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

Summary

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

Results information

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

Trial information

Trial identification

Sponsor protocol code	GED-0301-CD-004

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02641392
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Celgene Corporation
Sponsor organisation address	86 Morris Avenue, Summit, United States, 07901
Public contact	Clinical Trial Disclosure, Celgene Corporation, 01 888-260-1599, ClinicalTrialDisclosure@celgene.com
Scientific contact	Guillermo Rossiter, Celgene Corporation, 01 9088976467, grossiter@celgene.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	30 May 2018
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	04 January 2018
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

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

Protection of trial subjects:

Patient Confidentiality, Informed Consent, Archiving of Essential Documents

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	25 July 2016
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

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

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

Notes:

Subjects enrolled per age group	
In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	4
From 65 to 84 years	299
85 years and over	7

Subject disposition

Recruitment

Recruitment details:

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

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Pre-assignment

Screening details:

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

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	GED-0301 40 mg 4 Weeks Alt

Arm description:

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

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

Dosage and administration details:

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

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

Dosage and administration details:

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

Arm title	GED-0301 40 mg

Arm description:

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

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

Dosage and administration details:

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

Arm title	GED-0301 160 mg 4 Weeks Alt

Arm description:

Participants received one of three dose regimens up to week 208:
(1) alternating placebo daily for 4 weeks and GED-0301 160 mg daily for 4 weeks or
(2) alternating GED-0301 160 mg daily for 4 weeks and placebo daily for 4 weeks or
(3) GED-0301 160 mg daily for 12 weeks, followed by alternating placebo daily for 4 weeks and GED-0301 160 mg daily for 4 weeks.

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

Dosage and administration details:

Participants received one of three dose regimens up to week 208:
(1) alternating placebo daily for 4 weeks and GED-0301 160 mg daily for 4 weeks or
(2) alternating GED-0301 160 mg daily for 4 weeks and placebo daily for 4 weeks or
(3) GED-0301 160 mg daily for 12 weeks, followed by alternating placebo daily for 4 weeks and GED-0301 160 mg daily for 4 weeks.

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

Dosage and administration details:

Participants received one of three dose regimens up to week 208:
(1) alternating placebo daily for 4 weeks and GED-0301 160 mg daily for 4 weeks or
(2) alternating GED-0301 160 mg daily for 4 weeks and placebo daily for 4 weeks or
(3) GED-0301 160 mg daily for 12 weeks, followed by alternating placebo daily for 4 weeks and GED-0301 160 mg daily for 4 weeks

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

Baseline characteristics

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

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

Duration of Crohn's Disease			
Units: Years			
arithmetic mean	7.25	9.25	10.56
standard deviation	± 6.529	± 6.307	± 8.503
Baseline Crohn's Disease Activity (CDAI) Score			
The Crohn's Disease Activity Index (CDAI) is used to quantify the signs and symptoms of Crohn's disease and the effect on patient's quality of life. It consists of 8 variables which include patient reported outcomes over a 7 day period and physician assessments which are scored numerically and weighted. Scores range from 0 to 600, with the most severe disease defined >450			
Units: Units on a Scale			
arithmetic mean	316.9	309.2	307.5
standard deviation	± 96.90	± 43.10	± 62.74

Reporting group values	Total		
Number of subjects	310		
Age Categorical			
Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	0		
Newborns (0-27 days)	0		
Infants and toddlers (28 days-23 months)	0		
Children (2-11 years)	0		
Adolescents (12-17 years)	0		
Adults (18-64 years)	303		
From 65-84 years	7		
85 years and over	0		
Age Continuous			
Units: years			
arithmetic mean			
standard deviation	-		
Gender Categorical			
Units: Subjects			
Female	145		
Male	165		
Race/Ethnicity, Customized			
Units: Subjects			
American Indian or Alaska Native	2		
Asian	13		
Black or African American	3		
White	277		
Not Collected or Reported	11		
Other	4		
Duration of Crohn's Disease			
Units: Years			
arithmetic mean			
standard deviation	-		
Baseline Crohn's Disease Activity (CDAI) Score			
The Crohn's Disease Activity Index (CDAI) is used to quantify the signs and symptoms of Crohn's disease and the effect on patient's quality of life. It consists of 8 variables which include patient reported outcomes over a 7 day period and physician assessments which are scored numerically and weighted.			

Scores range from 0 to 600, with the most severe disease defined >450			
Units: Units on a Scale arithmetic mean standard deviation	- -		

End points

End points reporting groups

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

Primary: Number of Participants with Treatment Emergent Adverse Events

End point title	Number of Participants with Treatment Emergent Adverse Events[1]
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.	
End point type	Primary
End point timeframe:	
From the first day of GED-0301 until 28 days after the last dose of IP; maximum treatment duration was 16.1 weeks in the GED-0301 40 mg Alt dose; 16.3 weeks in the GED 40 mg continuous dose and 56.1 weeks in the GED-0301 160 mg Alt dose	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis were performed as the study was terminated.

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

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From the first day of GED-0301 until 28 days after the last dose of IP.

Adverse event reporting additional description:

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

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	20.0

Reporting groups

Reporting group title	GED-0301 40 mg 4 Weeks Alt

Reporting group description:

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

Reporting group title	GED-0301 40 mg

Reporting group description:

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

Reporting group title	GED-0301 160 mg 4 Weeks Alt

Reporting group description:

Participants received one of three dose regimens up to week 208;
(1) alternating placebo daily for 4 weeks and GED-0301 160 mg daily for 4 weeks or
(2) alternating GED-0301 160 mg daily for 4 weeks and placebo daily for 4 weeks or
(3) GED-0301 160 mg daily for 12 weeks, followed by alternating placebo daily for 4 weeks and GED-0301 160 mg daily for 4 weeks.

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

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

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

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

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

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

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

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

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

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

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
06 January 2017	1. The addition of adolescent subjects into this long-term active treatment extension study who previously participated in the Phase 3 Study GED-0301-CD-003. 2. New sections were added to the protocol that applied specifically to adolescent subjects. 3. The objectives, endpoints, inclusion/exclusion criteria, table of events, procedures, and assessments sections were separated for the adult and adolescent subjects throughout the protocol, where appropriate, to clearly indicate protocol information which applied specifically to adult versus adolescent subjects. 4. Previous GED-0301-CD-003 subjects were to have an ileocolonoscopy with intestinal mucosal biopsies during the screening period and at Week 12 in the core GED-0301-CD-003 study. A Week 40 ileocolonoscopy with intestinal mucosal biopsies was to be included in this study for these adult subjects, as well as the adolescent subjects, to determine if mucosal healing and/or endoscopic remission was achieved after 52 weeks of GED-0301 therapy from the combined studies (12 weeks from GED-0301-CD-003 and 40 weeks from GED-0301-CD-004) in the adult (and adolescent) populations. 5. The Week 12 clinical criteria were added for discontinuing subjects who did not achieve a minimum level of improvement by Week 12.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

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

Notes: