



Clinical trial results:

A Multicenter, Randomized, Double-Blind, Placebo Controlled Induction Study to Assess the Efficacy and Safety of Risankizumab in Subjects with Moderately to Severely Active Crohn's Disease Who Failed Prior Biologic Treatment

Summary

EudraCT number	2016-003190-17
Trial protocol	SK DK CZ DE GB PT IE BG AT LV PL NL EE LT ES GR BE FR HR
Global end of trial date	15 May 2021

Results information

Result version number	v1 (current)
This version publication date	21 November 2021
First version publication date	21 November 2021

Trial information

Trial identification

Sponsor protocol code	M15-991
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03104413
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, 001 8006339110, abbvieclinicaltrials@abbvie.com
Scientific contact	Global Medical Services, AbbVie, 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	19 May 2021
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	19 May 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The purpose of this study is to evaluate the efficacy and safety of risankizumab versus placebo during induction therapy in participants with moderately to severely active Crohn's disease (CD).

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	18 December 2017
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Belgium: 12
Country: Number of subjects enrolled	Bosnia and Herzegovina: 2
Country: Number of subjects enrolled	Bulgaria: 4
Country: Number of subjects enrolled	Canada: 63
Country: Number of subjects enrolled	Chile: 7
Country: Number of subjects enrolled	China: 1
Country: Number of subjects enrolled	Colombia: 2
Country: Number of subjects enrolled	Croatia: 7
Country: Number of subjects enrolled	Czechia: 19
Country: Number of subjects enrolled	Denmark: 14
Country: Number of subjects enrolled	Egypt: 22
Country: Number of subjects enrolled	Estonia: 1
Country: Number of subjects enrolled	France: 63
Country: Number of subjects enrolled	Germany: 26
Country: Number of subjects enrolled	Greece: 10
Country: Number of subjects enrolled	Ireland: 3
Country: Number of subjects enrolled	Israel: 14
Country: Number of subjects enrolled	Italy: 17
Country: Number of subjects enrolled	Korea, Democratic People's Republic of: 21
Country: Number of subjects enrolled	Latvia: 1

Country: Number of subjects enrolled	Spain: 15
Country: Number of subjects enrolled	Switzerland: 5
Country: Number of subjects enrolled	Taiwan: 10
Country: Number of subjects enrolled	United Kingdom: 18
Country: Number of subjects enrolled	United States: 150
Country: Number of subjects enrolled	Lithuania: 3
Country: Number of subjects enrolled	Netherlands: 5
Country: Number of subjects enrolled	New Zealand: 7
Country: Number of subjects enrolled	Poland: 9
Country: Number of subjects enrolled	Portugal: 13
Country: Number of subjects enrolled	Romania: 9
Country: Number of subjects enrolled	Russian Federation: 12
Country: Number of subjects enrolled	Serbia: 14
Country: Number of subjects enrolled	Singapore: 2
Country: Number of subjects enrolled	Slovakia: 18
Country: Number of subjects enrolled	South Africa: 4
Country: Number of subjects enrolled	Argentina: 7
Country: Number of subjects enrolled	Australia: 4
Country: Number of subjects enrolled	Austria: 3
Country: Number of subjects enrolled	Belarus: 1
Worldwide total number of subjects	618
EEA total number of subjects	252

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)	5
Adults (18-64 years)	582
From 65 to 84 years	31
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Subjects were randomized to receive 600mg risankizumab, 1200mg risankizumab or placebo during the double-blind, placebo-controlled Period 1. At Week 12, subjects who do not achieve clinical response were randomized into Period 2 to receive 180mg risankizumab, 360mg risankizumab or 1200mg risankizumab. Subjects who received placebo received 1200mg.

Pre-assignment

Screening details:

A total of 618 subjects were enrolled and 605 were included in the intent-to-treat (ITT) population; 569 of those had a baseline eligible Simple Endoscopic Score for Crohn's disease (SES-CD) of ≥ 6 (≥ 4 for isolated ileal disease) excluding the narrowing component and were included in the ITT1A population.

Period 1

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

Blinding implementation details:

All AbbVie personnel with direct oversight of the conduct and management of the trial (with the exception of AbbVie's Drug Supply Management Team) the Investigator, study site personnel and the subject remained blinded to each subject's treatment throughout the blinded period of the study.

Arms

Are arms mutually exclusive?	Yes
Arm title	Period 1 Placebo IV

Arm description:

Participants randomized to receive Placebo by intravenous (IV) infusion at Baseline, Weeks 4 and 8.

Arm type	Experimental
Investigational medicinal product name	Period 1 Placebo IV
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Participants received placebo intravenously at Baseline, Week 4 and Week 8.

Arm title	Period 1 Risankizumab 600mg IV
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Arm description:

Participants randomized to receive risankizumab 600mg by intravenous infusion at Baseline, Weeks 4 and 8.

Arm type	Experimental
Investigational medicinal product name	Period 1 Risankizumab 600mg IV
Investigational medicinal product code	ABBV-066
Other name	BI 655066, SKYRIZI
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Participants received risankizumab 600mg intravenously at Baseline, Week 4 and Week 8.

Arm title	Period 1 Risankizumab 1200mg IV
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Arm description:

Participants randomized to receive risankizumab 1200mg by intravenous infusion at Baseline, Weeks 4

and 8.

Arm type	Experimental
Investigational medicinal product name	Period 1 Risankizumab 1200mg IV
Investigational medicinal product code	ABBV-066
Other name	BI 655066, SKYRIZI
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Participants received risankizumab 1200mg intravenously at Baseline, Week 4 and Week 8.

Number of subjects in period 1	Period 1 Placebo IV	Period 1 Risankizumab 600mg IV	Period 1 Risankizumab 1200mg IV
Started	207	206	205
Completed	186	202	199
Not completed	21	4	6
Adverse event, non-fatal	9	-	4
Other, not specified	2	2	-
Lost to follow-up	2	-	-
Lack of efficacy	6	1	2
Withdrawal by subject	2	1	-

Period 2

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

Blinding implementation details:

All AbbVie personnel with direct oversight of the conduct and management of the trial (with the exception of AbbVie's Drug Supply Management Team) the Investigator, study site personnel and the subject remained blinded to each subject's treatment throughout the blinded period of the study.

Arms

Are arms mutually exclusive?	Yes
Arm title	Period 2 Risankizumab 180mg SC

Arm description:

Participants randomized to receive risankizumab 180mg by subcutaneous(SC) injection at Weeks 12 and 20.

Arm type	Experimental
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Investigational medicinal product name	Period 2 Risankizumab 180mg SC
Investigational medicinal product code	ABBV-066
Other name	BI 655066, SKYRIZI
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants received risankizumab 180mg subcutaneously at Weeks 12 and 20.

Arm title	Period 2 Risankizumab 360mg SC
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Arm description:

Participants randomized to receive risankizumab 360mg by subcutaneous injection at Weeks 12 and 20.

Arm type	Experimental
Investigational medicinal product name	Period 2 Risankizumab 360mg SC
Investigational medicinal product code	ABBV-066
Other name	BI 655066, SKYRIZI
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants received risankizumab 360mg subcutaneously at Weeks 12 and 20.

Arm title	Period 2 Risankizumab 1200mg IV
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Arm description:

Participants randomized to receive risankizumab 1200mg by intravenous infusion at Weeks 12, 16 and 20.

Arm type	Experimental
Investigational medicinal product name	Period 2 Risankizumab 1200mg IV
Investigational medicinal product code	ABBV-066
Other name	BI 655066, SKYRIZI
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Participants received risankizumab 1200mg intravenously at Weeks 12, 16, and 20.

Arm title	Period 2 Placebo/Risankizumab 1200mg IV
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Arm description:

Participants who received placebo in Induction Period 1 received 1200 mg risankizumab by intravenous infusion at Weeks 12, 16, and 20.

Arm type	Experimental
Investigational medicinal product name	Period 2 Placebo/Risankizumab 1200mg IV
Investigational medicinal product code	ABBV-066
Other name	BI 655066, SKYRIZI
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Participants who received placebo in Induction Period 1 received 1200 mg risankizumab intravenously at Weeks 12, 16, and 20.

Number of subjects in period 2^[1]	Period 2 Risankizumab 180mg SC	Period 2 Risankizumab 360mg SC	Period 2 Risankizumab 1200mg IV
Started	41	42	42
Completed	39	39	38
Not completed	2	3	4
Adverse event, non-fatal	1	1	1
Covid-19 Infection	-	-	-
Lost to follow-up	-	-	-
Missing study drug completion status	-	-	-
Lack of efficacy	1	1	1
Withdrawal by subject	-	1	2

Number of subjects in period 2^[1]	Period 2 Placebo/Risankizumab 1200mg IV
Started	86
Completed	76
Not completed	10
Adverse event, non-fatal	2
Covid-19 Infection	1
Lost to follow-up	1
Missing study drug completion status	1
Lack of efficacy	1
Withdrawal by subject	4

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: All participants who entered Induction Period 2.

Baseline characteristics

Reporting groups

Reporting group title	Period 1 Placebo IV
Reporting group description:	
Participants randomized to receive Placebo by intravenous (IV) infusion at Baseline, Weeks 4 and 8.	
Reporting group title	Period 1 Risankizumab 600mg IV
Reporting group description:	
Participants randomized to receive risankizumab 600mg by intravenous infusion at Baseline, Weeks 4 and 8.	
Reporting group title	Period 1 Risankizumab 1200mg IV
Reporting group description:	
Participants randomized to receive risankizumab 1200mg by intravenous infusion at Baseline, Weeks 4 and 8.	

Reporting group values	Period 1 Placebo IV	Period 1 Risankizumab 600mg IV	Period 1 Risankizumab 1200mg IV
Number of subjects	207	206	205
Age categorical Units: Subjects			

Age continuous Units: years arithmetic mean standard deviation	39.4 ± 13.28	40.4 ± 13.54	39.6 ± 12.85
Gender categorical Units: Subjects			
Female	104	106	99
Male	103	100	106
Ethnicity Units: Subjects			
Hispanic or Latino	22	16	15
Not Hispanic or Latino	185	190	190
Race Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	16	9	14
Black or African American	12	8	8
Native Hawaiian or Other Pacific Islander	2	0	0
White	176	189	182
More than one race	1	0	1

Reporting group values	Total		
Number of subjects	618		
Age categorical Units: Subjects			

Age continuous Units: years arithmetic mean standard deviation	-		
Gender categorical Units: Subjects			
Female	309		
Male	309		
Ethnicity Units: Subjects			
Hispanic or Latino	53		
Not Hispanic or Latino	565		
Race Units: Subjects			
American Indian or Alaska Native	0		
Asian	39		
Black or African American	28		
Native Hawaiian or Other Pacific Islander	2		
White	547		
More than one race	2		

End points

End points reporting groups

Reporting group title	Period 1 Placebo IV
Reporting group description: Participants randomized to receive Placebo by intravenous (IV) infusion at Baseline, Weeks 4 and 8.	
Reporting group title	Period 1 Risankizumab 600mg IV
Reporting group description: Participants randomized to receive risankizumab 600mg by intravenous infusion at Baseline, Weeks 4 and 8.	
Reporting group title	Period 1 Risankizumab 1200mg IV
Reporting group description: Participants randomized to receive risankizumab 1200mg by intravenous infusion at Baseline, Weeks 4 and 8.	
Reporting group title	Period 2 Risankizumab 180mg SC
Reporting group description: Participants randomized to receive risankizumab 180mg by subcutaneous(SC) injection at Weeks 12 and 20.	
Reporting group title	Period 2 Risankizumab 360mg SC
Reporting group description: Participants randomized to receive risankizumab 360mg by subcutaneous injection at Weeks 12 and 20.	
Reporting group title	Period 2 Risankizumab 1200mg IV
Reporting group description: Participants randomized to receive risankizumab 1200mg by intravenous infusion at Weeks 12, 16 and 20.	
Reporting group title	Period 2 Placebo/Risankizumab 1200mg IV
Reporting group description: Participants who received placebo in Induction Period 1 received 1200 mg risankizumab by intravenous infusion at Weeks 12, 16, and 20.	

Primary: Percentage of Participants With Clinical Remission at Week 12

End point title	Percentage of Participants With Clinical Remission at Week 12
End point description: Clinical remission is defined as using the average daily Stool Frequency (SF) ≤ 2.8 and not worse than Baseline AND average daily Abdominal Pain (AP) score ≤ 1 and not worse than Baseline. Intent to Treat 1A Population: all randomized subjects who received at least one dose of study drug during the 12-Week Induction Period, and had baseline eligible SES-CD of ≥ 6 (≥ 4 for isolated ileal disease) excluding the narrowing component.	
End point type	Primary
End point timeframe: Week 12	

End point values	Period 1 Placebo IV	Period 1 Risankizumab 600mg IV	Period 1 Risankizumab 1200mg IV	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	187	191	191	
Units: percentage of participants				
number (not applicable)	19.3	34.6	39.8	

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description: Risk difference = (risankizumab - placebo).	
Comparison groups	Period 1 Placebo IV v Period 1 Risankizumab 600mg IV
Number of subjects included in analysis	378
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference
Point estimate	15.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	6.4
upper limit	24

Statistical analysis title	Statistical Analysis 2
Statistical analysis description: Risk difference = (risankizumab - placebo).	
Comparison groups	Period 1 Risankizumab 1200mg IV v Period 1 Placebo IV
Number of subjects included in analysis	378
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference
Point estimate	20.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	11.5
upper limit	29.3

Primary: Percentage of Participants With Endoscopic Response at Week 12

End point title	Percentage of Participants With Endoscopic Response at Week 12
End point description:	
Endoscopic response was a decrease in Simplified Endoscopic Score for Crohn's Disease (SES-CD) > 50% from Baseline (or for subjects with isolated ileal disease and a Baseline SES-CD of 4, at least a 2 point reduction from Baseline).	
Intent to Treat 1A Population: all randomized subjects who received at least one dose of study drug during the 12-Week Induction Period and had baseline eligible SES-CD of ≥ 6 (≥ 4 for isolated ileal disease) excluding the narrowing component.	
End point type	Primary
End point timeframe:	
Week 12	

End point values	Period 1 Placebo IV	Period 1 Risankizumab 600mg IV	Period 1 Risankizumab 1200mg IV	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	187	191	191	
Units: percentage of participants				
number (not applicable)	11.2	28.8	34.2	

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description:	
Risk difference = (risankizumab - placebo).	
Comparison groups	Period 1 Placebo IV v Period 1 Risankizumab 600mg IV
Number of subjects included in analysis	378
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference
Point estimate	17.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	9.9
upper limit	25.4

Statistical analysis title	Statistical Analysis 2
Statistical analysis description:	
Risk difference = (risankizumab - placebo).	
Comparison groups	Period 1 Placebo IV v Period 1 Risankizumab 1200mg IV

Number of subjects included in analysis	378
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference
Point estimate	23.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	15.1
upper limit	31.1

Secondary: Percentage of Participants With Crohn's Disease Activity Index (CDAI) Clinical Remission at Week 12

End point title	Percentage of Participants With Crohn's Disease Activity Index (CDAI) Clinical Remission at Week 12
End point description:	
Crohn's Disease Activity Index (CDAI) is used to assess the symptoms of participants with Crohn's Disease. Higher CDAI scores indicate more severe disease. Clinical remission of Crohn's disease is defined as CDAI < 150.	
Intent to Treat 1A Population: all randomized subjects who received at least one dose of study drug during the 12-Week Induction Period and had baseline eligible SES-CD of ≥ 6 (≥ 4 for isolated ileal disease) excluding the narrowing component.	
End point type	Secondary
End point timeframe:	
Week 12	

End point values	Period 1 Placebo IV	Period 1 Risankizumab 600mg IV	Period 1 Risankizumab 1200mg IV	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	187	191	191	
Units: Percentage of participants				
number (not applicable)	19.8	42	40.3	

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description:	
Risk difference = (risankizumab - placebo).	
Comparison groups	Period 1 Placebo IV v Period 1 Risankizumab 600mg IV

Number of subjects included in analysis	378
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference
Point estimate	22.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	13.1
upper limit	31

Statistical analysis title	Statistical Analysis 2
Statistical analysis description: Risk difference = (risankizumab - placebo).	
Comparison groups	Period 1 Placebo IV v Period 1 Risankizumab 1200mg IV
Number of subjects included in analysis	378
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference
Point estimate	20.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	11.6
upper limit	29.5

Secondary: Percentage of Participants With Crohn's Disease Activity Index (CDAI) Clinical Response at Week 4

End point title	Percentage of Participants With Crohn's Disease Activity Index (CDAI) Clinical Response at Week 4
End point description: Crohn's Disease Activity Index (CDAI) is used to assess the symptoms of participants with Crohn's Disease. Higher CDAI scores indicate more severe disease. Clinical response is defined as reduction of CDAI \geq 100 points from baseline.	
Intent to Treat 1A Population: all randomized subjects who received at least one dose of study drug during the 12-Week Induction Period and had baseline eligible SES-CD of \geq 6 (\geq 4 for isolated ileal disease) excluding the narrowing component.	
End point type	Secondary
End point timeframe: Week 4	

End point values	Period 1 Placebo IV	Period 1 Risankizumab 600mg IV	Period 1 Risankizumab 1200mg IV	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	187	191	191	
Units: percentage of participants				
number (not applicable)	20.9	36.6	32.5	

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description: Risk difference = (risankizumab - placebo).	
Comparison groups	Period 1 Placebo IV v Period 1 Risankizumab 600mg IV
Number of subjects included in analysis	378
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference
Point estimate	15.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	6.8
upper limit	24.6

Statistical analysis title	Statistical Analysis 2
Statistical analysis description: Risk difference = (risankizumab - placebo).	
Comparison groups	Period 1 Placebo IV v Period 1 Risankizumab 1200mg IV
Number of subjects included in analysis	378
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.008
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference
Point estimate	11.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	3
upper limit	20.5

Secondary: Percentage of Participants With Clinical Remission at Week 4

End point title	Percentage of Participants With Clinical Remission at Week 4
End point description:	
Clinical remission is defined as using the average daily Stool Frequency (SF) ≤ 2.8 and not worse than Baseline AND average daily Abdominal Pain (AP) score ≤ 1 and not worse than Baseline.	
Intent to Treat 1A Population: all randomized subjects who received at least one dose of study drug during the 12-Week Induction Period and had baseline eligible SES-CD of ≥ 6 (≥ 4 for isolated ileal disease) excluding the narrowing component.	
End point type	Secondary
End point timeframe:	
Week 4	

End point values	Period 1 Placebo IV	Period 1 Risankizumab 600mg IV	Period 1 Risankizumab 1200mg IV	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	187	191	191	
Units: percentage of participants				
number (not applicable)	8	17.3	18.3	

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description:	
Risk difference = (risankizumab - placebo).	
Comparison groups	Period 1 Placebo IV v Period 1 Risankizumab 600mg IV
Number of subjects included in analysis	378
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.006
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference
Point estimate	9.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.6
upper limit	15.7

Statistical analysis title	Statistical Analysis 2
Statistical analysis description:	
Risk difference = (risankizumab - placebo).	
Comparison groups	Period 1 Placebo IV v Period 1 Risankizumab 1200mg IV

Number of subjects included in analysis	378
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.002
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference
Point estimate	10.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.7
upper limit	16.8

Secondary: Percentage of Participants With Crohn's Disease Activity Index (CDAI) Clinical Response at Week 12

End point title	Percentage of Participants With Crohn's Disease Activity Index (CDAI) Clinical Response at Week 12
End point description:	
Crohn's Disease Activity Index (CDAI) is used to assess the symptoms of participants with Crohn's Disease. Higher CDAI scores indicate more severe disease. Clinical response is defined as reduction of CDAI \geq 100 points from baseline.	
Intent to Treat 1A Population: all randomized subjects who received at least one dose of study drug during the 12-Week Induction Period and had baseline eligible SES-CD of \geq 6 (\geq 4 for isolated ileal disease) excluding the narrowing component.	
End point type	Secondary
End point timeframe:	
Week 12	

End point values	Period 1 Placebo IV	Period 1 Risankizumab 600mg IV	Period 1 Risankizumab 1200mg IV	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	187	191	191	
Units: percentage of participants				
number (not applicable)	30	59.5	60.7	

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description:	
Risk difference = (risankizumab - placebo).	
Comparison groups	Period 1 Placebo IV v Period 1 Risankizumab 600mg IV

Number of subjects included in analysis	378
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference
Point estimate	29.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	19.9
upper limit	39

Statistical analysis title	Statistical Analysis 2
Statistical analysis description: Risk difference = (risankizumab - placebo).	
Comparison groups	Period 1 Placebo IV v Period 1 Risankizumab 1200mg IV
Number of subjects included in analysis	378
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference
Point estimate	30.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	21.1
upper limit	40.1

Secondary: Change From Baseline of Induction in Functional Assessment of Chronic Illness Therapy (FACIT)-Fatigue at Week 12

End point title	Change From Baseline of Induction in Functional Assessment of Chronic Illness Therapy (FACIT)-Fatigue at Week 12
End point description: The FACIT-Fatigue scale is a 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.	
Intent to Treat 1A Population: all randomized subjects who received at least one dose of study drug during the 12-Week Induction Period and had baseline eligible SES-CD of ≥ 6 (≥ 4 for isolated ileal disease) excluding the narrowing component.	
End point type	Secondary
End point timeframe: Week 12	

End point values	Period 1 Placebo IV	Period 1 Risankizumab 600mg IV	Period 1 Risankizumab 1200mg IV	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	144	168	172	
Units: Units on a scale				
least squares mean (standard error)	7.7 (\pm 0.87)	10.5 (\pm 0.81)	10.8 (\pm 0.81)	

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description: Mean difference = (risankizumab - placebo).	
Comparison groups	Period 1 Placebo IV v Period 1 Risankizumab 600mg IV
Number of subjects included in analysis	312
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.02
Method	Mixed-Effect Model Repeat Measurement
Parameter estimate	LS Mean
Point estimate	2.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.4
upper limit	5.1

Statistical analysis title	Statistical Analysis 2
Statistical analysis description: Mean difference = (risankizumab - placebo).	
Comparison groups	Period 1 Placebo IV v Period 1 Risankizumab 1200mg IV
Number of subjects included in analysis	316
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.01
Method	Mixed-Effect Model Repeat Measurement
Parameter estimate	LS Mean
Point estimate	3
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.7
upper limit	5.3

Secondary: Change from baseline in Inflammatory Bowel Disease Questionnaire (IBDQ) total score at Week 12

End point title	Change from baseline in Inflammatory Bowel Disease Questionnaire (IBDQ) total score at Week 12
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End point description:

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.

Intent to Treat 1A Population: all randomized subjects who received at least one dose of study drug during the 12-Week Induction Period and had baseline eligible SES-CD of ≥ 6 (≥ 4 for isolated ileal disease) excluding the narrowing component.

End point type	Secondary
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End point timeframe:

Week 12

End point values	Period 1 Placebo IV	Period 1 Risankizumab 600mg IV	Period 1 Risankizumab 1200mg IV	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	144	168	172	
Units: Units on a Scale				
least squares mean (standard error)	27.2 (\pm 2.76)	39.6 (\pm 2.60)	42.2 (\pm 2.60)	

Statistical analyses

Statistical analysis title	Statistical Analysis 1
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Statistical analysis description:

Mean difference = (risankizumab - placebo).

Comparison groups	Period 1 Placebo IV v Period 1 Risankizumab 600mg IV
Number of subjects included in analysis	312
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.001
Method	Mixed-Effect Model Repeat Measurement
Parameter estimate	LS Mean
Point estimate	12.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	5
upper limit	19.8

Statistical analysis title	Statistical Analysis 2
Statistical analysis description: Mean difference = (risankizumab - placebo).	
Comparison groups	Period 1 Risankizumab 1200mg IV v Period 1 Placebo IV
Number of subjects included in analysis	316
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed-Effect Model Repeat Measurement
Parameter estimate	LS Mean
Point estimate	15
Confidence interval	
level	95 %
sides	2-sided
lower limit	7.7
upper limit	22.4

Secondary: Percentage of Participants With Enhanced Clinical Response and Endoscopic Response at Week 12

End point title	Percentage of Participants With Enhanced Clinical Response and Endoscopic Response at Week 12
End point description: Enhanced clinical response was defined as $\geq 60\%$ decrease in average daily Stool Frequency and/or $\geq 35\%$ decrease in average daily Abdominal Pain score and both not worse than baseline, and/or clinical remission. Endoscopic Response was defined as a decrease in Simplified Endoscopic Score for Crohn's Disease (SES-CD) $> 50\%$ from Baseline (or for subjects with isolated ileal disease and a Baseline SES-CD of 4, at least a 2 point reduction from Baseline).	
Intent to Treat 1A Population: all randomized subjects who received at least one dose of study drug during the 12-Week Induction Period and had baseline eligible SES-CD of ≥ 6 (≥ 4 for isolated ileal disease) excluding the narrowing component.	
End point type	Secondary
End point timeframe: Week 12	

End point values	Period 1 Placebo IV	Period 1 Risankizumab 600mg IV	Period 1 Risankizumab 1200mg IV	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	187	191	191	
Units: percentage of participants				
number (not applicable)	7	21	24.1	

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description: Risk difference = (risankizumab - placebo).	
Comparison groups	Period 1 Placebo IV v Period 1 Risankizumab 600mg IV
Number of subjects included in analysis	378
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference
Point estimate	13.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	7.1
upper limit	20.7

Statistical analysis title	Statistical Analysis 2
Statistical analysis description: Risk difference = (risankizumab - placebo).	
Comparison groups	Period 1 Placebo IV v Period 1 Risankizumab 1200mg IV
Number of subjects included in analysis	378
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference
Point estimate	17.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	10.3
upper limit	24.2

Secondary: Percentage of Participants With Endoscopic Remission at Week 12

End point title	Percentage of Participants With Endoscopic Remission at Week 12
End point description: Endoscopic remission was defined as SES-CD ≤ 4 and at least a 2-point reduction versus baseline and no subscore greater than 1 in any individual variable. Intent to Treat 1A Population: all randomized subjects who received at least one dose of study drug during the 12-Week Induction Period and had baseline eligible SES-CD of ≥ 6 (≥ 4 for isolated ileal disease) excluding the narrowing component.	
End point type	Secondary

End point timeframe:

Week 12

End point values	Period 1 Placebo IV	Period 1 Risankizumab 600mg IV	Period 1 Risankizumab 1200mg IV	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	187	191	191	
Units: percentage of participants				
number (not applicable)	4.3	19.4	20.4	

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description: Risk difference = (risankizumab - placebo).	
Comparison groups	Period 1 Placebo IV v Period 1 Risankizumab 600mg IV
Number of subjects included in analysis	378
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference
Point estimate	15
Confidence interval	
level	95 %
sides	2-sided
lower limit	8.9
upper limit	21.2

Statistical analysis title	Statistical Analysis 2
Statistical analysis description: Risk difference = (risankizumab - placebo).	
Comparison groups	Period 1 Placebo IV v Period 1 Risankizumab 1200mg IV
Number of subjects included in analysis	378
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference
Point estimate	16.2

Confidence interval	
level	95 %
sides	2-sided
lower limit	9.9
upper limit	22.4

Secondary: Percentage of Participants With Enhanced Clinical Response at Week 4

End point title	Percentage of Participants With Enhanced Clinical Response at Week 4
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End point description:

Enhanced clinical response was defined as $\geq 60\%$ decrease in average daily Stool Frequency and/or $\geq 35\%$ decrease in average daily Abdominal Pain score and both not worse than baseline, and/or clinical remission.

Intent to Treat 1A Population: all randomized subjects who received at least one dose of study drug during the 12-Week Induction Period and had baseline eligible SES-CD of ≥ 6 (≥ 4 for isolated ileal disease) excluding the narrowing component.

End point type	Secondary
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End point timeframe:

Week 4

End point values	Period 1 Placebo IV	Period 1 Risankizumab 600mg IV	Period 1 Risankizumab 1200mg IV	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	187	191	191	
Units: percentage of participants				
number (not applicable)	31.6	45	38.7	

Statistical analyses

Statistical analysis title	Statistical Analysis 1
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Statistical analysis description:

Risk difference = (risankizumab - placebo).

Comparison groups	Period 1 Placebo IV v Period 1 Risankizumab 600mg IV
Number of subjects included in analysis	378
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.006
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference
Point estimate	13.6

Confidence interval	
level	95 %
sides	2-sided
lower limit	4
upper limit	23.3

Statistical analysis title	Statistical Analysis 2
Statistical analysis description: Risk difference = (risankizumab - placebo).	
Comparison groups	Period 1 Placebo IV v Period 1 Risankizumab 1200mg IV
Number of subjects included in analysis	378
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.142
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference
Point estimate	7.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.4
upper limit	16.6

Secondary: Percentage of Participants With Ulcer-Free Endoscopy at Week 12

End point title	Percentage of Participants With Ulcer-Free Endoscopy at Week 12
End point description: Ulcer-free endoscopy was defined as SES-CD ulcerated surface subscore of 0 in subjects with SES-CD ulcerated surface subscore ≥ 1 at baseline. Intent to Treat 1A Population: all randomized subjects who received at least one dose of study drug during the 12-Week Induction Period and had baseline eligible SES-CD of ≥ 6 (≥ 4 for isolated ileal disease) excluding the narrowing component.	
End point type	Secondary
End point timeframe: Week 12	

End point values	Period 1 Placebo IV	Period 1 Risankizumab 600mg IV	Period 1 Risankizumab 1200mg IV	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	186	190	189	
Units: percentage of participants				
number (not applicable)	4.3	13.8	15.4	

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description: Risk difference = (risankizumab - placebo).	
Comparison groups	Period 1 Placebo IV v Period 1 Risankizumab 600mg IV
Number of subjects included in analysis	376
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference
Point estimate	9.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.8
upper limit	15.1

Statistical analysis title	Statistical Analysis 2
Statistical analysis description: Risk difference = (risankizumab - placebo).	
Comparison groups	Period 1 Placebo IV v Period 1 Risankizumab 1200mg IV
Number of subjects included in analysis	375
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference
Point estimate	11.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	5.3
upper limit	17

Secondary: Percentage of Participants With Enhanced Clinical Response at Week 12

End point title	Percentage of Participants With Enhanced Clinical Response at Week 12
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End point description:

Enhanced clinical response was defined as $\geq 60\%$ decrease in average daily Stool Frequency and/or $\geq 35\%$ decrease in average daily Abdominal Pain score and both not worse than baseline, and/or clinical remission.

Intent to Treat 1A Population: all randomized subjects who received at least one dose of study drug during the 12-Week Induction Period, and had baseline eligible SES-CD of ≥ 6 (≥ 4 for isolated ileal disease) excluding the narrowing component.

End point type	Secondary
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End point timeframe:

Week 12

End point values	Period 1 Placebo IV	Period 1 Risankizumab 600mg IV	Period 1 Risankizumab 1200mg IV	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	187	191	191	
Units: percentage of participants				
number (not applicable)	39.1	61.8	59.2	

Statistical analyses

Statistical analysis title	Statistical Analysis 1
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Statistical analysis description:

Risk difference = (risankizumab - placebo).

Comparison groups	Period 1 Placebo IV v Period 1 Risankizumab 600mg IV
Number of subjects included in analysis	378
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference
Point estimate	22.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	13
upper limit	32.5

Statistical analysis title	Statistical Analysis 2
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Statistical analysis description:

Risk difference = (risankizumab - placebo).

Comparison groups	Period 1 Placebo IV v Period 1 Risankizumab 1200mg IV
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Number of subjects included in analysis	378
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference
Point estimate	20
Confidence interval	
level	95 %
sides	2-sided
lower limit	10.2
upper limit	29.9

Secondary: Percentage of Participants With Resolution of Extra-Intestinal Manifestations (EIMs) at Week 12, in Participants With EIMs at Baseline

End point title	Percentage of Participants With Resolution of Extra-Intestinal Manifestations (EIMs) at Week 12, in Participants With EIMs at Baseline
End point description:	
Manifestations of Crohn's disease in areas of the body other than the digestive tract, including eyes, skin, joints, mouth, and liver.	
Intent to Treat 1A Population: all randomized subjects who received at least one dose of study drug during the 12-Week Induction Period and had baseline eligible SES-CD of ≥ 6 (≥ 4 for isolated ileal disease) excluding the narrowing component.	
End point type	Secondary
End point timeframe:	
Week 12	

End point values	Period 1 Placebo IV	Period 1 Risankizumab 600mg IV	Period 1 Risankizumab 1200mg IV	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	97	100	97	
Units: percentage of participants				
number (not applicable)	23.7	29.5	37.1	

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description:	
Risk difference = (risankizumab - placebo).	
Comparison groups	Period 1 Placebo IV v Period 1 Risankizumab 600mg IV

Number of subjects included in analysis	197
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.377
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference
Point estimate	5.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.8
upper limit	17.9

Statistical analysis title	Statistical Analysis 2
Statistical analysis description:	
Risk difference = (risankizumab - placebo).	
Comparison groups	Period 1 Placebo IV v Period 1 Risankizumab 1200mg IV
Number of subjects included in analysis	194
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.039
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference
Point estimate	13.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.7
upper limit	26.1

Secondary: Percentage of Participants With CD-Related Hospitalization through Week 12

End point title	Percentage of Participants With CD-Related Hospitalization through Week 12
End point description:	
Participants with at least one admission to the hospital due to Crohn's Disease.	
Intent to Treat 1A Population: all randomized subjects who received at least one dose of study drug during the 12-Week Induction Period and had baseline eligible SES-CD of ≥ 6 (≥ 4 for isolated ileal disease) excluding the narrowing component.	
End point type	Secondary
End point timeframe:	
Week 12	

End point values	Period 1 Placebo IV	Period 1 Risankizumab 600mg IV	Period 1 Risankizumab 1200mg IV	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	187	191	191	
Units: percentage of participants				
number (not applicable)	11.2	3.1	2.1	

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description: Risk difference = (risankizumab - placebo).	
Comparison groups	Period 1 Risankizumab 600mg IV v Period 1 Placebo IV
Number of subjects included in analysis	378
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.002
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference
Point estimate	-8.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-13.2
upper limit	-2.9

Statistical analysis title	Statistical Analysis 2
Statistical analysis description: Risk difference = (risankizumab - placebo).	
Comparison groups	Period 1 Placebo IV v Period 1 Risankizumab 1200mg IV
Number of subjects included in analysis	378
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference
Point estimate	-9.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-14.1
upper limit	-4.2

Secondary: Percentage of Participants Without Draining Fistulas at Week 12 in

Participants With Draining Fistulas at Baseline

End point title	Percentage of Participants Without Draining Fistulas at Week 12 in Participants With Draining Fistulas at Baseline
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End point description:

Participants without draining fistulas at Week 12 in participants who had draining fistulas at baseline.

Intent to Treat 1A Population: all randomized subjects who received at least one dose of study drug during the 12-Week Induction Period and had baseline eligible SES-CD of ≥ 6 (≥ 4 for isolated ileal disease) excluding the narrowing component.

End point type	Secondary
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End point timeframe:

Week 12

End point values	Period 1 Placebo IV	Period 1 Risankizumab 600mg IV	Period 1 Risankizumab 1200mg IV	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	15	14	16	
Units: percentage of participants				
number (not applicable)	13.3	7.1	43.8	

Statistical analyses

Statistical analysis title	Statistical Analysis 1
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Statistical analysis description:

Risk difference = (risankizumab - placebo).

Comparison groups	Period 1 Placebo IV v Period 1 Risankizumab 600mg IV
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Number of subjects included in analysis	29
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Analysis specification	Pre-specified
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Analysis type	superiority
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P-value	= 1
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Method	Cochran-Mantel-Haenszel
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Parameter estimate	Adjusted risk difference
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Point estimate	-6.2
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Confidence interval

level	95 %
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sides	2-sided
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lower limit	-28.1
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upper limit	15.7
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Statistical analysis title	Statistical Analysis 2
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Statistical analysis description:

Risk difference = (risankizumab - placebo).

Comparison groups	Period 1 Placebo IV v Period 1 Risankizumab 1200mg IV
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Number of subjects included in analysis	31
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.113
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference
Point estimate	30.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.6
upper limit	60.2

Secondary: Change from baseline in Work Productivity and Impairment Questionnaire – Crohn's disease (WPAI-CD) Overall Work Impairment at Week 12

End point title	Change from baseline in Work Productivity and Impairment Questionnaire – Crohn's disease (WPAI-CD) Overall Work Impairment at Week 12
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End point description:

WPAI: CD is a questionnaire used to evaluate lost productivity due to CD ; scores are presented as percentages (multiplying the scores by 100), with 0% representing no impact on productivity and 100% representing complete impact on productivity. Total work productivity impairment takes into account both hours missed due to CD symptoms and the patient's assessment of the degree to which CD affected their productivity while working (overall work impairment [OWI]). WPAI outcomes are expressed as impairment percentages, with higher numbers indicating greater impairment and less productivity.

Intent to Treat 1A Population: all randomized subjects who received at least one dose of study drug during the 12-Week Induction Period and had baseline eligible SES-CD of ≥ 6 (≥ 4 for isolated ileal disease) excluding the narrowing component.

End point type	Secondary
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End point timeframe:

Week 12

End point values	Period 1 Placebo IV	Period 1 Risankizumab 600mg IV	Period 1 Risankizumab 1200mg IV	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	68	73	86	
Units: units on a scale				
least squares mean (standard error)	-12.253 (\pm 3.3683)	-19.576 (\pm 3.2747)	-21.013 (\pm 3.0074)	

Statistical analyses

Statistical analysis title	Statistical Analysis 1
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Statistical analysis description:

Mean difference = (risankizumab - placebo).

Comparison groups	Period 1 Placebo IV v Period 1 Risankizumab 600mg IV
Number of subjects included in analysis	141
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.113
Method	Mixed-Effect Model Repeat Measurement
Parameter estimate	LS Mean
Point estimate	-7.323
Confidence interval	
level	95 %
sides	2-sided
lower limit	-16.399
upper limit	1.753

Statistical analysis title	Statistical Analysis 2
Statistical analysis description: Mean difference = (risankizumab - placebo).	
Comparison groups	Period 1 Placebo IV v Period 1 Risankizumab 1200mg IV
Number of subjects included in analysis	154
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.05
Method	Mixed-Effect Model Repeat Measurement
Parameter estimate	LS Mean
Point estimate	-8.759
Confidence interval	
level	95 %
sides	2-sided
lower limit	-17.518
upper limit	-0.001

Secondary: Change from baseline in Short Form-36 (SF-36) Physical Component Summary (PCS) score at Week 12

End point title	Change from baseline in Short Form-36 (SF-36) Physical Component Summary (PCS) score at Week 12
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End point description:

The Short Form-36 Health Survey determined participants' overall quality of life by assessing 1) limitations in physical functioning due to health problems; 2) limitations in usual role because of physical health problems; 3) bodily pain; 4) general health perceptions; 5) vitality; 6) limitations in social functioning because of physical or emotional problems; 7) limitations in usual role due to emotional problems; and 8) general mental health. Items 1-4 comprise the physical component of the SF-36. Scores on each item were summed and averaged (range = 0-100); a positive change from Baseline indicates improvement.

Intent to Treat 1A Population: all randomized subjects who received at least one dose of study drug during the 12-Week Induction Period and had baseline eligible SES-CD of ≥ 6 (≥ 4 for isolated ileal disease) excluding the narrowing component.

End point type	Secondary
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End point timeframe:

Week 12

End point values	Period 1 Placebo IV	Period 1 Risankizumab 600mg IV	Period 1 Risankizumab 1200mg IV	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	142	167	172	
Units: units on a Scale				
least squares mean (standard error)	5.237 (\pm 0.6166)	7.458 (\pm 0.5767)	7.951 (\pm 0.5749)	

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Period 1 Placebo IV v Period 1 Risankizumab 600mg IV
Number of subjects included in analysis	309
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.008
Method	Mixed-Effect Model Repeat Measurement
Parameter estimate	LS Mean
Point estimate	2.221
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.577
upper limit	3.865

Statistical analysis title	Statistical Analysis 2
Comparison groups	Period 1 Placebo IV v Period 1 Risankizumab 1200mg IV
Number of subjects included in analysis	314
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.001
Method	Mixed-Effect Model Repeat Measurement
Parameter estimate	LS Mean
Point estimate	2.714
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.077
upper limit	4.351

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From first dose of study drug until 140 days following last dose of study drug.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	23.1
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Reporting groups

Reporting group title	Period 1 Placebo IV
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Reporting group description:

Participants randomized to receive Placebo intravenous by intravenous infusion at Baseline, Weeks 4 and 8.

Reporting group title	Period 1 Risankizumab 1200mg IV
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Reporting group description:

Participants randomized to receive risankizumab 1200mg by intravenous infusion at Baseline, Weeks 4 and 8.

Reporting group title	Period 1 Risankizumab total
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Reporting group description: -

Reporting group title	Period 1 Risankizumab 600mg IV
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Reporting group description:

Participants randomized to receive risankizumab 600mg by intravenous infusion at Baseline, Weeks 4 and 8.

Reporting group title	Period 2 Risankizumab 180mg SC
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Reporting group description:

Participants randomized to receive risankizumab 180mg by subcutaneous injection at Weeks 12 and 20.

Reporting group title	Period 2 Risankizumab 360mg SC
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Reporting group description:

Participants randomized to receive risankizumab 360mg by subcutaneous injection at Weeks 12 and 20.

Reporting group title	Period 2 Risankizumab 1200mg IV
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Reporting group description:

Participants received risankizumab 1200mg by intravenous infusion at Weeks 12, 16, and 20.

Reporting group title	Period 2 Placebo/Risankizumab 1200mg IV
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Reporting group description:

Participants who received placebo in Induction Period 1 received 1200 mg risankizumab by intravenous infusion at Weeks 12, 16, and 20.

Reporting group title	Period 2 Risankizumab total
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Reporting group description: -

Serious adverse events	Period 1 Placebo IV	Period 1 Risankizumab 1200mg IV	Period 1 Risankizumab total
Total subjects affected by serious adverse events			
subjects affected / exposed	26 / 207 (12.56%)	9 / 205 (4.39%)	19 / 411 (4.62%)
number of deaths (all causes)	0	2	2
number of deaths resulting from adverse events	0	1	1

Neoplasms benign, malignant and unspecified (incl cysts and polyps) SQUAMOUS CELL CARCINOMA OF LUNG			
subjects affected / exposed	0 / 207 (0.00%)	1 / 205 (0.49%)	1 / 411 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders LERICHE SYNDROME			
subjects affected / exposed	0 / 207 (0.00%)	1 / 205 (0.49%)	1 / 411 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures INCISIONAL HERNIA REPAIR			
subjects affected / exposed	0 / 207 (0.00%)	1 / 205 (0.49%)	1 / 411 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pregnancy, puerperium and perinatal conditions ABORTION SPONTANEOUS			
subjects affected / exposed	0 / 207 (0.00%)	0 / 205 (0.00%)	0 / 411 (0.00%)
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	1 / 207 (0.48%)	1 / 205 (0.49%)	1 / 411 (0.24%)
occurrences causally related to treatment / all	1 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders ACUTE RESPIRATORY FAILURE			
subjects affected / exposed	0 / 207 (0.00%)	1 / 205 (0.49%)	1 / 411 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 1
PULMONARY EMBOLISM			

subjects affected / exposed	0 / 207 (0.00%)	1 / 205 (0.49%)	1 / 411 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
ANASTOMOTIC LEAK			
subjects affected / exposed	0 / 207 (0.00%)	0 / 205 (0.00%)	0 / 411 (0.00%)
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 HAEMORRHAGE			
subjects affected / exposed	0 / 207 (0.00%)	0 / 205 (0.00%)	0 / 411 (0.00%)
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			
ATRIAL FLUTTER			
subjects affected / exposed	0 / 207 (0.00%)	0 / 205 (0.00%)	1 / 411 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
ANAEMIA			
subjects affected / exposed	0 / 207 (0.00%)	2 / 205 (0.98%)	4 / 411 (0.97%)
occurrences causally related to treatment / all	0 / 0	2 / 2	2 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BONE MARROW FAILURE			
subjects affected / exposed	1 / 207 (0.48%)	0 / 205 (0.00%)	0 / 411 (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
MYELOSUPPRESSION			
subjects affected / exposed	1 / 207 (0.48%)	0 / 205 (0.00%)	0 / 411 (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
Gastrointestinal disorders			
ABDOMINAL PAIN			

subjects affected / exposed	1 / 207 (0.48%)	0 / 205 (0.00%)	0 / 411 (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
ANAL FISTULA			
subjects affected / exposed	0 / 207 (0.00%)	0 / 205 (0.00%)	1 / 411 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ANAL SPHINCTER ATONY			
subjects affected / exposed	1 / 207 (0.48%)	0 / 205 (0.00%)	0 / 411 (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
ANAL STENOSIS			
subjects affected / exposed	0 / 207 (0.00%)	0 / 205 (0.00%)	0 / 411 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ANORECTAL DISORDER			
subjects affected / exposed	1 / 207 (0.48%)	0 / 205 (0.00%)	0 / 411 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CROHN'S DISEASE			
subjects affected / exposed	20 / 207 (9.66%)	1 / 205 (0.49%)	2 / 411 (0.49%)
occurrences causally related to treatment / all	3 / 22	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DYSBIOSIS			
subjects affected / exposed	1 / 207 (0.48%)	0 / 205 (0.00%)	0 / 411 (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
HAEMATOCHYZIA			
subjects affected / exposed	0 / 207 (0.00%)	0 / 205 (0.00%)	1 / 411 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ILEAL STENOSIS			

subjects affected / exposed	1 / 207 (0.48%)	0 / 205 (0.00%)	0 / 411 (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
ILEUS			
subjects affected / exposed	0 / 207 (0.00%)	0 / 205 (0.00%)	1 / 411 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ILEUS PARALYTIC			
subjects affected / exposed	1 / 207 (0.48%)	0 / 205 (0.00%)	0 / 411 (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
INTESTINAL OBSTRUCTION			
subjects affected / exposed	0 / 207 (0.00%)	0 / 205 (0.00%)	0 / 411 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
JEJUNAL STENOSIS			
subjects affected / exposed	0 / 207 (0.00%)	0 / 205 (0.00%)	0 / 411 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
NAUSEA			
subjects affected / exposed	1 / 207 (0.48%)	0 / 205 (0.00%)	0 / 411 (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
SMALL INTESTINAL OBSTRUCTION			
subjects affected / exposed	2 / 207 (0.97%)	0 / 205 (0.00%)	1 / 411 (0.24%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
UMBILICAL HERNIA			
subjects affected / exposed	0 / 207 (0.00%)	0 / 205 (0.00%)	0 / 411 (0.00%)
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			
BILE DUCT STENOSIS			

subjects affected / exposed	0 / 207 (0.00%)	0 / 205 (0.00%)	1 / 411 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
ACUTE KIDNEY INJURY			
subjects affected / exposed	1 / 207 (0.48%)	0 / 205 (0.00%)	0 / 411 (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
CALCULUS URINARY			
subjects affected / exposed	1 / 207 (0.48%)	0 / 205 (0.00%)	0 / 411 (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
NEPHROLITHIASIS			
subjects affected / exposed	0 / 207 (0.00%)	1 / 205 (0.49%)	1 / 411 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
ARTHRALGIA			
subjects affected / exposed	1 / 207 (0.48%)	0 / 205 (0.00%)	0 / 411 (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
INTERVERTEBRAL DISC PROTRUSION			
subjects affected / exposed	0 / 207 (0.00%)	0 / 205 (0.00%)	1 / 411 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
ABDOMINAL ABSCESS			
subjects affected / exposed	1 / 207 (0.48%)	0 / 205 (0.00%)	0 / 411 (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
ANAL ABSCESS			

subjects affected / exposed	0 / 207 (0.00%)	0 / 205 (0.00%)	0 / 411 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BRONCHOPULMONARY ASPERGILLOSIS			
subjects affected / exposed	0 / 207 (0.00%)	0 / 205 (0.00%)	0 / 411 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CELLULITIS OF MALE EXTERNAL GENITAL ORGAN			
subjects affected / exposed	1 / 207 (0.48%)	0 / 205 (0.00%)	0 / 411 (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
CYTOMEGALOVIRUS INFECTION			
subjects affected / exposed	0 / 207 (0.00%)	0 / 205 (0.00%)	0 / 411 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GASTROENTERITIS ESCHERICHIA COLI			
subjects affected / exposed	0 / 207 (0.00%)	1 / 205 (0.49%)	1 / 411 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
NEUTROPENIC SEPSIS			
subjects affected / exposed	1 / 207 (0.48%)	0 / 205 (0.00%)	0 / 411 (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
PERIRECTAL ABSCESS			
subjects affected / exposed	1 / 207 (0.48%)	0 / 205 (0.00%)	0 / 411 (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
PNEUMONIA STAPHYLOCOCCAL			
subjects affected / exposed	0 / 207 (0.00%)	0 / 205 (0.00%)	0 / 411 (0.00%)
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	1 / 207 (0.48%)	1 / 205 (0.49%)	1 / 411 (0.24%)
occurrences causally related to treatment / all	1 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
VIRAL MYOCARDITIS			
subjects affected / exposed	1 / 207 (0.48%)	0 / 205 (0.00%)	0 / 411 (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
VIRAL PHARYNGITIS			
subjects affected / exposed	0 / 207 (0.00%)	0 / 205 (0.00%)	1 / 411 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
CACHEXIA			
subjects affected / exposed	1 / 207 (0.48%)	0 / 205 (0.00%)	0 / 411 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Period 1 Risankizumab 600mg IV	Period 2 Risankizumab 180mg SC	Period 2 Risankizumab 360mg SC
Total subjects affected by serious adverse events			
subjects affected / exposed	10 / 206 (4.85%)	2 / 41 (4.88%)	2 / 42 (4.76%)
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)			
SQUAMOUS CELL CARCINOMA OF LUNG			
subjects affected / exposed	0 / 206 (0.00%)	0 / 41 (0.00%)	0 / 42 (0.00%)
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			
LERICHE SYNDROME			
subjects affected / exposed	0 / 206 (0.00%)	0 / 41 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
INCISIONAL HERNIA REPAIR			

subjects affected / exposed	0 / 206 (0.00%)	0 / 41 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pregnancy, puerperium and perinatal conditions			
ABORTION SPONTANEOUS			
subjects affected / exposed	0 / 206 (0.00%)	0 / 41 (0.00%)	1 / 42 (2.38%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
PYREXIA			
subjects affected / exposed	0 / 206 (0.00%)	1 / 41 (2.44%)	0 / 42 (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
Respiratory, thoracic and mediastinal disorders			
ACUTE RESPIRATORY FAILURE			
subjects affected / exposed	0 / 206 (0.00%)	0 / 41 (0.00%)	0 / 42 (0.00%)
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 / 206 (0.00%)	0 / 41 (0.00%)	0 / 42 (0.00%)
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			
ANASTOMOTIC LEAK			
subjects affected / exposed	0 / 206 (0.00%)	0 / 41 (0.00%)	0 / 42 (0.00%)
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 HAEMORRHAGE			
subjects affected / exposed	0 / 206 (0.00%)	0 / 41 (0.00%)	0 / 42 (0.00%)
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			
ATRIAL FLUTTER			

subjects affected / exposed	1 / 206 (0.49%)	0 / 41 (0.00%)	0 / 42 (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
Blood and lymphatic system disorders			
ANAEMIA			
subjects affected / exposed	2 / 206 (0.97%)	0 / 41 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BONE MARROW FAILURE			
subjects affected / exposed	0 / 206 (0.00%)	0 / 41 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MYELOSUPPRESSION			
subjects affected / exposed	0 / 206 (0.00%)	0 / 41 (0.00%)	0 / 42 (0.00%)
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			
ABDOMINAL PAIN			
subjects affected / exposed	0 / 206 (0.00%)	2 / 41 (4.88%)	0 / 42 (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
ANAL FISTULA			
subjects affected / exposed	1 / 206 (0.49%)	0 / 41 (0.00%)	0 / 42 (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 SPHINCTER ATONY			
subjects affected / exposed	0 / 206 (0.00%)	0 / 41 (0.00%)	0 / 42 (0.00%)
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 STENOSIS			
subjects affected / exposed	0 / 206 (0.00%)	0 / 41 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ANORECTAL DISORDER			

subjects affected / exposed	0 / 206 (0.00%)	0 / 41 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CROHN'S DISEASE			
subjects affected / exposed	1 / 206 (0.49%)	0 / 41 (0.00%)	0 / 42 (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
DYSBIOSIS			
subjects affected / exposed	0 / 206 (0.00%)	0 / 41 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HAEMATOCHESIA			
subjects affected / exposed	1 / 206 (0.49%)	0 / 41 (0.00%)	0 / 42 (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
ILEAL STENOSIS			
subjects affected / exposed	0 / 206 (0.00%)	0 / 41 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ILEUS			
subjects affected / exposed	1 / 206 (0.49%)	0 / 41 (0.00%)	0 / 42 (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
ILEUS PARALYTIC			
subjects affected / exposed	0 / 206 (0.00%)	0 / 41 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INTESTINAL OBSTRUCTION			
subjects affected / exposed	0 / 206 (0.00%)	0 / 41 (0.00%)	1 / 42 (2.38%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
JEJUNAL STENOSIS			

subjects affected / exposed	0 / 206 (0.00%)	0 / 41 (0.00%)	0 / 42 (0.00%)
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 / 206 (0.00%)	1 / 41 (2.44%)	0 / 42 (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
SMALL INTESTINAL OBSTRUCTION			
subjects affected / exposed	1 / 206 (0.49%)	0 / 41 (0.00%)	0 / 42 (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
UMBILICAL HERNIA			
subjects affected / exposed	0 / 206 (0.00%)	0 / 41 (0.00%)	0 / 42 (0.00%)
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			
BILE DUCT STENOSIS			
subjects affected / exposed	1 / 206 (0.49%)	0 / 41 (0.00%)	0 / 42 (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 and urinary disorders			
ACUTE KIDNEY INJURY			
subjects affected / exposed	0 / 206 (0.00%)	0 / 41 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CALCULUS URINARY			
subjects affected / exposed	0 / 206 (0.00%)	0 / 41 (0.00%)	0 / 42 (0.00%)
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 / 206 (0.00%)	0 / 41 (0.00%)	0 / 42 (0.00%)
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				
ARTHRALGIA				
subjects affected / exposed	0 / 206 (0.00%)	0 / 41 (0.00%)	0 / 42 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0	
INTERVERTEBRAL DISC PROTRUSION				
subjects affected / exposed	1 / 206 (0.49%)	0 / 41 (0.00%)	0 / 42 (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				
ABDOMINAL ABSCESS				
subjects affected / exposed	0 / 206 (0.00%)	0 / 41 (0.00%)	0 / 42 (0.00%)	
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 / 206 (0.00%)	0 / 41 (0.00%)	0 / 42 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0	
BRONCHOPULMONARY ASPERGILLOSIS				
subjects affected / exposed	0 / 206 (0.00%)	0 / 41 (0.00%)	0 / 42 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0	
CELLULITIS OF MALE EXTERNAL GENITAL ORGAN				
subjects affected / exposed	0 / 206 (0.00%)	0 / 41 (0.00%)	0 / 42 (0.00%)	
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 / 206 (0.00%)	0 / 41 (0.00%)	0 / 42 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0	
GASTROENTERITIS ESCHERICHIA COLI				

subjects affected / exposed	0 / 206 (0.00%)	0 / 41 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
NEUTROPENIC SEPSIS			
subjects affected / exposed	0 / 206 (0.00%)	0 / 41 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PERIRECTAL ABSCESS			
subjects affected / exposed	0 / 206 (0.00%)	0 / 41 (0.00%)	0 / 42 (0.00%)
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 STAPHYLOCOCCAL			
subjects affected / exposed	0 / 206 (0.00%)	0 / 41 (0.00%)	0 / 42 (0.00%)
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 / 206 (0.00%)	0 / 41 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
VIRAL MYOCARDITIS			
subjects affected / exposed	0 / 206 (0.00%)	0 / 41 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
VIRAL PHARYNGITIS			
subjects affected / exposed	1 / 206 (0.49%)	0 / 41 (0.00%)	0 / 42 (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
Metabolism and nutrition disorders			
CACHEXIA			
subjects affected / exposed	0 / 206 (0.00%)	0 / 41 (0.00%)	0 / 42 (0.00%)
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	Period 2	Period 2	Period 2
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	Risankizumab 1200mg IV	Placebo/Risankizuma b 1200mg IV	Risankizumab total
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 42 (7.14%)	9 / 86 (10.47%)	16 / 211 (7.58%)
number of deaths (all causes)	1	0	1
number of deaths resulting from adverse events	1	0	1
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
SQUAMOUS CELL CARCINOMA OF LUNG			
subjects affected / exposed	0 / 42 (0.00%)	0 / 86 (0.00%)	0 / 211 (0.00%)
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			
LERICHE SYNDROME			
subjects affected / exposed	0 / 42 (0.00%)	0 / 86 (0.00%)	0 / 211 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
INCISIONAL HERNIA REPAIR			
subjects affected / exposed	0 / 42 (0.00%)	0 / 86 (0.00%)	0 / 211 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pregnancy, puerperium and perinatal conditions			
ABORTION SPONTANEOUS			
subjects affected / exposed	0 / 42 (0.00%)	0 / 86 (0.00%)	1 / 211 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
PYREXIA			
subjects affected / exposed	0 / 42 (0.00%)	0 / 86 (0.00%)	1 / 211 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
ACUTE RESPIRATORY FAILURE			

subjects affected / exposed	0 / 42 (0.00%)	0 / 86 (0.00%)	0 / 211 (0.00%)
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 / 42 (0.00%)	0 / 86 (0.00%)	0 / 211 (0.00%)
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			
ANASTOMOTIC LEAK			
subjects affected / exposed	1 / 42 (2.38%)	0 / 86 (0.00%)	1 / 211 (0.47%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
POST PROCEDURAL HAEMORRHAGE			
subjects affected / exposed	0 / 42 (0.00%)	1 / 86 (1.16%)	1 / 211 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
ATRIAL FLUTTER			
subjects affected / exposed	0 / 42 (0.00%)	0 / 86 (0.00%)	0 / 211 (0.00%)
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 / 42 (0.00%)	1 / 86 (1.16%)	1 / 211 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BONE MARROW FAILURE			
subjects affected / exposed	0 / 42 (0.00%)	0 / 86 (0.00%)	0 / 211 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MYELOSUPPRESSION			
subjects affected / exposed	0 / 42 (0.00%)	0 / 86 (0.00%)	0 / 211 (0.00%)
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			
ABDOMINAL PAIN			
subjects affected / exposed	0 / 42 (0.00%)	0 / 86 (0.00%)	2 / 211 (0.95%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ANAL FISTULA			
subjects affected / exposed	0 / 42 (0.00%)	0 / 86 (0.00%)	0 / 211 (0.00%)
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 SPHINCTER ATONY			
subjects affected / exposed	0 / 42 (0.00%)	0 / 86 (0.00%)	0 / 211 (0.00%)
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 STENOSIS			
subjects affected / exposed	0 / 42 (0.00%)	1 / 86 (1.16%)	1 / 211 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ANORECTAL DISORDER			
subjects affected / exposed	0 / 42 (0.00%)	0 / 86 (0.00%)	0 / 211 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CROHN'S DISEASE			
subjects affected / exposed	2 / 42 (4.76%)	2 / 86 (2.33%)	4 / 211 (1.90%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DYSBIOSIS			
subjects affected / exposed	0 / 42 (0.00%)	0 / 86 (0.00%)	0 / 211 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HAEMATOCHYZIA			
subjects affected / exposed	0 / 42 (0.00%)	0 / 86 (0.00%)	0 / 211 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ILEAL STENOSIS			

subjects affected / exposed	0 / 42 (0.00%)	1 / 86 (1.16%)	1 / 211 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ILEUS			
subjects affected / exposed	0 / 42 (0.00%)	0 / 86 (0.00%)	0 / 211 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ILEUS PARALYTIC			
subjects affected / exposed	0 / 42 (0.00%)	0 / 86 (0.00%)	0 / 211 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INTESTINAL OBSTRUCTION			
subjects affected / exposed	0 / 42 (0.00%)	0 / 86 (0.00%)	1 / 211 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
JEJUNAL STENOSIS			
subjects affected / exposed	0 / 42 (0.00%)	1 / 86 (1.16%)	1 / 211 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
NAUSEA			
subjects affected / exposed	0 / 42 (0.00%)	0 / 86 (0.00%)	1 / 211 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SMALL INTESTINAL OBSTRUCTION			
subjects affected / exposed	0 / 42 (0.00%)	0 / 86 (0.00%)	0 / 211 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
UMBILICAL HERNIA			
subjects affected / exposed	0 / 42 (0.00%)	1 / 86 (1.16%)	1 / 211 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
BILE DUCT STENOSIS			

subjects affected / exposed	0 / 42 (0.00%)	0 / 86 (0.00%)	0 / 211 (0.00%)
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			
ACUTE KIDNEY INJURY			
subjects affected / exposed	0 / 42 (0.00%)	1 / 86 (1.16%)	1 / 211 (0.47%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CALCULUS URINARY			
subjects affected / exposed	0 / 42 (0.00%)	0 / 86 (0.00%)	0 / 211 (0.00%)
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 / 42 (0.00%)	0 / 86 (0.00%)	0 / 211 (0.00%)
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			
ARTHRALGIA			
subjects affected / exposed	0 / 42 (0.00%)	0 / 86 (0.00%)	0 / 211 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INTERVERTEBRAL DISC PROTRUSION			
subjects affected / exposed	0 / 42 (0.00%)	0 / 86 (0.00%)	0 / 211 (0.00%)
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			
ABDOMINAL ABSCESS			
subjects affected / exposed	0 / 42 (0.00%)	0 / 86 (0.00%)	0 / 211 (0.00%)
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 / 42 (0.00%)	1 / 86 (1.16%)	1 / 211 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BRONCHOPULMONARY ASPERGILLOSIS			
subjects affected / exposed	0 / 42 (0.00%)	1 / 86 (1.16%)	1 / 211 (0.47%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CELLULITIS OF MALE EXTERNAL GENITAL ORGAN			
subjects affected / exposed	0 / 42 (0.00%)	0 / 86 (0.00%)	0 / 211 (0.00%)
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 / 42 (0.00%)	1 / 86 (1.16%)	1 / 211 (0.47%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GASTROENTERITIS ESCHERICHIA COLI			
subjects affected / exposed	0 / 42 (0.00%)	0 / 86 (0.00%)	0 / 211 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
NEUTROPENIC SEPSIS			
subjects affected / exposed	0 / 42 (0.00%)	0 / 86 (0.00%)	0 / 211 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PERIRECTAL ABSCESS			
subjects affected / exposed	0 / 42 (0.00%)	0 / 86 (0.00%)	0 / 211 (0.00%)
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 STAPHYLOCOCCAL			
subjects affected / exposed	0 / 42 (0.00%)	1 / 86 (1.16%)	1 / 211 (0.47%)
occurrences causally related to treatment / all	0 / 0	2 / 2	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SEPSIS			

subjects affected / exposed	1 / 42 (2.38%)	0 / 86 (0.00%)	1 / 211 (0.47%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1
VIRAL MYOCARDITIS			
subjects affected / exposed	0 / 42 (0.00%)	0 / 86 (0.00%)	0 / 211 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
VIRAL PHARYNGITIS			
subjects affected / exposed	0 / 42 (0.00%)	0 / 86 (0.00%)	0 / 211 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
CACHEXIA			
subjects affected / exposed	0 / 42 (0.00%)	0 / 86 (0.00%)	0 / 211 (0.00%)
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	Period 1 Placebo IV	Period 1 Risankizumab 1200mg IV	Period 1 Risankizumab total
Total subjects affected by non-serious adverse events			
subjects affected / exposed	51 / 207 (24.64%)	32 / 205 (15.61%)	64 / 411 (15.57%)
Nervous system disorders			
HEADACHE			
subjects affected / exposed	11 / 207 (5.31%)	10 / 205 (4.88%)	21 / 411 (5.11%)
occurrences (all)	12	11	25
Blood and lymphatic system disorders			
ANAEMIA			
subjects affected / exposed	11 / 207 (5.31%)	4 / 205 (1.95%)	7 / 411 (1.70%)
occurrences (all)	12	4	7
Gastrointestinal disorders			
CROHN'S DISEASE			
subjects affected / exposed	13 / 207 (6.28%)	3 / 205 (1.46%)	10 / 411 (2.43%)
occurrences (all)	13	3	10
NAUSEA			

subjects affected / exposed occurrences (all)	10 / 207 (4.83%) 10	3 / 205 (1.46%) 4	8 / 411 (1.95%) 10
Musculoskeletal and connective tissue disorders ARTHRALGIA subjects affected / exposed occurrences (all)	8 / 207 (3.86%) 8	9 / 205 (4.39%) 10	17 / 411 (4.14%) 18
Infections and infestations NASOPHARYNGITIS subjects affected / exposed occurrences (all)	11 / 207 (5.31%) 12	8 / 205 (3.90%) 8	16 / 411 (3.89%) 16

Non-serious adverse events	Period 1 Risankizumab 600mg IV	Period 2 Risankizumab 180mg SC	Period 2 Risankizumab 360mg SC
Total subjects affected by non-serious adverse events subjects affected / exposed	32 / 206 (15.53%)	5 / 41 (12.20%)	3 / 42 (7.14%)
Nervous system disorders HEADACHE subjects affected / exposed occurrences (all)	11 / 206 (5.34%) 14	1 / 41 (2.44%) 1	1 / 42 (2.38%) 1
Blood and lymphatic system disorders ANAEMIA subjects affected / exposed occurrences (all)	3 / 206 (1.46%) 3	0 / 41 (0.00%) 0	0 / 42 (0.00%) 0
Gastrointestinal disorders CROHN'S DISEASE subjects affected / exposed occurrences (all) NAUSEA subjects affected / exposed occurrences (all)	7 / 206 (3.40%) 7 5 / 206 (2.43%) 6	1 / 41 (2.44%) 1 0 / 41 (0.00%) 0	0 / 42 (0.00%) 0 1 / 42 (2.38%) 1
Musculoskeletal and connective tissue disorders ARTHRALGIA subjects affected / exposed occurrences (all)	8 / 206 (3.88%) 8	2 / 41 (4.88%) 3	1 / 42 (2.38%) 1
Infections and infestations NASOPHARYNGITIS			

subjects affected / exposed	8 / 206 (3.88%)	1 / 41 (2.44%)	0 / 42 (0.00%)
occurrences (all)	8	1	0

Non-serious adverse events	Period 2 Risankizumab 1200mg IV	Period 2 Placebo/Risankizumab 1200mg IV	Period 2 Risankizumab total
Total subjects affected by non-serious adverse events			
subjects affected / exposed	8 / 42 (19.05%)	12 / 86 (13.95%)	28 / 211 (13.27%)
Nervous system disorders			
HEADACHE			
subjects affected / exposed	3 / 42 (7.14%)	4 / 86 (4.65%)	9 / 211 (4.27%)
occurrences (all)	3	4	9
Blood and lymphatic system disorders			
ANAEMIA			
subjects affected / exposed	0 / 42 (0.00%)	2 / 86 (2.33%)	2 / 211 (0.95%)
occurrences (all)	0	3	3
Gastrointestinal disorders			
CROHN'S DISEASE			
subjects affected / exposed	2 / 42 (4.76%)	1 / 86 (1.16%)	4 / 211 (1.90%)
occurrences (all)	2	1	4
NAUSEA			
subjects affected / exposed	3 / 42 (7.14%)	0 / 86 (0.00%)	4 / 211 (1.90%)
occurrences (all)	3	0	4
Musculoskeletal and connective tissue disorders			
ARTHRALGIA			
subjects affected / exposed	1 / 42 (2.38%)	5 / 86 (5.81%)	9 / 211 (4.27%)
occurrences (all)	1	5	10
Infections and infestations			
NASOPHARYNGITIS			
subjects affected / exposed	2 / 42 (4.76%)	2 / 86 (2.33%)	5 / 211 (2.37%)
occurrences (all)	2	2	5

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
29 March 2017	<p>Major changes included:</p> <p>Changed title to remove double-dummy and prior anti-TNF to biologic. Text changed to support removal of vedolizumab comparator from the protocol and better explanation of biopsies during endoscopy and to remove patient reported diary parameter.</p>
05 July 2017	<p>Major changes included:</p> <p>Added CDAI criteria to the inclusion criteria. Updated to instruction on which hematocrit (Hct) value to use in calculating the CDAI for inclusion. Added "psychological or psychiatric cause" to exclusion criterion 29. Updated overall study design and plan: description, of study schematic figure, to remove reference to Weeks 2 and 6. Updated discontinuation of individual subjects, for subjects who do not have clinical response at Week 12. Updated contraception recommendations, and exclusion criterion 28. Updated pregnancy, for pregnancy reporting timing. Clarified the blind-breaking process. Updated tuberculosis (TB) requirements in exclusion criteria, benefits and risks, and efficacy and safety measurements assessed and flow chart. Added assent information for subjects less than 18 years old. Clarified stratification criteria.</p>
29 September 2017	<p>Major changes included:</p> <p>Added an anaphylaxis adjudication committee. Revised to allow for local regulations for the difference in minimum age for adults. Updated exclusion criterion 18 for CD related complications. Updated prohibited medications. Added international normalized ratio (INR) and anaphylaxis testing. Added endoscopic remission to ranked secondary endpoints and Patient Global Impression of Severity (PGIS) and Patient Global Impression of Change (PGIC) to non-ranked secondary endpoints. Added clinical and endoscopic remission over time as endpoints. Updated criteria for discontinuation of individual subjects. Revised to reduce redundancy. Revised to align with common toxicity criteria for adverse events (CTCAE) grading criteria for adverse events (AE)s. Revised to allow for additional types of anaphylactic reactions and to provide investigators with guidance on reporting of events. Updated alignment with template requirements and for consistency across the risankizumab programs. Clarified sample size calculations. Updated to reflect the most recent subject diary entries and addition of patient-reported outcome (PRO) for collection. Updated the schedule of activities to reflect changes made in the body of the protocol. Added information on the sample collection schedule. Revised to align with regulatory agency feedback.</p>

09 July 2018	<p>Major changes included:</p> <p>Extension of the AE collection period duration, final follow-up call, and period for prohibition of vaccines.</p> <p>Modified benefits and risks to align with the IB.</p> <p>Added blood collection for tryptase following a suspected drug administration hypersensitivity reaction.</p> <p>Added "worsening" CD to common AEs associated with underlying disease.</p> <p>Added "intramuscular" as possible route of administration for prohibited anti-infectives.</p> <p>Exclusion of subjects who receive exclusive enteral nutrition to treat CD.</p> <p>Added height measurement for pediatric subjects.</p> <p>Prohibition of local, routine testing for fecal calprotectin (FCP) and high-sensitivity C-reactive protein.</p> <p>Modified contraception language.</p> <p>Modified statistical methods for secondary endpoints to align with regulatory feedback.</p> <p>Removed stool sample collection for FCP at screening.</p> <p>Clarified repeat screening tests and the qualifications for a screening period extension.</p> <p>Documentation of the DMC opinion to continue the trial and pediatric enrollment.</p> <p>Clarified language to allow repeat testing if screening and baseline testing were more than 14 days apart and the circumstances that would qualify for a screening period extension.</p> <p>Clarified that indeterminate tuberculosis (TB) test results must be repeated.</p>
22 February 2019	<p>Major changes included:</p> <p>Documentation of the data monitoring committee (DMC) opinion to continue the trial and enroll 16 17 year olds.</p> <p>Added language to allow single repeat testing of transient exclusionary laboratory values during the screening period.</p> <p>Clarified the types of prohibited corticosteroids.</p> <p>Modified to permit enrollment of not more than 20% subjects with prior exposure, including intolerance or inadequate response, to ustekinumab.</p> <p>Specified that enrollment of subjects with Baseline SES-CD of ≥ 3 to < 6 for ileocolonic or colonic disease or Baseline SES-CD of 3 for isolated ileal disease, excluding the narrowing component, would be no more than 10% of the total population.</p> <p>Added of stratification factor of Baseline SES-CD.</p> <p>Updated definitions of endoscopic remission and endoscopic response.</p> <p>Revised to allow a commercially available assay to determine approved biologic washout.</p> <p>Clarified that TB prophylaxis is permissible.</p> <p>Revised the order and addition of ranked secondary endpoints, update of ranked secondary endpoints to non-ranked secondary endpoints, and addition of non-ranked secondary endpoint.</p> <p>Added CTCAE version.</p> <p>Clarified timing of database lock (DBL).</p> <p>Updated statistical assumptions for sample size determination.</p> <p>Added of details of multiplicity adjustment.</p> <p>Updated the missing imputation methodology to remove last observation carried forward (LOCF).</p>

19 December 2019	<p>Major changes included:</p> <p>Specified the total N of 579 for the primary ITT population used for efficacy analysis, that number of subjects with lower SES-CD subjects will be no more than 58, and that data collected from subjects with the lower SES-CD will be analyzed as an exploratory efficacy analysis.</p> <p>Specified that Hct from the preceding visit may be used to calculate the CDAI if there are technical issues.</p> <p>Revised the definition of endoscopic remission.</p> <p>Revised the term "endoscopic healing" to "ulcer-free endoscopy".</p> <p>Updated secondary endpoint ranking and combining and adding new ranked secondary endpoints.</p> <p>Clarified timing of DBL.</p> <p>Removed the missing imputation method OC from the sensitivity analysis of the continuous efficacy variables.</p> <p>Added missing data handling methods.</p> <p>Clarified the way continuous laboratory and vital signs would be summarized.</p> <p>Removed Fisher's exact test for risankizumab treatment group differences versus placebo for AEs.</p> <p>Added "Optional Blood Sample for Biologic Drug Level."</p>
28 July 2020	<p>Major changes included:</p> <p>Revised due to the COVID-19 pandemic, including benefit and risk, criteria to exclude subjects with active COVID-19, addition of COVID-19 AE data collection process, modification of study visits/protocol-specified procedures impacted by changes in local regulations, protocol deviations, missing data, data monitoring, and COVID-19 testing.</p> <p>Added language regarding site responsibility.</p> <p>Clarified HIV results language.</p>

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported