Clinical trial results:
A Phase 2, Double-blind, Randomized, Placebo-Controlled, Multicenter Study Evaluating the Safety and Efficacy of GS-5745 in Subjects with Moderately to Severely Active Crohn's Disease

Summary

EudraCT number	2015-001249-10
Trial protocol	HU DE CZ ES GB IS IT
Global end of trial date	22 December 2016

Results information

Result version number	v3 (current)
This version publication date	18 May 2019
First version publication date	19 November 2017
Version creation reason	• Correction of full data set Adding text to "Limitations and Caveats" section

Trial information

Trial identification

Sponsor protocol code	GS-US-395-1663

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02405442
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Gilead Sciences
Sponsor organisation address	333 Lakeside Drive, Foster City, CA, United States, 94404
Public contact	Clinical Trials Mailbox, Gilead Sciences International Ltd , ClinicalTrialDisclosures@gilead.com
Scientific contact	Clinical Trials Mailbox, Gilead Sciences International Ltd , ClinicalTrialDisclosures@gilead.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	22 December 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	30 November 2016
Global end of trial reached?	Yes
Global end of trial date	22 December 2016
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The primary objectives of this study were as follows:
1) To evaluate the efficacy of an 8-week induction regimen of andecaliximab (formerly GS-5745) to induce a clinical response, defined as a stool frequency and abdominal pain composite (PRO2) score ≤ 8 at Week 8
2) To evaluate the efficacy of an 8-week induction regimen of andecaliximab to induce an endoscopic response, defined as a reduction in the Simple Endoscopic Score for Crohn's Disease (SES-CD) of ≥ 50% from baseline at Week 8

The study consisted of a Blinded Treatment Period of 8 weeks followed by an Open-Label Extension. Participants who completed the Blinded Treatment Period were eligible to enroll in the optional Open-Label Extension for an additional 44 weeks. Participants who completed Week 52 assessments were eligible to enter the Extended Treatment Phase to continue treatment with andecaliximab for an additional 156 weeks.

Protection of trial subjects:

The protocol and consent/assent forms were submitted by each investigator to a duly constituted Independent Ethics Committee (IEC) or Institutional Review Board (IRB) for review and approval before study initiation. All revisions to the consent/assent forms (if applicable) after initial IEC/IRB approval were submitted by the investigator to the IEC/IRB for review and approval before implementation in accordance with regulatory requirements.

This study was conducted in accordance with recognized international scientific and ethical standards, including but not limited to the International Conference on Harmonization guideline for Good Clinical Practice (ICH GCP) and the original principles embodied in the Declaration of Helsinki.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	30 April 2015
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Australia: 9
Country: Number of subjects enrolled	New Zealand: 5
Country: Number of subjects enrolled	Canada: 4
Country: Number of subjects enrolled	South Africa: 3
Country: Number of subjects enrolled	Italy: 2
Country: Number of subjects enrolled	United States: 104
Country: Number of subjects enrolled	Poland: 16

Country: Number of subjects enrolled	Spain: 5
Country: Number of subjects enrolled	United Kingdom: 6
Country: Number of subjects enrolled	Czech Republic: 5
Country: Number of subjects enrolled	France: 8
Country: Number of subjects enrolled	Germany: 15
Country: Number of subjects enrolled	Hungary: 5
Worldwide total number of subjects	187
EEA total number of subjects	62

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)	179
From 65 to 84 years	8
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were enrolled at study sites in North America, Europe, South Africa, and Asia Pacific. The first participant was screened on 30 April 2015. The last study visit occurred on 22 December 2016.

Pre-assignment

Screening details:

315 participants were screened.

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	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Andecaliximab 150 mg every 2 weeks

Arm description:

• Double-blind Phase: 1 single-use prefilled syringe (PFS) of andecaliximab 150 mg and matching placebo coadministered at Weeks 0, 2, 4, and 6; 2 single-use PFS of placebo coadministered at Weeks 1, 3, 5, and 7
• Open-label Phase and Extended Treatment Phase: 1 single-use PFS of andecaliximab 150 mg administered weekly

Arm type	Experimental
Investigational medicinal product name	Andecaliximab
Investigational medicinal product code	
Other name	GS-5745
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

• Double-blind Phase: 1 single-use PFS of andecaliximab 150 mg every 2 weeks for 8 weeks
• Open-label Phase and Extended Treatment Phase: 1 single-use PFS of andecaliximab 150 mg administered weekly

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Double-blind Phase: 1 single-use PFS of placebo coadministered with andicaliximab at Weeks 0, 2, 4, and 6 and 2 single-use PFS of placebo administered at Weeks 1, 3, 5, and 7

Arm title	Andecaliximab 150 mg weekly

Arm description:

• Double-blind Phase: 1 single-use PFS of andecaliximab 150 mg and matching placebo coadministered weekly for 8 weeks
• Open-label Phase and Extended Treatment Phase: 1 single-use PFS of andecaliximab 150 mg administered weekly

Arm type	Experimental

Investigational medicinal product name	Andecaliximab
Investigational medicinal product code	
Other name	GS-5745
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

• Double-blind Phase: 1 single-use PFS of andecaliximab 150 mg weekly for 8 weeks
• Open-label Phase and Extended Treatment Phase: 1 single-use PFS of andecaliximab 150 mg administered weekly

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled injector
Routes of administration	Subcutaneous use

Dosage and administration details:

Double-blind Phase: 1 single-use PFS of placebo administered weekly for 8 weeks

Arm title	Andecaliximab 300 mg weekly

Arm description:

• Double-blind Phase: 2 single-use PFS of andecaliximab 150 mg coadministered weekly for 8 weeks
• Open-label Phase and Extended Treatment Phase: 1 single-use PFS of andecaliximab 150 mg administered weekly

Arm type	Experimental
Investigational medicinal product name	Andecaliximab
Investigational medicinal product code	
Other name	GS-5745
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

• Double-blind Phase: 2 single-use PFS of andecaliximab 150 mg weekly
• Open-label and Extended Treatment Phase: 1 single-use PFS of andecaliximab 150 mg administered weekly

Arm title	Placebo Group

Arm description:

• Double-blind Phase: 2 single-use PFS of placebo coadministered weekly for 8 weeks
• Open-label and Extended Treatment Phase: 1 single-use PFS of andecaliximab 150 mg administered weekly

Arm type	Experimental
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Double-blind Phase: 2 single-use PFS of placebo administered weekly for 8 weeks

Investigational medicinal product name	Andecaliximab
Investigational medicinal product code	
Other name	GS-5745
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Open-label Phase and Extended Treatment Phase: 1 single-use PFS of andecaliximab 150 mg weekly

Number of subjects in period 1	Andecaliximab 150 mg every 2 weeks	Andecaliximab 150 mg weekly	Andecaliximab 300 mg weekly
Started	53	53	53
Completed	0	0	0
Not completed	53	53	53
Study terminated by sponsor	31	31	31
Adverse event	5	2	6
Study disease-related symptoms	1	2	3
Investigator's discretion	15	13	10
Withdrew consent	1	3	3
Lost to follow-up	-	1	-
Lack of efficacy	-	1	-

Number of subjects in period 1	Placebo Group
Started	28
Completed	0
Not completed	28
Study terminated by sponsor	16
Adverse event	5
Study disease-related symptoms	2
Investigator's discretion	3
Withdrew consent	1
Lost to follow-up	-
Lack of efficacy	1

Baseline characteristics

Reporting groups

Reporting group title	Andecaliximab 150 mg every 2 weeks

Reporting group description:

• Double-blind Phase: 1 single-use prefilled syringe (PFS) of andecaliximab 150 mg and matching placebo coadministered at Weeks 0, 2, 4, and 6; 2 single-use PFS of placebo coadministered at Weeks 1, 3, 5, and 7
• Open-label Phase and Extended Treatment Phase: 1 single-use PFS of andecaliximab 150 mg administered weekly

Reporting group title	Andecaliximab 150 mg weekly

Reporting group description:

• Double-blind Phase: 1 single-use PFS of andecaliximab 150 mg and matching placebo coadministered weekly for 8 weeks
• Open-label Phase and Extended Treatment Phase: 1 single-use PFS of andecaliximab 150 mg administered weekly

Reporting group title	Andecaliximab 300 mg weekly

Reporting group description:

• Double-blind Phase: 2 single-use PFS of andecaliximab 150 mg coadministered weekly for 8 weeks
• Open-label Phase and Extended Treatment Phase: 1 single-use PFS of andecaliximab 150 mg administered weekly

Reporting group title	Placebo Group

Reporting group description:

• Double-blind Phase: 2 single-use PFS of placebo coadministered weekly for 8 weeks
• Open-label and Extended Treatment Phase: 1 single-use PFS of andecaliximab 150 mg administered weekly

Reporting group values	Andecaliximab 150 mg every 2 weeks	Andecaliximab 150 mg weekly	Andecaliximab 300 mg weekly
Number of subjects	53	53	53
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	38	39	42
standard deviation	± 12.8	± 13.5	± 11.7
Gender categorical Units: Subjects			
Female	25	28	22
Male	28	25	31
Race Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	1	1	0
Black or African American	3	4	3
Native Hawaiian or Pacific Islander	0	0	0
White	48	42	48
Other	1	0	1
Not Permitted	0	6	1

Ethnicity Units: Subjects			
Hispanic or Latino	1	1	5
Not Hispanic or Latino	52	46	47
Not Permitted	0	6	1

Reporting group values	Placebo Group	Total	
Number of subjects	28	187	
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	38		
standard deviation	± 13.5	-	
Gender categorical Units: Subjects			
Female	15	90	
Male	13	97	
Race Units: Subjects			
American Indian or Alaska Native	0	0	
Asian	1	3	
Black or African American	1	11	
Native Hawaiian or Pacific Islander	0	0	
White	22	160	
Other	3	5	
Not Permitted	1	8	
Ethnicity Units: Subjects			
Hispanic or Latino	1	8	
Not Hispanic or Latino	26	171	
Not Permitted	1	8	

End points

End points reporting groups

Reporting group title	Andecaliximab 150 mg every 2 weeks

Reporting group description:

• Double-blind Phase: 1 single-use prefilled syringe (PFS) of andecaliximab 150 mg and matching placebo coadministered at Weeks 0, 2, 4, and 6; 2 single-use PFS of placebo coadministered at Weeks 1, 3, 5, and 7
• Open-label Phase and Extended Treatment Phase: 1 single-use PFS of andecaliximab 150 mg administered weekly

Reporting group title	Andecaliximab 150 mg weekly

Reporting group description:

• Double-blind Phase: 1 single-use PFS of andecaliximab 150 mg and matching placebo coadministered weekly for 8 weeks
• Open-label Phase and Extended Treatment Phase: 1 single-use PFS of andecaliximab 150 mg administered weekly

Reporting group title	Andecaliximab 300 mg weekly

Reporting group description:

• Double-blind Phase: 2 single-use PFS of andecaliximab 150 mg coadministered weekly for 8 weeks
• Open-label Phase and Extended Treatment Phase: 1 single-use PFS of andecaliximab 150 mg administered weekly

Reporting group title	Placebo Group

Reporting group description:

• Double-blind Phase: 2 single-use PFS of placebo coadministered weekly for 8 weeks
• Open-label and Extended Treatment Phase: 1 single-use PFS of andecaliximab 150 mg administered weekly

Primary: Percentage of Participants Achieving Clinical Response (PRO2 score ≤ 8) at Week 8 of the Double-blind Phase

End point title	Percentage of Participants Achieving Clinical Response (PRO2 score ≤ 8) at Week 8 of the Double-blind Phase[1]

End point description:

1) Clinical response was defined as patient-reported outcomes (PRO2) score ≤ 8 at Week 8. PRO2 is the weighted average of the 2 variables of frequency of liquid or very soft stool and abdominal pain, based on 7-day participant diary data.
2) Full Analysis Set: all randomized participants who received at least 1 dose of study drug.
3) Week 8 refers to the analysis window of Day 43 to Day 70 and prior to the first open-label dose date.
4) Participants with a missing PRO2 value at the Week 8 analysis visit were imputed as not achieving the Clinical Response.

End point type	Primary

End point timeframe:

Week 8

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No hypothesis testing was performed for the primary efficacy endpoints.

End point values	Andecaliximab 150 mg every 2 weeks	Andecaliximab 150 mg weekly	Andecaliximab 300 mg weekly	Placebo Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	53	53	53	28
Units: Percentage of Participants				
number (confidence interval 95%)	17.0 (8.1 to 29.8)	13.2 (5.5 to 25.3)	11.3 (4.3 to 23.0)	14.3 (4.0 to 32.7)

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants Achieving Endoscopic Response (≥ 50% reduction from baseline SES-CD) at Week 8 of the Double-blind Phase

End point title	Percentage of Participants Achieving Endoscopic Response (≥ 50% reduction from baseline SES-CD) at Week 8 of the Double-blind Phase[2]

End point description:

1) Endoscopic response was defined as ≥ 50% reduction from baseline Simple Endoscopic Score for Crohn's Disease (SES-CD) at Week 8.
2) Participants in the Full Analysis Set were analyzed.
3) Week 8 refers to the analysis window of day 43 to day 70 and prior to the first Open-Label dose date.
4) Participants with missing SES-CD value at Week 8 analysis visit were imputed as not achieving Endoscopic Response

End point type	Primary

End point timeframe:

Week 8

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No hypothesis testing was performed for the primary efficacy endpoints.

End point values	Andecaliximab 150 mg every 2 weeks	Andecaliximab 150 mg weekly	Andecaliximab 300 mg weekly	Placebo Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	53	53	53	28
Units: Percentage of Participants				
number (confidence interval 95%)	11.3 (4.3 to 23.0)	13.2 (5.5 to 25.3)	7.5 (2.1 to 18.2)	10.7 (2.3 to 28.2)

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Achieving CDAI remission (CDAI ≤ 150) at Week 8 in the Double-Blind Phase

End point title	Percentage of Participants Achieving CDAI remission (CDAI ≤ 150) at Week 8 in the Double-Blind Phase

End point description:

1) Clinical remission was defined as Crohn's Disease Activity Index (CDAI) ≤ 150 at Week 8. 2) Participants in the Full Analysis Set set were analyzed.
3) Week 8 refers to the analysis window of day 43 to day 70 and prior to the first open-label dose date.
4) Participants with missing CDAI score at Week 8 analysis visit were imputed as not achieving CDAI remission.

End point type	Secondary

End point timeframe:

Week 8

End point values	Andecaliximab 150 mg every 2 weeks	Andecaliximab 150 mg weekly	Andecaliximab 300 mg weekly	Placebo Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	53	53	53	28
Units: Percentage of Participants				
number (confidence interval 95%)	20.8 (10.8 to 34.1)	17.0 (8.1 to 29.8)	11.3 (4.3 to 23.0)	21.4 (8.3 to 41.0)

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Achieving Mucosal Healing (SES-CD ulcer subscore = 0) at Week 8 of the Double-Blind Phase

End point title	Percentage of Participants Achieving Mucosal Healing (SES-CD ulcer subscore = 0) at Week 8 of the Double-Blind Phase

End point description:

The SES-CD evaluates 4 endoscopic variables: ulcer size, ulcerated surface, affected surface, and presence of narrowings. The SES-CD size-of-ulcer subscore ranges from 0 (none) to 3 (very large). Mucosal healing at Week 8 was defined as the size-of-ulcer subscore for segments with non-zero baseline value changes to zero at Week 8 AND the size-of-ulcer subscore for segments with zero value at baseline remain zero at Week 8. Week 8 refers to the analysis window of Day 43 to Day 70 and prior to the first Open-Label dose date. Participants with missing SES-CD size-of-ulcer subscore at Week 8 analysis visit were imputed as not achieving Mucosal Healing. Participants in the Full Analysis Set were analyzed.

End point type	Secondary

End point timeframe:

Week 8

End point values	Andecaliximab 150 mg every 2 weeks	Andecaliximab 150 mg weekly	Andecaliximab 300 mg weekly	Placebo Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	53	53	53	28
Units: Percentage of participants				
number (confidence interval 95%)	5.7 (1.2 to 15.7)	1.9 (0.0 to 10.1)	1.9 (0.0 to 10.1)	7.1 (0.9 to 23.5)

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Double-Blind Phase: First Dose of andecaliximab to Week 8;
Open-Label Phase: First Dose of open label andecaliximab to the last dose date (maximum: 67 weeks) plus 30 days

Adverse event reporting additional description:

Safety Analysis Set (Double-blind Phase and Open-label Phase): all participants who received at least 1 dose of study drug.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	19.1

Reporting groups

Reporting group title	Double-Blind Andecaliximab 150 mg Q2W (every 2 weeks)

Reporting group description:

1 single-use PFS of andecaliximab 150 mg and matching placebo coadministered at Weeks 0, 2, 4, and 6; 2 single-use PFS of placebo coadministered at Weeks 1, 3, 5 and 7

Reporting group title	Double-Blind Andecaliximab 150 mg QW (QW = weekly)

Reporting group description:

1 single-use PFS of andecaliximab 150 mg and matching placebo coadministered weekly for 8 weeks

Reporting group title	Double Blind Andecaliximab 300 mg QW

Reporting group description:

2 single-use PFS of andecaliximab 150 mg coadministered weekly for 8 weeks

Reporting group title	Double Blind Placebo

Reporting group description:

2 single-use PFS of placebo coadministered weekly for 8 weeks

Reporting group title	Open-Label Andecaliximab QW from Andecaliximab 150 mg Q2W

Reporting group description:

Participants from the Andecaliximab 150 mg Q2W group in the Double-blind Phase, who received open-label andecaliximab 150 mg weekly.

Reporting group title	Open-Label Andecaliximab QW from Andecaliximab 150 mg QW

Reporting group description:

Participants from the Andecaliximab 150 mg QW group in the Double-blind Phase, who received open-label andecaliximab 150 mg weekly.

Reporting group title	Open-Label Andecaliximab QW from Andecaliximab 300 mg QW

Reporting group description:

Participants from Andecaliximab 300 mg QW in the Double-blind Phase who received open-label andecaliximab 150 mg weekly.

Reporting group title	Open-Label Andecaliximab QW from Placebo

Reporting group description:

Participants from the Placebo group in the Double-blind Phase, who received open-label andecaliximab 150 mg weekly.

Serious adverse events	Double-Blind Andecaliximab 150 mg Q2W (every 2 weeks)	Double-Blind Andecaliximab 150 mg QW (QW = weekly)	Double Blind Andecaliximab 300 mg QW
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 53 (1.89%)	6 / 53 (11.32%)	8 / 53 (15.09%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Post procedural complication			
subjects affected / exposed	0 / 53 (0.00%)	0 / 53 (0.00%)	0 / 53 (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
Post procedural haematoma			
subjects affected / exposed	0 / 53 (0.00%)	0 / 53 (0.00%)	1 / 53 (1.89%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post procedural haemorrhage			
subjects affected / exposed	0 / 53 (0.00%)	0 / 53 (0.00%)	1 / 53 (1.89%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Procedural pain			
subjects affected / exposed	0 / 53 (0.00%)	0 / 53 (0.00%)	1 / 53 (1.89%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Peripheral ischaemia			
subjects affected / exposed	1 / 53 (1.89%)	0 / 53 (0.00%)	0 / 53 (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
Nervous system disorders			
Paraesthesia			
subjects affected / exposed	0 / 53 (0.00%)	0 / 53 (0.00%)	0 / 53 (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
Blood and lymphatic system disorders			

Anaemia			
subjects affected / exposed	0 / 53 (0.00%)	1 / 53 (1.89%)	1 / 53 (1.89%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Crohn's disease			
subjects affected / exposed	0 / 53 (0.00%)	3 / 53 (5.66%)	2 / 53 (3.77%)
occurrences causally related to treatment / all	0 / 0	0 / 4	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestinal obstruction			
subjects affected / exposed	0 / 53 (0.00%)	0 / 53 (0.00%)	0 / 53 (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
Abdominal pain			
subjects affected / exposed	0 / 53 (0.00%)	1 / 53 (1.89%)	1 / 53 (1.89%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anal fistula			
subjects affected / exposed	0 / 53 (0.00%)	0 / 53 (0.00%)	1 / 53 (1.89%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal obstruction			
subjects affected / exposed	0 / 53 (0.00%)	0 / 53 (0.00%)	0 / 53 (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
Constipation			
subjects affected / exposed	0 / 53 (0.00%)	0 / 53 (0.00%)	0 / 53 (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
Fistula of small intestine			
subjects affected / exposed	0 / 53 (0.00%)	0 / 53 (0.00%)	0 / 53 (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
Ileal stenosis			

subjects affected / exposed	0 / 53 (0.00%)	0 / 53 (0.00%)	0 / 53 (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
Intestinal perforation			
subjects affected / exposed	0 / 53 (0.00%)	0 / 53 (0.00%)	0 / 53 (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
Large intestinal stenosis			
subjects affected / exposed	0 / 53 (0.00%)	0 / 53 (0.00%)	0 / 53 (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
Large intestine perforation			
subjects affected / exposed	0 / 53 (0.00%)	0 / 53 (0.00%)	1 / 53 (1.89%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Proctalgia			
subjects affected / exposed	0 / 53 (0.00%)	1 / 53 (1.89%)	0 / 53 (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
Rectal haemorrhage			
subjects affected / exposed	0 / 53 (0.00%)	1 / 53 (1.89%)	0 / 53 (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
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	0 / 53 (0.00%)	0 / 53 (0.00%)	0 / 53 (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
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	0 / 53 (0.00%)	0 / 53 (0.00%)	1 / 53 (1.89%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 53 (0.00%)	1 / 53 (1.89%)	0 / 53 (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
Acute prerenal failure			
subjects affected / exposed	1 / 53 (1.89%)	0 / 53 (0.00%)	0 / 53 (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
Nephrolithiasis			
subjects affected / exposed	0 / 53 (0.00%)	0 / 53 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Abdominal abscess			
subjects affected / exposed	0 / 53 (0.00%)	0 / 53 (0.00%)	0 / 53 (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
Anal abscess			
subjects affected / exposed	0 / 53 (0.00%)	0 / 53 (0.00%)	0 / 53 (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
Appendicitis			
subjects affected / exposed	0 / 53 (0.00%)	0 / 53 (0.00%)	0 / 53 (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
Bacterial pyelonephritis			
subjects affected / exposed	0 / 53 (0.00%)	0 / 53 (0.00%)	0 / 53 (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
Clostridium difficile infection			
subjects affected / exposed	0 / 53 (0.00%)	0 / 53 (0.00%)	0 / 53 (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

Cytomegalovirus infection			
subjects affected / exposed	0 / 53 (0.00%)	0 / 53 (0.00%)	0 / 53 (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
Enteritis infectious			
subjects affected / exposed	0 / 53 (0.00%)	0 / 53 (0.00%)	0 / 53 (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
Perirectal abscess			
subjects affected / exposed	0 / 53 (0.00%)	0 / 53 (0.00%)	0 / 53 (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
Pneumonia			
subjects affected / exposed	1 / 53 (1.89%)	0 / 53 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Hypocalcaemia			
subjects affected / exposed	1 / 53 (1.89%)	0 / 53 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypokalaemia			
subjects affected / exposed	0 / 53 (0.00%)	0 / 53 (0.00%)	1 / 53 (1.89%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Double Blind Placebo	Open-Label Andecaliximab QW from Andecaliximab 150 mg Q2W	Open-Label Andecaliximab QW from Andecaliximab 150 mg QW
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 28 (10.71%)	9 / 52 (17.31%)	10 / 48 (20.83%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Post procedural complication			

subjects affected / exposed	0 / 28 (0.00%)	0 / 52 (0.00%)	0 / 48 (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
Post procedural haematoma			
subjects affected / exposed	0 / 28 (0.00%)	0 / 52 (0.00%)	0 / 48 (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
Post procedural haemorrhage			
subjects affected / exposed	0 / 28 (0.00%)	0 / 52 (0.00%)	0 / 48 (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
Procedural pain			
subjects affected / exposed	0 / 28 (0.00%)	0 / 52 (0.00%)	0 / 48 (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
Vascular disorders			
Peripheral ischaemia			
subjects affected / exposed	0 / 28 (0.00%)	0 / 52 (0.00%)	0 / 48 (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
Nervous system disorders			
Paraesthesia			
subjects affected / exposed	1 / 28 (3.57%)	0 / 52 (0.00%)	0 / 48 (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
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 28 (0.00%)	0 / 52 (0.00%)	0 / 48 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Crohn's disease			

subjects affected / exposed	0 / 28 (0.00%)	4 / 52 (7.69%)	5 / 48 (10.42%)
occurrences causally related to treatment / all	0 / 0	0 / 4	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestinal obstruction			
subjects affected / exposed	0 / 28 (0.00%)	2 / 52 (3.85%)	1 / 48 (2.08%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain			
subjects affected / exposed	0 / 28 (0.00%)	0 / 52 (0.00%)	0 / 48 (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
Anal fistula			
subjects affected / exposed	1 / 28 (3.57%)	0 / 52 (0.00%)	0 / 48 (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
Intestinal obstruction			
subjects affected / exposed	0 / 28 (0.00%)	1 / 52 (1.92%)	1 / 48 (2.08%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Constipation			
subjects affected / exposed	0 / 28 (0.00%)	0 / 52 (0.00%)	1 / 48 (2.08%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fistula of small intestine			
subjects affected / exposed	0 / 28 (0.00%)	1 / 52 (1.92%)	0 / 48 (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
Ileal stenosis			
subjects affected / exposed	0 / 28 (0.00%)	1 / 52 (1.92%)	0 / 48 (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
Intestinal perforation			

subjects affected / exposed	0 / 28 (0.00%)	1 / 52 (1.92%)	0 / 48 (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
Large intestinal stenosis			
subjects affected / exposed	0 / 28 (0.00%)	0 / 52 (0.00%)	1 / 48 (2.08%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Large intestine perforation			
subjects affected / exposed	0 / 28 (0.00%)	0 / 52 (0.00%)	0 / 48 (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
Proctalgia			
subjects affected / exposed	0 / 28 (0.00%)	0 / 52 (0.00%)	0 / 48 (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
Rectal haemorrhage			
subjects affected / exposed	0 / 28 (0.00%)	0 / 52 (0.00%)	0 / 48 (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
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	1 / 28 (3.57%)	0 / 52 (0.00%)	0 / 48 (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
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	0 / 28 (0.00%)	0 / 52 (0.00%)	0 / 48 (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
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 28 (0.00%)	0 / 52 (0.00%)	0 / 48 (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

Acute prerenal failure			
subjects affected / exposed	0 / 28 (0.00%)	0 / 52 (0.00%)	0 / 48 (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
Nephrolithiasis			
subjects affected / exposed	0 / 28 (0.00%)	0 / 52 (0.00%)	0 / 48 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Abdominal abscess			
subjects affected / exposed	0 / 28 (0.00%)	1 / 52 (1.92%)	0 / 48 (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
Anal abscess			
subjects affected / exposed	0 / 28 (0.00%)	0 / 52 (0.00%)	1 / 48 (2.08%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Appendicitis			
subjects affected / exposed	0 / 28 (0.00%)	0 / 52 (0.00%)	0 / 48 (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
Bacterial pyelonephritis			
subjects affected / exposed	0 / 28 (0.00%)	0 / 52 (0.00%)	0 / 48 (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
Clostridium difficile infection			
subjects affected / exposed	0 / 28 (0.00%)	0 / 52 (0.00%)	1 / 48 (2.08%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cytomegalovirus infection			
subjects affected / exposed	0 / 28 (0.00%)	0 / 52 (0.00%)	0 / 48 (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
Enteritis infectious			

subjects affected / exposed	0 / 28 (0.00%)	0 / 52 (0.00%)	1 / 48 (2.08%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Perirectal abscess			
subjects affected / exposed	1 / 28 (3.57%)	0 / 52 (0.00%)	0 / 48 (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
Pneumonia			
subjects affected / exposed	0 / 28 (0.00%)	0 / 52 (0.00%)	0 / 48 (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			
Hypocalcaemia			
subjects affected / exposed	0 / 28 (0.00%)	0 / 52 (0.00%)	0 / 48 (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
Hypokalaemia			
subjects affected / exposed	0 / 28 (0.00%)	0 / 52 (0.00%)	0 / 48 (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	Open-Label Andecaliximab QW from Andecaliximab 300 mg QW	Open-Label Andecaliximab QW from Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 47 (14.89%)	6 / 26 (23.08%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Injury, poisoning and procedural complications			
Post procedural complication			
subjects affected / exposed	1 / 47 (2.13%)	0 / 26 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural haematoma			

subjects affected / exposed	0 / 47 (0.00%)	0 / 26 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural haemorrhage			
subjects affected / exposed	0 / 47 (0.00%)	0 / 26 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Procedural pain			
subjects affected / exposed	0 / 47 (0.00%)	0 / 26 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Peripheral ischaemia			
subjects affected / exposed	0 / 47 (0.00%)	0 / 26 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Paraesthesia			
subjects affected / exposed	0 / 47 (0.00%)	0 / 26 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 47 (0.00%)	1 / 26 (3.85%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Crohn's disease			
subjects affected / exposed	4 / 47 (8.51%)	3 / 26 (11.54%)	
occurrences causally related to treatment / all	1 / 4	2 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestinal obstruction			

subjects affected / exposed	2 / 47 (4.26%)	0 / 26 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain			
subjects affected / exposed	1 / 47 (2.13%)	0 / 26 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anal fistula			
subjects affected / exposed	0 / 47 (0.00%)	0 / 26 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal obstruction			
subjects affected / exposed	0 / 47 (0.00%)	0 / 26 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Constipation			
subjects affected / exposed	0 / 47 (0.00%)	0 / 26 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fistula of small intestine			
subjects affected / exposed	0 / 47 (0.00%)	0 / 26 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ileal stenosis			
subjects affected / exposed	0 / 47 (0.00%)	0 / 26 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal perforation			
subjects affected / exposed	0 / 47 (0.00%)	0 / 26 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large intestinal stenosis			

subjects affected / exposed	0 / 47 (0.00%)	0 / 26 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large intestine perforation			
subjects affected / exposed	0 / 47 (0.00%)	0 / 26 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Proctalgia			
subjects affected / exposed	0 / 47 (0.00%)	0 / 26 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal haemorrhage			
subjects affected / exposed	0 / 47 (0.00%)	0 / 26 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	0 / 47 (0.00%)	0 / 26 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	0 / 47 (0.00%)	0 / 26 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 47 (0.00%)	0 / 26 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute prerenal failure			
subjects affected / exposed	0 / 47 (0.00%)	0 / 26 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Nephrolithiasis			
subjects affected / exposed	0 / 47 (0.00%)	1 / 26 (3.85%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Abdominal abscess			
subjects affected / exposed	0 / 47 (0.00%)	0 / 26 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anal abscess			
subjects affected / exposed	0 / 47 (0.00%)	0 / 26 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendicitis			
subjects affected / exposed	0 / 47 (0.00%)	1 / 26 (3.85%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacterial pyelonephritis			
subjects affected / exposed	0 / 47 (0.00%)	1 / 26 (3.85%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clostridium difficile infection			
subjects affected / exposed	0 / 47 (0.00%)	0 / 26 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cytomegalovirus infection			
subjects affected / exposed	1 / 47 (2.13%)	0 / 26 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enteritis infectious			
subjects affected / exposed	0 / 47 (0.00%)	0 / 26 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Perirectal abscess			

subjects affected / exposed	0 / 47 (0.00%)	0 / 26 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	0 / 47 (0.00%)	0 / 26 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Hypocalcaemia			
subjects affected / exposed	0 / 47 (0.00%)	0 / 26 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypokalaemia			
subjects affected / exposed	0 / 47 (0.00%)	0 / 26 (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: 5 %

Non-serious adverse events	Double-Blind Andecaliximab 150 mg Q2W (every 2 weeks)	Double-Blind Andecaliximab 150 mg QW (QW = weekly)	Double Blind Andecaliximab 300 mg QW
Total subjects affected by non-serious adverse events			
subjects affected / exposed	15 / 53 (28.30%)	25 / 53 (47.17%)	25 / 53 (47.17%)
Investigations			
Hepatic enzyme increased			
subjects affected / exposed	0 / 53 (0.00%)	0 / 53 (0.00%)	0 / 53 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 53 (0.00%)	0 / 53 (0.00%)	0 / 53 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 53 (0.00%)	4 / 53 (7.55%)	5 / 53 (9.43%)
occurrences (all)	0	5	5

Dizziness			
subjects affected / exposed	0 / 53 (0.00%)	5 / 53 (9.43%)	2 / 53 (3.77%)
occurrences (all)	0	6	2
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 53 (0.00%)	2 / 53 (3.77%)	6 / 53 (11.32%)
occurrences (all)	0	2	6
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 53 (1.89%)	3 / 53 (5.66%)	0 / 53 (0.00%)
occurrences (all)	1	3	0
Fatigue			
subjects affected / exposed	6 / 53 (11.32%)	0 / 53 (0.00%)	5 / 53 (9.43%)
occurrences (all)	6	0	5
Gastrointestinal disorders			
Crohn's disease			
subjects affected / exposed	1 / 53 (1.89%)	1 / 53 (1.89%)	2 / 53 (3.77%)
occurrences (all)	1	1	2
Abdominal pain			
subjects affected / exposed	1 / 53 (1.89%)	7 / 53 (13.21%)	4 / 53 (7.55%)
occurrences (all)	1	7	4
Nausea			
subjects affected / exposed	3 / 53 (5.66%)	1 / 53 (1.89%)	7 / 53 (13.21%)
occurrences (all)	3	1	7
Vomiting			
subjects affected / exposed	2 / 53 (3.77%)	1 / 53 (1.89%)	1 / 53 (1.89%)
occurrences (all)	2	1	1
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	0 / 53 (0.00%)	0 / 53 (0.00%)	1 / 53 (1.89%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 53 (0.00%)	4 / 53 (7.55%)	1 / 53 (1.89%)
occurrences (all)	0	4	1
Back pain			

subjects affected / exposed	1 / 53 (1.89%)	2 / 53 (3.77%)	0 / 53 (0.00%)
occurrences (all)	1	2	0
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	2 / 53 (3.77%)	1 / 53 (1.89%)	4 / 53 (7.55%)
occurrences (all)	2	1	6
Urinary tract infection			
subjects affected / exposed	1 / 53 (1.89%)	2 / 53 (3.77%)	1 / 53 (1.89%)
occurrences (all)	1	2	1
Upper respiratory tract infection			
subjects affected / exposed	1 / 53 (1.89%)	0 / 53 (0.00%)	1 / 53 (1.89%)
occurrences (all)	1	0	1
Clostridium difficile infection			
subjects affected / exposed	0 / 53 (0.00%)	1 / 53 (1.89%)	0 / 53 (0.00%)
occurrences (all)	0	1	0
Rhinitis			
subjects affected / exposed	1 / 53 (1.89%)	0 / 53 (0.00%)	0 / 53 (0.00%)
occurrences (all)	1	0	0
Herpes zoster			
subjects affected / exposed	0 / 53 (0.00%)	0 / 53 (0.00%)	0 / 53 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Hypokalaemia			
subjects affected / exposed	1 / 53 (1.89%)	3 / 53 (5.66%)	4 / 53 (7.55%)
occurrences (all)	1	3	4

Non-serious adverse events	Double Blind Placebo	Open-Label Andecaliximab QW from Andecaliximab 150 mg Q2W	Open-Label Andecaliximab QW from Andecaliximab 150 mg QW
Total subjects affected by non-serious adverse events			
subjects affected / exposed	16 / 28 (57.14%)	22 / 52 (42.31%)	21 / 48 (43.75%)
Investigations			
Hepatic enzyme increased			
subjects affected / exposed	0 / 28 (0.00%)	0 / 52 (0.00%)	0 / 48 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			

Contusion			
subjects affected / exposed	0 / 28 (0.00%)	3 / 52 (5.77%)	0 / 48 (0.00%)
occurrences (all)	0	3	0
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 28 (3.57%)	2 / 52 (3.85%)	1 / 48 (2.08%)
occurrences (all)	1	2	1
Dizziness			
subjects affected / exposed	0 / 28 (0.00%)	0 / 52 (0.00%)	0 / 48 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 28 (0.00%)	1 / 52 (1.92%)	1 / 48 (2.08%)
occurrences (all)	0	1	4
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	4 / 28 (14.29%)	2 / 52 (3.85%)	1 / 48 (2.08%)
occurrences (all)	5	2	1
Fatigue			
subjects affected / exposed	1 / 28 (3.57%)	1 / 52 (1.92%)	1 / 48 (2.08%)
occurrences (all)	1	1	1
Gastrointestinal disorders			
Crohn's disease			
subjects affected / exposed	2 / 28 (7.14%)	6 / 52 (11.54%)	10 / 48 (20.83%)
occurrences (all)	2	8	13
Abdominal pain			
subjects affected / exposed	3 / 28 (10.71%)	7 / 52 (13.46%)	1 / 48 (2.08%)
occurrences (all)	3	8	1
Nausea			
subjects affected / exposed	5 / 28 (17.86%)	3 / 52 (5.77%)	4 / 48 (8.33%)
occurrences (all)	5	3	4
Vomiting			
subjects affected / exposed	1 / 28 (3.57%)	3 / 52 (5.77%)	0 / 48 (0.00%)
occurrences (all)	1	4	0
Renal and urinary disorders			

Nephrolithiasis			
subjects affected / exposed	2 / 28 (7.14%)	2 / 52 (3.85%)	1 / 48 (2.08%)
occurrences (all)	2	2	1
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	2 / 28 (7.14%)	2 / 52 (3.85%)	0 / 48 (0.00%)
occurrences (all)	2	2	0
Back pain			
subjects affected / exposed	2 / 28 (7.14%)	0 / 52 (0.00%)	1 / 48 (2.08%)
occurrences (all)	2	0	1
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	0 / 28 (0.00%)	4 / 52 (7.69%)	3 / 48 (6.25%)
occurrences (all)	0	4	3
Urinary tract infection			
subjects affected / exposed	1 / 28 (3.57%)	0 / 52 (0.00%)	3 / 48 (6.25%)
occurrences (all)	1	0	3
Upper respiratory tract infection			
subjects affected / exposed	2 / 28 (7.14%)	1 / 52 (1.92%)	1 / 48 (2.08%)
occurrences (all)	2	1	1
Clostridium difficile infection			
subjects affected / exposed	0 / 28 (0.00%)	0 / 52 (0.00%)	0 / 48 (0.00%)
occurrences (all)	0	0	0
Rhinitis			
subjects affected / exposed	0 / 28 (0.00%)	0 / 52 (0.00%)	0 / 48 (0.00%)
occurrences (all)	0	0	0
Herpes zoster			
subjects affected / exposed	2 / 28 (7.14%)	0 / 52 (0.00%)	0 / 48 (0.00%)
occurrences (all)	2	0	0
Metabolism and nutrition disorders			
Hypokalaemia			
subjects affected / exposed	1 / 28 (3.57%)	2 / 52 (3.85%)	2 / 48 (4.17%)
occurrences (all)	1	2	3

Non-serious adverse events	Open-Label Andecaliximab QW from Andecaliximab 300 mg QW	Open-Label Andecaliximab QW from Placebo	
Total subjects affected by non-serious			

adverse events subjects affected / exposed	17 / 47 (36.17%)	16 / 26 (61.54%)	
Investigations Hepatic enzyme increased subjects affected / exposed occurrences (all)	0 / 47 (0.00%) 0	2 / 26 (7.69%) 2	
Injury, poisoning and procedural complications Contusion subjects affected / exposed occurrences (all)	0 / 47 (0.00%) 0	0 / 26 (0.00%) 0	
Nervous system disorders Headache subjects affected / exposed occurrences (all) Dizziness subjects affected / exposed occurrences (all)	1 / 47 (2.13%) 1 1 / 47 (2.13%) 1	0 / 26 (0.00%) 0 0 / 26 (0.00%) 0	
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all)	1 / 47 (2.13%) 1	1 / 26 (3.85%) 2	
General disorders and administration site conditions Pyrexia subjects affected / exposed occurrences (all) Fatigue subjects affected / exposed occurrences (all)	2 / 47 (4.26%) 2 0 / 47 (0.00%) 0	2 / 26 (7.69%) 3 0 / 26 (0.00%) 0	
Gastrointestinal disorders Crohn's disease subjects affected / exposed occurrences (all) Abdominal pain subjects affected / exposed occurrences (all) Nausea	4 / 47 (8.51%) 4 3 / 47 (6.38%) 3	5 / 26 (19.23%) 5 1 / 26 (3.85%) 1	

subjects affected / exposed	1 / 47 (2.13%)	2 / 26 (7.69%)	
occurrences (all)	1	2	
Vomiting			
subjects affected / exposed	2 / 47 (4.26%)	0 / 26 (0.00%)	
occurrences (all)	2	0	
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	0 / 47 (0.00%)	0 / 26 (0.00%)	
occurrences (all)	0	0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 47 (2.13%)	2 / 26 (7.69%)	
occurrences (all)	1	2	
Back pain			
subjects affected / exposed	0 / 47 (0.00%)	1 / 26 (3.85%)	
occurrences (all)	0	1	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	4 / 47 (8.51%)	1 / 26 (3.85%)	
occurrences (all)	4	1	
Urinary tract infection			
subjects affected / exposed	1 / 47 (2.13%)	1 / 26 (3.85%)	
occurrences (all)	1	2	
Upper respiratory tract infection			
subjects affected / exposed	0 / 47 (0.00%)	0 / 26 (0.00%)	
occurrences (all)	0	0	
Clostridium difficile infection			
subjects affected / exposed	0 / 47 (0.00%)	2 / 26 (7.69%)	
occurrences (all)	0	2	
Rhinitis			
subjects affected / exposed	0 / 47 (0.00%)	2 / 26 (7.69%)	
occurrences (all)	0	2	
Herpes zoster			
subjects affected / exposed	0 / 47 (0.00%)	0 / 26 (0.00%)	
occurrences (all)	0	0	
Metabolism and nutrition disorders			

Hypokalaemia subjects affected / exposed occurrences (all)	1 / 47 (2.13%) 2	1 / 26 (3.85%) 1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
16 February 2015	1. Revised the primary objectives, study design, and criteria for evaluation to address the FDA recommendation to conduct a dose-ranging study and move towards a responder definition (primary efficacy endpoint) in Crohn's disease that was comprised of both key clinical signs and symptoms as well as endoscopic findings 2. Revised the secondary objectives to address the FDA recommendation to change the CDAI remission objective from a primary objective to a secondary objective 3. Revised the exploratory objectives to reflect changes made in the study design 4. Added that up to 50% of subjects enrolled may have had evidence of fistula at screening 5. Revised study design in response to the FDA recommendation to conduct a dose-ranging study 6. Increased number of subjects planned to accommodate 2 additional treatment groups 7. Revised the inclusion criteria to provide a clearly defined moderately or severely active Crohn's disease study population from which to assess response and remission based on clinical signs and symptoms as well as endoscopic findings 8. Broadened the exclusion criteria to capture perianal abscess and abscesses involving the urogenital system, which could present in Crohn's disease and require appropriate antibiotic and/or surgical management 9. Added short bowel syndrome to the exclusion criteria 10. Clarified that all endpoint assessments would be conducted at Week 8 11. Added SES-CD as a validated tool to score the endoscopic findings 12. Provided additional detail regarding screening and randomization procedures 13. Added how the CDAI stool frequency and abdominal pain composite score would be calculated
10 March 2015	1. Clarified in the exploratory objectives that matrix metallopeptidase-9 (MMP9) activity and MMP9 expression in biopsies would be examined and added biopsy collection time points 2. Clarified the exclusion criteria to allow subjects who have had resected non-melanoma skin cancer to participate in the study 3. Added that the primary analysis would be conducted when all randomized subjects completed the Double-blind Phase or prematurely discontinued 4. Clarified in the study rationale that 300 mg SC dosing occurred weekly and 150 mg SC dosing occurred weekly or every other week 5. Revised dosage and administration of andecaliximab and placebo to allow medical professionals at the site to determine the most suitable area for the SC injections 6. Clarified calculation of the CDAI, PRO2, and full ileocolonoscopy 7. Removed nonessential CDAI assessments and scoring 8. Decreased the number of nonessential biopsies for analysis and clarified the colonoscopy procedure 9. Clarified that subjects could not begin the Open-label Phase prior to completing the Week 8 ileocolonoscopy

24 February 2016	1. Added an additional exploratory objective to assess long term safety of andecaliximab during the Extended Treatment Phase 2. Added the Extended Treatment Phase to the study design to allow subjects who had completed Week 52 assessments to receive andecaliximab 150 mg for an additional 156 weekly doses 3. Added an additional time point (Week 52/early termination) to the MRE substudy to better ascertain changes in disease activity over time with andecaliximab 4. Clarified that sparse PK samples were not collected at Week 52 and were collected during the Extended Treatment Phase 5. Clarified clinically significant worsening of underlying Crohn's disease in discontinuation criteria, per VHP conditional approval 6. Clarified prohibited medications during the Extended Treatment Phase 7. Added details and clarification of the MRE substudy procedures

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
01 November 2016	After all participants completed the Double-blind (DB) Phase, a primary efficacy analysis was conducted to evaluate the clinical response, defined as PRO2 score ≤ 8, and the endoscopic response, defined as reduction in the SES-CD of ≥ 50% from baseline. No treatment difference was observed between andecaliximab and placebo. Accordingly, Gilead terminated the Open-label Phase and Extended Treatment Phase of GS-US-395-1663, effective 01 November 2016. A prespecified topline analysis was performed after the last enrolled subject received the 8-week DB induction treatment. Based on this review, Gilead terminated the Open-label and Extended Treatment Phases of the study due to lack of efficacy.	-

Notes:

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

An unplanned review of unblinded clinical trial data was performed in this study that was not prospectively specified in the protocol. There was no impact on the overall integrity or conclusions of the study.

Notes: