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

Summary

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

Results information

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

Trial information

Trial identification

Sponsor protocol code	GED-0301-CD-005

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Celgene Corporation
Sponsor organisation address	86 Morris Avenue, Summit, United States, 07901
Public contact	Clinical Trial Disclosure, Celgene Corporation, 01 888-260-1599, ClinicalTrialDisclosure@Celgene.com
Scientific contact	Keith Usiskin, Celgene Corporation, 01 908.897.6550 , kusiskin@celgene.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	05 April 2018
Is this the analysis of the primary completion data?	No

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

Notes:

General information about the trial

Main objective of the trial:

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

Protection of trial subjects:

Patient Confidentiality, Personal Data Protection, Archiving of Essential Documents

Background therapy: -

Evidence for comparator: -

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

Notes:

Population of trial subjects

Subjects enrolled per country

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

Notes:

Subjects enrolled per age group

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

Subject disposition

Recruitment

Recruitment details:

18 subjects were enrolled from 2 sites in Italy.

Pre-assignment

Screening details:

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

Period 1

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

Arms

Arm title	GED-0301 160 mg

Arm description:

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

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

Dosage and administration details:

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

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

Period 2

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

Arms

Arm title	GED-0301 160 mg /Alt 4 Weeks

Arm description:

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

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

Dosage and administration details:

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

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

Notes:

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

Baseline characteristics

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

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

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

End points

End points reporting groups

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

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

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

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Statistical comparisons between treatment groups were not conducted in this study.

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

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

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

End point type	Secondary

End point timeframe:

Week 12

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

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

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

End point type	Secondary

End point timeframe:

Weeks 4, 8 and 12

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

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

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

End point type	Secondary

End point timeframe:

Baseline to Week 12

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

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

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

End point type	Secondary

End point timeframe:

Baseline to Week 52

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

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

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

End point type	Secondary

End point timeframe:

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

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

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

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

End point type	Secondary

End point timeframe:

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

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

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

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

Adverse event reporting additional description:

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

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	20.0

Reporting groups

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

Reporting group description:

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

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

Reporting group description:

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

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

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

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

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

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

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

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

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

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

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

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

Notes: