



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	9 / 175 (5.14%)		
occurrences (all)	11		
General disorders and administration site conditions			
PYREXIA			
subjects affected / exposed	0 / 175 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders			
ABDOMINAL PAIN			
subjects affected / exposed	15 / 175 (8.57%)		
occurrences (all)	17		
CROHN'S DISEASE			
subjects affected / exposed	15 / 175 (8.57%)		
occurrences (all)	16		
DIARRHOEA			
subjects affected / exposed	0 / 175 (0.00%)		
occurrences (all)	0		
NAUSEA			
subjects affected / exposed	9 / 175 (5.14%)		
occurrences (all)	9		
Musculoskeletal and connective tissue disorders			
ARTHRALGIA			
subjects affected / exposed	25 / 175 (14.29%)		
occurrences (all)	27		
BACK PAIN			
subjects affected / exposed	0 / 175 (0.00%)		
occurrences (all)	0		
Infections and infestations			
VIRAL UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	16 / 175 (9.14%)		
occurrences (all)	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: