Clinical trial results:
Early Phase 2 Clinical Trial of E6011 in Patients With Active Crohn's Disease

Summary

EudraCT number	2018-002109-70
Trial protocol	HU CZ
Global end of trial date	03 April 2024

Results information

Result version number	v1 (current)
This version publication date	20 March 2025
First version publication date	20 March 2025

Trial information

Trial identification

Sponsor protocol code	E6011-ET2

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03733314
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	EA Pharma Co., Ltd
Sponsor organisation address	2-1-1 Irifune, Chuo-ku, Tokyo, Japan, 104-0042
Public contact	Corporate Communication Dept., EA Pharma Co., Ltd, +81 0362809600, contact_ea@eapharma.co.jp
Scientific contact	Corporate Communication Dept., EA Pharma Co., Ltd, +81 0362809600, contact_ea@eapharma.co.jp

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	13 September 2024
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	03 April 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study was to examine the efficacy and safety of E6011 at 12 weeks after administration by means of double-blind placebo-controlled trial.

Protection of trial subjects:

This study was conducted in accordance with International Conference on Harmonization (ICH) Good Clinical Practice (GCP) guidelines and applicable national regulations. Essential documents were retained in accordance with ICH GCP.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	25 April 2019
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: 20
Country: Number of subjects enrolled	Poland: 3
Country: Number of subjects enrolled	Hungary: 1
Country: Number of subjects enrolled	Russian Federation: 1
Worldwide total number of subjects	25
EEA total number of subjects	4

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)	25
From 65 to 84 years	0

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Subjects took part in the study at 49 investigative sites in Japan, Czech Republic, Hungary, Poland, and Russia from 25 April 2019 to 03 April 2024.

Pre-assignment

Screening details:

A total of 65 subjects were screened, of which 40 were screen failures and 25 were enrolled to receive study treatment.

Period 1

Period 1 title	Remission-induction Period: (Weeks 0-12)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Carer, Investigator, Data analyst, Assessor, Subject

Arms

Are arms mutually exclusive?	Yes
Arm title	Remission Induction Period: E6011 10 mg/kg

Arm description:

Subjects with moderate to severe active Crohn’s disease received E6011 10 milligram per kilogram (mg/kg), intravenous (IV) infusion once, at Weeks 0, 1, 2 then every 2 weeks up Week 10 during the Remission Induction Period.

Arm type	Experimental
Investigational medicinal product name	E6011
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

E6011 10 mg/kg administered as IV infusion.

Arm title	Remission Induction Period: Placebo

Arm description:

Subjects with moderate to severe active Crohn’s disease received placebo, IV infusion once, at Weeks 0, 1, 2 then every 2 weeks up Week 10 during the Remission Induction Period.

Arm type	Experimental
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

E6011 placebo administered as IV infusion.

Number of subjects in period 1	Remission Induction Period: E6011 10 mg/kg	Remission Induction Period: Placebo
Started	12	13
CDAI Responders at Week 12	5 [1]	6 [2]
CDAI Non-responders at Week 12	5 [3]	7 [4]
Completed	10	13
Not completed	2	0
Consent withdrawn by subject	2	-

Notes:

[1] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: These are the CDAI responders at Week 24 and therefore the number is not equal to or greater than the started.

[2] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: These are the CDAI responders at Week 24 and therefore the number is not equal to or greater than the started.

[3] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: These are the CDAI responders at Week 12 and therefore the number is not equal to or greater than the started.

[4] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: These are the CDAI responders at Week 12 and therefore the number is not equal to or greater than the started.

Period 2

Period 2 title	Rescue Period: (Weeks 12 to 24)
Is this the baseline period?	No
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	No
Arm title	Rescue Period: E6011 10 mg/kg

Arm description:

Subjects with moderate to severe active Crohn’s disease received E6011 10 mg/kg, IV infusion once, at Weeks 12, 13, 14 then every 2 weeks up to Week 22 during Rescue Period.

Arm type	Experimental
Investigational medicinal product name	E6011
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

E6011 10 mg/kg administered as IV infusion.

Arm title	Rescue Period: Placebo to E6011 10 mg/kg

Arm description:

Subjects with moderate to severe active Crohn’s disease who received placebo in the remission induction period received E6011 10 mg/kg, IV infusion once, at Weeks 12, 13, 14 then every 2 weeks

up to Week 22 during Rescue the Period.

Arm type	Experimental
Investigational medicinal product name	E6011
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

E6011 10 mg/kg administered as IV infusion.

Number of subjects in period 2	Rescue Period: E6011 10 mg/kg	Rescue Period: Placebo to E6011 10 mg/kg
Started	5	7
CDAI Responders at Week 24	2 [5]	2 [6]
CDAI Non-responders at Week 24	2 [7]	1 [8]
Completed	4	3
Not completed	1	4
Consent withdrawn by subject	1	2
Progressive disease	-	2

Notes:

[5] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: These are the CDAI responders at Week 12 and therefore the number is not equal to or greater than the started.

[6] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: These are the CDAI responders at Week 24 and therefore the number is not equal to or greater than the started.

[7] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: These are the CDAI responders at Week 12 and therefore the number is not equal to or greater than the started.

[8] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: These are the CDAI responders at Week 24 and therefore the number is not equal to or greater than the started.

Period 3

Period 3 title	Extension Period:(Week 12-52/Week 24-64)
Is this the baseline period?	No
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	No

Arm title	Extension Period: E6011 10 mg/kg

Arm description:

Subjects with moderate to severe active Crohn’s disease and with response at Week 12 and Week 24 received E6011 10 mg/kg, IV infusion once, every 4 weeks from Week 12 to Week 48 and Week 24 to Week 60, respectively, during the Extension Period.

Arm type	Experimental
Investigational medicinal product name	E6011
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

E6011 10 mg/kg administered as IV infusion.

Arm title	Extension Period: Placebo to E6011 10 mg/kg

Arm description:

Subjects with moderate to severe active Crohn’s disease who received placebo in the remission induction period, who had response at Week 12 and Week 24 received E6011 10 mg/kg, IV infusion once, every 4 weeks from Week 12 to Week 48 and Week 24 to Week 60, respectively during the Extension Period.

Arm type	Experimental
Investigational medicinal product name	E6011
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

E6011 10 mg/kg administered as IV infusion.

Number of subjects in period 3	Extension Period: E6011 10 mg/kg	Extension Period: Placebo to E6011 10 mg/kg
Started	7	8
Completed	2	5
Not completed	5	3
Unspecified	3	2
Progressive disease	1	-
Lack of efficacy	1	1

Period 4

Period 4 title	Post-observation Period
Is this the baseline period?	No
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms	
Are arms mutually exclusive?	No
Arm title	Post-observation Period: E6011 10 mg/kg

Arm description:

Subjects with moderate to severe active Crohn’s disease who received E6011 10 mg/kg in any of the treatment periods were observed during Post-observation Period for 70 days after last dose.

Arm type	No intervention

No investigational medicinal product assigned in this arm

Arm title	Post-observation Period: Placebo to E6011 10 mg/kg

Arm description:

Subjects with moderate to severe active Crohn’s disease who received placebo in the remission induction period and who were switched to receive E6011 10 mg/kg in Rescue or Extension periods were observed during Post-observation Period for 70 days after last dose.

Arm type	No intervention

No investigational medicinal product assigned in this arm

Number of subjects in period 4	Post-observation Period: E6011 10 mg/kg	Post-observation Period: Placebo to E6011 10 mg/kg
Started	12	13
Completed	12	13

Baseline characteristics

Reporting groups	
Reporting group title	Remission Induction Period: E6011 10 mg/kg
Reporting group description:	
Subjects with moderate to severe active Crohn's disease received E6011 10 milligram per kilogram (mg/kg), intravenous (IV) infusion once, at Weeks 0, 1, 2 then every 2 weeks up Week 10 during the Remission Induction Period.	
Reporting group title	Remission Induction Period: Placebo
Reporting group description:	
Subjects with moderate to severe active Crohn's disease received placebo, IV infusion once, at Weeks 0, 1, 2 then every 2 weeks up Week 10 during the Remission Induction Period.	

Reporting group values	Remission Induction Period: E6011 10 mg/kg	Remission Induction Period: Placebo	Total
Number of subjects	12	13	25
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)	12	13	25
From 65-84 years	0	0	0
85 years and over	0	0	0
Age Continuous Units: years			
arithmetic mean	29.8	33.2	
standard deviation	± 8.7	± 12.0	-
Sex: Female, Male Units: subjects			
Female	2	5	7
Male	10	8	18
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	11	9	20
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	0
White	1	4	5
More than one race	0	0	0
Unknown or Not Reported	0	0	0
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	0	0	0
Not Hispanic or Latino	12	13	25

Unknown or Not Reported	0	0	0

End points

End points reporting groups

Reporting group title	Remission Induction Period: E6011 10 mg/kg

Reporting group description:

Subjects with moderate to severe active Crohn's disease received E6011 10 milligram per kilogram (mg/kg), intravenous (IV) infusion once, at Weeks 0, 1, 2 then every 2 weeks up Week 10 during the Remission Induction Period.

Reporting group title	Remission Induction Period: Placebo

Reporting group description:

Subjects with moderate to severe active Crohn's disease received placebo, IV infusion once, at Weeks 0, 1, 2 then every 2 weeks up Week 10 during the Remission Induction Period.

Reporting group title	Rescue Period: E6011 10 mg/kg

Reporting group description:

Subjects with moderate to severe active Crohn's disease received E6011 10 mg/kg, IV infusion once, at Weeks 12, 13, 14 then every 2 weeks up to Week 22 during Rescue Period.

Reporting group title	Rescue Period: Placebo to E6011 10 mg/kg

Reporting group description:

Subjects with moderate to severe active Crohn's disease who received placebo in the remission induction period received E6011 10 mg/kg, IV infusion once, at Weeks 12, 13, 14 then every 2 weeks up to Week 22 during Rescue the Period.

Reporting group title	Extension Period: E6011 10 mg/kg

Reporting group description:

Subjects with moderate to severe active Crohn's disease and with response at Week 12 and Week 24 received E6011 10 mg/kg, IV infusion once, every 4 weeks from Week 12 to Week 48 and Week 24 to Week 60, respectively, during the Extension Period.

Reporting group title	Extension Period: Placebo to E6011 10 mg/kg

Reporting group description:

Subjects with moderate to severe active Crohn's disease who received placebo in the remission induction period, who had response at Week 12 and Week 24 received E6011 10 mg/kg, IV infusion once, every 4 weeks from Week 12 to Week 48 and Week 24 to Week 60, respectively during the Extension Period.

Reporting group title	Post-observation Period: E6011 10 mg/kg

Reporting group description:

Subjects with moderate to severe active Crohn's disease who received E6011 10 mg/kg in any of the treatment periods were observed during Post-observation Period for 70 days after last dose.

Reporting group title	Post-observation Period: Placebo to E6011 10 mg/kg

Reporting group description:

Subjects with moderate to severe active Crohn's disease who received placebo in the remission induction period and who were switched to receive E6011 10 mg/kg in Rescue or Extension periods were observed during Post-observation Period for 70 days after last dose.

Subject analysis set title	E6011 10 mg/kg
Subject analysis set type	Full analysis

Subject analysis set description:

Subjects with moderate to severe active Crohn's disease received E6011 10 milligram per kilogram (mg/kg), intravenous (IV) infusion once, at Weeks 0, 1, 2 then every 2 weeks up Week 10 during the Remission Induction Period, thereafter, non-responder subjects continued E6011 treatment at Weeks 12, 13, 14 then every 2 weeks up to Week 22 during the Rescue Period. Responder subjects at Week 12 continued E6011 treatment, every 4 weeks from Week 12 to Week 48 and responders at Week 24 continued E6011 treatment, every 4 weeks, from Week 24 to Week 60 during the Extension Period.

Subject analysis set title	Placebo then E6011 10 mg/kg
Subject analysis set type	Full analysis

Subject analysis set description:

Subjects with moderate to severe active Crohn's disease received placebo, IV infusion once, at Weeks 0, 1, 2 then every 2 weeks up Week 10 during the Remission Induction Period, thereafter, non-responder subjects received E6011 10 mg/kg, IV infusion once, at Weeks 12, 13, 14 then every 2 weeks up to Week 22 during the Rescue Period. Responder subjects at Week 12 continued E6011 treatment, every 4

weeks from Week 12 to Week 48 and responders at Week 24 continued E6011 treatment, every 4 weeks, from Week 24 to Week 60 during the Extension Period.

Primary: Percentage of Subjects With Clinical Response (CR) 100 (CR100) at Week 12

End point title	Percentage of Subjects With Clinical Response (CR) 100 (CR100) at Week 12

End point description:

The CDAI system was a composite index of 8 disease activity variables: severity of abdominal pain, general well-being, very soft/liquid stool frequency, extra-intestinal symptoms, need for antidiarrheal drugs, presence of an abdominal mass, body weight and hematocrit. The sub scores of abdominal pain (0-3), general well-being (0-4, higher values mean worse well-being), and number of very soft or liquid stools were then summed. Additionally, the remaining predictors were also noted and weighted to create the total CDAI score which ranged from 0-600 with a higher score indicating a worse outcome. The Full analysis set (FAS) included subjects to whom the IMP has been administered after randomization, and who had 1 or more evaluable, post-IMP administration primary efficacy endpoint (that is, to have an evaluable CDAI value at baseline and any other post baseline).

End point type	Primary

End point timeframe:

At Week 12

End point values	Remission Induction Period: E6011 10 mg/kg	Remission Induction Period: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	13		
Units: percentage of subjects				
number (confidence interval 95%)	33.3 (9.9 to 65.1)	23.1 (5.0 to 53.8)		

Statistical analyses

Statistical analysis title	E6011 10 mg/kg vs Placebo then E6011 10 mg/kg
Comparison groups	Remission Induction Period: E6011 10 mg/kg v Remission Induction Period: Placebo
Number of subjects included in analysis	25
Analysis specification	Pre-specified
Analysis type	superiority[1]
Parameter estimate	Difference
Point estimate	10.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-24.9
upper limit	45.4

Notes:

[1] - The difference of percentage was calculated as E6011 minus placebo.

Secondary: Percentage of Subjects With CR70 and CR100

End point title	Percentage of Subjects With CR70 and CR100

End point description:

CR70=reduction of >=70 points in CDAI from baseline. CR100=reduction of >=100 points in CDAI from baseline. CDAI was composite index of 8 disease activity variables: severity of abdominal pain, general well-being, very soft/liquid stool frequency, extra-intestinal symptoms, need for antidiarrheal drugs, presence of abdominal mass, body weight, hematocrit. Sub scores of abdominal pain (0-3), general well-being (0-4), number of very soft or liquid stools were summed. Remaining predictors were also noted and weighted to create total CDAI score ranged from 0-600 with higher score=worse outcome. FAS was used for analysis. "n"=subjects evaluable at given time points,99999=no data was calculated as no subjects analyzed. As planned, combined data for all periods (remission-induction, rescue and extension periods) was collected and reported in endpoint due to same dosing of E6011. From Week 14-24, subjects data analyzed simultaneously for rescue and extension period and reported collectively.

End point type	Secondary

End point timeframe:

At Weeks 2, 4, 8, 12, 14, 16, 20, 24, 28, 32, 36, 40, 44, 48, 52, 56, 60 and 64

End point values	E6011 10 mg/kg	Placebo then E6011 10 mg/kg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	12	13		
Units: percentage of subjects				
number (not applicable)				
CR70: Week 2 (n=12,13)	16.7	23.1		
CR70: Week 4 (n=11,13)	45.5	23.1		
CR70: Week 8 (n=10,13)	50.0	38.5		
CR70: Week 12 (n=10,13)	50.0	46.2		
CR70: Week 14 (n=4,6)	25.0	33.3		
CR70: Week 16 (n=10,10)	70.0	60.0		
CR70: Week 20 (n=9,8)	66.7	62.5		
CR70: Week 24 (n=8,7)	62.5	71.4		
CR70: Week 28 (n=4,7)	100.0	85.7		
CR70: Week 32 (n=4,6)	50.0	83.3		
CR70: Week 36 (n=4,6)	100.0	83.3		
CR70: Week 40 (n=3,4)	100.0	75.0		
CR70: Week 44 (n=3,5)	100.0	80.0		
CR70: Week 48 (n=3,4)	66.7	100.0		
CR70: Week 52 (n=3,3)	66.7	66.7		
CR70: Week 56 (n=0,1)	99999	100.0		
CR70: Week 60 (n=0,2)	99999	100.0		
CR70: Week 64 (n=0,1)	99999	100.0		
CR100: Week 2 (n=12,13)	16.7	15.4		
CR100: Week 4 (n=11,13)	18.2	23.1		
CR100: Week 8 (n=10,13)	30.0	30.8		
CR100: Week 12 (n=10,13)	40.0	23.1		
CR100: Week 14 (n=4,6)	25.0	33.3		
CR100: Week 16 (n=10,10)	70.0	50.0		
CR100: Week 20 (n=9,8)	55.6	50.0		
CR100: Week 24 (n=8,7)	50.0	57.1		
CR100: Week 28 (n=4,7)	100.0	71.4		
CR100: Week 32 (n=4,6)	50.0	83.3		
CR100: Week 36 (n=4,6)	75.0	50.0		

CR100: Week 40 (n=3,4)	100.0	75.0		
CR100: Week 44 (n=3,5)	66.7	80.0		
CR100: Week 48 (n=3,4)	66.7	75.0		
CR100: Week 52 (n=3,3)	66.7	66.7		
CR100: Week 56 (n=0,1)	99999	100.0		
CR100: Week 60 (n=0,2)	99999	50.0		
CR100: Week 64 (n=0,1)	99999	100.0		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Below 150 CDAI Points

End point title	Percentage of Subjects With Below 150 CDAI Points

End point description:

CDAI remission was defined as CDAI score below (<) 150 points. CDAI was composite index of 8 disease activity variables: severity of abdominal pain, general well-being, very soft/liquid stool frequency, extra-intestinal symptoms, need for antidiarrheal drugs, presence of abdominal mass, body weight, hematocrit. Sub scores of abdominal pain (0-3), general well-being (0-4), number of very soft or liquid stools were summed. Remaining predictors were also noted and weighted to create total CDAI score ranged from 0-600 with higher score=worse outcome. FAS was used for analysis. Here "n" = subjects who were evaluable for this endpoint at given time points and 99999 = no data was calculated as no subjects analyzed. As planned, combined data for all the periods (remission-induction, rescue and extension periods) was collected and reported in endpoint due to same dosing of E6011. From Week 14-24, subjects data analyzed simultaneously for rescue and extension period and reported collectively.

End point type	Secondary

End point timeframe:

At Weeks 2, 4, 8, 12, 14, 16, 20, 24, 28, 32, 36, 40, 44, 48, 52, 56, 60 and 64

End point values	E6011 10 mg/kg	Placebo then E6011 10 mg/kg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	12	13		
Units: percentage of subjects				
number (not applicable)				
CDAI <150 points: Week 2 (n=12,13)	0.0	7.7		
CDAI <150 points: Week 4 (n=11,13)	0.0	15.4		
CDAI <150 points: Week 8 (n=10,13)	20.0	30.8		
CDAI <150 points: Week 12 (n=10,13)	10.0	15.4		
CDAI <150 points: Week 14 (n=4,6)	0.0	16.7		
CDAI <150 points: Week 16 (n=10,10)	20.0	30.0		
CDAI <150 points: Week 20 (n=9,8)	11.1	37.5		
CDAI <150 points: Week 24 (n=8,7)	12.5	42.9		
CDAI <150 points: Week 28 (n=4,7)	100.0	42.9		
CDAI <150 points: Week 32 (n=4,6)	50.0	83.3		
CDAI <150 points: Week 36 (n=4,6)	25.0	33.3		
CDAI <150 points: Week 40 (n=3,4)	66.7	50.0		
CDAI <150 points: Week 44 (n=3,5)	33.3	60.0		

CDAI <150 points: Week 48 (n=3,4)	0.0	50.0		
CDAI <150 points: Week 52 (n=3,3)	33.3	66.7		
CDAI <150 points: Week 56 (n=0,1)	99999	100.0		
CDAI <150 points: Week 60 (n=0,2)	99999	50.0		
CDAI <150 points: Week 64 (n=0,1)	99999	100.0		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With at Least 5-point and 8-point Reduction From Baseline in Patient Reported Outcome 2 (PRO2)

End point title	Percentage of Subjects With at Least 5-point and 8-point Reduction From Baseline in Patient Reported Outcome 2 (PRO2)

End point description:

Patient reported outcome 2-clinical response 5 (PRO2-CR5) and PRO2-CR8 = CR with reduction of 5 or more and 8 or more points in PRO2 score from baseline. PRO2 scale is derived from the CDAI and focuses on two main symptoms: abdominal pain and stool frequency. The scores from these two components are combined to give an overall PRO2 score ranging from 0 to no upper limit, with a higher score=worse outcome. FAS was used for analysis. "n" = subjects evaluable at given time points; 99999 = no data was calculated as no subjects analyzed. As planned, combined data for all periods (remission-induction, rescue and extension periods) was collected/reported in endpoint due to same dosing of E6011. From Week 14-24, subjects data analyzed simultaneously for rescue and extension period and reported collectively.

End point type	Secondary

End point timeframe:

At Weeks 2, 4, 8, 12, 14, 16, 20, 24, 28, 32, 36, 40, 44, 48, 52, 56, 60 and 64

End point values	E6011 10 mg/kg	Placebo then E6011 10 mg/kg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	12	13		
Units: percentage of subjects				
number (not applicable)				
>=5-point reduction: Week 2 (n=12,13)	25.0	38.5		
>=5-point reduction: Week 4 (n=11,13)	45.5	38.5		
>=5-point reduction: Week 8 (n=10,13)	60.0	53.8		
>=5-point reduction: Week 12 (n=10,13)	50.0	53.8		
>=5-point reduction: Week 14 (n=4,6)	25.0	50.0		
>=5-point reduction: Week 16 (n=10,10)	70.0	60.0		
>=5-point reduction: Week 20 (n=9,8)	77.8	75.0		
>=5-point reduction: Week 24 (n=8,7)	62.5	71.4		
>=5-point reduction: Week 28 (n=4,7)	100.0	85.7		
>=5-point reduction: Week 32 (n=4,6)	50.0	100.0		
>=5-point reduction: Week 36 (n=4,6)	75.0	83.3		
>=5-point reduction: Week 40 (n=3,4)	100.0	50.0		
>=5-point reduction: Week 44 (n=3,5)	100.0	60.0		

>=5-point reduction: Week 48 (n=3,4)	100.0	75.0		
>=5-point reduction: Week 52 (n=3,3)	100.0	66.7		
>=5-point reduction: Week 56 (n=0,1)	99999	100.0		
>=5-point reduction: Week 60 (n=0,2)	99999	100.0		
>=5-point reduction: Week 64 (n=0,1)	99999	100.0		
>=8-point reduction: Week 2 (n=12,13)	16.7	15.4		
>=8-point reduction: Week 4 (n=11,13)	27.3	30.8		
>=8-point reduction: Week 8 (n=10,13)	40.0	30.8		
>=8-point reduction: Week 12 (n=10,13)	40.0	30.8		
>=8-point reduction: Week 14 (n=4,6)	25.0	16.7		
>=8-point reduction: Week 16 (n=10,10)	60.0	40.0		
>=8-point reduction: Week 20 (n=9,8)	55.6	62.5		
>=8-point reduction: Week 24 (n=8,7)	50.0	57.1		
>=8-point reduction: Week 28 (n=4,7)	100.0	57.1		
>=8-point reduction: Week 32 (n=4,6)	50.0	66.7		
>=8-point reduction: Week 36 (n=4,6)	75.0	33.3		
>=8-point reduction: Week 40 (n=3,4)	100.0	50.0		
>=8-point reduction: Week 44 (n=3,5)	100.0	60.0		
>=8-point reduction: Week 48 (n=3,4)	100.0	75.0		
>=8-point reduction: Week 52 (n=3,3)	66.7	66.7		
>=8-point reduction: Week 56 (n=0,1)	99999	100.0		
>=8-point reduction: Week 60 (n=0,2)	99999	50.0		
>=8-point reduction: Week 64 (n=0,1)	99999	100.0		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Below 8 Points in PRO2

End point title	Percentage of Subjects With Below 8 Points in PRO2

End point description:

PRO2 scale is derived from the CDAI and focuses on two main symptoms: abdominal pain and stool frequency. The scores from these two components are combined to give an overall PRO2 score ranging from 0 to no upper limit, with a higher score=worse outcome. FAS was used for analysis. Here "n" = subjects who were evaluable for this endpoint at given time points and 99999 = no data was calculated as no subjects analyzed. As planned, combined data for all the periods (remission-induction, rescue and extension periods) was collected and reported in endpoint due to same dosing of E6011. From Week 14-24, subjects data analyzed simultaneously for rescue and extension period and reported collectively.

End point type	Secondary

End point timeframe:

At Weeks 2, 4, 8, 12, 14, 16, 20, 24, 28, 32, 36, 40, 44, 48, 52, 56, 60 and 64

End point values	E6011 10 mg/kg	Placebo then E6011 10 mg/kg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	12	13		
Units: percentage of subjects				
number (not applicable)				
PRO2 <8 points: Week 2 (n=12,13)	8.3	7.7		
PRO2 <8 points: Week 4 (n=11,13)	9.1	7.7		
PRO2 <8 points: Week 8 (n=10,13)	20.0	23.1		
PRO2 <8 points: Week 12 (n=10,13)	10.0	15.4		
PRO2 <8 points: Week 14 (n=4,6)	0.0	16.7		
PRO2 <8 points: Week 16 (n=10,10)	10.0	30.0		
PRO2 <8 points: Week 20 (n=9,8)	0.0	37.5		
PRO2 <8 points: Week 24 (n=8,7)	12.5	28.6		
PRO2 <8 points: Week 28 (n=4,7)	25.0	14.3		
PRO2 <8 points: Week 32 (n=4,6)	25.0	33.3		
PRO2 <8 points: Week 36 (n=4,6)	0.0	16.7		
PRO2 <8 points: Week 40 (n=3,4)	33.3	25.0		
PRO2 <8 points: Week 44 (n=3,5)	0.0	40.0		
PRO2 <8 points: Week 48 (n=3,4)	0.0	50.0		
PRO2 <8 points: Week 52 (n=3,3)	33.3	66.7		
PRO2 <8 points: Week 56 (n=0,1)	99999	100.0		
PRO2 <8 points: Week 60 (n=0,2)	99999	50.0		
PRO2 <8 points: Week 64 (n=0,1)	99999	100.0		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With at Least 50 Percent (%) Improvement in (Endoscopic Response) Simple Endoscopic Score for Crohn's Disease (SES-CD) Score at Week 12

End point title	Percentage of Subjects With at Least 50 Percent (%) Improvement in (Endoscopic Response) Simple Endoscopic Score for Crohn's Disease (SES-CD) Score at Week 12

End point description:

Endoscopic response was defined as an improvement in SES-CD of at least 50% from baseline. The SES-CD assesses following 4 components: size of ulcers, ulcerated surface, affected surface, and presence of narrowing. Each of these components was scored on scale of 0 (none/unaffected) to 3 (worst). In SES-CD, each of these 4 components are assessed in 5 segments: terminal ileum, right colon, transverse colon, left colon, and rectum. The SES-CD was the sum of the individual scores of each of the components across the five segments. The range of SES-CD scores was 0 - 12 for each segment, and 0 - 60 for the overall SES-CD score, with larger scores indicating greater severity of disease. FAS was used for analysis.

End point type	Secondary

End point timeframe:

At Week 12

End point values	Remission Induction Period: E6011 10 mg/kg	Remission Induction Period: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	13		
Units: percentage of subjects				
number (confidence interval 95%)	8.3 (0.2 to 38.5)	15.4 (1.9 to 45.4)		

Statistical analyses

Statistical analysis title	E6011 10 mg/kg vs Placebo then E6011 10 mg/kg
Comparison groups	Remission Induction Period: E6011 10 mg/kg v Remission Induction Period: Placebo
Number of subjects included in analysis	25
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference
Point estimate	-7.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-32.1
upper limit	18

Secondary: Change From Baseline in CDAI Score

End point title	Change From Baseline in CDAI Score

End point description:

CDAI was composite index of 8 disease activity variables: severity of abdominal pain, general well-being, very soft/liquid stool frequency, extra-intestinal symptoms, need for antidiarrheal drugs, presence of abdominal mass, body weight, hematocrit. Sub scores of abdominal pain (0-3), general well-being (0-4), number of very soft or liquid stools were summed. Remaining predictors were also noted and weighted to create total CDAI score ranged from 0-600 with higher score=worse outcome. FAS was used for analysis. Here "n" = subjects who were evaluable for this endpoint at given time points and 99999 = no data was calculated due to less subjects. As planned, combined data for all the periods (remission-induction, rescue and extension periods) was collected and reported in this endpoint due to same dosing of E6011. From Week 14-24, subjects data analyzed simultaneously for rescue and extension period and reported collectively.

End point type	Secondary

End point timeframe:

Baseline, at Weeks 2, 4, 8, 12, 14, 16, 20, 24, 28, 32, 36, 40, 44, 48, 52, 56, 60 and 64

End point values	E6011 10 mg/kg	Placebo then E6011 10 mg/kg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	12	13		
Units: score on a scale				
arithmetic mean (standard deviation)				
Change at Week 2 (n=12,13)	-38.0 (± 96.1)	-50.3 (± 56.7)		
Change at Week 4 (n=11,13)	-60.5 (± 102.7)	-64.5 (± 91.0)		
Change at Week 8 (n=10,13)	-92.8 (± 109.8)	-70.5 (± 113.3)		
Change at Week 12 (n=10,13)	-92.4 (± 109.0)	-69.6 (± 107.0)		
Change at Week 14 (n=4,6)	-22.0 (± 78.1)	-25.8 (± 100.8)		
Change at Week 16 (n=9,9)	-102.8 (± 95.2)	-89.3 (± 120.1)		
Change at Week 20 (n=9,7)	-115.4 (± 66.1)	-119.1 (± 136.4)		
Change at Week 24 (n=8,7)	-115.5 (± 90.1)	-100.0 (± 120.3)		
Change at Week 28 (n=3,7)	-160.7 (± 28.1)	-153.1 (± 93.5)		
Change at Week 32 (n=4,6)	-97.3 (± 95.1)	-183.7 (± 79.1)		
Change at Week 36 (n=4,6)	-136.0 (± 44.2)	-143.0 (± 109.8)		
Change at Week 40 (n=3,4)	-173.7 (± 49.0)	-157.0 (± 84.0)		
Change at Week 44 (n=3,5)	-147.3 (± 75.8)	-185.2 (± 102.9)		
Change at Week 48 (n=3,4)	-127.3 (± 56.1)	-209.8 (± 99.2)		
Change at Week 52 (n=3,3)	-103.7 (± 102.8)	-171.3 (± 162.4)		
Change at Week 56 (n=0,1)	99999 (± 99999)	-211.0 (± 99999)		
Change at Week 60 (n=0,2)	99999 (± 99999)	-145.0 (± 97.6)		
Change at Week 64 (n=0,1)	99999 (± 99999)	-240.0 (± 99999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Less Than or Equal to (<=) 2 (Endoscopic Remission) SES-CD Score at Week 12

End point title	Percentage of Subjects With Less Than or Equal to (<=) 2 (Endoscopic Remission) SES-CD Score at Week 12

End point description:

Endoscopic remission was defined as 2 or less points on SES-CD. The SES-CD assesses following 4 components: size of ulcers, ulcerated surface, affected surface, and presence of narrowing. Each of these components was scored on scale of 0 (none/unaffected) to 3 (worst). In SES-CD, each of these 4 components are assessed in 5 segments: terminal ileum, right colon, transverse colon, left colon, and rectum. The SES-CD was the sum of the individual scores of each of the components across the five

segments. The range of SES-CD scores was 0 - 12 for each segment, and 0 - 60 for the overall SES-CD score, with larger scores indicating greater severity of disease. FAS was used for analysis.

End point type	Secondary

End point timeframe:

At Week 12

End point values	Remission Induction Period: E6011 10 mg/kg	Remission Induction Period: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	13		
Units: percentage of subjects				
number (confidence interval 95%)	8.3 (0.2 to 38.5)	0.0 (0.0 to 24.7)		

Statistical analyses

Statistical analysis title	E6011 10 mg/kg vs Placebo then E6011 10 mg/kg
Comparison groups	Remission Induction Period: E6011 10 mg/kg v Remission Induction Period: Placebo
Number of subjects included in analysis	25
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference
Point estimate	8.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.3
upper limit	24

Secondary: Percent Change From Baseline in CDAI Score

End point title	Percent Change From Baseline in CDAI Score

End point description:

CDAI was composite index of 8 disease activity variables: severity of abdominal pain, general well-being, very soft/liquid stool frequency, extra-intestinal symptoms, need for antidiarrheal drugs, presence of abdominal mass, body weight, hematocrit. Sub scores of abdominal pain (0-3), general well-being (0-4), number of very soft or liquid stools were summed. Remaining predictors were also noted and weighted to create total CDAI score ranged from 0-600 with higher score=worse outcome. FAS was used for analysis. Here "n" = subjects who were evaluable for this endpoint at given time points and 99999 = no data was calculated due to less subjects. As planned, combined data for all the periods (remission-induction, rescue and extension periods) was collected and reported in this endpoint due to same dosing of E6011. From Week 14-24, subjects data analyzed simultaneously for rescue and extension period and reported collectively.

End point type	Secondary

End point timeframe:

Baseline, at Weeks 2, 4, 8, 12, 14, 16, 20, 24, 28, 32, 36, 40, 44, 48, 52, 56, 60 and 64

End point values	E6011 10 mg/kg	Placebo then E6011 10 mg/kg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	12	13		
Units: percent change				
arithmetic mean (standard deviation)				
Percent Change at Week 2 (n=12,13)	-8.9 (± 24.6)	-16.7 (± 21.1)		
Percent Change at Week 4 (n=11,13)	-16.0 (± 26.1)	-20.6 (± 26.6)		
Percent Change at Week 8 (n=10,13)	-25.8 (± 27.7)	-23.1 (± 37.1)		
Percent Change at Week 12 (n=10,13)	-25.3 (± 27.1)	-21.8 (± 33.9)		
Percent Change at Week 14 (n=4,6)	-8.3 (± 28.4)	-9.3 (± 36.6)		
Percent Change at Week 16 (n=9,9)	-29.3 (± 23.6)	-27.5 (± 37.0)		
Percent Change at Week 20 (n=9,7)	-34.5 (± 17.5)	-36.6 (± 45.4)		
Percent Change at Week 24 (n=8,7)	-34.8 (± 25.3)	-32.6 (± 44.1)		
Percent Change at Week 28 (n=3,7)	-53.6 (± 3.4)	-48.3 (± 26.2)		
Percent Change at Week 32 (n=4,6)	-31.4 (± 29.3)	-60.1 (± 28.3)		
Percent Change at Week 36 (n=4,6)	-43.3 (± 10.3)	-43.5 (± 30.2)		
Percent Change at Week 40 (n=3,4)	-53.9 (± 15.7)	-50.2 (± 23.7)		
Percent Change at Week 44 (n=3,5)	-45.7 (± 23.1)	-56.8 (± 27.1)		
Percent Change at Week 48 (n=3,4)	-39.6 (± 17.8)	-63.7 (± 25.5)		
Percent Change at Week 52 (n=3,3)	-33.0 (± 32.4)	-53.8 (± 48.2)		
Percent Change at Week 56 (n=0,1)	99999 (± 99999)	-77.0 (± 99999)		
Percent Change at Week 60 (n=0,2)	99999 (± 99999)	-51.9 (± 99999)		
Percent Change at Week 64 (n=0,1)	99999 (± 99999)	-87.6 (± 99999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in PRO2

End point title	Change From Baseline in PRO2

End point description:

PRO2 scale is derived from the CDAI and focuses on two main symptoms: abdominal pain and stool frequency. The scores from these two components are combined to give an overall PRO2 score ranging from 0 to no upper limit, with a higher score=worse outcome. FAS was used for analysis. Here "n" = subjects who were evaluable for this endpoint at given time points and 99999 =no data was calculated due to less subjects. As planned, combined data for all the periods (remission-induction, rescue and extension periods) was collected and reported in this endpoint due to same dosing of E6011. From Week 14-24, subjects data analyzed simultaneously for rescue and extension period and reported collectively.

End point type	Secondary

End point timeframe:

Baseline, at Weeks 2, 4, 8, 12, 14, 16, 20, 24, 28, 32, 36, 40, 44, 48, 52, 56, 60 and 64

End point values	E6011 10 mg/kg	Placebo then E6011 10 mg/kg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	12	13		
Units: score on a scale				
arithmetic mean (standard deviation)				
Change at Week 2 (n=12,13)	-3.1 (± 6.5)	-4.3 (± 4.0)		
Change at Week 4 (n=11,13)	-5.3 (± 6.6)	-4.9 (± 6.5)		
Change at Week 8 (n=10,13)	-6.9 (± 7.3)	-5.8 (± 7.1)		
Change at Week 12 (n=10,13)	-6.5 (± 6.2)	-5.5 (± 6.7)		
Change at Week 14 (n=4,6)	-3.0 (± 6.7)	-2.7 (± 5.4)		
Change at Week 16 (n=10,9)	-8.1 (± 5.7)	-6.1 (± 7.6)		
Change at Week 20 (n=9,7)	-7.9 (± 4.2)	-8.3 (± 9.2)		
Change at Week 24 (n=8,7)	-6.5 (± 6.4)	-6.9 (± 7.4)		
Change at Week 28 (n=3,7)	-9.0 (± 1.0)	-9.6 (± 5.7)		
Change at Week 32 (n=4,6)	-5.5 (± 6.1)	-12.0 (± 6.2)		
Change at Week 36 (n=4,6)	-9.0 (± 7.0)	-9.0 (± 6.1)		
Change at Week 40 (n=3,4)	-13.0 (± 1.7)	-6.3 (± 6.8)		
Change at Week 44 (n=3,5)	-11.0 (± 2.0)	-9.4 (± 7.7)		
Change at Week 48 (n=3,4)	-8.7 (± 0.6)	-11.8 (± 6.6)		
Change at Week 52 (n=3,3)	-8.3 (± 3.1)	-11.0 (± 8.5)		
Change at Week 56 (n=0,1)	99999 (± 99999)	-13.0 (± 99999)		
Change at Week 60 (n=0,2)	99999 (± 99999)	-9.5 (± 6.4)		
Change at Week 64 (n=0,1)	99999 (± 99999)	-15.0 (± 99999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline in PRO2

End point title	Percent Change From Baseline in PRO2

End point description:

PRO2 scale is derived from the CDAI and focuses on two main symptoms: abdominal pain and stool frequency. The scores from these two components are combined to give an overall PRO2 score ranging from 0 to no upper limit, with a higher score=worse outcome. FAS was used for analysis. Here "n" = subjects who were evaluable for this endpoint at given time points and 99999 = no data was calculated due to less subjects. As planned, combined data for all the periods (remission-induction, rescue and extension periods) was collected and reported in this endpoint due to same dosing of E6011. From Week 14-24, subjects data analyzed simultaneously for rescue and extension period and reported collectively.

End point type	Secondary

End point timeframe:

At Weeks 2, 4, 8, 12, 14, 16, 20, 24, 28, 32, 36, 40, 44, 48, 52, 56, 60 and 64

End point values	E6011 10 mg/kg	Placebo then E6011 10 mg/kg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	12	13		
Units: percent change				
arithmetic mean (standard deviation)				
Percent Change at Week 2 (n=12,13)	-13.5 (± 31.3)	-20.9 (± 20.0)		
Percent Change at Week 4 (n=11,13)	-23.0 (± 29.8)	-22.9 (± 28.4)		
Percent Change at Week 8 (n=10,13)	-30.1 (± 33.0)	-29.2 (± 34.6)		
Percent Change at Week 12 (n=10,13)	-29.4 (± 28.0)	-25.8 (± 31.0)		
Percent Change at Week 14 (n=4,6)	-13.4 (± 28.6)	-17.6 (± 32.7)		
Percent Change at Week 16 (n=10,9)	-36.8 (± 25.0)	-27.9 (± 34.4)		
Percent Change at Week 20 (n=9,7)	-36.2 (± 16.8)	-37.6 (± 46.7)		
Percent Change at Week 24 (n=8,7)	-30.0 (± 28.0)	-35.9 (± 41.1)		
Percent Change at Week 28 (n=3,7)	-47.7 (± 9.2)	-46.2 (± 23.7)		
Percent Change at Week 32 (n=4,6)	-25.1 (± 32.7)	-58.3 (± 30.3)		
Percent Change at Week 36 (n=4,6)	-37.1 (± 25.5)	-42.9 (± 24.6)		
Percent Change at Week 40 (n=3,4)	-56.4 (± 14.3)	-31.2 (± 32.6)		
Percent Change at Week 44 (n=3,5)	-46.9 (± 9.1)	-45.3 (± 32.5)		
Percent Change at Week 48 (n=3,4)	-37.3 (± 7.2)	-57.2 (± 26.7)		
Percent Change at Week 52 (n=3,3)	-38.4 (± 22.2)	-56.1 (± 34.6)		
Percent Change at Week 56 (n=0,1)	99999 (± 99999)	-81.3 (± 99999)		
Percent Change at Week 60 (n=0,2)	99999 (± 99999)	-59.4 (± 39.8)		
Percent Change at Week 64 (n=0,1)	99999 (± 99999)	-93.8 (± 99999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in SES-CD Score at Week 12

End point title	Change From Baseline in SES-CD Score at Week 12

End point description:

The SES-CD assesses the following 4 components: size of ulcers, ulcerated surface, affected surface, and presence of narrowing. Each of these components was scored on a scale of 0 (none/unaffected) to 3 (worst). In the SES-CD, each of these 4 components are assessed in the five segments: terminal ileum, right colon, transverse colon, left colon, and rectum. The SES-CD was the sum of the individual scores of each of the components across the five segments. The range of SES-CD scores was 0 - 12 for each segment, and 0 - 60 for the overall SES-CD score, with larger scores indicating greater severity of disease. FAS was used for analysis. Here, "number of subjects analyzed” = subjects who were evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Baseline, at Week 12

End point values	Remission Induction Period: E6011 10 mg/kg	Remission Induction Period: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	13		
Units: score on a scale				
arithmetic mean (standard deviation)	1.4 (± 4.9)	-3.5 (± 4.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Steroid Dosage in Subjects Concomitantly Using Adrenocorticosteroids up to Week 64

End point title	Change from Baseline in Steroid Dosage in Subjects Concomitantly Using Adrenocorticosteroids up to Week 64

End point description:

Change from baseline in steroid dosage in subjects concomitantly using adrenocorticosteroids up to Week 64 was reported. FAS was used for analysis. Here, "number of subjects analyzed" = subjects who were evaluable for this endpoint. As planned, combined data for all the periods (remission-induction, rescue, extension and post observation periods) was collected and reported in outcome measure due to same dosing of E6011.

End point type	Secondary

End point timeframe:

Baseline up to Week 64

End point values	E6011 10 mg/kg	Placebo then E6011 10 mg/kg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	3	6		
Units: milligram per day (mg/day)				
arithmetic mean (standard deviation)	0 (± 0)	0 (± 0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline in Steroid Dosage in Subjects Concomitantly Using Adrenocorticosteroids up to Week 64

End point title	Percent Change From Baseline in Steroid Dosage in Subjects Concomitantly Using Adrenocorticosteroids up to Week 64

End point description:

Percent change from baseline in steroid dosage in subjects concomitantly using adrenocorticosteroids up to Week 64 was reported. FAS was used for analysis. Here, "number of subjects analyzed" = subjects who were evaluable for this endpoint. As planned, combined data for all the periods (remission-induction, rescue, extension and post observation periods) was collected and reported in outcome measure due to same dosing of E6011.

End point type	Secondary

End point timeframe:

Baseline up to Week 64

End point values	E6011 10 mg/kg	Placebo then E6011 10 mg/kg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	3	6		
Units: percent change				
arithmetic mean (standard deviation)	0 (± 0)	0 (± 0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Who Achieved Steroid-free Improvement up to Week 64

End point title	Percentage of Subjects Who Achieved Steroid-free Improvement up to Week 64

End point description:

Steroid-free clinical improvement=clinical response(CR70,CR100,PRO2-CR5;PRO2-CR8 responses) in subjects who became steroid free through steroid reduction.CR70; CR100=clinical response with decrease of >=70;>=100 point from baseline,respectively.PRO2-CR5 and PRO2-CR8=clinical response with decrease of >=5 or 8 point from baseline,respectively.CDAI score ranged from 0-600;higher score=worse outcome. . PRO2 scale is derived from the CDAI and focuses on two main symptoms: abdominal pain and stool frequency. The scores from these two components are combined to give an overall PRO2 score ranging from 0 to no upper limit, with a higher score=worse outcome. FAS was used."N"=subjects evaluable for endpoint.As planned, combined data for all periods(remission-induction, rescue and extension periods)was collected/reported in endpoint due to same dosing of E6011.Steroid-free remission was assessed in subjects who were concomitantly taking adrenocorticosteroid.

End point type	Secondary

End point timeframe:

Up to Week 64

End point values	E6011 10 mg/kg	Placebo then E6011 10 mg/kg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	3	6		
Units: percentage of subjects	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Who Achieved Steroid-free Remission up to Week 64

End point title	Percentage of Subjects Who Achieved Steroid-free Remission up to Week 64

End point description:

Steroid-free remission =clinical remission (CDAI remission or PRO2-remission) in subjects who became steroid free through steroid reduction. CDAI = score below 150 points. PRO2-remission = PRO2- score less than 8-points. CDAI system was composite index of 8 disease activity variables. Total CDAI score ranged from 0-600 with higher score=worse outcome. . PRO2 scale is derived from the CDAI and focuses on two main symptoms: abdominal pain and stool frequency. The scores from these two components are combined to give an overall PRO2 score ranging from 0 to no upper limit, with a higher score=worse outcome. FAS was used. "N" =subjects who were evaluable for endpoint. As planned, combined data for all periods (remission-induction, rescue and extension periods) was collected/reported in endpoint due to same dosing of E6011. Steroid-free remission was assessed in subjects who were concomitantly taking adrenocorticosteroid.

End point type	Secondary

End point timeframe:

Up to Week 64

End point values	E6011 10 mg/kg	Placebo then E6011 10 mg/kg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	3	6		
Units: percentage of subjects	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline in SES-CD Score at Week 12

End point title	Percent Change From Baseline in SES-CD Score at Week 12

End point description:

The SES-CD assesses the following 4 components: size of ulcers, ulcerated surface, affected surface, and presence of narrowing. Each of these components was scored on a scale of 0 (none/unaffected) to 3 (worst). In the SES-CD, each of these 4 components are assessed in the five segments: terminal ileum, right colon, transverse colon, left colon, and rectum. The SES-CD was the sum of the individual scores of each of the components across the five segments. The range of SES-CD scores was 0 - 12 for each segment, and 0 - 60 for the overall SES-CD score, with larger scores indicating greater severity of disease. FAS was used for analysis. Here, "number of subjects analyzed" = subjects who were evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Baseline, at Week 12

End point values	Remission Induction Period: E6011 10 mg/kg	Remission Induction Period: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	13		
Units: percent change				
arithmetic mean (standard deviation)	-0.3 (± 45.6)	-19.2 (± 33.2)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Remission induction period: From the first dose of the study drug (Week 0) up to Week 12; Rescue period: From Week 12 up to Week 24; Extension period: Week 12 up to Week 64; Post-observation period: Up to 70 days after last dose of study drug

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	25.0

Reporting groups

Reporting group title	Remission Induction Period: E6011 10 mg/kg

Reporting group description:

Subjects received E6011 10 mg/kg, IV infusion once, at Weeks 0,1, 2 then every 2 weeks up Week 10 during Remission Induction Period.

Reporting group title	Remission Induction Period: Placebo

Reporting group description:

Subjects received placebo, IV infusion once, at Weeks 0,1, 2 then every 2 weeks up Week 10 during Remission Induction Period.

Reporting group title	Rescue Period: E6011 10 mg/kg

Reporting group description:

Subjects received E6011 10 mg/kg, IV infusion once, at Weeks 12, 13, 14 then every 2 weeks up to Week 22 during Rescue Period.

Reporting group title	Post-observation Period: Placebo to E6011 10 mg/kg

Reporting group description:

Subjects who received placebo in the remission induction period and who were switched to receive E6011 10 mg/kg in Rescue or Extension periods were observed during Post-observation Period for 70 days after last dose.

Reporting group title	Extension Period: E6011 10 mg/kg

Reporting group description:

Subjects with response at Week 12 and Week 24 received E6011 10 mg/kg, IV infusion once, every 4 weeks from Week 12 to Week 48 and Week 24 to Week 60, respectively, during the Extension Period.

Reporting group title	Extension Period: Placebo to E6011 10 mg/kg

Reporting group description:

Subjects who received placebo in the remission induction period, who had response at Week 12 and Week 24 received E6011 10 mg/kg, IV infusion once, every 4 weeks from Week 12 to Week 48 and Week 24 to Week 60, respectively during the Extension Period.

Reporting group title	Post-observation Period: E6011 10 mg/kg

Reporting group description:

Subjects who received E6011 10 mg/kg in any of the treatment periods were observed during Post-observation Period for 70 days after last dose.

Reporting group title	Rescue Period: Placebo to E6011 10 mg/kg

Reporting group description:

Subjects who received placebo in the remission induction period received E6011 10 mg/kg, IV infusion once, at Weeks 12, 13, 14 then every 2 weeks up to Week 22 during Rescue the Period.

Serious adverse events	Remission Induction Period: E6011 10 mg/kg	Remission Induction Period: Placebo	Rescue Period: E6011 10 mg/kg
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 12 (0.00%)	1 / 13 (7.69%)	0 / 5 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Gastrointestinal disorders			
Lower Gastrointestinal Haemorrhage			
subjects affected / exposed	0 / 12 (0.00%)	0 / 13 (0.00%)	0 / 5 (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
Crohn's Disease			
subjects affected / exposed	0 / 12 (0.00%)	0 / 13 (0.00%)	0 / 5 (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
Metabolism and nutrition disorders			
Hypokalaemia			
subjects affected / exposed	0 / 12 (0.00%)	1 / 13 (7.69%)	0 / 5 (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

Serious adverse events	Post-observation Period: Placebo to E6011 10 mg/kg	Extension Period: E6011 10 mg/kg	Extension Period: Placebo to E6011 10 mg/kg
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 13 (7.69%)	0 / 7 (0.00%)	0 / 8 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Gastrointestinal disorders			
Lower Gastrointestinal Haemorrhage			
subjects affected / exposed	0 / 13 (0.00%)	0 / 7 (0.00%)	0 / 8 (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
Crohn's Disease			
subjects affected / exposed	1 / 13 (7.69%)	0 / 7 (0.00%)	0 / 8 (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
Metabolism and nutrition disorders			

Hypokalaemia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 7 (0.00%)	0 / 8 (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

Serious adverse events	Post-observation Period: E6011 10 mg/kg	Rescue Period: Placebo to E6011 10 mg/kg	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 12 (0.00%)	2 / 7 (28.57%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Gastrointestinal disorders			
Lower Gastrointestinal Haemorrhage			
subjects affected / exposed	0 / 12 (0.00%)	1 / 7 (14.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Crohn's Disease			
subjects affected / exposed	0 / 12 (0.00%)	1 / 7 (14.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Hypokalaemia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Remission Induction Period: E6011 10 mg/kg	Remission Induction Period: Placebo	Rescue Period: E6011 10 mg/kg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 12 (50.00%)	5 / 13 (38.46%)	3 / 5 (60.00%)
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 12 (8.33%)	0 / 13 (0.00%)	1 / 5 (20.00%)
occurrences (all)	1	0	2

Immune system disorders			
Immunisation Reaction			
subjects affected / exposed	0 / 12 (0.00%)	0 / 13 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Investigations			
Weight Decreased			
subjects affected / exposed	0 / 12 (0.00%)	0 / 13 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Blood Creatine Phosphokinase Increased			
subjects affected / exposed	0 / 12 (0.00%)	0 / 13 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Injury, poisoning and procedural complications			
Compression Fracture			
subjects affected / exposed	0 / 12 (0.00%)	0 / 13 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Cardiomyopathy			
subjects affected / exposed	0 / 12 (0.00%)	0 / 13 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Atrioventricular Block First Degree			
subjects affected / exposed	0 / 12 (0.00%)	0 / 13 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Facial Paralysis			
subjects affected / exposed	0 / 12 (0.00%)	1 / 13 (7.69%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Headache			
subjects affected / exposed	1 / 12 (8.33%)	1 / 13 (7.69%)	0 / 5 (0.00%)
occurrences (all)	1	1	0
Migraine			
subjects affected / exposed	0 / 12 (0.00%)	1 / 13 (7.69%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 12 (8.33%)	0 / 13 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal disorders			

Crohn's Disease			
subjects affected / exposed	0 / 12 (0.00%)	0 / 13 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Abdominal Pain Upper			
subjects affected / exposed	1 / 12 (8.33%)	0 / 13 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Toothache			
subjects affected / exposed	0 / 12 (0.00%)	1 / 13 (7.69%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Haemorrhoids			
subjects affected / exposed	0 / 12 (0.00%)	0 / 13 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Stomatitis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 13 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	1 / 12 (8.33%)	0 / 13 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	0 / 12 (0.00%)	0 / 13 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 12 (8.33%)	0 / 13 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Temporomandibular Joint Syndrome			
subjects affected / exposed	0 / 12 (0.00%)	1 / 13 (7.69%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Myalgia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 13 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Muscle Spasms			
subjects affected / exposed	0 / 12 (0.00%)	0 / 13 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1

Infections and infestations			
Covid-19			
subjects affected / exposed	1 / 12 (8.33%)	0 / 13 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Conjunctivitis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 13 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Respiratory Tract Infection			
subjects affected / exposed	0 / 12 (0.00%)	0 / 13 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Upper Respiratory Tract Infection			
subjects affected / exposed	0 / 12 (0.00%)	0 / 13 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Hypokalaemia			
subjects affected / exposed	0 / 12 (0.00%)	1 / 13 (7.69%)	0 / 5 (0.00%)
occurrences (all)	0	2	0

Non-serious adverse events	Post-observation Period: Placebo to E6011 10 mg/kg	Extension Period: E6011 10 mg/kg	Extension Period: Placebo to E6011 10 mg/kg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 13 (7.69%)	1 / 7 (14.29%)	5 / 8 (62.50%)
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 7 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Immune system disorders			
Immunisation Reaction			
subjects affected / exposed	0 / 13 (0.00%)	1 / 7 (14.29%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Investigations			
Weight Decreased			
subjects affected / exposed	0 / 13 (0.00%)	0 / 7 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Blood Creatine Phosphokinase Increased			
subjects affected / exposed	0 / 13 (0.00%)	0 / 7 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0

Injury, poisoning and procedural complications			
Compression Fracture			
subjects affected / exposed	0 / 13 (0.00%)	0 / 7 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Cardiac disorders			
Cardiomyopathy			
subjects affected / exposed	0 / 13 (0.00%)	0 / 7 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Atrioventricular Block First Degree			
subjects affected / exposed	0 / 13 (0.00%)	0 / 7 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Nervous system disorders			
Facial Paralysis			
subjects affected / exposed	0 / 13 (0.00%)	0 / 7 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Headache			
subjects affected / exposed	0 / 13 (0.00%)	0 / 7 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Migraine			
subjects affected / exposed	0 / 13 (0.00%)	0 / 7 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 7 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
Crohn's Disease			
subjects affected / exposed	0 / 13 (0.00%)	0 / 7 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Abdominal Pain Upper			
subjects affected / exposed	0 / 13 (0.00%)	0 / 7 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Toothache			
subjects affected / exposed	0 / 13 (0.00%)	0 / 7 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Haemorrhoids			

subjects affected / exposed	0 / 13 (0.00%)	0 / 7 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Stomatitis			
subjects affected / exposed	1 / 13 (7.69%)	0 / 7 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	0 / 13 (0.00%)	0 / 7 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	0 / 13 (0.00%)	0 / 7 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 7 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Temporomandibular Joint Syndrome			
subjects affected / exposed	0 / 13 (0.00%)	0 / 7 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Myalgia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 7 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Muscle Spasms			
subjects affected / exposed	0 / 13 (0.00%)	0 / 7 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Covid-19			
subjects affected / exposed	0 / 13 (0.00%)	0 / 7 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Conjunctivitis			
subjects affected / exposed	0 / 13 (0.00%)	0 / 7 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Respiratory Tract Infection			
subjects affected / exposed	0 / 13 (0.00%)	0 / 7 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1

Upper Respiratory Tract Infection subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	0 / 7 (0.00%) 0	1 / 8 (12.50%) 3
Metabolism and nutrition disorders Hypokalaemia subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	0 / 7 (0.00%) 0	0 / 8 (0.00%) 0

Non-serious adverse events	Post-observation Period: E6011 10 mg/kg	Rescue Period: Placebo to E6011 10 mg/kg	
Total subjects affected by non-serious adverse events subjects affected / exposed	2 / 12 (16.67%)	4 / 7 (57.14%)	
General disorders and administration site conditions Pyrexia subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	2 / 7 (28.57%) 2	
Immune system disorders Immunisation Reaction subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 7 (0.00%) 0	
Investigations Weight Decreased subjects affected / exposed occurrences (all) Blood Creatine Phosphokinase Increased subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0 0 / 12 (0.00%) 0	1 / 7 (14.29%) 1 0 / 7 (0.00%) 0	
Injury, poisoning and procedural complications Compression Fracture subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 7 (0.00%) 0	
Cardiac disorders Cardiomyopathy subjects affected / exposed occurrences (all) Atrioventricular Block First Degree	0 / 12 (0.00%) 0	0 / 7 (0.00%) 0	

subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 7 (0.00%) 0	
Nervous system disorders Facial Paralysis subjects affected / exposed occurrences (all) Headache subjects affected / exposed occurrences (all) Migraine subjects affected / exposed occurrences (all)	 0 / 12 (0.00%) 0 0 / 12 (0.00%) 0 0 / 12 (0.00%) 0	 0 / 7 (0.00%) 0 0 / 7 (0.00%) 0 0 / 7 (0.00%) 0	
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all)	 0 / 12 (0.00%) 0	 0 / 7 (0.00%) 0	
Gastrointestinal disorders Crohn's Disease subjects affected / exposed occurrences (all) Abdominal Pain Upper subjects affected / exposed occurrences (all) Toothache subjects affected / exposed occurrences (all) Haemorrhoids subjects affected / exposed occurrences (all) Stomatitis subjects affected / exposed occurrences (all)	 1 / 12 (8.33%) 1 0 / 12 (0.00%) 0 0 / 12 (0.00%) 0 0 / 12 (0.00%) 0 0 / 12 (0.00%) 0	 0 / 7 (0.00%) 0 0 / 7 (0.00%) 0 0 / 7 (0.00%) 0 0 / 7 (0.00%) 0 0 / 7 (0.00%) 0	
Skin and subcutaneous tissue disorders Pruritus subjects affected / exposed occurrences (all)	 0 / 12 (0.00%) 0	 0 / 7 (0.00%) 0	
Renal and urinary disorders			

Dysuria			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Temporomandibular Joint Syndrome			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Myalgia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Muscle Spasms			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Infections and infestations			
Covid-19			
subjects affected / exposed	0 / 12 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Conjunctivitis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Respiratory Tract Infection			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Upper Respiratory Tract Infection			
subjects affected / exposed	0 / 12 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Metabolism and nutrition disorders			
Hypokalaemia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
19 September 2018	Protocol amendment 1: The main changes included: The expected number of sites was increased from 16 to 17. Some corrections were made.
05 November 2018	Protocol amendment 2 (continued): The emergency code break procedure (section 9.5.4.5) was adapted from web-based to IWRS based. The first secondary endpoint was amended to include CDAI remission rate (proportion of subjects with below 150 points). The second secondary endpoint was changed from "Proportion of subjects with at least 5- point reduction in PRO2 from baseline (PRO2-CR5 response rate), proportion of subjects with at least 8-point reduction from baseline (PRO2-CR8 response rate), and proportion of subjects with reductions below 8 points (PRO2-resmission rate) at each CDAI remission rate evaluation time." to "Proportion of subjects with at least 5-point reduction in PRO2 from baseline (PRO2-CR5 response rate), proportion of subjects with at least 8-point reduction from baseline (PRO2-CR8 response rate), and proportion of subjects with below 8 points (PRO2-resmission rate) at each evaluation time". The last secondary endpoint was changed from: "Steroid-free remission rate and steroid-free response rate in subjects concomitantly using adrenocorticosteroids is to be tabulated by treatment group and evaluation time. Summary statistics for steroid dosage, change and percent change from baseline are also to be calculated for each treatment group and evaluation time" to "In subjects who were concomitantly taking adrenocorticosteroid, dosage, change and percent change of adrenocorticosteroid from baseline". In section 11.4: Data recording, the following sentence was deleted: "For the CDAI assessment items assessed by the investigator, the data entered by investigators in the site staff part of the electronic patient reported outcomes are to be used for evaluations.
05 November 2018	Protocol amendment 2: The study design in the synopsis was amended to specify that the screening test had to be carried out within 42 days prior to the start of the IMP administration after obtaining consent, and before the double-blind period. The expected number of sites was increased from 17 to 18. Exclusion criterion 28 and 34 was amended: to clarify that subject with cervical cancers with no metastasis or recurrence observed for 5 more years at the time of giving consent were not excluded from the study. The highly effective contraception methods were altered from including “Contraceptive ring (IUD) or intrauterine progesterone-releasing system (IUS)” to “Use of intrauterine device (IUD)”. (As the use of an intrauterine progesterone-releasing system (IUS) was allowed in the Japanese protocol, exclusion criteria 34 was not altered in the Japanese protocol.) It was stated in the synopsis that safety was analysed using the safety analysis set. The process of keeping the IMP blinded in section 9.4.1. was amended by adding non-transparent sealing covers and seal stickers, which had to be intact during administration. Section 9.4.3: Method of allocating subjects to treatment groups: Statements about stratified allocation algorithm created by IWRS and randomization manager creating a drug number table of randomized drugs were removed. Section 9.4.6.2: Maintenance of Blinding: A statement that randomization manager is to seal the allocation number table immediately upon creating it, and carefully store it until code break, was removed. Section 9.5.1.2.1: History of Crohn's disease: disease types were changed from "enteritis, enterocolitis, colitis" to "small intestine-type, small and large intestine-type, or large intestine-type". Blood sampled for viral and TB test was reduced from 22 mL to 18 mL. (The blood sample for viral and TB testing was 23 mL throughout the study in the Japanese protocol.)

03 April 2020	Protocol amendment 6: Inclusion criterion 5 was changed to amend the number of biologics that the subjects could have taken without response to be eligible to enter the clinical study from one to "one or two". In addition, "subjects who cannot taper oral adrenocorticosteroids" was changed to "subjects who cannot taper adrenocorticosteroids". Exclusion criterion 17 was amended to exclude subjects with AST or ALT three times the upper limit (previously: twice the upper limit) and subjects with serum creatinine levels more than 1.5 times the upper normal limit (previously: 1.5 mg/dL). Vedolizumab intake was moved from exclusion criterion 27, where it was not permitted any time in the past to exclusion criterion 24, where it was not permitted within 8 weeks prior to the start of the IMP administration. Chest X-ray tests were removed as standard safety examinations throughout the protocol, and were only to be done during screening. Updates in the study schedule (recruitment planned: September 2018 to April 2021, treatment planned: October 2018 to June 2021, follow-up planned: June 2021 to June 2023, close out: July 2023). Added, that the haematocrit value used to calculate the CDAI score at Week 0 or screening test (screening test value may also be used if this is within 7 days of the date of the CDAI assessment).
01 June 2020	Protocol amendment 7: Russia was added as a study country. Inclusion criterion 5 was changed to delete the number of biologics ("one or two") that the subjects could have taken without response to be eligible to enter the clinical study.
01 October 2020	Protocol amendment 8: The anticipated number of Japanese subjects was updated from 12 to 22, the anticipated number of non-Japanese subjects was updated from 28 to 18. Updates in the study schedule (end of recruitment planned: October 2020). The analysis of blood biomarkers was added to the protocol.
09 April 2021	Protocol amendment 10: Exclusion criterion 10 was amended to include. "In addition, subjects who tested positive for HCV antibody and who were at least 24 weeks post-treatment may participate in clinical trial as long as negative HCV-RNA is confirmed during screening period." This was also added to section 9.5.1.2.4: Other items assessed during screening period in this clinical trial or specific to disease area. Exclusion criterion 20 was changed from "Subjects with an infectious disease requiring hospitalisation or intravenous administration of antibiotics (including antiviral drugs) within 4 weeks prior to the start of IMP administration, or oral administration of antibiotics (including antiviral drugs) within 2 weeks prior to start of IMP administration" to "Subjects who required any one of following treatments of infection; "hospitalization within 4 weeks prior to start of IMP administration", "intravenous treatment of antibiotics (including antiviral drugs) within 4 weeks prior to start of IMP administration", or "oral treatment of antibiotics (including antiviral drugs) within 2 weeks prior to start of IMP administration". Furthermore, with regard to novel coronavirus infection (COVID-19), subjects who required any one of following treatments: "hospitalization within 4 weeks prior to start of IMP administration", "any intravenous treatment within 4 weeks prior to start of IMP administration" or "any oral treatment within 2 weeks prior to start of IMP administration". Exclusion criterion 25 was amended to include vaccines with toxicity equivalent to that of live vaccine. The same changes were made in section 9.4.7: Prior treatment and concomitant treatment and section 9.4.7.1.1: Prohibited concomitant therapies and concomitant drugs. Section 9.4.7.1.2 Restricted concomitant drugs was amended to include: "The SARS-CoV-2 vaccine may be used concomitantly, but it should not be administered within 7 days before or after IMP administration."
17 September 2021	Protocol Amendment 11: Exclusion criterion 25 was amended. Vaccines with a toxicity equivalent to that of a live vaccine were deleted and "vaccine that is considered to have a risk of infection, such as a virus vector vaccine that uses a virus that retains its ability to proliferate" was added. The same changes were made in section 9.4.7: Prior treatment and concomitant treatment and section 9.4.7.1.1: Prohibited concomitant therapies and concomitant drugs. Updates in the study schedule (end of treatment planned: January 2023, end of follow-up planned: January 2025, close out: February 2025).
18 April 2022	Protocol Amendment 12: Updates in the study schedule (end of treatment planned: April 2022 instead of January 2023, end of follow-up planned: April 2024 instead of January 2025, close out: May 2024 instead of February 2025). The target sample size in section 9.7.2 was reduced to 25, which was the number of enrolled subjects at the end of recruitment. However, the analyses were not changed.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported