



Clinical trial results:

A Phase 3, randomized, double-blind, placebo-controlled, multicenter study to investigate the efficacy and safety of mongersen (GED-0301) for the treatment of subjects with active Crohn's disease.

Summary

| | |
|--------------------------|--|
| EudraCT number | 2015-001925-18 |
| Trial protocol | GB SE SK LV EE DE PT HU CZ AT ES DK BE NO BG GR HR FI IT |
| Global end of trial date | 22 January 2018 |

Results information

| | |
|--------------------------------|-----------------|
| Result version number | v1 (current) |
| This version publication date | 25 January 2019 |
| First version publication date | 25 January 2019 |

Trial information

Trial identification

| | |
|-----------------------|-----------------|
| Sponsor protocol code | GED-0301-CD-002 |
|-----------------------|-----------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT02596893 |
| 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, MD, Celgene Corporation, 01 908-897-6467, 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 | 02 May 2018 |
| Is this the analysis of the primary completion data? | No |

| | |
|----------------------------------|-----------------|
| Global end of trial reached? | Yes |
| Global end of trial date | 22 January 2018 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy of GED-0301 compared with placebo on clinical activity at Week 12 in subjects with active CD.

Protection of trial subjects:

Patient Confidentiality, Personal Data Protection; Archiving of essential documents.

Background therapy: -

Evidence for comparator: -

| | |
|---|------------------|
| Actual start date of recruitment | 08 December 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: 26 |
| Country: Number of subjects enrolled | Austria: 17 |
| Country: Number of subjects enrolled | Belgium: 14 |
| Country: Number of subjects enrolled | Bulgaria: 9 |
| Country: Number of subjects enrolled | Canada: 56 |
| Country: Number of subjects enrolled | Croatia: 6 |
| Country: Number of subjects enrolled | Czech Republic: 5 |
| Country: Number of subjects enrolled | Denmark: 16 |
| Country: Number of subjects enrolled | Estonia: 1 |
| Country: Number of subjects enrolled | France: 49 |
| Country: Number of subjects enrolled | Germany: 107 |
| Country: Number of subjects enrolled | Greece: 12 |
| Country: Number of subjects enrolled | Hungary: 15 |
| Country: Number of subjects enrolled | Israel: 34 |
| Country: Number of subjects enrolled | Italy: 48 |
| Country: Number of subjects enrolled | Korea, Democratic People's Republic of: 21 |
| Country: Number of subjects enrolled | Latvia: 7 |
| Country: Number of subjects enrolled | Netherlands: 18 |
| Country: Number of subjects enrolled | Norway: 9 |
| Country: Number of subjects enrolled | Poland: 12 |
| Country: Number of subjects enrolled | Portugal: 9 |
| Country: Number of subjects enrolled | Romania: 5 |

| | |
|--------------------------------------|------------------------|
| Country: Number of subjects enrolled | Russian Federation: 22 |
| Country: Number of subjects enrolled | Serbia: 5 |
| Country: Number of subjects enrolled | Slovakia: 17 |
| Country: Number of subjects enrolled | Spain: 9 |
| Country: Number of subjects enrolled | Sweden: 3 |
| Country: Number of subjects enrolled | Switzerland: 5 |
| Country: Number of subjects enrolled | Turkey: 15 |
| Country: Number of subjects enrolled | Ukraine: 22 |
| Country: Number of subjects enrolled | United States: 86 |
| Country: Number of subjects enrolled | United Kingdom: 21 |
| Worldwide total number of subjects | 701 |
| EEA total number of subjects | 409 |

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) | 681 |
| From 65 to 84 years | 20 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

701 subjects were enrolled from the United States, Canada, Eastern and Western Europe, Australia, Korea and Russia.

Pre-assignment

Screening details:

Treatment assignment at baseline (Week 0) was stratified based on concomitant use of corticosteroids (yes/no), concomitant use of immunosuppressants (yes/no) or and previous exposure to biologics (yes/no).

Period 1

| | |
|------------------------------|---|
| Period 1 title | Double-Blind Period Weeks 0-52 (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator, Monitor, Data analyst |

Blinding implementation details:

During the study, coded GED-0301 or placebo tablets were dispensed in accordance with the randomization number assigned by the Interactive Response System. The blind was not to be broken unless, it was absolutely necessary to safely treat the subject. The decision to break the blind in emergency situations was the responsibility of the treating physician.

Arms

| | |
|------------------------------|---------|
| Are arms mutually exclusive? | Yes |
| Arm title | Placebo |

Arm description:

Participants received placebo daily up to week 52.

| | |
|--|----------|
| Arm type | Placebo |
| 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 placebo daily up to week 52.

| | |
|------------------|--|
| Arm title | GED-0301 160 mg / GED-0301 40 mg 4 Weeks Alt |
|------------------|--|

Arm description:

Participants received GED-0301 160 mg daily for 12 weeks, followed by alternating placebo daily for 4 weeks and GED-0301 40 mg daily for 4 weeks, up to week 52.

| | |
|--|--------------|
| 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 GED-0301 160 mg daily for 12 weeks, followed by alternating placebo daily for 4 weeks and GED-0301 40 mg daily for 4 weeks, up to week 52.

| | |
|------------------|----------------------------------|
| Arm title | GED-0301 160 mg / GED-0301 40 mg |
|------------------|----------------------------------|

Arm description:

Participants received GED-0301 160 mg daily for 12 weeks, followed by continuous GED-0301 40 mg

daily up to week 52.

| | |
|--|--------------|
| 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 GED-0301 160 mg daily for 12 weeks, followed by continuous GED-0301 40 mg daily, up to week 52.

| | |
|------------------|--|
| Arm title | GED-0301 160 mg / GED-0301 160 mg 4 Week Alt |
|------------------|--|

Arm description:

Participants received 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, up to week 52.

| | |
|--|--------------|
| 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 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, up to week 52.

| Number of subjects in period 1 | Placebo | GED-0301 160 mg / GED-0301 40 mg 4 Weeks Alt | GED-0301 160 mg / GED-0301 40 mg |
|---------------------------------------|---------|--|-------------------------------------|
| Started | 174 | 176 | 176 |
| Completed | 10 | 8 | 14 |
| Not completed | 164 | 168 | 162 |
| Adverse event, serious fatal | - | - | 1 |
| Consent withdrawn by subject | 10 | 4 | 13 |
| Non-compliance with Study Drug | - | - | 1 |
| Adverse event, non-fatal | 11 | 15 | 15 |
| Miscellaneous | 1 | 2 | - |
| Early Escape | 66 | 76 | 69 |
| Pregnancy | - | - | - |
| Study Terminated by Sponsor | 61 | 56 | 48 |
| Lost to follow-up | - | 1 | 1 |
| Lack of efficacy | 15 | 14 | 14 |
| Protocol deviation | - | - | - |

| Number of subjects in period 1 | GED-0301 160 mg / GED-0301 160 mg 4 Week Alt |
|---------------------------------------|--|
| Started | 175 |

| | |
|--------------------------------|-----|
| Completed | 9 |
| Not completed | 166 |
| Adverse event, serious fatal | - |
| Consent withdrawn by subject | 5 |
| Non-compliance with Study Drug | 2 |
| Adverse event, non-fatal | 12 |
| Miscellaneous | 2 |
| Early Escape | 70 |
| Pregnancy | 1 |
| Study Terminated by Sponsor | 58 |
| Lost to follow-up | 1 |
| Lack of efficacy | 13 |
| Protocol deviation | 2 |

Baseline characteristics

Reporting groups

| | |
|---|--|
| Reporting group title | Placebo |
| Reporting group description: Participants received placebo daily up to week 52. | |
| Reporting group title | GED-0301 160 mg / GED-0301 40 mg 4 Weeks Alt |
| Reporting group description: Participants received GED-0301 160 mg daily for 12 weeks, followed by alternating placebo daily for 4 weeks and GED-0301 40 mg daily for 4 weeks, up to week 52. | |
| Reporting group title | GED-0301 160 mg / GED-0301 40 mg |
| Reporting group description: Participants received GED-0301 160 mg daily for 12 weeks, followed by continuous GED-0301 40 mg daily up to week 52. | |
| Reporting group title | GED-0301 160 mg / GED-0301 160 mg 4 Week Alt |
| Reporting group description: Participants received 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, up to week 52. | |

| Reporting group values | Placebo | GED-0301 160 mg / GED-0301 40 mg 4 Weeks Alt | GED-0301 160 mg / GED-0301 40 mg |
|---|---------|--|-------------------------------------|
| Number of subjects | 174 | 176 | 176 |
| Age categorical Units: Subjects | | | |
| In utero | 0 | 0 | 0 |
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | 0 |
| Newborns (0-27 days) | 0 | 0 | 0 |
| Infants and toddlers (28 days-23 months) | 0 | 0 | 0 |
| Children (2-11 years) | 0 | 0 | 0 |
| Adolescents (12-17 years) | 0 | 0 | 0 |
| Adults (18-64 years) | 168 | 172 | 171 |
| From 65-84 years | 6 | 4 | 5 |
| 85 years and over | 0 | 0 | 0 |
| Age Continuous Units: Years | | | |
| arithmetic mean | 38.5 | 37.6 | 39.6 |
| standard deviation | ± 12.88 | ± 12.84 | ± 12.90 |
| Sex: Female, Male Units: Subjects | | | |
| Female | 76 | 98 | 92 |
| Male | 98 | 78 | 84 |
| Race/Ethnicity, Customized Units: Subjects | | | |
| American Indian or Alaska Native | 1 | 0 | 1 |
| Asian | 11 | 2 | 8 |
| Black or African American | 4 | 4 | 2 |
| White | 150 | 165 | 152 |
| Not Collected or Reported | 5 | 4 | 9 |

| | | | |
|---------------------------|---|---|---|
| Other (No classification) | 3 | 1 | 4 |
|---------------------------|---|---|---|

| | | | |
|---|------------------|------------------|------------------|
| Duration of Crohn's Disease Units: Years arithmetic mean standard deviation | 9.57 ± 9.106 | 8.63 ± 7.877 | 9.84 ± 8.746 |
| 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 | 307.9 ± 64.31 | 292.8 ± 69.33 | 308.3 ± 65.50 |
| Baseline Endoscopic Score for Crohn's Disease (Central Read) | | | |
| 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 standard deviation | 14.4 ± 7.88 | 14.3 ± 8.41 | 13.8 ± 7.69 |

| Reporting group values | GED-0301 160 mg / GED-0301 160 mg 4 Week Alt | Total | |
|---|--|-------|--|
| Number of subjects | 175 | 701 | |
| Age categorical 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) | 170 | 681 | |
| From 65-84 years | 5 | 20 | |
| 85 years and over | 0 | 0 | |
| Age Continuous Units: Years arithmetic mean standard deviation | 38.2 ± 12.47 | - | |
| Sex: Female, Male Units: Subjects | | | |
| Female | 80 | 346 | |
| Male | 95 | 355 | |
| Race/Ethnicity, Customized Units: Subjects | | | |
| American Indian or Alaska Native | 0 | 2 | |
| Asian | 8 | 29 | |

| | | | |
|---|---------|-----|--|
| Black or African American | 2 | 12 | |
| White | 158 | 625 | |
| Not Collected or Reported | 5 | 23 | |
| Other (No classification) | 2 | 10 | |
| Duration of Crohn's Disease | | | |
| Units: Years | | | |
| arithmetic mean | 10.15 | | |
| standard deviation | ± 9.353 | - | |
| 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 | 309.9 | | |
| standard deviation | ± 66.32 | - | |
| Baseline Endoscopic Score for Crohn's Disease (Central Read) | | | |
| 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 | 14.5 | | |
| standard deviation | ± 8.30 | - | |

End points

End points reporting groups

| | |
|---|--|
| Reporting group title | Placebo |
| Reporting group description: Participants received placebo daily up to week 52. | |
| Reporting group title | GED-0301 160 mg / GED-0301 40 mg 4 Weeks Alt |
| Reporting group description: Participants received GED-0301 160 mg daily for 12 weeks, followed by alternating placebo daily for 4 weeks and GED-0301 40 mg daily for 4 weeks, up to week 52. | |
| Reporting group title | GED-0301 160 mg / GED-0301 40 mg |
| Reporting group description: Participants received GED-0301 160 mg daily for 12 weeks, followed by continuous GED-0301 40 mg daily up to week 52. | |
| Reporting group title | GED-0301 160 mg / GED-0301 160 mg 4 Week Alt |
| Reporting group description: Participants received 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, up to week 52. | |

Primary: The Percentage of Participants Who Achieved a Clinical Remission at Week 12

| | |
|--|---|
| End point title | The Percentage of Participants Who Achieved a Clinical Remission at Week 12 |
| End point description: Clinical remission is defined as a Crohn's Disease Activity Index (CDAI) score < 150. The Crohn's Disease Activity Index 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. Includes intent to treat population, and included participants who had either completed that timepoint visit or discontinued at any time due to reasons other than study terminated | |
| End point type | Primary |
| End point timeframe: Week 12 | |

| End point values | Placebo | GED-0301 160 mg / GED-0301 40 mg 4 Weeks Alt | GED-0301 160 mg / GED-0301 40 mg | GED-0301 160 mg / GED-0301 160 mg 4 Week Alt |
|-----------------------------------|---------------------|--|----------------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 160 | 162 | 164 | 157 |
| Units: Percentage of Participants | | | | |
| number (confidence interval 95%) | 25.0 (18.9 to 32.2) | 25.3 (19.2 to 32.5) | 21.3 (15.8 to 28.2) | 21.7 (15.9 to 28.7) |

Statistical analyses

| | |
|---|--|
| Statistical analysis title | Statistical Analysis 1 |
| Statistical analysis description: | |
| The weighted average of the treatment differences across the strata with the CMH weights. | |
| Comparison groups | Placebo v GED-0301 160 mg / GED-0301 40 mg 4 Weeks Alt |
| Number of subjects included in analysis | 322 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.9141 |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Stratified Difference |
| Point estimate | 0.5 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -8.9 |
| upper limit | 10 |

| | |
|---|--|
| Statistical analysis title | Statistical Analysis 2 |
| Statistical analysis description: | |
| The weighted average of the treatment differences across the strata with the CMH weights. | |
| Comparison groups | Placebo v GED-0301 160 mg / GED-0301 40 mg |
| Number of subjects included in analysis | 324 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.4286 |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Stratified Difference |
| Point estimate | -3.6 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -12.8 |
| upper limit | 5.6 |

| | |
|---|--|
| Statistical analysis title | Statistical Analysis 3 |
| Statistical analysis description: | |
| The weighted average of the treatment differences across the strata with the CMH weights. | |
| Comparison groups | Placebo v GED-0301 160 mg / GED-0301 160 mg 4 Week Alt |
| Number of subjects included in analysis | 317 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.5591 |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Stratified Difference |
| Point estimate | -2.7 |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -12 |
| upper limit | 6.6 |

Secondary: Percentage of Participants Who Achieved Clinical Remission at Week 52

| | |
|-----------------|---|
| End point title | Percentage of Participants Who Achieved Clinical Remission at Week 52 |
|-----------------|---|

End point description:

Clinical remission is defined as a CDAI score < 150 and 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. Intent to Treat Population; includes Included participants who had either completed that timepoint visit or discontinued at any time due to reasons other than study terminated by sponsor. NRI.

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

End point timeframe:

Week 52

| End point values | Placebo | GED-0301 160 mg / GED-0301 40 mg 4 Weeks Alt | GED-0301 160 mg / GED-0301 40 mg | GED-0301 160 mg / GED-0301 160 mg 4 Week Alt |
|-----------------------------------|-------------------|--|----------------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 113 | 120 | 128 | 117 |
| Units: percentage of participants | | | | |
| number (confidence interval 95%) | 5.3 (2.5 to 11.1) | 2.5 (0.9 to 7.1) | 9.4 (5.4 to 15.7) | 3.4 (1.3 to 8.5) |

Statistical analyses

| | |
|----------------------------|------------------------|
| Statistical analysis title | Statistical Analysis 1 |
|----------------------------|------------------------|

Statistical analysis description:

The weighted average of the treatment differences across the strata with the CMH weights.

| | |
|---|--|
| Comparison groups | Placebo v GED-0301 160 mg / GED-0301 40 mg 4 Weeks Alt |
| Number of subjects included in analysis | 233 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.2523 |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Stratified Difference |
| Point estimate | -2.9 |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -9.7 |
| upper limit | 3.9 |

| | |
|---|--|
| Statistical analysis title | Statistical Analysis 2 |
| Statistical analysis description: | |
| The weighted average of the treatment differences across the strata with the CMH weights. | |
| Comparison groups | Placebo v GED-0301 160 mg / GED-0301 40 mg |
| Number of subjects included in analysis | 241 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.1626 |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Stratified Difference |
| Point estimate | 4.8 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -3 |
| upper limit | 11.8 |

| | |
|---|--|
| Statistical analysis title | Statistical Analysis 3 |
| Statistical analysis description: | |
| The weighted average of the treatment differences across the strata with the CMH weights. | |
| Comparison groups | Placebo v GED-0301 160 mg / GED-0301 160 mg 4 Week Alt |
| Number of subjects included in analysis | 230 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.442 |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Stratified Difference |
| Point estimate | -2.1 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -9.1 |
| upper limit | 5.3 |

| | |
|--|--|
| Secondary: Percentage of Participants With Endoscopic Response-50 Centrally Read at Week 52 | |
| End point title | Percentage of Participants With Endoscopic Response-50 Centrally Read at Week 52 |

End point description:

An endoscopic response-50 is defined as a reduction of at least 50% compared to baseline in the simple endoscopic score for Crohn's disease (SES-CD). The SES-CD assesses the size of mucosal ulcers, the extent of ulcerated surface, the extent of affected surface, and the presence and type of narrowings. Scores range from 0 to 60 with higher scores reflecting more severe disease. The SES-CD calculations include: - Ulcers scored as: 0: no 1: aphthous (0.1-0.5 cm) 2: large (0.5-2 cm) 3: very large (>2 cm) - Surface involved disease 0: 0% 1: <50% 2: 50-75% 3: >75% Surface involved by ulcerations: 0: 0% 1: <10% 2: 10-30% 3: >30% - Narrowings: 0: No 1: Single, can be passed 2: Multiple, can be passed 3: Cannot be passed Grand Total = SES-CD score. ITT population. Included participants who had either completed that timepoint visit or discontinued at any time due to reasons other than study terminated by sponsor. NRI.

| | |
|----------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Week 52 | |

| End point values | Placebo | GED-0301 160 mg / GED-0301 40 mg 4 Weeks Alt | GED-0301 160 mg / GED-0301 40 mg | GED-0301 160 mg / GED-0301 160 mg 4 Week Alt |
|-----------------------------------|------------------|--|----------------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 113 | 120 | 128 | 117 |
| Units: percentage pf participants | | | | |
| number (confidence interval 95%) | 3.5 (1.4 to 8.7) | 0.8 (0.1 to 4.6) | 1.6 (0.4 to 5.5) | 1.7 (0.5 to 6.0) |

Statistical analyses

| | |
|---|--|
| Statistical analysis title | Statistical Analysis 1 |
| Statistical analysis description: | |
| The weighted average of the treatment differences across the strata with the CMH weights. | |
| Comparison groups | Placebo v GED-0301 160 mg / GED-0301 40 mg 4 Weeks Alt |
| Number of subjects included in analysis | 233 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.1799 |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Stratified Difference |
| Point estimate | -2.6 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -9.5 |
| upper limit | 5 |

| | |
|---|--|
| Statistical analysis title | Statistical Analysis 2 |
| Statistical analysis description: | |
| The weighted average of the treatment differences across the strata with the CMH weights. | |
| Comparison groups | Placebo v GED-0301 160 mg / GED-0301 40 mg |

| | |
|---|-------------------------|
| Number of subjects included in analysis | 241 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.2309 |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Stratified Difference |
| Point estimate | -2.4 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -9.4 |
| upper limit | 4.9 |

| | |
|--|--|
| Statistical analysis title | Statistical Analysis 3 |
| Statistical analysis description: The weighted average of the treatment differences across the strata with the CMH weights. | |
| Comparison groups | Placebo v GED-0301 160 mg / GED-0301 160 mg 4 Week Alt |
| Number of subjects included in analysis | 230 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.3264 |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Stratified Difference |
| Point estimate | -2.1 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -9.1 |
| upper limit | 4.6 |

Secondary: The Percentage of Participants Who Achieved a Clinical Response at Week 12

| | |
|--|--|
| End point title | The Percentage of Participants Who Achieved a Clinical Response at Week 12 |
| End point description: A clinical response is defined as a CDAI score decrease from baseline ≥ 100 points. The 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 . ITT Population. Included participants who had either completed that timepoint visit or discontinued at any time due to reasons other than study terminated by sponsor. NRI. | |
| End point type | Secondary |
| End point timeframe: Week 12 | |

| End point values | Placebo | GED-0301 160 mg / GED-0301 40 mg 4 Weeks Alt | GED-0301 160 mg / GED-0301 40 mg | GED-0301 160 mg / GED-0301 160 mg 4 Week Alt |
|-----------------------------------|---------------------|--|----------------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 160 | 162 | 164 | 157 |
| Units: percentage of participants | | | | |
| number (confidence interval 95%) | 44.4 (36.9 to 52.1) | 32.1 (25.4 to 39.6) | 34.1 (27.3 to 41.7) | 33.8 (26.8 to 41.5) |

Statistical analyses

| Statistical analysis title | Statistical Analysis 1 |
|--|--|
| Statistical analysis description: The weighted average of the treatment differences across the strata with the CMH weights. | |
| Comparison groups | Placebo v GED-0301 160 mg / GED-0301 40 mg 4 Weeks Alt |
| Number of subjects included in analysis | 322 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0299 |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Stratified Difference |
| Point estimate | -11.7 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -22 |
| upper limit | -1.1 |

| Statistical analysis title | Statistical Analysis 2 |
|--|--|
| Statistical analysis description: The weighted average of the treatment differences across the strata with the CMH weights. | |
| Comparison groups | Placebo v GED-0301 160 mg / GED-0301 40 mg |
| Number of subjects included in analysis | 324 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0582 |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Stratified difference |
| Point estimate | -9.9 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -20.3 |
| upper limit | 0.7 |

| | |
|---|--|
| Statistical analysis title | Statistical Analysis 3 |
| Comparison groups | Placebo v GED-0301 160 mg / GED-0301 160 mg 4 Week Alt |
| Number of subjects included in analysis | 317 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0741 |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Stratified difference |
| Point estimate | -9.7 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -20.1 |
| upper limit | 1 |

Secondary: The Percentage of Participants Who Achieved a Clinical Response at Week 4

| | |
|--|---|
| End point title | The Percentage of Participants Who Achieved a Clinical Response at Week 4 |
| End point description: A clinical response is defined as a decrease from baseline in CDAI \geq 100 points. The Crohn's Disease Activity Index 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 . ITT Population. NRI. | |
| End point type | Secondary |
| End point timeframe: Week 4 | |

| End point values | Placebo | GED-0301 160 mg / GED-0301 40 mg 4 Weeks Alt | GED-0301 160 mg / GED-0301 40 mg | GED-0301 160 mg / GED-0301 160 mg 4 Week Alt |
|-----------------------------------|---------------------|--|----------------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 169 | 172 | 170 | 169 |
| Units: percentage of participants | | | | |
| number (confidence interval 95%) | 34.3 (27.6 to 41.8) | 28.5 (22.3 to 35.6) | 32.4 (25.8 to 39.7) | 27.8 (21.6 to 35.0) |

Statistical analyses

| | |
|--|--|
| Statistical analysis title | Statistical Analysis 1 |
| Statistical analysis description: The weighted average of the treatment differences across the strata with the CMH weights. | |
| Comparison groups | Placebo v GED-0301 160 mg / GED-0301 40 mg 4 Weeks Alt |

| | |
|---|-------------------------|
| Number of subjects included in analysis | 341 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.2493 |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Stratified difference |
| Point estimate | -5.8 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -15.5 |
| upper limit | 4 |

| | |
|-----------------------------------|------------------------|
| Statistical analysis title | Statistical Analysis 2 |
|-----------------------------------|------------------------|

Statistical analysis description:

The weighted average of the treatment differences across the strata with the CMH weights.

| | |
|---|--|
| Comparison groups | Placebo v GED-0301 160 mg / GED-0301 40 mg |
| Number of subjects included in analysis | 339 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.716 |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Stratified difference |
| Point estimate | -1.8 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -11.8 |
| upper limit | 8.2 |

| | |
|-----------------------------------|------------------------|
| Statistical analysis title | Statistical Analysis 3 |
|-----------------------------------|------------------------|

Statistical analysis description:

The weighted average of the treatment differences across the strata with the CMH weights.

| | |
|---|--|
| Comparison groups | Placebo v GED-0301 160 mg / GED-0301 160 mg 4 Week Alt |
| Number of subjects included in analysis | 338 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.2452 |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Stratified difference |
| Point estimate | -5.8 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -15.5 |
| upper limit | 4.1 |

Secondary: The Percentage of Participants Who Achieved a Clinical Remission at Week 4

| | |
|---|--|
| End point title | The Percentage of Participants Who Achieved a Clinical Remission at Week 4 |
| End point description: A clinical remission is a CDAI score < 150. The Crohn's Disease Activity Index 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. ITT Population. NRI. | |
| End point type | Secondary |
| End point timeframe: Week 4 | |

| End point values | Placebo | GED-0301 160 mg / GED-0301 40 mg 4 Weeks Alt | GED-0301 160 mg / GED-0301 40 mg | GED-0301 160 mg / GED-0301 160 mg 4 Week Alt |
|-----------------------------------|---------------------|--|----------------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 169 | 172 | 170 | 169 |
| Units: percentage of participants | | | | |
| number (confidence interval 95%) | 20.1 (14.8 to 26.8) | 18.6 (13.5 to 25.1) | 16.5 (11.6 to 22.8) | 15.4 (10.7 to 21.6) |

Statistical analyses

| | |
|--|--|
| Statistical analysis title | Statistical Analysis 1 |
| Statistical analysis description: The weighted average of the treatment differences across the strata with the CMH weights. | |
| Comparison groups | Placebo v GED-0301 160 mg / GED-0301 40 mg 4 Weeks Alt |
| Number of subjects included in analysis | 341 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.7541 |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Stratified difference |
| Point estimate | -1.3 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -9.8 |
| upper limit | 7.1 |

| | |
|---|--|
| Statistical analysis title | Statistical Analysis 2 |
| Statistical analysis description: | |
| The weighted average of the treatment differences across the strata with the CMH weights. | |
| Comparison groups | Placebo v GED-0301 160 mg / GED-0301 40 mg |
| Number of subjects included in analysis | 339 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.3784 |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Stratified difference |
| Point estimate | -3.7 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -12 |
| upper limit | 4.6 |

| | |
|---|--|
| Statistical analysis title | Statistical Analysis 3 |
| Statistical analysis description: | |
| The weighted average of the treatment differences across the strata with the CMH weights. | |
| Comparison groups | Placebo v GED-0301 160 mg / GED-0301 160 mg 4 Week Alt |
| Number of subjects included in analysis | 338 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.2865 |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Stratified difference |
| Point estimate | -4.4 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -12.6 |
| upper limit | 3.8 |

Secondary: The Percentage of Participants Who Achieved a Corticosteroid-Free Clinical Remission at Week 52

| | |
|---|---|
| End point title | The Percentage of Participants Who Achieved a Corticosteroid-Free Clinical Remission at Week 52 |
| End point description: | |
| <p>The percentage of participants who were receiving oral corticosteroids for Crohn's disease, at baseline and achieved a clinical remission (CDAI score <150) at Week 52 without corticosteroids. The Crohn's Disease Activity Index 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. ITT Population. Includes participants who received oral corticosteroids at baseline and had either completed that timepoint visit or discontinued at any time due to reasons other than study terminated by sponsor. NRI.</p> | |
| End point type | Secondary |

End point timeframe:

Week 52

| End point values | Placebo | GED-0301 160 mg / GED-0301 40 mg 4 Weeks Alt | GED-0301 160 mg / GED-0301 40 mg | GED-0301 160 mg / GED-0301 160 mg 4 Week Alt |
|-----------------------------------|-------------------|--|----------------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 46 | 39 | 43 | 42 |
| Units: percentage of participants | | | | |
| number (confidence interval 95%) | 2.2 (0.4 to 11.3) | 0.0 (0.0 to 9.0) | 7.0 (2.4 to 18.6) | 2.4 (0.4 to 12.3) |

Statistical analyses

| Statistical analysis title | Statistical Analysis 1 |
|----------------------------|------------------------|
|----------------------------|------------------------|

Statistical analysis description:

2-sided 95% CI were based on the unstratified Newcombe method.

| | |
|---|--|
| Comparison groups | Placebo v GED-0301 160 mg / GED-0301 40 mg 4 Weeks Alt |
| Number of subjects included in analysis | 85 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.3572 ^[1] |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Unstratified CMH |
| Point estimate | -2.2 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -11.3 |
| upper limit | 7 |

Notes:

[1] - p-values were based on the unstratified CMH test when 1 and only 1 of the 2 treatment groups being compared had no subjects in a stratum.

| Statistical analysis title | Statistical Analysis 2 |
|----------------------------|------------------------|
|----------------------------|------------------------|

Statistical analysis description:

The weighted average of the treatment differences across the strata with the CMH weights.

| | |
|---|--|
| Comparison groups | Placebo v GED-0301 160 mg / GED-0301 40 mg |
| Number of subjects included in analysis | 89 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.2823 |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Stratified difference |
| Point estimate | 4.7 |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -8.8 |
| upper limit | 18.9 |

| | |
|---|--|
| Statistical analysis title | Statistical Analysis 3 |
| Statistical analysis description: | |
| The weighted average of the treatment differences across the strata with the CMH weights. | |
| Comparison groups | Placebo v GED-0301 160 mg / GED-0301 160 mg 4 Week Alt |
| Number of subjects included in analysis | 88 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | > 0.9999 |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Stratified difference |
| Point estimate | 0 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -12.8 |
| upper limit | 13.7 |

Secondary: Percentage of Participants Who Achieved a Sustained Clinical Remission at Both Week 12 and 52

| | |
|--|---|
| End point title | Percentage of Participants Who Achieved a Sustained Clinical Remission at Both Week 12 and 52 |
| End point description: | |
| For participants who achieved a sustained clinical remission at both week 12 and 52, the clinical remission is a CDAI score < 150. The Crohn's Disease Activity Index 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. ITT Population. NRI. | |
| End point type | Secondary |
| End point timeframe: | |
| Weeks 12 and 52 | |

| End point values | Placebo | GED-0301 160 mg / GED-0301 40 mg 4 Weeks Alt | GED-0301 160 mg / GED-0301 40 mg | GED-0301 160 mg / GED-0301 160 mg 4 Week Alt |
|-----------------------------------|------------------|--|----------------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 113 | 120 | 128 | 117 |
| Units: percentage of participants | | | | |
| number (confidence interval 95%) | 2.7 (0.9 to 7.5) | 2.5 (0.9 to 7.1) | 3.9 (1.7 to 8.8) | 1.7 (0.5 to 5.0) |

Statistical analyses

| | |
|--|--|
| Statistical analysis title | Statistical Analysis 1 |
| Statistical analysis description: The weighted average of the treatment differences across the strata with CMH weights. | |
| Comparison groups | Placebo v GED-0301 160 mg / GED-0301 40 mg 4 Weeks Alt |
| Number of subjects included in analysis | 233 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.8031 |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Stratified difference |
| Point estimate | -0.5 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -6.7 |
| upper limit | 5.9 |

| | |
|--|--|
| Statistical analysis title | Statistical Analysis 2 |
| Statistical analysis description: The weighted average of the treatment differences across the strata with CMH weights. | |
| Comparison groups | Placebo v GED-0301 160 mg / GED-0301 40 mg |
| Number of subjects included in analysis | 241 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.5583 |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Stratified difference |
| Point estimate | 1.4 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -5.1 |
| upper limit | 7.3 |

| | |
|--|--|
| Statistical analysis title | Statistical Analysis 3 |
| Statistical analysis description: The weighted average of the treatment differences across the strata with CMH weights. | |
| Comparison groups | Placebo v GED-0301 160 mg / GED-0301 160 mg 4 Week Alt |

| | |
|---|-------------------------|
| Number of subjects included in analysis | 230 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.6123 |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Stratified difference |
| Point estimate | -1 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -7.2 |
| upper limit | 6.8 |

Secondary: Percentage of Participants With Endoscopic Response-25 Centrally Read at Week 12

| | |
|-----------------|--|
| End point title | Percentage of Participants With Endoscopic Response-25 Centrally Read at Week 12 |
|-----------------|--|

End point description:

An endoscopic response-25 is defined as a reduction of at least 25% compared to baseline in simple endoscopic score for Crohn's disease (SES-CD). The SES-CD assesses the size of mucosal ulcers, the extent of ulcerated surface, the extent of affected surface, and the presence and type of narrowings. Scores range from 0 to 60 with higher scores reflecting more severe disease. The SES-CD calculations include: - Ulcers scored as: 0: no 1: aphthous (0.1-0.5 cm) 2: large (0.5-2 cm) 3: very large (>2 cm) - Surface involved disease 0: 0% 1: <50% 2: 50-75% 3: >75% Surface involved by ulcerations: 0: 0% 1: <10% 2: 10-30% 3: >30% - Narrowings: 0: No 1: Single, can be passed 2: Multiple, can be passed 3: Cannot be passed Grand Total = SES-CD score. ITT Population. NRI.

| | |
|----------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Week 0, Week 12 | |

| End point values | Placebo | GED-0301 160 mg / GED-0301 40 mg 4 Weeks Alt | GED-0301 160 mg / GED-0301 40 mg | GED-0301 160 mg / GED-0301 160 mg 4 Week Alt |
|-----------------------------------|---------------------|--|----------------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 160 | 162 | 164 | 157 |
| Units: percentage pf participants | | | | |
| number (confidence interval 95%) | 28.1 (21.7 to 35.5) | 17.3 (12.2 to 23.8) | 27.4 (21.2 to 34.7) | 24.2 (18.2 to 31.5) |

Statistical analyses

| | |
|----------------------------|------------------------|
| Statistical analysis title | Statistical Analysis 1 |
|----------------------------|------------------------|

Statistical analysis description:

The weighted average of the treatment differences across the strata with the CMH weights.

| | |
|-------------------|--|
| Comparison groups | Placebo v GED-0301 160 mg / GED-0301 40 mg 4 Weeks Alt |
|-------------------|--|

| | |
|---|-------------------------|
| Number of subjects included in analysis | 322 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0239 |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Stratified difference |
| Point estimate | -10.6 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -19.6 |
| upper limit | -1.4 |

| | |
|-----------------------------------|------------------------|
| Statistical analysis title | Statistical Analysis 2 |
|-----------------------------------|------------------------|

Statistical analysis description:

The weighted average of the treatment differences across the strata with the CMH weights.

| | |
|---|--|
| Comparison groups | Placebo v GED-0301 160 mg / GED-0301 40 mg |
| Number of subjects included in analysis | 324 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.8334 |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Stratified difference |
| Point estimate | -1 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -10.8 |
| upper limit | 8.7 |

| | |
|-----------------------------------|------------------------|
| Statistical analysis title | Statistical Analysis 3 |
|-----------------------------------|------------------------|

Statistical analysis description:

The weighted average of the treatment differences across the strata with the CMH weights.

| | |
|---|--|
| Comparison groups | Placebo v GED-0301 160 mg / GED-0301 160 mg 4 Week Alt |
| Number of subjects included in analysis | 317 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.4383 |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Stratified difference |
| Point estimate | -3.9 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -13.5 |
| upper limit | 5.8 |

Secondary: Percentage of Participants With Endoscopic Remission Centrally Read at Week 52

| | |
|-----------------|--|
| End point title | Percentage of Participants With Endoscopic Remission Centrally Read at Week 52 |
|-----------------|--|

End point description:

Endoscopic remission is defined as a simple endoscopic score for Crohn's disease (SES-CD) of ≤ 2 at the specified timeframe. The SES-CD assesses the size of mucosal ulcers, the extent of ulcerated surface, the extent of affected surface, and the presence and type of narrowings. Scores range from 0 to 60 with higher scores reflecting more severe disease. The SES-CD calculations include: - Ulcers scored as: 0: no 1: aphthous (0.1-0.5 cm) 2: large (0.5-2 cm) 3: very large (>2 cm) - Surface involved disease 0: 0% 1: $<50\%$ 2: 50-75% 3: $>75\%$ Surface involved by ulcerations: 0: 0% 1: $<10\%$ 2: 10-30% 3: $>30\%$ - Narrowings: 0: No 1: Single, can be passed 2: Multiple, can be passed 3: Cannot be passed Grand Total = SES-CD score. ITT Population. NRI.

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

End point timeframe:

Week 52

| End point values | Placebo | GED-0301 160 mg / GED-0301 40 mg 4 Weeks Alt | GED-0301 160 mg / GED-0301 40 mg | GED-0301 160 mg / GED-0301 160 mg 4 Week Alt |
|-----------------------------------|------------------|--|----------------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 113 | 120 | 128 | 117 |
| Units: percentage pf participants | | | | |
| number (confidence interval 95%) | 2.7 (0.9 to 7.5) | 0.8 (0.1 to 4.6) | 0.8 (0.1 to 4.3) | 0.9 (0.2 to 4.7) |

Statistical analyses

| | |
|----------------------------|------------------------|
| Statistical analysis title | Statistical Analysis 1 |
|----------------------------|------------------------|

Statistical analysis description:

The weighted average of the treatment differences across the strata with CMH weights.

| | |
|---|--|
| Comparison groups | Placebo v GED-0301 160 mg / GED-0301 40 mg 4 Weeks Alt |
| Number of subjects included in analysis | 233 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.3573 |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Stratified difference |
| Point estimate | -1.6 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -8.3 |
| upper limit | 5.9 |

| | |
|--|--|
| Statistical analysis title | Statistical Analysis 2 |
| Statistical analysis description: The weighted average of the treatment differences across the strata with CMH weights. | |
| Comparison groups | Placebo v GED-0301 160 mg / GED-0301 40 mg |
| Number of subjects included in analysis | 241 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.2221 |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Stratified difference |
| Point estimate | -2 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -8.7 |
| upper limit | 5.1 |

| | |
|--|--|
| Statistical analysis title | Statistical Analysis 3 |
| Statistical analysis description: The weighted average of the treatment differences across the strata with CMH weights. | |
| Comparison groups | Placebo v GED-0301 160 mg / GED-0301 160 mg 4 Week Alt |
| Number of subjects included in analysis | 230 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.2578 |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Stratified difference |
| Point estimate | -2 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -8.7 |
| upper limit | 5.6 |

Secondary: The Number of Participants Who Experienced Treatment Emergent Adverse Events (TEAE) from Week 0 to Week 52

| | |
|-----------------|--|
| End point title | The Number of Participants Who Experienced Treatment Emergent Adverse Events (TEAE) from Week 0 to Week 52 |
|-----------------|--|

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 (could be non-serious or serious) = symptoms causing severe discomfort/pain. Safety population includes subjects who received at least one dose of GED-0301.

| | |
|---|-----------|
| End point type | Secondary |
| End point timeframe: | |
| From the first day of GED-0301 until 28 days after the last dose of investigational product (IP); maximum treatment duration was 52.6 weeks | |

| End point values | Placebo | GED-0301 160 mg / GED-0301 40 mg 4 Weeks Alt | GED-0301 160 mg / GED-0301 40 mg | GED-0301 160 mg / GED-0301 160 mg 4 Week Alt |
|-------------------------------------|-----------------|--|----------------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 174 | 176 | 176 | 175 |
| Units: participants | | | | |
| Any TEAE | 124 | 128 | 129 | 113 |
| Any IP-Related TEAE | 31 | 35 | 30 | 20 |
| Any Severe TEAE | 14 | 22 | 21 | 15 |
| Any Serious TEAE (SAE) | 16 | 28 | 22 | 15 |
| Any Serious IP-Related TEAE | 3 | 2 | 2 | 0 |
| Any TEAE Leading to IP Withdrawal | 11 | 15 | 16 | 12 |
| Any TEAE Leading to IP Interruption | 4 | 4 | 5 | 4 |
| Any TEAE Leading to Death | 0 | 0 | 1 | 1 |

Statistical analyses

No statistical analyses for this end point

Secondary: The Number of Participants Who Discontinued IP due to an Treatment Emergent Adverse Events

| | |
|-----------------|--|
| End point title | The Number of Participants Who Discontinued IP due to an Treatment Emergent Adverse Events |
|-----------------|--|

End point description:

A TEAE was defined as any AE occurring or worsening on or after the first dose 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. Safety Population.

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

End point timeframe:

From the first day of GED-0301 until 28 days after the last dose of IP; maximum treatment duration was 52.6 weeks

| End point values | Placebo | GED-0301 160 mg / GED-0301 40 mg 4 Weeks Alt | GED-0301 160 mg / GED-0301 40 mg | GED-0301 160 mg / GED-0301 160 mg 4 Week Alt |
|-----------------------------|-----------------|--|----------------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 174 | 176 | 176 | 175 |
| Units: participants | 11 | 15 | 16 | 12 |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From day 1 of GED-0301 until 28 days after the last dose of IP 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:

Maximum treatment duration was 52.6 weeks

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

Dictionary used

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

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

Reporting groups

| | |
|-----------------------|---------|
| Reporting group title | Placebo |
|-----------------------|---------|

Reporting group description:

Participants received placebo daily up to week 52.

| | |
|-----------------------|---|
| Reporting group title | GED-0301 160 mg / GED-0301 40 mg 4 Week Alt |
|-----------------------|---|

Reporting group description:

Participants received GED-0301 160 mg daily for 12 weeks, followed by alternating placebo daily for 4 weeks and GED-0301 40 mg daily for 4 weeks, up to week 52.

| | |
|-----------------------|----------------------------------|
| Reporting group title | GED-0301 160 mg / GED-0301 40 mg |
|-----------------------|----------------------------------|

Reporting group description:

Participants received GED-0301 160 mg daily for 12 weeks, followed by continuous GED-0301 40 mg daily, up to week 52.

| | |
|-----------------------|--|
| Reporting group title | GED-0301 160 mg / GED-0301 160 mg 4 Week Alt |
|-----------------------|--|

Reporting group description:

Participants received 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, up to week 52.

| Serious adverse events | Placebo | GED-0301 160 mg / GED-0301 40 mg 4 Week Alt | GED-0301 160 mg / GED-0301 40 mg |
|---|------------------|---|-------------------------------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 16 / 174 (9.20%) | 28 / 176 (15.91%) | 22 / 176 (12.50%) |
| number of deaths (all causes) | 0 | 0 | 1 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| CERVIX NEOPLASM | | | |
| subjects affected / exposed | 0 / 174 (0.00%) | 0 / 176 (0.00%) | 1 / 176 (0.57%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| NEUROENDOCRINE TUMOUR | | | |

| | | | |
|--|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 174 (0.00%) | 0 / 176 (0.00%) | 0 / 176 (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 |
| General disorders and administration site conditions | | | |
| ASTHENIA | | | |
| subjects affected / exposed | 0 / 174 (0.00%) | 1 / 176 (0.57%) | 0 / 176 (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 |
| DRUG WITHDRAWAL SYNDROME | | | |
| subjects affected / exposed | 0 / 174 (0.00%) | 0 / 176 (0.00%) | 0 / 176 (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 |
| FATIGUE | | | |
| subjects affected / exposed | 0 / 174 (0.00%) | 1 / 176 (0.57%) | 0 / 176 (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 |
| PYREXIA | | | |
| subjects affected / exposed | 0 / 174 (0.00%) | 0 / 176 (0.00%) | 1 / 176 (0.57%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Reproductive system and breast disorders | | | |
| PERINEAL DISORDER | | | |
| subjects affected / exposed | 0 / 174 (0.00%) | 0 / 176 (0.00%) | 0 / 176 (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 |
| Psychiatric disorders | | | |
| ALCOHOLISM | | | |
| subjects affected / exposed | 0 / 174 (0.00%) | 0 / 176 (0.00%) | 1 / 176 (0.57%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Product issues | | | |
| DEVICE DISLOCATION | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 1 / 174 (0.57%) | 0 / 176 (0.00%) | 0 / 176 (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 |
| Investigations | | | |
| WEIGHT DECREASED | | | |
| subjects affected / exposed | 0 / 174 (0.00%) | 0 / 176 (0.00%) | 0 / 176 (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 |
| Injury, poisoning and procedural complications | | | |
| POST PROCEDURAL HAEMORRHAGE | | | |
| subjects affected / exposed | 0 / 174 (0.00%) | 1 / 176 (0.57%) | 0 / 176 (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 |
| PROCEDURAL INTESTINAL PERFORATION | | | |
| subjects affected / exposed | 0 / 174 (0.00%) | 0 / 176 (0.00%) | 1 / 176 (0.57%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| THORACIC VERTEBRAL FRACTURE | | | |
| subjects affected / exposed | 0 / 174 (0.00%) | 0 / 176 (0.00%) | 1 / 176 (0.57%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nervous system disorders | | | |
| HEADACHE | | | |
| subjects affected / exposed | 0 / 174 (0.00%) | 1 / 176 (0.57%) | 0 / 176 (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 |
| SCIATICA | | | |
| subjects affected / exposed | 1 / 174 (0.57%) | 0 / 176 (0.00%) | 0 / 176 (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 / 174 (0.00%) | 0 / 176 (0.00%) | 0 / 176 (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 | | | |
| ABDOMINAL ADHESIONS | | | |
| subjects affected / exposed | 0 / 174 (0.00%) | 1 / 176 (0.57%) | 0 / 176 (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 |
| ABDOMINAL PAIN | | | |
| subjects affected / exposed | 3 / 174 (1.72%) | 1 / 176 (0.57%) | 1 / 176 (0.57%) |
| occurrences causally related to treatment / all | 1 / 3 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| ANAL FISSURE | | | |
| subjects affected / exposed | 0 / 174 (0.00%) | 1 / 176 (0.57%) | 0 / 176 (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 FISTULA | | | |
| subjects affected / exposed | 0 / 174 (0.00%) | 2 / 176 (1.14%) | 2 / 176 (1.14%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| COLITIS | | | |
| subjects affected / exposed | 0 / 174 (0.00%) | 0 / 176 (0.00%) | 0 / 176 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| CROHN'S DISEASE | | | |
| subjects affected / exposed | 4 / 174 (2.30%) | 9 / 176 (5.11%) | 8 / 176 (4.55%) |
| occurrences causally related to treatment / all | 0 / 4 | 1 / 10 | 0 / 8 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| ENTEROVESICAL FISTULA | | | |
| subjects affected / exposed | 0 / 174 (0.00%) | 0 / 176 (0.00%) | 0 / 176 (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 |
| HAEMATOCHYZIA | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 174 (0.00%) | 0 / 176 (0.00%) | 1 / 176 (0.57%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| ILEAL STENOSIS | | | |
| subjects affected / exposed | 0 / 174 (0.00%) | 1 / 176 (0.57%) | 0 / 176 (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 STENOSIS | | | |
| subjects affected / exposed | 0 / 174 (0.00%) | 1 / 176 (0.57%) | 0 / 176 (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 | 1 / 174 (0.57%) | 0 / 176 (0.00%) | 0 / 176 (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 |
| LARGE INTESTINE PERFORATION | | | |
| subjects affected / exposed | 0 / 174 (0.00%) | 1 / 176 (0.57%) | 0 / 176 (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 |
| MELAENA | | | |
| subjects affected / exposed | 1 / 174 (0.57%) | 0 / 176 (0.00%) | 0 / 176 (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 |
| NAUSEA | | | |
| subjects affected / exposed | 0 / 174 (0.00%) | 1 / 176 (0.57%) | 0 / 176 (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 |
| PANCREATITIS ACUTE | | | |
| subjects affected / exposed | 0 / 174 (0.00%) | 0 / 176 (0.00%) | 0 / 176 (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 |
| SMALL INTESTINAL OBSTRUCTION | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 1 / 174 (0.57%) | 2 / 176 (1.14%) | 1 / 176 (0.57%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 3 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| VOMITING | | | |
| subjects affected / exposed | 2 / 174 (1.15%) | 0 / 176 (0.00%) | 0 / 176 (0.00%) |
| occurrences causally related to treatment / all | 1 / 3 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatobiliary disorders | | | |
| CHOLECYSTITIS ACUTE | | | |
| subjects affected / exposed | 0 / 174 (0.00%) | 1 / 176 (0.57%) | 0 / 176 (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 |
| HEPATIC VEIN THROMBOSIS | | | |
| subjects affected / exposed | 0 / 174 (0.00%) | 0 / 176 (0.00%) | 1 / 176 (0.57%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| HEPATITIS | | | |
| subjects affected / exposed | 0 / 174 (0.00%) | 1 / 176 (0.57%) | 0 / 176 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Skin and subcutaneous tissue disorders | | | |
| ACUTE FEBRILE NEUTROPHILIC DERMATOSIS | | | |
| subjects affected / exposed | 1 / 174 (0.57%) | 0 / 176 (0.00%) | 0 / 176 (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 |
| PSORIASIS | | | |
| subjects affected / exposed | 1 / 174 (0.57%) | 0 / 176 (0.00%) | 0 / 176 (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 |
| PYODERMA GANGRENOSUM | | | |
| subjects affected / exposed | 1 / 174 (0.57%) | 0 / 176 (0.00%) | 1 / 176 (0.57%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|-----------------|-----------------|-----------------|
| Renal and urinary disorders | | | |
| STRESS URINARY INCONTINENCE | | | |
| subjects affected / exposed | 1 / 174 (0.57%) | 0 / 176 (0.00%) | 0 / 176 (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 |
| Musculoskeletal and connective tissue disorders | | | |
| MUSCULOSKELETAL PAIN | | | |
| subjects affected / exposed | 0 / 174 (0.00%) | 1 / 176 (0.57%) | 0 / 176 (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 |
| Infections and infestations | | | |
| ABDOMINAL ABSCESS | | | |
| subjects affected / exposed | 0 / 174 (0.00%) | 0 / 176 (0.00%) | 1 / 176 (0.57%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| ANAL ABSCESS | | | |
| subjects affected / exposed | 1 / 174 (0.57%) | 1 / 176 (0.57%) | 1 / 176 (0.57%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| CELLULITIS | | | |
| subjects affected / exposed | 1 / 174 (0.57%) | 0 / 176 (0.00%) | 0 / 176 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| EPSTEIN-BARR VIRUS INFECTION | | | |
| subjects affected / exposed | 1 / 174 (0.57%) | 0 / 176 (0.00%) | 0 / 176 (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 |
| GASTROENTERITIS | | | |
| subjects affected / exposed | 0 / 174 (0.00%) | 1 / 176 (0.57%) | 0 / 176 (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 |
| GASTROENTERITIS NOROVIRUS | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 174 (0.00%) | 1 / 176 (0.57%) | 0 / 176 (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 |
| HERPES SIMPLEX OESOPHAGITIS | | | |
| subjects affected / exposed | 0 / 174 (0.00%) | 1 / 176 (0.57%) | 0 / 176 (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 |
| HERPES ZOSTER | | | |
| subjects affected / exposed | 0 / 174 (0.00%) | 0 / 176 (0.00%) | 1 / 176 (0.57%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| PNEUMONIA | | | |
| subjects affected / exposed | 0 / 174 (0.00%) | 0 / 176 (0.00%) | 1 / 176 (0.57%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| STAPHYLOCOCCAL SEPSIS | | | |
| subjects affected / exposed | 0 / 174 (0.00%) | 0 / 176 (0.00%) | 1 / 176 (0.57%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metabolism and nutrition disorders | | | |
| MALNUTRITION | | | |
| subjects affected / exposed | 1 / 174 (0.57%) | 0 / 176 (0.00%) | 0 / 176 (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 |

| | | | |
|---|--|--|--|
| Serious adverse events | GED-0301 160 mg / GED-0301 160 mg 4 Week Alt | | |
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 15 / 175 (8.57%) | | |
| number of deaths (all causes) | 1 | | |
| number of deaths resulting from adverse events | 0 | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| CERVIX NEOPLASM | | | |

| | | | |
|--|-----------------|--|--|
| subjects affected / exposed | 0 / 175 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| NEUROENDOCRINE TUMOUR | | | |
| subjects affected / exposed | 1 / 175 (0.57%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| General disorders and administration site conditions | | | |
| ASTHENIA | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| DRUG WITHDRAWAL SYNDROME | | | |
| subjects affected / exposed | 1 / 175 (0.57%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| FATIGUE | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| PYREXIA | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Reproductive system and breast disorders | | | |
| PERINEAL DISORDER | | | |
| subjects affected / exposed | 1 / 175 (0.57%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Psychiatric disorders | | | |
| ALCOHOLISM | | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 0 / 175 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Product issues | | | |
| DEVICE DISLOCATION | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Investigations | | | |
| WEIGHT DECREASED | | | |
| subjects affected / exposed | 1 / 175 (0.57%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Injury, poisoning and procedural complications | | | |
| POST PROCEDURAL HAEMORRHAGE | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| PROCEDURAL INTESTINAL PERFORATION | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| THORACIC VERTEBRAL FRACTURE | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Nervous system disorders | | | |
| HEADACHE | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| SCIATICA | | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 0 / 175 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Blood and lymphatic system disorders | | | |
| ANAEMIA | | | |
| subjects affected / exposed | 1 / 175 (0.57%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastrointestinal disorders | | | |
| ABDOMINAL ADHESIONS | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| ABDOMINAL PAIN | | | |
| subjects affected / exposed | 2 / 175 (1.14%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| ANAL FISSURE | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| ANAL FISTULA | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| COLITIS | | | |
| subjects affected / exposed | 1 / 175 (0.57%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| CROHN'S DISEASE | | | |
| subjects affected / exposed | 5 / 175 (2.86%) | | |
| occurrences causally related to treatment / all | 0 / 6 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| ENTEROVESICAL FISTULA | | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 1 / 175 (0.57%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| HAEMATOECHEZIA | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| ILEAL STENOSIS | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| INTESTINAL STENOSIS | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| LARGE INTESTINAL STENOSIS | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| LARGE INTESTINE PERFORATION | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| MELAENA | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| NAUSEA | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| PANCREATITIS ACUTE | | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 1 / 175 (0.57%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| SMALL INTESTINAL OBSTRUCTION | | | |
| subjects affected / exposed | 2 / 175 (1.14%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 1 | | |
| VOMITING | | | |
| subjects affected / exposed | 1 / 175 (0.57%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hepatobiliary disorders | | | |
| CHOLECYSTITIS ACUTE | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| HEPATIC VEIN THROMBOSIS | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| HEPATITIS | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Skin and subcutaneous tissue disorders | | | |
| ACUTE FEBRILE NEUTROPHILIC DERMATOSIS | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| PSORIASIS | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

| | | | |
|---|-----------------|--|--|
| PYODERMA GANGRENOSUM | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Renal and urinary disorders | | | |
| STRESS URINARY INCONTINENCE | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Musculoskeletal and connective tissue disorders | | | |
| MUSCULOSKELETAL PAIN | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Infections and infestations | | | |
| ABDOMINAL ABSCESS | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| ANAL ABSCESS | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| CELLULITIS | | | |
| subjects affected / exposed | 1 / 175 (0.57%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| EPSTEIN-BARR VIRUS INFECTION | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| GASTROENTERITIS | | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 0 / 175 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| GASTROENTERITIS NOROVIRUS | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| HERPES SIMPLEX OESOPHAGITIS | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| HERPES ZOSTER | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| PNEUMONIA | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| STAPHYLOCOCCAL SEPSIS | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Metabolism and nutrition disorders | | | |
| MALNUTRITION | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

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

| Non-serious adverse events | Placebo | GED-0301 160 mg / GED-0301 40 mg 4 Week Alt | GED-0301 160 mg / GED-0301 40 mg |
|--|---|---|--|
| Total subjects affected by non-serious adverse events subjects affected / exposed | 78 / 174 (44.83%) | 72 / 176 (40.91%) | 74 / 176 (42.05%) |
| Nervous system disorders HEADACHE subjects affected / exposed occurrences (all) | 15 / 174 (8.62%) 16 | 10 / 176 (5.68%) 10 | 12 / 176 (6.82%) 20 |
| General disorders and administration site conditions PYREXIA subjects affected / exposed occurrences (all) | 10 / 174 (5.75%) 11 | 13 / 176 (7.39%) 24 | 14 / 176 (7.95%) 20 |
| Gastrointestinal disorders ABDOMINAL PAIN subjects affected / exposed occurrences (all) CROHN'S DISEASE subjects affected / exposed occurrences (all) DIARRHOEA subjects affected / exposed occurrences (all) NAUSEA subjects affected / exposed occurrences (all) | 19 / 174 (10.92%) 19 15 / 174 (8.62%) 18 0 / 174 (0.00%) 0 12 / 174 (6.90%) 12 | 20 / 176 (11.36%) 22 14 / 176 (7.95%) 19 10 / 176 (5.68%) 28 9 / 176 (5.11%) 9 | 14 / 176 (7.95%) 16 14 / 176 (7.95%) 14 0 / 176 (0.00%) 0 10 / 176 (5.68%) 10 |
| Musculoskeletal and connective tissue disorders ARTHRALGIA subjects affected / exposed occurrences (all) BACK PAIN subjects affected / exposed occurrences (all) | 15 / 174 (8.62%) 15 9 / 174 (5.17%) 10 | 20 / 176 (11.36%) 21 0 / 176 (0.00%) 0 | 23 / 176 (13.07%) 37 0 / 176 (0.00%) 0 |
| Infections and infestations VIRAL UPPER RESPIRATORY TRACT INFECTION subjects affected / exposed occurrences (all) | 15 / 174 (8.62%) 18 | 18 / 176 (10.23%) 21 | 14 / 176 (7.95%) 18 |

| | | | |
|--|--|--|--|
| Non-serious adverse events | GED-0301 160 mg / GED-0301 160 mg 4 Week Alt | | |
| Total subjects affected by non-serious adverse events subjects affected / exposed | 63 / 175 (36.00%) | | |
| Nervous system disorders HEADACHE subjects affected / exposed occurrences (all) | 9 / 175 (5.14%) 11 | | |
| General disorders and administration site conditions PYREXIA subjects affected / exposed occurrences (all) | 0 / 175 (0.00%) 0 | | |
| Gastrointestinal disorders ABDOMINAL PAIN subjects affected / exposed occurrences (all) CROHN'S DISEASE subjects affected / exposed occurrences (all) DIARRHOEA subjects affected / exposed occurrences (all) NAUSEA subjects affected / exposed occurrences (all) | 15 / 175 (8.57%) 17 15 / 175 (8.57%) 16 0 / 175 (0.00%) 0 9 / 175 (5.14%) 9 | | |
| Musculoskeletal and connective tissue disorders ARTHRALGIA subjects affected / exposed occurrences (all) BACK PAIN subjects affected / exposed occurrences (all) | 25 / 175 (14.29%) 27 0 / 175 (0.00%) 0 | | |
| Infections and infestations VIRAL UPPER RESPIRATORY TRACT INFECTION subjects affected / exposed occurrences (all) | 16 / 175 (9.14%) 18 | | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|-------------------|---|
| 23 September 2015 | <p>Addition of Inclusion Criteria for Patient-reported Outcomes-2.</p> <p>The primary purpose of this protocol amendment was to add inclusion criteria for the PROs of abdominal pain and stool frequency. The rationale for this amendment was to align with the current critical endpoints for abdominal pain and stool frequency.</p> <p>Update of Exclusion Criterion Number 12</p> <p>Exclusion criterion number 12 was updated to allow stable doses of antibiotics for the treatment of CD, provided that the dose had been stable for at least 2 weeks prior to the Screening Visit. In earlier GED-0301 studies, the use of antibiotics for the treatment of CD was prohibited.</p> <p>Following discussions with clinical investigators, the use of antibiotics could be commonly used as background therapy in subjects with CD and there was no reason to suspect a diminished effect of GED-0301 with its different mechanism of action. This change supported a broader subject population to be studied in this Phase 3 study.</p> <p>Revision of Exclusion Criterion Number 13</p> <p>Exclusion criterion number 13 was revised to exclude subjects with prior treatment with 3 biologics as opposed to 2 biologics.</p> <p>The rationale was based on the expectation of responsiveness to GED-0301 (with a different mechanism of action than biologic therapy) in terms of clinical and endoscopic benefit, which was expected to be substantively similar in subjects having been exposed to either 2 or 3 biologics. The intention, therefore, was to study a broader group of subjects with prior biologic exposure. The target of 65% of the subjects in this study to be naive to prior biologic therapy was unchanged.</p> |
| 25 October 2016 | <p>The purpose of the amendment was to prioritize the evaluation of clinical remission and endoscopic outcomes as primary and secondary endpoints. Endpoints were listed by 2 regions (US and rest of world). The primary efficacy measure was clinical remission at Week 12. The secondary efficacy measures include the evaluation of endoscopic remission at Week 52; clinical remission based on CDAI score at Week 12 (US only); clinical remission (based on stool frequency/abdominal pain and CDAI score for US, and CDAI score for ROW) at Week (Wk) 52; clinical response at Wk 12; ER-50 sustained clinical remission at Wk 12 and Wk 52; steroid-free clinical remission at Week 52; ER-25 at Wk 12; clinical remission at Wk 4; clinical response at Wk 4; and clinical remission (based on CDAI score) at Week 4. Inclusion/Exclusion Changes: Aminosalicylates were removed as one of the therapies that subjects may have failed to grant eligibility. Failed treatment with biologics was further specified to include infliximab, adalimumab, certolizumab, or vedolizumab. Clarification: the presence of active CD was to be determined by ileocolonoscopy at screening and Pan-colonic screening surveillance was removed. Those with increased risk of colorectal cancer should have had a colonoscopy with pan-colonic surveillance biopsies. The inclusion criterion requiring male subjects to use barrier contraception was removed and those taking an oral contraceptive as an alternative method of birth control based on physician judgment. The exclusion criteria were revised to clarify the requirements with respect to strictures. Prior use of biologics was updated to specify infliximab, adalimumab, certolizumab, or vedolizumab. Exclusion criteria considered the duration of 5 elimination half-lives for biologics, in addition to the 8-week and 1-month washout periods for biologics and investigational drug. Those with a diagnosis of colorectal dysplasia were excluded. Those with serious infections were also excluded.</p> |

| | |
|----------------|---|
| 15 August 2017 | <p>The primary purpose of the amendment was to harmonize and reprioritize the order of endpoints based on regulatory agency feedback. There was now one set of endpoints for all regions. The primary efficacy measure was clinical remission (defined as a CDAI score < 150) at Week 12. Key secondary efficacy measures included: clinical remission at Week 52, ER-50 (defined as a reduction of at least 50% compared with baseline in the SES-CD) at Week 52, clinical response (defined as a decrease from baseline in CDAI \geq 100 points) at Week 12, clinical response at Week 4, clinical remission at Week 4, steroid-free clinical remission at Week 52, sustained clinical remission at both Week 12 and Week 52, ER-25 (defined as a reduction of at least 25% compared with baseline in SES-CD) at Week 12, and the evaluation of endoscopic remission (defined as SES-CD \leq 2) at Week 52. New exploratory endpoints included the proportion of subjects who achieved clinical remission for at least 80% of visits (for all subjects through Week 52, and from Weeks 12 to 52 for subjects with clinical remission at Week 12). Exploratory endpoints regarding corticosteroid-free clinical remission were revised for clarity. Monitoring of Liver Function Tests (LFTs) Additional guidance was added for those who developed changes in LFTs including, but not limited to, repeat testing, evaluation for cause, and close observation. Criteria were also provided to consider IP interruption or study discontinuation. This additional guidance was added at the request of the US FDA and was not specific to any signals observed with GED-0301. Discontinuation Criteria Text was updated to specify potential reasons for discontinuation including but not limited to subject safety (eg, LFT abnormalities), CD-related surgeries, initiation of biologics, and initiation of specific CD-related medications. The reasons for treatment and study discontinuation were updated to include lack of efficacy.</p> |
|----------------|---|

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 DMC, this study was terminated early by the sponsor on 19 Oct 2017 due to a lack of emerging benefit; no emergent safety findings were noted.

Notes: