# Clinical trial results:
# A PHASE 2B RANDOMISED, DOUBLE-BLIND, PLACEBO-CONTROLLED, PARALLEL ADAPTIVE 2-STAGE, MULTI-CENTRE STUDY TO EVALUATE THE SAFETY AND EFFICACY OF ORAL PTG-100 INDUCTION IN SUBJECTS WITH MODERATE TO SEVERE ACTIVE ULCERATIVE COLITIS

## Summary

| | |
|---|---|
| EudraCT number | 2016-003452-75 |
| Trial protocol | LV HU BE CZ NL PL HR |
| Global end of trial date | 26 March 2018 |

**Results information**

| | |
|---|---|
| Result version number | v1 (current) |
| This version publication date | 11 April 2019 |
| First version publication date | 11 April 2019 |

## Trial information

**Trial identification**

| | |
|---|---|
| Sponsor protocol code | PTG-100-02 |

**Additional study identifiers**

| | |
|---|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT02895100 |
| WHO universal trial number (UTN) | - |

Notes:

**Sponsors**

| | |
|---|---|
| Sponsor organisation name | Protagonist Therapeutics, Inc |
| Sponsor organisation address | 7707 Gateway Boulevard, Suite 140, Newark, United States, CA 94560-1160 |
| Public contact | Clinical trials information, Protagonist Therapeutics, Inc, clinical@protagonist-inc.com |
| Scientific contact | Clinical trials information, Protagonist Therapeutics, Inc, clinical@protagonist-inc.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 | Interim |
| Date of interim/final analysis | 23 March 2018 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 23 March 2018 |
| Global end of trial reached? | Yes |
| Global end of trial date | 26 March 2018 |
| Was the trial ended prematurely? | Yes |

Notes:

## General information about the trial

Main objective of the trial:

1. To evaluate the safety and tolerability of PTG-100

2. To evaluate the efficacy of PTG-100 in the induction treatment of subjects with moderate to severe active UC compared to placebo.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and in compliance with all International Council for Harmonization (ICH) Good Clinical Practice (GCP) Guidelines. All the local regulatory requirements pertinent to safety of trials subjects were followed.

Background therapy: -

Evidence for comparator: -

| | |
|---|---|
| Actual start date of recruitment | 10 January 2017 |
| 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 | Netherlands: 3 |
| Country: Number of subjects enrolled | Poland: 5 |
| Country: Number of subjects enrolled | Czech Republic: 3 |
| Country: Number of subjects enrolled | Germany: 2 |
| Country: Number of subjects enrolled | Hungary: 7 |
| Country: Number of subjects enrolled | Latvia: 2 |
| Country: Number of subjects enrolled | Australia: 2 |
| Country: Number of subjects enrolled | Bosnia and Herzegovina: 2 |
| Country: Number of subjects enrolled | Canada: 2 |
| Country: Number of subjects enrolled | New Zealand: 2 |
| Country: Number of subjects enrolled | Serbia: 17 |
| Country: Number of subjects enrolled | Korea, Republic of: 3 |
| Country: Number of subjects enrolled | Russian Federation: 14 |
| Country: Number of subjects enrolled | Ukraine: 13 |
| Country: Number of subjects enrolled | United States: 21 |
| Worldwide total number of subjects | 98 |
| EEA total number of subjects | 22 |

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) | 90 |
| From 65 to 84 years | 8 |
| 85 years and over | 0 |

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

Subjects were screened for eligibility according to the inclusion/ exclusion criteria within 42 days of dosing. Eligible subjects returned for sigmoidoscopy/ biopsy and baseline Mayo Score within 14 days of randomization. A total of 183 subjects were screened. A total of 103 subjects were randomized and 98 subjects received study drug.

### Period 1

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

### Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | PTG-100 150 mg |

Arm description: -

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | PTG-100 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

Subject was administered 1 × 150mg PTG-100 capsule and 2 × placebo capsules QD

| | |
|---|---|
| **Arm title** | PTG-100 300 mg |

Arm description: -

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | PTG-100 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

Subject was administered 2 × 150mg PTG-100 capsules and 1 × placebo capsule QD

| | |
|---|---|
| **Arm title** | PTG-100 900 mg |

Arm description: -

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | PTG-100 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

Subject was administered 3 × 300mg PTG-100 capsules QD

| | |
|---|---|
| **Arm title** | Placebo |

| Arm description: - | |
|---|---|
| Arm type | Placebo |
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

Subject administered 3 x placebo capsules QD

| **Number of subjects in period 1** | PTG-100 150 mg | PTG-100 300 mg | PTG-100 900 mg |
|---|---|---|---|
| Started | 25 | 25 | 23 |
| Completed | 14 | 14 | 15 |
| Not completed | 11 | 11 | 8 |
| Physician decision | 2 | - | - |
| Study terminated by Sponsor | 6 | 5 | 5 |
| Adverse event, non-fatal | 1 | - | 1 |
| Other | - | 2 | 1 |
| Lost to follow-up | 1 | - | - |
| Withdrawal by subject | 1 | 4 | 1 |

| **Number of subjects in period 1** | Placebo |
|---|---|
| Started | 25 |
| Completed | 15 |
| Not completed | 10 |
| Physician decision | 1 |
| Study terminated by Sponsor | 7 |
| Adverse event, non-fatal | - |
| Other | - |
| Lost to follow-up | - |
| Withdrawal by subject | 2 |

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | PTG-100 150 mg |
| Reporting group description: - | |
| Reporting group title | PTG-100 300 mg |
| Reporting group description: - | |
| Reporting group title | PTG-100 900 mg |
| Reporting group description: - | |
| Reporting group title | Placebo |
| Reporting group description: - | |

| Reporting group values | PTG-100 150 mg | PTG-100 300 mg | PTG-100 900 mg |
|---|---|---|---|
| Number of subjects | 25 | 25 | 23 |
| Age categorical<br>Units: Subjects | | | |
| In utero<br>Preterm newborn infants (gestational age < 37 wks)<br>Newborns (0-27 days)<br>Infants and toddlers (28 days-23 months)<br>Children (2-11 years)<br>Adolescents (12-17 years)<br>Adults (18-64 years)<br>From 65-84 years<br>85 years and over | | | |
| Age continuous<br>Units: years | | | |
| arithmetic mean | 45.2 | 43.8 | 40.6 |
| standard deviation | ± 13.8 | ± 17.0 | ± 14.1 |
| Gender categorical<br>Units: Subjects | | | |
| Female | 7 | 15 | 14 |
| Male | 18 | 10 | 9 |
| Race<br>Units: Subjects | | | |
| White | 19 | 23 | 22 |
| Asian | 4 | 1 | 0 |
| Black or African American | 2 | 0 | 1 |
| Other | 0 | 1 | 0 |
| Ethnicity<br>Units: Subjects | | | |
| Hispanic or Latino | 0 | 2 | 1 |
| Not Hispanic or Latino | 25 | 23 | 22 |
| Weight<br>Units: kg | | | |
| arithmetic mean | 77.8 | 70.7 | 72.3 |
| standard deviation | ± 16.3 | ± 15.4 | ± 19.1 |

| | | | |
|---|---|---|---|
| Height | | | |
| Units: cm | | | |
| arithmetic mean | 173.2 | 169.8 | 173.0 |
| standard deviation | ± 7.3 | ± 9.7 | ± 9.1 |
| BMI | | | |
| Units: kg/m2 | | | |
| arithmetic mean | 25.7 | 24.5 | 23.9 |
| standard deviation | ± 4.7 | ± 5.2 | ± 4.5 |

| **Reporting group values** | Placebo | Total | |
|---|---|---|---|
| Number of subjects | 25 | 98 | |
| 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) | | 0 | |
| From 65-84 years | | 0 | |
| 85 years and over | | 0 | |
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | 42.2 | | |
| standard deviation | ± 14.9 | - | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 10 | 46 | |
| Male | 15 | 52 | |
| Race | | | |
| Units: Subjects | | | |
| White | 23 | 87 | |
| Asian | 0 | 5 | |
| Black or African American | 2 | 5 | |
| Other | 0 | 1 | |
| Ethnicity | | | |
| Units: Subjects | | | |
| Hispanic or Latino | 1 | 4 | |
| Not Hispanic or Latino | 24 | 94 | |
| Weight | | | |
| Units: kg | | | |
| arithmetic mean | 69.5 | | |
| standard deviation | ± 16.1 | - | |
| Height | | | |
| Units: cm | | | |
| arithmetic mean | 171.1 | | |
| standard deviation | ± 8.3 | - | |
| BMI | | | |
| Units: kg/m2 | | | |

| | | | |
|---|---|---|---|
| arithmetic mean | 23.7 | | |
| standard deviation | ± 4.7 | - | |

## End points

### End points reporting groups

| | |
|---|---|
| Reporting group title | PTG-100 150 mg |
| Reporting group description: - | |
| Reporting group title | PTG-100 300 mg |
| Reporting group description: - | |
| Reporting group title | PTG-100 900 mg |
| Reporting group description: - | |
| Reporting group title | Placebo |
| Reporting group description: - | |

### Primary: Efficacy: proportion of subjects receiving PTG-100 with clinical remission at Week 12

| | |
|---|---|
| End point title | Efficacy: proportion of subjects receiving PTG-100 with clinical remission at Week 12[1] |

End point description:

The primary efficacy endpoint for this study was the proportion of subjects receiving PTG-100 with clinical remission at Week 12. Clinical remission was defined using the Mayo subscores of stool frequency, rectal bleeding, and endoscopy.

| | |
|---|---|
| End point type | Primary |

End point timeframe:

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: This trial was discontinued due to a futile outcome from the unblinded interim analysis by the independent DMC, therefore statistical analyses are not reported.

| End point values | PTG-100 150 mg | PTG-100 300 mg | PTG-100 900 mg | Placebo |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 16 | 16 | 16 | 17 |
| Units: Subjects | | | | |
| Clinical Remission | 1 | 2 | 3 | 4 |

### Statistical analyses

No statistical analyses for this end point

## Adverse events

| Adverse events information | |
|---|---|
| Timeframe for reporting adverse events: Day 0 to week 12 | |
| Assessment type | Systematic |

| Dictionary used | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 21 |

| Reporting groups | |
|---|---|
| Reporting group title | PTG-100 150 mg |
| Reporting group description: - | |
| Reporting group title | PTG-100 300 mg |
| Reporting group description: - | |
| Reporting group title | PTG-100 900 mg |
| Reporting group description: - | |
| Reporting group title | Placebo |
| Reporting group description: - | |

| Serious adverse events | PTG-100 150 mg | PTG-100 300 mg | PTG-100 900 mg |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 2 / 25 (8.00%) | 2 / 25 (8.00%) | 1 / 23 (4.35%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Pregnancy, puerperium and perinatal conditions | | | |
| Pregnancy | | | |
| subjects affected / exposed | 0 / 25 (0.00%) | 1 / 25 (4.00%) | 0 / 23 (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 |
| Gastrointestinal disorders | | | |
| Ulcerative colitis flare | | | |
| subjects affected / exposed | 1 / 25 (4.00%) | 0 / 25 (0.00%) | 0 / 23 (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 |
| Colitis ulcerative | | | |
| subjects affected / exposed | 0 / 25 (0.00%) | 0 / 25 (0.00%) | 1 / 23 (4.35%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Exacerbation of ulcerative colitis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 25 (0.00%) | 1 / 25 (4.00%) | 0 / 23 (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 ischaemia | | | |
| subjects affected / exposed | 0 / 25 (0.00%) | 0 / 25 (0.00%) | 0 / 23 (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 |
| Infections and infestations | | | |
| Perirectal abscess | | | |
| subjects affected / exposed | 1 / 25 (4.00%) | 0 / 25 (0.00%) | 0 / 23 (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** | Placebo | | |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 1 / 25 (4.00%) | | |
| number of deaths (all causes) | 1 | | |
| number of deaths resulting from adverse events | 1 | | |
| Pregnancy, puerperium and perinatal conditions | | | |
| Pregnancy | | | |
| subjects affected / exposed | 0 / 25 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastrointestinal disorders | | | |
| Ulcerative colitis flare | | | |
| subjects affected / exposed | 0 / 25 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Colitis ulcerative | | | |
| subjects affected / exposed | 0 / 25 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Exacerbation of ulcerative colitis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 25 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Intestinal ischaemia | | | |
| subjects affected / exposed | 1 / 25 (4.00%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 1 | | |
| Infections and infestations | | | |
| Perirectal abscess | | | |
| subjects affected / exposed | 0 / 25 (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** | PTG-100 150 mg | PTG-100 300 mg | PTG-100 900 mg |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 7 / 25 (28.00%) | 11 / 25 (44.00%) | 14 / 23 (60.87%) |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 0 / 25 (0.00%) | 0 / 25 (0.00%) | 4 / 23 (17.39%) |
| occurrences (all) | 0 | 0 | 4 |
| General disorders and administration site conditions | | | |
| Fatigue | | | |
| subjects affected / exposed | 0 / 25 (0.00%) | 0 / 25 (0.00%) | 2 / 23 (8.70%) |
| occurrences (all) | 0 | 0 | 3 |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 0 / 25 (0.00%) | 2 / 25 (8.00%) | 1 / 23 (4.35%) |
| occurrences (all) | 0 | 2 | 1 |
| Gastrointestinal disorders | | | |
| Colitis ulcerative | | | |
| subjects affected / exposed | 0 / 25 (0.00%) | 2 / 25 (8.00%) | 3 / 23 (13.04%) |
| occurrences (all) | 0 | 2 | 3 |
| Abdominal pain | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 25 (0.00%) | 2 / 25 (8.00%) | 0 / 23 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 0 / 25 (0.00%) | 0 / 25 (0.00%) | 2 / 23 (8.70%) |
| occurrences (all) | 0 | 0 | 2 |
| Arthritis | | | |
| subjects affected / exposed | 0 / 25 (0.00%) | 2 / 25 (8.00%) | 0 / 23 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Infections and infestations | | | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 0 / 25 (0.00%) | 3 / 25 (12.00%) | 0 / 23 (0.00%) |
| occurrences (all) | 0 | 3 | 0 |

| **Non-serious adverse events** | Placebo | | |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 11 / 25 (44.00%) | | |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 2 / 25 (8.00%) | | |
| occurrences (all) | 2 | | |
| General disorders and administration site conditions | | | |
| Fatigue | | | |
| subjects affected / exposed | 1 / 25 (4.00%) | | |
| occurrences (all) | 1 | | |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 1 / 25 (4.00%) | | |
| occurrences (all) | 1 | | |
| Gastrointestinal disorders | | | |
| Colitis ulcerative | | | |
| subjects affected / exposed | 0 / 25 (0.00%) | | |
| occurrences (all) | 0 | | |
| Abdominal pain | | | |
| subjects affected / exposed | 0 / 25 (0.00%) | | |
| occurrences (all) | 0 | | |
| Musculoskeletal and connective tissue disorders | | | |

| | | | |
|---|---|---|---|
| Arthralgia<br>subjects affected / exposed<br>occurrences (all)<br><br>Arthritis<br>subjects affected / exposed<br>occurrences (all) | 0 / 25 (0.00%)<br>0<br><br>0 / 25 (0.00%)<br>0 | | |
| Infections and infestations<br>Nasopharyngitis<br>subjects affected / exposed<br>occurrences (all) | 1 / 25 (4.00%)<br>1 | | |

## More information

## Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---|---|
| 01 November 2016 | The Protocol (Protocol Amendment 1, dated 26 September 2016) was revised to Protocol Amendment 2, dated 01 November 2016 in response to a Food and Drug Administration (FDA) request to add measures pertinent to the progressive multifocal encephalopathy (PML) monitoring plan in the trial following review of the PTG-100 Investigational New Drug application. The revisions included:<br><br>1. Clarification that a complete neurological examination would be conducted at Screening and subjects with abnormal neurological findings would be excluded.<br>2. Addition of a phone follow-up 6 months after the end of study treatment to assess signs and symptoms of PML, and incorporation of features to enhance the completeness of follow up.<br>3. Modification of the protocol's monitoring program for PML such that it included education of site personnel and subjects about the signs and symptoms of PML and advised subjects to report to designated personnel if they experienced any of these signs or symptoms. Clarification of the conditions in which a neurologist would be consulted for the follow-up PML assessments.<br>4. Creation of a specific algorithm/action plan for all subjects suspected of having PML and referencing of this plan in the protocol, including details indicating which portions of the algorithm could be conducted by the Investigator or a consulting neurologist, and the conditions whereby a case would be referred to an outside panel of PML experts (with at least one neurologist) for final determination of whether or not the subject had PML.<br>5. Modification of Appendix D to include both a subjective and objective PML assessment checklist for screening and evaluation of suspected PML, to add further information regarding PML assessment. |
| 16 November 2017 | The Protocol Amendment 2 was revised to Protocol Amendment 3, dated 16 November 2017 in order to include the following changes:<br>1. Extension of the Screening window by 1 week, although sites were still encouraged to complete Screening as soon as possible.<br>2. Allowing for the option to have a combined Screening visit that included endoscopy.<br>3. Clarification of Inclusion Criteria #5d and addition of #5e, regarding contraception requirements that applied to sexual activity with a non-sterile male partner.<br>4. Clarification of the Exclusion Criteria #4 for Clostridium difficile to be based on the toxin result and not the PCR result. In addition, clarified that subjects with prior HCV infection who were successfully treated could be enrolled.<br>5. Clarification added to the synopsis that PD samples were to be collected at selected sites only (in line with the main body of the protocol).<br>6. Removal of the statement that all visit procedures needed to be performed prior to the final dose on Day 84.<br>7. Clarification of the resting time needed prior to ECG assessments.<br>8. Inclusion of a statement to clarify that if there was a delay to the IP shipment for Day 0 dosing, that would not be considered a protocol deviation.<br>9. Updating of the Sponsor's Medical Director's name and title.<br>10. Clarification that the 6-month phone call could occur before this date if the subject terminated early from the study.<br>11. Clarification for which subjects would be considered in the Interim Analysis.<br>12. Removal of references to dipstick in the protocol as all subjects had a macro analysis performed instead.<br>13. Clarification that subject numbering would be assigned by an Interactive Web Response System and not by the clinical site staff.<br>14. Inclusion of language to clarify how Mayo scores for rectal bleeding and stool frequency were to be calculated if the Screening visit was combined.<br>15. Removal of text regarding the addition of an additional dose arm (not tested in Stage 1 |

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.

Unblinded IA was performed by the DMC on 65 subjects who had completed 12 weeks dosing/terminated early. Futility was based on failure to achieve 10% conditional power for the primary efficacy endpoint. The trial was declared futile and terminated.

Notes: