Clinical trial results:
BI 655066/ABBV-066 (Risankizumab) versus Ustekinumab and Placebo Comparators in a Randomized Double Blind Trial for Maintenance Use in Moderate to Severe Plaque Type Psoriasis-2

Summary

EudraCT number	2015-003622-13
Trial protocol	BE DE AT PT ES PL IT
Global end of trial date	04 September 2017

Results information

Result version number	v1 (current)
This version publication date	20 September 2018
First version publication date	20 September 2018

Trial information

Trial identification

Sponsor protocol code	1311.28

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02684357
WHO universal trial number (UTN)	-
Other trial identifiers	AbbVie: M15-995

Notes:

Sponsors

Sponsor organisation name	Boehringer Ingelheim
Sponsor organisation address	Binger Strasse 173, Ingelheim am Rhein, Germany, 55216
Public contact	QRPE Processes and Systems Coordination, Clinical Trial Information Disclosure, Boehringer Ingelheim, 001 8002430127, clintriage.rdg@boehringer-ingelheim.com
Scientific contact	QRPE Processes and Systems Coordination, Clinical Trial Information Disclosure, Boehringer Ingelheim, 001 8002430127, clintriage.rdg@boehringer-ingelheim.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	17 October 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	31 December 2016
Global end of trial reached?	Yes
Global end of trial date	04 September 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objectives of this study were to assess the efficacy and safety of risankizumab, compared to ustekinumab and placebo, in subjects with moderate to severe chronic plaque psoriasis. In addition, this study was to assess pharmacokinetics (PK) and the emergence of anti-drug antibodies and their effect on efficacy and safety.

Protection of trial subjects:

Only subjects that met all the study inclusion and none of the exclusion criteria were to be entered in the study. All subjects were free to withdraw from the clinical trial at any time for any reason given. Close monitoring of all subjects was adhered to throughout the trial conduct. Rescue medication was allowed for all patients as required.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	31 March 2016
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Austria: 14
Country: Number of subjects enrolled	Belgium: 15
Country: Number of subjects enrolled	Canada: 155
Country: Number of subjects enrolled	France: 28
Country: Number of subjects enrolled	Germany: 27
Country: Number of subjects enrolled	Mexico: 22
Country: Number of subjects enrolled	Poland: 15
Country: Number of subjects enrolled	Portugal: 7
Country: Number of subjects enrolled	Spain: 30
Country: Number of subjects enrolled	United States: 264
Worldwide total number of subjects	577
EEA total number of subjects	136

Notes:

Subjects enrolled per age group

In utero	0

Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	505
From 65 to 84 years	72
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Participants were randomized to placebo, ustekinumab, or risankizumab in Part A. Participants who received placebo in Part A switched to risankizumab in Part B; participants who received ustekinumab in Part A continued ustekinumab in Part B; and participants who received risankizumab in Part A continued risankizumab in Part B.

Period 1

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

Blinding implementation details:

All participants received 2 sets of injections to maintain the blind (the placebo arm received placebo for risankizumab and placebo for ustekinumab) the risankizumab arm received risankizumab and placebo for ustekinumab and the ustekinumab arm received ustekinumab and placebo for risankizumab

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo (Part A)

Arm description:

Participants randomized to receive double-blind (DB) placebo by subcutaneous (SC) injection at Weeks 0 and 4 (Part A).

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants randomized to receive double-blind (DB) placebo by subcutaneous (SC) injection at Weeks 0 and 4
(Part A).

Arm title	Ustekinumab (Part A)

Arm description:

Participants randomized to receive double-blind (DB) ustekinumab 45 or 90 mg (based on screening weight) by subcutaneous (SC) injection at Weeks 0 and 4 (Part A).
They received 2 sets of injections to maintain the blind (ustekinumab and placebo for risankizumab)

Arm type	Active comparator
Investigational medicinal product name	Placebo for Risankizumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants randomized to receive Placebo for Risankizumab subcutaneous (SC) injection at Weeks 0 and 4 (Part A).

Investigational medicinal product name	Ustekinumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants randomized to receive double-blind (DB) ustekinumab 45 or 90 mg (based on screening weight) by subcutaneous (SC) injection at Weeks 0 and 4 (Part A).

Arm title	Risankizumab (Part A)

Arm description:

Participants randomized to receive double-blind (DB) risankizumab 150 mg by subcutaneous (SC) injection at Weeks 0 and 4 (Part A).
They received 2 sets of injections to maintain the blind (risankizumab and placebo for ustekinumab)

Arm type	Experimental
Investigational medicinal product name	Risankizumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants randomized to receive double-blind (DB) risankizumab 150 mg by subcutaneous (SC) injection at Weeks 0 and 4 (Part A).

Investigational medicinal product name	Placebo for Ustekinumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants randomized to receive Placebo for Ustekinumab subcutaneous (SC) injection at Weeks 0 and 4 (Part A).

Number of subjects in period 1[1]	Placebo (Part A)	Ustekinumab (Part A)	Risankizumab (Part A)
Started	98	99	294
Completed	94	96	292
Not completed	4	3	2
Consent withdrawn by subject	3	-	-
Not specified	-	1	-
Adverse Event (Worsening of Disease)	1	-	-
Lost to follow-up	-	2	2

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: The number of subjects starting the period 1 (Part A) have switched their treatments in period 2 (Part B)

Period 2

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

Blinding implementation details:

All participants received 2 sets of injections to maintain the blind (the placebo arm received placebo for risankizumab and placebo for ustekinumab) the risankizumab arm received risankizumab and placebo for ustekinumab and the ustekinumab arm received ustekinumab and placebo for risankizumab

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo/Risankizumab (Part B)

Arm description:

Participants randomized to receive placebo in Part A switched to risankizumab 150 mg by subcutaneous (SC) injection at Weeks 16,
28, and 40 (Part B).

Arm type	Experimental
Investigational medicinal product name	Risankizumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants randomized to receive placebo in Part A switched to risankizumab 150 mg by subcutaneous (SC) injection at Weeks 16, 28, and 40 (Part B).

Arm title	Ustekinumab/Ustekinumab (Part B)

Arm description:

Participants randomized to receive ustekinumab in Part A continued to receive ustekinumab 45 mg or 90 mg (based on screening weight) by subcutaneous (SC) injection at Weeks 16, 28, and 40 (Part B).

Arm type	Active comparator
Investigational medicinal product name	Ustekinumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants randomized to receive ustekinumab in Part A continued to receive ustekinumab 45 mg or 90 mg(based on screening weight) by subcutaneous (SC) injection at Weeks 16, 28, and 40 (Part B).

Arm title	Risankizumab/Risankizumab (Part B)

Arm description:

Participants randomized to receive risankizumab in Part A continued to receive risankizumab 150 mg by subcutaneous (SC) injection at Weeks 16, 28, and 40 (Part B).

Arm type	Experimental
Investigational medicinal product name	Risankizumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants randomized to receive risankizumab in Part A continued to receive risankizumab 150 mg by subcutaneous (SC) injection at Weeks 16, 28, and 40 (Part B).

Number of subjects in period 2[2]	Placebo/Risankizumab (Part B)	Ustekinumab/Ustekinumab (Part B)	Risankizumab/Risankizumab (Part B)
Started	94	94	291
Completed	91	90	278
Not completed	3	4	13
Consent withdrawn by subject	-	2	4
Adverse Event (Other)	1	1	1
Not specified	1	-	1
Lost to follow-up	1	1	7

Notes:

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

Justification: The number of subjects starting the period 1 (Part A) have switched their treatments in period 2 (Part B)

Baseline characteristics

Reporting groups	
Reporting group title	Placebo (Part A)
Reporting group description:	
Participants randomized to receive double-blind (DB) placebo by subcutaneous (SC) injection at Weeks 0 and 4 (Part A).	
Reporting group title	Ustekinumab (Part A)
Reporting group description:	
Participants randomized to receive double-blind (DB) ustekinumab 45 or 90 mg (based on screening weight) by subcutaneous (SC) injection at Weeks 0 and 4 (Part A). They received 2 sets of injections to maintain the blind (ustekinumab and placebo for risankizumab)	
Reporting group title	Risankizumab (Part A)
Reporting group description:	
Participants randomized to receive double-blind (DB) risankizumab 150 mg by subcutaneous (SC) injection at Weeks 0 and 4 (Part A). They received 2 sets of injections to maintain the blind (risankizumab and placebo for ustekinumab)	

Reporting group values	Placebo (Part A)	Ustekinumab (Part A)	Risankizumab (Part A)
Number of subjects	98	99	294
Age categorical Units: Subjects			
Age Continuous			
Intent-to-treat (ITT) population: all randomized participants			
Units: years			
arithmetic mean	46.3	48.6	46.2
standard deviation	± 13.26	± 14.81	± 13.68
Sex: Female, Male			
Intent-to-treat (ITT) population: all randomized participants			
Units: Subjects			
Female	31	33	91
Male	67	66	203
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	19	12	44
Not Hispanic or Latino	79	87	250
Unknown or Not Reported	0	0	0
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	1	0	2
Asian	7	4	25
Native Hawaiian or Other Pacific Islander	1	1	0
Black or African American	2	2	10
White	87	91	255
More than one race	0	1	2
Unknown or Not Reported	0	0	0

Reporting group values	Total		

Number of subjects	491		
Age categorical Units: Subjects			

Age Continuous			
Intent-to-treat (ITT) population: all randomized participants			
Units: years arithmetic mean standard deviation	- -		
Sex: Female, Male			
Intent-to-treat (ITT) population: all randomized participants			
Units: Subjects			
Female	155		
Male	336		
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	75		
Not Hispanic or Latino	416		
Unknown or Not Reported	0		
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	3		
Asian	36		
Native Hawaiian or Other Pacific Islander	2		
Black or African American	14		
White	433		
More than one race	3		
Unknown or Not Reported	0		

End points

End points reporting groups

Reporting group title	Placebo (Part A)
Reporting group description:	
Participants randomized to receive double-blind (DB) placebo by subcutaneous (SC) injection at Weeks 0 and 4 (Part A).	
Reporting group title	Ustekinumab (Part A)
Reporting group description:	
Participants randomized to receive double-blind (DB) ustekinumab 45 or 90 mg (based on screening weight) by subcutaneous (SC) injection at Weeks 0 and 4 (Part A). They received 2 sets of injections to maintain the blind (ustekinumab and placebo for risankizumab)	
Reporting group title	Risankizumab (Part A)
Reporting group description:	
Participants randomized to receive double-blind (DB) risankizumab 150 mg by subcutaneous (SC) injection at Weeks 0 and 4 (Part A). They received 2 sets of injections to maintain the blind (risankizumab and placebo for ustekinumab)	
Reporting group title	Placebo/Risankizumab (Part B)
Reporting group description:	
Participants randomized to receive placebo in Part A switched to risankizumab 150 mg by subcutaneous (SC) injection at Weeks 16, 28, and 40 (Part B).	
Reporting group title	Ustekinumab/Ustekinumab (Part B)
Reporting group description:	
Participants randomized to receive ustekinumab in Part A continued to receive ustekinumab 45 mg or 90 mg (based on screening weight) by subcutaneous (SC) injection at Weeks 16, 28, and 40 (Part B).	
Reporting group title	Risankizumab/Risankizumab (Part B)
Reporting group description:	
Participants randomized to receive risankizumab in Part A continued to receive risankizumab 150 mg by subcutaneous (SC) injection at Weeks 16, 28, and 40 (Part B).	
Subject analysis set title	Placebo/Risankizumab (Part B)
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Participants randomized to receive placebo in Part A switched to risankizumab 150 mg by subcutaneous (SC) injection at Weeks 16, 28, and 40 (Part B).	
Subject analysis set title	Ustekinumab/Ustekinumab (Part B)
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Participants randomized to receive ustekinumab in Part A continued to receive ustekinumab 45 mg or 90 mg (based on screening weight) by subcutaneous (SC) injection at Weeks 16, 28, and 40 (Part B).	
Subject analysis set title	Risankizumab/Risankizumab (Part B)
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Participants randomized to receive risankizumab in Part A continued to receive risankizumab 150 mg by subcutaneous (SC) injection at Weeks 16, 28, and 40 (Part B).	

Primary: Percentage of Participants Achieving 90% Improvement in Psoriasis Area and Severity Index (PASI) Score (PASI90) at Week 16 in participants who received risankizumab compared with placebo (Part A)

End point title	Percentage of Participants Achieving 90% Improvement in Psoriasis Area and Severity Index (PASI) Score (PASI90) at Week 16 in participants who received risankizumab compared with placebo (Part A)[1]
End point description:	
PASI is a composite score based on the degree of effect on body surface area of psoriasis and the extension of erythema (reddening), induration (thickness), desquamation (scaling) of the lesions and	

area affected as observed on the day of examination. The severity of each sign was assessed using a 5-point scale, where 0=no symptoms, 1=slight, 2=moderate, 3=marked, 4=very marked. The PASI score ranges from 0 to 72, where 0 indicates no psoriasis and 72 indicates very severe psoriasis. PASI90 is defined as at least a 90% reduction in PASI score compared with the Baseline PASI score. The percent reduction in score is calculated as (PASI score at Baseline - score at follow-up visit) / PASI score at Baseline * 100. Non-responder imputation (NRI) was used for missing data.

Intent-to-treat (ITT) population: all randomized participants.

End point type	Primary

End point timeframe:

Week 16

Notes:

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Only those arms for which the comparisons are presented in the clinical trial report thus, those that would yield meaningful results were reported.

End point values	Placebo (Part A)	Risankizumab (Part A)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	98[2]	294[3]		
Units: percentage of participants				
number (not applicable)	2.0	74.8		

Notes:

[2] - ITT

[3] - ITT

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

95% CI for adjusted difference of 2 treatment groups, calculated from the Cochran-Mantel-Haenszel test adjusted for the comparison of 2 treatment groups. If there was a stratum containing zero count, 0.1 was added to each cell.

Comparison groups	Placebo (Part A) v Risankizumab (Part A)
Number of subjects included in analysis	392
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001 [4]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted percentage difference
Point estimate	72.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	66.8
upper limit	78.2

Notes:

[4] - Cochran-Mantel-Haenszel test adjusted for strata (baseline weight [≤100 kg vs >100 kg] and prior exposure to tumor necrosis factor [TNF] antagonists [0 vs ≥1]). If there was a stratum containing zero count, 0.1 was added to each cell.

Primary: Percentage of participants achieving a static Physician Global Assessment (sPGA) score of clear or almost clear at Week 16 in participants who received Risankizumab compared with Placebo (Part A)

End point title	Percentage of participants achieving a static Physician Global Assessment (sPGA) score of clear or almost clear at Week 16 in

	participants who received Risankizumab compared with Placebo (Part A)[5]

End point description:

The sPGA is an assessment by the investigator of the overall disease severity at the time of evaluation. Erythema (E), induration (I), and desquamation (D) are scored on a 5-point scale ranging from 0 (none) to 4 (severe). The sPGA ranges from 0 to 4, and is calculated as Clear (0) = 0 for all three; Almost clear (1) = mean >0, <1.5; Mild (2) = mean ≥1.5, <2.5; Moderate (3) = mean ≥2.5, <3.5; and Severe (4) = mean ≥3.5. NRI was used for missing data.

End point type	Primary

End point timeframe:

Week 16

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Only those arms for which the comparisons are presented in the clinical trial report thus, those that would yield meaningful results were reported.

End point values	Placebo (Part A)	Risankizumab (Part A)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	98[6]	294[7]		
Units: percentage of participants				
number (not applicable)	5.1	83.7		

Notes:

[6] - ITT

[7] - ITT

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

95% CI for adjusted difference of 2 treatment groups, calculated by the Cochran-Mantel-Haenszel test adjusted for the comparison of 2 treatment groups. If there was a stratum containing zero count, 0.1 was added to each cell.

Comparison groups	Placebo (Part A) v Risankizumab (Part A)
Number of subjects included in analysis	392
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001 [8]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted percentage difference
Point estimate	78.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	72.4
upper limit	84.5

Notes:

[8] - Cochran-Mantel-Haenszel test adjusted for strata (baseline weight [≤100 kg vs >100 kg] and prior exposure to tumor necrosis factor [TNF] antagonists [0 vs ≥1]). If there was a stratum containing zero count, 0.1 was added to each cell.

Secondary: Percentage of participants achieving sPGA score of clear at Week 16 in participants who received Risankizumab compared with Placebo (Part A)

End point title	Percentage of participants achieving sPGA score of clear at Week 16 in participants who received Risankizumab compared with Placebo (Part A)[9]

End point description:

The sPGA is an assessment by the investigator of the overall disease severity at the time of evaluation. Erythema (E), induration (I), and desquamation (D) are scored on a 5-point scale ranging from 0 (none) to 4 (severe). The sPGA ranges from 0 to 4, and is calculated as Clear (0) = 0 for all three; Almost clear (1) = mean >0, <1.5; Mild (2) = mean ≥1.5, <2.5; Moderate (3) = mean ≥2.5, <3.5; and Severe (4) = mean ≥3.5. NRI was used for missing data.

End point type	Secondary

End point timeframe:

Week 16

Notes:

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only those arms for which the comparisons are presented in the clinical trial report thus, those that would yield meaningful results were reported.

End point values	Placebo (Part A)	Risankizumab (Part A)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	98[10]	294[11]		
Units: percentage of participants				
number (not applicable)	3.1	51.0		

Notes:

[10] - ITT

[11] - ITT

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

95% CI for adjusted difference of 2 treatment groups, calculated from the Cochran-Mantel-Haenszel test adjusted for the comparison of 2 treatment groups. If there was a stratum containing zero count, 0.1 was added to each cell.

Comparison groups	Placebo (Part A) v Risankizumab (Part A)
Number of subjects included in analysis	392
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001 [12]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted percentage difference
Point estimate	47.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	40.9
upper limit	54.2

Notes:

[12] - Cochran-Mantel-Haenszel test adjusted for strata (baseline weight [≤100 kg vs >100 kg] and prior exposure to tumor necrosis factor [TNF] antagonists [0 vs ≥1]). If there was a stratum containing zero count, 0.1 was added to each cell.

Secondary: Percentage of Participants Achieving PASI100 at Week 16 in participants who received Risankizumab compared with Placebo (Part A)

End point title	Percentage of Participants Achieving PASI100 at Week 16 in participants who received Risankizumab compared with Placebo (Part A)[13]

End point description:

PASI is a composite score based on the degree of effect on body surface area of psoriasis and the extension of erythema (reddening), induration (thickness), desquamation (scaling) of the lesions and area affected as observed on the day of examination. The severity of each sign was assessed using a 5-point scale, where 0=no symptoms, 1=slight, 2=moderate, 3=marked, 4=very marked. The PASI score ranges from 0 to 72, where 0 indicates no psoriasis and 72 indicates very severe psoriasis. PASI100 is defined as a 100% reduction in PASI score compared with the Baseline PASI score. The percent reduction in score is calculated as (PASI score at Baseline - score at follow-up visit) / PASI score at Baseline * 100. NRI was used for missing data.

End point type	Secondary

End point timeframe:

Week 16

Notes:

[13] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only those arms for which the comparisons are presented in the clinical trial report thus, those that would yield meaningful results were reported.

End point values	Placebo (Part A)	Risankizumab (Part A)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	98[14]	294[15]		
Units: percentage of participants				
number (not applicable)	2.0	50.7		

Notes:

[14] - ITT

[15] - ITT

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

95% CI for adjusted difference of 2 treatment groups, calculated from the Cochran-Mantel-Haenszel test adjusted for the comparison of 2 treatment groups. If there was a stratum containing zero count, 0.1 was added to each cell.

Comparison groups	Placebo (Part A) v Risankizumab (Part A)
Number of subjects included in analysis	392
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001 [16]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted percentage difference
Point estimate	48.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	41.9
upper limit	54.6

Notes:

[16] - Cochran-Mantel-Haenszel test adjusted for strata (baseline weight [≤100 kg vs >100 kg] and prior exposure to tumor necrosis factor [TNF] antagonists [0 vs ≥1]). If there was a stratum containing zero count, 0.1 was added to each cell.

Secondary: Percentage of participants achieving a Dermatology Life Quality Index (DLQI) score of 0 or 1 at Week 16 in participants who received Risankizumab compared with Placebo (Part A)

End point title	Percentage of participants achieving a Dermatology Life Quality Index (DLQI) score of 0 or 1 at Week 16 in participants who received Risankizumab compared with Placebo (Part A)[17]

End point description:

DLQI is a 10-question questionnaire that asks the participant to evaluate the degree that psoriasis has affected their quality of life in the last week and includes 6 domains (symptoms and feelings, daily activities, leisure, work and school, personal relationships, and treatment). Responses to each domain are not relevant (0), not at all (0), a little (1), a lot (2), and very much (3). The DLQI is calculated by summing the scores of the questions and ranges from 0 to 30, where 0-1 = no effect on patient's life, 2-5 = small effect, 6-10 = moderate effect, 11-20 = very large effect, and 21-30 = extremely large effect on patient's life. The higher the score, the more the quality of life is impaired. A 5-point change from baseline is considered a clinically important difference. NRI was used for missing data.

End point type	Secondary

End point timeframe:

Week 16

Notes:

[17] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only those arms for which the comparisons are presented in the clinical trial report thus, those that would yield meaningful results were reported.

End point values	Placebo (Part A)	Risankizumab (Part A)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	98[18]	294[19]		
Units: percentage of participants				
number (not applicable)	4.1	66.7		

Notes:

[18] - ITT

[19] - ITT

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

95% CI for adjusted difference of 2 treatment groups, calculated from the Cochran-Mantel-Haenszel test adjusted for the comparison of 2 treatment groups. If there was a stratum containing zero count, 0.1 was added to each cell.

Comparison groups	Placebo (Part A) v Risankizumab (Part A)
Number of subjects included in analysis	392
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001 [20]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted percentage difference
Point estimate	62.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	55.5
upper limit	68.9

Notes:

[20] - Cochran-Mantel-Haenszel test adjusted for strata (baseline weight [≤100 kg vs >100 kg] and prior exposure to tumor necrosis factor [TNF] antagonists [0 vs ≥1]). If there was a stratum containing zero count, 0.1 was added to each cell.

Secondary: Percentage of Participants Achieving a Psoriasis Symptom Scale (PSS) Score of 0 at Week 16 in participants who received Risankizumab compared with Placebo (Part A)

End point title	Percentage of Participants Achieving a Psoriasis Symptom Scale (PSS) Score of 0 at Week 16 in participants who received Risankizumab compared with Placebo (Part A)[21]

End point description:

The PSS asks the participant to rate the severity of symptoms of psoriasis in the last 24 hours (pain, redness, itching, and burning) using a 5-point Likert –type scale ranging from 0 (none) to 4 (very severe). The PSS is calculated by summing the scores of the questions and ranges from 0 to 16, where the higher the score, the greater the severity of psoriasis symptoms. NRI was used for missing data.

End point type	Secondary

End point timeframe:

Week 16

Notes:

[21] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only those arms for which the comparisons are presented in the clinical trial report thus, those that would yield meaningful results were reported.

End point values	Placebo (Part A)	Risankizumab (Part A)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	98[22]	294[23]		
Units: percentage of participants				
number (not applicable)	0	31.3		

Notes:

[22] - ITT

[23] - ITT

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

95% CI for adjusted difference of 2 treatment groups, calculated from the Cochran-Mantel-Haenszel test adjusted for the comparison of 2 treatment groups. If there was a stratum containing zero count, 0.1 was added to each cell.

Comparison groups	Placebo (Part A) v Risankizumab (Part A)
Number of subjects included in analysis	392
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001 [24]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted percentage difference
Point estimate	31.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	25.7
upper limit	36.6

Notes:

[24] - Cochran-Mantel-Haenszel test adjusted for strata (baseline weight [≤100 kg vs >100 kg] and prior exposure to tumor necrosis factor [TNF] antagonists [0 vs ≥1]). If there was a stratum containing zero count, 0.1 was added to each cell.

Secondary: Percentage of participants achieving PASI90 at Week 16 in participants who received Risankizumab compared with Ustekinumab (Part A)

End point title	Percentage of participants achieving PASI90 at Week 16 in participants who received Risankizumab compared with Ustekinumab (Part A)[25]

End point description:

PASI is a composite score based on the degree of effect on body surface area of psoriasis and the extension of erythema (reddening), induration (thickness), desquamation (scaling) of the lesions and area affected as observed on the day of examination. The severity of each sign was assessed using a 5-point scale, where 0=no symptoms, 1=slight, 2=moderate, 3=marked, 4=very marked. The PASI score ranges from 0 to 72, where 0 indicates no psoriasis and 72 indicates very severe psoriasis. PASI90 is defined as at least a 90% reduction in PASI score compared with the Baseline PASI score. The percent reduction in score is calculated as (PASI score at Baseline - score at follow-up visit) / PASI score at Baseline * 100. NRI was used for missing data.

End point type	Secondary

End point timeframe:

Week 16

Notes:

[25] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only those arms for which the comparisons are presented in the clinical trial report thus, those that would yield meaningful results were reported.

End point values	Ustekinumab (Part A)	Risankizumab (Part A)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	99[26]	294[27]		
Units: percentage of participants				
number (not applicable)	47.5	74.8		

Notes:

[26] - ITT

[27] - ITT

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

95% CI for adjusted difference of 2 treatment groups, calculated from the Cochran-Mantel-Haenszel test adjusted for the comparison of 2 treatment groups. If there was a stratum containing zero count, 0.1 was added to each cell.

Comparison groups	Ustekinumab (Part A) v Risankizumab (Part A)
Number of subjects included in analysis	393
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001 [28]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted percentage difference
Point estimate	27.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	16.7
upper limit	38.5

Notes:

[28] - Cochran-Mantel-Haenszel test adjusted for strata (baseline weight [≤100 kg vs >100 kg] and prior exposure to tumor necrosis factor [TNF] antagonists [0 vs ≥1]). If there was a stratum containing zero count, 0.1 was added to each cell.

Secondary: Percentage of participants achieving sPGA score of clear or almost clear at Week 16 in participants who received Risankizumab compared with Ustekinumab (Part A)

End point title	Percentage of participants achieving sPGA score of clear or almost clear at Week 16 in participants who received Risankizumab compared with Ustekinumab (Part A)[29]

End point description:

The sPGA is an assessment by the investigator of the overall disease severity at the time of evaluation. Erythema (E), induration (I), and desquamation (D) are scored on a 5-point scale ranging from 0 (none) to 4 (severe). The sPGA ranges from 0 to 4, and is calculated as Clear (0) = 0 for all three; Almost clear (1) = mean >0, <1.5; Mild (2) = mean ≥1.5, <2.5; Moderate (3) = mean ≥2.5, <3.5; and Severe (4) = mean ≥3.5. NRI was used for missing data.

End point type	Secondary

End point timeframe:

Week 16

Notes:

[29] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only those arms for which the comparisons are presented in the clinical trial report thus, those that would yield meaningful results were reported.

End point values	Ustekinumab (Part A)	Risankizumab (Part A)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	99[30]	294[31]		
Units: percentage of participants				
number (not applicable)	61.6	83.7		

Notes:

[30] - ITT

[31] - ITT

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

95% CI for adjusted difference of 2 treatment groups, calculated from the Cochran-Mantel-Haenszel test adjusted for the comparison of 2
treatment groups. If there was a stratum containing zero count, 0.1 was added to each cell.

Comparison groups	Ustekinumab (Part A) v Risankizumab (Part A)
Number of subjects included in analysis	393
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001 [32]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted percentage difference
Point estimate	22.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	12
upper limit	32.5

Notes:

[32] - Cochran-Mantel-Haenszel test adjusted for strata (baseline weight [≤100 kg vs >100 kg] and prior exposure to tumor necrosis factor [TNF] antagonists [0 vs ≥1]). If there was a stratum containing zero count, 0.1 was added to each cell.

Secondary: Percentage of participants achieving PASI100 at Week 16 in participants who received Risankizumab compared with Ustekinumab (Part A)

End point title	Percentage of participants achieving PASI100 at Week 16 in participants who received Risankizumab compared with Ustekinumab (Part A)[33]

End point description:

PASI is a composite score based on the degree of effect on body surface area of psoriasis and the extension of erythema (reddening), induration (thickness), desquamation (scaling) of the lesions and area affected as observed on the day of examination. The severity of each sign was assessed using a 5-point scale, where 0=no symptoms, 1=slight, 2=moderate, 3=marked, 4=very marked. The PASI score ranges from 0 to 72, where 0 indicates no psoriasis and 72 indicates very severe psoriasis. PASI00 is defined as a 100% reduction in PASI score compared with the Baseline PASI score. The percent reduction in score is calculated as (PASI score at Baseline - score at follow-up visit) / PASI score at Baseline * 100. NRI was used for missing data.

End point type	Secondary

End point timeframe:

Week 16

Notes:

[33] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only those arms for which the comparisons are presented in the clinical trial report thus, those that would yield meaningful results were reported.

End point values	Ustekinumab (Part A)	Risankizumab (Part A)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	99[34]	294[35]		
Units: percentage of participants				
number (not applicable)	24.2	50.7		

Notes:

[34] - ITT

[35] - ITT

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

95% CI for adjusted difference of 2 treatment groups, calculated from the Cochran-Mantel-Haenszel test adjusted for the comparison of 2 treatment groups. If there was a stratum containing zero count, 0.1 was added to each cell.

Comparison groups	Ustekinumab (Part A) v Risankizumab (Part A)
Number of subjects included in analysis	393
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001 [36]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted percentage difference
Point estimate	27

Confidence interval	
level	95 %
sides	2-sided
lower limit	17
upper limit	37

Notes:

[36] - Cochran-Mantel-Haenszel test adjusted for strata (baseline weight [≤100 kg vs >100 kg] and prior exposure to tumor necrosis factor [TNF] antagonists [0 vs ≥1]). If there was a stratum containing zero count, 0.1 was added to each cell.

Secondary: Percentage of participants achieving sPGA score of clear at Week 16 in participants who received Risankizumab compared with Ustekinumab (Part A)

End point title	Percentage of participants achieving sPGA score of clear at Week 16 in participants who received Risankizumab compared with Ustekinumab (Part A)[37]

End point description:

The sPGA is an assessment by the investigator of the overall disease severity at the time of evaluation. Erythema (E), induration (I), and desquamation (D) are scored on a 5-point scale ranging from 0 (none) to 4 (severe). The sPGA ranges from 0 to 4, and is calculated as Clear (0) = 0 for all three; Almost clear (1) = mean >0, <1.5; Mild (2) = mean ≥1.5, <2.5; Moderate (3) = mean ≥2.5, <3.5; and Severe (4) = mean ≥3.5. NRI was used for missing data.

End point type	Secondary

End point timeframe:

Week 16

Notes:

[37] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only those arms for which the comparisons are presented in the clinical trial report thus, those that would yield meaningful results were reported.

End point values	Ustekinumab (Part A)	Risankizumab (Part A)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	99[38]	294[39]		
Units: percentage of participants				
number (not applicable)	25.3	51.0		

Notes:

[38] - ITT

[39] - ITT

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

95% CI for adjusted difference of 2 treatment groups, calculated from the Cochran-Mantel-Haenszel test adjusted for the comparison of 2 treatment groups. If there was a stratum containing zero count, 0.1 was added to each cell.

Comparison groups	Ustekinumab (Part A) v Risankizumab (Part A)
Number of subjects included in analysis	393
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001 [40]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted percentage difference
Point estimate	26.3

Confidence interval	
level	95 %
sides	2-sided
lower limit	16.1
upper limit	36.4

Notes:

[40] - Cochran-Mantel-Haenszel test adjusted for strata (baseline weight [≤100 kg vs >100 kg] and prior exposure to tumor necrosis factor [TNF] antagonists [0 vs ≥1]). If there was a stratum containing zero count, 0.1 was added to each cell.

Secondary: Percentage of participants Achieving PASI90 at Week 52 in participants who received Risankizumab compared with Ustekinumab (Part B)

End point title	Percentage of participants Achieving PASI90 at Week 52 in participants who received Risankizumab compared with Ustekinumab (Part B)

End point description:

PASI is a composite score based on the degree of effect on body surface area of psoriasis and the extension of erythema (reddening), induration (thickness), desquamation (scaling) of the lesions and area affected as observed on the day of examination. The severity of each sign was assessed using a 5-point scale, where 0=no symptoms, 1=slight, 2=moderate, 3=marked, 4=very marked. The PASI score ranges from 0 to 72, where 0 indicates no psoriasis and 72 indicates very severe psoriasis. PASI90 is defined as at least a 90% reduction in PASI score compared with the Baseline PASI score. The percent reduction in score is calculated as (PASI score at Baseline - score at follow-up visit) / PASI score at Baseline * 100. NRI was used for missing data.

End point type	Secondary

End point timeframe:

Week 52

End point values	Ustekinumab/Ustekinumab (Part B)	Risankizumab/Risankizumab (Part B)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	99[41]	294[42]		
Units: percentage of participants				
number (not applicable)	50.5	80.6		

Notes:

[41] - ITT

[42] - ITT

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

95% CI for adjusted difference of 2 treatment groups, calculated from the Cochran-Mantel-Haenszel test adjusted for the comparison of 2 treatment groups. If there was a stratum containing zero count, 0.1 was added to each cell.

Comparison groups	Ustekinumab/Ustekinumab (Part B) v Risankizumab/Risankizumab (Part B)

Number of subjects included in analysis	393
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001 [43]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted percentage difference
Point estimate	30.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	19.6
upper limit	40.9

Notes:

[43] - Cochran-Mantel-Haenszel test adjusted for strata (baseline weight [≤100 kg vs >100 kg] and prior exposure to tumor necrosis factor [TNF] antagonists [0 vs ≥1]). If there was a stratum containing zero count, 0.1 was added to each cell.

Secondary: Percentage of participants achieving PASI100 at Week 52 in participants who received Risankizumab compared with Ustekinumab (Part B)

End point title	Percentage of participants achieving PASI100 at Week 52 in participants who received Risankizumab compared with Ustekinumab (Part B)

End point description:

PASI is a composite score based on the degree of effect on body surface area of psoriasis and the extension of erythema (reddening), induration (thickness), desquamation (scaling) of the lesions and area affected as observed on the day of examination. The severity of each sign was assessed using a 5-point scale, where 0=no symptoms, 1=slight, 2=moderate, 3=marked, 4=very marked. The PASI score ranges from 0 to 72, where 0 indicates no psoriasis and 72 indicates very severe psoriasis. PASI00 is defined as a 100% reduction in PASI score compared with the Baseline PASI score. The percent reduction in score is calculated as (PASI score at Baseline - score at follow-up visit) / PASI score at Baseline * 100. NRI was used for missing data.

End point type	Secondary

End point timeframe:

Week 52

End point values	Ustekinumab/Ustekinumab (Part B)	Risankizumab/Risankizumab (Part B)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	99[44]	294[45]		
Units: percentage of participants				
number (not applicable)	30.3	59.5		

Notes:

[44] - ITT

[45] - ITT

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

95% CI for adjusted difference of 2 treatment groups, calculated from the Cochran-Mantel-Haenszel test adjusted for the comparison of 2 treatment groups. If there was a stratum containing zero count, 0.1 was added to each cell.

Comparison groups	Ustekinumab/Ustekinumab (Part B) v

	Risankizumab/Risankizumab (Part B)
Number of subjects included in analysis	393
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001 [46]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted percentage difference
Point estimate	29.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	18.9
upper limit	40.1

Notes:

[46] - Cochran-Mantel-Haenszel test adjusted for strata (baseline weight [≤100 kg vs >100 kg] and prior exposure to tumor necrosis factor [TNF] antagonists [0 vs ≥1]). If there was a stratum containing zero count, 0.1 was added to each cell.

Secondary: Percentage of participants achieving sPGA score of clear at Week 52 in participants who received Risankizumab compared with Ustekinumab (Part B)

End point title	Percentage of participants achieving sPGA score of clear at Week 52 in participants who received Risankizumab compared with Ustekinumab (Part B)

End point description:

The sPGA is an assessment by the investigator of the overall disease severity at the time of evaluation. Erythema (E), induration (I), and desquamation (D) are scored on a 5-point scale ranging from 0 (none) to 4 (severe). The sPGA ranges from 0 to 4, and is calculated as Clear (0) = 0 for all three; Almost clear (1) = mean >0, <1.5; Mild (2) = mean ≥1.5, <2.5; Moderate (3) = mean ≥2.5, <3.5; and Severe (4) = mean ≥3.5. NRI was used for missing data.

End point type	Secondary

End point timeframe:

Week 52

End point values	Ustekinumab/Ustekinumab (Part B)	Risankizumab/Risankizumab (Part B)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	99[47]	294[48]		
Units: percentage of participants				
number (not applicable)	30.3	59.5		

Notes:

[47] - ITT

[48] - ITT

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

95% CI for adjusted difference of 2 treatment groups, calculated from the Cochran-Mantel-Haenszel test adjusted for the comparison of 2 treatment groups. If there was a stratum containing zero count, 0.1 was added to each cell.

Comparison groups	Ustekinumab/Ustekinumab (Part B) v Risankizumab/Risankizumab (Part B)

Number of subjects included in analysis	393
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001 [49]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted percentage difference
Point estimate	29.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	18.9
upper limit	40.1

Notes:

[49] - Cochran-Mantel-Haenszel test adjusted for strata (baseline weight [≤100 kg vs >100 kg] and prior exposure to tumor necrosis factor [TNF] antagonists [0 vs ≥1]). If there was a stratum containing zero count, 0.1 was added to each cell.

Secondary: Percentage of Participants Achieving PASI75 at Week 12 in participants who received Risankizumab compared with Ustekinumab (Part A)

End point title	Percentage of Participants Achieving PASI75 at Week 12 in participants who received Risankizumab compared with Ustekinumab (Part A)[50]

End point description:

PASI is a composite score based on the degree of effect on body surface area of psoriasis and the extension of erythema (reddening), induration (thickness), desquamation (scaling) of the lesions and area affected as observed on the day of examination. The severity of each sign was assessed using a 5-point scale, where 0=no symptoms, 1=slight, 2=moderate, 3=marked, 4=very marked. The PASI score ranges from 0 to 72, where 0 indicates no psoriasis and 72 indicates very severe psoriasis. PASI75 is defined as at least a 75% reduction in PASI score compared with the Baseline PASI score. The percent reduction in score is calculated as (PASI score at Baseline - score at follow-up visit) / PASI score at Baseline * 100. NRI was used for missing data.

End point type	Secondary

End point timeframe:

Week 12

Notes:

[50] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only those arms for which the comparisons are presented in the clinical trial report thus, those that would yield meaningful results were reported.

End point values	Ustekinumab (Part A)	Risankizumab (Part A)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	99[51]	294[52]		
Units: percentage of participants				
number (not applicable)	69.7	88.8		

Notes:

[51] - ITT

[52] - ITT

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

95% CI for adjusted difference of 2 treatment groups, calculated from the Cochran-Mantel-Haenszel test adjusted for the comparison of 2 treatment groups. If there was a stratum containing zero count, 0.1 was added to each cell.

Comparison groups	Ustekinumab (Part A) v Risankizumab (Part A)
Number of subjects included in analysis	393
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001 [53]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted percentage difference
Point estimate	19.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	9.5
upper limit	28.8

Notes:

[53] - Cochran-Mantel-Haenszel test adjusted for strata (baseline weight [≤100 kg vs >100 kg] and prior exposure to tumor necrosis factor [TNF] antagonists [0 vs ≥1]). If there was a stratum containing zero count, 0.1 was added to each cell.

Secondary: Percentage of participants achieving sPGA score of clear or almost clear at Week 12 in participants who received Risankizumab compared with Ustekinumab (Part A)

End point title	Percentage of participants achieving sPGA score of clear or almost clear at Week 12 in participants who received Risankizumab compared with Ustekinumab (Part A)[54]

End point description:

The sPGA is an assessment by the investigator of the overall disease severity at the time of evaluation. Erythema (E), induration (I), and desquamation (D) are scored on a 5-point scale ranging from 0 (none) to 4 (severe). The sPGA ranges from 0 to 4, and is calculated as Clear (0) = 0 for all three; Almost clear (1) = mean >0, <1.5; Mild (2) = mean ≥1.5, <2.5; Moderate (3) = mean ≥2.5, <3.5; and Severe (4) = mean ≥3.5. NRI was used for missing data.

End point type	Secondary

End point timeframe:

Week 12

Notes:

[54] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only those arms for which the comparisons are presented in the clinical trial report thus, those that would yield meaningful results were reported.

End point values	Ustekinumab (Part A)	Risankizumab (Part A)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	99[55]	294[56]		
Units: percentage of participants				
number (not applicable)	64.6	82.3		

Notes:

[55] - ITT

[56] - ITT

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

95% CI for adjusted difference of 2 treatment groups, calculated from the Cochran-Mantel-Haenszel test adjusted for the comparison of 2 treatment groups. If there was a stratum containing zero count, 0.1 was added to each cell.

Comparison groups	Ustekinumab (Part A) v Risankizumab (Part A)
Number of subjects included in analysis	393
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001 [57]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted percentage difference
Point estimate	18
Confidence interval	
level	95 %
sides	2-sided
lower limit	7.8
upper limit	28.3

Notes:

[57] - Cochran-Mantel-Haenszel test adjusted for strata (baseline weight [≤100 kg vs >100 kg] and prior exposure to tumor necrosis factor [TNF] antagonists [0 vs ≥1]). If there was a stratum containing zero count, 0.1 was added to each cell.

Secondary: Percentage of participants achieving a DLQI score of 0 or 1 at Week 16 in participants who received Risankizumab compared with Ustekinumab (Part A)

End point title	Percentage of participants achieving a DLQI score of 0 or 1 at Week 16 in participants who received Risankizumab compared with Ustekinumab (Part A)[58]

End point description:

DLQI is a 10-question questionnaire that asks the participant to evaluate the degree that psoriasis has affected their quality of life in the last week and includes 6 domains (symptoms and feelings, daily activities, leisure, work and school, personal relationships, and treatment). Responses to each domain are not relevant (0), not at all (0), a little (1), a lot (2), and very much (3). The DLQI is calculated by summing the scores of the questions and ranges from 0 to 30, where 0-1 = no effect on patient's life, 2-5 = small effect, 6-10 = moderate effect, 11-20 = very large effect, and 21-30 = extremely large effect on patient's life. The higher the score, the more the quality of life is impaired. A 5-point change from baseline is considered a clinically important difference. NRI was used for missing data.

End point type	Secondary

End point timeframe:

Week 16

Notes:

[58] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only those arms for which the comparisons are presented in the clinical trial report thus, those that would yield meaningful results were reported.

End point values	Ustekinumab (Part A)	Risankizumab (Part A)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	99[59]	294[60]		
Units: percentage of participants				
number (not applicable)	46.5	66.7		

Notes:

[59] - ITT

[60] - ITT

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

95% CI for adjusted difference of 2 treatment groups, calculated from the Cochran-Mantel-Haenszel test

adjusted for the comparison of 2 treatment groups. If there was a stratum containing zero count, 0.1 was added to each cell.

Comparison groups	Ustekinumab (Part A) v Risankizumab (Part A)
Number of subjects included in analysis	393
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001 [61]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted percentage difference
Point estimate	20.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	9.1
upper limit	31.4

Notes:

[61] - Cochran-Mantel-Haenszel test adjusted for strata (baseline weight [≤100 kg vs >100 kg] and prior exposure to tumor necrosis factor [TNF] antagonists [0 vs ≥1]). If there was a stratum containing zero count, 0.1 was added to each cell.

Secondary: Change from baseline in PSS total score at week 16 in participants who received Risankizumab compared with Placebo (Part A)

End point title	Change from baseline in PSS total score at week 16 in participants who received Risankizumab compared with Placebo (Part A)[62]

End point description:

The PSS asks the participant to rate the severity of symptoms of psoriasis in the last 24 hours (pain, redness, itching, and burning) using a 5-point Likert –type scale ranging from 0 (none) to 4 (very severe). The PSS is calculated by summing the scores of the questions and ranges from 0 to 16, where the higher the score, the greater the severity of psoriasis symptoms. Last observation carried forward (LOCF) imputation was used for missing data.
A negative change in PSS total score indicates improvement.

End point type	Secondary

End point timeframe:

Week 16

Notes:

[62] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only those arms for which the comparisons are presented in the clinical trial report thus, those that would yield meaningful results were reported.

End point values	Placebo (Part A)	Risankizumab (Part A)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	85[63]	227[64]		
Units: units on a scale				
least squares mean (standard error)	-0.027 (± 0.3316)	-6.402 (± 0.2193)		

Notes:

[63] - ITT

[64] - ITT

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

P-value calculated by the van Elteren test stratified for baseline weight (≤100 kg vs >100 kg) and prior exposure to TNF antagonists (0 vs ≥1).

Comparison groups	Placebo (Part A) v Risankizumab (Part A)
Number of subjects included in analysis	312
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	van Elteren test
Parameter estimate	Mean difference (final values)
Point estimate	-6.375
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.102
upper limit	-5.648

Secondary: Percentage of participants Achieving PASI75 at Week 16 in participants who received Risankizumab compared with Placebo (Part A)

End point title	Percentage of participants Achieving PASI75 at Week 16 in participants who received Risankizumab compared with Placebo (Part A)[65]

End point description:

PASI is a composite score based on the degree of effect on body surface area of psoriasis and the extension of erythema (reddening), induration (thickness), desquamation (scaling) of the lesions and area affected as observed on the day of examination. The severity of each sign was assessed using a 5-point scale, where 0=no symptoms, 1=slight, 2=moderate, 3=marked, 4=very marked. The PASI score ranges from 0 to 72, where 0 indicates no psoriasis and 72 indicates very severe psoriasis. PASI75 is defined as at least a 75% reduction in PASI score compared with the Baseline PASI score. The percent reduction in score is calculated as (PASI score at Baseline - score at follow-up visit) / PASI score at Baseline * 100. NRI was used for missing data.

End point type	Secondary

End point timeframe:

Week 16

Notes:

[65] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only those arms for which the comparisons are presented in the clinical trial report thus, those that would yield meaningful results were reported.

End point values	Placebo (Part A)	Risankizumab (Part A)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	98[66]	294[67]		
Units: percentage of participants				
number (not applicable)	6.1	90.8		

Notes:

[66] - ITT

[67] - ITT

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

95% CI for adjusted difference of 2 treatment groups, calculated from the Cochran-Mantel-Haenszel test adjusted for the comparison of 2 treatment groups. If there was a stratum containing zero count, 0.1 was added to each cell.

Comparison groups	Placebo (Part A) v Risankizumab (Part A)
Number of subjects included in analysis	392
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001 [68]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted percentage difference
Point estimate	84.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	79
upper limit	90.4

Notes:

[68] - Cochran-Mantel-Haenszel test adjusted for strata (baseline weight [≤100 kg vs >100 kg] and prior exposure to tumor necrosis factor [TNF] antagonists [0 vs ≥1]). If there was a stratum containing zero count, 0.1 was added to each cell.

Secondary: Percentage of participants achieving sPGA score of clear or almost clear at Week 52 in participants who received Risankizumab compared with Ustekinumab (Part B)

End point title	Percentage of participants achieving sPGA score of clear or almost clear at Week 52 in participants who received Risankizumab compared with Ustekinumab (Part B)

End point description:

The sPGA is an assessment by the investigator of the overall disease severity at the time of evaluation. Erythema (E), induration (I), and desquamation (D) are scored on a 5-point scale ranging from 0 (none) to 4 (severe). The sPGA ranges from 0 to 4, and is calculated as Clear (0) = 0 for all three; Almost clear (1) = mean >0, <1.5; Mild (2) = mean ≥1.5, <2.5; Moderate (3) = mean ≥2.5, <3.5; and Severe (4) = mean ≥3.5. NRI was used for missing data.

End point type	Secondary

End point timeframe:

Week 52

End point values	Ustekinumab/Ustekinumab (Part B)	Risankizumab/Risankizumab (Part B)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	99[69]	294[70]		
Units: percentage of participants				
number (not applicable)	54.5	83.3		

Notes:

[69] - ITT

[70] - ITT

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

95% CI for adjusted difference of 2 treatment groups, calculated from the Cochran-Mantel-Haenszel test adjusted for the comparison of 2 treatment groups. If there was a stratum containing zero count, 0.1 was added to each cell.

Comparison groups	Ustekinumab/Ustekinumab (Part B) v Risankizumab/Risankizumab (Part B)
Number of subjects included in analysis	393
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001 [71]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted percentage difference
Point estimate	29.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	18.5
upper limit	39.6

Notes:

[71] - Cochran-Mantel-Haenszel test adjusted for strata (baseline weight [≤100 kg vs >100 kg] and prior exposure to tumor necrosis factor [TNF] antagonists [0 vs ≥1]). If there was a stratum containing zero count, 0.1 was added to each cell.

Secondary: Percentage of participants Achieving PASI75 at Week 52 in participants who received Risankizumab compared with Ustekinumab (Part B)

End point title	Percentage of participants Achieving PASI75 at Week 52 in participants who received Risankizumab compared with Ustekinumab (Part B)

End point description:

PASI is a composite score based on the degree of effect on body surface area of psoriasis and the extension of erythema (reddening), induration (thickness), desquamation (scaling) of the lesions and area affected as observed on the day of examination. The severity of each sign was assessed using a 5-point scale, where 0=no symptoms, 1=slight, 2=moderate, 3=marked, 4=very marked. The PASI score ranges from 0 to 72, where 0 indicates no psoriasis and 72 indicates very severe psoriasis. PASI75 is defined as at least a 75% reduction in PASI score compared with the Baseline PASI score. The percent reduction in score is calculated as (PASI score at Baseline - score at follow-up visit) / PASI score at Baseline * 100. NRI was used for missing data.

End point type	Secondary

End point timeframe:

Week 52

End point values	Ustekinumab/Ustekinumab (Part B)	Risankizumab/Risankizumab (Part B)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	99[72]	294[73]		
Units: percentage of participants				
number (not applicable)	76.8	91.5		

Notes:

[72] - ITT

[73] - ITT

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

95% CI for adjusted difference of 2 treatment groups, calculated from the Cochran-Mantel-Haenszel test adjusted for the comparison of treatment groups. If there was a stratum containing zero count, 0.1 was added to each cell.

Comparison groups	Ustekinumab/Ustekinumab (Part B) v Risankizumab/Risankizumab (Part B)
Number of subjects included in analysis	393
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.001 [74]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted percentage difference
Point estimate	14.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	5.9
upper limit	23.5

Notes:

[74] - Cochran-Mantel-Haenszel test adjusted for strata (baseline weight [≤100 kg vs >100 kg] and prior exposure to tumor necrosis factor [TNF] antagonists [0 vs ≥1]). If there was a stratum containing zero count, 0.1 was added to each cell.

Adverse events information

Timeframe for reporting adverse events:

Treatment-emergent adverse events (TEAEs) and serious adverse events (TESAEs) were collected from first dose of study drug until 15 weeks after the last dose of study drug (up to 55 weeks).

Adverse event reporting additional description:

TEAEs and TESAEs in Part A: Events from first dose of study drug in Part A until prior to first dose in Part B (Week 16) or up to 105 days after last dose of study drug if the participant discontinued in Part A; TEAEs and TESAEs in Part B: Events from first dose of study drug in Part B (Week 16) until up to 105 days after last dose of study drug.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	20.0

Reporting groups

Reporting group title	Placebo (Part A)

Reporting group description:

Participants randomized to receive double-blind (DB) placebo by subcutaneous (SC) injection at Weeks 0 and 4 (Part A).

Reporting group title	Ustekinumab (Part A)

Reporting group description:

Participants randomized to receive double-blind (DB) ustekinumab 45 or 90 mg (based on screening weight) by subcutaneous (SC) injection at Weeks 0 and 4 (Part A).

Reporting group title	Risankizumab (Part A)

Reporting group description:

Participants randomized to receive double-blind (DB) risankizumab 150 mg by subcutaneous (SC) injection at Weeks 0 and 4 (Part A).

Reporting group title	Placebo/Risankizumab (Part B)

Reporting group description:

Participants randomized to receive placebo in Part A switched to risankizumab 150 mg by subcutaneous (SC) injection at Weeks 16, 28, and 40 (Part B).

Reporting group title	Ustekinumab/Ustekinumab (Part B)

Reporting group description:

Participants randomized to receive ustekinumab in Part A continued to receive ustekinumab 45 mg or 90 mg (based on screening weight) by subcutaneous (SC) injection at Weeks 16, 28, and 40 (Part B).

Reporting group title	Risankizumab/Risankizumab (Part B)

Reporting group description:

Participants randomized to receive risankizumab in Part A continued to receive risankizumab 150 mg by subcutaneous (SC) injection at Weeks 16, 28, and 40 (Part B).

Serious adverse events	Placebo (Part A)	Ustekinumab (Part A)	Risankizumab (Part A)
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 98 (1.02%)	3 / 99 (3.03%)	6 / 294 (2.04%)
number of deaths (all causes)	0	0	1
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			

Basal cell carcinoma			
subjects affected / exposed	0 / 98 (0.00%)	0 / 99 (0.00%)	1 / 294 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Breast cancer			
subjects affected / exposed	0 / 98 (0.00%)	0 / 99 (0.00%)	0 / 294 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Prostate cancer			
subjects affected / exposed	0 / 98 (0.00%)	0 / 99 (0.00%)	0 / 294 (0.00%)
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			
Abortion induced			
subjects affected / exposed	0 / 98 (0.00%)	1 / 99 (1.01%)	0 / 294 (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
Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous			
subjects affected / exposed	0 / 98 (0.00%)	0 / 99 (0.00%)	0 / 294 (0.00%)
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			
Non-cardiac chest pain			
subjects affected / exposed	0 / 98 (0.00%)	0 / 99 (0.00%)	0 / 294 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Menometrorrhagia			
subjects affected / exposed	1 / 98 (1.02%)	0 / 99 (0.00%)	0 / 294 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			

Respiratory failure			
subjects affected / exposed	0 / 98 (0.00%)	0 / 99 (0.00%)	0 / 294 (0.00%)
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			
Fall			
subjects affected / exposed	0 / 98 (0.00%)	1 / 99 (1.01%)	0 / 294 (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
Fibula fracture			
subjects affected / exposed	0 / 98 (0.00%)	1 / 99 (1.01%)	0 / 294 (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
Meniscus injury			
subjects affected / exposed	0 / 98 (0.00%)	0 / 99 (0.00%)	0 / 294 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tibia fracture			
subjects affected / exposed	0 / 98 (0.00%)	1 / 99 (1.01%)	0 / 294 (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
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 98 (0.00%)	0 / 99 (0.00%)	0 / 294 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial flutter			
subjects affected / exposed	0 / 98 (0.00%)	0 / 99 (0.00%)	0 / 294 (0.00%)
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 aneurysm			
subjects affected / exposed	0 / 98 (0.00%)	0 / 99 (0.00%)	0 / 294 (0.00%)
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 failure congestive			
subjects affected / exposed	0 / 98 (0.00%)	0 / 99 (0.00%)	1 / 294 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac ventricular thrombosis			
subjects affected / exposed	0 / 98 (0.00%)	0 / 99 (0.00%)	0 / 294 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary artery disease			
subjects affected / exposed	0 / 98 (0.00%)	0 / 99 (0.00%)	1 / 294 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Seizure			
subjects affected / exposed	0 / 98 (0.00%)	0 / 99 (0.00%)	0 / 294 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transient ischaemic attack			
subjects affected / exposed	0 / 98 (0.00%)	0 / 99 (0.00%)	0 / 294 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Glaucoma			
subjects affected / exposed	0 / 98 (0.00%)	0 / 99 (0.00%)	0 / 294 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Retinal detachment			
subjects affected / exposed	0 / 98 (0.00%)	0 / 99 (0.00%)	0 / 294 (0.00%)
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			
Colitis			

subjects affected / exposed	0 / 98 (0.00%)	0 / 99 (0.00%)	0 / 294 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enterovesical fistula			
subjects affected / exposed	0 / 98 (0.00%)	0 / 99 (0.00%)	1 / 294 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric dilatation			
subjects affected / exposed	0 / 98 (0.00%)	0 / 99 (0.00%)	1 / 294 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hiatus hernia			
subjects affected / exposed	0 / 98 (0.00%)	0 / 99 (0.00%)	0 / 294 (0.00%)
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 / 98 (0.00%)	0 / 99 (0.00%)	0 / 294 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal colic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 99 (0.00%)	0 / 294 (0.00%)
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			
Lumbar spinal stenosis			
subjects affected / exposed	0 / 98 (0.00%)	0 / 99 (0.00%)	0 / 294 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Muscular weakness			
subjects affected / exposed	0 / 98 (0.00%)	0 / 99 (0.00%)	0 / 294 (0.00%)
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			
Cellulitis			
subjects affected / exposed	0 / 98 (0.00%)	0 / 99 (0.00%)	1 / 294 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulitis			
subjects affected / exposed	0 / 98 (0.00%)	0 / 99 (0.00%)	1 / 294 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes zoster			
subjects affected / exposed	0 / 98 (0.00%)	1 / 99 (1.01%)	1 / 294 (0.34%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteomyelitis			
subjects affected / exposed	0 / 98 (0.00%)	0 / 99 (0.00%)	1 / 294 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 98 (0.00%)	0 / 99 (0.00%)	0 / 294 (0.00%)
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 / 98 (0.00%)	0 / 99 (0.00%)	1 / 294 (0.34%)
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			
Dehydration			
subjects affected / exposed	0 / 98 (0.00%)	0 / 99 (0.00%)	0 / 294 (0.00%)
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	Placebo/Risankizumab (Part B)	Ustekinumab/Ustekinumab (Part B)	Risankizumab/Risankizumab (Part B)
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 94 (3.19%)	4 / 94 (4.26%)	13 / 291 (4.47%)
number of deaths (all causes)	0	0	1

number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	0 / 94 (0.00%)	0 / 94 (0.00%)	1 / 291 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Breast cancer			
subjects affected / exposed	1 / 94 (1.06%)	0 / 94 (0.00%)	0 / 291 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Prostate cancer			
subjects affected / exposed	0 / 94 (0.00%)	1 / 94 (1.06%)	0 / 291 (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
Surgical and medical procedures			
Abortion induced			
subjects affected / exposed	0 / 94 (0.00%)	0 / 94 (0.00%)	0 / 291 (0.00%)
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 / 94 (0.00%)	1 / 94 (1.06%)	0 / 291 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Non-cardiac chest pain			
subjects affected / exposed	0 / 94 (0.00%)	0 / 94 (0.00%)	1 / 291 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Menometrorrhagia			

subjects affected / exposed	0 / 94 (0.00%)	0 / 94 (0.00%)	0 / 291 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Respiratory failure			
subjects affected / exposed	0 / 94 (0.00%)	0 / 94 (0.00%)	1 / 291 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 94 (0.00%)	0 / 94 (0.00%)	0 / 291 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fibula fracture			
subjects affected / exposed	0 / 94 (0.00%)	0 / 94 (0.00%)	0 / 291 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meniscus injury			
subjects affected / exposed	0 / 94 (0.00%)	0 / 94 (0.00%)	1 / 291 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tibia fracture			
subjects affected / exposed	0 / 94 (0.00%)	0 / 94 (0.00%)	0 / 291 (0.00%)
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 fibrillation			
subjects affected / exposed	0 / 94 (0.00%)	0 / 94 (0.00%)	1 / 291 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial flutter			

subjects affected / exposed	1 / 94 (1.06%)	0 / 94 (0.00%)	0 / 291 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac aneurysm			
subjects affected / exposed	0 / 94 (0.00%)	0 / 94 (0.00%)	1 / 291 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure congestive			
subjects affected / exposed	0 / 94 (0.00%)	0 / 94 (0.00%)	1 / 291 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac ventricular thrombosis			
subjects affected / exposed	0 / 94 (0.00%)	0 / 94 (0.00%)	1 / 291 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary artery disease			
subjects affected / exposed	1 / 94 (1.06%)	0 / 94 (0.00%)	0 / 291 (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
Nervous system disorders			
Seizure			
subjects affected / exposed	0 / 94 (0.00%)	0 / 94 (0.00%)	1 / 291 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Transient ischaemic attack			
subjects affected / exposed	0 / 94 (0.00%)	0 / 94 (0.00%)	1 / 291 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Glaucoma			
subjects affected / exposed	0 / 94 (0.00%)	1 / 94 (1.06%)	0 / 291 (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
Retinal detachment			

subjects affected / exposed	0 / 94 (0.00%)	0 / 94 (0.00%)	1 / 291 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Colitis			
subjects affected / exposed	0 / 94 (0.00%)	1 / 94 (1.06%)	0 / 291 (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
Enterovesical fistula			
subjects affected / exposed	0 / 94 (0.00%)	0 / 94 (0.00%)	0 / 291 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric dilatation			
subjects affected / exposed	0 / 94 (0.00%)	0 / 94 (0.00%)	0 / 291 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hiatus hernia			
subjects affected / exposed	0 / 94 (0.00%)	0 / 94 (0.00%)	1 / 291 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 94 (0.00%)	0 / 94 (0.00%)	1 / 291 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal colic			
subjects affected / exposed	0 / 94 (0.00%)	0 / 94 (0.00%)	1 / 291 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Lumbar spinal stenosis			
subjects affected / exposed	0 / 94 (0.00%)	0 / 94 (0.00%)	1 / 291 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Muscular weakness			
subjects affected / exposed	1 / 94 (1.06%)	0 / 94 (0.00%)	0 / 291 (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			
Cellulitis			
subjects affected / exposed	0 / 94 (0.00%)	0 / 94 (0.00%)	0 / 291 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulitis			
subjects affected / exposed	0 / 94 (0.00%)	0 / 94 (0.00%)	0 / 291 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes zoster			
subjects affected / exposed	0 / 94 (0.00%)	0 / 94 (0.00%)	0 / 291 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteomyelitis			
subjects affected / exposed	0 / 94 (0.00%)	0 / 94 (0.00%)	0 / 291 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 94 (0.00%)	0 / 94 (0.00%)	2 / 291 (0.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	0 / 94 (0.00%)	0 / 94 (0.00%)	0 / 291 (0.00%)
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			
Dehydration			
subjects affected / exposed	0 / 94 (0.00%)	0 / 94 (0.00%)	1 / 291 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
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	Placebo (Part A)	Ustekinumab (Part A)	Risankizumab (Part A)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	8 / 98 (8.16%)	14 / 99 (14.14%)	29 / 294 (9.86%)
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	3 / 98 (3.06%)	5 / 99 (5.05%)	3 / 294 (1.02%)
occurrences (all)	3	6	3
Infections and infestations			
Influenza			
subjects affected / exposed	1 / 98 (1.02%)	0 / 99 (0.00%)	6 / 294 (2.04%)
occurrences (all)	1	0	6
Upper respiratory tract infection			
subjects affected / exposed	2 / 98 (2.04%)	4 / 99 (4.04%)	11 / 294 (3.74%)
occurrences (all)	2	4	11
Viral upper respiratory tract infection			
subjects affected / exposed	2 / 98 (2.04%)	5 / 99 (5.05%)	10 / 294 (3.40%)
occurrences (all)	2	5	10

Non-serious adverse events	Placebo/Risankizumab (Part B)	Ustekinumab/Ustekinumab (Part B)	Risankizumab/Risankizumab (Part B)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	26 / 94 (27.66%)	27 / 94 (28.72%)	67 / 291 (23.02%)
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	3 / 94 (3.19%)	2 / 94 (2.13%)	6 / 291 (2.06%)
occurrences (all)	3	2	6
Infections and infestations			
Influenza			
subjects affected / exposed	5 / 94 (5.32%)	2 / 94 (2.13%)	4 / 291 (1.37%)
occurrences (all)	7	2	5
Upper respiratory tract infection			

subjects affected / exposed	8 / 94 (8.51%)	9 / 94 (9.57%)	24 / 291 (8.25%)
occurrences (all)	8	13	28
Viral upper respiratory tract infection			
subjects affected / exposed	14 / 94 (14.89%)	17 / 94 (18.09%)	34 / 291 (11.68%)
occurrences (all)	16	22	40

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
24 May 2016	Substantive changes from the original protocol to Amendment 1 were to require an additional anti-drug antibody (ADA) sample at Week 4, to clarify the definition of analysis sets in the Statistical Methods upon a request from Health Authorities, and to add a definition for "time to onset of endpoint."
12 October 2016	Substantive changes from Amendment 1 to Amendment 2 were to transition the United States (US) Investigational New Drug application for risankizumab from BI to AbbVie, to change the sponsor for Study M15-995 within the US to AbbVie, and to change the Sponsor information and the ownership of various study responsibilities (e.g., statistical analysis).

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported