + Mesalazine placebo	Mesalazine 3g + D9421-C placebo
Started	56	56
Completed	50	45
Not completed	6	11
Subject Decision	2	7
Adverse event, non-fatal	4	4

Baseline characteristics

Reporting groups	
Reporting group title	D9421-C 9mg + Mesalazine placebo
Reporting group description:	
Patients randomised to D9421-C 9 mg took 3 capsules of D9421-C capsule 3 mg once daily before breakfast and 4 tablets of Mesalazine tablets placebo three times a day after each meal for 8 weeks.	
Reporting group title	Mesalazine 3g + D9421-C placebo
Reporting group description:	
Patients randomised to Mesalazine 3 g took 3 capsules of D9421-C capsule placebo once daily before breakfast and 4 tablets of Mesalazine tablets 250 mg three times a day after each meal for 8 weeks.	

Reporting group values	D9421-C 9mg + Mesalazine placebo	Mesalazine 3g + D9421-C placebo	Total
Number of subjects	56	56	112
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)	1	0	1
Adults (18-64 years)	53	56	109
From 65-84 years	2	0	2
85 years and over	0	0	0
Age Continuous | Units: Years			
arithmetic mean	38.1	35.8	
standard deviation	± 13.43	± 10.71	-
Gender, Male/Female Units: Participants			
Female	19	13	32
Male	37	43	80
Age, Customized Units: Subjects			
<30 Years	19	20	39
>=30 Years	37	36	73

End points

End points reporting groups

Reporting group title	D9421-C 9mg + Mesalazine placebo
Reporting group description:	
Patients randomised to D9421-C 9 mg took 3 capsules of D9421-C capsule 3 mg once daily before breakfast and 4 tablets of Mesalazine tablets placebo three times a day after each meal for 8 weeks.	
Reporting group title	Mesalazine 3g + D9421-C placebo
Reporting group description:	
Patients randomised to Mesalazine 3 g took 3 capsules of D9421-C capsule placebo once daily before breakfast and 4 tablets of Mesalazine tablets 250 mg three times a day after each meal for 8 weeks.	

Primary: Proportion of patients with remission at Week 8

End point title	Proportion of patients with remission at Week 8
End point description:	
For the primary efficacy variable “Remission after 8 weeks of treatment”, Crohn’s Disease Activity Index CDAI scores was used to determine the patient’s response. Remission for this study is defined as a CDAI score of ≤150. A patient who drops out without any remission before week 8 was considered as a nonresponder (no remission) for this analysis. A patient who drops out before Week 8, but was in remission at the time of dropout, was considered in remission after dropout in this analysis.	
End point type	Primary
End point timeframe:	
8 Week	

End point values	D9421-C 9mg + Mesalazine placebo	Mesalazine 3g + D9421-C placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	56	56		
Units: Participants	17	14		

Statistical analyses

Statistical analysis title	Remission rates at Week 8
Statistical analysis description:	
Remission rates at Week 8 for D9421-C 9 mg as compared to Mesalazine 3 g.	
Comparison groups	D9421-C 9mg + Mesalazine placebo v Mesalazine 3g + D9421-C placebo
Number of subjects included in analysis	112
Analysis specification	Pre-specified
Analysis type	non-inferiority[1]
P-value	= 0.526
Method	Chi-squared
Parameter estimate	Difference of proportion
Point estimate	5.4

Secondary: Proportion of patients with remission at Week 4

End point title	Proportion of patients with remission at Week 4

End point description:

For the secondary efficacy variable “Remission after 4 weeks of treatment”, Crohn’s Disease Activity Index CDAI scores was used to determine the patient’s response. Remission for this study is defined as a CDAI score of ≤150.

End point type	Secondary

End point timeframe:

4 Week

End point values	D9421-C 9mg + Mesalazine placebo	Mesalazine 3g + D9421-C placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	56	56		
Units: Participants	12	7		

Statistical analyses

Statistical analysis title	Remission rates at Week 4
Comparison groups	D9421-C 9mg + Mesalazine placebo v Mesalazine 3g + D9421-C placebo
Number of subjects included in analysis	112
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.208
Method	Chi-squared
Parameter estimate	Difference of proportion
Point estimate	8.9
Confidence interval	
level	90 %
sides	2-sided
lower limit	-2.87
upper limit	20.58

Secondary: Change in CDAI scores from baseline to Week 2

End point title	Change in CDAI scores from baseline to Week 2

End point description:

Crohn’s Disease Activity Index (CDAI) score is calculated based on the data collected in the diary card. The patients is asked to fill the following items in the diary card (from the morning in preceding day to the morning in current day). (1) Number of liquid or very soft stools (2) Abdominal pain rating (none, mild, moderate, severe) (3) General well-being (generally well, slightly under par, poor, very poor, terrible) (4) Body temperature (if a patient feels fever) (5) Intake of loperamide or other opiates for

diarrhoea. The data for the calculation of CDAI score in diary card is then transcribed by the investigator(s) into the eCRFs at each clinical visit. The higher total CDAI score indicates severe condition and total CDAI score 150 less or equal is evaluated as a remission.

End point type	Secondary

End point timeframe:

2 Week

End point values	D9421-C 9mg + Mesalazine placebo	Mesalazine 3g + D9421-C placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	53	53		
Units: Scores on a scale				
least squares mean (standard error)	-38.5 (± 8.91)	-15.7 (± 7.66)		

Statistical analyses

Statistical analysis title	Change in CDAI scores from baseline to Weeks 2
Comparison groups	D9421-C 9mg + Mesalazine placebo v Mesalazine 3g + D9421-C placebo
Number of subjects included in analysis	106
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.058
Method	Mixed models analysis
Parameter estimate	LS mean difference between groups
Point estimate	-22.8
Confidence interval	
level	90 %
sides	2-sided
lower limit	-42.55
upper limit	-3.09
Variability estimate	Standard error of the mean
Dispersion value	11.89

Secondary: Change in CDAI scores from baseline to Week 4

End point title	Change in CDAI scores from baseline to Week 4

End point description:

Crohn's Disease Activity Index (CDAI) score is calculated based on the data collected in the diary card. The patients is asked to fill the following items in the diary card (from the morning in preceding day to the morning in current day). (1) Number of liquid or very soft stools (2) Abdominal pain rating (none, mild, moderate, severe) (3) General well-being (generally well, slightly under par, poor, very poor, terrible) (4) Body temperature (if a patient feels fever) (5) Intake of loperamide or other opiates for diarrhoea. The data for the calculation of CDAI score in diary card is then transcribed by the investigator(s) into the eCRFs at each clinical visit. The higher total CDAI score indicates severe condition and total CDAI score 150 less or equal is evaluated as a remission.

End point type	Secondary

End point timeframe:
4 Week

End point values	D9421-C 9mg + Mesalazine placebo	Mesalazine 3g + D9421-C placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	55	50		
Units: Scores on a scale				
least squares mean (standard error)	-58.7 (± 9.44)	-28.7 (± 7.29)		

Statistical analyses

Statistical analysis title	Change in CDAI scores from baseline to Weeks 4
Comparison groups	D9421-C 9mg + Mesalazine placebo v Mesalazine 3g + D9421-C placebo
Number of subjects included in analysis	105
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.014
Method	Mixed models analysis
Parameter estimate	LS mean difference between group
Point estimate	-30
Confidence interval	
level	90 %
sides	2-sided
lower limit	-49.95
upper limit	-9.96
Variability estimate	Standard error of the mean
Dispersion value	12.05

Secondary: Change in CDAI scores from baseline to Week 8

End point title	Change in CDAI scores from baseline to Week 8

End point description:

Crohn's Disease Activity Index (CDAI) score is calculated based on the data collected in the diary card. The patients is asked to fill the following items in the diary card (from the morning in preceding day to the morning in current day). (1) Number of liquid or very soft stools (2) Abdominal pain rating (none, mild, moderate, severe) (3) General well-being (generally well, slightly under par, poor, very poor, terrible) (4) Body temperature (if a patient feels fever) (5) Intake of loperamide or other opiates for diarrhoea. The data for the calculation of CDAI score in diary card is then transcribed by the investigator(s) into the eCRFs at each clinical visit. The higher total CDAI score indicates severe condition and total CDAI score 150 less or equal is evaluated as a remission.

End point type	Secondary

End point timeframe:

8 Week

End point values	D9421-C 9mg + Mesalazine placebo	Mesalazine 3g + D9421-C placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	51	45		
Units: Scores on a scale				
least squares mean (standard error)	-67 (± 11.17)	-45.7 (± 9.11)		

Statistical analyses

Statistical analysis title	Change in CDAI scores from baseline to Week 8
Comparison groups	D9421-C 9mg + Mesalazine placebo v Mesalazine 3g + D9421-C placebo
Number of subjects included in analysis	96
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.144
Method	Mixed models analysis
Parameter estimate	LS mean difference between group
Point estimate	-21.4
Confidence interval	
level	90 %
sides	2-sided
lower limit	-45.47
upper limit	2.74
Variability estimate	Standard error of the mean
Dispersion value	14.53

Secondary: Cumulative remission rate at Week 2

End point title	Cumulative remission rate at Week 2
End point description:	
Remission rate is defined as CDAI score of less than or equal to 150. Cumulative remission rate at Week 2 is obtained by Kaplan-Meier (KM) estimates.	
End point type	Secondary
End point timeframe:	
2 Week	

End point values	D9421-C 9mg + Mesalazine placebo	Mesalazine 3g + D9421-C placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	56	56		
Units: Percentage of participants				
number (confidence interval)	12.5 (5.23 to 19.77)	10.7 (3.92 to 17.51)		

Statistical analyses

No statistical analyses for this end point

Secondary: Cumulative remission rate at Week 4

End point title	Cumulative remission rate at Week 4

End point description:

Remission rate is defined as CDAI score of less than or equal to 150. Cumulative remission rate at Week 4 is obtained by Kaplan-Meier (KM) estimates.

End point type	Secondary

End point timeframe:

4 Week

End point values	D9421-C 9mg + Mesalazine placebo	Mesalazine 3g + D9421-C placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	56	56		
Units: Percentage of participants				
number (confidence interval)	25 (15.48 to 34.52)	17.9 (9.44 to 26.28)		

Statistical analyses

No statistical analyses for this end point

Secondary: Cumulative remission rate at Week 8

End point title	Cumulative remission rate at Week 8

End point description:

Remission rate is defined as CDAI score of less than or equal to 150. Cumulative remission rate at Week 8 is obtained by Kaplan-Meier (KM) estimates.

End point type	Secondary

End point timeframe:

8 Week

End point values	D9421-C 9mg + Mesalazine placebo	Mesalazine 3g + D9421-C placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	56	56		
Units: Percentage of participants				
number (confidence interval)	37.5 (26.86 to 48.14)	30.4 (20.25 to 40.46)		

Statistical analyses

No statistical analyses for this end point

Secondary: Clinical improvement rates at Week 2 (70 points)

End point title	Clinical improvement rates at Week 2 (70 points)

End point description:

Clinical improvement is defined as CDAI score of <=150 or a decrease in CDAI score from baseline of at least 70 points.

End point type	Secondary

End point timeframe:

2 Week

End point values	D9421-C 9mg + Mesalazine placebo	Mesalazine 3g + D9421-C placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	56	56		
Units: Participants	19	11		

Statistical analyses

Statistical analysis title	Clinical improvement rates at Weeks 2 (70 points)
Comparison groups	D9421-C 9mg + Mesalazine placebo v Mesalazine 3g + D9421-C placebo
Number of subjects included in analysis	112
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference of proportions
Point estimate	14.3

Confidence interval	
level	90 %
sides	2-sided
lower limit	0.5
upper limit	27.4

Secondary: Clinical improvement rates at Week 4 (70 points)

End point title	Clinical improvement rates at Week 4 (70 points)

End point description:

Clinical improvement is defined as CDAI score of <=150 or a decrease in CDAI score from baseline of at least 70 points.

End point type	Secondary

End point timeframe:

4 Week

End point values	D9421-C 9mg + Mesalazine placebo	Mesalazine 3g + D9421-C placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	56	56		
Units: Participants	22	13		

Statistical analyses

Statistical analysis title	Clinical improvement rates at Week 4 (70 points)
Comparison groups	D9421-C 9mg + Mesalazine placebo v Mesalazine 3g + D9421-C placebo
Number of subjects included in analysis	112
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference of proportions
Point estimate	16.1
Confidence interval	
level	90 %
sides	2-sided
lower limit	1.66
upper limit	29.61

Secondary: Clinical improvement rates at Week 8 (70 points)

End point title	Clinical improvement rates at Week 8 (70 points)

End point description:

Clinical improvement is defined as CDAI score of <=150 or a decrease in CDAI score from baseline of at least 70 points.

End point type	Secondary
End point timeframe: 8 Week	

End point values	D9421-C 9mg + Mesalazine placebo	Mesalazine 3g + D9421-C placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	56	56		
Units: Participants	27	18		

Statistical analyses

Statistical analysis title	Clinical improvement rate at Week 8 (70 points)
Comparison groups	D9421-C 9mg + Mesalazine placebo v Mesalazine 3g + D9421-C placebo
Number of subjects included in analysis	112
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference of proportions
Point estimate	16.1
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.85
upper limit	30.29

Secondary: Clinical improvement rates at Week 2 (100 points)	
End point title	Clinical improvement rates at Week 2 (100 points)
End point description: Clinical improvement is defined as CDAI score of <=150 or a decrease in CDAI score from baseline of at least 100 points.	
End point type	Secondary
End point timeframe: 2 Week	

End point values	D9421-C 9mg + Mesalazine placebo	Mesalazine 3g + D9421-C placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	56	56		
Units: Participants	14	10		

Statistical analyses

Statistical analysis title	Clinical improvement rates at Week 2 (100 points)
Comparison groups	D9421-C 9mg + Mesalazine placebo v Mesalazine 3g + D9421-C placebo
Number of subjects included in analysis	112
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference of proportions
Point estimate	7.1
Confidence interval	
level	90 %
sides	2-sided
lower limit	-5.67
upper limit	19.71

Secondary: Clinical improvement rates at Week 4 (100 points)	
End point title	Clinical improvement rates at Week 4 (100 points)
End point description: Clinical improvement is defined as CDAI score of <=150 or a decrease in CDAI score from baseline of at least 100 points.	
End point type	Secondary
End point timeframe: 4 Week	

End point values	D9421-C 9mg + Mesalazine placebo	Mesalazine 3g + D9421-C placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	56	56		
Units: Participants	19	11		

Statistical analyses

Statistical analysis title	Clinical improvement rate at Week 4 (100 points)
Comparison groups	D9421-C 9mg + Mesalazine placebo v Mesalazine 3g + D9421-C placebo

Number of subjects included in analysis	112
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference of proportions
Point estimate	14.3
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.5
upper limit	27.4

Secondary: Clinical improvement rates at Week 8

End point title	Clinical improvement rates at Week 8
End point description:	
Clinical improvement is defined as CDAI score of <=150 or a decrease in CDAI score from baseline of at least 100 points.	
End point type	Secondary
End point timeframe:	
8 Week	

End point values	D9421-C 9mg + Mesalazine placebo	Mesalazine 3g + D9421-C placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	56	56		
Units: Participants	24	17		

Statistical analyses

Statistical analysis title	Clinical improvement rate at Week 8 (100 points)
Comparison groups	D9421-C 9mg + Mesalazine placebo v Mesalazine 3g + D9421-C placebo
Number of subjects included in analysis	112
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference of proportions
Point estimate	12.5
Confidence interval	
level	90 %
sides	2-sided
lower limit	-2.44
upper limit	26.68

ranging from 1 to 7, where 7 is the most favourable. Ten questions are related to bowel symptoms, five to systemic symptoms, twelve to emotional function, and five to social function. The corresponding answers will be added to form four subscores and a total score: bowel function score (10 – 70), systemic symptom score (5 – 35), emotional function score (12 – 84), social function score (5 – 35) and the total score (32 – 224), with higher scores indicating more favorable outcome.

End point type	Secondary

End point timeframe:

4 Week

End point values	D9421-C 9mg + Mesalazine placebo	Mesalazine 3g + D9421-C placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	55	50		
Units: Scores on a scale				
least squares mean (standard error)	19.4 (± 3.03)	6.8 (± 2.44)		

Statistical analyses

Statistical analysis title	Change in total IBDQ scores at Week 4
Comparison groups	D9421-C 9mg + Mesalazine placebo v Mesalazine 3g + D9421-C placebo
Number of subjects included in analysis	105
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	LS mean difference between group
Point estimate	12.6
Confidence interval	
level	90 %
sides	2-sided
lower limit	6.07
upper limit	19.11
Variability estimate	Standard error of the mean
Dispersion value	3.93

Secondary: Change in total IBDQ scores from baseline to Week 8

End point title	Change in total IBDQ scores from baseline to Week 8

End point description:

The Inflammatory Bowel Disease Questionnaire (IBDQ) is a standard measure of HRQL in Crohn's disease patients (Guyatt G et al 1989). The validated Japanese version of the IBDQ was used in this study (Hashimoto H et al 2003). The IBDQ contains 32 questions; each with seven possible answers ranging from 1 to 7, where 7 is the most favourable. Ten questions are related to bowel symptoms, five to systemic symptoms, twelve to emotional function, and five to social function. The corresponding answers will be added to form four subscores and a total score: bowel function score (10 – 70), systemic symptom score (5 – 35), emotional function score (12 – 84), social function score (5 – 35) and the total score (32 – 224), with higher scores indicating more favorable outcome.

End point type	Secondary

End point timeframe:
8 Week

End point values	D9421-C 9mg + Mesalazine placebo	Mesalazine 3g + D9421-C placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	51	45		
Units: Scores on a scale				
least squares mean (standard error)	18.3 (± 2.93)	5.8 (± 3.16)		

Statistical analyses

Statistical analysis title	Change in total IBDQ scores at Week 8
Comparison groups	D9421-C 9mg + Mesalazine placebo v Mesalazine 3g + D9421-C placebo
Number of subjects included in analysis	96
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference between group
Point estimate	12.6
Confidence interval	
level	90 %
sides	2-sided
lower limit	5.4
upper limit	19.72
Variability estimate	Standard error of the mean
Dispersion value	4.31

Secondary: Change in total IBDQ scores from baseline to Week 10

End point title	Change in total IBDQ scores from baseline to Week 10

End point description:

The Inflammatory Bowel Disease Questionnaire (IBDQ) is a standard measure of HRQL in Crohn's disease patients (Guyatt G et al 1989). The validated Japanese version of the IBDQ was used in this study (Hashimoto H et al 2003). The IBDQ contains 32 questions; each with seven possible answers ranging from 1 to 7, where 7 is the most favourable. Ten questions are related to bowel symptoms, five to systemic symptoms, twelve to emotional function, and five to social function. The corresponding answers will be added to form four subscores and a total score: bowel function score (10 – 70), systemic symptom score (5 – 35), emotional function score (12 – 84), social function score (5 – 35) and the total score (32 – 224), with higher scores indicating more favorable outcome.

End point type	Secondary

End point timeframe:

10 Week

End point values	D9421-C 9mg + Mesalazine placebo	Mesalazine 3g + D9421-C placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50	45		
Units: Scores on a scale				
least squares mean (standard error)	21.1 (± 3.11)	7.1 (± 2.96)		

Statistical analyses

Statistical analysis title	Change in total IBDQ scores at Week 10
Comparison groups	D9421-C 9mg + Mesalazine placebo v Mesalazine 3g + D9421-C placebo
Number of subjects included in analysis	95
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference between group
Point estimate	14.1
Confidence interval	
level	90 %
sides	2-sided
lower limit	6.9
upper limit	21.23
Variability estimate	Standard error of the mean
Dispersion value	4.32

Secondary: Change in IBDQ scores from baseline to Week 2 - Bowel function

End point title	Change in IBDQ scores from baseline to Week 2 - Bowel function

End point description:

The Inflammatory Bowel Disease Questionnaire (IBDQ) is a standard measure of HRQL in Crohn's disease patients (Guyatt G et al 1989). The validated Japanese version of the IBDQ was used in this study (Hashimoto H et al 2003). The IBDQ contains 32 questions; each with seven possible answers ranging from 1 to 7, where 7 is the most favourable. Ten questions are related to bowel symptoms, five to systemic symptoms, twelve to emotional function, and five to social function. The corresponding answers will be added to form four subscores and a total score: bowel function score (10 – 70), systemic symptom score (5 – 35), emotional function score (12 – 84), social function score (5 – 35) and the total score (32 – 224), with higher scores indicating more favorable outcome.

End point type	Secondary

End point timeframe:

2 Week

End point values	D9421-C 9mg + Mesalazine placebo	Mesalazine 3g + D9421-C placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	56	54		
Units: Scores on a scale				
least squares mean (standard error)	6.1 (± 0.77)	2.7 (± 0.82)		

Statistical analyses

Statistical analysis title	Change in IBDQ scores at W2 - Bowel function
Comparison groups	D9421-C 9mg + Mesalazine placebo v Mesalazine 3g + D9421-C placebo
Number of subjects included in analysis	110
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference between group
Point estimate	3.4
Confidence interval	
level	90 %
sides	2-sided
lower limit	1.49
upper limit	5.29
Variability estimate	Standard error of the mean
Dispersion value	1.14

Secondary: Change in IBDQ scores from baseline to Week 4 - Bowel function

End point title	Change in IBDQ scores from baseline to Week 4 - Bowel function

End point description:

The Inflammatory Bowel Disease Questionnaire (IBDQ) is a standard measure of HRQL in Crohn's disease patients (Guyatt G et al 1989). The validated Japanese version of the IBDQ was used in this study (Hashimoto H et al 2003). The IBDQ contains 32 questions; each with seven possible answers ranging from 1 to 7, where 7 is the most favourable. Ten questions are related to bowel symptoms, five to systemic symptoms, twelve to emotional function, and five to social function. The corresponding answers will be added to form four subscores and a total score: bowel function score (10 – 70), systemic symptom score (5 – 35), emotional function score (12 – 84), social function score (5 – 35) and the total score (32 – 224), with higher scores indicating more favorable outcome.

End point type	Secondary

End point timeframe:

4 Week

End point values	D9421-C 9mg + Mesalazine placebo	Mesalazine 3g + D9421-C placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	55	50		
Units: Scores on a scale				
least squares mean (standard error)	6.6 (± 0.99)	2.8 (± 0.84)		

Statistical analyses

Statistical analysis title	Change in IBDQ scores at W4 - Bowel function
Comparison groups	D9421-C 9mg + Mesalazine placebo v Mesalazine 3g + D9421-C placebo
Number of subjects included in analysis	105
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference between group
Point estimate	3.8
Confidence interval	
level	90 %
sides	2-sided
lower limit	1.64
upper limit	5.97
Variability estimate	Standard error of the mean
Dispersion value	1.31

Secondary: Change in IBDQ scores from baseline to Week 8 - Bowel function

End point title	Change in IBDQ scores from baseline to Week 8 - Bowel function

End point description:

The Inflammatory Bowel Disease Questionnaire (IBDQ) is a standard measure of HRQL in Crohn's disease patients (Guyatt G et al 1989). The validated Japanese version of the IBDQ was used in this study (Hashimoto H et al 2003). The IBDQ contains 32 questions; each with seven possible answers ranging from 1 to 7, where 7 is the most favourable. Ten questions are related to bowel symptoms, five to systemic symptoms, twelve to emotional function, and five to social function. The corresponding answers will be added to form four subscores and a total score: bowel function score (10 – 70), systemic symptom score (5 – 35), emotional function score (12 – 84), social function score (5 – 35) and the total score (32 – 224), with higher scores indicating more favorable outcome.

End point type	Secondary

End point timeframe:

8 Week

End point values	D9421-C 9mg + Mesalazine placebo	Mesalazine 3g + D9421-C placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	51	45		
Units: Scores on a scale				
least squares mean (standard error)	6.5 (± 1.04)	2.4 (± 1.11)		

Statistical analyses

Statistical analysis title	Change in IBDQ scores at W8 - Bowel function
Comparison groups	D9421-C 9mg + Mesalazine placebo v Mesalazine 3g + D9421-C placebo
Number of subjects included in analysis	96
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference between group
Point estimate	4.1
Confidence interval	
level	90 %
sides	2-sided
lower limit	1.58
upper limit	6.64
Variability estimate	Standard error of the mean
Dispersion value	1.53

Secondary: Change in IBDQ scores from baseline to Week 10 - Bowel function

End point title	Change in IBDQ scores from baseline to Week 10 - Bowel function

End point description:

The Inflammatory Bowel Disease Questionnaire (IBDQ) is a standard measure of HRQL in Crohn's disease patients (Guyatt G et al 1989). The validated Japanese version of the IBDQ was used in this study (Hashimoto H et al 2003). The IBDQ contains 32 questions; each with seven possible answers ranging from 1 to 7, where 7 is the most favourable. Ten questions are related to bowel symptoms, five to systemic symptoms, twelve to emotional function, and five to social function. The corresponding answers will be added to form four subscores and a total score: bowel function score (10 – 70), systemic symptom score (5 – 35), emotional function score (12 – 84), social function score (5 – 35) and the total score (32 – 224), with higher scores indicating more favorable outcome.

End point type	Secondary

End point timeframe:

10 Week

End point values	D9421-C 9mg + Mesalazine placebo	Mesalazine 3g + D9421-C placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50	45		
Units: Scores on a scale				
least squares mean (standard error)	6.9 (± 1.08)	3.6 (± 0.98)		

Statistical analyses

Statistical analysis title	Change in IBDQ scores at W10 - Bowel function
Comparison groups	D9421-C 9mg + Mesalazine placebo v Mesalazine 3g + D9421-C placebo
Number of subjects included in analysis	95
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference between group
Point estimate	3.3
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.9
upper limit	5.76
Variability estimate	Standard error of the mean
Dispersion value	1.47

Secondary: Change in IBDQ scores from baseline to Week 2 - Systemic symptom

End point title	Change in IBDQ scores from baseline to Week 2 - Systemic symptom

End point description:

The Inflammatory Bowel Disease Questionnaire (IBDQ) is a standard measure of HRQL in Crohn's disease patients (Guyatt G et al 1989). The validated Japanese version of the IBDQ was used in this study (Hashimoto H et al 2003). The IBDQ contains 32 questions; each with seven possible answers ranging from 1 to 7, where 7 is the most favourable. Ten questions are related to bowel symptoms, five to systemic symptoms, twelve to emotional function, and five to social function. The corresponding answers will be added to form four subscores and a total score: bowel function score (10 – 70), systemic symptom score (5 – 35), emotional function score (12 – 84), social function score (5 – 35) and the total score (32 – 224), with higher scores indicating more favorable outcome.

End point type	Secondary

End point timeframe:

2 Week

End point values	D9421-C 9mg + Mesalazine placebo	Mesalazine 3g + D9421-C placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	56	54		
Units: Scores on a scale				
least squares mean (standard error)	3 (± 0.49)	1 (± 0.48)		

Statistical analyses

Statistical analysis title	Change in IBDQ scores at W2 - Systemic symptom
Comparison groups	D9421-C 9mg + Mesalazine placebo v Mesalazine 3g + D9421-C placebo
Number of subjects included in analysis	110
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference between group
Point estimate	2
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.89
upper limit	3.17
Variability estimate	Standard error of the mean
Dispersion value	0.69

Secondary: Change in IBDQ scores from baseline to Week 4 - Systemic symptom

End point title	Change in IBDQ scores from baseline to Week 4 - Systemic symptom

End point description:

The Inflammatory Bowel Disease Questionnaire (IBDQ) is a standard measure of HRQL in Crohn's disease patients (Guyatt G et al 1989). The validated Japanese version of the IBDQ was used in this study (Hashimoto H et al 2003). The IBDQ contains 32 questions; each with seven possible answers ranging from 1 to 7, where 7 is the most favourable. Ten questions are related to bowel symptoms, five to systemic symptoms, twelve to emotional function, and five to social function. The corresponding answers will be added to form four subscores and a total score: bowel function score (10 – 70), systemic symptom score (5 – 35), emotional function score (12 – 84), social function score (5 – 35) and the total score (32 – 224), with higher scores indicating more favorable outcome.

End point type	Secondary

End point timeframe:

4 Week

End point values	D9421-C 9mg + Mesalazine placebo	Mesalazine 3g + D9421-C placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	55	50		
Units: Scores on a scale				
least squares mean (standard error)	3.3 (± 0.57)	1.3 (± 0.47)		

Statistical analyses

Statistical analysis title	Change in IBDQ scores at W4 - Systemic symptom
Comparison groups	D9421-C 9mg + Mesalazine placebo v Mesalazine 3g + D9421-C placebo
Number of subjects included in analysis	105
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference between group
Point estimate	2
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.73
upper limit	3.19
Variability estimate	Standard error of the mean
Dispersion value	0.74

Secondary: Change in IBDQ scores from baseline to Week 8 - Systemic symptom

End point title	Change in IBDQ scores from baseline to Week 8 - Systemic symptom

End point description:

The Inflammatory Bowel Disease Questionnaire (IBDQ) is a standard measure of HRQL in Crohn's disease patients (Guyatt G et al 1989). The validated Japanese version of the IBDQ was used in this study (Hashimoto H et al 2003). The IBDQ contains 32 questions; each with seven possible answers ranging from 1 to 7, where 7 is the most favourable. Ten questions are related to bowel symptoms, five to systemic symptoms, twelve to emotional function, and five to social function. The corresponding answers will be added to form four subscores and a total score: bowel function score (10 – 70), systemic symptom score (5 – 35), emotional function score (12 – 84), social function score (5 – 35) and the total score (32 – 224), with higher scores indicating more favorable outcome.

End point type	Secondary

End point timeframe:

8 Week

End point values	D9421-C 9mg + Mesalazine placebo	Mesalazine 3g + D9421-C placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	51	45		
Units: Scores on a scale				
least squares mean (standard error)	3.5 (± 0.58)	1.2 (± 0.61)		

Statistical analyses

Statistical analysis title	Change in IBDQ scores at W8 - Systemic symptom
Comparison groups	D9421-C 9mg + Mesalazine placebo v Mesalazine 3g + D9421-C placebo
Number of subjects included in analysis	96
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference between group
Point estimate	2.4
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.96
upper limit	3.76
Variability estimate	Standard error of the mean
Dispersion value	0.84

Secondary: Change in IBDQ scores from baseline to Week 10 - Systemic symptom

End point title	Change in IBDQ scores from baseline to Week 10 - Systemic symptom

End point description:

The Inflammatory Bowel Disease Questionnaire (IBDQ) is a standard measure of HRQL in Crohn's disease patients (Guyatt G et al 1989). The validated Japanese version of the IBDQ was used in this study (Hashimoto H et al 2003). The IBDQ contains 32 questions; each with seven possible answers ranging from 1 to 7, where 7 is the most favourable. Ten questions are related to bowel symptoms, five to systemic symptoms, twelve to emotional function, and five to social function. The corresponding answers will be added to form four subscores and a total score: bowel function score (10 – 70), systemic symptom score (5 – 35), emotional function score (12 – 84), social function score (5 – 35) and the total score (32 – 224), with higher scores indicating more favorable outcome.

End point type	Secondary

End point timeframe:

10 Week

End point values	D9421-C 9mg + Mesalazine placebo	Mesalazine 3g + D9421-C placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50	45		
Units: Scores on a scale				
least squares mean (standard error)	3.8 (± 0.64)	1.2 (± 0.62)		

Statistical analyses

Statistical analysis title	Change in IBDQ scores at W10 - Systemic symptom
Comparison groups	D9421-C 9mg + Mesalazine placebo v Mesalazine 3g + D9421-C placebo
Number of subjects included in analysis	95
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference between group
Point estimate	2.6
Confidence interval	
level	90 %
sides	2-sided
lower limit	1.15
upper limit	4.09
Variability estimate	Standard error of the mean
Dispersion value	0.89

Secondary: Change in IBDQ scores from baseline to Week 2 - Emotional function

End point title	Change in IBDQ scores from baseline to Week 2 - Emotional function

End point description:

The Inflammatory Bowel Disease Questionnaire (IBDQ) is a standard measure of HRQL in Crohn's disease patients (Guyatt G et al 1989). The validated Japanese version of the IBDQ was used in this study (Hashimoto H et al 2003). The IBDQ contains 32 questions; each with seven possible answers ranging from 1 to 7, where 7 is the most favourable. Ten questions are related to bowel symptoms, five to systemic symptoms, twelve to emotional function, and five to social function. The corresponding answers will be added to form four subscores and a total score: bowel function score (10 – 70), systemic symptom score (5 – 35), emotional function score (12 – 84), social function score (5 – 35) and the total score (32 – 224), with higher scores indicating more favorable outcome.

End point type	Secondary

End point timeframe:

2 Week

End point values	D9421-C 9mg + Mesalazine placebo	Mesalazine 3g + D9421-C placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	55	50		
Units: Scores on a scale				
least squares mean (standard error)	7 (± 1.25)	2.1 (± 1.08)		

Statistical analyses

Statistical analysis title	Change in IBDQ scores at W4 - Emotional function
Comparison groups	D9421-C 9mg + Mesalazine placebo v Mesalazine 3g + D9421-C placebo
Number of subjects included in analysis	105
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference between group
Point estimate	4.9
Confidence interval	
level	90 %
sides	2-sided
lower limit	2.14
upper limit	7.65
Variability estimate	Standard error of the mean
Dispersion value	1.66

Secondary: Change in IBDQ scores from baseline to Week 8 - Emotional function

End point title	Change in IBDQ scores from baseline to Week 8 - Emotional function

End point description:

The Inflammatory Bowel Disease Questionnaire (IBDQ) is a standard measure of HRQL in Crohn's disease patients (Guyatt G et al 1989). The validated Japanese version of the IBDQ was used in this study (Hashimoto H et al 2003). The IBDQ contains 32 questions; each with seven possible answers ranging from 1 to 7, where 7 is the most favourable. Ten questions are related to bowel symptoms, five to systemic symptoms, twelve to emotional function, and five to social function. The corresponding answers will be added to form four subscores and a total score: bowel function score (10 – 70), systemic symptom score (5 – 35), emotional function score (12 – 84), social function score (5 – 35) and the total score (32 – 224), with higher scores indicating more favorable outcome.

End point type	Secondary

End point timeframe:

8 Week

End point values	D9421-C 9mg + Mesalazine placebo	Mesalazine 3g + D9421-C placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	51	45		
Units: Scores on a scale				
least squares mean (standard error)	5.9 (± 1.18)	1.6 (± 1.31)		

Statistical analyses

Statistical analysis title	Change in IBDQ scores at W8 - Emotional function
Comparison groups	D9421-C 9mg + Mesalazine placebo v Mesalazine 3g + D9421-C placebo
Number of subjects included in analysis	96
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference between group
Point estimate	4.3
Confidence interval	
level	90 %
sides	2-sided
lower limit	1.4
upper limit	7.25
Variability estimate	Standard error of the mean
Dispersion value	1.76

Secondary: Change in IBDQ scores from baseline to Week 10 - Emotional function

End point title	Change in IBDQ scores from baseline to Week 10 - Emotional function

End point description:

The Inflammatory Bowel Disease Questionnaire (IBDQ) is a standard measure of HRQL in Crohn's disease patients (Guyatt G et al 1989). The validated Japanese version of the IBDQ was used in this study (Hashimoto H et al 2003). The IBDQ contains 32 questions; each with seven possible answers ranging from 1 to 7, where 7 is the most favourable. Ten questions are related to bowel symptoms, five to systemic symptoms, twelve to emotional function, and five to social function. The corresponding answers will be added to form four subscores and a total score: bowel function score (10 – 70), systemic symptom score (5 – 35), emotional function score (12 – 84), social function score (5 – 35) and the total score (32 – 224), with higher scores indicating more favorable outcome.

End point type	Secondary

End point timeframe:

10 Week

End point values	D9421-C 9mg + Mesalazine placebo	Mesalazine 3g + D9421-C placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50	45		
Units: Scores on a scale				
least squares mean (standard error)	8 (± 1.28)	1.3 (± 1.34)		

Statistical analyses

Statistical analysis title	Change in IBDQ scores at W10 - Emotional function
Comparison groups	D9421-C 9mg + Mesalazine placebo v Mesalazine 3g + D9421-C placebo
Number of subjects included in analysis	95
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference between group
Point estimate	6.6
Confidence interval	
level	90 %
sides	2-sided
lower limit	3.56
upper limit	9.72
Variability estimate	Standard error of the mean
Dispersion value	1.86

Secondary: Change in IBDQ scores from baseline to Week 2 - Social function

End point title	Change in IBDQ scores from baseline to Week 2 - Social function

End point description:

The Inflammatory Bowel Disease Questionnaire (IBDQ) is a standard measure of HRQL in Crohn's disease patients (Guyatt G et al 1989). The validated Japanese version of the IBDQ was used in this study (Hashimoto H et al 2003). The IBDQ contains 32 questions; each with seven possible answers ranging from 1 to 7, where 7 is the most favourable. Ten questions are related to bowel symptoms, five to systemic symptoms, twelve to emotional function, and five to social function. The corresponding answers will be added to form four subscores and a total score: bowel function score (10 – 70), systemic symptom score (5 – 35), emotional function score (12 – 84), social function score (5 – 35) and the total score (32 – 224), with higher scores indicating more favorable outcome.

End point type	Secondary

End point timeframe:

2 Week

End point values	D9421-C 9mg + Mesalazine placebo	Mesalazine 3g + D9421-C placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	56	54		
Units: Scores on a scale				
least squares mean (standard error)	1.9 (± 0.45)	0.6 (± 0.55)		

Statistical analyses

Statistical analysis title	Change in IBDQ scores at W2 - Social function
Comparison groups	D9421-C 9mg + Mesalazine placebo v Mesalazine 3g + D9421-C placebo
Number of subjects included in analysis	110
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference between group
Point estimate	1.2
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.01
upper limit	2.43
Variability estimate	Standard error of the mean
Dispersion value	0.73

Secondary: Change in IBDQ scores from baseline to Week 4 - Social function

End point title	Change in IBDQ scores from baseline to Week 4 - Social function

End point description:

The Inflammatory Bowel Disease Questionnaire (IBDQ) is a standard measure of HRQL in Crohn's disease patients (Guyatt G et al 1989). The validated Japanese version of the IBDQ was used in this study (Hashimoto H et al 2003). The IBDQ contains 32 questions; each with seven possible answers ranging from 1 to 7, where 7 is the most favourable. Ten questions are related to bowel symptoms, five to systemic symptoms, twelve to emotional function, and five to social function. The corresponding answers will be added to form four subscores and a total score: bowel function score (10 – 70), systemic symptom score (5 – 35), emotional function score (12 – 84), social function score (5 – 35) and the total score (32 – 224), with higher scores indicating more favorable outcome.

End point type	Secondary

End point timeframe:

4 Week

End point values	D9421-C 9mg + Mesalazine placebo	Mesalazine 3g + D9421-C placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	55	50		
Units: Scores on a scale				
least squares mean (standard error)	2.5 (± 0.58)	0.7 (± 0.56)		

Statistical analyses

Statistical analysis title	Change in IBDQ scores at W4 - Social function
Comparison groups	D9421-C 9mg + Mesalazine placebo v Mesalazine 3g + D9421-C placebo
Number of subjects included in analysis	105
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference between group
Point estimate	1.8
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.42
upper limit	3.12
Variability estimate	Standard error of the mean
Dispersion value	0.81

Secondary: Change in IBDQ scores from baseline to Week 8 - Social function

End point title	Change in IBDQ scores from baseline to Week 8 - Social function

End point description:

The Inflammatory Bowel Disease Questionnaire (IBDQ) is a standard measure of HRQL in Crohn's disease patients (Guyatt G et al 1989). The validated Japanese version of the IBDQ was used in this study (Hashimoto H et al 2003). The IBDQ contains 32 questions; each with seven possible answers ranging from 1 to 7, where 7 is the most favourable. Ten questions are related to bowel symptoms, five to systemic symptoms, twelve to emotional function, and five to social function. The corresponding answers will be added to form four subscores and a total score: bowel function score (10 – 70), systemic symptom score (5 – 35), emotional function score (12 – 84), social function score (5 – 35) and the total score (32 – 224), with higher scores indicating more favorable outcome.

End point type	Secondary

End point timeframe:

8 Week

End point values	D9421-C 9mg + Mesalazine placebo	Mesalazine 3g + D9421-C placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	51	45		
Units: Scores on a scale				
least squares mean (standard error)	2.3 (± 0.57)	0.7 (± 0.63)		

Statistical analyses

Statistical analysis title	Change in IBDQ scores at W8 - Social function
Comparison groups	D9421-C 9mg + Mesalazine placebo v Mesalazine 3g + D9421-C placebo
Number of subjects included in analysis	96
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference between group
Point estimate	1.6
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.19
upper limit	3.04
Variability estimate	Standard error of the mean
Dispersion value	0.86

Secondary: Change in IBDQ scores from baseline to Week 10 - Social function

End point title	Change in IBDQ scores from baseline to Week 10 - Social function

End point description:

The Inflammatory Bowel Disease Questionnaire (IBDQ) is a standard measure of HRQL in Crohn's disease patients (Guyatt G et al 1989). The validated Japanese version of the IBDQ was used in this study (Hashimoto H et al 2003). The IBDQ contains 32 questions; each with seven possible answers ranging from 1 to 7, where 7 is the most favourable. Ten questions are related to bowel symptoms, five to systemic symptoms, twelve to emotional function, and five to social function. The corresponding answers will be added to form four subscores and a total score: bowel function score (10 – 70), systemic symptom score (5 – 35), emotional function score (12 – 84), social function score (5 – 35) and the total score (32 – 224), with higher scores indicating more favorable outcome.

End point type	Secondary

End point timeframe:

10 Week

End point values	D9421-C 9mg + Mesalazine placebo	Mesalazine 3g + D9421-C placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50	45		
Units: Scores on a scale				
least squares mean (standard error)	2.4 (± 0.63)	1.2 (± 0.56)		

Statistical analyses

Statistical analysis title	Change in IBDQ scores at W10 - Social function
Comparison groups	D9421-C 9mg + Mesalazine placebo v Mesalazine 3g + D9421-C placebo
Number of subjects included in analysis	95
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference between group
Point estimate	1.3
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.15
upper limit	2.76
Variability estimate	Standard error of the mean
Dispersion value	0.85

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events collected from the date of signing of informed consent to Visit 6 or withdrawal visit (including the tapering period)

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.0

Reporting groups

Reporting group title	D9421-C 9mg + Mesalazine placebo

Reporting group description:

Patients randomised to D9421-C 9 mg took 3 capsules of D9421-C capsule 3 mg once daily before breakfast and 4 tablets of Mesalazine tablets placebo three times a day after each meal for 8 weeks.

Reporting group title	Mesalazine 3g + D9421-C placebo

Reporting group description:

Patients randomised to Mesalazine 3 g took 3 capsules of D9421-C capsule placebo once daily before breakfast and 4 tablets of Mesalazine tablets 250 mg three times a day after each meal for 8 weeks.

Serious adverse events	D9421-C 9mg + Mesalazine placebo	Mesalazine 3g + D9421-C placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 56 (5.36%)	1 / 56 (1.79%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Gastrointestinal disorders			
Ileus			
subjects affected / exposed	1 / 56 (1.79%)	1 / 56 (1.79%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumatosis intestinalis			
subjects affected / exposed	1 / 56 (1.79%)	0 / 56 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower gastrointestinal haemorrhage			
subjects affected / exposed	1 / 56 (1.79%)	0 / 56 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	D9421-C 9mg + Mesalazine placebo	Mesalazine 3g + D9421-C placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	11 / 56 (19.64%)	16 / 56 (28.57%)	
Nervous system disorders			
Headache			
subjects affected / exposed	3 / 56 (5.36%)	0 / 56 (0.00%)	
occurrences (all)	4	0	
Gastrointestinal disorders			
Crohn's disease			
subjects affected / exposed	1 / 56 (1.79%)	3 / 56 (5.36%)	
occurrences (all)	1	3	
Vomiting			
subjects affected / exposed	3 / 56 (5.36%)	0 / 56 (0.00%)	
occurrences (all)	3	0	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	6 / 56 (10.71%)	10 / 56 (17.86%)	
occurrences (all)	6	10	
Pharyngitis			
subjects affected / exposed	0 / 56 (0.00%)	3 / 56 (5.36%)	
occurrences (all)	0	3	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
08 December 2011	Amendment 1
04 April 2012	Amendment 2
01 March 2013	Amendment 3
25 September 2013	Amendment 4

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported