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	v1
This version publication date	25 May 2024
First version publication date	25 May 2024

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	01 April 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:

Induction study included Sub Studies 1 and 2 (Phase 2b dose-finding induction and Phase 3 efficacy/safety induction studies, respectively). Both sub studies included Periods 1 and 2: S1P1 12 weeks-Double-Blind and Open-Label; S1P2 12 weeks for clinical non-responders in S1P1; S2P1: 12 weeks; S2P2 12 weeks for clinical non-responders from S2P1.

Pre-assignment

Screening details:

In SS1 Double-blind (DB) Dose Finding Induction Period 1 (S1P1) (ITT1A), 240 subjects enrolled 180 received at least 1 dose of study drug ; Open-Label (ITT1B), 341 subjects enrolled 340 received drug. S1P2 (ITT1P2): 215 subjects enrolled 214 received drug. In S2P1 (ITT2), 977 randomized 650 received drug. S2P2 (ITT2P2), 384 enrolled and 382 treated

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: The study included Sub Studies 1 and 2 (Phase 2b dose-finding induction and Phase 3 efficacy/safety induction studies, respectively). Both sub studies included a Period 1 followed by a Period 2. Within Substudy 1 and 2, subjects who did not achieve clinical response at Week 12 in the respective substudy were eligible to receive blinded risankizumab treatment in the study period 2.

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 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[2]	61[3]	61[4]	58[5]
Units: Participants	1	7	6	6

Notes:

[2] - ITT1A randomized subjects who received at least 1 dose of drug during Induction Period 1 Substudy 1.
[3] - ITT1A randomized subjects who received at least 1 dose of drug during Induction Period 1 Substudy 1
[4] - ITT1A randomized subjects who received at least 1 dose of drug during Induction Period 1 Substudy 1
[5] - ITT1A randomized subjects who received at least 1 dose of drug during Induction Period 1 Substudy 1

End point values	S1P1: OL -			

	Risankizumab 1800mg IV			
Subject group type	Reporting group			
Number of subjects analysed	340[6]			
Units: Participants	42			

Notes:

[6] - ITT1B includes all the additional subjects who received at least one dose of risankizumab 1800 mg IV

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 [7]
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:

[7] - 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 [8]
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:

[8] - 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 [9]
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:

[9] - 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[10]

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:

[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	S2P1: DB – Placebo IV	S2P1: DB Risankizumab 1200mg IV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	325[11]	650[12]		
Units: Percentage of Participants				
arithmetic mean (confidence interval 95%)	6.2 (3.6 to 8.9)	20.3 (17.2 to 23.4)		

Notes:

[11] - ITT2 population.

[12] - 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[13]
P-value	< 0.0001 [14]
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:

[13] - Stratified by Advanced Therapy-IR status (yes vs no), Baseline steroid use (yes vs. no) and Baseline Adapted Mayo Score (≤ 7, > 7).
[14] - 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[15]

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:

[15] - 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[16]	61[17]	61[18]	58[19]
Units: Participants	3	15	8	9

Notes:

[16] - Includes ITT1A population.

[17] - Includes ITT1A population.

[18] - Includes ITT1A population.

[19] - Includes ITT1A population.

End point values	S1P1: OL - Risankizumab 1800mg IV			

Subject group type	Reporting group			
Number of subjects analysed	340[20]			
Units: Participants	61			

Notes:

[20] - 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	121
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0028 [21]
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:

[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	= 0.0968 [22]
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:

[22] - 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 [23]
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:

[23] - 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 FullMayo 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 FullMayo Score of 6 to 12 at Baseline[24]

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:

[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	0[25]	0[26]	0[27]	0[28]
Units: Participants				

Notes:

[25] - Data could not be analyzed due to data gathering/validation issues.

[26] - Data could not be analyzed due to data gathering/validation issues.

[27] - Data could not be analyzed due to data gathering/validation issues.

[28] - Data could not be analyzed due to data gathering/validation issues.

End point values	S1P1: OL - Risankizumab 1800mg IV			
Subject group type	Reporting group			
Number of subjects analysed	0[29]			

Units: Participants				

Notes:

[29] - Data could not be analyzed due to data gathering/validation issues.

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[30]

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 ≥ 30%, plus a decrease in RBS ≥ 1 or an absolute RBS ≤ 1.

End point type	Secondary

End point timeframe:

Week 12

Notes:

[30] - 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[31]	61[32]	61[33]	58[34]
Units: Participants	12	26	28	31

Notes:

[31] - Includes ITT1A population.

[32] - Includes ITT1A population.

[33] - Includes ITT1A population.

[34] - Includes ITT1A population.

End point values	S1P1: OL - Risankizumab 1800mg IV			
Subject group type	Reporting group			
Number of subjects analysed	340[35]			
Units: Participants	157			

Notes:

[35] - 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	121
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0022 [36]
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:

[36] - 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 [37]
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:

[37] - 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 [38]
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:

[38] - 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[39]

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 ≥ 30% from Baseline, plus a decrease in RBS ≥ 1 or an absolute RBS ≤ 1.

End point type	Secondary

End point timeframe:

Week 4

Notes:

[39] - 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[40]	61[41]	61[42]	58[43]
Units: Participants	15	20	28	22

Notes:

[40] - Includes ITT1A population.

[41] - Includes ITT1A population.

[42] - Includes ITT1A population.

[43] - Includes ITT1A population.

End point values	S1P1: OL - Risankizumab 1800mg IV			
Subject group type	Reporting group			
Number of subjects analysed	340[44]			
Units: Participants	148			

Notes:

[44] - 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	121
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1842 [45]
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:

[45] - 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 [46]
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:

[46] - 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 [47]
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:

[47] - 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[48]

End point description:

Endoscopic remission was defined as endoscopy subscore of 0.

End point type	Secondary

End point timeframe:

Week 12

Notes:

[48] - 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[49]	61[50]	61[51]	58[52]
Units: Participants	0	5	3	5

Notes:

[49] - Includes ITT1A population.

[50] - Includes ITT1A population.

[51] - Includes ITT1A population.

[52] - Includes ITT1A population.

End point values	S1P1: OL - Risankizumab 1800mg IV			
Subject group type	Reporting group			
Number of subjects analysed	340[53]			
Units: Participants	22			

Notes:

[53] - 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	121
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0192 [54]
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:

[54] - 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 [55]
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:

[55] - 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 [56]
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:

[56] - 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[57]

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:

[57] - 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[58]	61[59]	61[60]	58[61]
Units: Participants	5	6	4	3

Notes:

[58] - Includes ITT1A population.

[59] - Includes ITT1A population.

[60] - Includes ITT1A population.

[61] - Includes ITT1A population.

End point values	S1P1: OL - Risankizumab 1800mg IV			
Subject group type	Reporting group			
Number of subjects analysed	340[62]			
Units: Participants	19			

Notes:

[62] - 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	121
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7737 [63]
Method	Chi-squared

Notes:

[63] - 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 [64]
Method	Fisher exact

Notes:

[64] - 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 [65]
Method	Fisher exact

Notes:

[65] - 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)[66]

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; andGrade 5, erosions or ulceration.

End point type	Secondary

End point timeframe:

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	60[67]	61[68]	61[69]	58[70]
Units: Participants	0	3	2	1

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	340[71]			
Units: Participants	10			

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	121
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0722 [72]
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:

[72] - 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 [73]
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:

[73] - 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 [74]
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:

[74] - 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)[75]

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:

[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	50[76]	52[77]	56[78]	53[79]
Units: Units on a scale				
least squares mean (standard error)	-7.4 (± 1.53)	-13.8 (± 1.50)	-15.6 (± 1.46)	-15.1 (± 1.51)

Notes:

[76] - Includes ITT1A population.

[77] - Includes ITT1A population.

[78] - Includes ITT1A population.

[79] - Includes ITT1A population.

End point values	S1P1: OL - Risankizumab 1800mg IV			
Subject group type	Reporting group			
Number of subjects analysed	286[80]			
Units: Units on a scale				
least squares mean (standard error)	-17.1 (± 0.58)			

Notes:

[80] - 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 [81]
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:

[81] - P-value ≤ 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 [82]
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:

[82] - P-value ≤ 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 [83]
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:

[83] - P-value ≤ 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)[84]

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:

[84] - 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[85]	55[86]	59[87]	54[88]
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:

[85] - Includes ITT1A population.

[86] - Includes ITT1A population.

[87] - Includes ITT1A population.

[88] - Includes ITT1A population.

End point values	S1P1: OL - Risankizumab 1800mg IV			
Subject group type	Reporting group			
Number of subjects analysed	305[89]			
Units: Units on a scale				
least squares mean (standard error)	49.5 (± 1.86)			

Notes:

[89] - 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 [90]
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:

[90] - P-value ≤ 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 [91]
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:

[91] - P-value ≤ 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 [92]
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:

[92] - P-value ≤ 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

	Component[93]

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:

[93] - 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[94]	54[95]	59[96]	54[97]
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:

[94] - Includes ITT1A population.

[95] - Includes ITT1A population.

[96] - Includes ITT1A population.

[97] - Includes ITT1A population.

End point values	S1P1: OL - Risankizumab 1800mg IV			
Subject group type	Reporting group			
Number of subjects analysed	298[98]			
Units: Units on a scale				
least squares mean (standard error)	7.719 (± 0.3929)			

Notes:

[98] - 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 [99]
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:

[99] - P-value ≤ 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 [100]
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:

[100] - P-value ≤ 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)[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:

Baseline Through 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	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[102]	54[103]	59[104]	54[105]
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:

[102] - Includes ITT1A population.

[103] - Includes ITT1A population..

[104] - Includes ITT1A population.

[105] - Includes ITT1A population.

End point values	S1P1: OL - Risankizumab 1800mg IV			
Subject group type	Reporting group			
Number of subjects analysed	298[106]			
Units: units on a scale				
least squares mean (standard error)	10.7 (± 0.54)			

Notes:

[106] - 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 [107]
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:

[107] - P-value ≤ 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 [108]
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:

[108] - P-value ≤ 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 [109]
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:

[109] - P-value ≤ 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[110]

End point description:

Participants who underwent surgery related to UC.

End point type	Secondary

End point timeframe:

Through Week 12

Notes:

[110] - 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[111]	61[112]	61[113]	58[114]
Units: Participants	0	1	0	0

Notes:

[111] - Includes ITT1A population.

[112] - Includes ITT1A population.

[113] - Includes ITT1A population.

[114] - Includes ITT1A population.

End point values	S1P1: OL - Risankizumab 1800mg IV			
Subject group type	Reporting group			
Number of subjects analysed	340[115]			
Units: Participants	7			

Notes:

[115] - 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	121
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 1 [116]
Method	Fisher exact

Notes:

[116] - 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[117]

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 ≥ 30% from baseline, and a decrease in RBS ≥ 1 or an absolute RBS ≤ 1).

End point type	Secondary

End point timeframe:

Week 12

Notes:

[117] - 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[118]	650[119]		
Units: Participants	116	418		

Notes:

[118] - ITT2

[119] - ITT2

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[120]
P-value	< 0.0001 [121]
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:

[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: Percentage of Participants Achieving Endoscopic Improvement

End point title	Sub-Study 2: Percentage of Participants Achieving Endoscopic Improvement[122]

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:

[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	325[123]	650[124]		
Units: Participants	39	237		

Notes:

[123] - ITT2

[124] - 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[125]
P-value	< 0.0001 [126]
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:

[125] - Between-group diff. and 95% CI calculated using Mantel-Haenszel common rate diff. (Greenland and Robins (1985)).
[126] - 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)[127]

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:

[127] - 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[128]	650[129]		
Units: Participants	25	159		

Notes:

[128] - ITT2

[129] - 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[130]
P-value	< 0.0001 [131]
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:

[130] - Between-group diff. and 95% CI calculated using Mantel-Haenszel common rate diff. (Greenland and Robins (1985)).
[131] - 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[132]

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:

[132] - 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[133]	650[134]		
Units: Participants	11	69		

Notes:

[133] - ITT2

[134] - 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[135]
P-value	< 0.0001 [136]
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:

[135] - Between-group diff. and 95% CI calculated using Mantel-Haenszel common rate diff. (Greenland and Robins (1985)).
[136] - 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[137]

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 ≥ 30% from Baseline, plus a decrease in RBS ≥ 1 or an absolute RBS ≤ 1.

End point type	Secondary

End point timeframe:

Week 4

Notes:

[137] - 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[138]	650[139]		
Units: Participants	99	339		

Notes:

[138] - ITT2

[139] - 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[140]
P-value	< 0.0001 [141]
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:

[140] - Between-group diff. and 95% CI calculated using Mantel-Haenszel common rate diff. (Greenland and Robins (1985)).
[141] - 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[142]

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:

[142] - 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[143]	650[144]		
Units: Participants	90	287		

Notes:

[143] - ITT2

[144] - 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[145]
P-value	< 0.0001 [146]
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:

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

[146] - 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[147]

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:

[147] - 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[148]	650[149]		
Units: Participants	86	232		

Notes:

[148] - ITT2

[149] - 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[150]
P-value	= 0.0021 [151]
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:

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

[151] - 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[152]

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:

[152] - 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[153]	650[154]		
Units: Participants	2	41		

Notes:

[153] - ITT2

[154] - 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[155]
P-value	< 0.0001 [156]
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:

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

[156] - 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)[157]

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:

[157] - 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[158]	614[159]		
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:

[158] - ITT2

[159] - 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[160]
P-value	< 0.0001 [161]
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
Variability estimate	Standard error of the mean
Dispersion value	0.72

Notes:

[160] - Between-group diff. and 95% CI calculated using ANCOVA/MMRM with RTB-MI for continuous endpoints.
[161] - 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[162]

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:

[162] - 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[163]	619[164]		
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:

[163] - ITT2

[164] - 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[165]
P-value	< 0.0001 [166]
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
Variability estimate	Standard error of the mean
Dispersion value	2.52

Notes:

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

[166] - 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[167]

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:

[167] - 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[168]	650[169]		
Units: Count of participants				
least squares mean (confidence interval 95%)	5.5 (3.1 to 8.0)	0.8 (0.1 to 1.4)		

Notes:

[168] - ITT2

[169] - 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[170]
P-value	< 0.0001 [171]
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:

[170] - 95% CI for treatment differences is based on normal approximation of the binomial proportions

[171] - 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[172]

End point description:

Percentage of participants who reported no nocturnal bowel movements.

End point type	Secondary

End point timeframe:

Week 12

Notes:

[172] - 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[173]	650[174]		
Units: Participants	140	437		

Notes:

[173] - ITT2

[174] - 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[175]
P-value	< 0.0001 [176]
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:

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

[176] - 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[177]

End point description:

Percentage of participants who reported no tenesmus.

End point type	Secondary

End point timeframe:

Week 12

Notes:

[177] - 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[178]	650[179]		
Units: Participants	98	317		

Notes:
[178] - ITT2
[179] - 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[180]
P-value	< 0.0001 [181]
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:
[180] - Between-group diff. and 95% CI calculated using Mantel-Haenszel common rate diff. (Greenland and Robins (1985)).
[181] - 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[182]

End point description:
Change in number of fecal incontinence episodes per week.

End point type	Secondary

End point timeframe:
Baseline to Week 12

Notes:
[182] - 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: Count of participants				
least squares mean (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[183]
P-value	< 0.0001 [184]
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
Variability estimate	Standard error of the mean
Dispersion value	0.3865

Notes:

[183] - Between-group diff. and 95% CI calculated using ANCOVA/MMRM with RTB-MI for continuous endpoints.
[184] - 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[185]

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:

[185] - 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[186]	602[187]		
Units: Count of Participants				
least squares mean (confidence interval 95%)	-1.505 (-1.7969 to	-2.485 (-2.6872 to		

	-1.2122)	-2.2831)

Notes:

[186] - ITT2

[187] - 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 [188]
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
Variability estimate	Standard error of the mean
Dispersion value	0.1775

Notes:

[188] - 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[189]

End point description:

End point type	Secondary

End point timeframe:

Baseline through Week 12

Notes:

[189] - 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[190]	54[191]	59[192]	54[193]
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:

[190] - Includes ITT1A population.

[191] - Includes ITT1A population.

[192] - Includes ITT1A population.

[193] - Includes ITT1A population.

End point values	S1P1: OL - Risankizumab 1800mg IV			
Subject group type	Reporting group			
Number of subjects analysed	298[194]			
Units: Units on a scale				
least squares mean (standard error)	7.777 (± 0.4777)			

Notes:

[194] - 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 [195]
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:

[195] - 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 [196]
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:

[196] - 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 [197]
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:

[197] - 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 information

Timeframe for reporting adverse events:

All-cause mortality and Serious AE were reported from time of informed consent until 140 days following last dose of study drug, or the first dose of next period/study, whichever occurs first.

Adverse event reporting additional description:

All other AE were reported from time of first dose until 140 days following last dose of study drug, or the first dose of next period/study, whichever occurs earlier.

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_1200mgIV
Reporting group description: -	
Reporting group title	SS1_P1_Risa_600mgIV
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_P2_Risa_180mgSC
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	SS1_P2_Risa_360mgSC
Reporting group description: -	
Reporting group title	SS2_P1_PlbIV
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_Risa_360mgSC

Reporting group description: -

Serious adverse events	SS1_P1_PlbIV	SS1_P1_Risa_1200 mgIV	SS1_P1_Risa_600m gIV
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 59 (10.17%)	4 / 61 (6.56%)	6 / 62 (9.68%)
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 / 61 (0.00%)	0 / 62 (0.00%)
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 / 61 (0.00%)	0 / 62 (0.00%)
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 / 61 (0.00%)	0 / 62 (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 / 61 (0.00%)	0 / 62 (0.00%)
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 / 61 (0.00%)	0 / 62 (0.00%)
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 / 59 (0.00%)	0 / 61 (0.00%)	1 / 62 (1.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYPERTENSION			

subjects affected / exposed	0 / 59 (0.00%)	0 / 61 (0.00%)	0 / 62 (0.00%)
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 / 61 (0.00%)	0 / 62 (0.00%)
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 / 59 (0.00%)	0 / 61 (0.00%)	1 / 62 (1.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	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 / 61 (0.00%)	0 / 62 (0.00%)
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 / 61 (0.00%)	0 / 62 (0.00%)
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 / 61 (0.00%)	0 / 62 (0.00%)
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 / 61 (0.00%)	0 / 62 (0.00%)
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 / 61 (0.00%)	0 / 62 (0.00%)
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 / 61 (0.00%)	0 / 62 (0.00%)
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 / 61 (0.00%)	0 / 62 (0.00%)
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 / 61 (0.00%)	0 / 62 (0.00%)
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 / 61 (0.00%)	0 / 62 (0.00%)
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 / 61 (0.00%)	0 / 62 (0.00%)
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 / 61 (0.00%)	0 / 62 (0.00%)
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 / 61 (0.00%)	0 / 62 (0.00%)
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 / 61 (0.00%)	0 / 62 (0.00%)
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 / 61 (0.00%)	0 / 62 (0.00%)
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 / 61 (0.00%)	0 / 62 (0.00%)
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 / 61 (0.00%)	0 / 62 (0.00%)
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 / 61 (0.00%)	0 / 62 (0.00%)
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 / 61 (0.00%)	0 / 62 (0.00%)
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 / 61 (0.00%)	0 / 62 (0.00%)
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%)	2 / 61 (3.28%)	0 / 62 (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 / 59 (0.00%)	0 / 61 (0.00%)	0 / 62 (0.00%)
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 / 61 (0.00%)	0 / 62 (0.00%)
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 / 61 (0.00%)	0 / 62 (0.00%)
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%)	0 / 61 (0.00%)	1 / 62 (1.61%)
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 ULCERATIVE			
subjects affected / exposed	3 / 59 (5.08%)	0 / 61 (0.00%)	1 / 62 (1.61%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ENTERITIS			
subjects affected / exposed	0 / 59 (0.00%)	0 / 61 (0.00%)	0 / 62 (0.00%)
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 / 59 (0.00%)	0 / 61 (0.00%)	0 / 62 (0.00%)
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 / 61 (0.00%)	0 / 62 (0.00%)
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 / 61 (0.00%)	0 / 62 (0.00%)
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 / 61 (0.00%)	0 / 62 (0.00%)
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 / 61 (0.00%)	0 / 62 (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 / 61 (0.00%)	0 / 62 (0.00%)
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 / 61 (0.00%)	0 / 62 (0.00%)
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 / 59 (0.00%)	0 / 61 (0.00%)	0 / 62 (0.00%)
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 / 59 (0.00%)	1 / 61 (1.64%)	0 / 62 (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 / 59 (0.00%)	0 / 61 (0.00%)	0 / 62 (0.00%)
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 / 61 (0.00%)	0 / 62 (0.00%)
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 / 61 (0.00%)	0 / 62 (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 / 61 (0.00%)	0 / 62 (0.00%)
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 / 61 (0.00%)	0 / 62 (0.00%)
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 / 61 (0.00%)	0 / 62 (0.00%)
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 / 61 (0.00%)	0 / 62 (0.00%)
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 / 61 (0.00%)	0 / 62 (0.00%)
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 / 61 (0.00%)	0 / 62 (0.00%)
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 / 61 (0.00%)	0 / 62 (0.00%)
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%)	0 / 61 (0.00%)	1 / 62 (1.61%)
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 / 59 (0.00%)	0 / 61 (0.00%)	0 / 62 (0.00%)
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 / 61 (0.00%)	0 / 62 (0.00%)
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 / 61 (0.00%)	0 / 62 (0.00%)
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 / 61 (0.00%)	0 / 62 (0.00%)
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%)	1 / 61 (1.64%)	0 / 62 (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 / 59 (0.00%)	0 / 61 (0.00%)	0 / 62 (0.00%)
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 / 61 (0.00%)	0 / 62 (0.00%)
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 / 61 (0.00%)	0 / 62 (0.00%)
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 / 61 (0.00%)	0 / 62 (0.00%)
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%)	0 / 61 (0.00%)	1 / 62 (1.61%)
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 MYCOPLASMAL			
subjects affected / exposed	0 / 59 (0.00%)	0 / 61 (0.00%)	0 / 62 (0.00%)
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 / 61 (0.00%)	0 / 62 (0.00%)
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 / 61 (0.00%)	0 / 62 (0.00%)
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 / 61 (0.00%)	0 / 62 (0.00%)
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 / 61 (0.00%)	0 / 62 (0.00%)
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 / 61 (0.00%)	0 / 62 (0.00%)
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_1800mgIV	SS1_P2_Risa_180mgSC	SS2_P2_PlbIV_Risa_1200mgIV
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 58 (5.17%)	6 / 71 (8.45%)	4 / 173 (2.31%)
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 / 71 (0.00%)	0 / 173 (0.00%)
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 / 71 (0.00%)	0 / 173 (0.00%)
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 / 71 (0.00%)	0 / 173 (0.00%)
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 / 71 (0.00%)	0 / 173 (0.00%)
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%)	1 / 71 (1.41%)	0 / 173 (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
DEEP VEIN THROMBOSIS			
subjects affected / exposed	0 / 58 (0.00%)	0 / 71 (0.00%)	0 / 173 (0.00%)
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 / 71 (0.00%)	0 / 173 (0.00%)
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%)	1 / 71 (1.41%)	0 / 173 (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
General disorders and administration site conditions			
PYREXIA			
subjects affected / exposed	0 / 58 (0.00%)	1 / 71 (1.41%)	0 / 173 (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

Immune system disorders			
ANAPHYLACTIC REACTION			
subjects affected / exposed	0 / 58 (0.00%)	0 / 71 (0.00%)	0 / 173 (0.00%)
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 / 58 (0.00%)	0 / 71 (0.00%)	0 / 173 (0.00%)
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 / 58 (0.00%)	0 / 71 (0.00%)	0 / 173 (0.00%)
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 / 58 (0.00%)	0 / 71 (0.00%)	0 / 173 (0.00%)
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 / 58 (0.00%)	0 / 71 (0.00%)	0 / 173 (0.00%)
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 / 58 (0.00%)	0 / 71 (0.00%)	0 / 173 (0.00%)
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 / 58 (0.00%)	0 / 71 (0.00%)	0 / 173 (0.00%)
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 / 58 (0.00%)	0 / 71 (0.00%)	0 / 173 (0.00%)
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 / 71 (0.00%)	0 / 173 (0.00%)
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 / 71 (0.00%)	0 / 173 (0.00%)
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 / 71 (0.00%)	1 / 173 (0.58%)
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 / 71 (0.00%)	0 / 173 (0.00%)
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 / 71 (0.00%)	0 / 173 (0.00%)
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 / 71 (0.00%)	0 / 173 (0.00%)
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 / 71 (0.00%)	0 / 173 (0.00%)
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 / 71 (0.00%)	0 / 173 (0.00%)
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 / 71 (0.00%)	0 / 173 (0.00%)
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 / 71 (0.00%)	0 / 173 (0.00%)
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 / 71 (0.00%)	0 / 173 (0.00%)
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%)	0 / 71 (0.00%)	0 / 173 (0.00%)
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 / 58 (0.00%)	0 / 71 (0.00%)	0 / 173 (0.00%)
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 / 71 (0.00%)	0 / 173 (0.00%)
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 / 71 (0.00%)	0 / 173 (0.00%)
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 / 71 (0.00%)	0 / 173 (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%)	3 / 71 (4.23%)	1 / 173 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ENTERITIS			
subjects affected / exposed	0 / 58 (0.00%)	0 / 71 (0.00%)	0 / 173 (0.00%)
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 / 58 (0.00%)	0 / 71 (0.00%)	0 / 173 (0.00%)
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 / 71 (0.00%)	1 / 173 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
NAUSEA			
subjects affected / exposed	0 / 58 (0.00%)	0 / 71 (0.00%)	0 / 173 (0.00%)
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 / 71 (0.00%)	0 / 173 (0.00%)
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 / 71 (0.00%)	0 / 173 (0.00%)
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 / 71 (0.00%)	0 / 173 (0.00%)
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%)	1 / 71 (1.41%)	0 / 173 (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
NEPHROLITHIASIS			
subjects affected / exposed	0 / 58 (0.00%)	1 / 71 (1.41%)	0 / 173 (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
RENAL COLIC			
subjects affected / exposed	0 / 58 (0.00%)	0 / 71 (0.00%)	0 / 173 (0.00%)
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 / 58 (0.00%)	0 / 71 (0.00%)	0 / 173 (0.00%)
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 / 71 (0.00%)	0 / 173 (0.00%)
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 / 71 (0.00%)	0 / 173 (0.00%)
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 / 58 (0.00%)	0 / 71 (0.00%)	0 / 173 (0.00%)
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 / 71 (0.00%)	0 / 173 (0.00%)
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 / 71 (0.00%)	0 / 173 (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 / 71 (0.00%)	1 / 173 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19			
subjects affected / exposed	0 / 58 (0.00%)	0 / 71 (0.00%)	0 / 173 (0.00%)
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 / 71 (0.00%)	0 / 173 (0.00%)
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 / 71 (0.00%)	1 / 173 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CYTOMEGALOVIRUS INFECTION			

subjects affected / exposed	0 / 58 (0.00%)	0 / 71 (0.00%)	0 / 173 (0.00%)
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 / 71 (0.00%)	0 / 173 (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 / 71 (0.00%)	0 / 173 (0.00%)
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 / 71 (0.00%)	0 / 173 (0.00%)
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 / 71 (0.00%)	0 / 173 (0.00%)
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%)	0 / 71 (0.00%)	0 / 173 (0.00%)
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 / 58 (0.00%)	0 / 71 (0.00%)	0 / 173 (0.00%)
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 / 71 (0.00%)	0 / 173 (0.00%)
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 / 71 (0.00%)	0 / 173 (0.00%)
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 / 71 (0.00%)	0 / 173 (0.00%)
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 / 71 (0.00%)	0 / 173 (0.00%)
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 / 71 (0.00%)	0 / 173 (0.00%)
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 / 71 (0.00%)	0 / 173 (0.00%)
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 / 71 (0.00%)	0 / 173 (0.00%)
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 / 71 (0.00%)	0 / 173 (0.00%)
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 / 71 (0.00%)	0 / 173 (0.00%)
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 / 71 (0.00%)	0 / 173 (0.00%)
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_Risa_1200 mgIV	SS1_P2_Risa_360m gSC	SS2_P1_PlbIV
Total subjects affected by serious adverse events			
subjects affected / exposed	15 / 651 (2.30%)	7 / 70 (10.00%)	33 / 324 (10.19%)
number of deaths (all causes)	1	0	0
number of deaths resulting from adverse events	1	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
BREAST CANCER			
subjects affected / exposed	0 / 651 (0.00%)	0 / 70 (0.00%)	1 / 324 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PITUITARY TUMOUR BENIGN			
subjects affected / exposed	0 / 651 (0.00%)	0 / 70 (0.00%)	1 / 324 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PROSTATE CANCER			
subjects affected / exposed	0 / 651 (0.00%)	0 / 70 (0.00%)	0 / 324 (0.00%)
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 / 651 (0.00%)	0 / 70 (0.00%)	1 / 324 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
ARTERIAL OCCLUSIVE DISEASE			
subjects affected / exposed	0 / 651 (0.00%)	0 / 70 (0.00%)	0 / 324 (0.00%)
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 / 651 (0.15%)	0 / 70 (0.00%)	1 / 324 (0.31%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYPERTENSION			
subjects affected / exposed	0 / 651 (0.00%)	1 / 70 (1.43%)	0 / 324 (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 / 651 (0.00%)	0 / 70 (0.00%)	0 / 324 (0.00%)
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 / 651 (0.00%)	0 / 70 (0.00%)	0 / 324 (0.00%)
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 / 651 (0.00%)	1 / 70 (1.43%)	0 / 324 (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 / 651 (0.00%)	0 / 70 (0.00%)	0 / 324 (0.00%)
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 / 651 (0.00%)	0 / 70 (0.00%)	0 / 324 (0.00%)
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	2 / 651 (0.31%)	0 / 70 (0.00%)	1 / 324 (0.31%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RESPIRATORY DISTRESS			
subjects affected / exposed	0 / 651 (0.00%)	1 / 70 (1.43%)	0 / 324 (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	0 / 651 (0.00%)	0 / 70 (0.00%)	1 / 324 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GENERALISED ANXIETY DISORDER			
subjects affected / exposed	0 / 651 (0.00%)	0 / 70 (0.00%)	1 / 324 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MAJOR DEPRESSION			
subjects affected / exposed	1 / 651 (0.15%)	0 / 70 (0.00%)	0 / 324 (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
SUICIDAL IDEATION			
subjects affected / exposed	0 / 651 (0.00%)	0 / 70 (0.00%)	0 / 324 (0.00%)
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 / 651 (0.00%)	0 / 70 (0.00%)	1 / 324 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
ROAD TRAFFIC ACCIDENT			
subjects affected / exposed	0 / 651 (0.00%)	0 / 70 (0.00%)	0 / 324 (0.00%)
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	1 / 651 (0.15%)	0 / 70 (0.00%)	0 / 324 (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 LACERATION			
subjects affected / exposed	1 / 651 (0.15%)	0 / 70 (0.00%)	0 / 324 (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
SUBDURAL HAEMATOMA			
subjects affected / exposed	1 / 651 (0.15%)	0 / 70 (0.00%)	0 / 324 (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
Cardiac disorders			
ARTERIOSCLEROSIS CORONARY ARTERY			
subjects affected / exposed	0 / 651 (0.00%)	0 / 70 (0.00%)	1 / 324 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
TACHYCARDIA			
subjects affected / exposed	0 / 651 (0.00%)	1 / 70 (1.43%)	0 / 324 (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	1 / 651 (0.15%)	0 / 70 (0.00%)	0 / 324 (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
CEREBROVASCULAR ACCIDENT			
subjects affected / exposed	0 / 651 (0.00%)	1 / 70 (1.43%)	0 / 324 (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	0 / 651 (0.00%)	0 / 70 (0.00%)	1 / 324 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Blood and lymphatic system disorders			
ANAEMIA			
subjects affected / exposed	2 / 651 (0.31%)	1 / 70 (1.43%)	2 / 324 (0.62%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
CATARACT			
subjects affected / exposed	0 / 651 (0.00%)	0 / 70 (0.00%)	0 / 324 (0.00%)
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 / 651 (0.00%)	0 / 70 (0.00%)	2 / 324 (0.62%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ANAL PROLAPSE			
subjects affected / exposed	0 / 651 (0.00%)	0 / 70 (0.00%)	0 / 324 (0.00%)
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 / 651 (0.00%)	0 / 70 (0.00%)	0 / 324 (0.00%)
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	2 / 651 (0.31%)	2 / 70 (2.86%)	16 / 324 (4.94%)
occurrences causally related to treatment / all	1 / 2	1 / 2	2 / 17
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ENTERITIS			
subjects affected / exposed	0 / 651 (0.00%)	0 / 70 (0.00%)	0 / 324 (0.00%)
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	1 / 651 (0.15%)	0 / 70 (0.00%)	0 / 324 (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
HAEMATEMESIS			
subjects affected / exposed	0 / 651 (0.00%)	0 / 70 (0.00%)	0 / 324 (0.00%)
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 / 651 (0.00%)	0 / 70 (0.00%)	1 / 324 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
HEPATIC CIRRHOSIS			
subjects affected / exposed	0 / 651 (0.00%)	0 / 70 (0.00%)	1 / 324 (0.31%)
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 and subcutaneous tissue disorders			
ERYTHEMA NODOSUM			
subjects affected / exposed	0 / 651 (0.00%)	0 / 70 (0.00%)	0 / 324 (0.00%)
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 / 651 (0.00%)	0 / 70 (0.00%)	0 / 324 (0.00%)
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 / 651 (0.00%)	0 / 70 (0.00%)	0 / 324 (0.00%)
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 / 651 (0.00%)	0 / 70 (0.00%)	0 / 324 (0.00%)
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 / 651 (0.00%)	0 / 70 (0.00%)	0 / 324 (0.00%)
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 / 651 (0.00%)	0 / 70 (0.00%)	0 / 324 (0.00%)
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 / 651 (0.00%)	0 / 70 (0.00%)	0 / 324 (0.00%)
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 / 651 (0.15%)	0 / 70 (0.00%)	0 / 324 (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	1 / 651 (0.15%)	0 / 70 (0.00%)	0 / 324 (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
ANAL ABSCESS			
subjects affected / exposed	0 / 651 (0.00%)	0 / 70 (0.00%)	0 / 324 (0.00%)
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 / 651 (0.00%)	0 / 70 (0.00%)	1 / 324 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CLOSTRIDIUM DIFFICILE INFECTION			
subjects affected / exposed	0 / 651 (0.00%)	0 / 70 (0.00%)	0 / 324 (0.00%)
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	1 / 651 (0.15%)	0 / 70 (0.00%)	0 / 324 (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
COVID-19 PNEUMONIA			
subjects affected / exposed	1 / 651 (0.15%)	0 / 70 (0.00%)	0 / 324 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
CYSTITIS			
subjects affected / exposed	0 / 651 (0.00%)	0 / 70 (0.00%)	0 / 324 (0.00%)
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 / 651 (0.00%)	0 / 70 (0.00%)	0 / 324 (0.00%)
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 / 651 (0.00%)	0 / 70 (0.00%)	0 / 324 (0.00%)
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 / 651 (0.00%)	0 / 70 (0.00%)	1 / 324 (0.31%)
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 INFECTIOUS			
subjects affected / exposed	0 / 651 (0.00%)	0 / 70 (0.00%)	1 / 324 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ERYSIPELAS			
subjects affected / exposed	0 / 651 (0.00%)	0 / 70 (0.00%)	0 / 324 (0.00%)
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 / 651 (0.00%)	0 / 70 (0.00%)	0 / 324 (0.00%)
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 / 651 (0.00%)	0 / 70 (0.00%)	0 / 324 (0.00%)
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 / 651 (0.00%)	0 / 70 (0.00%)	1 / 324 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PHARYNGEAL ABSCESS			
subjects affected / exposed	0 / 651 (0.00%)	0 / 70 (0.00%)	1 / 324 (0.31%)
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			
subjects affected / exposed	1 / 651 (0.15%)	0 / 70 (0.00%)	0 / 324 (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 HAEMOPHILUS			
subjects affected / exposed	0 / 651 (0.00%)	0 / 70 (0.00%)	0 / 324 (0.00%)
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 / 651 (0.00%)	1 / 70 (1.43%)	0 / 324 (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 / 651 (0.00%)	0 / 70 (0.00%)	0 / 324 (0.00%)
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 / 651 (0.00%)	0 / 70 (0.00%)	0 / 324 (0.00%)
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 / 651 (0.00%)	0 / 70 (0.00%)	0 / 324 (0.00%)
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 / 651 (0.00%)	0 / 70 (0.00%)	0 / 324 (0.00%)
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 / 651 (0.00%)	1 / 70 (1.43%)	0 / 324 (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

Serious adverse events	SS2_P2_Risa_180mgSC	SS2_P2_Risa_1200mgIV	SS2_P2_Risa_360mgSC
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 71 (5.63%)	1 / 68 (1.47%)	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	0 / 71 (0.00%)	0 / 68 (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
PITUITARY TUMOUR BENIGN			
subjects affected / exposed	0 / 71 (0.00%)	0 / 68 (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
PROSTATE CANCER			
subjects affected / exposed	0 / 71 (0.00%)	0 / 68 (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	0 / 71 (0.00%)	0 / 68 (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
Vascular disorders			
ARTERIAL OCCLUSIVE DISEASE			
subjects affected / exposed	0 / 71 (0.00%)	0 / 68 (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	0 / 71 (0.00%)	0 / 68 (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
HYPERTENSION			
subjects affected / exposed	0 / 71 (0.00%)	0 / 68 (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
PERIPHERAL ARTERY OCCLUSION			
subjects affected / exposed	0 / 71 (0.00%)	0 / 68 (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 / 71 (0.00%)	0 / 68 (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 / 71 (0.00%)	0 / 68 (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
Reproductive system and breast disorders			
UTERINE PROLAPSE			

subjects affected / exposed	1 / 71 (1.41%)	0 / 68 (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, thoracic and mediastinal disorders			
PLEURAL EFFUSION			
subjects affected / exposed	0 / 71 (0.00%)	0 / 68 (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	0 / 71 (0.00%)	0 / 68 (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 DISTRESS			
subjects affected / exposed	0 / 71 (0.00%)	0 / 68 (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
Psychiatric disorders			
ADJUSTMENT DISORDER			
subjects affected / exposed	0 / 71 (0.00%)	0 / 68 (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
GENERALISED ANXIETY DISORDER			
subjects affected / exposed	0 / 71 (0.00%)	0 / 68 (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
MAJOR DEPRESSION			
subjects affected / exposed	0 / 71 (0.00%)	0 / 68 (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 / 71 (0.00%)	0 / 68 (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	0 / 71 (0.00%)	0 / 68 (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
Injury, poisoning and procedural complications			
ROAD TRAFFIC ACCIDENT			
subjects affected / exposed	1 / 71 (1.41%)	0 / 68 (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
SKELETAL INJURY			
subjects affected / exposed	0 / 71 (0.00%)	0 / 68 (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 / 71 (0.00%)	0 / 68 (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 / 71 (0.00%)	0 / 68 (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	0 / 71 (0.00%)	0 / 68 (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
TACHYCARDIA			
subjects affected / exposed	0 / 71 (0.00%)	0 / 68 (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
Nervous system disorders			
CEREBRAL MASS EFFECT			

subjects affected / exposed	0 / 71 (0.00%)	0 / 68 (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 / 71 (0.00%)	0 / 68 (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
DIZZINESS			
subjects affected / exposed	0 / 71 (0.00%)	0 / 68 (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
Blood and lymphatic system disorders			
ANAEMIA			
subjects affected / exposed	0 / 71 (0.00%)	0 / 68 (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
Eye disorders			
CATARACT			
subjects affected / exposed	0 / 71 (0.00%)	0 / 68 (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	0 / 71 (0.00%)	0 / 68 (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 PROLAPSE			
subjects affected / exposed	0 / 71 (0.00%)	0 / 68 (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 / 71 (0.00%)	0 / 68 (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	1 / 71 (1.41%)	0 / 68 (0.00%)	1 / 70 (1.43%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ENTERITIS			
subjects affected / exposed	1 / 71 (1.41%)	0 / 68 (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
GASTRITIS EROSIVE			
subjects affected / exposed	0 / 71 (0.00%)	0 / 68 (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 / 71 (0.00%)	0 / 68 (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	0 / 71 (0.00%)	0 / 68 (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
Hepatobiliary disorders			
HEPATIC CIRRHOSIS			
subjects affected / exposed	0 / 71 (0.00%)	0 / 68 (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 and subcutaneous tissue disorders			
ERYTHEMA NODOSUM			
subjects affected / exposed	0 / 71 (0.00%)	0 / 68 (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 / 71 (0.00%)	0 / 68 (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 / 71 (0.00%)	0 / 68 (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 / 71 (0.00%)	0 / 68 (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 / 71 (0.00%)	0 / 68 (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 / 71 (0.00%)	0 / 68 (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 / 71 (0.00%)	0 / 68 (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 / 71 (0.00%)	0 / 68 (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 / 71 (0.00%)	0 / 68 (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 / 71 (0.00%)	0 / 68 (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	0 / 71 (0.00%)	0 / 68 (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
CLOSTRIDIUM DIFFICILE INFECTION			
subjects affected / exposed	0 / 71 (0.00%)	0 / 68 (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 / 71 (0.00%)	1 / 68 (1.47%)	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
COVID-19 PNEUMONIA			
subjects affected / exposed	0 / 71 (0.00%)	0 / 68 (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 / 71 (0.00%)	0 / 68 (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 / 71 (0.00%)	0 / 68 (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 / 71 (0.00%)	0 / 68 (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	0 / 71 (0.00%)	0 / 68 (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
ENTERITIS INFECTIOUS			
subjects affected / exposed	0 / 71 (0.00%)	0 / 68 (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
ERYSIPELAS			
subjects affected / exposed	0 / 71 (0.00%)	0 / 68 (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 / 71 (0.00%)	0 / 68 (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 / 71 (0.00%)	0 / 68 (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	0 / 71 (0.00%)	0 / 68 (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
PHARYNGEAL ABSCESS			
subjects affected / exposed	0 / 71 (0.00%)	0 / 68 (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			
subjects affected / exposed	0 / 71 (0.00%)	0 / 68 (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 / 71 (0.00%)	0 / 68 (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 / 71 (0.00%)	0 / 68 (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
POST PROCEDURAL INFECTION			
subjects affected / exposed	0 / 71 (0.00%)	0 / 68 (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 / 71 (0.00%)	0 / 68 (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 / 71 (0.00%)	0 / 68 (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 / 71 (0.00%)	0 / 68 (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 / 71 (0.00%)	0 / 68 (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

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

Non-serious adverse events	SS1_P1_PlbIV	SS1_P1_Risa_1200 mgIV	SS1_P1_Risa_600m gIV
Total subjects affected by non-serious adverse events			
subjects affected / exposed	14 / 59 (23.73%)	12 / 61 (19.67%)	13 / 62 (20.97%)
Nervous system disorders			
HEADACHE			
subjects affected / exposed	3 / 59 (5.08%)	3 / 61 (4.92%)	2 / 62 (3.23%)
occurrences (all)	4	3	2
Blood and lymphatic system disorders			
ANAEMIA			
subjects affected / exposed	2 / 59 (3.39%)	2 / 61 (3.28%)	0 / 62 (0.00%)
occurrences (all)	2	3	0
Gastrointestinal disorders			
COLITIS ULCERATIVE			
subjects affected / exposed	4 / 59 (6.78%)	3 / 61 (4.92%)	1 / 62 (1.61%)
occurrences (all)	5	3	1
HAEMORRHOIDS			
subjects affected / exposed	3 / 59 (5.08%)	0 / 61 (0.00%)	0 / 62 (0.00%)
occurrences (all)	3	0	0
Skin and subcutaneous tissue disorders			
DRY SKIN			
subjects affected / exposed	0 / 59 (0.00%)	0 / 61 (0.00%)	2 / 62 (3.23%)
occurrences (all)	0	0	2
Infections and infestations			
BRONCHITIS			
subjects affected / exposed	0 / 59 (0.00%)	1 / 61 (1.64%)	4 / 62 (6.45%)
occurrences (all)	0	1	4
COVID-19			
subjects affected / exposed	0 / 59 (0.00%)	0 / 61 (0.00%)	0 / 62 (0.00%)
occurrences (all)	0	0	0
NASOPHARYNGITIS			
subjects affected / exposed	4 / 59 (6.78%)	3 / 61 (4.92%)	5 / 62 (8.06%)
occurrences (all)	5	5	5
PHARYNGITIS			
subjects affected / exposed	1 / 59 (1.69%)	0 / 61 (0.00%)	1 / 62 (1.61%)
occurrences (all)	1	0	1
SINUSITIS			

subjects affected / exposed	0 / 59 (0.00%)	1 / 61 (1.64%)	0 / 62 (0.00%)
occurrences (all)	0	1	0

Non-serious adverse events	SS1_P2_Risa_1800mgIV	SS1_P2_PlbIV_Risa_1800mgIV	SS1_P1_OL_Risa_1800mgIV
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_1800mgIV	SS1_P2_Risa_180mgSC	SS2_P2_PlbIV_Risa_1200mgIV
Total subjects affected by non-serious adverse events			
subjects affected / exposed	12 / 58 (20.69%)	4 / 71 (5.63%)	22 / 173 (12.72%)
Nervous system disorders			
HEADACHE			
subjects affected / exposed	4 / 58 (6.90%)	2 / 71 (2.82%)	3 / 173 (1.73%)
occurrences (all)	5	2	3
Blood and lymphatic system disorders			
ANAEMIA			
subjects affected / exposed	1 / 58 (1.72%)	1 / 71 (1.41%)	4 / 173 (2.31%)
occurrences (all)	1	1	4
Gastrointestinal disorders			
COLITIS ULCERATIVE			
subjects affected / exposed	1 / 58 (1.72%)	0 / 71 (0.00%)	3 / 173 (1.73%)
occurrences (all)	1	0	3
HAEMORRHOIDS			
subjects affected / exposed	0 / 58 (0.00%)	0 / 71 (0.00%)	0 / 173 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
DRY SKIN			
subjects affected / exposed	0 / 58 (0.00%)	0 / 71 (0.00%)	0 / 173 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
BRONCHITIS			
subjects affected / exposed	0 / 58 (0.00%)	0 / 71 (0.00%)	1 / 173 (0.58%)
occurrences (all)	0	0	1
COVID-19			
subjects affected / exposed	0 / 58 (0.00%)	0 / 71 (0.00%)	10 / 173 (5.78%)
occurrences (all)	0	0	10
NASOPHARYNGITIS			

subjects affected / exposed	5 / 58 (8.62%)	1 / 71 (1.41%)	3 / 173 (1.73%)
occurrences (all)	6	1	3
PHARYNGITIS			
subjects affected / exposed	0 / 58 (0.00%)	0 / 71 (0.00%)	1 / 173 (0.58%)
occurrences (all)	0	0	1
SINUSITIS			
subjects affected / exposed	1 / 58 (1.72%)	0 / 71 (0.00%)	0 / 173 (0.00%)
occurrences (all)	1	0	0

Non-serious adverse events	SS2_P1_Risa_1200 mgIV	SS1_P2_Risa_360m gSC	SS2_P1_PlbIV
Total subjects affected by non-serious adverse events			
subjects affected / exposed	100 / 651 (15.36%)	16 / 70 (22.86%)	63 / 324 (19.44%)
Nervous system disorders			
HEADACHE			
subjects affected / exposed	19 / 651 (2.92%)	5 / 70 (7.14%)	7 / 324 (2.16%)
occurrences (all)	25	5	8
Blood and lymphatic system disorders			
ANAEMIA			
subjects affected / exposed	20 / 651 (3.07%)	1 / 70 (1.43%)	18 / 324 (5.56%)
occurrences (all)	20	1	20
Gastrointestinal disorders			
COLITIS ULCERATIVE			
subjects affected / exposed	9 / 651 (1.38%)	3 / 70 (4.29%)	17 / 324 (5.25%)
occurrences (all)	9	3	17
HAEMORRHOIDS			
subjects affected / exposed	5 / 651 (0.77%)	1 / 70 (1.43%)	0 / 324 (0.00%)
occurrences (all)	6	1	0
Skin and subcutaneous tissue disorders			
DRY SKIN			
subjects affected / exposed	3 / 651 (0.46%)	1 / 70 (1.43%)	2 / 324 (0.62%)
occurrences (all)	3	1	2
Infections and infestations			
BRONCHITIS			
subjects affected / exposed	2 / 651 (0.31%)	0 / 70 (0.00%)	0 / 324 (0.00%)
occurrences (all)	3	0	0
COVID-19			

subjects affected / exposed	30 / 651 (4.61%)	0 / 70 (0.00%)	19 / 324 (5.86%)
occurrences (all)	30	0	19
NASOPHARYNGITIS			
subjects affected / exposed	18 / 651 (2.76%)	6 / 70 (8.57%)	8 / 324 (2.47%)
occurrences (all)	18	6	9
PHARYNGITIS			
subjects affected / exposed	0 / 651 (0.00%)	1 / 70 (1.43%)	0 / 324 (0.00%)
occurrences (all)	0	1	0
SINUSITIS			
subjects affected / exposed	1 / 651 (0.15%)	2 / 70 (2.86%)	1 / 324 (0.31%)
occurrences (all)	1	2	1

Non-serious adverse events	SS2_P2_Risa_180mgSC	SS2_P2_Risa_1200mgIV	SS2_P2_Risa_360mgSC
Total subjects affected by non-serious adverse events			
subjects affected / exposed	10 / 71 (14.08%)	9 / 68 (13.24%)	23 / 70 (32.86%)
Nervous system disorders			
HEADACHE			
subjects affected / exposed	1 / 71 (1.41%)	2 / 68 (2.94%)	6 / 70 (8.57%)
occurrences (all)	1	4	6
Blood and lymphatic system disorders			
ANAEMIA			
subjects affected / exposed	2 / 71 (2.82%)	1 / 68 (1.47%)	6 / 70 (8.57%)
occurrences (all)	2	1	6
Gastrointestinal disorders			
COLITIS ULCERATIVE			
subjects affected / exposed	3 / 71 (4.23%)	1 / 68 (1.47%)	0 / 70 (0.00%)
occurrences (all)	3	1	0
HAEMORRHOIDS			
subjects affected / exposed	1 / 71 (1.41%)	0 / 68 (0.00%)	1 / 70 (1.43%)
occurrences (all)	1	0	1
Skin and subcutaneous tissue disorders			
DRY SKIN			
subjects affected / exposed	0 / 71 (0.00%)	0 / 68 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
BRONCHITIS			

subjects affected / exposed	0 / 71 (0.00%)	1 / 68 (1.47%)	1 / 70 (1.43%)
occurrences (all)	0	1	1
COVID-19			
subjects affected / exposed	4 / 71 (5.63%)	4 / 68 (5.88%)	6 / 70 (8.57%)
occurrences (all)	4	4	6
NASOPHARYNGITIS			
subjects affected / exposed	1 / 71 (1.41%)	0 / 68 (0.00%)	4 / 70 (5.71%)
occurrences (all)	1	0	4
PHARYNGITIS			
subjects affected / exposed	0 / 71 (0.00%)	0 / 68 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
SINUSITIS			
subjects affected / exposed	0 / 71 (0.00%)	0 / 68 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
18 October 2017	Global amendment 1 • 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	Global Amendment 2 • 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	Global amendment 3: • 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	Global amendment 4: • 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: