



Clinical trial results:

A Multicenter, Randomized, Double-Blind, Placebo Controlled Induction Study to Evaluate the Efficacy and Safety of Risankizumab in Subjects With Moderately to Severely Active Ulcerative Colitis

Summary

| | |
|--------------------------|--|
| EudraCT number | 2016-004677-40 |
| Trial protocol | BE SK AT SE ES NL PT GR DK LT PL DE GB LV SI BG HR FR IT |
| Global end of trial date | 11 May 2023 |

Results information

| | |
|--------------------------------|---|
| Result version number | v2 (current) |
| This version publication date | 28 May 2025 |
| First version publication date | 25 May 2024 |
| Version creation reason | • Correction of full data set clarifying text and data. |

Trial information

Trial identification

| | |
|-----------------------|---------|
| Sponsor protocol code | M16-067 |
|-----------------------|---------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT03398148 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | AbbVie Deutschland GmbH & Co. KG |
| Sponsor organisation address | AbbVie House, Vanwall Business Park, Vanwall Road,, Maidenhead, Berkshire, United Kingdom, SL6 4UB |
| Public contact | Global Medical Services, AbbVie, AbbVie Deutschland GmbH & Co. KG, 001 8006339110, abbvieclinicaltrials@abbvie.com |
| Scientific contact | Global Medical Services, AbbVie, AbbVie Deutschland GmbH & Co. KG, 001 8006339110, abbvieclinicaltrials@abbvie.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 | 11 May 2023 |
| Is this the analysis of the primary completion data? | No |

| | |
|----------------------------------|-------------|
| Global end of trial reached? | Yes |
| Global end of trial date | 11 May 2023 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

This study comprises two sub-studies:

The purpose of Substudy 1 (SS1) is to characterize the efficacy, safety, and pharmacokinetics of Risankizumab as induction treatment in subjects with moderately to severely active Ulcerative Colitis (UC) and to identify the appropriate induction dose of Risankizumab for further evaluation in Substudy 2 (SS2).

The purpose of SS2 is to evaluate the efficacy and safety of Risankizumab compared to placebo in inducing clinical remission in subjects with moderately to severely active UC.

Protection of trial subjects:

Subject and/or legal guardian read and understood the information provided about the study and gave written permission.

Background therapy: -

Evidence for comparator: -

| | |
|---|---------------|
| Actual start date of recruitment | 07 March 2018 |
| 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 | Israel: 55 |
| Country: Number of subjects enrolled | Argentina: 12 |
| Country: Number of subjects enrolled | Netherlands: 20 |
| Country: Number of subjects enrolled | Poland: 118 |
| Country: Number of subjects enrolled | Portugal: 15 |
| Country: Number of subjects enrolled | Slovakia: 37 |
| Country: Number of subjects enrolled | Slovenia: 4 |
| Country: Number of subjects enrolled | Spain: 38 |
| Country: Number of subjects enrolled | United Kingdom: 28 |
| Country: Number of subjects enrolled | Croatia: 20 |
| Country: Number of subjects enrolled | Austria: 40 |
| Country: Number of subjects enrolled | Belgium: 75 |
| Country: Number of subjects enrolled | Bulgaria: 5 |
| Country: Number of subjects enrolled | Czechia: 10 |
| Country: Number of subjects enrolled | Denmark: 4 |
| Country: Number of subjects enrolled | France: 17 |
| Country: Number of subjects enrolled | Germany: 102 |

| | |
|--------------------------------------|------------------------|
| Country: Number of subjects enrolled | Greece: 26 |
| Country: Number of subjects enrolled | Italy: 109 |
| Country: Number of subjects enrolled | Latvia: 7 |
| Country: Number of subjects enrolled | Lithuania: 15 |
| Country: Number of subjects enrolled | Brazil: 29 |
| Country: Number of subjects enrolled | Canada: 52 |
| Country: Number of subjects enrolled | Chile: 19 |
| Country: Number of subjects enrolled | Colombia: 2 |
| Country: Number of subjects enrolled | China: 88 |
| Country: Number of subjects enrolled | Egypt: 22 |
| Country: Number of subjects enrolled | Japan: 207 |
| Country: Number of subjects enrolled | Korea, Republic of: 39 |
| Country: Number of subjects enrolled | Mexico: 1 |
| Country: Number of subjects enrolled | New Zealand: 31 |
| Country: Number of subjects enrolled | Romania: 15 |
| Country: Number of subjects enrolled | Russian Federation: 20 |
| Country: Number of subjects enrolled | Serbia: 37 |
| Country: Number of subjects enrolled | Singapore: 2 |
| Country: Number of subjects enrolled | South Africa: 22 |
| Country: Number of subjects enrolled | Sweden: 3 |
| Country: Number of subjects enrolled | Switzerland: 19 |
| Country: Number of subjects enrolled | Taiwan: 15 |
| Country: Number of subjects enrolled | Ukraine: 8 |
| Country: Number of subjects enrolled | United States: 167 |
| Country: Number of subjects enrolled | Türkiye: 3 |
| Worldwide total number of subjects | 1558 |
| EEA total number of subjects | 680 |

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) | 1451 |
| From 65 to 84 years | 107 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

This study was comprised of 2 SubStudies, each had 2 Periods. Substudy 1 Period 1 had both a doubleblind (DB) Dose Finding Induction Period (S1P1, Analysis populations = ITT1A, N=240) and an Open-Label Period (S1P1, ITT1B, N=341); Subjects with inadequate response in S1P1 could move on to S1P2 (ITT2B, N=215).

Pre-assignment

Screening details:

Substudy 2 was a phase 2 induction study: S2P1 was a DB placebo-controlled study (ITT2, N=977); Subjects with inadequate response in S2P1 could move on to S2P2 (ITT2P2, N=384). N=all enrolled.

Period 1

| | |
|------------------------------|-------------------------|
| Period 1 title | S1P1 and S2P1 |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator |

Blinding implementation details:

During Substudy 1, Induction Period 1 (S1P1), Participants received Risankizumab 1800mg administered by intravenous (IV) infusion in an Open-Label manner. All other Substudies were Double-Blinded.

Arms

| | |
|------------------------------|-----------------------|
| Are arms mutually exclusive? | Yes |
| Arm title | S1P1: DB - Placebo IV |

Arm description:

Substudy 1, Induction Period 1 (S1P1): Double-blind (DB) Participants randomized to receive Placebo for Risankizumab administered by intravenous (IV) infusion.

| | |
|--|--------------------------|
| Arm type | Placebo |
| Investigational medicinal product name | Placebo for Risankizumab |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Injection/infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Placebo for Risankizumab administered by intravenous (IV) infusion.

| | |
|------------------|----------------------------------|
| Arm title | S1P1: DB - Risankizumab 600mg IV |
|------------------|----------------------------------|

Arm description:

Substudy 1, Induction Period 1 (S1P1): Double-blind (DB) Participants randomized to receive Risankizumab 600mg administered by intravenous (IV) infusion.

| | |
|--|---------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Risankizumab |
| Investigational medicinal product code | |
| Other name | ABBV-066, BI 655066 |
| Pharmaceutical forms | Injection/infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Risankizumab 600mg administered by intravenous (IV) infusion

| | |
|------------------|-----------------------------------|
| Arm title | S1P1: DB - Risankizumab 1200mg IV |
|------------------|-----------------------------------|

| | |
|---|-----------------------------------|
| Arm description: | |
| Substudy 1, Induction Period 1 (S1P1): Double-blind (DB) Participants randomized to receive Risankizumab 1200mg administered by intravenous (IV) infusion. | |
| Arm type | Experimental |
| Investigational medicinal product name | Risankizumab |
| Investigational medicinal product code | |
| Other name | ABBV-066, BI 655066 |
| Pharmaceutical forms | Injection/infusion |
| Routes of administration | Intravenous use |
| Dosage and administration details: | |
| Risankizumab 1200mg administered by intravenous (IV) infusion | |
| Arm title | S1P1: DB - Risankizumab 1800mg IV |
| Arm description: | |
| Substudy 1, Induction Period 1 (S1P1): Double-blind (DB) Participants randomized to receive Risankizumab 1800mg administered by intravenous (IV) infusion. | |
| Arm type | Experimental |
| Investigational medicinal product name | Risankizumab |
| Investigational medicinal product code | |
| Other name | ABBV-066, BI 655066 |
| Pharmaceutical forms | Injection/infusion |
| Routes of administration | Intravenous use |
| Dosage and administration details: | |
| Risankizumab 1800mg administered by intravenous (IV) infusion | |
| Arm title | S1P1: OL - Risankizumab 1800mg IV |
| Arm description: | |
| Substudy 1, Induction Period 1 (S1P1): Open-label (OL) Participants received Risankizumab 1800mg administered by intravenous (IV) infusion. | |
| Arm type | Experimental |
| Investigational medicinal product name | Risankizumab |
| Investigational medicinal product code | |
| Other name | ABBV-066, BI 655066 |
| Pharmaceutical forms | Injection/infusion |
| Routes of administration | Intravenous use |
| Dosage and administration details: | |
| Risankizumab 1800mg administered by intravenous (IV) infusion | |
| Arm title | S2P1: DB – Placebo IV |
| Arm description: | |
| Substudy 2, Induction Period 1 (S2P1): Double-blind (DB) received placebo for risankizumab administered by intravenous (IV) infusion. | |
| Arm type | Placebo |
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Injection/infusion |
| Routes of administration | Intravenous use |
| Dosage and administration details: | |
| Placebo for risankizumab administered by intravenous (IV) infusion. | |
| Arm title | S2P1: DB Risankizumab 1200mg IV |
| Arm description: | |
| Substudy 2, Induction Period 1 (S2P1): Double-blind (DB) received risankizumab 1200mg administered by intravenous (IV) infusion. | |
| Arm type | Experimental |

| | |
|--|---------------------|
| Investigational medicinal product name | risankizumab |
| Investigational medicinal product code | |
| Other name | ABBV-066, BI 655066 |
| Pharmaceutical forms | Injection/infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

risankizumab 1200mg administered by intravenous (IV) infusion.

| Number of subjects in period 1 ^[1] | S1P1: DB - Placebo IV | S1P1: DB - Risankizumab 600mg IV | S1P1: DB - Risankizumab 1200mg IV |
|--|--------------------------|--|---|
| | | | |
| Started | 60 | 61 | 61 |
| Completed | 53 | 55 | 58 |
| Not completed | 7 | 6 | 3 |
| COVID-19 INFECTION | - | - | - |
| Consent withdrawn by subject | 1 | 2 | - |
| Adverse event, non-fatal | 5 | 2 | 2 |
| COVID-19 LOGISTICAL RESTRICTIONS | - | - | - |
| Not Specified | - | 1 | - |
| Lack of efficacy | 1 | 1 | 1 |

| Number of subjects in period 1 ^[1] | S1P1: DB - Risankizumab 1800mg IV | S1P1: OL - Risankizumab 1800mg IV | S2P1: DB - Placebo IV |
|--|---|---|--------------------------|
| | | | |
| Started | 58 | 340 | 325 |
| Completed | 57 | 306 | 297 |
| Not completed | 1 | 34 | 28 |
| COVID-19 INFECTION | - | - | - |
| Consent withdrawn by subject | 1 | 3 | 6 |
| Adverse event, non-fatal | - | 8 | 12 |
| COVID-19 LOGISTICAL RESTRICTIONS | - | - | - |
| Not Specified | - | 3 | 4 |
| Lack of efficacy | - | 20 | 6 |

| Number of subjects in period 1 ^[1] | S2P1: DB Risankizumab 1200mg IV |
|--|---------------------------------------|
| Started | 650 |
| Completed | 637 |
| Not completed | 13 |
| COVID-19 INFECTION | 1 |
| Consent withdrawn by subject | 4 |
| Adverse event, non-fatal | 2 |
| COVID-19 LOGISTICAL RESTRICTIONS | 1 |

| | |
|------------------|---|
| Not Specified | 4 |
| Lack of efficacy | 1 |

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: In S1P1: Open-label Risankizumab 1800mg IV arm, a total of 341 subjects were enrolled, but only 340 subjects were treated.

In the S2P1: Double-blind Risankizumab 1200mg IV arm, a total of 652 subjects were randomized, but only 650 subjects were treated.

Period 2

| | |
|------------------------------|-------------------------|
| Period 2 title | S1P2 and S2P2 |
| Is this the baseline period? | No |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator |

Arms

| | |
|------------------------------|----------------------------------|
| Are arms mutually exclusive? | Yes |
| Arm title | S1P2: DB - Risankizumab 180mg SC |

Arm description:

Substudy 1, Induction Period 2 (S1P2): Double-blind (DB) Participants who received risankizumab with inadequate response in Induction 1 randomized to receive risankizumab 180mg administered by subcutaneous (SC) injection.

| | |
|--|---------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Risankizumab |
| Investigational medicinal product code | |
| Other name | ABBV-066, BI 655066 |
| Pharmaceutical forms | Injection/infusion |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Risankizumab 180mg administered by subcutaneous (SC) injection.

| | |
|------------------|----------------------------------|
| Arm title | S1P2: DB – Risankizumab 360mg SC |
|------------------|----------------------------------|

Arm description:

Substudy 1, Induction Period 2 (S1P2): Double-blind (DB) Participants who received risankizumab with inadequate response in Induction 1 randomized to receive Risankizumab 360mg administered by subcutaneous (SC) injection.

| | |
|--|---------------------|
| Arm type | Experimental |
| Investigational medicinal product name | risankizumab |
| Investigational medicinal product code | |
| Other name | ABBV-066, BI 655066 |
| Pharmaceutical forms | Injection/infusion |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Risankizumab 360mg administered by subcutaneous (SC) injection

| | |
|------------------|-----------------------------------|
| Arm title | S1P2: DB – Risankizumab 1800mg IV |
|------------------|-----------------------------------|

Arm description:

Substudy 1, Induction Period 2 (S1P2): Double-blind (DB) Participants who received risankizumab with inadequate response in Induction 1 randomized to receive 1800mg administered by intravenous (IV) infusion

| | |
|----------|--------------|
| Arm type | Experimental |
|----------|--------------|

| | |
|---|---------------------------------------|
| Investigational medicinal product name | risankizumab |
| Investigational medicinal product code | |
| Other name | ABBV-066, BI 655066 |
| Pharmaceutical forms | Injection/infusion |
| Routes of administration | Intravenous use |
| Dosage and administration details: | |
| Risankizumab 1800mg administered by intravenous (IV) infusion | |
| Arm title | S1P2: DB – Risankizumab 1800mg IV Pbo |
| Arm description: | |
| Substudy 1, Induction Period 2 (S1P2): Double-blind (DB) participants who received placebo with inadequate response in Induction 1 receive risankizumab 1800mg administered by intravenous (IV) infusion | |
| Arm type | Experimental |
| Investigational medicinal product name | risankizumab |
| Investigational medicinal product code | |
| Other name | ABBV-066, BI 655066 |
| Pharmaceutical forms | Injection/infusion |
| Routes of administration | Intravenous use |
| Dosage and administration details: | |
| risankizumab 1800mg administered by intravenous (IV) infusion | |
| Arm title | S2P2 DB – Risankizumab 180mg SC |
| Arm description: | |
| Substudy 2, Induction Period 2 (S2P2): Double-blind (DB) participants who received risankizumab with inadequate response in Induction 1 randomized to receive risankizumab 180mg administered by subcutaneous (SC) injection | |
| Arm type | Experimental |
| Investigational medicinal product name | risankizumab |
| Investigational medicinal product code | |
| Other name | ABBV-066, BI 655066 |
| Pharmaceutical forms | Injection/infusion |
| Routes of administration | Subcutaneous use |
| Dosage and administration details: | |
| risankizumab 180mg administered by subcutaneous (SC) injection | |
| Arm title | S2P2 DB – Risankizumab 360mg SC |
| Arm description: | |
| Substudy 2, Induction Period 2 (S2P2): Double-blind (DB) participants who received risankizumab with inadequate response in Induction 1 randomized to receive risankizumab 360mg administered by subcutaneous (SC) injection. | |
| Arm type | Experimental |
| Investigational medicinal product name | risankizumab |
| Investigational medicinal product code | |
| Other name | ABBV-066, BI 655066 |
| Pharmaceutical forms | Injection/infusion |
| Routes of administration | Subcutaneous use |
| Dosage and administration details: | |
| Risankizumab 360mg administered by subcutaneous (SC) injection. | |
| Arm title | S2P2 DB – Risankizumab 1200mg IV |
| Arm description: | |
| Substudy 2, Induction Period 2 (S2P2): Double-blind (DB) participants who received risankizumab with inadequate response in Induction 1 randomized to receive Risankizumab 1200mg administered by intravenous (IV) infusion. | |
| Arm type | Experimental |

| | |
|--|--------------------------------------|
| Investigational medicinal product name | risankizumab |
| Investigational medicinal product code | |
| Other name | ABBV-066, BI 655066 |
| Pharmaceutical forms | Injection/infusion |
| Routes of administration | Intravenous use |
| Dosage and administration details: | |
| Risankizumab 1200mg administered by intravenous (IV) infusion. | |
| Arm title | S2P2 DB – Risankizumab 1200mg IV Pbo |

Arm description:

Substudy 2, Induction Period 2 (S2P2): Double-blind (DB) participants received placebo with inadequate response in Induction 1 randomized to receive risankizumab 1200mg administered by intravenous (IV) infusion.

| | |
|--|---------------------|
| Arm type | Experimental |
| Investigational medicinal product name | risankizumab |
| Investigational medicinal product code | |
| Other name | ABBV-066, BI 655066 |
| Pharmaceutical forms | Injection/infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Risankizumab 1200mg administered by intravenous (IV) infusion.

| Number of subjects in period 2^[2] | S1P2: DB - Risankizumab 180mg SC | S1P2: DB – Risankizumab 360mg SC | S1P2: DB – Risankizumab 1800mg IV |
|---|--|--|---|
| Started | 72 | 69 | 36 |
| Completed | 65 | 57 | 34 |
| Not completed | 7 | 12 | 2 |
| Consent withdrawn by subject | - | 1 | 2 |
| Adverse event, non-fatal | 2 | 4 | - |
| COVID-19 LOGISTICAL RESTRICTIONS | - | 1 | - |
| Not Specified | - | 1 | - |
| Lost to follow-up | - | - | - |
| Lack of efficacy | 5 | 5 | - |

| Number of subjects in period 2^[2] | S1P2: DB – Risankizumab 1800mg IV Pbo | S2P2 DB – Risankizumab 180mg SC | S2P2 DB – Risankizumab 360mg SC |
|---|---|---------------------------------------|---------------------------------------|
| Started | 37 | 71 | 70 |
| Completed | 35 | 65 | 65 |
| Not completed | 2 | 6 | 5 |
| Consent withdrawn by subject | - | 4 | - |
| Adverse event, non-fatal | - | - | - |
| COVID-19 LOGISTICAL RESTRICTIONS | - | - | - |
| Not Specified | - | - | - |
| Lost to follow-up | - | 1 | 1 |

| | | | |
|------------------|---|---|---|
| Lack of efficacy | 2 | 1 | 4 |
|------------------|---|---|---|

| Number of subjects in period 2^[2] | S2P2 DB – Risankizumab 1200mg IV | S2P2 DB – Risankizumab 1200mg IV Pbo |
|---|---|---|
| Started | 68 | 173 |
| Completed | 61 | 164 |
| Not completed | 7 | 9 |
| Consent withdrawn by subject | 2 | 1 |
| Adverse event, non-fatal | 1 | 3 |
| COVID-19 LOGISTICAL RESTRICTIONS | - | - |
| Not Specified | 1 | 1 |
| Lost to follow-up | - | - |
| Lack of efficacy | 3 | 4 |

Notes:

[2] - 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: Double-blind Risankizumab 1200mg IV arm, a total of 652 subjects were randomized, but only 650 subjects were treated.

Baseline characteristics

Reporting groups

| | |
|---|-----------------------------------|
| Reporting group title | S1P1: DB - Placebo IV |
| Reporting group description: | |
| Substudy 1, Induction Period 1 (S1P1): Double-blind (DB) Participants randomized to receive Placebo for Risankizumab administered by intravenous (IV) infusion. | |
| Reporting group title | S1P1: DB - Risankizumab 600mg IV |
| Reporting group description: | |
| Substudy 1, Induction Period 1 (S1P1): Double-blind (DB) Participants randomized to receive Risankizumab 600mg administered by intravenous (IV) infusion. | |
| Reporting group title | S1P1: DB - Risankizumab 1200mg IV |
| Reporting group description: | |
| Substudy 1, Induction Period 1 (S1P1): Double-blind (DB) Participants randomized to receive Risankizumab 1200mg administered by intravenous (IV) infusion. | |
| Reporting group title | S1P1: DB - Risankizumab 1800mg IV |
| Reporting group description: | |
| Substudy 1, Induction Period 1 (S1P1): Double-blind (DB) Participants randomized to receive Risankizumab 1800mg administered by intravenous (IV) infusion. | |
| Reporting group title | S1P1: OL - Risankizumab 1800mg IV |
| Reporting group description: | |
| Substudy 1, Induction Period 1 (S1P1): Open-label (OL) Participants received Risankizumab 1800mg administered by intravenous (IV) infusion. | |
| Reporting group title | S2P1: DB – Placebo IV |
| Reporting group description: | |
| Substudy 2, Induction Period 1 (S2P1): Double-blind (DB) received placebo for risankizumab administered by intravenous (IV) infusion. | |
| Reporting group title | S2P1: DB Risankizumab 1200mg IV |
| Reporting group description: | |
| Substudy 2, Induction Period 1 (S2P1): Double-blind (DB) received risankizumab 1200mg administered by intravenous (IV) infusion. | |

| Reporting group values | S1P1: DB - Placebo IV | S1P1: DB - Risankizumab 600mg IV | S1P1: DB - Risankizumab 1200mg IV |
|------------------------------------|-----------------------|----------------------------------|-----------------------------------|
| Number of subjects | 60 | 61 | 61 |
| Age categorical Units: Subjects | | | |

| | | | |
|--|---------|---------|---------|
| Age continuous Units: years | | | |
| arithmetic mean | 44.4 | 43.0 | 41.8 |
| standard deviation | ± 14.09 | ± 14.90 | ± 13.80 |
| Gender categorical Units: Subjects | | | |
| Female | 24 | 21 | 26 |
| Male | 36 | 40 | 35 |
| Ethnicity (NIH/OMB) Units: Subjects | | | |
| Hispanic or Latino | 3 | 2 | 6 |
| Not Hispanic or Latino | 57 | 59 | 55 |
| Unknown or Not Reported | 0 | 0 | 0 |

| | | | |
|---|----------|----------|----------|
| Race (NIH/OMB) | | | |
| Units: Subjects | | | |
| American Indian or Alaska Native | 0 | 0 | 0 |
| Asian | 14 | 11 | 15 |
| Native Hawaiian or Other Pacific Islander | 0 | 0 | 0 |
| Black or African American | 2 | 1 | 1 |
| White | 44 | 49 | 45 |
| More than one race | 0 | 0 | 0 |
| Unknown or Not Reported | 0 | 0 | 0 |
| Adapted Mayo Score | | | |
| Measure Description: The Adapted Mayo Score is a composite score of UC disease activity based on the following 3 subscores: 1. Stool frequency subscore (SFS), scored from 0 (normal number of stools) to 3 (5 or more stools more than normal) 2. Rectal bleeding subscore (RBS), scored from 0 (no blood seen) to 3 (blood alone passed) 3. Endoscopic subscore, scored from 0 (normal or inactive disease) to 3 (severe disease, spontaneous bleeding, ulceration) The overall Adapted Mayo score ranges from 0 to 9 where higher scores represent more severe disease. | | | |
| Units: Adapted Mayo Score 0 - 9 | | | |
| arithmetic mean | 7.012 | 6.929 | 7.011 |
| standard deviation | ± 1.1645 | ± 1.2240 | ± 1.1288 |

| Reporting group values | S1P1: DB - Risankizumab 1800mg IV | S1P1: OL - Risankizumab 1800mg IV | S2P1: DB – Placebo IV |
|------------------------|---|---|--------------------------|
| Number of subjects | 58 | 340 | 325 |
| Age categorical | | | |
| Units: Subjects | | | |

| | | | |
|---|---------|---------|---------|
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | 40.9 | 40.4 | 42.8 |
| standard deviation | ± 13.73 | ± 14.17 | ± 14.30 |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 27 | 145 | 124 |
| Male | 31 | 195 | 201 |
| Ethnicity (NIH/OMB) | | | |
| Units: Subjects | | | |
| Hispanic or Latino | 1 | 21 | 20 |
| Not Hispanic or Latino | 57 | 319 | 305 |
| Unknown or Not Reported | 0 | 0 | 0 |
| Race (NIH/OMB) | | | |
| Units: Subjects | | | |
| American Indian or Alaska Native | 0 | 0 | 0 |
| Asian | 11 | 47 | 96 |
| Native Hawaiian or Other Pacific Islander | 0 | 0 | 0 |
| Black or African American | 2 | 3 | 7 |
| White | 45 | 290 | 218 |
| More than one race | 0 | 0 | 4 |
| Unknown or Not Reported | 0 | 0 | 0 |

| | | | |
|---|----------|----------|----------|
| Adapted Mayo Score | | | |
| Measure Description: The Adapted Mayo Score is a composite score of UC disease activity based on the following 3 subscores: 1. Stool frequency subscore (SFS), scored from 0 (normal number of stools) to 3 (5 or more stools more than normal) 2. Rectal bleeding subscore (RBS), scored from 0 (no blood seen) to 3 (blood alone passed) 3. Endoscopic subscore, scored from 0 (normal or inactive disease) to 3 (severe disease, spontaneous bleeding, ulceration) The overall Adapted Mayo score ranges from 0 to 9 where higher scores represent more severe disease. | | | |
| Units: Adapted Mayo Score 0 - 9 | | | |
| arithmetic mean | 7.15 | 7.179 | 7.052 |
| standard deviation | ± 1.3908 | ± 1.2279 | ± 1.2800 |

| Reporting group values | S2P1: DB Risankizumab 1200mg IV | Total | |
|------------------------|---------------------------------------|-------|--|
| Number of subjects | 650 | 1555 | |
| Age categorical | | | |
| Units: Subjects | | | |

| | | | |
|---|---------|------|--|
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | 41.8 | | |
| standard deviation | ± 13.47 | - | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 265 | 632 | |
| Male | 385 | 923 | |
| Ethnicity (NIH/OMB) | | | |
| Units: Subjects | | | |
| Hispanic or Latino | 44 | 97 | |
| Not Hispanic or Latino | 606 | 1458 | |
| Unknown or Not Reported | 0 | 0 | |
| Race (NIH/OMB) | | | |
| Units: Subjects | | | |
| American Indian or Alaska Native | 1 | 1 | |
| Asian | 171 | 365 | |
| Native Hawaiian or Other Pacific Islander | 0 | 0 | |
| Black or African American | 12 | 28 | |
| White | 461 | 1152 | |
| More than one race | 5 | 9 | |
| Unknown or Not Reported | 0 | 0 | |
| Adapted Mayo Score | | | |

| | | | |
|---|----------|---|--|
| Measure Description: The Adapted Mayo Score is a composite score of UC disease activity based on the following 3 subscores: 1. Stool frequency subscore (SFS), scored from 0 (normal number of stools) to 3 (5 or more stools more than normal) 2. Rectal bleeding subscore (RBS), scored from 0 (no blood seen) to 3 (blood alone passed) 3. Endoscopic subscore, scored from 0 (normal or inactive disease) to 3 (severe disease, spontaneous bleeding, ulceration) The overall Adapted Mayo score ranges from 0 to 9 where higher scores represent more severe disease. | | | |
| Units: Adapted Mayo Score 0 - 9 | | | |
| arithmetic mean | 7.068 | | |
| standard deviation | ± 1.2173 | - | |

End points

End points reporting groups

| | |
|---|---------------------------------------|
| Reporting group title | S1P1: DB - Placebo IV |
| Reporting group description: Substudy 1, Induction Period 1 (S1P1): Double-blind (DB) Participants randomized to receive Placebo for Risankizumab administered by intravenous (IV) infusion. | |
| Reporting group title | S1P1: DB - Risankizumab 600mg IV |
| Reporting group description: Substudy 1, Induction Period 1 (S1P1): Double-blind (DB) Participants randomized to receive Risankizumab 600mg administered by intravenous (IV) infusion. | |
| Reporting group title | S1P1: DB - Risankizumab 1200mg IV |
| Reporting group description: Substudy 1, Induction Period 1 (S1P1): Double-blind (DB) Participants randomized to receive Risankizumab 1200mg administered by intravenous (IV) infusion. | |
| Reporting group title | S1P1: DB - Risankizumab 1800mg IV |
| Reporting group description: Substudy 1, Induction Period 1 (S1P1): Double-blind (DB) Participants randomized to receive Risankizumab 1800mg administered by intravenous (IV) infusion. | |
| Reporting group title | S1P1: OL - Risankizumab 1800mg IV |
| Reporting group description: Substudy 1, Induction Period 1 (S1P1): Open-label (OL) Participants received Risankizumab 1800mg administered by intravenous (IV) infusion. | |
| Reporting group title | S2P1: DB – Placebo IV |
| Reporting group description: Substudy 2, Induction Period 1 (S2P1): Double-blind (DB) received placebo for risankizumab administered by intravenous (IV) infusion. | |
| Reporting group title | S2P1: DB Risankizumab 1200mg IV |
| Reporting group description: Substudy 2, Induction Period 1 (S2P1): Double-blind (DB) received risankizumab 1200mg administered by intravenous (IV) infusion. | |
| Reporting group title | S1P2: DB - Risankizumab 180mg SC |
| Reporting group description: Substudy 1, Induction Period 2 (S1P2): Double-blind (DB) Participants who received risankizumab with inadequate response in Induction 1 randomized to receive risankizumab 180mg administered by subcutaneous (SC) injection. | |
| Reporting group title | S1P2: DB – Risankizumab 360mg SC |
| Reporting group description: Substudy 1, Induction Period 2 (S1P2): Double-blind (DB) Participants who received risankizumab with inadequate response in Induction 1 randomized to receive Risankizumab 360mg administered by subcutaneous (SC) injection. | |
| Reporting group title | S1P2: DB – Risankizumab 1800mg IV |
| Reporting group description: Substudy 1, Induction Period 2 (S1P2): Double-blind (DB) Participants who received risankizumab with inadequate response in Induction 1 randomized to receive 1800mg administered by intravenous (IV) infusion | |
| Reporting group title | S1P2: DB – Risankizumab 1800mg IV Pbo |
| Reporting group description: Substudy 1, Induction Period 2 (S1P2): Double-blind (DB) participants who received placebo with inadequate response in Induction 1 receive risankizumab 1800mg administered by intravenous (IV) infusion | |
| Reporting group title | S2P2 DB – Risankizumab 180mg SC |
| Reporting group description: Substudy 2, Induction Period 2 (S2P2): Double-blind (DB) participants who received risankizumab with inadequate response in Induction 1 randomized to receive risankizumab 180mg administered by subcutaneous (SC) injection | |

| | |
|---|--------------------------------------|
| Reporting group title | S2P2 DB – Risankizumab 360mg SC |
| Reporting group description: | |
| Substudy 2, Induction Period 2 (S2P2): Double-blind (DB) participants who received risankizumab with inadequate response in Induction 1 randomized to receive risankizumab 360mg administered by subcutaneous (SC) injection. | |
| Reporting group title | S2P2 DB – Risankizumab 1200mg IV |
| Reporting group description: | |
| Substudy 2, Induction Period 2 (S2P2): Double-blind (DB) participants who received risankizumab with inadequate response in Induction 1 randomized to receive Risankizumab 1200mg administered by intravenous (IV) infusion. | |
| Reporting group title | S2P2 DB – Risankizumab 1200mg IV Pbo |
| Reporting group description: | |
| Substudy 2, Induction Period 2 (S2P2): Double-blind (DB) participants received placebo with inadequate response in Induction 1 randomized to receive risankizumab 1200mg administered by intravenous (IV) infusion. | |

Primary: Sub-Study 1: Percentage of Participants Achieving Clinical Remission Per Adapted Mayo Score

| | |
|--|--|
| End point title | Sub-Study 1: Percentage of Participants Achieving Clinical Remission Per Adapted Mayo Score ^[1] |
| End point description: | |
| The Adapted Mayo Score is a composite score of UC disease activity based on the following 3 subscores: | |
| 1. Stool frequency subscore (SFS), scored from 0 (normal number of stools) to 3 (5 or more stools more than normal) | |
| 2. Rectal bleeding subscore (RBS), scored from 0 (no blood seen) to 3 (blood alone passed) | |
| 3. Endoscopic subscore, scored from 0 (normal or inactive disease) to 3 (severe disease, spontaneous bleeding, ulceration) | |
| The overall Adapted Mayo score ranges from 0 to 9 where higher scores represent more severe disease. For Sub-Study 1, clinical remission was defined as SFS ≤ 1, and not greater than baseline, RBS of 0, and endoscopic subscore ≤ 1. | |
| End point type | Primary |
| End point timeframe: | |
| Week 12 | |

Notes:

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: The study included Sub Studies 1 and 2 (Phase 2b dose-finding induction and Phase 3 efficacy/safety induction studies, respectively). The arms as shown are aligned with the sub study and planned analysis population for this end point per protocol and statistical analysis plan.

| End point values | S1P1: DB - Placebo IV | S1P1: DB - Risankizumab 600mg IV | S1P1: DB - Risankizumab 1200mg IV | S1P1: DB - Risankizumab 1800mg IV |
|-----------------------------------|-----------------------|----------------------------------|-----------------------------------|-----------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 60 | 61 | 61 | 58 |
| Units: Percentage of Participants | | | | |
| number (not applicable) | 1.7 | 11.5 | 9.8 | 10.3 |

| End point values | S1P1: OL - Risankizumab 1800mg IV | | | |
|-----------------------------|-----------------------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 340 | | | |

| | | | | |
|-----------------------------------|------|--|--|--|
| Units: Percentage of Participants | | | | |
| number (not applicable) | 12.4 | | | |

Statistical analyses

| | |
|---|--|
| Statistical analysis title | Primary Analysis |
| Comparison groups | S1P1: DB - Placebo IV v S1P1: DB - Risankizumab 600mg IV |
| Number of subjects included in analysis | 121 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0324 ^[2] |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Adjusted Risk Difference |
| Point estimate | 9.6 |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | 2.2 |
| upper limit | 17 |

Notes:

[2] - P-value ≤ 0.05 . Based on Cochran-Mantel-Haenszel (CMH) test stratified by baseline corticosteroid use (yes, no) and baseline adapted mayo score (≤ 7 , > 7).

Risk difference = (risankizumab – Placebo).

| | |
|---|---|
| Statistical analysis title | Primary Analysis |
| Comparison groups | S1P1: DB - Placebo IV v S1P1: DB - Risankizumab 1200mg IV |
| Number of subjects included in analysis | 121 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.046 ^[3] |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Adjusted Risk Difference |
| Point estimate | 8.4 |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | 1.5 |
| upper limit | 15.3 |

Notes:

[3] - P-value ≤ 0.05 . Based on Cochran-Mantel-Haenszel (CMH) test stratified by baseline corticosteroid use (yes, no) and baseline adapted mayo score (≤ 7 , > 7).

Risk difference = (risankizumab – Placebo).

| | |
|-----------------------------------|---|
| Statistical analysis title | Primary Analysis |
| Comparison groups | S1P1: DB - Placebo IV v S1P1: DB - Risankizumab 1800mg IV |

| | |
|---|--------------------------|
| Number of subjects included in analysis | 118 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0397 ^[4] |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Adjusted Risk Difference |
| Point estimate | 8.7 |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | 1.7 |
| upper limit | 15.6 |

Notes:

[4] - P-value ≤ 0.05 . Based on Cochran-Mantel-Haenszel (CMH) test stratified by baseline corticosteroid use (yes, no) and baseline adapted mayo score (≤ 7 , > 7).

Risk difference = (risankizumab – Placebo)

Primary: Sub-Study 2: Percentage of Participants Achieving Clinical Remission Per Adapted Mayo Score

| | |
|-----------------|--|
| End point title | Sub-Study 2: Percentage of Participants Achieving Clinical Remission Per Adapted Mayo Score ^[5] |
|-----------------|--|

End point description:

The Adapted Mayo Score is a composite score of UC disease activity based on the following 3 subscores:

1. Stool frequency subscore (SFS), scored from 0 (normal number of stools) to 3 (5 or more stools more than normal)
2. Rectal bleeding subscore (RBS), scored from 0 (no blood seen) to 3 (blood alone passed)
3. Endoscopic subscore, scored from 0 (normal or inactive disease) to 3 (severe disease, spontaneous bleeding, ulceration)

The overall Adapted Mayo score ranges from 0 to 9 where higher scores represent more severe disease.

For Sub-Study 2, clinical remission was defined as SFS ≤ 1 , and not greater than baseline, RBS of 0, and endoscopic subscore ≤ 1 . Evidence of friability during endoscopy in subjects with otherwise "mild" endoscopic activity will confer an endoscopic subscore of 2.

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

End point timeframe:

Week 12

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: The study included Sub Studies 1 and 2 (Phase 2b dose-finding induction and Phase 3 efficacy/safety induction studies, respectively). The arms as shown are aligned with the sub study and planned analysis population for this end point per protocol and statistical analysis plan.

| End point values | S2P1: DB – Placebo IV | S2P1: DB Risankizumab 1200mg IV | | |
|---|-----------------------|---------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 325 ^[6] | 650 ^[7] | | |
| Units: Percentage of Participants | | | | |
| arithmetic mean (confidence interval 95%) | 6.2 (3.6 to 8.9) | 20.3 (17.2 to 23.4) | | |

Notes:

[6] - ITT2 population.

[7] - ITT2 population.

Statistical analyses

| | |
|---|---|
| Statistical analysis title | Primary Analysis |
| Comparison groups | S2P1: DB – Placebo IV v S2P1: DB Risankizumab 1200mg IV |
| Number of subjects included in analysis | 975 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[8] |
| P-value | < 0.0001 ^[9] |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Adjusted Risk Difference |
| Point estimate | 14 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 10 |
| upper limit | 18 |

Notes:

[8] - Stratified by Advanced Therapy-IR status (yes vs no), Baseline steroid use (yes vs. no) and Baseline Adapted Mayo Score (≤ 7 , > 7).

[9] - Achieved statistical significance at the 2-sided α level of 0.05 under overall Type I error rate control.

Secondary: Sub-Study 1: Percentage of Participants Achieving Endoscopic Improvement

| | |
|-----------------|--|
| End point title | Sub-Study 1: Percentage of Participants Achieving Endoscopic Improvement ^[10] |
|-----------------|--|

End point description:

Endoscopic improvement is defined as endoscopy subscore of 0 or 1.

Endoscopies were assessed by a blinded central reader and scored according to the following scale: 0 = Normal or inactive disease; 1 = Mild disease (erythema, decreased vascular pattern); 2 = Moderate disease (marked erythema, lack of vascular pattern, any friability, erosions); 3 = Severe disease (spontaneous bleeding, ulceration).

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

End point timeframe:

Week 12

Notes:

[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The study included Sub Studies 1 and 2 (Phase 2b dose-finding induction and Phase 3 efficacy/safety induction studies, respectively). The arms as shown are aligned with the sub study and planned analysis population for this end point per protocol and statistical analysis plan.

| End point values | S1P1: DB - Placebo IV | S1P1: DB - Risankizumab 600mg IV | S1P1: DB - Risankizumab 1200mg IV | S1P1: DB - Risankizumab 1800mg IV |
|-----------------------------------|-----------------------|----------------------------------|-----------------------------------|-----------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 60 | 61 | 61 | 58 |
| Units: Percentage of Participants | | | | |
| number (not applicable) | 5.0 | 24.6 | 13.1 | 15.5 |

| End point values | S1P1: OL - Risankizumab 1800mg IV | | | |
|-----------------------------|-----------------------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 340 | | | |

| | | | | |
|-----------------------------------|------|--|--|--|
| Units: Percentage of Participants | | | | |
| number (not applicable) | 17.9 | | | |

Statistical analyses

| | |
|---|--|
| Statistical analysis title | Primary Analysis |
| Comparison groups | S1P1: DB - Placebo IV v S1P1: DB - Risankizumab 600mg IV |
| Number of subjects included in analysis | 121 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0028 ^[11] |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Adjusted Risk Difference |
| Point estimate | 18.7 |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | 8.4 |
| upper limit | 29 |

Notes:

[11] - P-value ≤ 0.01 . Stratified by baseline corticosteroid use (yes, no) and baseline adapted mayo score (≤ 7 , > 7).

Risk difference = (risankizumab – Placebo).

| | |
|---|---|
| Statistical analysis title | Primary Analysis |
| Comparison groups | S1P1: DB - Placebo IV v S1P1: DB - Risankizumab 1200mg IV |
| Number of subjects included in analysis | 121 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0968 ^[12] |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Adjusted Risk Difference |
| Point estimate | 8.4 |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | 0.1 |
| upper limit | 16.7 |

Notes:

[12] - P-value ≤ 0.1 . Stratified by baseline corticosteroid use (yes, no) and baseline adapted mayo score (≤ 7 , > 7).

Risk difference = (risankizumab – Placebo).

| | |
|-----------------------------------|---|
| Statistical analysis title | Primary Analysis |
| Comparison groups | S1P1: DB - Placebo IV v S1P1: DB - Risankizumab 1800mg IV |

| | |
|---|--------------------------|
| Number of subjects included in analysis | 118 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0512 ^[13] |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Adjusted Risk Difference |
| Point estimate | 10.5 |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | 1.6 |
| upper limit | 19.3 |

Notes:

[13] - P-value ≤ 0.1 . Stratified by baseline corticosteroid use (yes, no) and baseline adapted mayo score (≤ 7 , > 7).

Risk difference = (risankizumab – Placebo).

Secondary: Sub-Study 1: Percentage of Participants Achieving Clinical Remission Per Full Mayo Score in Participants With a Full Mayo Score of 6 to 12 at Baseline

| | |
|-----------------|--|
| End point title | Sub-Study 1: Percentage of Participants Achieving Clinical Remission Per Full Mayo Score in Participants With a Full Mayo Score of 6 to 12 at Baseline ^[14] |
|-----------------|--|

End point description:

The Mayo score is a tool designed to measure disease activity for ulcerative colitis. The Full Mayo score (FMS) ranges from 0 (normal or inactive disease) to 12 (severe disease) and is calculated as the sum of 4 subscores (stool frequency, rectal bleeding, endoscopy [confirmed by a central reader], and physician's global assessment), each of which ranges from 0 (normal) to 3 (severe disease). Negative changes indicate improvement.

Clinical remission per FMS is defined as Mayo Score ≤ 2 and no individual subscore > 1 .

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

End point timeframe:

Week 12

Notes:

[14] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The study included Sub Studies 1 and 2 (Phase 2b dose-finding induction and Phase 3 efficacy/safety induction studies, respectively). The arms as shown are aligned with the sub study and planned analysis population for this end point per protocol and statistical analysis plan.

| End point values | S1P1: DB - Placebo IV | S1P1: DB - Risankizumab 600mg IV | S1P1: DB - Risankizumab 1200mg IV | S1P1: DB - Risankizumab 1800mg IV |
|-----------------------------|-----------------------|----------------------------------|-----------------------------------|-----------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 0 ^[15] | 0 ^[16] | 0 ^[17] | 0 ^[18] |
| Units: Participants | | | | |

Notes:

[15] - No data was collected.

[16] - No data was collected.

[17] - No data was collected.

[18] - No data was collected.

| End point values | S1P1: OL - Risankizumab 1800mg IV | | | |
|-----------------------------|-----------------------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 0 ^[19] | | | |

| | | | | |
|---------------------|--|--|--|--|
| Units: Participants | | | | |
|---------------------|--|--|--|--|

Notes:

[19] - No data was collected.

Statistical analyses

No statistical analyses for this end point

Secondary: Sub-Study 1: Percentage of Participants Achieving Clinical Response Per Adapted Mayo Score

| | |
|-----------------|--|
| End point title | Sub-Study 1: Percentage of Participants Achieving Clinical Response Per Adapted Mayo Score ^[20] |
|-----------------|--|

End point description:

The Adapted Mayo Score is a composite score of UC disease activity based on the following 3 subscores:

1. Stool frequency subscore (SFS), scored from 0 (normal number of stools) to 3 (5 or more stools more than normal)
2. Rectal bleeding subscore (RBS), scored from 0 (no blood seen) to 3 (blood alone passed)
3. Endoscopic subscore, scored from 0 (normal or inactive disease) to 3 (severe disease, spontaneous bleeding, ulceration)

The overall Adapted Mayo Score ranges from 0 to 9 where higher scores represent more severe disease. Clinical response per Adapted Mayo Score was defined as decrease from baseline in Adapted Mayo Score ≥ 2 points and $\geq 30\%$, plus a decrease in RBS ≥ 1 or an absolute RBS ≤ 1 .

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

End point timeframe:

Week 12

Notes:

[20] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The study included Sub Studies 1 and 2 (Phase 2b dose-finding induction and Phase 3 efficacy/safety induction studies, respectively). The arms as shown are aligned with the sub study and planned analysis population for this end point per protocol and statistical analysis plan.

| End point values | S1P1: DB - Placebo IV | S1P1: DB - Risankizumab 600mg IV | S1P1: DB - Risankizumab 1200mg IV | S1P1: DB - Risankizumab 1800mg IV |
|-----------------------------------|-----------------------|----------------------------------|-----------------------------------|-----------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 60 | 61 | 61 | 58 |
| Units: Percentage of Participants | | | | |
| number (not applicable) | 20.0 | 42.6 | 45.9 | 53.4 |

| End point values | S1P1: OL - Risankizumab 1800mg IV | | | |
|-----------------------------------|-----------------------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 340 | | | |
| Units: Percentage of Participants | | | | |
| number (not applicable) | 46.2 | | | |

Statistical analyses

| Statistical analysis title | Primary Analysis |
|---|--|
| Comparison groups | S1P1: DB - Placebo IV v S1P1: DB - Risankizumab 600mg IV |
| Number of subjects included in analysis | 121 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0022 ^[21] |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Adjusted Risk Difference |
| Point estimate | 23.9 |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | 11 |
| upper limit | 36.7 |

Notes:

[21] - P-value ≤ 0.01 .

Stratified by baseline corticosteroid use (yes, no) and baseline adapted mayo score (≤ 7 , > 7).

Risk difference = (risankizumab - Placebo).

| Statistical analysis title | Primary Analysis |
|---|---|
| Comparison groups | S1P1: DB - Placebo IV v S1P1: DB - Risankizumab 1200mg IV |
| Number of subjects included in analysis | 121 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0002 ^[22] |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Adjusted Risk Difference |
| Point estimate | 28.4 |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | 15.7 |
| upper limit | 41.1 |

Notes:

[22] - P-value ≤ 0.001 .

Stratified by baseline corticosteroid use (yes, no) and baseline adapted mayo score (≤ 7 , > 7). Risk

difference = (risankizumab - Placebo).

| Statistical analysis title | Primary Analysis |
|---|---|
| Comparison groups | S1P1: DB - Placebo IV v S1P1: DB - Risankizumab 1800mg IV |
| Number of subjects included in analysis | 118 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 ^[23] |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Adjusted Risk Difference |
| Point estimate | 33.8 |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | 20.7 |
| upper limit | 46.9 |

Notes:

[23] - P-value ≤ 0.001 .

Stratified by baseline corticosteroid use (yes, no) and baseline adapted mayo score (≤ 7 , > 7).

Risk difference = (risankizumab - Placebo).

Secondary: Sub-Study 1: Percentage of Participants Achieving Clinical Response Per Partial Adapted Mayo Score

| | |
|-----------------|--|
| End point title | Sub-Study 1: Percentage of Participants Achieving Clinical Response Per Partial Adapted Mayo Score ^[24] |
|-----------------|--|

End point description:

Clinical response per Partial Adapted Mayo Score (without endoscopy).

The Partial Mayo Score is a composite score of UC disease activity based on the following 2 subscores:

1. Stool frequency subscore (SFS), scored from 0 (normal number of stools) to 3 (5 or more stools more than normal)

2. Rectal bleeding subscore (RBS), scored from 0 (no blood seen) to 3 (blood alone passed)

The overall Partial Mayo Score ranges from 0 to 6 with higher scores representing more severe disease.

Clinical response per Partial Mayo Score is defined as a decrease in Partial Adapted Mayo score ≥ 1 point and $\geq 30\%$ from Baseline, plus a decrease in RBS ≥ 1 or an absolute RBS ≤ 1 .

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

End point timeframe:

Week 4

Notes:

[24] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The study included Sub Studies 1 and 2 (Phase 2b dose-finding induction and Phase 3 efficacy/safety induction studies, respectively). The arms as shown are aligned with the sub study and planned analysis population for this end point per protocol and statistical analysis plan.

| End point values | S1P1: DB - Placebo IV | S1P1: DB - Risankizumab 600mg IV | S1P1: DB - Risankizumab 1200mg IV | S1P1: DB - Risankizumab 1800mg IV |
|-----------------------------------|-----------------------|----------------------------------|-----------------------------------|-----------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 60 | 61 | 61 | 58 |
| Units: Percentage of Participants | | | | |
| number (not applicable) | 25.0 | 32.8 | 45.9 | 37.9 |

| End point values | S1P1: OL - Risankizumab 1800mg IV | | | |
|-----------------------------------|-----------------------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 340 | | | |
| Units: Percentage of Participants | | | | |
| number (not applicable) | 43.5 | | | |

Statistical analyses

| | |
|----------------------------|--|
| Statistical analysis title | Primary Analysis |
| Comparison groups | S1P1: DB - Placebo IV v S1P1: DB - Risankizumab 600mg IV |

| | |
|---|--------------------------|
| Number of subjects included in analysis | 121 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.1842 ^[25] |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Adjusted Risk Difference |
| Point estimate | 10.2 |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | -2.4 |
| upper limit | 22.9 |

Notes:

[25] - Stratified by baseline corticosteroid use (yes, no) and baseline adapted mayo score (≤ 7 , > 7).
Risk difference = (risankizumab - Placebo).

| | |
|---|---|
| Statistical analysis title | Primary Analysis |
| Comparison groups | S1P1: DB - Placebo IV v S1P1: DB - Risankizumab 1200mg IV |
| Number of subjects included in analysis | 121 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0041 ^[26] |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Adjusted Risk Difference |
| Point estimate | 23.2 |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | 9.9 |
| upper limit | 36.4 |

Notes:

[26] - P-value ≤ 0.01 .
Stratified by baseline corticosteroid use (yes, no) and baseline adapted mayo score (≤ 7 , > 7).
Risk difference = (risankizumab - Placebo).

| | |
|---|---|
| Statistical analysis title | Primary Analysis |
| Comparison groups | S1P1: DB - Placebo IV v S1P1: DB - Risankizumab 1800mg IV |
| Number of subjects included in analysis | 118 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.1117 ^[27] |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Adjusted Risk Difference |
| Point estimate | 13.1 |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | -0.4 |
| upper limit | 26.6 |

Notes:

[27] - Stratified by baseline corticosteroid use (yes, no) and baseline adapted mayo score (≤ 7 , > 7).
Risk difference = (risankizumab - Placebo).

Secondary: Sub-Study 1: Percentage of Participants Achieving Endoscopic Remission

| | |
|--|--|
| End point title | Sub-Study 1: Percentage of Participants Achieving Endoscopic Remission ^[28] |
| End point description: Endoscopic remission was defined as endoscopy subscore of 0. | |
| End point type | Secondary |
| End point timeframe: Week 12 | |

Notes:

[28] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The study included Sub Studies 1 and 2 (Phase 2b dose-finding induction and Phase 3 efficacy/safety induction studies, respectively). The arms as shown are aligned with the sub study and planned analysis population for this end point per protocol and statistical analysis plan.

| End point values | S1P1: DB - Placebo IV | S1P1: DB - Risankizumab 600mg IV | S1P1: DB - Risankizumab 1200mg IV | S1P1: DB - Risankizumab 1800mg IV |
|-----------------------------------|-----------------------|----------------------------------|-----------------------------------|-----------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 60 | 61 | 61 | 58 |
| Units: Percentage of Participants | | | | |
| number (not applicable) | 0 | 8.2 | 4.9 | 8.6 |

| End point values | S1P1: OL - Risankizumab 1800mg IV | | | |
|-----------------------------------|-----------------------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 340 | | | |
| Units: Percentage of Participants | | | | |
| number (not applicable) | 6.5 | | | |

Statistical analyses

| Statistical analysis title | Primary Analysis |
|---|--|
| Comparison groups | S1P1: DB - Placebo IV v S1P1: DB - Risankizumab 600mg IV |
| Number of subjects included in analysis | 121 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0192 ^[29] |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Adjusted Risk Difference |
| Point estimate | 8.3 |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | 2.5 |
| upper limit | 14.1 |

Notes:

[29] - P-value ≤ 0.05 .

Stratified by baseline corticosteroid use (yes, no) and baseline adapted mayo score (≤ 7 , > 7).

Risk difference = (risankizumab - Placebo).

| | |
|---|---|
| Statistical analysis title | Primary Analysis |
| Comparison groups | S1P1: DB - Placebo IV v S1P1: DB - Risankizumab 1200mg IV |
| Number of subjects included in analysis | 121 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0706 ^[30] |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Adjusted Risk Difference |
| Point estimate | 4.8 |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | 0.4 |
| upper limit | 9.1 |

Notes:

[30] - P-value ≤ 0.1 .

Stratified by baseline corticosteroid use (yes, no) and baseline adapted mayo score (≤ 7 , > 7).

Risk difference = (risankizumab - Placebo).

| | |
|---|---|
| Statistical analysis title | Primary Analysis |
| Comparison groups | S1P1: DB - Placebo IV v S1P1: DB - Risankizumab 1800mg IV |
| Number of subjects included in analysis | 118 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.017 ^[31] |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Adjusted Risk Difference |
| Point estimate | 8.7 |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | 2.7 |
| upper limit | 14.6 |

Notes:

[31] - P-value ≤ 0.05 .

Stratified by baseline corticosteroid use (yes, no) and baseline adapted mayo score (≤ 7 , > 7).

Risk difference = (risankizumab - Placebo).

Secondary: Sub-Study 1: Percentage of Participants With Hospitalization

| | |
|---|--|
| End point title | Sub-Study 1: Percentage of Participants With Hospitalization ^[32] |
| End point description: | |
| Participants with an event that results in admission to the hospital. | |
| End point type | Secondary |
| End point timeframe: | |
| Through Week 12 | |

Notes:

[32] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The study included Sub Studies 1 and 2 (Phase 2b dose-finding induction and Phase 3 efficacy/safety induction studies, respectively). The arms as shown are aligned with the sub study and planned analysis population for this end point per protocol and statistical analysis plan.

| End point values | S1P1: DB - Placebo IV | S1P1: DB - Risankizumab 600mg IV | S1P1: DB - Risankizumab 1200mg IV | S1P1: DB - Risankizumab 1800mg IV |
|-----------------------------------|-----------------------|----------------------------------|-----------------------------------|-----------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 60 | 61 | 61 | 58 |
| Units: Percentage of Participants | | | | |
| number (not applicable) | 8.3 | 9.8 | 6.6 | 5.2 |

| End point values | S1P1: OL - Risankizumab 1800mg IV | | | |
|-----------------------------------|-----------------------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 340 | | | |
| Units: Percentage of Participants | | | | |
| number (not applicable) | 5.6 | | | |

Statistical analyses

| Statistical analysis title | Primary Analysis |
|---|--|
| Comparison groups | S1P1: DB - Placebo IV v S1P1: DB - Risankizumab 600mg IV |
| Number of subjects included in analysis | 121 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.7737 ^[33] |
| Method | Chi-squared |

Notes:

[33] - P value for comparisons between treatment groups and placebo group using chi-square test or Fisher's exact test.

| Statistical analysis title | Primary Analysis |
|---|---|
| Comparison groups | S1P1: DB - Placebo IV v S1P1: DB - Risankizumab 1200mg IV |
| Number of subjects included in analysis | 121 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.7432 ^[34] |
| Method | Fisher exact |

Notes:

[34] - P value for comparisons between treatment groups and placebo group using chi-square test or Fisher's exact test.

| Statistical analysis title | Primary Analysis |
|----------------------------|---|
| Comparison groups | S1P1: DB - Placebo IV v S1P1: DB - Risankizumab 1800mg IV |

| | |
|---|--------------------------|
| Number of subjects included in analysis | 118 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.7172 ^[35] |
| Method | Fisher exact |

Notes:

[35] - P value for comparisons between treatment groups and placebo group using chi-square test or Fisher's exact test.

Secondary: Sub-Study 1: Percentage of Participants Achieving Histologic Endoscopic Mucosal Remission (HEMR)

| | |
|-----------------|--|
| End point title | Sub-Study 1: Percentage of Participants Achieving Histologic Endoscopic Mucosal Remission (HEMR) ^[36] |
|-----------------|--|

End point description:

Mucosal healing defined as endoscopic and histologic remission.

Mucosal healing is defined as an endoscopic score of 0 and Geboes score < 2.0. The endoscopic subscore ranges from 0 (normal or inactive disease) to 3 (severe disease with spontaneous bleeding, ulceration).

The Geboes histologic index includes seven histological features (architectural change, chronic inflammatory infiltrate, lamina propria neutrophils and eosinophils, neutrophils in epithelium, crypt destruction and erosion or ulcers). The Geboes score has 6 grades, each with 3-5 subgrades: Grade 0, structural change only; Grade 1, chronic inflammation; Grade 2, lamina propria neutrophils and eosinophils; Grade 3, neutrophils in epithelium; Grade 4, crypt destruction; and Grade 5, erosions or ulceration.

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

End point timeframe:

Week 12

Notes:

[36] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The study included Sub Studies 1 and 2 (Phase 2b dose-finding induction and Phase 3 efficacy/safety induction studies, respectively). The arms as shown are aligned with the sub study and planned analysis population for this end point per protocol and statistical analysis plan.

| End point values | S1P1: DB - Placebo IV | S1P1: DB - Risankizumab 600mg IV | S1P1: DB - Risankizumab 1200mg IV | S1P1: DB - Risankizumab 1800mg IV |
|-----------------------------------|-----------------------|----------------------------------|-----------------------------------|-----------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 60 | 61 | 61 | 58 |
| Units: Percentage of Participants | | | | |
| number (not applicable) | 0 | 4.9 | 3.3 | 1.7 |

| End point values | S1P1: OL - Risankizumab 1800mg IV | | | |
|-----------------------------------|-----------------------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 340 | | | |
| Units: Percentage of Participants | | | | |
| number (not applicable) | 2.9 | | | |

Statistical analyses

| | |
|---|--|
| Statistical analysis title | Primary Analysis |
| Comparison groups | S1P1: DB - Placebo IV v S1P1: DB - Risankizumab 600mg IV |
| Number of subjects included in analysis | 121 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0722 ^[37] |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Adjusted Risk Difference |
| Point estimate | 4.7 |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | 0.4 |
| upper limit | 9 |

Notes:

[37] - P-value ≤ 0.1 .

Stratified by baseline corticosteroid use (yes, no) and baseline adapted mayo score (≤ 7 , > 7).

Risk difference = (risankizumab - Placebo).

| | |
|---|---|
| Statistical analysis title | Primary Analysis |
| Comparison groups | S1P1: DB - Placebo IV v S1P1: DB - Risankizumab 1200mg IV |
| Number of subjects included in analysis | 121 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.148 ^[38] |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Adjusted Risk Difference |
| Point estimate | 3.1 |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | -0.4 |
| upper limit | 6.6 |

Notes:

[38] - Stratified by baseline corticosteroid use (yes, no) and baseline adapted mayo score (≤ 7 , > 7).

Risk difference = (risankizumab - Placebo).

| | |
|---|---|
| Statistical analysis title | Primary Analysis |
| Comparison groups | S1P1: DB - Placebo IV v S1P1: DB - Risankizumab 1800mg IV |
| Number of subjects included in analysis | 118 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.3042 ^[39] |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Adjusted Risk Difference |
| Point estimate | 1.7 |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | -1 |
| upper limit | 4.5 |

Notes:

[39] - Stratified by baseline corticosteroid use (yes, no) and baseline adapted mayo score (≤ 7 , > 7).
Risk difference = (risankizumab - Placebo).

Secondary: Sub-Study 1: Change in Ulcerative Colitis Symptom Questionnaire (UC-SQ)

| | |
|-----------------|---|
| End point title | Sub-Study 1: Change in Ulcerative Colitis Symptom Questionnaire (UC-SQ) ^[40] |
|-----------------|---|

End point description:

The UC-SQ is a patient questionnaire to assess severity of Ulcerative Colitis Symptom

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

End point timeframe:

Baseline Through Week 12

Notes:

[40] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The study included Sub Studies 1 and 2 (Phase 2b dose-finding induction and Phase 3 efficacy/safety induction studies, respectively). The arms as shown are aligned with the sub study and planned analysis population for this end point per protocol and statistical analysis plan.

| End point values | S1P1: DB - Placebo IV | S1P1: DB - Risankizumab 600mg IV | S1P1: DB - Risankizumab 1200mg IV | S1P1: DB - Risankizumab 1800mg IV |
|-------------------------------------|-----------------------|----------------------------------|-----------------------------------|-----------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 50 ^[41] | 52 ^[42] | 56 ^[43] | 53 ^[44] |
| Units: Units on a scale | | | | |
| least squares mean (standard error) | -7.4 (\pm 1.53) | -13.8 (\pm 1.50) | -15.6 (\pm 1.46) | -15.1 (\pm 1.51) |

Notes:

[41] - Includes ITT1A population.

[42] - Includes ITT1A population.

[43] - Includes ITT1A population.

[44] - Includes ITT1A population.

| End point values | S1P1: OL - Risankizumab 1800mg IV | | | |
|-------------------------------------|-----------------------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 286 ^[45] | | | |
| Units: Units on a scale | | | | |
| least squares mean (standard error) | -17.1 (\pm 0.58) | | | |

Notes:

[45] - Includes ITT1B population.

Statistical analyses

| Statistical analysis title | Primary Analysis |
|---|--|
| Comparison groups | S1P1: DB - Placebo IV v S1P1: DB - Risankizumab 600mg IV |
| Number of subjects included in analysis | 102 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.003 ^[46] |
| Method | Mixed-effect model repeated measurement |
| Parameter estimate | Least Squares (LS) Mean Difference |
| Point estimate | -6.4 |

| | |
|----------------------|----------------------------|
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | -9.94 |
| upper limit | -2.89 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 2.13 |

Notes:

[46] - P-value \leq 0.01.

| | |
|---|---|
| Statistical analysis title | Primary Analysis |
| Comparison groups | S1P1: DB - Placebo IV v S1P1: DB - Risankizumab 1200mg IV |
| Number of subjects included in analysis | 106 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0001 ^[47] |
| Method | Mixed-effect model repeated measurement |
| Parameter estimate | Least Squares (LS) Mean Difference |
| Point estimate | -8.2 |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | -11.67 |
| upper limit | -4.71 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 2.11 |

Notes:

[47] - P-value \leq 0.001

| | |
|---|---|
| Statistical analysis title | Primary Analysis |
| Comparison groups | S1P1: DB - Placebo IV v S1P1: DB - Risankizumab 1800mg IV |
| Number of subjects included in analysis | 103 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0004 ^[48] |
| Method | Mixed-effect model repeated measurement |
| Parameter estimate | Least Squares (LS) Mean Difference |
| Point estimate | -7.7 |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | -11.27 |
| upper limit | -4.19 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 2.14 |

Notes:

[48] - P-value \leq 0.001

Secondary: Sub-Study 1: Change in Inflammatory Bowel Disease Questionnaire (IBDQ)

| | |
|-----------------|--|
| End point title | Sub-Study 1: Change in Inflammatory Bowel Disease Questionnaire (IBDQ) ^[49] |
|-----------------|--|

End point description:

The IBDQ is used to assess the quality of life of patients with inflammatory bowel disease. The IBDQ is a 32-item (ranges 1 - 7) self-report questionnaire for patients with IBD to evaluate the patient reported outcomes across 4 dimensions: bowel symptoms (loose stools, abdominal pain), systemic symptoms (fatigue, altered sleep pattern), social function (work attendance, need to cancel social events), and emotional function (anger, depression, irritability). The IBDQ total Score ranges from 32 to 224 with a higher score indicating better outcome.

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

End point timeframe:

Baseline Through Week 12

Notes:

[49] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The study included Sub Studies 1 and 2 (Phase 2b dose-finding induction and Phase 3 efficacy/safety induction studies, respectively). The arms as shown are aligned with the sub study and planned analysis population for this end point per protocol and statistical analysis plan.

| End point values | S1P1: DB - Placebo IV | S1P1: DB - Risankizumab 600mg IV | S1P1: DB - Risankizumab 1200mg IV | S1P1: DB - Risankizumab 1800mg IV |
|-------------------------------------|-----------------------|----------------------------------|-----------------------------------|-----------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 51 ^[50] | 55 ^[51] | 59 ^[52] | 54 ^[53] |
| Units: Units on a scale | | | | |
| least squares mean (standard error) | 20.1 (± 4.67) | 37.4 (± 4.56) | 40.3 (± 4.38) | 40.0 (± 4.55) |

Notes:

[50] - Includes ITT1A population.

[51] - Includes ITT1A population.

[52] - Includes ITT1A population.

[53] - Includes ITT1A population.

| End point values | S1P1: OL - Risankizumab 1800mg IV | | | |
|-------------------------------------|-----------------------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 305 ^[54] | | | |
| Units: Units on a scale | | | | |
| least squares mean (standard error) | 49.5 (± 1.86) | | | |

Notes:

[54] - Includes ITT1B population.

Statistical analyses

| Statistical analysis title | Primary Analysis |
|---|--|
| Comparison groups | S1P1: DB - Placebo IV v S1P1: DB - Risankizumab 600mg IV |
| Number of subjects included in analysis | 106 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0081 ^[55] |
| Method | Mixed-effect model repeated measurement |
| Parameter estimate | Least Squares (LS) Mean Difference |
| Point estimate | 17.3 |

| | |
|----------------------|----------------------------|
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | 6.61 |
| upper limit | 28 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 6.47 |

Notes:

[55] - P-value \leq 0.01.

| | |
|---|---|
| Statistical analysis title | Primary Analysis |
| Comparison groups | S1P1: DB - Placebo IV v S1P1: DB - Risankizumab 1200mg IV |
| Number of subjects included in analysis | 110 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0017 ^[56] |
| Method | Mixed-effect model repeated measurement |
| Parameter estimate | Least Squares (LS) Mean Difference |
| Point estimate | 20.3 |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | 9.74 |
| upper limit | 30.79 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 6.37 |

Notes:

[56] - P-value \leq 0.01

| | |
|---|---|
| Statistical analysis title | Primary Analysis |
| Comparison groups | S1P1: DB - Placebo IV v S1P1: DB - Risankizumab 1800mg IV |
| Number of subjects included in analysis | 105 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0024 ^[57] |
| Method | Mixed-effect model repeated measurement |
| Parameter estimate | Least Squares (LS) Mean Difference |
| Point estimate | 19.9 |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | 9.22 |
| upper limit | 30.67 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 6.49 |

Notes:

[57] - P-value \leq 0.01

Secondary: Sub-Study 1: Change in Short Form-36 (SF-36) - Physical Component

| | |
|-----------------|---|
| End point title | Sub-Study 1: Change in Short Form-36 (SF-36) - Physical |
|-----------------|---|

End point description:

The SF-36 is an indicator of overall health status.

The Short Form 36-Item Health Survey (SF-36) Version 2 is a self-administered questionnaire that measures the impact of disease on overall quality of life during the past 4 weeks. The SF-36 consists of 36 questions in eight domains (physical function, pain, general and mental health, vitality, social function, physical and emotional health).

End point type

Secondary

End point timeframe:

Baseline Through Week 12

Notes:

[58] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The study included Sub Studies 1 and 2 (Phase 2b dose-finding induction and Phase 3 efficacy/safety induction studies, respectively). The arms as shown are aligned with the sub study and planned analysis population for this end point per protocol and statistical analysis plan.

| End point values | S1P1: DB - Placebo IV | S1P1: DB - Risankizumab 600mg IV | S1P1: DB - Risankizumab 1200mg IV | S1P1: DB - Risankizumab 1800mg IV |
|-------------------------------------|-----------------------|----------------------------------|-----------------------------------|-----------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 51 ^[59] | 54 ^[60] | 59 ^[61] | 54 ^[62] |
| Units: Units on a scale | | | | |
| least squares mean (standard error) | 3.904 (± 0.8907) | 5.112 (± 0.8751) | 6.350 (± 0.8341) | 6.296 (± 0.8675) |

Notes:

[59] - Includes ITT1A population.

[60] - Includes ITT1A population.

[61] - Includes ITT1A population.

[62] - Includes ITT1A population.

| End point values | S1P1: OL - Risankizumab 1800mg IV | | | |
|-------------------------------------|-----------------------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 298 ^[63] | | | |
| Units: Units on a scale | | | | |
| least squares mean (standard error) | 7.719 (± 0.3929) | | | |

Notes:

[63] - Includes ITT1B population.

Statistical analyses

| Statistical analysis title | Primary Analysis |
|---|--|
| Comparison groups | S1P1: DB - Placebo IV v S1P1: DB - Risankizumab 600mg IV |
| Number of subjects included in analysis | 105 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.3315 |
| Method | Mixed-effect model repeated measurement |
| Parameter estimate | Least Squares (LS) Mean Difference |
| Point estimate | 1.208 |

| | |
|----------------------|----------------------------|
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | -0.8429 |
| upper limit | 3.2596 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 1.2416 |

| | |
|---|---|
| Statistical analysis title | Primary Analysis |
| Comparison groups | S1P1: DB - Placebo IV v S1P1: DB - Risankizumab 1200mg IV |
| Number of subjects included in analysis | 110 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0451 ^[64] |
| Method | Mixed-effect model repeated measurement |
| Parameter estimate | Least Squares (LS) Mean Difference |
| Point estimate | 2.447 |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | 0.4415 |
| upper limit | 4.4519 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 1.2137 |

Notes:

[64] - P-value \leq 0.05

| | |
|---|---|
| Statistical analysis title | Primary Analysis |
| Comparison groups | S1P1: DB - Placebo IV v S1P1: DB - Risankizumab 1800mg IV |
| Number of subjects included in analysis | 105 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0543 ^[65] |
| Method | Mixed-effect model repeated measurement |
| Parameter estimate | Least Squares (LS) Mean Difference |
| Point estimate | 2.392 |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | 0.3498 |
| upper limit | 4.4352 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 1.2364 |

Notes:

[65] - P-value \leq 0.1

Secondary: Sub-Study 1: Change in Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-Fatigue)

| | |
|---|---|
| End point title | Sub-Study 1: Change in Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-Fatigue) ^[66] |
| End point description: | |
| The FACIT-Fatigue Scale is a validated self-administered 13-item tool that measures an individual's level of fatigue during their usual daily activities over the past 7 days. Each of the fatigue and impact of fatigue items are measured on a four-point Likert scale. The FACIT Fatigue Scale is the sum of the individual 13 scores and ranges from 0 to 52 where higher scores indicate better the quality of life. A positive change from baseline indicates improvement. | |
| End point type | Secondary |
| End point timeframe: | |
| Baseline Through Week 12 | |

Notes:

[66] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The study included Sub Studies 1 and 2 (Phase 2b dose-finding induction and Phase 3 efficacy/safety induction studies, respectively). The arms as shown are aligned with the sub study and planned analysis population for this end point per protocol and statistical analysis plan.

| End point values | S1P1: DB - Placebo IV | S1P1: DB - Risankizumab 600mg IV | S1P1: DB - Risankizumab 1200mg IV | S1P1: DB - Risankizumab 1800mg IV |
|-------------------------------------|-----------------------|----------------------------------|-----------------------------------|-----------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 51 ^[67] | 54 ^[68] | 59 ^[69] | 54 ^[70] |
| Units: units on a scale | | | | |
| least squares mean (standard error) | 3.7 (± 1.37) | 7.6 (± 1.35) | 9.0 (± 1.29) | 8.3 (± 1.33) |

Notes:

[67] - Includes ITT1A population.

[68] - Includes ITT1A population..

[69] - Includes ITT1A population.

[70] - Includes ITT1A population.

| End point values | S1P1: OL - Risankizumab 1800mg IV | | | |
|-------------------------------------|-----------------------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 298 ^[71] | | | |
| Units: units on a scale | | | | |
| least squares mean (standard error) | 10.7 (± 0.54) | | | |

Notes:

[71] - Includes ITT1B population.

Statistical analyses

| Statistical analysis title | Primary Analysis |
|---|--|
| Comparison groups | S1P1: DB - Placebo IV v S1P1: DB - Risankizumab 600mg IV |
| Number of subjects included in analysis | 105 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0422 ^[72] |
| Method | Mixed-effect model repeated measurement |
| Parameter estimate | Least Squares (LS) Mean Difference |
| Point estimate | 3.9 |

| | |
|----------------------|----------------------------|
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | 0.75 |
| upper limit | 7.06 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 1.91 |

Notes:

[72] - P-value \leq 0.05

| | |
|---|---|
| Statistical analysis title | Primary Analysis |
| Comparison groups | S1P1: DB - Placebo IV v S1P1: DB - Risankizumab 1200mg IV |
| Number of subjects included in analysis | 110 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0049 ^[73] |
| Method | Mixed-effect model repeated measurement |
| Parameter estimate | Least Squares (LS) Mean Difference |
| Point estimate | 5.3 |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | 2.23 |
| upper limit | 8.42 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 1.87 |

Notes:

[73] - P-value \leq 0.01

| | |
|---|---|
| Statistical analysis title | Primary Analysis |
| Comparison groups | S1P1: DB - Placebo IV v S1P1: DB - Risankizumab 1800mg IV |
| Number of subjects included in analysis | 105 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0156 ^[74] |
| Method | Mixed-effect model repeated measurement |
| Parameter estimate | Least Squares (LS) Mean Difference |
| Point estimate | 4.6 |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | 1.5 |
| upper limit | 7.8 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 1.91 |

Notes:

[74] - P-value \leq 0.05

Secondary: Sub-Study 1: Percentage of Participants Undergoing Ulcerative Colitis (UC)-Related Surgeries

| | |
|---|--|
| End point title | Sub-Study 1: Percentage of Participants Undergoing Ulcerative Colitis (UC)-Related Surgeries ^[75] |
| End point description: Participants who underwent surgery related to UC. | |
| End point type | Secondary |
| End point timeframe: Through Week 12 | |

Notes:

[75] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The study included Sub Studies 1 and 2 (Phase 2b dose-finding induction and Phase 3 efficacy/safety induction studies, respectively). The arms as shown are aligned with the sub study and planned analysis population for this end point per protocol and statistical analysis plan.

| End point values | S1P1: DB - Placebo IV | S1P1: DB - Risankizumab 600mg IV | S1P1: DB - Risankizumab 1200mg IV | S1P1: DB - Risankizumab 1800mg IV |
|-----------------------------------|-----------------------|----------------------------------|-----------------------------------|-----------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 60 | 61 | 61 | 58 |
| Units: Percentage of Participants | | | | |
| number (not applicable) | 0 | 1.6 | 0 | 0 |

| End point values | S1P1: OL - Risankizumab 1800mg IV | | | |
|-----------------------------------|-----------------------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 340 | | | |
| Units: Percentage of Participants | | | | |
| number (not applicable) | 2.1 | | | |

Statistical analyses

| | |
|---|--|
| Statistical analysis title | Primary Analysis |
| Comparison groups | S1P1: DB - Placebo IV v S1P1: DB - Risankizumab 600mg IV |
| Number of subjects included in analysis | 121 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 1 ^[76] |
| Method | Fisher exact |

Notes:

[76] - P-Value for comparisons between treatment groups and placebo group using Fisher's exact test.

Secondary: Sub-Study 2: Percentage of Participants Achieving Clinical Response Per Adapted Mayo Score

| | |
|-----------------|--|
| End point title | Sub-Study 2: Percentage of Participants Achieving Clinical Response Per Adapted Mayo Score ^[77] |
|-----------------|--|

End point description:

The Adapted Mayo Score is a composite score of UC disease activity based on the following 3 subscores: Stool frequency subscore (SFS), scored from 0 (normal number of stools) to 3 (5 or more stools more

than normal)

Rectal bleeding subscore (RBS), scored from 0 (no blood seen) to 3 (blood alone passed)

Endoscopic subscore, scored from 0 (normal or inactive disease) to 3 (severe disease, spontaneous bleeding, ulceration)

The overall Adapted Mayo Score ranges from 0 to 9 where higher scores represent more severe disease.

Clinical Response is defined as a decrease from baseline in the Adapted Mayo Score ≥ 2 points and $\geq 30\%$ from baseline, and a decrease in RBS ≥ 1 or an absolute RBS ≤ 1).

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

End point timeframe:

Week 12

Notes:

[77] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The study included Sub Studies 1 and 2 (Phase 2b dose-finding induction and Phase 3 efficacy/safety induction studies, respectively). The arms as shown are aligned with the sub study and planned analysis population for this end point per protocol and statistical analysis plan.

| End point values | S2P1: DB – Placebo IV | S2P1: DB Risankizumab 1200mg IV | | |
|-----------------------------------|-----------------------|---------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 325 | 650 | | |
| Units: Percentage of Participants | | | | |
| number (confidence interval 95%) | 35.7 (30.5 to 40.9) | 64.3 (60.6 to 67.9) | | |

Statistical analyses

| Statistical analysis title | Primary Analysis |
|---|---|
| Comparison groups | S2P1: DB Risankizumab 1200mg IV v S2P1: DB – Placebo IV |
| Number of subjects included in analysis | 975 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[78] |
| P-value | < 0.0001 ^[79] |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Adjusted Risk Difference |
| Point estimate | 28.6 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 22.3 |
| upper limit | 34.8 |

Notes:

[78] - Between-group diff. and 95% CI calculated using Mantel-Haenszel common rate diff. (Greenland and Robins (1985)).

[79] - Statistical significance is determined via the graphical multiple testing procedure controlling the overall type I error rate of primary and key secondary endpoints at the 0.05 level.

Secondary: Sub-Study 2: Percentage of Participants Achieving Endoscopic Improvement

| | |
|-----------------|--|
| End point title | Sub-Study 2: Percentage of Participants Achieving Endoscopic Improvement ^[80] |
|-----------------|--|

End point description:

Endoscopic Improvement is defined as an endoscopic subscore of 0 or 1.

Endoscopies were assessed by a blinded central reader and scored according to the following scale: 0 = Normal or inactive disease; 1 = Mild disease (erythema, decreased vascular pattern); 2 = Moderate disease (marked erythema, lack of vascular pattern, any friability, erosions); 3 = Severe disease (spontaneous bleeding, ulceration).

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

Notes:

[80] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The study included Sub Studies 1 and 2 (Phase 2b dose-finding induction and Phase 3 efficacy/safety induction studies, respectively). The arms as shown are aligned with the sub study and planned analysis population for this end point per protocol and statistical analysis plan.

| End point values | S2P1: DB – Placebo IV | S2P1: DB Risankizumab 1200mg IV | | |
|-----------------------------------|-----------------------|---------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 325 | 650 | | |
| Units: Percentage of Participants | | | | |
| number (confidence interval 95%) | 12.1 (8.5 to 15.6) | 36.5 (32.8 to 40.2) | | |

Statistical analyses

| Statistical analysis title | Primary Analysis |
|---|---|
| Comparison groups | S2P1: DB – Placebo IV v S2P1: DB Risankizumab 1200mg IV |
| Number of subjects included in analysis | 975 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[81] |
| P-value | < 0.0001 ^[82] |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Adjusted Risk Difference |
| Point estimate | 24.3 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 19.3 |
| upper limit | 29.4 |

Notes:

[81] - Between-group diff. and 95% CI calculated using Mantel-Haenszel common rate diff. (Greenland and Robins (1985)).

[82] - Statistical significance is determined via the graphical multiple testing procedure controlling the overall type I error rate of primary and key secondary endpoints at the 0.05 level.

Secondary: Sub-Study 2: Percentage of Participants Achieving Histologic Endoscopic Mucosal Improvement (HEMI)

| | |
|-----------------|--|
| End point title | Sub-Study 2: Percentage of Participants Achieving Histologic Endoscopic Mucosal Improvement (HEMI) ^[83] |
|-----------------|--|

End point description:

Histologic-Endoscopic Mucosal Improvement is defined as an endoscopic subscore of 0 or 1 without evidence of friability and a Geboes score ≤ 3.1.

The endoscopic subscore ranges from 0 (normal or inactive disease) to 3 (severe disease with spontaneous bleeding, ulceration).

The Geboes histologic index includes seven histological features (architectural change, chronic inflammatory infiltrate, lamina propria neutrophils and eosinophils, neutrophils in epithelium, crypt destruction and erosion or ulcers).

The Geboes score has 6 grades, each with 3-5 subgrades: Grade 0, structural change only; Grade 1, chronic inflammation; Grade 2, lamina propria neutrophils and eosinophils; Grade 3, neutrophils in epithelium; Grade 4, crypt destruction; and Grade 5, erosions or ulceration.

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

End point timeframe:

Week 12

Notes:

[83] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The study included Sub Studies 1 and 2 (Phase 2b dose-finding induction and Phase 3 efficacy/safety induction studies, respectively). The arms as shown are aligned with the sub study and planned analysis population for this end point per protocol and statistical analysis plan.

| End point values | S2P1: DB – Placebo IV | S2P1: DB Risankizumab 1200mg IV | | |
|-----------------------------------|-----------------------|---------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 325 | 650 | | |
| Units: Percentage of Participants | | | | |
| number (confidence interval 95%) | 7.7 (4.8 to 10.6) | 24.5 (21.2 to 27.8) | | |

Statistical analyses

| Statistical analysis title | Primary Analysis |
|---|---|
| Comparison groups | S2P1: DB – Placebo IV v S2P1: DB Risankizumab 1200mg IV |
| Number of subjects included in analysis | 975 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[84] |
| P-value | < 0.0001 ^[85] |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Adjusted Risk Difference |
| Point estimate | 16.6 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 12.3 |
| upper limit | 21 |

Notes:

[84] - Between-group diff. and 95% CI calculated using Mantel-Haenszel common rate diff. (Greenland and Robins (1985)).

[85] - Statistical significance is determined via the graphical multiple testing procedure controlling the overall type I error rate of primary and key secondary endpoints at the 0.05 level. Adjusted Risk Difference.

Secondary: Sub-Study 2: Percentage of Participants Achieving Endoscopic Remission

| | |
|-----------------|--|
| End point title | Sub-Study 2: Percentage of Participants Achieving Endoscopic Remission ^[86] |
|-----------------|--|

End point description:

Endoscopic remission per endoscopy subscore.

Endoscopic Remission: SES-CD ≤ 4 and at least a 2-point reduction versus baseline and no subscore greater than 1 in any individual variable.

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

End point timeframe:

Week 12

Notes:

[86] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The study included Sub Studies 1 and 2 (Phase 2b dose-finding induction and Phase 3 efficacy/safety induction studies, respectively). The arms as shown are aligned with the sub study and planned analysis population for this end point per protocol and statistical analysis plan.

| End point values | S2P1: DB – Placebo IV | S2P1: DB Risankizumab 1200mg IV | | |
|-----------------------------------|-----------------------|---------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 325 | 650 | | |
| Units: Percentage of Participants | | | | |
| number (confidence interval 95%) | 3.4 (1.4 to 5.4) | 10.6 (8.2 to 13.0) | | |

Statistical analyses

| Statistical analysis title | Primary Analysis |
|---|---|
| Comparison groups | S2P1: DB – Placebo IV v S2P1: DB Risankizumab 1200mg IV |
| Number of subjects included in analysis | 975 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[87] |
| P-value | < 0.0001 ^[88] |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Adjusted Risk Difference |
| Point estimate | 7.2 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 4.2 |
| upper limit | 10.2 |

Notes:

[87] - Between-group diff. and 95% CI calculated using Mantel-Haenszel common rate diff. (Greenland and Robins (1985)).

[88] - Statistical significance is determined via the graphical multiple testing procedure controlling the overall type I error rate of primary and key secondary endpoints at the 0.05 level.

Secondary: Sub-Study 2: Percentage of Participants Achieving Clinical Response Per Partial Adapted Mayo Score at Week 4

| | |
|-----------------|--|
| End point title | Sub-Study 2: Percentage of Participants Achieving Clinical Response Per Partial Adapted Mayo Score at Week 4 ^[89] |
|-----------------|--|

End point description:

Clinical response per Partial Adapted Mayo Score (without endoscopy).

The Partial Mayo Score is a composite score of UC disease activity based on the following 2 subscores: Stool frequency subscore (SFS), scored from 0 (normal number of stools) to 3 (5 or more stools more than normal)

Rectal bleeding subscore (RBS), scored from 0 (no blood seen) to 3 (blood alone passed)

The overall Partial Mayo Score ranges from 0 to 6 with higher scores representing more severe disease.

Clinical Response per Partial Mayo Score is defined as a decrease in Partial Adapted Mayo Score ≥ 1 points and $\geq 30\%$ from Baseline, plus a decrease in RBS ≥ 1 or an absolute RBS ≤ 1 .

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

End point timeframe:

Week 4

Notes:

[89] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The study included Sub Studies 1 and 2 (Phase 2b dose-finding induction and Phase 3 efficacy/safety induction studies, respectively). The arms as shown are aligned with the sub study and planned analysis population for this end point per protocol and statistical analysis plan.

| End point values | S2P1: DB – Placebo IV | S2P1: DB Risankizumab 1200mg IV | | |
|-----------------------------------|-----------------------|---------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 325 | 650 | | |
| Units: Percentage of Participants | | | | |
| number (confidence interval 95%) | 30.5 (25.5 to 35.5) | 52.2 (48.3 to 56.0) | | |

Statistical analyses

| Statistical analysis title | Primary Analysis |
|---|---|
| Comparison groups | S2P1: DB – Placebo IV v S2P1: DB Risankizumab 1200mg IV |
| Number of subjects included in analysis | 975 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[90] |
| P-value | < 0.0001 ^[91] |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Adjusted Risk Difference |
| Point estimate | 21.8 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 15.6 |
| upper limit | 28.1 |

Notes:

[90] - Between-group diff. and 95% CI calculated using Mantel-Haenszel common rate diff. (Greenland and Robins (1985)).

[91] - Statistical significance is determined via the graphical multiple testing procedure controlling the overall type I error rate of primary and key secondary endpoints at the 0.05 level.

Secondary: Sub-Study 2: Percentage of Participants Achieving No Bowel Urgency

| | |
|-----------------|--|
| End point title | Sub-Study 2: Percentage of Participants Achieving No Bowel Urgency ^[92] |
|-----------------|--|

End point description:

Percentage of participants who reported no bowel urgency. Bowel urgency was assessed by participants in a subject diary completed once a day.

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

End point timeframe:

Week 12

Notes:

[92] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The study included Sub Studies 1 and 2 (Phase 2b dose-finding induction and Phase 3 efficacy/safety induction studies, respectively). The arms as shown are aligned with the sub study and planned analysis population for this end point per protocol and statistical analysis plan.

| End point values | S2P1: DB – Placebo IV | S2P1: DB Risankizumab 1200mg IV | | |
|-----------------------------------|-----------------------|---------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 325 | 650 | | |
| Units: Percentage of Participants | | | | |
| number (confidence interval 95%) | 27.7 (22.8 to 32.6) | 44.1 (40.3 to 47.9) | | |

Statistical analyses

| Statistical analysis title | Primary Analysis |
|---|---|
| Comparison groups | S2P1: DB – Placebo IV v S2P1: DB Risankizumab 1200mg IV |
| Number of subjects included in analysis | 975 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[93] |
| P-value | < 0.0001 ^[94] |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Adjusted Risk Difference |
| Point estimate | 16.3 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 10.3 |
| upper limit | 22.4 |

Notes:

[93] - Between-group diff. and 95% CI calculated using Mantel-Haenszel common rate diff. (Greenland and Robins (1985)).

[94] - Statistical significance is determined via the graphical multiple testing procedure controlling the overall type I error rate of primary and key secondary endpoints at the 0.05 level.

Secondary: Sub-Study 2: Percentage of Participants Achieving No Abdominal Pain

| | |
|-----------------|---|
| End point title | Sub-Study 2: Percentage of Participants Achieving No Abdominal Pain ^[95] |
|-----------------|---|

End point description:

Percentage of participants who reported no abdominal pain. Abdominal pain was assessed by participants in a subject diary completed once a day.

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

End point timeframe:

Week 12

Notes:

[95] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The study included Sub Studies 1 and 2 (Phase 2b dose-finding induction and Phase 3 efficacy/safety induction studies, respectively). The arms as shown are aligned with the sub study and planned analysis population for this end point per protocol and statistical analysis plan.

| End point values | S2P1: DB – Placebo IV | S2P1: DB Risankizumab 1200mg IV | | |
|-----------------------------------|-----------------------|---------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 325 | 650 | | |
| Units: Percentage of Participants | | | | |
| number (confidence interval 95%) | 26.5 (21.7 to 31.3) | 35.8 (32.1 to 39.4) | | |

Statistical analyses

| Statistical analysis title | Primary Analysis |
|---|---|
| Comparison groups | S2P1: DB – Placebo IV v S2P1: DB Risankizumab 1200mg IV |
| Number of subjects included in analysis | 975 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[96] |
| P-value | = 0.0021 ^[97] |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Adjusted Risk Difference |
| Point estimate | 9.3 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 3.4 |
| upper limit | 15.3 |

Notes:

[96] - Between-group diff. and 95% CI calculated using Mantel-Haenszel common rate diff. (Greenland and Robins (1985)).

[97] - Statistical significance is determined via the graphical multiple testing procedure controlling the overall type I error rate of primary and key secondary endpoints at the 0.05 level.

Secondary: Sub-Study 2: Percentage of Participants Achieving Histologic Endoscopic Mucosal Remission (HEMR): Endoscopy Subscore of 0 and Geboes Score < 2.0) at Week 12

| | |
|-----------------|--|
| End point title | Sub-Study 2: Percentage of Participants Achieving Histologic Endoscopic Mucosal Remission (HEMR): Endoscopy Subscore of 0 and Geboes Score < 2.0) at Week 12 ^[98] |
|-----------------|--|

End point description:

Mucosal healing defined as endoscopic and histologic remission.

Mucosal healing is defined as an endoscopic score of 0 and Geboes score < 2.0. The endoscopic subscore ranges from 0 (normal or inactive disease) to 3 (severe disease with spontaneous bleeding, ulceration).

The Geboes histologic index includes seven histological features (architectural change, chronic inflammatory infiltrate, lamina propria neutrophils and eosinophils, neutrophils in epithelium, crypt destruction and erosion or ulcers). The Geboes score has 6 grades, each with 3-5 subgrades: Grade 0, structural change only; Grade 1, chronic inflammation; Grade 2, lamina propria neutrophils and eosinophils; Grade 3, neutrophils in epithelium; Grade 4, crypt destruction; and Grade 5, erosions or ulceration.

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

End point timeframe:

Week 12

Notes:

[98] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The study included Sub Studies 1 and 2 (Phase 2b dose-finding induction and Phase 3 efficacy/safety induction studies, respectively). The arms as shown are aligned with the sub study and planned analysis population for this end point per protocol and statistical analysis plan.

| End point values | S2P1: DB – Placebo IV | S2P1: DB Risankizumab 1200mg IV | | |
|-----------------------------------|-----------------------|---------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 325 | 650 | | |
| Units: Percentage of Participants | | | | |
| number (confidence interval 95%) | 0.6 (0.0 to 1.5) | 6.3 (4.4 to 8.2) | | |

Statistical analyses

| Statistical analysis title | Primary Analysis |
|---|---|
| Comparison groups | S2P1: DB – Placebo IV v S2P1: DB Risankizumab 1200mg IV |
| Number of subjects included in analysis | 975 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[99] |
| P-value | < 0.0001 ^[100] |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Adjusted Risk Difference |
| Point estimate | 5.6 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 3.5 |
| upper limit | 7.7 |

Notes:

[99] - Between-group diff. and 95% CI calculated using Mantel-Haenszel common rate diff. (Greenland and Robins (1985)).

[100] - Statistical significance is determined via the graphical multiple testing procedure controlling the overall type I error rate of primary and key secondary endpoints at the 0.05 level.

Secondary: Sub-Study 2: Change in Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-Fatigue)

| | |
|-----------------|--|
| End point title | Sub-Study 2: Change in Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-Fatigue) ^[101] |
|-----------------|--|

End point description:

The FACIT-Fatigue Scale is a validated self-administered 13-item tool that measures an individual's level of fatigue during their usual daily activities over the past 7 days. Each of the fatigue and impact of fatigue items are measured on a four-point Likert scale.

The FACIT Fatigue Scale is the sum of the individual 13 scores and ranges from 0 to 52 where higher scores indicate better the quality of life. A positive change from baseline indicates improvement.

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

End point timeframe:

Week 12

Notes:

[101] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The study included Sub Studies 1 and 2 (Phase 2b dose-finding induction and Phase 3 efficacy/safety induction studies, respectively). The arms as shown are aligned with the sub study and planned analysis population for this end point per protocol and statistical analysis plan.

| End point values | S2P1: DB – Placebo IV | S2P1: DB Risankizumab 1200mg IV | | |
|--|-----------------------|---------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 308 ^[102] | 614 ^[103] | | |
| Units: Units on scale | | | | |
| least squares mean (confidence interval 95%) | 3.3 (2.12 to 4.50) | 7.9 (7.03 to 8.69) | | |

Notes:

[102] - ITT2

[103] - ITT2

Statistical analyses

| Statistical analysis title | Primary Analysis |
|---|---|
| Comparison groups | S2P1: DB – Placebo IV v S2P1: DB Risankizumab 1200mg IV |
| Number of subjects included in analysis | 922 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[104] |
| P-value | < 0.0001 ^[105] |
| Method | ANCOVA |
| Parameter estimate | Least Squares (LS) Mean Difference |
| Point estimate | 4.5 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 3.13 |
| upper limit | 5.97 |

Notes:

[104] - Between-group diff. and 95% CI calculated using ANCOVA/MMRM with RTB-MI for continuous endpoints.

[105] - Statistical significance is determined via the graphical multiple testing procedure controlling the overall type I error rate of primary and key secondary endpoints at the 0.05 level.

Secondary: Sub-Study 2: Change in Inflammatory Bowel Disease Questionnaire (IBDQ) Total Score

| | |
|-----------------|---|
| End point title | Sub-Study 2: Change in Inflammatory Bowel Disease Questionnaire (IBDQ) Total Score ^[106] |
|-----------------|---|

End point description:

The IBDQ is used to assess the quality of life of patients with inflammatory bowel disease. The IBDQ is a 32-item (ranges 1 - 7) self-report questionnaire for patients with IBD to evaluate the patient reported outcomes across 4 dimensions: bowel symptoms (loose stools, abdominal pain), systemic symptoms (fatigue, altered sleep pattern), social function (work attendance, need to cancel social events), and emotional function (anger, depression, irritability). The IBDQ total Score ranges from 32 to 224 with a higher score indicating better outcome.

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

End point timeframe:

Baseline to Week 12

Notes:

[106] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The study included Sub Studies 1 and 2 (Phase 2b dose-finding induction and Phase 3 efficacy/safety induction studies, respectively). The arms as shown are aligned with the sub study and planned analysis population for this end point per protocol and statistical analysis plan.

| End point values | S2P1: DB – Placebo IV | S2P1: DB Risankizumab 1200mg IV | | |
|--|-----------------------|---------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 310 ^[107] | 619 ^[108] | | |
| Units: Units on scale | | | | |
| least squares mean (confidence interval 95%) | 24.3 (20.19 to 28.46) | 42.6 (39.72 to 45.57) | | |

Notes:

[107] - ITT2

[108] - ITT2

Statistical analyses

| Statistical analysis title | Primary Analysis |
|---|---|
| Comparison groups | S2P1: DB – Placebo IV v S2P1: DB Risankizumab 1200mg IV |
| Number of subjects included in analysis | 929 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[109] |
| P-value | < 0.0001 ^[110] |
| Method | ANCOVA |
| Parameter estimate | Least Squares (LS) Mean Difference |
| Point estimate | 18.3 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 13.38 |
| upper limit | 23.25 |

Notes:

[109] - Between-group diff. and 95% CI calculated using ANCOVA/MMRM with RTB-MI for continuous endpoints.

[110] - Statistical significance is determined via the graphical multiple testing procedure controlling the overall type I error rate of primary and key secondary endpoints at the 0.05 level.

Secondary: Sub-Study 2: Occurrence of UC-related Hospitalizations

| | |
|------------------------|--|
| End point title | Sub-Study 2: Occurrence of UC-related Hospitalizations ^[111] |
| End point description: | Participants with an UC-related event that results in admission to the hospital. |
| End point type | Secondary |
| End point timeframe: | Baseline Through Week 12 |

Notes:

[111] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The study included Sub Studies 1 and 2 (Phase 2b dose-finding induction and Phase 3 efficacy/safety induction studies, respectively). The arms as shown are aligned with the sub study and planned analysis population for this end point per protocol and statistical analysis plan.

| End point values | S2P1: DB – Placebo IV | S2P1: DB Risankizumab 1200mg IV | | |
|-----------------------------------|-----------------------|---------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 325 ^[112] | 650 ^[113] | | |
| Units: percentage of participants | | | | |
| number (confidence interval 95%) | 5.5 (3.1 to 8.0) | 0.8 (0.1 to 1.4) | | |

Notes:

[112] - ITT2

[113] - ITT2

Statistical analyses

| | |
|---|---|
| Statistical analysis title | Primary Analysis |
| Comparison groups | S2P1: DB – Placebo IV v S2P1: DB Risankizumab 1200mg IV |
| Number of subjects included in analysis | 975 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[114] |
| P-value | < 0.0001 ^[115] |
| Method | Chi-squared |
| Parameter estimate | Risk difference=(Risankizumab - Placebo) |
| Point estimate | -4.8 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -7.3 |
| upper limit | -2.2 |

Notes:

[114] - 95% CI for treatment differences is based on normal approximation of the binomial proportions

[115] - Statistical significance is determined via the graphical multiple testing procedure controlling the overall type I error rate of primary and key secondary endpoints at the 0.05 level.

Secondary: Sub-Study 2: Percentage of Participants Achieving No Nocturnal Bowel Movements

| | |
|------------------------|---|
| End point title | Sub-Study 2: Percentage of Participants Achieving No Nocturnal Bowel Movements ^[116] |
| End point description: | Percentage of participants who reported no nocturnal bowel movements. |
| End point type | Secondary |
| End point timeframe: | |
| Week 12 | |

Notes:

[116] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The study included Sub Studies 1 and 2 (Phase 2b dose-finding induction and Phase 3 efficacy/safety induction studies, respectively). The arms as shown are aligned with the sub study and planned analysis population for this end point per protocol and statistical analysis plan.

| | | | | |
|-----------------------------------|-----------------------|---------------------------------|--|--|
| End point values | S2P1: DB – Placebo IV | S2P1: DB Risankizumab 1200mg IV | | |
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 325 | 650 | | |
| Units: Percentage of Participants | | | | |
| number (confidence interval 95%) | 43.1 (37.7 to 48.5) | 67.3 (63.7 to 70.9) | | |

Statistical analyses

| | |
|---|---|
| Statistical analysis title | Primary Analysis |
| Comparison groups | S2P1: DB – Placebo IV v S2P1: DB Risankizumab 1200mg IV |
| Number of subjects included in analysis | 975 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[117] |
| P-value | < 0.0001 ^[118] |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Adjusted Risk Difference |
| Point estimate | 24.2 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 17.9 |
| upper limit | 30.5 |

Notes:

[117] - Between-group diff. and 95% CI calculated using Mantel-Haenszel common rate difference. (Greenland and Robins (1985)).

[118] - Statistical significance is determined via the graphical multiple testing procedure controlling the overall type I error rate of primary and key secondary endpoints at the 0.05 level.

Secondary: Sub-Study 2: Percentage of Participants Achieving No Tenesmus

| | |
|------------------------|--|
| End point title | Sub-Study 2: Percentage of Participants Achieving No Tenesmus ^[119] |
| End point description: | Percentage of participants who reported no tenesmus. |
| End point type | Secondary |
| End point timeframe: | |
| Week 12 | |

Notes:

[119] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The study included Sub Studies 1 and 2 (Phase 2b dose-finding induction and Phase 3 efficacy/safety induction studies, respectively). The arms as shown are aligned with the sub study and planned analysis population for this end point per protocol and statistical analysis plan.

| | | | | |
|-----------------------------------|-----------------------|---------------------------------|--|--|
| End point values | S2P1: DB – Placebo IV | S2P1: DB Risankizumab 1200mg IV | | |
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 325 | 650 | | |
| Units: Percentage of Participants | | | | |
| number (confidence interval 95%) | 30.2 (25.2 to 35.1) | 48.7 (44.9 to 52.6) | | |

Statistical analyses

| | |
|---|---|
| Statistical analysis title | Primary Analysis |
| Comparison groups | S2P1: DB – Placebo IV v S2P1: DB Risankizumab 1200mg IV |
| Number of subjects included in analysis | 975 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[120] |
| P-value | < 0.0001 ^[121] |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Adjusted Risk Difference |
| Point estimate | 18.6 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 12.4 |
| upper limit | 24.8 |

Notes:

[120] - Between-group diff. and 95% CI calculated using Mantel-Haenszel common rate diff. (Greenland and Robins (1985)).

[121] - Statistical significance is determined via the graphical multiple testing procedure controlling the overall type I error rate of primary and key secondary endpoints at the 0.05 level.

Secondary: Sub-Study 2: Change in Number of Fecal Incontinence Episodes Per Week

| | |
|------------------------|--|
| End point title | Sub-Study 2: Change in Number of Fecal Incontinence Episodes Per Week ^[122] |
| End point description: | Change in number of fecal incontinence episodes per week. |
| End point type | Secondary |
| End point timeframe: | Baseline to Week 12 |

Notes:

[122] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The study included Sub Studies 1 and 2 (Phase 2b dose-finding induction and Phase 3 efficacy/safety induction studies, respectively). The arms as shown are aligned with the sub study and planned analysis population for this end point per protocol and statistical analysis plan.

| | | | | |
|--|-----------------------------|---------------------------------|--|--|
| End point values | S2P1: DB – Placebo IV | S2P1: DB Risankizumab 1200mg IV | | |
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 288 | 602 | | |
| Units: Fecal Incontinence Episodes/ week | | | | |
| number (confidence interval 95%) | -2.213 (-2.8526 to -1.5726) | -3.839 (-4.2687 to -3.4099) | | |

Statistical analyses

| | |
|---|---|
| Statistical analysis title | Primary Analysis |
| Comparison groups | S2P1: DB – Placebo IV v S2P1: DB Risankizumab 1200mg IV |
| Number of subjects included in analysis | 890 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[123] |
| P-value | < 0.0001 ^[124] |
| Method | Mixed-Effect Model Repeated Measures |
| Parameter estimate | Least Squares (LS) Mean Difference |
| Point estimate | -1.627 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.3846 |
| upper limit | -0.8689 |

Notes:

[123] - Between-group diff. and 95% CI calculated using ANCOVA/MMRM with RTB-MI for continuous endpoints.

[124] - Statistical significance is determined via the graphical multiple testing procedure controlling the overall type I error rate of primary and key secondary endpoints at the 0.05 level.

Secondary: Sub-Study 2: Change in Number of Days Per Week With Sleep Interrupted Due to UC Symptoms

| | |
|------------------------|---|
| End point title | Sub-Study 2: Change in Number of Days Per Week With Sleep Interrupted Due to UC Symptoms ^[125] |
| End point description: | Change from baseline in number of days per week with sleep interrupted due to UC symptoms. |
| End point type | Secondary |
| End point timeframe: | Baseline to Week 12 |

Notes:

[125] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The study included Sub Studies 1 and 2 (Phase 2b dose-finding induction and Phase 3 efficacy/safety induction studies, respectively). The arms as shown are aligned with the sub study and planned analysis population for this end point per protocol and statistical analysis plan.

| | | | | |
|----------------------------------|-----------------------------|---------------------------------|--|--|
| End point values | S2P1: DB – Placebo IV | S2P1: DB Risankizumab 1200mg IV | | |
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 288 ^[126] | 602 ^[127] | | |
| Units: Days | | | | |
| number (confidence interval 95%) | -1.505 (-1.7969 to -1.2122) | -2.485 (-2.6872 to -2.2831) | | |

Notes:

[126] - ITT2

[127] - ITT2

Statistical analyses

| | |
|---|---|
| Statistical analysis title | Primary Analysis |
| Comparison groups | S2P1: DB – Placebo IV v S2P1: DB Risankizumab 1200mg IV |
| Number of subjects included in analysis | 890 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 ^[128] |
| Method | Mixed-effect model repeated measurement |
| Parameter estimate | Least Squares (LS) Mean Difference |
| Point estimate | -0.981 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.3285 |
| upper limit | -0.6326 |

Notes:

[128] - Statistical significance is determined via the graphical multiple testing procedure controlling the overall type I error rate of primary and key secondary endpoints at the 0.05 level.

Secondary: Sub-Study 1: Change From Baseline in Short Form-36 (SF-36) - Mental Component

| | |
|-----------------|--|
| End point title | Sub-Study 1: Change From Baseline in Short Form-36 (SF-36) - Mental Component ^[129] |
|-----------------|--|

End point description:

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

End point timeframe:

Baseline through Week 12

Notes:

[129] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The study included Sub Studies 1 and 2 (Phase 2b dose-finding induction and Phase 3 efficacy/safety induction studies, respectively). The arms as shown are aligned with the sub study and planned analysis population for this end point per protocol and statistical analysis plan.

| End point values | S1P1: DB - Placebo IV | S1P1: DB - Risankizumab 600mg IV | S1P1: DB - Risankizumab 1200mg IV | S1P1: DB - Risankizumab 1800mg IV |
|-------------------------------------|-----------------------|----------------------------------|-----------------------------------|-----------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 51 ^[130] | 54 ^[131] | 59 ^[132] | 54 ^[133] |
| Units: Units on a scale | | | | |
| least squares mean (standard error) | 3.094 (± 1.2533) | 6.756 (± 1.2319) | 7.284 (± 1.1739) | 5.442 (± 1.2185) |

Notes:

[130] - Includes ITT1A population.

[131] - Includes ITT1A population.

[132] - Includes ITT1A population.

[133] - Includes ITT1A population.

| | | | | |
|-------------------------------------|---|--|--|--|
| End point values | S1P1: OL - Risankizumab 1800mg IV | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 298 ^[134] | | | |
| Units: Units on a scale | | | | |
| least squares mean (standard error) | 7.777 (± 0.4777) | | | |

Notes:

[134] - Includes ITT1B population.

Statistical analyses

| | |
|---|--|
| Statistical analysis title | Primary Analysis |
| Comparison groups | S1P1: DB - Placebo IV v S1P1: DB - Risankizumab 600mg IV |
| Number of subjects included in analysis | 105 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0367 ^[135] |
| Method | Mixed-effect model repeated measurement |
| Parameter estimate | LS Mean of Difference |
| Point estimate | 3.662 |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | 0.7841 |
| upper limit | 6.5402 |

Notes:

[135] - P-value for test of difference between each Risankizumab dose group and placebo for mean change from baseline using the mixed-effect repeated measure model The unstructured covariance structure was used to estimate within subject errors.

| | |
|---|---|
| Statistical analysis title | Primary Analysis |
| Comparison groups | S1P1: DB - Placebo IV v S1P1: DB - Risankizumab 1200mg IV |
| Number of subjects included in analysis | 110 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0151 ^[136] |
| Method | Mixed-effect model repeated measurement |
| Parameter estimate | LS Mean of Difference |
| Point estimate | 4.19 |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | 1.3656 |
| upper limit | 7.0144 |

Notes:

[136] - P-value for test of difference between each Risankizumab dose group and placebo for mean change from baseline using the mixed-effect repeated measure model The unstructured covariance structure was used to estimate within subject errors.

| | |
|---|---|
| Statistical analysis title | Primary Analysis |
| Comparison groups | S1P1: DB - Placebo IV v S1P1: DB - Risankizumab 1800mg IV |
| Number of subjects included in analysis | 105 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.1795 ^[137] |
| Method | Mixed-effect model repeated measurement |
| Parameter estimate | LS Mean of Difference |
| Point estimate | 2.348 |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | -0.5322 |
| upper limit | 5.2281 |

Notes:

[137] - P-value for test of difference between each Risankizumab dose group and placebo for mean change from baseline using the mixed-effect repeated measure model The unstructured covariance structure was used to estimate within subject errors.

Adverse events

Adverse events information

Timeframe for reporting adverse events:

In S1P1, median time on follow-up was 86, 86, 85, 87, & 87 days (d) for S1P1 DB-PboIV, S1P1 DB-Risankizumab(Risa) 600mgIV, S1P1 DB-Risa 1200mgIV, S1P1 DB-Risa 1800mgIV, and S1P1 OL-Risa1800mgIV; respectively. In S1P2, it was 87, 106, 93 & 93d for arms

Adverse event reporting additional description:

S1P2 DB-Risa 1800mgIVPbo, S1P2 DB-Risa1800mgIV, S1P2 DB-Risa 180mgSC, and S1P2 DB-Risa 360mgSC; respectively. In S2P1, it was 87 & 89d for arms S2P1 DB-PboIV, S2P1 DB-Risa1200mgIV, respectively. In S2P2, it was 143.5, 159, 197 & 193d for arms, S2P2 DB-Risa1200mgIVPbo, S2P2 DB-Risa 1200mgIV, S2P2 DB-Risa 180mgSC, and S2P2 DB-Risa 360mgSC; respectively.

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

Dictionary used

| | |
|--------------------|--------|
| Dictionary name | MedDRA |
| Dictionary version | 25.1 |

Reporting groups

| | |
|-----------------------|--------------|
| Reporting group title | SS1_P1_PlbIV |
|-----------------------|--------------|

Reporting group description: -

| | |
|-----------------------|---------------------|
| Reporting group title | SS1_P1_Risa_600mgIV |
|-----------------------|---------------------|

Reporting group description: -

| | |
|-----------------------|---------------------|
| Reporting group title | SS1_P2_Risa_180mgSC |
|-----------------------|---------------------|

Reporting group description: -

| | |
|-----------------------|----------------------|
| Reporting group title | SS1_P2_Risa_1800mgIV |
|-----------------------|----------------------|

Reporting group description: -

| | |
|-----------------------|----------------------------|
| Reporting group title | SS1_P2_PlbIV_Risa_1800mgIV |
|-----------------------|----------------------------|

Reporting group description: -

| | |
|-----------------------|-------------------------|
| Reporting group title | SS1_P1_OL_Risa_1800mgIV |
|-----------------------|-------------------------|

Reporting group description: -

| | |
|-----------------------|-------------------------|
| Reporting group title | SS1_P1_DB_Risa_1800mgIV |
|-----------------------|-------------------------|

Reporting group description: -

| | |
|-----------------------|----------------------|
| Reporting group title | SS1_P1_Risa_1200mgIV |
|-----------------------|----------------------|

Reporting group description: -

| | |
|-----------------------|---------------------|
| Reporting group title | SS2_P2_Risa_180mgSC |
|-----------------------|---------------------|

Reporting group description: -

| | |
|-----------------------|----------------------|
| Reporting group title | SS2_P2_Risa_1200mgIV |
|-----------------------|----------------------|

Reporting group description: -

| | |
|-----------------------|----------------------------|
| Reporting group title | SS2_P2_PlbIV_Risa_1200mgIV |
|-----------------------|----------------------------|

Reporting group description: -

| | |
|-----------------------|----------------------|
| Reporting group title | SS2_P1_Risa_1200mgIV |
|-----------------------|----------------------|

Reporting group description: -

| | |
|-----------------------|--------------|
| Reporting group title | SS2_P1_PlbIV |
|-----------------------|--------------|

Reporting group description: -

| | |
|-----------------------|---------------------|
| Reporting group title | SS1_P2_Risa_360mgSC |
|-----------------------|---------------------|

Reporting group description: -

| | |
|-----------------------|---------------------|
| Reporting group title | SS2_P2_Risa_360mgSC |
|-----------------------|---------------------|

Reporting group description: -

| Serious adverse events | SS1_P1_PlbIV | SS1_P1_Risa_600mgIV | SS1_P2_Risa_180mgSC |
|---|-----------------|---------------------|---------------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 6 / 59 (10.17%) | 6 / 62 (9.68%) | 6 / 71 (8.45%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| BREAST CANCER | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 62 (0.00%) | 0 / 71 (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 |
| PITUITARY TUMOUR BENIGN | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 62 (0.00%) | 0 / 71 (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 |
| PROSTATE CANCER | | | |
| subjects affected / exposed | 1 / 59 (1.69%) | 0 / 62 (0.00%) | 0 / 71 (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 |
| RENAL CANCER | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 62 (0.00%) | 0 / 71 (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 |
| Vascular disorders | | | |
| ARTERIAL OCCLUSIVE DISEASE | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 62 (0.00%) | 1 / 71 (1.41%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| DEEP VEIN THROMBOSIS | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 1 / 62 (1.61%) | 0 / 71 (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 |
| HYPERTENSION | | | |

| | | | |
|--|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 62 (0.00%) | 0 / 71 (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 |
| PERIPHERAL ARTERY OCCLUSION | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 62 (0.00%) | 1 / 71 (1.41%) |
| 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 | | | |
| PYREXIA | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 1 / 62 (1.61%) | 1 / 71 (1.41%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Immune system disorders | | | |
| ANAPHYLACTIC REACTION | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 62 (0.00%) | 0 / 71 (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 |
| Reproductive system and breast disorders | | | |
| UTERINE PROLAPSE | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 62 (0.00%) | 0 / 71 (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 |
| Respiratory, thoracic and mediastinal disorders | | | |
| PLEURAL EFFUSION | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 62 (0.00%) | 0 / 71 (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 |
| PULMONARY EMBOLISM | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 62 (0.00%) | 0 / 71 (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 |
| RESPIRATORY DISTRESS | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 62 (0.00%) | 0 / 71 (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 | | | |
| ADJUSTMENT DISORDER | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 62 (0.00%) | 0 / 71 (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 |
| GENERALISED ANXIETY DISORDER | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 62 (0.00%) | 0 / 71 (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 |
| MAJOR DEPRESSION | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 62 (0.00%) | 0 / 71 (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 |
| SUICIDAL IDEATION | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 62 (0.00%) | 0 / 71 (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 |
| Investigations | | | |
| HAEMOGLOBIN DECREASED | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 62 (0.00%) | 0 / 71 (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 | | | |
| ROAD TRAFFIC ACCIDENT | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 62 (0.00%) | 0 / 71 (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 |
| SKELETAL INJURY | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 62 (0.00%) | 0 / 71 (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 |

| | | | |
|---|----------------|----------------|----------------|
| SKIN LACERATION | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 62 (0.00%) | 0 / 71 (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 |
| SUBDURAL HAEMATOMA | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 62 (0.00%) | 0 / 71 (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 |
| Cardiac disorders | | | |
| ARTERIOSCLEROSIS CORONARY ARTERY | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 62 (0.00%) | 0 / 71 (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 |
| TACHYCARDIA | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 62 (0.00%) | 0 / 71 (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 |
| Nervous system disorders | | | |
| CEREBRAL MASS EFFECT | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 62 (0.00%) | 0 / 71 (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 |
| CEREBROVASCULAR ACCIDENT | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 62 (0.00%) | 0 / 71 (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 |
| DIZZINESS | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 62 (0.00%) | 0 / 71 (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 |
| Blood and lymphatic system disorders | | | |
| ANAEMIA | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 62 (0.00%) | 0 / 71 (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 |
| Eye disorders | | | |
| CATARACT | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 62 (0.00%) | 0 / 71 (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 | | | |
| ANAL FISTULA | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 62 (0.00%) | 0 / 71 (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 |
| ANAL PROLAPSE | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 62 (0.00%) | 0 / 71 (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 |
| COLITIS | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 1 / 62 (1.61%) | 0 / 71 (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 |
| COLITIS ULCERATIVE | | | |
| subjects affected / exposed | 3 / 59 (5.08%) | 1 / 62 (1.61%) | 3 / 71 (4.23%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 1 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| ENTERITIS | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 62 (0.00%) | 0 / 71 (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 |
| GASTRITIS EROSIIVE | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 62 (0.00%) | 0 / 71 (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 |
| HAEMATEMESIS | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 62 (0.00%) | 0 / 71 (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 |
| NAUSEA | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 62 (0.00%) | 0 / 71 (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 |
| Hepatobiliary disorders | | | |
| HEPATIC CIRRHOSIS | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 62 (0.00%) | 0 / 71 (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 |
| Skin and subcutaneous tissue disorders | | | |
| ERYTHEMA NODOSUM | | | |
| subjects affected / exposed | 1 / 59 (1.69%) | 0 / 62 (0.00%) | 0 / 71 (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 |
| PEMPHIGOID | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 62 (0.00%) | 0 / 71 (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 |
| Renal and urinary disorders | | | |
| CALCULUS URINARY | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 62 (0.00%) | 1 / 71 (1.41%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| NEPHROLITHIASIS | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 62 (0.00%) | 1 / 71 (1.41%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| RENAL COLIC | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 62 (0.00%) | 0 / 71 (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 |

| | | | |
|---|----------------|----------------|----------------|
| RENAL FAILURE | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 62 (0.00%) | 0 / 71 (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 |
| Musculoskeletal and connective tissue disorders | | | |
| FLANK PAIN | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 62 (0.00%) | 0 / 71 (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 |
| OSTEONECROSIS | | | |
| subjects affected / exposed | 1 / 59 (1.69%) | 0 / 62 (0.00%) | 0 / 71 (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 |
| Infections and infestations | | | |
| ABSCESS LIMB | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 62 (0.00%) | 0 / 71 (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 |
| ANAL ABSCESS | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 62 (0.00%) | 0 / 71 (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 |
| APPENDICITIS | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 62 (0.00%) | 0 / 71 (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 |
| CLOSTRIDIUM DIFFICILE INFECTION | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 62 (0.00%) | 0 / 71 (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 |
| COVID-19 | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 62 (0.00%) | 0 / 71 (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 |

| | | | |
|---|----------------|----------------|----------------|
| COVID-19 PNEUMONIA | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 62 (0.00%) | 0 / 71 (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 |
| CYSTITIS | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 62 (0.00%) | 0 / 71 (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 |
| CYTOMEGALOVIRUS INFECTION | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 1 / 62 (1.61%) | 0 / 71 (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 |
| DEVICE RELATED SEPSIS | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 62 (0.00%) | 0 / 71 (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 |
| ENDOCARDITIS | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 62 (0.00%) | 0 / 71 (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 |
| ENTERITIS INFECTIOUS | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 62 (0.00%) | 0 / 71 (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 |
| ERYSIPELAS | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 62 (0.00%) | 0 / 71 (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 |
| LARGE INTESTINE INFECTION | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 62 (0.00%) | 0 / 71 (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 |
| LUNG ABSCESS | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 62 (0.00%) | 0 / 71 (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 |
| PAROTID ABSCESS | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 62 (0.00%) | 0 / 71 (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 |
| PHARYNGEAL ABSCESS | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 62 (0.00%) | 0 / 71 (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 |
| PNEUMONIA | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 62 (0.00%) | 0 / 71 (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 |
| PNEUMONIA HAEMOPHILUS | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 1 / 62 (1.61%) | 0 / 71 (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 |
| PNEUMONIA MYCOPLASMAL | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 62 (0.00%) | 0 / 71 (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 |
| POST PROCEDURAL INFECTION | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 62 (0.00%) | 0 / 71 (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 |
| POSTOPERATIVE WOUND INFECTION | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 62 (0.00%) | 0 / 71 (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 |
| RECTAL ABSCESS | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 62 (0.00%) | 0 / 71 (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 |
| SALMONELLOSIS | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 62 (0.00%) | 0 / 71 (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 |
| SEPSIS | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 62 (0.00%) | 0 / 71 (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 |

| Serious adverse events | SS1_P2_Risa_1800 mgIV | SS1_P2_PlbIV_Risa_ 1800mgIV | SS1_P1_OL_Risa_18 00mgIV |
|---|--------------------------|--------------------------------|-----------------------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 1 / 37 (2.70%) | 3 / 36 (8.33%) | 20 / 340 (5.88%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| BREAST CANCER | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 36 (0.00%) | 0 / 340 (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 |
| PITUITARY TUMOUR BENIGN | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 36 (0.00%) | 0 / 340 (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 |
| PROSTATE CANCER | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 36 (0.00%) | 0 / 340 (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 |
| RENAL CANCER | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 36 (0.00%) | 0 / 340 (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 |

| | | | |
|--|----------------|----------------|-----------------|
| Vascular disorders | | | |
| ARTERIAL OCCLUSIVE DISEASE | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 36 (0.00%) | 0 / 340 (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 |
| DEEP VEIN THROMBOSIS | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 36 (0.00%) | 0 / 340 (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 |
| HYPERTENSION | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 36 (0.00%) | 0 / 340 (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 |
| PERIPHERAL ARTERY OCCLUSION | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 36 (0.00%) | 0 / 340 (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 | | | |
| PYREXIA | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 36 (0.00%) | 0 / 340 (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 |
| Immune system disorders | | | |
| ANAPHYLACTIC REACTION | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 36 (0.00%) | 0 / 340 (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 |
| Reproductive system and breast disorders | | | |
| UTERINE PROLAPSE | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 36 (0.00%) | 0 / 340 (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 |
| Respiratory, thoracic and mediastinal disorders | | | |

| | | | |
|---|----------------|----------------|-----------------|
| PLEURAL EFFUSION | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 36 (0.00%) | 1 / 340 (0.29%) |
| 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 EMBOLISM | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 36 (0.00%) | 0 / 340 (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 |
| RESPIRATORY DISTRESS | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 36 (0.00%) | 0 / 340 (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 | | | |
| ADJUSTMENT DISORDER | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 36 (0.00%) | 0 / 340 (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 |
| GENERALISED ANXIETY DISORDER | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 36 (0.00%) | 0 / 340 (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 |
| MAJOR DEPRESSION | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 36 (0.00%) | 0 / 340 (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 |
| SUICIDAL IDEATION | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 36 (0.00%) | 1 / 340 (0.29%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Investigations | | | |
| HAEMOGLOBIN DECREASED | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 36 (0.00%) | 0 / 340 (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 | | | |
| ROAD TRAFFIC ACCIDENT | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 36 (0.00%) | 0 / 340 (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 |
| SKELETAL INJURY | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 36 (0.00%) | 0 / 340 (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 |
| SKIN LACERATION | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 36 (0.00%) | 0 / 340 (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 |
| SUBDURAL HAEMATOMA | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 36 (0.00%) | 0 / 340 (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 |
| Cardiac disorders | | | |
| ARTERIOSCLEROSIS CORONARY ARTERY | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 36 (0.00%) | 0 / 340 (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 |
| TACHYCARDIA | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 36 (0.00%) | 0 / 340 (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 |
| Nervous system disorders | | | |
| CEREBRAL MASS EFFECT | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 36 (0.00%) | 0 / 340 (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 |
| CEREBROVASCULAR ACCIDENT | | | |

| | | | |
|---|----------------|----------------|------------------|
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 36 (0.00%) | 0 / 340 (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 |
| DIZZINESS | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 36 (0.00%) | 0 / 340 (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 |
| Blood and lymphatic system disorders | | | |
| ANAEMIA | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 36 (0.00%) | 0 / 340 (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 |
| Eye disorders | | | |
| CATARACT | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 36 (0.00%) | 1 / 340 (0.29%) |
| 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 | | | |
| ANAL FISTULA | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 36 (0.00%) | 0 / 340 (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 |
| ANAL PROLAPSE | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 36 (0.00%) | 1 / 340 (0.29%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| COLITIS | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 36 (0.00%) | 0 / 340 (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 |
| COLITIS ULCERATIVE | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 1 / 36 (2.78%) | 12 / 340 (3.53%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 1 / 12 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|----------------|----------------|-----------------|
| ENTERITIS | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 36 (0.00%) | 0 / 340 (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 |
| GASTRITIS EROSIVE | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 36 (0.00%) | 0 / 340 (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 |
| HAEMATEMESIS | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 36 (0.00%) | 0 / 340 (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 |
| NAUSEA | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 36 (0.00%) | 0 / 340 (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 |
| Hepatobiliary disorders | | | |
| HEPATIC CIRRHOSIS | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 36 (0.00%) | 0 / 340 (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 |
| Skin and subcutaneous tissue disorders | | | |
| ERYTHEMA NODOSUM | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 36 (0.00%) | 0 / 340 (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 |
| PEMPHIGOID | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 1 / 36 (2.78%) | 0 / 340 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal and urinary disorders | | | |
| CALCULUS URINARY | | | |

| | | | |
|---|----------------|----------------|-----------------|
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 36 (0.00%) | 0 / 340 (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 |
| NEPHROLITHIASIS | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 36 (0.00%) | 0 / 340 (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 |
| RENAL COLIC | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 36 (0.00%) | 0 / 340 (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 |
| RENAL FAILURE | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 36 (0.00%) | 1 / 340 (0.29%) |
| 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 | | | |
| FLANK PAIN | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 36 (0.00%) | 1 / 340 (0.29%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| OSTEONECROSIS | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 1 / 36 (2.78%) | 0 / 340 (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 | | | |
| ABSCESS LIMB | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 36 (0.00%) | 0 / 340 (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 |
| ANAL ABSCESS | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 36 (0.00%) | 2 / 340 (0.59%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|----------------|----------------|-----------------|
| APPENDICITIS | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 36 (0.00%) | 0 / 340 (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 |
| CLOSTRIDIUM DIFFICILE INFECTION | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 36 (0.00%) | 0 / 340 (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 |
| COVID-19 | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 36 (0.00%) | 0 / 340 (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 |
| COVID-19 PNEUMONIA | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 36 (0.00%) | 0 / 340 (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 |
| CYSTITIS | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 36 (0.00%) | 0 / 340 (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 |
| CYTOMEGALOVIRUS INFECTION | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 36 (0.00%) | 1 / 340 (0.29%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| DEVICE RELATED SEPSIS | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 36 (0.00%) | 0 / 340 (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 |
| ENDOCARDITIS | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 36 (0.00%) | 0 / 340 (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 |
| ENTERITIS INFECTIOUS | | | |

| | | | |
|---|----------------|----------------|-----------------|
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 36 (0.00%) | 0 / 340 (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 |
| ERYSIPELAS | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 1 / 36 (2.78%) | 0 / 340 (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 |
| LARGE INTESTINE INFECTION | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 36 (0.00%) | 0 / 340 (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 |
| LUNG ABSCESS | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 1 / 36 (2.78%) | 0 / 340 (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 |
| PAROTID ABSCESS | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 36 (0.00%) | 0 / 340 (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 |
| PHARYNGEAL ABSCESS | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 36 (0.00%) | 0 / 340 (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 |
| PNEUMONIA | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 36 (0.00%) | 0 / 340 (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 |
| PNEUMONIA HAEMOPHILUS | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 36 (0.00%) | 0 / 340 (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 |
| PNEUMONIA MYCOPLASMAL | | | |

| | | | |
|---|----------------|----------------|-----------------|
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 36 (0.00%) | 0 / 340 (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 |
| POST PROCEDURAL INFECTION | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 36 (0.00%) | 1 / 340 (0.29%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| POSTOPERATIVE WOUND INFECTION | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 36 (0.00%) | 1 / 340 (0.29%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| RECTAL ABSCESS | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 36 (0.00%) | 1 / 340 (0.29%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| SALMONELLOSIS | | | |
| subjects affected / exposed | 1 / 37 (2.70%) | 0 / 36 (0.00%) | 0 / 340 (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 |
| SEPSIS | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 36 (0.00%) | 0 / 340 (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 |

| Serious adverse events | SS1_P1_DB_Risa_1 800mgIV | SS1_P1_Risa_1200 mgIV | SS2_P2_Risa_180m gSC |
|---|-----------------------------|--------------------------|-------------------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 3 / 58 (5.17%) | 4 / 61 (6.56%) | 4 / 71 (5.63%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| BREAST CANCER | | | |
| subjects affected / exposed | 0 / 58 (0.00%) | 0 / 61 (0.00%) | 0 / 71 (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 |

| | | | |
|--|----------------|----------------|----------------|
| PITUITARY TUMOUR BENIGN | | | |
| subjects affected / exposed | 0 / 58 (0.00%) | 0 / 61 (0.00%) | 0 / 71 (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 |
| PROSTATE CANCER | | | |
| subjects affected / exposed | 0 / 58 (0.00%) | 0 / 61 (0.00%) | 0 / 71 (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 |
| RENAL CANCER | | | |
| subjects affected / exposed | 0 / 58 (0.00%) | 0 / 61 (0.00%) | 0 / 71 (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 |
| Vascular disorders | | | |
| ARTERIAL OCCLUSIVE DISEASE | | | |
| subjects affected / exposed | 0 / 58 (0.00%) | 0 / 61 (0.00%) | 0 / 71 (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 |
| DEEP VEIN THROMBOSIS | | | |
| subjects affected / exposed | 0 / 58 (0.00%) | 0 / 61 (0.00%) | 0 / 71 (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 |
| HYPERTENSION | | | |
| subjects affected / exposed | 0 / 58 (0.00%) | 0 / 61 (0.00%) | 0 / 71 (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 |
| PERIPHERAL ARTERY OCCLUSION | | | |
| subjects affected / exposed | 0 / 58 (0.00%) | 0 / 61 (0.00%) | 0 / 71 (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 | | | |
| PYREXIA | | | |
| subjects affected / exposed | 0 / 58 (0.00%) | 0 / 61 (0.00%) | 0 / 71 (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 |

| | | | |
|---|----------------------------------|----------------------------------|----------------------------------|
| Immune system disorders ANAPHYLACTIC REACTION subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 58 (0.00%) 0 / 0 0 / 0 | 0 / 61 (0.00%) 0 / 0 0 / 0 | 0 / 71 (0.00%) 0 / 0 0 / 0 |
| Reproductive system and breast disorders UTERINE PROLAPSE subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 58 (0.00%) 0 / 0 0 / 0 | 0 / 61 (0.00%) 0 / 0 0 / 0 | 1 / 71 (1.41%) 0 / 1 0 / 0 |
| Respiratory, thoracic and mediastinal disorders PLEURAL EFFUSION subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 58 (0.00%) 0 / 0 0 / 0 | 0 / 61 (0.00%) 0 / 0 0 / 0 | 0 / 71 (0.00%) 0 / 0 0 / 0 |
| PULMONARY EMBOLISM subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 58 (0.00%) 0 / 0 0 / 0 | 0 / 61 (0.00%) 0 / 0 0 / 0 | 0 / 71 (0.00%) 0 / 0 0 / 0 |
| RESPIRATORY DISTRESS subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 58 (0.00%) 0 / 0 0 / 0 | 0 / 61 (0.00%) 0 / 0 0 / 0 | 0 / 71 (0.00%) 0 / 0 0 / 0 |
| Psychiatric disorders ADJUSTMENT DISORDER subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 58 (0.00%) 0 / 0 0 / 0 | 0 / 61 (0.00%) 0 / 0 0 / 0 | 0 / 71 (0.00%) 0 / 0 0 / 0 |
| GENERALISED ANXIETY DISORDER subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 58 (0.00%) 0 / 0 0 / 0 | 0 / 61 (0.00%) 0 / 0 0 / 0 | 0 / 71 (0.00%) 0 / 0 0 / 0 |
| MAJOR DEPRESSION | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 58 (0.00%) | 0 / 61 (0.00%) | 0 / 71 (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 |
| SUICIDAL IDEATION | | | |
| subjects affected / exposed | 0 / 58 (0.00%) | 0 / 61 (0.00%) | 0 / 71 (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 |
| Investigations | | | |
| HAEMOGLOBIN DECREASED | | | |
| subjects affected / exposed | 0 / 58 (0.00%) | 0 / 61 (0.00%) | 0 / 71 (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 | | | |
| ROAD TRAFFIC ACCIDENT | | | |
| subjects affected / exposed | 0 / 58 (0.00%) | 0 / 61 (0.00%) | 1 / 71 (1.41%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| SKELETAL INJURY | | | |
| subjects affected / exposed | 0 / 58 (0.00%) | 0 / 61 (0.00%) | 0 / 71 (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 |
| SKIN LACERATION | | | |
| subjects affected / exposed | 0 / 58 (0.00%) | 0 / 61 (0.00%) | 0 / 71 (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 |
| SUBDURAL HAEMATOMA | | | |
| subjects affected / exposed | 0 / 58 (0.00%) | 0 / 61 (0.00%) | 0 / 71 (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 |
| Cardiac disorders | | | |
| ARTERIOSCLEROSIS CORONARY ARTERY | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 58 (0.00%) | 0 / 61 (0.00%) | 0 / 71 (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 |
| TACHYCARDIA | | | |
| subjects affected / exposed | 0 / 58 (0.00%) | 0 / 61 (0.00%) | 0 / 71 (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 |
| Nervous system disorders | | | |
| CEREBRAL MASS EFFECT | | | |
| subjects affected / exposed | 0 / 58 (0.00%) | 0 / 61 (0.00%) | 0 / 71 (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 |
| CEREBROVASCULAR ACCIDENT | | | |
| subjects affected / exposed | 0 / 58 (0.00%) | 0 / 61 (0.00%) | 0 / 71 (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 |
| DIZZINESS | | | |
| subjects affected / exposed | 0 / 58 (0.00%) | 0 / 61 (0.00%) | 0 / 71 (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 |
| Blood and lymphatic system disorders | | | |
| ANAEMIA | | | |
| subjects affected / exposed | 0 / 58 (0.00%) | 2 / 61 (3.28%) | 0 / 71 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Eye disorders | | | |
| CATARACT | | | |
| subjects affected / exposed | 0 / 58 (0.00%) | 0 / 61 (0.00%) | 0 / 71 (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 | | | |
| ANAL FISTULA | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 58 (0.00%) | 0 / 61 (0.00%) | 0 / 71 (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 |
| ANAL PROLAPSE | | | |
| subjects affected / exposed | 0 / 58 (0.00%) | 0 / 61 (0.00%) | 0 / 71 (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 |
| COLITIS | | | |
| subjects affected / exposed | 1 / 58 (1.72%) | 0 / 61 (0.00%) | 0 / 71 (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 / 58 (0.00%) | 0 / 61 (0.00%) | 1 / 71 (1.41%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| ENTERITIS | | | |
| subjects affected / exposed | 0 / 58 (0.00%) | 0 / 61 (0.00%) | 1 / 71 (1.41%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| GASTRITIS EROSIIVE | | | |
| subjects affected / exposed | 0 / 58 (0.00%) | 0 / 61 (0.00%) | 0 / 71 (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 |
| HAEMATEMESIS | | | |
| subjects affected / exposed | 0 / 58 (0.00%) | 0 / 61 (0.00%) | 0 / 71 (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 |
| NAUSEA | | | |
| subjects affected / exposed | 0 / 58 (0.00%) | 0 / 61 (0.00%) | 0 / 71 (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 |
| Hepatobiliary disorders | | | |
| HEPATIC CIRRHOSIS | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 58 (0.00%) | 0 / 61 (0.00%) | 0 / 71 (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 |
| Skin and subcutaneous tissue disorders | | | |
| ERYTHEMA NODOSUM | | | |
| subjects affected / exposed | 0 / 58 (0.00%) | 0 / 61 (0.00%) | 0 / 71 (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 |
| PEMPHIGOID | | | |
| subjects affected / exposed | 0 / 58 (0.00%) | 0 / 61 (0.00%) | 0 / 71 (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 |
| Renal and urinary disorders | | | |
| CALCULUS URINARY | | | |
| subjects affected / exposed | 0 / 58 (0.00%) | 0 / 61 (0.00%) | 0 / 71 (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 |
| NEPHROLITHIASIS | | | |
| subjects affected / exposed | 0 / 58 (0.00%) | 0 / 61 (0.00%) | 0 / 71 (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 |
| RENAL COLIC | | | |
| subjects affected / exposed | 0 / 58 (0.00%) | 1 / 61 (1.64%) | 0 / 71 (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 |
| RENAL FAILURE | | | |
| subjects affected / exposed | 0 / 58 (0.00%) | 0 / 61 (0.00%) | 0 / 71 (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 |
| Musculoskeletal and connective tissue disorders | | | |
| FLANK PAIN | | | |
| subjects affected / exposed | 0 / 58 (0.00%) | 0 / 61 (0.00%) | 0 / 71 (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 |

| | | | |
|---|----------------|----------------|----------------|
| OSTEONECROSIS | | | |
| subjects affected / exposed | 0 / 58 (0.00%) | 0 / 61 (0.00%) | 0 / 71 (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 | | | |
| ABSCCESS LIMB | | | |
| subjects affected / exposed | 0 / 58 (0.00%) | 0 / 61 (0.00%) | 0 / 71 (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 |
| ANAL ABSCESS | | | |
| subjects affected / exposed | 0 / 58 (0.00%) | 0 / 61 (0.00%) | 0 / 71 (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 |
| APPENDICITIS | | | |
| subjects affected / exposed | 1 / 58 (1.72%) | 0 / 61 (0.00%) | 0 / 71 (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 |
| CLOSTRIDIUM DIFFICILE INFECTION | | | |
| subjects affected / exposed | 0 / 58 (0.00%) | 0 / 61 (0.00%) | 0 / 71 (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 |
| COVID-19 | | | |
| subjects affected / exposed | 0 / 58 (0.00%) | 0 / 61 (0.00%) | 0 / 71 (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 |
| COVID-19 PNEUMONIA | | | |
| subjects affected / exposed | 0 / 58 (0.00%) | 0 / 61 (0.00%) | 0 / 71 (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 |
| CYSTITIS | | | |
| subjects affected / exposed | 0 / 58 (0.00%) | 0 / 61 (0.00%) | 0 / 71 (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 |
| CYTOMEGALOVIRUS INFECTION | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 58 (0.00%) | 0 / 61 (0.00%) | 0 / 71 (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 |
| DEVICE RELATED SEPSIS | | | |
| subjects affected / exposed | 1 / 58 (1.72%) | 0 / 61 (0.00%) | 0 / 71 (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 |
| ENDOCARDITIS | | | |
| subjects affected / exposed | 0 / 58 (0.00%) | 0 / 61 (0.00%) | 0 / 71 (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 |
| ENTERITIS INFECTIOUS | | | |
| subjects affected / exposed | 0 / 58 (0.00%) | 0 / 61 (0.00%) | 0 / 71 (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 |
| ERYSIPELAS | | | |
| subjects affected / exposed | 0 / 58 (0.00%) | 0 / 61 (0.00%) | 0 / 71 (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 |
| LARGE INTESTINE INFECTION | | | |
| subjects affected / exposed | 0 / 58 (0.00%) | 1 / 61 (1.64%) | 0 / 71 (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 |
| LUNG ABSCESS | | | |
| subjects affected / exposed | 0 / 58 (0.00%) | 0 / 61 (0.00%) | 0 / 71 (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 |
| PAROTID ABSCESS | | | |
| subjects affected / exposed | 0 / 58 (0.00%) | 0 / 61 (0.00%) | 0 / 71 (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 |
| PHARYNGEAL ABSCESS | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 58 (0.00%) | 0 / 61 (0.00%) | 0 / 71 (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 |
| PNEUMONIA | | | |
| subjects affected / exposed | 0 / 58 (0.00%) | 0 / 61 (0.00%) | 0 / 71 (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 |
| PNEUMONIA HAEMOPHILUS | | | |
| subjects affected / exposed | 0 / 58 (0.00%) | 0 / 61 (0.00%) | 0 / 71 (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 |
| PNEUMONIA MYCOPLASMAL | | | |
| subjects affected / exposed | 0 / 58 (0.00%) | 0 / 61 (0.00%) | 0 / 71 (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 |
| POST PROCEDURAL INFECTION | | | |
| subjects affected / exposed | 0 / 58 (0.00%) | 0 / 61 (0.00%) | 0 / 71 (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 |
| POSTOPERATIVE WOUND INFECTION | | | |
| subjects affected / exposed | 0 / 58 (0.00%) | 0 / 61 (0.00%) | 0 / 71 (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 |
| RECTAL ABSCESS | | | |
| subjects affected / exposed | 0 / 58 (0.00%) | 0 / 61 (0.00%) | 0 / 71 (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 |
| SALMONELLOSIS | | | |
| subjects affected / exposed | 0 / 58 (0.00%) | 0 / 61 (0.00%) | 0 / 71 (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 |
| SEPSIS | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 58 (0.00%) | 0 / 61 (0.00%) | 0 / 71 (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 |

| Serious adverse events | SS2_P2_Risa_1200 mgIV | SS2_P2_PlbIV_Risa_ 1200mgIV | SS2_P1_Risa_1200 mgIV |
|---|--------------------------|--------------------------------|--------------------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 1 / 68 (1.47%) | 4 / 173 (2.31%) | 15 / 651 (2.30%) |
| number of deaths (all causes) | 0 | 0 | 1 |
| number of deaths resulting from adverse events | 0 | 0 | 1 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| BREAST CANCER | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | 0 / 173 (0.00%) | 0 / 651 (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 |
| PITUITARY TUMOUR BENIGN | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | 0 / 173 (0.00%) | 0 / 651 (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 |
| PROSTATE CANCER | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | 0 / 173 (0.00%) | 0 / 651 (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 |
| RENAL CANCER | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | 0 / 173 (0.00%) | 0 / 651 (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 |
| Vascular disorders | | | |
| ARTERIAL OCCLUSIVE DISEASE | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | 0 / 173 (0.00%) | 0 / 651 (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 |
| DEEP VEIN THROMBOSIS | | | |

| | | | |
|---|----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 68 (0.00%) | 0 / 173 (0.00%) | 1 / 651 (0.15%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| HYPERTENSION | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | 0 / 173 (0.00%) | 0 / 651 (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 |
| PERIPHERAL ARTERY OCCLUSION | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | 0 / 173 (0.00%) | 0 / 651 (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 | | | |
| PYREXIA | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | 0 / 173 (0.00%) | 0 / 651 (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 |
| Immune system disorders | | | |
| ANAPHYLACTIC REACTION | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | 0 / 173 (0.00%) | 0 / 651 (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 |
| Reproductive system and breast disorders | | | |
| UTERINE PROLAPSE | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | 0 / 173 (0.00%) | 0 / 651 (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 |
| Respiratory, thoracic and mediastinal disorders | | | |
| PLEURAL EFFUSION | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | 0 / 173 (0.00%) | 0 / 651 (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 |
| PULMONARY EMBOLISM | | | |

| | | | |
|---|----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 68 (0.00%) | 0 / 173 (0.00%) | 2 / 651 (0.31%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| RESPIRATORY DISTRESS | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | 0 / 173 (0.00%) | 0 / 651 (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 | | | |
| ADJUSTMENT DISORDER | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | 0 / 173 (0.00%) | 0 / 651 (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 |
| GENERALISED ANXIETY DISORDER | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | 0 / 173 (0.00%) | 0 / 651 (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 |
| MAJOR DEPRESSION | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | 0 / 173 (0.00%) | 1 / 651 (0.15%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| SUICIDAL IDEATION | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | 0 / 173 (0.00%) | 0 / 651 (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 |
| Investigations | | | |
| HAEMOGLOBIN DECREASED | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | 0 / 173 (0.00%) | 0 / 651 (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 | | | |
| ROAD TRAFFIC ACCIDENT | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | 1 / 173 (0.58%) | 0 / 651 (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 |

| | | | |
|---|----------------|-----------------|-----------------|
| SKELETAL INJURY | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | 0 / 173 (0.00%) | 1 / 651 (0.15%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| SKIN LACERATION | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | 0 / 173 (0.00%) | 1 / 651 (0.15%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| SUBDURAL HAEMATOMA | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | 0 / 173 (0.00%) | 1 / 651 (0.15%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac disorders | | | |
| ARTERIOSCLEROSIS CORONARY ARTERY | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | 0 / 173 (0.00%) | 0 / 651 (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 |
| TACHYCARDIA | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | 0 / 173 (0.00%) | 0 / 651 (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 |
| Nervous system disorders | | | |
| CEREBRAL MASS EFFECT | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | 0 / 173 (0.00%) | 1 / 651 (0.15%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| CEREBROVASCULAR ACCIDENT | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | 0 / 173 (0.00%) | 0 / 651 (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 |
| DIZZINESS | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | 0 / 173 (0.00%) | 0 / 651 (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 |

| | | | |
|---|----------------|-----------------|-----------------|
| Blood and lymphatic system disorders | | | |
| ANAEMIA | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | 0 / 173 (0.00%) | 2 / 651 (0.31%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Eye disorders | | | |
| CATARACT | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | 0 / 173 (0.00%) | 0 / 651 (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 | | | |
| ANAL FISTULA | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | 0 / 173 (0.00%) | 0 / 651 (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 |
| ANAL PROLAPSE | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | 0 / 173 (0.00%) | 0 / 651 (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 |
| COLITIS | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | 0 / 173 (0.00%) | 0 / 651 (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 |
| COLITIS ULCERATIVE | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | 1 / 173 (0.58%) | 2 / 651 (0.31%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 1 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| ENTERITIS | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | 0 / 173 (0.00%) | 0 / 651 (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 |
| GASTRITIS EROSIVE | | | |

| | | | |
|---|----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 68 (0.00%) | 0 / 173 (0.00%) | 1 / 651 (0.15%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| HAEMATEMESIS | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | 1 / 173 (0.58%) | 0 / 651 (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 |
| NAUSEA | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | 0 / 173 (0.00%) | 0 / 651 (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 |
| Hepatobiliary disorders | | | |
| HEPATIC CIRRHOSIS | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | 0 / 173 (0.00%) | 0 / 651 (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 |
| Skin and subcutaneous tissue disorders | | | |
| ERYTHEMA NODOSUM | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | 0 / 173 (0.00%) | 0 / 651 (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 |
| PEMPHIGOID | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | 0 / 173 (0.00%) | 0 / 651 (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 |
| Renal and urinary disorders | | | |
| CALCULUS URINARY | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | 0 / 173 (0.00%) | 0 / 651 (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 |
| NEPHROLITHIASIS | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | 0 / 173 (0.00%) | 0 / 651 (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 |

| | | | |
|---|----------------|-----------------|-----------------|
| RENAL COLIC | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | 0 / 173 (0.00%) | 0 / 651 (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 |
| RENAL FAILURE | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | 0 / 173 (0.00%) | 0 / 651 (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 |
| Musculoskeletal and connective tissue disorders | | | |
| FLANK PAIN | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | 0 / 173 (0.00%) | 0 / 651 (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 |
| OSTEONECROSIS | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | 0 / 173 (0.00%) | 1 / 651 (0.15%) |
| 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 | | | |
| ABSCESS LIMB | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | 0 / 173 (0.00%) | 1 / 651 (0.15%) |
| 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 / 68 (0.00%) | 0 / 173 (0.00%) | 0 / 651 (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 |
| APPENDICITIS | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | 0 / 173 (0.00%) | 0 / 651 (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 |
| CLOSTRIDIUM DIFFICILE INFECTION | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | 1 / 173 (0.58%) | 0 / 651 (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 |

| | | | |
|---|----------------|-----------------|-----------------|
| COVID-19 | | | |
| subjects affected / exposed | 1 / 68 (1.47%) | 0 / 173 (0.00%) | 1 / 651 (0.15%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| COVID-19 PNEUMONIA | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | 0 / 173 (0.00%) | 1 / 651 (0.15%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| CYSTITIS | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | 1 / 173 (0.58%) | 0 / 651 (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 |
| CYTOMEGALOVIRUS INFECTION | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | 0 / 173 (0.00%) | 0 / 651 (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 |
| DEVICE RELATED SEPSIS | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | 0 / 173 (0.00%) | 0 / 651 (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 |
| ENDOCARDITIS | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | 0 / 173 (0.00%) | 0 / 651 (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 |
| ENTERITIS INFECTIOUS | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | 0 / 173 (0.00%) | 0 / 651 (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 |
| ERYSIPELAS | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | 0 / 173 (0.00%) | 0 / 651 (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 |
| LARGE INTESTINE INFECTION | | | |

| | | | |
|---|----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 68 (0.00%) | 0 / 173 (0.00%) | 0 / 651 (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 |
| LUNG ABSCESS | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | 0 / 173 (0.00%) | 0 / 651 (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 |
| PAROTID ABSCESS | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | 0 / 173 (0.00%) | 0 / 651 (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 |
| PHARYNGEAL ABSCESS | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | 0 / 173 (0.00%) | 0 / 651 (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 |
| PNEUMONIA | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | 0 / 173 (0.00%) | 1 / 651 (0.15%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| PNEUMONIA HAEMOPHILUS | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | 0 / 173 (0.00%) | 0 / 651 (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 |
| PNEUMONIA MYCOPLASMAL | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | 0 / 173 (0.00%) | 0 / 651 (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 |
| POST PROCEDURAL INFECTION | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | 0 / 173 (0.00%) | 0 / 651 (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 |
| POSTOPERATIVE WOUND INFECTION | | | |

| | | | |
|---|----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 68 (0.00%) | 0 / 173 (0.00%) | 0 / 651 (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 |
| RECTAL ABSCESS | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | 0 / 173 (0.00%) | 0 / 651 (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 |
| SALMONELLOSIS | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | 0 / 173 (0.00%) | 0 / 651 (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 |
| SEPSIS | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | 0 / 173 (0.00%) | 0 / 651 (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 |

| Serious adverse events | SS2_P1_PlbIV | SS1_P2_Risa_360m gSC | SS2_P2_Risa_360m gSC |
|--|-------------------|-------------------------|-------------------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 33 / 324 (10.19%) | 7 / 70 (10.00%) | 1 / 70 (1.43%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| BREAST CANCER | | | |
| subjects affected / exposed | 1 / 324 (0.31%) | 0 / 70 (0.00%) | 0 / 70 (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 |
| PITUITARY TUMOUR BENIGN | | | |
| subjects affected / exposed | 1 / 324 (0.31%) | 0 / 70 (0.00%) | 0 / 70 (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 |
| PROSTATE CANCER | | | |
| subjects affected / exposed | 0 / 324 (0.00%) | 0 / 70 (0.00%) | 0 / 70 (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 |

| | | | |
|--|-----------------|----------------|----------------|
| RENAL CANCER | | | |
| subjects affected / exposed | 1 / 324 (0.31%) | 0 / 70 (0.00%) | 0 / 70 (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 |
| Vascular disorders | | | |
| ARTERIAL OCCLUSIVE DISEASE | | | |
| subjects affected / exposed | 0 / 324 (0.00%) | 0 / 70 (0.00%) | 0 / 70 (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 |
| DEEP VEIN THROMBOSIS | | | |
| subjects affected / exposed | 1 / 324 (0.31%) | 0 / 70 (0.00%) | 0 / 70 (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 |
| HYPERTENSION | | | |
| subjects affected / exposed | 0 / 324 (0.00%) | 1 / 70 (1.43%) | 0 / 70 (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 |
| PERIPHERAL ARTERY OCCLUSION | | | |
| subjects affected / exposed | 0 / 324 (0.00%) | 0 / 70 (0.00%) | 0 / 70 (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 | | | |
| PYREXIA | | | |
| subjects affected / exposed | 0 / 324 (0.00%) | 0 / 70 (0.00%) | 0 / 70 (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 |
| Immune system disorders | | | |
| ANAPHYLACTIC REACTION | | | |
| subjects affected / exposed | 0 / 324 (0.00%) | 1 / 70 (1.43%) | 0 / 70 (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 |
| Reproductive system and breast disorders | | | |
| UTERINE PROLAPSE | | | |

| | | | |
|---|-----------------|----------------|----------------|
| subjects affected / exposed | 0 / 324 (0.00%) | 0 / 70 (0.00%) | 0 / 70 (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 |
| Respiratory, thoracic and mediastinal disorders | | | |
| PLEURAL EFFUSION | | | |
| subjects affected / exposed | 0 / 324 (0.00%) | 0 / 70 (0.00%) | 0 / 70 (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 |
| PULMONARY EMBOLISM | | | |
| subjects affected / exposed | 1 / 324 (0.31%) | 0 / 70 (0.00%) | 0 / 70 (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 |
| RESPIRATORY DISTRESS | | | |
| subjects affected / exposed | 0 / 324 (0.00%) | 1 / 70 (1.43%) | 0 / 70 (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 |
| Psychiatric disorders | | | |
| ADJUSTMENT DISORDER | | | |
| subjects affected / exposed | 1 / 324 (0.31%) | 0 / 70 (0.00%) | 0 / 70 (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 |
| GENERALISED ANXIETY DISORDER | | | |
| subjects affected / exposed | 1 / 324 (0.31%) | 0 / 70 (0.00%) | 0 / 70 (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 |
| MAJOR DEPRESSION | | | |
| subjects affected / exposed | 0 / 324 (0.00%) | 0 / 70 (0.00%) | 0 / 70 (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 |
| SUICIDAL IDEATION | | | |
| subjects affected / exposed | 0 / 324 (0.00%) | 0 / 70 (0.00%) | 0 / 70 (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 |

| | | | |
|---|-----------------|----------------|----------------|
| Investigations | | | |
| HAEMOGLOBIN DECREASED | | | |
| subjects affected / exposed | 1 / 324 (0.31%) | 0 / 70 (0.00%) | 0 / 70 (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 |
| Injury, poisoning and procedural complications | | | |
| ROAD TRAFFIC ACCIDENT | | | |
| subjects affected / exposed | 0 / 324 (0.00%) | 0 / 70 (0.00%) | 0 / 70 (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 |
| SKELETAL INJURY | | | |
| subjects affected / exposed | 0 / 324 (0.00%) | 0 / 70 (0.00%) | 0 / 70 (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 |
| SKIN LACERATION | | | |
| subjects affected / exposed | 0 / 324 (0.00%) | 0 / 70 (0.00%) | 0 / 70 (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 |
| SUBDURAL HAEMATOMA | | | |
| subjects affected / exposed | 0 / 324 (0.00%) | 0 / 70 (0.00%) | 0 / 70 (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 |
| Cardiac disorders | | | |
| ARTERIOSCLEROSIS CORONARY ARTERY | | | |
| subjects affected / exposed | 1 / 324 (0.31%) | 0 / 70 (0.00%) | 0 / 70 (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 |
| TACHYCARDIA | | | |
| subjects affected / exposed | 0 / 324 (0.00%) | 1 / 70 (1.43%) | 0 / 70 (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 |
| Nervous system disorders | | | |
| CEREBRAL MASS EFFECT | | | |

| | | | |
|---|-----------------|----------------|----------------|
| subjects affected / exposed | 0 / 324 (0.00%) | 0 / 70 (0.00%) | 0 / 70 (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 |
| CEREBROVASCULAR ACCIDENT | | | |
| subjects affected / exposed | 0 / 324 (0.00%) | 1 / 70 (1.43%) | 0 / 70 (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 |
| DIZZINESS | | | |
| subjects affected / exposed | 1 / 324 (0.31%) | 0 / 70 (0.00%) | 0 / 70 (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 |
| Blood and lymphatic system disorders | | | |
| ANAEMIA | | | |
| subjects affected / exposed | 2 / 324 (0.62%) | 1 / 70 (1.43%) | 0 / 70 (0.00%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Eye disorders | | | |
| CATARACT | | | |
| subjects affected / exposed | 0 / 324 (0.00%) | 0 / 70 (0.00%) | 0 / 70 (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 | | | |
| ANAL FISTULA | | | |
| subjects affected / exposed | 2 / 324 (0.62%) | 0 / 70 (0.00%) | 0 / 70 (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 |
| ANAL PROLAPSE | | | |
| subjects affected / exposed | 0 / 324 (0.00%) | 0 / 70 (0.00%) | 0 / 70 (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 |
| COLITIS | | | |
| subjects affected / exposed | 0 / 324 (0.00%) | 0 / 70 (0.00%) | 0 / 70 (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 |

| | | | |
|---|------------------|----------------|----------------|
| COLITIS ULCERATIVE | | | |
| subjects affected / exposed | 16 / 324 (4.94%) | 2 / 70 (2.86%) | 1 / 70 (1.43%) |
| occurrences causally related to treatment / all | 2 / 17 | 1 / 2 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| ENTERITIS | | | |
| subjects affected / exposed | 0 / 324 (0.00%) | 0 / 70 (0.00%) | 0 / 70 (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 |
| GASTRITIS EROSIIVE | | | |
| subjects affected / exposed | 0 / 324 (0.00%) | 0 / 70 (0.00%) | 0 / 70 (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 |
| HAEMATEMESIS | | | |
| subjects affected / exposed | 0 / 324 (0.00%) | 0 / 70 (0.00%) | 0 / 70 (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 |
| NAUSEA | | | |
| subjects affected / exposed | 1 / 324 (0.31%) | 0 / 70 (0.00%) | 0 / 70 (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 |
| Hepatobiliary disorders | | | |
| HEPATIC CIRRHOSIS | | | |
| subjects affected / exposed | 1 / 324 (0.31%) | 0 / 70 (0.00%) | 0 / 70 (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 |
| Skin and subcutaneous tissue disorders | | | |
| ERYTHEMA NODOSUM | | | |
| subjects affected / exposed | 0 / 324 (0.00%) | 0 / 70 (0.00%) | 0 / 70 (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 |
| PEMPHIGOID | | | |
| subjects affected / exposed | 0 / 324 (0.00%) | 0 / 70 (0.00%) | 0 / 70 (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 |

| | | | |
|---|-----------------|----------------|----------------|
| Renal and urinary disorders | | | |
| CALCULUS URINARY | | | |
| subjects affected / exposed | 0 / 324 (0.00%) | 0 / 70 (0.00%) | 0 / 70 (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 |
| NEPHROLITHIASIS | | | |
| subjects affected / exposed | 0 / 324 (0.00%) | 0 / 70 (0.00%) | 0 / 70 (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 |
| RENAL COLIC | | | |
| subjects affected / exposed | 0 / 324 (0.00%) | 0 / 70 (0.00%) | 0 / 70 (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 |
| RENAL FAILURE | | | |
| subjects affected / exposed | 0 / 324 (0.00%) | 0 / 70 (0.00%) | 0 / 70 (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 |
| Musculoskeletal and connective tissue disorders | | | |
| FLANK PAIN | | | |
| subjects affected / exposed | 0 / 324 (0.00%) | 0 / 70 (0.00%) | 0 / 70 (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 |
| OSTEONECROSIS | | | |
| subjects affected / exposed | 0 / 324 (0.00%) | 0 / 70 (0.00%) | 0 / 70 (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 | | | |
| ABSCESS LIMB | | | |
| subjects affected / exposed | 0 / 324 (0.00%) | 0 / 70 (0.00%) | 0 / 70 (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 |
| ANAL ABSCESS | | | |

| | | | |
|---|-----------------|----------------|----------------|
| subjects affected / exposed | 0 / 324 (0.00%) | 0 / 70 (0.00%) | 0 / 70 (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 |
| APPENDICITIS | | | |
| subjects affected / exposed | 1 / 324 (0.31%) | 0 / 70 (0.00%) | 0 / 70 (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 |
| CLOSTRIDIUM DIFFICILE INFECTION | | | |
| subjects affected / exposed | 0 / 324 (0.00%) | 0 / 70 (0.00%) | 0 / 70 (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 |
| COVID-19 | | | |
| subjects affected / exposed | 0 / 324 (0.00%) | 0 / 70 (0.00%) | 0 / 70 (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 |
| COVID-19 PNEUMONIA | | | |
| subjects affected / exposed | 0 / 324 (0.00%) | 0 / 70 (0.00%) | 0 / 70 (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 |
| CYSTITIS | | | |
| subjects affected / exposed | 0 / 324 (0.00%) | 0 / 70 (0.00%) | 0 / 70 (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 |
| CYTOMEGALOVIRUS INFECTION | | | |
| subjects affected / exposed | 0 / 324 (0.00%) | 0 / 70 (0.00%) | 0 / 70 (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 |
| DEVICE RELATED SEPSIS | | | |
| subjects affected / exposed | 0 / 324 (0.00%) | 0 / 70 (0.00%) | 0 / 70 (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 |
| ENDOCARDITIS | | | |

| | | | |
|---|-----------------|----------------|----------------|
| subjects affected / exposed | 1 / 324 (0.31%) | 0 / 70 (0.00%) | 0 / 70 (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 |
| ENTERITIS INFECTIOUS | | | |
| subjects affected / exposed | 1 / 324 (0.31%) | 0 / 70 (0.00%) | 0 / 70 (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 |
| ERYSIPELAS | | | |
| subjects affected / exposed | 0 / 324 (0.00%) | 0 / 70 (0.00%) | 0 / 70 (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 |
| LARGE INTESTINE INFECTION | | | |
| subjects affected / exposed | 0 / 324 (0.00%) | 0 / 70 (0.00%) | 0 / 70 (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 |
| LUNG ABSCESS | | | |
| subjects affected / exposed | 0 / 324 (0.00%) | 0 / 70 (0.00%) | 0 / 70 (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 |
| PAROTID ABSCESS | | | |
| subjects affected / exposed | 1 / 324 (0.31%) | 0 / 70 (0.00%) | 0 / 70 (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 |
| PHARYNGEAL ABSCESS | | | |
| subjects affected / exposed | 1 / 324 (0.31%) | 0 / 70 (0.00%) | 0 / 70 (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 |
| PNEUMONIA | | | |
| subjects affected / exposed | 0 / 324 (0.00%) | 0 / 70 (0.00%) | 0 / 70 (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 |
| PNEUMONIA HAEMOPHILUS | | | |

| | | | |
|---|-----------------|----------------|----------------|
| subjects affected / exposed | 0 / 324 (0.00%) | 0 / 70 (0.00%) | 0 / 70 (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 |
| PNEUMONIA MYCOPLASMAL | | | |
| subjects affected / exposed | 0 / 324 (0.00%) | 1 / 70 (1.43%) | 0 / 70 (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 |
| POST PROCEDURAL INFECTION | | | |
| subjects affected / exposed | 0 / 324 (0.00%) | 0 / 70 (0.00%) | 0 / 70 (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 |
| POSTOPERATIVE WOUND INFECTION | | | |
| subjects affected / exposed | 0 / 324 (0.00%) | 0 / 70 (0.00%) | 0 / 70 (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 |
| RECTAL ABSCESS | | | |
| subjects affected / exposed | 0 / 324 (0.00%) | 0 / 70 (0.00%) | 0 / 70 (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 |
| SALMONELLOSIS | | | |
| subjects affected / exposed | 0 / 324 (0.00%) | 0 / 70 (0.00%) | 0 / 70 (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 |
| SEPSIS | | | |
| subjects affected / exposed | 0 / 324 (0.00%) | 1 / 70 (1.43%) | 0 / 70 (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 |

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

| Non-serious adverse events | SS1_P1_PlbIV | SS1_P1_Risa_600mgIV | SS1_P2_Risa_180mgSC |
|--|--|--|--|
| Total subjects affected by non-serious adverse events subjects affected / exposed | 14 / 59 (23.73%) | 13 / 62 (20.97%) | 4 / 71 (5.63%) |
| Nervous system disorders HEADACHE subjects affected / exposed occurrences (all) | 3 / 59 (5.08%) 4 | 2 / 62 (3.23%) 2 | 2 / 71 (2.82%) 2 |
| Blood and lymphatic system disorders ANAEMIA subjects affected / exposed occurrences (all) | 2 / 59 (3.39%) 2 | 0 / 62 (0.00%) 0 | 1 / 71 (1.41%) 1 |
| Gastrointestinal disorders COLITIS ULCERATIVE subjects affected / exposed occurrences (all) HAEMORRHOIDS subjects affected / exposed occurrences (all) | 4 / 59 (6.78%) 5 3 / 59 (5.08%) 3 | 1 / 62 (1.61%) 1 0 / 62 (0.00%) 0 | 0 / 71 (0.00%) 0 0 / 71 (0.00%) 0 |
| Skin and subcutaneous tissue disorders DRY SKIN subjects affected / exposed occurrences (all) | 0 / 59 (0.00%) 0 | 2 / 62 (3.23%) 2 | 0 / 71 (0.00%) 0 |
| Infections and infestations BRONCHITIS subjects affected / exposed occurrences (all) COVID-19 subjects affected / exposed occurrences (all) NASOPHARYNGITIS subjects affected / exposed occurrences (all) PHARYNGITIS subjects affected / exposed occurrences (all) SINUSITIS | 0 / 59 (0.00%) 0 0 / 59 (0.00%) 0 4 / 59 (6.78%) 5 1 / 59 (1.69%) 1 | 4 / 62 (6.45%) 4 0 / 62 (0.00%) 0 5 / 62 (8.06%) 5 1 / 62 (1.61%) 1 | 0 / 71 (0.00%) 0 0 / 71 (0.00%) 0 1 / 71 (1.41%) 1 0 / 71 (0.00%) 0 |

| | | | |
|-----------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 62 (0.00%) | 0 / 71 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| Non-serious adverse events | SS1_P2_Risa_1800 mgIV | SS1_P2_PlbIV_Risa_ 1800mgIV | SS1_P1_OL_Risa_18 00mgIV |
|---|--------------------------|--------------------------------|-----------------------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 6 / 37 (16.22%) | 11 / 36 (30.56%) | 75 / 340 (22.06%) |
| Nervous system disorders | | | |
| HEADACHE | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 2 / 36 (5.56%) | 21 / 340 (6.18%) |
| occurrences (all) | 0 | 2 | 24 |
| Blood and lymphatic system disorders | | | |
| ANAEMIA | | | |
| subjects affected / exposed | 1 / 37 (2.70%) | 0 / 36 (0.00%) | 12 / 340 (3.53%) |
| occurrences (all) | 1 | 0 | 12 |
| Gastrointestinal disorders | | | |
| COLITIS ULCERATIVE | | | |
| subjects affected / exposed | 1 / 37 (2.70%) | 1 / 36 (2.78%) | 12 / 340 (3.53%) |
| occurrences (all) | 1 | 1 | 12 |
| HAEMORRHOIDS | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 1 / 36 (2.78%) | 0 / 340 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Skin and subcutaneous tissue disorders | | | |
| DRY SKIN | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 2 / 36 (5.56%) | 4 / 340 (1.18%) |
| occurrences (all) | 0 | 2 | 4 |
| Infections and infestations | | | |
| BRONCHITIS | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 36 (0.00%) | 1 / 340 (0.29%) |
| occurrences (all) | 0 | 0 | 1 |
| COVID-19 | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 36 (0.00%) | 1 / 340 (0.29%) |
| occurrences (all) | 0 | 0 | 1 |
| NASOPHARYNGITIS | | | |
| subjects affected / exposed | 4 / 37 (10.81%) | 2 / 36 (5.56%) | 24 / 340 (7.06%) |
| occurrences (all) | 5 | 2 | 26 |
| PHARYNGITIS | | | |

| | | | |
|-----------------------------|----------------|----------------|-----------------|
| subjects affected / exposed | 0 / 37 (0.00%) | 2 / 36 (5.56%) | 3 / 340 (0.88%) |
| occurrences (all) | 0 | 2 | 3 |
| SINUSITIS | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 2 / 36 (5.56%) | 3 / 340 (0.88%) |
| occurrences (all) | 0 | 3 | 3 |

| Non-serious adverse events | SS1_P1_DB_Risa_1 800mgIV | SS1_P1_Risa_1200 mgIV | SS2_P2_Risa_180m gSC |
|---|-----------------------------|--------------------------|-------------------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 12 / 58 (20.69%) | 12 / 61 (19.67%) | 10 / 71 (14.08%) |
| Nervous system disorders | | | |
| HEADACHE | | | |
| subjects affected / exposed | 4 / 58 (6.90%) | 3 / 61 (4.92%) | 1 / 71 (1.41%) |
| occurrences (all) | 5 | 3 | 1 |
| Blood and lymphatic system disorders | | | |
| ANAEMIA | | | |
| subjects affected / exposed | 1 / 58 (1.72%) | 2 / 61 (3.28%) | 2 / 71 (2.82%) |
| occurrences (all) | 1 | 3 | 2 |
| Gastrointestinal disorders | | | |
| COLITIS ULCERATIVE | | | |
| subjects affected / exposed | 1 / 58 (1.72%) | 3 / 61 (4.92%) | 3 / 71 (4.23%) |
| occurrences (all) | 1 | 3 | 3 |
| HAEMORRHOIDS | | | |
| subjects affected / exposed | 0 / 58 (0.00%) | 0 / 61 (0.00%) | 1 / 71 (1.41%) |
| occurrences (all) | 0 | 0 | 1 |
| Skin and subcutaneous tissue disorders | | | |
| DRY SKIN | | | |
| subjects affected / exposed | 0 / 58 (0.00%) | 0 / 61 (0.00%) | 0 / 71 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Infections and infestations | | | |
| BRONCHITIS | | | |
| subjects affected / exposed | 0 / 58 (0.00%) | 1 / 61 (1.64%) | 0 / 71 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| COVID-19 | | | |
| subjects affected / exposed | 0 / 58 (0.00%) | 0 / 61 (0.00%) | 4 / 71 (5.63%) |
| occurrences (all) | 0 | 0 | 4 |
| NASOPHARYNGITIS | | | |

| | | | |
|-----------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 5 / 58 (8.62%) | 3 / 61 (4.92%) | 1 / 71 (1.41%) |
| occurrences (all) | 6 | 5 | 1 |
| PHARYNGITIS | | | |
| subjects affected / exposed | 0 / 58 (0.00%) | 0 / 61 (0.00%) | 0 / 71 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| SINUSITIS | | | |
| subjects affected / exposed | 1 / 58 (1.72%) | 1 / 61 (1.64%) | 0 / 71 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |

| Non-serious adverse events | SS2_P2_Risa_1200 mgIV | SS2_P2_PlbIV_Risa_ 1200mgIV | SS2_P1_Risa_1200 mgIV |
|---|--------------------------|--------------------------------|--------------------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 9 / 68 (13.24%) | 22 / 173 (12.72%) | 100 / 651 (15.36%) |
| Nervous system disorders | | | |
| HEADACHE | | | |
| subjects affected / exposed | 2 / 68 (2.94%) | 3 / 173 (1.73%) | 19 / 651 (2.92%) |
| occurrences (all) | 4 | 3 | 25 |
| Blood and lymphatic system disorders | | | |
| ANAEMIA | | | |
| subjects affected / exposed | 1 / 68 (1.47%) | 4 / 173 (2.31%) | 20 / 651 (3.07%) |
| occurrences (all) | 1 | 4 | 20 |
| Gastrointestinal disorders | | | |
| COLITIS ULCERATIVE | | | |
| subjects affected / exposed | 1 / 68 (1.47%) | 3 / 173 (1.73%) | 9 / 651 (1.38%) |
| occurrences (all) | 1 | 3 | 9 |
| HAEMORRHOIDS | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | 0 / 173 (0.00%) | 5 / 651 (0.77%) |
| occurrences (all) | 0 | 0 | 6 |
| Skin and subcutaneous tissue disorders | | | |
| DRY SKIN | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | 0 / 173 (0.00%) | 3 / 651 (0.46%) |
| occurrences (all) | 0 | 0 | 3 |
| Infections and infestations | | | |
| BRONCHITIS | | | |
| subjects affected / exposed | 1 / 68 (1.47%) | 1 / 173 (0.58%) | 2 / 651 (0.31%) |
| occurrences (all) | 1 | 1 | 3 |
| COVID-19 | | | |

| | | | |
|-----------------------------|----------------|------------------|------------------|
| subjects affected / exposed | 4 / 68 (5.88%) | 10 / 173 (5.78%) | 30 / 651 (4.61%) |
| occurrences (all) | 4 | 10 | 30 |
| NASOPHARYNGITIS | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | 3 / 173 (1.73%) | 18 / 651 (2.76%) |
| occurrences (all) | 0 | 3 | 18 |
| PHARYNGITIS | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | 1 / 173 (0.58%) | 0 / 651 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| SINUSITIS | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | 0 / 173 (0.00%) | 1 / 651 (0.15%) |
| occurrences (all) | 0 | 0 | 1 |

| Non-serious adverse events | SS2_P1_PlbIV | SS1_P2_Risa_360m gSC | SS2_P2_Risa_360m gSC |
|---|-------------------|-------------------------|-------------------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 63 / 324 (19.44%) | 16 / 70 (22.86%) | 23 / 70 (32.86%) |
| Nervous system disorders | | | |
| HEADACHE | | | |
| subjects affected / exposed | 7 / 324 (2.16%) | 5 / 70 (7.14%) | 6 / 70 (8.57%) |
| occurrences (all) | 8 | 5 | 6 |
| Blood and lymphatic system disorders | | | |
| ANAEMIA | | | |
| subjects affected / exposed | 18 / 324 (5.56%) | 1 / 70 (1.43%) | 6 / 70 (8.57%) |
| occurrences (all) | 20 | 1 | 6 |
| Gastrointestinal disorders | | | |
| COLITIS ULCERATIVE | | | |
| subjects affected / exposed | 17 / 324 (5.25%) | 3 / 70 (4.29%) | 0 / 70 (0.00%) |
| occurrences (all) | 17 | 3 | 0 |
| HAEMORRHOIDS | | | |
| subjects affected / exposed | 0 / 324 (0.00%) | 1 / 70 (1.43%) | 1 / 70 (1.43%) |
| occurrences (all) | 0 | 1 | 1 |
| Skin and subcutaneous tissue disorders | | | |
| DRY SKIN | | | |
| subjects affected / exposed | 2 / 324 (0.62%) | 1 / 70 (1.43%) | 0 / 70 (0.00%) |
| occurrences (all) | 2 | 1 | 0 |
| Infections and infestations | | | |
| BRONCHITIS | | | |

| | | | |
|-----------------------------|------------------|----------------|----------------|
| subjects affected / exposed | 0 / 324 (0.00%) | 0 / 70 (0.00%) | 1 / 70 (1.43%) |
| occurrences (all) | 0 | 0 | 1 |
| COVID-19 | | | |
| subjects affected / exposed | 19 / 324 (5.86%) | 0 / 70 (0.00%) | 6 / 70 (8.57%) |
| occurrences (all) | 19 | 0 | 6 |
| NASOPHARYNGITIS | | | |
| subjects affected / exposed | 8 / 324 (2.47%) | 6 / 70 (8.57%) | 4 / 70 (5.71%) |
| occurrences (all) | 9 | 6 | 4 |
| PHARYNGITIS | | | |
| subjects affected / exposed | 0 / 324 (0.00%) | 1 / 70 (1.43%) | 0 / 70 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| SINUSITIS | | | |
| subjects affected / exposed | 1 / 324 (0.31%) | 2 / 70 (2.86%) | 0 / 70 (0.00%) |
| occurrences (all) | 1 | 2 | 0 |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|------------------|--|
| 18 October 2017 | <p>Global amendment 1</p> <ul style="list-style-type: none"> Modified the number of days prior to each study visit needed to calculate the Subscores for Rectal Bleeding, Stool Frequency, and the Physician's Global Assessment. Corrected typographical errors. |
| 14 February 2018 | <p>Global Amendment 2</p> <ul style="list-style-type: none"> Added text that the subjects dosed in the Dose-analysis period will receive open-label risankizumab. Modify the adverse event follow-up time, duration of contraception use after last dose and time during which live or attenuated vaccines are not allowed. Add language to confirm that the dose and sample size will be reassessed after the completion of Sub-Study 1. To change the study duration up to 45 weeks. Correct typographical errors. Clarified when INR test is drawn. Modified the justification for the statistical methodology used for dose selection in Sub-Study 1. Updated Secondary Efficacy Variables, Sub-study 2. Modified the assumptions used for power calculation Corrected the study activities table. |
| 01 October 2020 | <p>Global amendment 3:</p> <ul style="list-style-type: none"> Updated the Sponsor address text. Modified Benefits and Risks text to include assessment of clinical data from Sub-study 1 (Phase 2b) of Study M16-067 and in the light of the COVID-19 pandemic. Updated text throughout the protocol to include the dose selected based on completion of Sub-study 1. Update study title, study population and eligibility criteria to include enrollment of non-bio-IR in Sub-study 2. Update the number of subjects to be enrolled in Sub-study 2 and total number of subjects throughout the protocol. Update the randomization stratification factors for Sub-study 2. Updated DMC text. Specified the types of prohibited corticosteroids. Clarified the types of biopsies collected during the study. Removed the open label filler arm after Sub-study 2. Clarified that anti-infectives used for TB prophylaxis are permissible. Removed statistical tests for demographics and baseline characteristics. Removed the missing imputation method LOCF and the analysis of continuous efficacy endpoint. Changed CMH test to MN test in statistical analysis for binary endpoint. Updated text for statistical testing procedures. Addition of exclusion criteria to exclude subjects with active COVID-19 infection from enrollment into study. modified study visits/protocol-specified procedures impacted by changes in local regulations due to the COVID-19 pandemic. Clarified HIV results language throughout. Clarifying text throughout. Additions to the study activities table. |

| | |
|------------------|--|
| 16 December 2022 | <p>Global amendment 4:</p> <ul style="list-style-type: none"> • Updated Secondary Endpoints and Additional Endpoints for Sub-Study 2. • Clarified randomization stratification factors for Period 2 of Sub-Studies 1 and 2. • Clarified the safety analyses population text. • Replaced, added, edited text regarding handling of missing data in binary and in continuous endpoints. • Updated the language of baseline summary for clarity. • Updated CMH test as the primary method for binary endpoints instead of M-N test. • Advanced Therapy-IR status (yes vs no), in replacement of "number of prior failed biologics (0, 1, >1)", will be used as a stratification factor in the CMH test. • Updated multiple testing procedure language for Sub-Study 2. • Added RTB-MI analysis method for secondary efficacy endpoints. • Clarified efficacy analysis methods for secondary endpoints. |
|------------------|--|

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.

None reported.

Notes: