# 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 | v2 |
| This version publication date | 03 April 2019 |
| First version publication date | 19 November 2017 |
| Version creation reason | • Correction of full data set<br>• Measure type changed from "arithmetic mean" to "number" for all endpoints<br>• Added data for mucosal healing endpoint<br>• Updated maximum time frame in AE section for Open-Label Phase |

## 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<br><br>, ClinicalTrialDisclosures@gilead.com |
| Scientific contact | Clinical Trials Mailbox, Gilead Sciences International Ltd<br><br>, 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<br>Units: Subjects | | | |
| Age continuous<br>Units: years | | | |
| arithmetic mean | 38 | 39 | 42 |
| standard deviation | ± 12.8 | ± 13.5 | ± 11.7 |
| Gender categorical<br>Units: Subjects | | | |
| Female | 25 | 28 | 22 |
| Male | 28 | 25 | 31 |
| Race<br>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<br>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<br>Units: Subjects | | | |
| Age continuous<br>Units: years | | | |
| arithmetic mean | 38 | | |
| standard deviation | ± 13.5 | - | |
| Gender categorical<br>Units: Subjects | | | |
| Female | 15 | 90 | |
| Male | 13 | 97 | |
| Race<br>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<br>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 | 0 / 47 (0.00%) | 2 / 26 (7.69%) | |
| occurrences (all) | 0 | 2 | |
| Injury, poisoning and procedural complications | | | |
| Contusion | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 0 / 26 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 1 / 47 (2.13%) | 0 / 26 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Dizziness | | | |
| subjects affected / exposed | 1 / 47 (2.13%) | 0 / 26 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 1 / 47 (2.13%) | 1 / 26 (3.85%) | |
| occurrences (all) | 1 | 2 | |
| General disorders and administration site conditions | | | |
| Pyrexia | | | |
| subjects affected / exposed | 2 / 47 (4.26%) | 2 / 26 (7.69%) | |
| occurrences (all) | 2 | 3 | |
| Fatigue | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 0 / 26 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Gastrointestinal disorders | | | |
| Crohn's disease | | | |
| subjects affected / exposed | 4 / 47 (8.51%) | 5 / 26 (19.23%) | |
| occurrences (all) | 4 | 5 | |
| Abdominal pain | | | |
| subjects affected / exposed | 3 / 47 (6.38%) | 1 / 26 (3.85%) | |
| occurrences (all) | 3 | 1 | |
| Nausea | | | |

| | | | |
|---|---|---|---|
| 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<br>subjects affected / exposed<br>occurrences (all) | 1 / 47 (2.13%)<br>2 | 1 / 26 (3.85%)<br>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<br>and symptoms as well as endoscopic findings<br>2. Revised the secondary objectives to address the FDA recommendation to change the CDAI remission objective from a primary objective to a secondary objective<br>3. Revised the exploratory objectives to reflect changes made in the study design<br>4. Added that up to 50% of subjects enrolled may have had evidence of fistula at screening<br>5. Revised study design in response to the FDA recommendation to conduct a dose-ranging<br>study<br>6. Increased number of subjects planned to accommodate 2 additional treatment groups<br>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<br>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<br>9. Added short bowel syndrome to the exclusion criteria<br>10. Clarified that all endpoint assessments would be conducted at Week 8<br>11. Added SES-CD as a validated tool to score the endoscopic findings<br>12. Provided additional detail regarding screening and randomization procedures<br>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<br>2. Clarified the exclusion criteria to allow subjects who have had resected non-melanoma skin cancer to participate in the study<br>3. Added that the primary analysis would be conducted when all randomized subjects completed the Double-blind Phase or prematurely discontinued<br>4. Clarified in the study rationale that 300 mg SC dosing occurred weekly and 150 mg SC dosing occurred weekly or every other week<br>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<br>6. Clarified calculation of the CDAI, PRO2, and full ileocolonoscopy<br>7. Removed nonessential CDAI assessments and scoring<br>8. Decreased the number of nonessential biopsies for analysis and clarified the colonoscopy procedure<br>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<br>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<br>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<br>4. Clarified that sparse PK samples were not collected at Week 52 and were collected during the Extended Treatment Phase<br>5. Clarified clinically significant worsening of underlying Crohn's disease in discontinuation criteria, per VHP conditional approval<br>6. Clarified prohibited medications during the Extended Treatment Phase<br>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. | - |

Notes:

## Limitations and caveats

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

| |
|---|
| 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: