# Clinical trial results:
# A Phase 2, Open-label Study to Explore the Pharmacodynamic and Clinical Effects of Mongersen (GED-0301) in Subjects with Active Crohn's Disease

## Summary

| | |
|---|---|
| EudraCT number | 2015-001693-18 |
| Trial protocol | IT |
| Global end of trial date | 23 April 2018 |

**Results information**

| | |
|---|---|
| Result version number | v1 (current) |
| This version publication date | 14 March 2019 |
| First version publication date | 14 March 2019 |

## Trial information

**Trial identification**

| | |
|---|---|
| Sponsor protocol code | GED-0301-CD-005 |

**Additional study identifiers**

| | |
|---|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT02685683 |
| WHO universal trial number (UTN) | - |

Notes:

**Sponsors**

| | |
|---|---|
| Sponsor organisation name | Celgene Corporation |
| Sponsor organisation address | 86 Morris Avenue, Summit, United States, 07901 |
| Public contact | Clinical Trial Disclosure, Celgene Corporation, 01 888-260-1599, ClinicalTrialDisclosure@Celgene.com |
| Scientific contact | Keith Usiskin, Celgene Corporation, 01 908.897.6550 , kusiskin@celgene.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 | 05 April 2018 |
| Is this the analysis of the primary completion data? | No |

| | |
|---|---|
| Global end of trial reached? | Yes |
| Global end of trial date | 23 April 2018 |
| Was the trial ended prematurely? | Yes |

Notes:

## General information about the trial

Main objective of the trial:

To explore the mechanism of action of mongersen (GED-0301) 160 mg once daily (QD) in subjects with active Crohn’s Disease.

Protection of trial subjects:

Patient Confidentiality, Personal Data Protection, Archiving of Essential Documents

Background therapy: -

Evidence for comparator: -

| | |
|---|---|
| Actual start date of recruitment | 07 April 2016 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | No |

Notes:

## Population of trial subjects

### Subjects enrolled per country

| | |
|---|---|
| Country: Number of subjects enrolled | Italy: 18 |
| Worldwide total number of subjects | 18 |
| EEA total number of subjects | 18 |

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) | 18 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

## Subject disposition

### Recruitment

Recruitment details:

18 subjects were enrolled from 2 sites in Italy.

### Pre-assignment

Screening details:

Study subjects must have had a diagnosis of Crohn's Disease (CD) for at least 3 months prior to starting screening assessments.

### Period 1

| | |
|---|---|
| Period 1 title | Induction Period Week 0 to 12 |
| Is this the baseline period? | Yes |
| Allocation method | Not applicable |
| Blinding used | Not blinded |

### Arms

| | |
|---|---|
| **Arm title** | GED-0301 160 mg |

Arm description:

Participants received GED-0301 160 mg tablets daily during the induction period from week 0 up to week 12.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | GED-0301 |
| Investigational medicinal product code | |
| Other name | Mongersen |
| Pharmaceutical forms | Coated tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Participants received GED-0301 160 mg tablets daily during the induction period from week 0 up to week 12.

| **Number of subjects in period 1** | GED-0301 160 mg |
|---|---|
| Started | 18 |
| Completed | 17 |
| Not completed | 1 |
| Lack of efficacy | 1 |

### Period 2

| | |
|---|---|
| Period 2 title | Maintenance Period Week 12 to 100 |
| Is this the baseline period? | No |
| Allocation method | Non-randomised - controlled |
| Blinding used | Not blinded |

## Arms

| **Arm title** | GED-0301 160 mg /Alt 4 Weeks |
|---|---|

Arm description:

Participants began the maintenance period after the Week 12 visit and initially received no GED-0301 from weeks 12 to 16, then received GED-0301 160 mg daily on an alternating schedule of 4 weeks on GED-0301 160 mg daily and 4 weeks off GED-0301 up to week 100.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | GED-0301 |
| Investigational medicinal product code | |
| Other name | Mongersen |
| Pharmaceutical forms | Coated tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Participants received GED-0301 160 mg tablets daily from week 12 to week 52 visit with an alternating schedule of 4 weeks off GED-0301 160 mg and 4 weeks on.

| **Number of subjects in period 2[1]** | GED-0301 160 mg /Alt 4 Weeks |
|---|---|
| Started | 16 |
| Received Treatment | 15 |
| Completed | 6 |
| Not completed | 10 |
| Terminated by Sponsor | 5 |
| Adverse event, non-fatal | 1 |
| Lack of efficacy | 4 |

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.
Justification: One subject did not enter the maintenance period due to lack of efficacy.

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | GED-0301 160 mg |
| Reporting group description: | |
| Participants received GED-0301 160 mg tablets daily during the induction period from week 0 up to week 12. | |

| Reporting group values | GED-0301 160 mg | Total | |
|---|---|---|---|
| Number of subjects | 18 | 18 | |
| Age Categorical<br>Units: Subjects | | | |
| In utero | 0 | 0 | |
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | |
| Newborns (0-27 days) | 0 | 0 | |
| Infants and toddlers (28 days-23 months) | 0 | 0 | |
| Children (2-11 years) | 0 | 0 | |
| Adolescents (12-17 years) | 0 | 0 | |
| Adults (18-64 years) | 18 | 18 | |
| From 65-84 years | 0 | 0 | |
| 85 years and over | 0 | 0 | |
| Age Continuous<br>Units: years | | | |
| arithmetic mean | 39.1 | | |
| standard deviation | ± 11.10 | - | |
| Gender Categorical<br>Units: Subjects | | | |
| Female | 7 | 7 | |
| Male | 11 | 11 | |
| Race<br>Units: Subjects | | | |
| White | 18 | 18 | |
| Duration of Crohn's Disease<br>Units: Years | | | |
| arithmetic mean | 10.75 | | |
| standard deviation | ± 7.558 | - | |
| Baseline Crohn's Disease Activity Index (CDAI) Score | | | |
| The Crohn's Disease Activity Index (CDAI) is used to quantify the signs and symptoms of Crohn's disease and the affect on patient's quality of life. It consists of 8 variables which include patient reported outcomes over a 7 day period and physician assessments which are scored numerically and weighted. Scores range from 0 to 600, with the most severe disease defined > 450. | | | |
| Units: units on scale | | | |
| arithmetic mean | 299.1 | | |
| standard deviation | ± 70.10 | - | |
| Baseline Simple Endoscopic Score (SES-CD) | | | |
| The Simple Endoscopic Score for Crohn's disease (SES-CD) is a validated index used to quantify the presence and size of ulcers, extent of ulcerated surface, extent of affected surface and presence and type of narrowings across 5 segments across the distal ileum and colon. Scores range from 0 to 60 with | | | |

| higher scores reflecting more severe disease. | | | |
|---|---|---|---|
| Units: units on a scale | | | |
| arithmetic mean | 14.8 | | |
| standard deviation | ± 10.04 | - | |

## End points

### End points reporting groups

| | |
|---|---|
| Reporting group title | GED-0301 160 mg |
| Reporting group description: | |
| Participants received GED-0301 160 mg tablets daily during the induction period from week 0 up to week 12. | |
| Reporting group title | GED-0301 160 mg /Alt 4 Weeks |
| Reporting group description: | |
| Participants began the maintenance period after the Week 12 visit and initially received no GED-0301 from weeks 12 to 16, then received GED-0301 160 mg daily on an alternating schedule of 4 weeks on GED-0301 160 mg daily and 4 weeks off GED-0301 up to week 100. | |

### Primary: Percent Change from Baseline of Smad7 Protein in the Intestinal Mucosa at Week 12

| | |
|---|---|
| End point title | Percent Change from Baseline of Smad7 Protein in the Intestinal Mucosa at Week 12[1] |
| End point description: | |
| Smad7 protein expression in the intestinal mucosa was evaluated from biopsy samples taken during ileocolonoscopy. Crohn's disease related inflammation is characterized by reduced activity of the immunosuppressive cytokine transforming growth factor β1 (TGF-β1) due to high levels of Smad7, an inhibitor of TGF-β1 signaling. The pharmacodynamic population included subjects who entered the study and had evaluable pharmacodynamic data. | |
| End point type | Primary |
| End point timeframe: | |
| Baseline to Week 12 | |

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: Statistical comparisons between treatment groups were not conducted in this study.

| End point values | GED-0301 160 mg | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 17 | | | |
| Units: percent change | | | | |
| median (confidence interval 95%) | -33.302 (-63.456 to 6.669) | | | |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Percent Change from Baseline in the Messenger Ribonucleic Acid (mRNA) Expression of Inflammatory Cytokines in the Intestinal Mucosa at Week 12

| | |
|---|---|
| End point title | Percent Change from Baseline in the Messenger Ribonucleic Acid (mRNA) Expression of Inflammatory Cytokines in the Intestinal Mucosa at Week 12 |

End point description:

Messenger RNA (mRNA) expression of inflammatory cytokines in the intestinal mucosa were evaluated from biopsy samples taken during ileocolonoscopy. Several inflammatory cytokines were assessed, including Interferon-Gamma (IFN-gamma), Interleukin-17A (IL-17), IL-21, Transforming Growth Factor-Beta (TGF-ß) and Tumor Necrosis Factor-Alpha (TNF)-α. The pharmacodynamic population included subjects who entered the study and had evaluable pharmacodynamic data.

| End point type | Secondary |
|---|---|

End point timeframe:

Week 12

| **End point values** | GED-0301 160 mg | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 17 | | | |
| Units: percent change | | | | |
| median (confidence interval 95%) | | | | |
| IFN-gamma | -12.63049 (-28.93519 to 106.87257) | | | |
| IL-17A | -43.28111 (-81.91115 to 27.94879) | | | |
| IL-21 | -9.03189 (-96.99325 to 39.07209) | | | |
| TGF-ß | 18.29742 (-1.16654 to 28.51651) | | | |
| TNF-α | -37.11355 (-70.18706 to 108.33319) | | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Participants who Achieved Clinical Remission Defined as CDAI score < 150 at Weeks 4, 8, and 12

| End point title | Percentage of Participants who Achieved Clinical Remission Defined as CDAI score < 150 at Weeks 4, 8, and 12 |
|---|---|

End point description:

Clinical remission is defined as a CDAI score < 150. The CDAI is used to quantify the signs and symptoms of Crohn's disease and the affect on patient's quality of life. It consists of 8 variables which include patient reported outcomes over a 7 day period and physician assessments which are scored numerically and weighted. Scores range from 0 to 600, with the most severe disease defined > 450. The intent to treat population included all subjects who received at least one dose of GED-0301. NRI = nonresponder imputation; subjects with insufficient data for response determination at the time point under consideration were considered nonresponders.

| End point type | Secondary |
|---|---|

End point timeframe:

Weeks 4, 8 and 12

| End point values | GED-0301 160 mg | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 18 | | | |
| Units: percentage of participants | | | | |
| number (confidence interval 95%) | | | | |
| Week 4 | 38.9 (20.3 to 61.4) | | | |
| Week 8 | 55.6 (33.7 to 75.4) | | | |
| Week 12 | 50.0 (29.0 to 71.0) | | | |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Change from Baseline in the Simple Endoscopic Score for Crohn’s Disease at Weeks 12

| End point title | Change from Baseline in the Simple Endoscopic Score for Crohn’s Disease at Weeks 12 |
|---|---|

End point description:

The Simple Endoscopic Score for Crohn's disease (SES-CD) is a validated index used to quantify the presence and size of ulcers, extent of ulcerated surface, extent of affected surface and presence and type of narrowings across 5 segments across the distal ileum and colon. Scores range from 0 to 60 with higher scores reflecting more severe disease. The intent to treat population included all subjects who received at least one dose of GED-0301. Subjects with at least 1 value (either baseline or postbaseline) were included in the longitudinal data analysis model. Data as observed. (DAO). The sample size at each time point was the number of subjects who had a value at that time point for inclusion in the model.

| End point type | Secondary |
|---|---|

End point timeframe:

Baseline to Week 12

| End point values | GED-0301 160 mg | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 17 | | | |
| Units: units on a scale | | | | |
| least squares mean (confidence interval 95%) | 0.2 (-1.7 to 2.0) | | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Change from Baseline in the Simple Endoscopic Score for Crohn’s Disease at Week 52

| End point title | Change from Baseline in the Simple Endoscopic Score for Crohn’s Disease at Week 52 |
|---|---|

End point description:

The Simple Endoscopic Score for Crohn's disease (SES-CD) is a validated index used to quantify the presence and size of ulcers, extent of ulcerated surface, extent of affected surface and presence and type of narrowings across 5 segments across the distal ileum and colon. Scores range from 0 to 60 with higher scores reflecting more severe disease. The intent to treat population included all subjects who received at least one dose of GED-0301. Subjects with at least 1 value (either baseline or postbaseline) were included in the longitudinal data analysis model; data as observed. (DAO).

| End point type | Secondary |
|---|---|

End point timeframe:

Baseline to Week 52

| **End point values** | GED-0301 160 mg /Alt 4 Weeks | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 7 | | | |
| Units: units on a scale | | | | |
| least squares mean (confidence interval 95%) | -2.7 (-11.1 to 5.6) | | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Participants with Treatment Emergent Adverse Events (TEAE) During the Induction Period: Week 0 to 12

| End point title | Number of Participants with Treatment Emergent Adverse Events (TEAE) During the Induction Period: Week 0 to 12 |
|---|---|

End point description:

A TEAE was defined as any adverse event (AE) occurring or worsening on or after the first treatment of GED-0301 and up to 28 days after the last GED-0301 dose or the last follow-up date, whichever occurred earlier. A serious AE = any AE which results in death; is life-threatening; requires inpatient hospitalization or prolongation of existing hospitalization; results in persistent or significant disability/incapacity, is a congenital anomaly/birth defect, constitutes an important medical event. The severity of AEs was assessed by the investigator and based on the following scale: Mild = asymptomatic or mild symptoms, clinical or diagnostic observations only; Moderate = symptoms cause moderate discomfort; Severe symptoms causing severe discomfort/pain. The safety population included all subjects who entered the study and received at least 1 dose of GED-0301.

| End point type | Secondary |
|---|---|

End point timeframe:

From the date of the first dose of GED-0301 during the induction period to the date of the last GED-0301 dose of the induction period. The median treatment duration was 12.05 weeks.

| End point values | GED-0301 160 mg | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 18 | | | |
| Units: Participants | | | | |
| Any TEAE | 8 | | | |
| Any Drug-related TEAE | 0 | | | |
| Any Severe TEAE | 0 | | | |
| Any Serious TEAE | 1 | | | |
| Any Serious Drug-related TEAE | 0 | | | |
| Any TEAE Leading to Drug Withdrawal | 0 | | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Participants with Treatment Emergent Adverse Events During the Maintenance Period: Week 12 to Week 100.

| End point title | Number of Participants with Treatment Emergent Adverse Events During the Maintenance Period: Week 12 to Week 100. |
|---|---|

End point description:

A TEAE was defined as any adverse event (AE) occurring or worsening on or after the first treatment of GED-0301 and up to 28 days after the last GED-0301 dose or the last follow-up date, whichever occurred earlier. A serious AE = any AE which results in death; is life-threatening; requires inpatient hospitalization or prolongation of existing hospitalization; results in persistent or significant disability/incapacity, is a congenital anomaly/birth defect, constitutes an important medical event. The severity of AEs was assessed by the investigator and based on the following scale: Mild = asymptomatic or mild symptoms, clinical or diagnostic observations only; Moderate = symptoms cause moderate discomfort; Severe symptoms causing severe discomfort/pain. The safety population included all subjects who entered the study and received at least 1 dose of GED-0301.

| End point type | Secondary |
|---|---|

End point timeframe:

From the first day of the first GED-0301 dose during the maintenance period and no later than 28 days after the last dose date of the maintenance period or the last follow-up date, whichever was earlier. The median treatment duration was 28.10 weeks.

| End point values | GED-0301 160 mg /Alt 4 Weeks | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 15 | | | |
| Units: participants | | | | |
| Any TEAE | 9 | | | |
| Any Drug-Related TEAE | 0 | | | |
| Any Severe TEAE | 1 | | | |
| Any Serious TEAE | 2 | | | |
| Any Serious Drug-related TEAE | 0 | | | |
| Any TEAE Leading to Drug Withdrawal | 1 | | | |

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

From the first day of GED-0301 until 28 days after the last dose of investigational product as well as those SAEs made known to the Investigator at any time thereafter that are suspected of being related to IP

Adverse event reporting additional description:

Induction Period - median treatment duration was 12.05 weeks. Maintenance Period - median treatment duration was 28.10 weeks; total GED-0301 Exposure Period -median treatment duration was 39.65 weeks

| | |
|---|---|
| Assessment type | Systematic |

### Dictionary used

| | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 20.0 |

### Reporting groups

| | |
|---|---|
| Reporting group title | GED-0301 160 mg Induction Period Week 0 to 12 |

Reporting group description:

Participants received GED-0301 160 mg daily from Week 0 up to Week 12.

| | |
|---|---|
| Reporting group title | GED-0301 160 mg/Alt 4 Weeks Maintenace Period Week 12 to 100 |

Reporting group description:

Participants began the maintenance period after the Week 12 visit and initially received no GED-0301 from weeks 12 to 16, then received GED-0301 160 mg daily on an alternating schedule of 4 weeks on GED-0301 160 mg daily and 4 weeks off GED-0301 up to week 100.

| Serious adverse events | GED-0301 160 mg Induction Period Week 0 to 12 | GED-0301 160 mg/Alt 4 Weeks Maintenace Period Week 12 to 100 | |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 2 / 15 (13.33%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | 0 | 0 | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Chondrosarcoma | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 15 (6.67%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal disorders | | | |
| Abdominal pain | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 15 (6.67%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|---|---|---|
| Infections and infestations | | | |
| Anal abscess | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 15 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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

| **Non-serious adverse events** | GED-0301 160 mg Induction Period Week 0 to 12 | GED-0301 160 mg/Alt 4 Weeks Maintenace Period Week 12 to 100 | |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 8 / 18 (44.44%) | 7 / 15 (46.67%) | |
| Investigations | | | |
| C-reactive protein increased | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 15 (6.67%) | |
| occurrences (all) | 0 | 1 | |
| Faecal calprotectin increased | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 1 / 15 (6.67%) | |
| occurrences (all) | 1 | 1 | |
| Weight decreased | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 15 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Injury, poisoning and procedural complications | | | |
| Radius fracture | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 15 (6.67%) | |
| occurrences (all) | 0 | 1 | |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 15 (6.67%) | |
| occurrences (all) | 0 | 1 | |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 15 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| General disorders and administration site conditions | | | |

| | | | |
|---|---|---|---|
| Oedema peripheral | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 15 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Pyrexia | | | |
| subjects affected / exposed | 4 / 18 (22.22%) | 1 / 15 (6.67%) | |
| occurrences (all) | 10 | 1 | |
| Gastrointestinal disorders | | | |
| Abdominal pain | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 15 (6.67%) | |
| occurrences (all) | 0 | 3 | |
| Anal fissure | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 15 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Dental caries | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 15 (6.67%) | |
| occurrences (all) | 0 | 1 | |
| Diarrhoea | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 15 (6.67%) | |
| occurrences (all) | 0 | 2 | |
| Diverticulum | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 15 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Haemorrhoids | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 15 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Nausea | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 1 / 15 (6.67%) | |
| occurrences (all) | 1 | 1 | |
| Proctalgia | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 15 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Vomiting | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 15 (6.67%) | |
| occurrences (all) | 0 | 6 | |
| Respiratory, thoracic and mediastinal disorders | | | |

| | | | |
|---|---|---|---|
| Asthma | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 1 / 15 (6.67%) | |
| occurrences (all) | 1 | 1 | |
| Skin and subcutaneous tissue disorders | | | |
| Dermatitis allergic | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 15 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Papule | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 1 / 15 (6.67%) | |
| occurrences (all) | 1 | 1 | |
| Psychiatric disorders | | | |
| Anxiety | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 15 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 2 / 18 (11.11%) | 2 / 15 (13.33%) | |
| occurrences (all) | 2 | 2 | |
| Infections and infestations | | | |
| Anal abscess | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 15 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Gastroenteritis | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 15 (6.67%) | |
| occurrences (all) | 0 | 1 | |
| Influenza | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 15 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Varicella | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 15 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Metabolism and nutrition disorders | | | |
| Hyperkalaemia | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 15 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Hypoglycaemia | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 15 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Vitamin D deficiency | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 15 (0.00%) | |
| occurrences (all) | 1 | 0 | |

## More information

## Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---|---|
| 08 August 2016 | 1. Added Week 52 endoscopy and key PD assessments 2. Added of Year 2 3. Added/revised endpoints based on the addition of the Week 52 endoscopic and PD outcomes and the addition of Year 2, (included safety, clinical efficacy, and PD outcomes through Week 100). 4. Revised Inclusion Criteria #5, to clarify that the presence of active CD must be determined by ileocolonoscopy at screening and #8 to remove aminosalicylates as one of the therapies that subjects may have failed to allow for study eligibility. Certolizumab was added as one of the therapies that subjects may have failed to allow for study eligibility. 5. Revised Exclusion Criteria #3 and #4, to clarify the protocol requirements to manifestations and complications of CD; exclusion criterion #14 (previously exclusion criterion #13) revised to exclude all bile acid sequestrants, not only cholestyramine; exclusion criterion #16 to prohibit subjects with prior exposure to biologics for the treatment of CD, approved or investigational; exclusion #17 (previously Exclusion Criterion #15 to clarify that subjects with prior exposure with > 2 TNF-α blockers were excluded, and biologic exposure was limited to the medications specified in exclusion criterion #16; exclusion criteria #18 (previously exclusion criterion #16) and exclusion criterion #29 (previously exclusion criterion #28) to note that a necessary longer washout duration was needed in the event that 5 elimination half-lives of the previous agent was longer than the 8-week washout period for biologics and 1-month washout period for other investigational drugs. 6. Revised baseline FCP collection time point from Visit 2 to Visit 1 7. Added corticosteroid tapering procedure for subjects who continued to take a stable dose upon study entry at screening and during the study. 8. Updated subject dosing instructions. 9. Added that subject may have been allowed to re-screen with approval from sponsor 10. Minor clarifications and corrections |
| 02 February 2017 | 1. Added endoscopic and clinical improvement criteria (≥ 50% reduction from baseline in the central reader SES-CD and HBI ≤ 7, respectively) at Year 1 (Week 52) to determine if subjects should have continued into Year 2 of the study 2. Added discontinuation criteria (HBI ≤ 7) if subject experienced "lack of efficacy" during Year 2; subjects who had an HBI > 7 for 2 consecutive study visits, at least 14 days apart, were required to be discontinued from the study 3. Minor clarifications and corrections. |

Notes:

## Interruptions (globally)

Were there any global interruptions to the trial? No

## Limitations and caveats

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

Following a recommendation by the Data Monitoring Committee (DMC), the study was terminated early by Celgene on 19 Oct 2017 due to a lack of emerging benefit; no emergent safety findings were noted.

Notes: