



## Clinical trial results:

### A Phase 3, long-term active treatment extension study of mongersen (GED-0301) in subjects with Crohn's disease

#### Summary

|                          |   |
|--------------------------|---|
| EudraCT number           | 2015-001963-37  |
| Trial protocol           | LV EE SK SE HU AT CZ GB DE ES PT BE DK BG GR HR FI IT |
| Global end of trial date | 04 January 2018                                       |

#### Results information

|                                |                 |
|--------------------------------|-----------------|
| Result version number          | v1 (current)    |
| This version publication date  | 24 January 2019 |
| First version publication date | 24 January 2019 |

#### Trial information

##### Trial identification

|                       |                 |
|-----------------------|-----------------|
| Sponsor protocol code | GED-0301-CD-004 |
|-----------------------|-----------------|

##### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT02641392 |
| 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           | Guillermo Rossiter, Celgene Corporation, 01 9088976467, grossiter@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                       | 30 May 2018     |
| Is this the analysis of the primary completion data? | No              |
| Global end of trial reached?                         | Yes             |
| Global end of trial date                             | 04 January 2018 |
| Was the trial ended prematurely?                     | Yes             |

Notes:

## General information about the trial

Main objective of the trial:

The primary objective of the study is to evaluate the long-term safety of oral GED-0301 in subjects with Crohn's disease (CD).

Protection of trial subjects:

Patient Confidentiality, Informed Consent, Archiving of Essential Documents

Background therapy: -

Evidence for comparator: -

|   |              |
|---|--------------|
| Actual start date of recruitment                          | 25 July 2016 |
| 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: 10         |
| Country: Number of subjects enrolled | Austria: 13           |
| Country: Number of subjects enrolled | Belgium: 12           |
| Country: Number of subjects enrolled | Bulgaria: 3           |
| Country: Number of subjects enrolled | Canada: 29            |
| Country: Number of subjects enrolled | Croatia: 2            |
| Country: Number of subjects enrolled | Czech Republic: 2     |
| Country: Number of subjects enrolled | Denmark: 11           |
| Country: Number of subjects enrolled | France: 24            |
| Country: Number of subjects enrolled | Germany: 57           |
| Country: Number of subjects enrolled | Greece: 3             |
| Country: Number of subjects enrolled | Hungary: 6            |
| Country: Number of subjects enrolled | Israel: 23            |
| Country: Number of subjects enrolled | Italy: 20             |
| Country: Number of subjects enrolled | Korea, Republic of: 9 |
| Country: Number of subjects enrolled | Latvia: 2             |
| Country: Number of subjects enrolled | Netherlands: 8        |
| Country: Number of subjects enrolled | Norway: 4             |
| Country: Number of subjects enrolled | Poland: 2             |
| Country: Number of subjects enrolled | Russian Federation: 5 |
| Country: Number of subjects enrolled | Serbia: 1             |
| Country: Number of subjects enrolled | Sweden: 2             |

|                                      |                   |
|--------------------------------------|-------------------|
| Country: Number of subjects enrolled | Switzerland: 2    |
| Country: Number of subjects enrolled | Turkey: 5         |
| Country: Number of subjects enrolled | Ukraine: 11       |
| Country: Number of subjects enrolled | United Kingdom: 1 |
| Country: Number of subjects enrolled | United States: 29 |
| Country: Number of subjects enrolled | Slovakia: 7       |
| Country: Number of subjects enrolled | Spain: 7          |
| Worldwide total number of subjects   | 310               |
| EEA total number of subjects         | 186               |

Notes:

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### **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)                      | 4   |
| From 65 to 84 years                       | 299 |
| 85 years and over                         | 7   |

## Subject disposition

### Recruitment

Recruitment details:

310 adult participants who had previously participated in the main study GED-0301-CD-002 were enrolled at 167 study sites in 29 countries.

### Pre-assignment

Screening details:

Includes participants with Crohn's disease who had previously participated in the main study GED-0301-CD-002 through Week 12 at minimum and completed participation through the last treatment visit at Week 52, or met the "early escape criteria" and were discontinued beginning at Week 12 through Week 52.

### Period 1

|                              |  |
|------------------------------|--|
| Period 1 title               | Overall Period (overall period)              |
| Is this the baseline period? | Yes  |
| Allocation method            | Non-randomised - controlled                  |
| Blinding used                | Double blind                                 |
| Roles blinded                | Subject, Investigator, Monitor, Data analyst |

### Arms

|                              |                            |
|------------------------------|----------------------------|
| Are arms mutually exclusive? | Yes                        |
| <b>Arm title</b>             | GED-0301 40 mg 4 Weeks Alt |

Arm description:

Participants received alternating placebo daily for 4 weeks and GED-0301 40 mg daily for 4 weeks, up to week 208.

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

Dosage and administration details:

Participants received alternating placebo daily for 4 weeks and GED-0301 40 mg daily for 4 weeks, up to week 208

|  |          |
|--|----------|
| Investigational medicinal product name | Placebo  |
| Investigational medicinal product code |          |
| Other name                             |          |
| Pharmaceutical forms                   | Tablet   |
| Routes of administration               | Oral use |

Dosage and administration details:

Participants received alternating placebo daily for 4 weeks and GED-0301 40 mg daily for 4 weeks, up to week 208

|                  |                |
|------------------|----------------|
| <b>Arm title</b> | GED-0301 40 mg |
|------------------|----------------|

Arm description:

Participants received continuous GED-0301 40 mg daily up to week 208.

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

Dosage and administration details:

Participants received continuous GED-0301 40 mg daily, up to week 208.

|  |                             |
|--|-----------------------------|
| <b>Arm title</b>   | GED-0301 160 mg 4 Weeks Alt |
| Arm description:   |                             |
| Participants received one of three dose regimens up to week 208:<br>(1) alternating placebo daily for 4 weeks and GED-0301 160 mg daily for 4 weeks or<br>(2) alternating GED-0301 160 mg daily for 4 weeks and placebo daily for 4 weeks or<br>(3) GED-0301 160 mg daily for 12 weeks, followed by alternating placebo daily for 4 weeks and GED-0301 160 mg daily for 4 weeks. |                             |
| Arm type   | Experimental                |
| Investigational medicinal product name   | GED-0301                    |
| Investigational medicinal product code   |                             |
| Other name   | Mongersen                   |
| Pharmaceutical forms   | Tablet                      |
| Routes of administration   | Oral use                    |

Dosage and administration details:

Participants received one of three dose regimens up to week 208:

- (1) alternating placebo daily for 4 weeks and GED-0301 160 mg daily for 4 weeks or
- (2) alternating GED-0301 160 mg daily for 4 weeks and placebo daily for 4 weeks or
- (3) GED-0301 160 mg daily for 12 weeks, followed by alternating placebo daily for 4 weeks and GED-0301 160 mg daily for 4 weeks.

|  |          |
|--|----------|
| Investigational medicinal product name | Placebo  |
| Investigational medicinal product code |          |
| Other name                             |          |
| Pharmaceutical forms                   | Tablet   |
| Routes of administration               | Oral use |

Dosage and administration details:

Participants received one of three dose regimens up to week 208:

- (1) alternating placebo daily for 4 weeks and GED-0301 160 mg daily for 4 weeks or
- (2) alternating GED-0301 160 mg daily for 4 weeks and placebo daily for 4 weeks or
- (3) GED-0301 160 mg daily for 12 weeks, followed by alternating placebo daily for 4 weeks and GED-0301 160 mg daily for 4 weeks

| <b>Number of subjects in period 1</b> | GED-0301 40 mg 4 Weeks Alt | GED-0301 40 mg | GED-0301 160 mg 4 Weeks Alt |
|---------------------------------------|----------------------------|----------------|-----------------------------|
| Started                               | 4                          | 13             | 293                         |
| Completed                             | 0                          | 0              | 0                           |
| Not completed                         | 4                          | 13             | 293                         |
| Adverse event, serious fatal          | -                          | -              | 1                           |
| Consent withdrawn by subject          | -                          | -              | 17                          |
| Adverse event, non-fatal              | -                          | 1              | 25                          |
| Miscellaneous                         | -                          | -              | 3                           |
| Study Terminated by Sponsor           | 4                          | 12             | 144                         |
| Lost to follow-up                     | -                          | -              | 2                           |
| Lack of efficacy                      | -                          | -              | 101                         |



## Baseline characteristics

### Reporting groups

|                              |  |
|------------------------------|--|
| Reporting group title        | GED-0301 40 mg 4 Weeks Alt   |
| Reporting group description: | Participants received alternating placebo daily for 4 weeks and GED-0301 40 mg daily for 4 weeks, up to week 208.  |
| Reporting group title        | GED-0301 40 mg   |
| Reporting group description: | Participants received continuous GED-0301 40 mg daily up to week 208.  |
| Reporting group title        | GED-0301 160 mg 4 Weeks Alt  |
| Reporting group description: | Participants received one of three dose regimens up to week 208:<br>(1) alternating placebo daily for 4 weeks and GED-0301 160 mg daily for 4 weeks or<br>(2) alternating GED-0301 160 mg daily for 4 weeks and placebo daily for 4 weeks or<br>(3) GED-0301 160 mg daily for 12 weeks, followed by alternating placebo daily for 4 weeks and GED-0301 160 mg daily for 4 weeks. |

| Reporting group values                             | GED-0301 40 mg 4 Weeks Alt | GED-0301 40 mg | GED-0301 160 mg 4 Weeks Alt |
|--|----------------------------|----------------|-----------------------------|
| Number of subjects                                 | 4                          | 13             | 293                         |
| Age Categorical<br>Units: Subjects                 |                            |                |                             |
| In utero   | 0                          | 0              | 0                           |
| Preterm newborn infants (gestational age < 37 wks) | 0                          | 0              | 0                           |
| Newborns (0-27 days)                               | 0                          | 0              | 0                           |
| Infants and toddlers (28 days-23 months)           | 0                          | 0              | 0                           |
| Children (2-11 years)                              | 0                          | 0              | 0                           |
| Adolescents (12-17 years)                          | 0                          | 0              | 0                           |
| Adults (18-64 years)                               | 4                          | 13             | 286                         |
| From 65-84 years                                   | 0                          | 0              | 7                           |
| 85 years and over                                  | 0                          | 0              | 0                           |
| Age Continuous<br>Units: years                     |                            |                |                             |
| arithmetic mean                                    | 35.3                       | 41.8           | 38.1                        |
| standard deviation                                 | ± 12.34                    | ± 14.21        | ± 12.30                     |
| Gender Categorical<br>Units: Subjects              |                            |                |                             |
| Female   | 3                          | 6              | 136                         |
| Male   | 1                          | 7              | 157                         |
| Race/Ethnicity, Customized<br>Units: Subjects      |                            |                |                             |
| American Indian or Alaska Native                   | 0                          | 0              | 2                           |
| Asian  | 0                          | 3              | 10                          |
| Black or African American                          | 0                          | 0              | 3                           |
| White  | 4                          | 9              | 264                         |
| Not Collected or Reported                          | 0                          | 1              | 10                          |
| Other  | 0                          | 0              | 4                           |

|  |                  |                  |                  |
|--|------------------|------------------|------------------|
| Duration of Crohn's Disease<br>Units: Years<br>arithmetic mean<br>standard deviation   | 7.25<br>± 6.529  | 9.25<br>± 6.307  | 10.56<br>± 8.503 |
| Baseline Crohn's Disease Activity (CDAI) Score   |                  |                  |                  |
| The Crohn's Disease Activity Index (CDAI) is used to quantify the signs and symptoms of Crohn's disease and the effect 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 a Scale<br>arithmetic mean<br>standard deviation   | 316.9<br>± 96.90 | 309.2<br>± 43.10 | 307.5<br>± 62.74 |

|  |       |  |  |
|--|-------|--|--|
| <b>Reporting group values</b>  | Total |  |  |
| Number of subjects   | 310   |  |  |
| Age Categorical<br>Units: Subjects   |       |  |  |
| In utero   | 0     |  |  |
| Preterm newborn infants (gestational age < 37 wks)   | 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)   | 303   |  |  |
| From 65-84 years   | 7     |  |  |
| 85 years and over  | 0     |  |  |
| Age Continuous<br>Units: years<br>arithmetic mean<br>standard deviation  | -     |  |  |
| Gender Categorical<br>Units: Subjects  |       |  |  |
| Female   | 145   |  |  |
| Male   | 165   |  |  |
| Race/Ethnicity, Customized<br>Units: Subjects  |       |  |  |
| American Indian or Alaska Native   | 2     |  |  |
| Asian  | 13    |  |  |
| Black or African American  | 3     |  |  |
| White  | 277   |  |  |
| Not Collected or Reported  | 11    |  |  |
| Other  | 4     |  |  |
| Duration of Crohn's Disease<br>Units: Years<br>arithmetic mean<br>standard deviation   | -     |  |  |
| Baseline Crohn's Disease Activity (CDAI) Score   |       |  |  |
| The Crohn's Disease Activity Index (CDAI) is used to quantify the signs and symptoms of Crohn's disease and the effect 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 a Scale   |   |  |  |
| arithmetic mean   |   |  |  |
| standard deviation  | - |  |  |

## End points

### End points reporting groups

|  |                             |
|--|-----------------------------|
| Reporting group title  | GED-0301 40 mg 4 Weeks Alt  |
| Reporting group description:<br>Participants received alternating placebo daily for 4 weeks and GED-0301 40 mg daily for 4 weeks, up to week 208.  |                             |
| Reporting group title  | GED-0301 40 mg              |
| Reporting group description:<br>Participants received continuous GED-0301 40 mg daily up to week 208.  |                             |
| Reporting group title  | GED-0301 160 mg 4 Weeks Alt |
| Reporting group description:<br>Participants received one of three dose regimens up to week 208:<br>(1) alternating placebo daily for 4 weeks and GED-0301 160 mg daily for 4 weeks or<br>(2) alternating GED-0301 160 mg daily for 4 weeks and placebo daily for 4 weeks or<br>(3) GED-0301 160 mg daily for 12 weeks, followed by alternating placebo daily for 4 weeks and GED-0301 160 mg daily for 4 weeks. |                             |

### Primary: Number of Participants with Treatment Emergent Adverse Events

|   |  |
|---|--|
| End point title   | Number of Participants with Treatment Emergent Adverse Events <sup>[1]</sup> |
| End point description:<br>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 (could be non- serious or serious) = symptoms causing severe discomfort/pain. |  |
| End point type  | Primary  |
| End point timeframe:<br>From the first day of GED-0301 until 28 days after the last dose of IP; maximum treatment duration was 16.1 weeks in the GED-0301 40 mg Alt dose; 16.3 weeks in the GED 40 mg continuous dose and 56.1 weeks in the GED-0301 160 mg Alt dose  |  |
| Notes:<br>[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.<br>Justification: No statistical analysis were performed as the study was terminated.   |  |

| End point values                    | GED-0301 40 mg 4 Weeks Alt | GED-0301 40 mg  | GED-0301 160 mg 4 Weeks Alt |  |
|-------------------------------------|----------------------------|-----------------|-----------------------------|--|
| Subject group type                  | Reporting group            | Reporting group | Reporting group             |  |
| Number of subjects analysed         | 4                          | 13              | 293                         |  |
| Units: Participants                 |                            |                 |                             |  |
| Any TEAE                            | 1                          | 6               | 189                         |  |
| Any Drug-Related TEAE               | 0                          | 1               | 43                          |  |
| Any Severe TEAE                     | 0                          | 0               | 38                          |  |
| Any Serious TEAE (SAE)              | 1                          | 0               | 41                          |  |
| Any Serious Drug-Related TEAE       | 0                          | 0               | 4                           |  |
| Any TEAE Leading to IP Interruption | 0                          | 0               | 7                           |  |
| Any TEAE Leading to IP Withdrawal   | 0                          | 1               | 27                          |  |
| Any TEAE Leading to Death           | 0                          | 0               | 1                           |  |

## **Statistical analyses**

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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 IP.

Adverse event reporting additional description:

Maximum treatment duration was 16.1 weeks in the GED-0301 40 mg Alt dose; 16.3 weeks in the GED 40 mg continuous dose and 56.1 weeks in the GED-0301 160 mg Alt dose.

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

### Dictionary used

|                 |        |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

|                    |      |
|--------------------|------|
| Dictionary version | 20.0 |
|--------------------|------|

### Reporting groups

|                       |                            |
|-----------------------|----------------------------|
| Reporting group title | GED-0301 40 mg 4 Weeks Alt |
|-----------------------|----------------------------|

Reporting group description:

Participants received alternating placebo daily for 4 weeks and GED-0301 40 mg daily for 4 weeks, up to week 208.

|                       |                |
|-----------------------|----------------|
| Reporting group title | GED-0301 40 mg |
|-----------------------|----------------|

Reporting group description:

Participants received continuous GED-0301 40 mg daily, up to week 208

|                       |                             |
|-----------------------|-----------------------------|
| Reporting group title | GED-0301 160 mg 4 Weeks Alt |
|-----------------------|-----------------------------|

Reporting group description:

Participants received one of three dose regimens up to week 208;

(1) alternating placebo daily for 4 weeks and GED-0301 160 mg daily for 4 weeks or

(2) alternating GED-0301 160 mg daily for 4 weeks and placebo daily for 4 weeks or

(3) GED-0301 160 mg daily for 12 weeks, followed by alternating placebo daily for 4 weeks and GED-0301 160 mg daily for 4 weeks.

| <b>Serious adverse events</b>                     | GED-0301 40 mg 4 Weeks Alt | GED-0301 40 mg | GED-0301 160 mg 4 Weeks Alt |
|---|----------------------------|----------------|-----------------------------|
| Total subjects affected by serious adverse events |                            |                |                             |
| subjects affected / exposed                       | 1 / 4 (25.00%)             | 0 / 13 (0.00%) | 41 / 293 (13.99%)           |
| number of deaths (all causes)                     | 0                          | 0              | 1                           |
| number of deaths resulting from adverse events    | 0                          | 0              | 0                           |
| Investigations                                    |                            |                |                             |
| ELECTROCARDIOGRAM T WAVE INVERSION                |                            |                |                             |
| subjects affected / exposed                       | 1 / 4 (25.00%)             | 0 / 13 (0.00%) | 0 / 293 (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                       |
| HEPATIC ENZYME INCREASED                          |                            |                |                             |
| subjects affected / exposed                       | 0 / 4 (0.00%)              | 0 / 13 (0.00%) | 1 / 293 (0.34%)             |
| occurrences causally related to treatment / all   | 0 / 0                      | 0 / 0          | 1 / 1                       |
| deaths causally related to treatment / all        | 0 / 0                      | 0 / 0          | 0 / 0                       |

|  |               |                |                 |
|--|---------------|----------------|-----------------|
| Injury, poisoning and procedural complications       |               |                |                 |
| ANASTOMOTIC ULCER<br>HAEMORRHAGE                     |               |                |                 |
| subjects affected / exposed                          | 0 / 4 (0.00%) | 0 / 13 (0.00%) | 1 / 293 (0.34%) |
| occurrences causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 1           |
| deaths causally related to treatment / all           | 0 / 0         | 0 / 0          | 0 / 0           |
| Blood and lymphatic system disorders                 |               |                |                 |
| ANAEMIA  |               |                |                 |
| subjects affected / exposed                          | 0 / 4 (0.00%) | 0 / 13 (0.00%) | 1 / 293 (0.34%) |
| occurrences causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 1           |
| deaths causally related to treatment / all           | 0 / 0         | 0 / 0          | 0 / 0           |
| General disorders and administration site conditions |               |                |                 |
| DROWNING   |               |                |                 |
| subjects affected / exposed                          | 0 / 4 (0.00%) | 0 / 13 (0.00%) | 1 / 293 (0.34%) |
| occurrences causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 1           |
| deaths causally related to treatment / all           | 0 / 0         | 0 / 0          | 0 / 1           |
| FATIGUE  |               |                |                 |
| subjects affected / exposed                          | 0 / 4 (0.00%) | 0 / 13 (0.00%) | 1 / 293 (0.34%) |
| occurrences causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 1           |
| deaths causally related to treatment / all           | 0 / 0         | 0 / 0          | 0 / 0           |
| HYPERTHERMIA   |               |                |                 |
| subjects affected / exposed                          | 0 / 4 (0.00%) | 0 / 13 (0.00%) | 1 / 293 (0.34%) |
| occurrences causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 1           |
| deaths causally related to treatment / all           | 0 / 0         | 0 / 0          | 0 / 0           |
| Gastrointestinal disorders                           |               |                |                 |
| ABDOMINAL PAIN                                       |               |                |                 |
| subjects affected / exposed                          | 0 / 4 (0.00%) | 0 / 13 (0.00%) | 2 / 293 (0.68%) |
| occurrences causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 2           |
| deaths causally related to treatment / all           | 0 / 0         | 0 / 0          | 0 / 0           |
| ANAL FISTULA   |               |                |                 |
| subjects affected / exposed                          | 0 / 4 (0.00%) | 0 / 13 (0.00%) | 2 / 293 (0.68%) |
| occurrences causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 3           |
| deaths causally related to treatment / all           | 0 / 0         | 0 / 0          | 0 / 0           |
| ANAL STENOSIS  |               |                |                 |

|   |               |                |                  |
|---|---------------|----------------|------------------|
| subjects affected / exposed                     | 0 / 4 (0.00%) | 0 / 13 (0.00%) | 1 / 293 (0.34%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 2            |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0            |
| <b>CROHN'S DISEASE</b>                          |               |                |                  |
| subjects affected / exposed                     | 0 / 4 (0.00%) | 0 / 13 (0.00%) | 12 / 293 (4.10%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 14           |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0            |
| <b>ILEAL STENOSIS</b>                           |               |                |                  |
| subjects affected / exposed                     | 0 / 4 (0.00%) | 0 / 13 (0.00%) | 5 / 293 (1.71%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 5            |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0            |
| <b>INTESTINAL HAEMORRHAGE</b>                   |               |                |                  |
| subjects affected / exposed                     | 0 / 4 (0.00%) | 0 / 13 (0.00%) | 1 / 293 (0.34%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0            |
| <b>INTESTINAL STENOSIS</b>                      |               |                |                  |
| subjects affected / exposed                     | 0 / 4 (0.00%) | 0 / 13 (0.00%) | 1 / 293 (0.34%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0            |
| <b>LARGE INTESTINAL STENOSIS</b>                |               |                |                  |
| subjects affected / exposed                     | 0 / 4 (0.00%) | 0 / 13 (0.00%) | 4 / 293 (1.37%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 4            |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0            |
| <b>RECTAL HAEMORRHAGE</b>                       |               |                |                  |
| subjects affected / exposed                     | 0 / 4 (0.00%) | 0 / 13 (0.00%) | 1 / 293 (0.34%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0            |
| <b>SMALL INTESTINAL OBSTRUCTION</b>             |               |                |                  |
| subjects affected / exposed                     | 0 / 4 (0.00%) | 0 / 13 (0.00%) | 1 / 293 (0.34%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0            |
| <b>SUBILEUS</b>                                 |               |                |                  |

|  |               |                |                 |
|--|---------------|----------------|-----------------|
| subjects affected / exposed                            | 0 / 4 (0.00%) | 0 / 13 (0.00%) | 2 / 293 (0.68%) |
| occurrences causally related to treatment / all        | 0 / 0         | 0 / 0          | 0 / 2           |
| deaths causally related to treatment / all             | 0 / 0         | 0 / 0          | 0 / 0           |
| <b>Skin and subcutaneous tissue disorders</b>          |               |                |                 |
| <b>ACUTE FEBRILE NEUTROPHILIC DERMATOSIS</b>           |               |                |                 |
| subjects affected / exposed                            | 0 / 4 (0.00%) | 0 / 13 (0.00%) | 1 / 293 (0.34%) |
| occurrences causally related to treatment / all        | 0 / 0         | 0 / 0          | 1 / 1           |
| deaths causally related to treatment / all             | 0 / 0         | 0 / 0          | 0 / 0           |
| <b>Renal and urinary disorders</b>                     |               |                |                 |
| <b>VESICAL FISTULA</b>                                 |               |                |                 |
| subjects affected / exposed                            | 0 / 4 (0.00%) | 0 / 13 (0.00%) | 1 / 293 (0.34%) |
| occurrences causally related to treatment / all        | 0 / 0         | 0 / 0          | 0 / 1           |
| deaths causally related to treatment / all             | 0 / 0         | 0 / 0          | 0 / 0           |
| <b>Musculoskeletal and connective tissue disorders</b> |               |                |                 |
| <b>ANKYLOSING SPONDYLITIS</b>                          |               |                |                 |
| subjects affected / exposed                            | 0 / 4 (0.00%) | 0 / 13 (0.00%) | 1 / 293 (0.34%) |
| occurrences causally related to treatment / all        | 0 / 0         | 0 / 0          | 0 / 1           |
| deaths causally related to treatment / all             | 0 / 0         | 0 / 0          | 0 / 0           |
| <b>BACK PAIN</b>                                       |               |                |                 |
| subjects affected / exposed                            | 0 / 4 (0.00%) | 0 / 13 (0.00%) | 1 / 293 (0.34%) |
| occurrences causally related to treatment / all        | 0 / 0         | 0 / 0          | 0 / 1           |
| deaths causally related to treatment / all             | 0 / 0         | 0 / 0          | 0 / 0           |
| <b>Infections and infestations</b>                     |               |                |                 |
| <b>ABDOMINAL ABSCESS</b>                               |               |                |                 |
| subjects affected / exposed                            | 0 / 4 (0.00%) | 0 / 13 (0.00%) | 1 / 293 (0.34%) |
| occurrences causally related to treatment / all        | 0 / 0         | 0 / 0          | 0 / 1           |
| deaths causally related to treatment / all             | 0 / 0         | 0 / 0          | 0 / 0           |
| <b>ANAL ABSCESS</b>                                    |               |                |                 |
| subjects affected / exposed                            | 0 / 4 (0.00%) | 0 / 13 (0.00%) | 3 / 293 (1.02%) |
| occurrences causally related to treatment / all        | 0 / 0         | 0 / 0          | 1 / 3           |
| deaths causally related to treatment / all             | 0 / 0         | 0 / 0          | 0 / 0           |
| <b>APPENDICITIS</b>                                    |               |                |                 |

|   |               |                |                 |
|---|---------------|----------------|-----------------|
| subjects affected / exposed                     | 0 / 4 (0.00%) | 0 / 13 (0.00%) | 1 / 293 (0.34%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0           |
| <b>CAMPYLOBACTER GASTROENTERITIS</b>            |               |                |                 |
| subjects affected / exposed                     | 0 / 4 (0.00%) | 0 / 13 (0.00%) | 1 / 293 (0.34%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0           |
| <b>GROIN ABSCESS</b>                            |               |                |                 |
| subjects affected / exposed                     | 0 / 4 (0.00%) | 0 / 13 (0.00%) | 1 / 293 (0.34%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0           |
| <b>INFECTIOUS COLITIS</b>                       |               |                |                 |
| subjects affected / exposed                     | 0 / 4 (0.00%) | 0 / 13 (0.00%) | 1 / 293 (0.34%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0           |
| <b>PERIRECTAL ABSCESS</b>                       |               |                |                 |
| subjects affected / exposed                     | 0 / 4 (0.00%) | 0 / 13 (0.00%) | 2 / 293 (0.68%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 2           |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0           |
| <b>POSTOPERATIVE ABSCESS</b>                    |               |                |                 |
| subjects affected / exposed                     | 0 / 4 (0.00%) | 0 / 13 (0.00%) | 1 / 293 (0.34%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0           |
| <b>PULMONARY SEPSIS</b>                         |               |                |                 |
| subjects affected / exposed                     | 0 / 4 (0.00%) | 0 / 13 (0.00%) | 1 / 293 (0.34%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 1 / 1           |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0           |
| <b>SALMONELLOSIS</b>                            |               |                |                 |
| subjects affected / exposed                     | 0 / 4 (0.00%) | 0 / 13 (0.00%) | 1 / 293 (0.34%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0           |
| <b>URINARY TRACT INFECTION</b>                  |               |                |                 |

|   |               |                |                 |
|---|---------------|----------------|-----------------|
| subjects affected / exposed                     | 0 / 4 (0.00%) | 0 / 13 (0.00%) | 1 / 293 (0.34%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0           |
| <b>VULVAL ABSCESS</b>                           |               |                |                 |
| subjects affected / exposed                     | 0 / 4 (0.00%) | 0 / 13 (0.00%) | 1 / 293 (0.34%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0           |

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

| <b>Non-serious adverse events</b>                     | GED-0301 40 mg 4 Weeks Alt | GED-0301 40 mg  | GED-0301 160 mg 4 Weeks Alt |
|---|----------------------------|-----------------|-----------------------------|
| Total subjects affected by non-serious adverse events |                            |                 |                             |
| subjects affected / exposed                           | 1 / 4 (25.00%)             | 6 / 13 (46.15%) | 92 / 293 (31.40%)           |
| Investigations  |                            |                 |                             |
| ELECTROCARDIOGRAM T WAVE INVERSION                    |                            |                 |                             |
| subjects affected / exposed                           | 1 / 4 (25.00%)             | 0 / 13 (0.00%)  | 0 / 293 (0.00%)             |
| occurrences (all)                                     | 1                          | 0               | 0                           |
| Injury, poisoning and procedural complications        |                            |                 |                             |
| RADIUS FRACTURE                                       |                            |                 |                             |
| subjects affected / exposed                           | 0 / 4 (0.00%)              | 1 / 13 (7.69%)  | 0 / 293 (0.00%)             |
| occurrences (all)                                     | 0                          | 1               | 0                           |
| Cardiac disorders                                     |                            |                 |                             |
| CARDIAC VALVE DISEASE                                 |                            |                 |                             |
| subjects affected / exposed                           | 1 / 4 (25.00%)             | 0 / 13 (0.00%)  | 0 / 293 (0.00%)             |
| occurrences (all)                                     | 1                          | 0               | 0                           |
| Nervous system disorders                              |                            |                 |                             |
| HEADACHE  |                            |                 |                             |
| subjects affected / exposed                           | 0 / 4 (0.00%)              | 0 / 13 (0.00%)  | 16 / 293 (5.46%)            |
| occurrences (all)                                     | 0                          | 0               | 18                          |
| Gastrointestinal disorders                            |                            |                 |                             |
| ABDOMINAL PAIN  |                            |                 |                             |
| subjects affected / exposed                           | 0 / 4 (0.00%)              | 1 / 13 (7.69%)  | 29 / 293 (9.90%)            |
| occurrences (all)                                     | 0                          | 1               | 35                          |
| ANAL FISTULA  |                            |                 |                             |

|   |                     |                      |                         |
|---|---------------------|----------------------|-------------------------|
| subjects affected / exposed<br>occurrences (all)  | 0 / 4 (0.00%)<br>0  | 1 / 13 (7.69%)<br>1  | 0 / 293 (0.00%)<br>0    |
| APHTHOUS ULCER<br>subjects affected / exposed<br>occurrences (all)  | 0 / 4 (0.00%)<br>0  | 1 / 13 (7.69%)<br>1  | 0 / 293 (0.00%)<br>0    |
| CROHN'S DISEASE<br>subjects affected / exposed<br>occurrences (all)   | 0 / 4 (0.00%)<br>0  | 1 / 13 (7.69%)<br>1  | 30 / 293 (10.24%)<br>35 |
| DIARRHOEA<br>subjects affected / exposed<br>occurrences (all)   | 0 / 4 (0.00%)<br>0  | 1 / 13 (7.69%)<br>1  | 0 / 293 (0.00%)<br>0    |
| ILEAL STENOSIS<br>subjects affected / exposed<br>occurrences (all)  | 0 / 4 (0.00%)<br>0  | 1 / 13 (7.69%)<br>1  | 0 / 293 (0.00%)<br>0    |
| Hepatobiliary disorders<br>GALLBLADDER DISORDER<br>subjects affected / exposed<br>occurrences (all)               | 1 / 4 (25.00%)<br>1 | 0 / 13 (0.00%)<br>0  | 0 / 293 (0.00%)<br>0    |
| Musculoskeletal and connective tissue disorders<br>ARTHRALGIA<br>subjects affected / exposed<br>occurrences (all) | 0 / 4 (0.00%)<br>0  | 2 / 13 (15.38%)<br>2 | 27 / 293 (9.22%)<br>29  |
| Infections and infestations<br>CYSTITIS<br>subjects affected / exposed<br>occurrences (all)                       | 0 / 4 (0.00%)<br>0  | 1 / 13 (7.69%)<br>1  | 0 / 293 (0.00%)<br>0    |
| UPPER RESPIRATORY TRACT INFECTION<br>subjects affected / exposed<br>occurrences (all)                             | 0 / 4 (0.00%)<br>0  | 1 / 13 (7.69%)<br>1  | 0 / 293 (0.00%)<br>0    |
| VIRAL UPPER RESPIRATORY TRACT INFECTION<br>subjects affected / exposed<br>occurrences (all)                       | 1 / 4 (25.00%)<br>1 | 1 / 13 (7.69%)<br>2  | 20 / 293 (6.83%)<br>28  |
| Metabolism and nutrition disorders<br>HYPERLIPIDAEMIA   |                     |                      |                         |

|                             |                |                |                 |
|-----------------------------|----------------|----------------|-----------------|
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 13 (0.00%) | 0 / 293 (0.00%) |
| occurrences (all)           | 1              | 0              | 0               |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date            | Amendment   |
|-----------------|---|
| 06 January 2017 | <ol style="list-style-type: none"><li>1. The addition of adolescent subjects into this long-term active treatment extension study who previously participated in the Phase 3 Study GED-0301-CD-003.</li><li>2. New sections were added to the protocol that applied specifically to adolescent subjects.</li><li>3. The objectives, endpoints, inclusion/exclusion criteria, table of events, procedures, and assessments sections were separated for the adult and adolescent subjects throughout the protocol, where appropriate, to clearly indicate protocol information which applied specifically to adult versus adolescent subjects.</li><li>4. Previous GED-0301-CD-003 subjects were to have an ileocolonoscopy with intestinal mucosal biopsies during the screening period and at Week 12 in the core GED-0301-CD-003 study. A Week 40 ileocolonoscopy with intestinal mucosal biopsies was to be included in this study for these adult subjects, as well as the adolescent subjects, to determine if mucosal healing and/or endoscopic remission was achieved after 52 weeks of GED-0301 therapy from the combined studies (12 weeks from GED-0301-CD-003 and 40 weeks from GED-0301-CD-004) in the adult (and adolescent) populations.</li><li>5. The Week 12 clinical criteria were added for discontinuing subjects who did not achieve a minimum level of improvement by Week 12.</li></ol> |

Notes:

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### 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: