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

Summary

EudraCT number	2014-005117-23
Trial protocol	DE CZ
Global end of trial date	18 September 2017

Results information

Result version number	v2 (current)
This version publication date	17 July 2019
First version publication date	21 September 2018
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	1311.3

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02684370
WHO universal trial number (UTN)	-

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, +1 800 243 0127, clintriage.rdg@boehringer-ingelheim.com
Scientific contact	QRPE Processes and Systems Coordination Clinical Trial Information Disclosure, Boehringer Ingelheim, +1 800 243 0127, 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	18 October 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	22 December 2016
Global end of trial reached?	Yes
Global end of trial date	18 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 informed that they were free to withdraw their consent at any time during the study without penalty or prejudice. The subjects were informed that their personal trial related data would be considered confidential and used by BI in accordance with the local data protection laws. The level of disclosure was explained to the subjects. The subjects were also informed that their medical records could be examined by Clinical Quality Assurance auditors appointed by BI, by members of the appropriate Independent Ethics Committee (IEC), and by inspectors from regulatory authorities. Confidentiality of subject data was ensured by the use of depersonalised subject identification codes (subject numbers). If a subject continued to take trial medication, close monitoring was adhered to and all adverse events recorded. The terms and conditions of the insurance cover were available to the investigator and the subjects in the Investigator Site File (ISF).

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	24 February 2016
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	Australia: 46
Country: Number of subjects enrolled	Canada: 108
Country: Number of subjects enrolled	Czech Republic: 12
Country: Number of subjects enrolled	France: 17
Country: Number of subjects enrolled	Germany: 42
Country: Number of subjects enrolled	Japan: 51
Country: Number of subjects enrolled	Korea, Republic of: 52
Country: Number of subjects enrolled	United States: 232
Worldwide total number of subjects	560
EEA total number of subjects	71

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)	492
From 65 to 84 years	67
85 years and over	1

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 and risankizumab in Part A continued the same in Part B. Total 560 subjects were enrolled 54 subjects failed screening and are excluded from the analyses

Period 1

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

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:

Matching placebo were administered by subcutaneous (SC) injection at Weeks 0 and 4

Arm title	Ustekinumab (Part A)

Arm description:

Participants randomized to receive double-blind (DB) ustekinumab 45 milligram (mg) 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	Ustekinumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Ustekinumab 45 mg or 90 mg were administered by subcutaneous (SC) injection at Weeks 0 and 4

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).

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:

Risankizumab 150 mg were administered by subcutaneous (SC) injection at Weeks 0 and 4

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	102	100	304
Completed	98	99	299
Not completed	4	1	5
Adverse event, non-fatal	2	-	1
Not specified	-	-	1
Lost to follow-up	1	1	-
Withdrawal by subject	1	-	3

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: Baseline characteristics are based on the patients who were randomised at week 0 after successfully completing the screening period

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, Monitor, Data analyst, Assessor

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.

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	Experimental
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.

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.

Number of subjects in period 2[2]	Placebo/Risankizumab (Part B)	Ustekinumab/Ustekinumab (Part B)	Risankizumab/Risankizumab (Part B)
Started	97	99	297
Completed	95	94	289
Not completed	2	5	8
Adverse event, non-fatal	-	2	1
Subject Withdrawal	1	1	2
Lost to follow-up	1	2	5

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 milligram (mg) 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	102	100	304
Age categorical			
Units: Subjects			

Age Continuous			
Age of all patients included in the study. Intent-to-treat (ITT) population: All participants who were randomized at Week 0.			
Units: years			
arithmetic mean	49.3	46.5	48.3
standard deviation	± 13.63	± 13.42	± 13.39
Sex: Female, Male			
Gender distribution of all patients included in the study. ITT population was used for this assessment.			
Units: Subjects			
Female	23	30	92
Male	79	70	212
Ethnicity (NIH/OMB)			
Ethnicity of all patients included in the study. ITT population was used for this assessment.			
Units: Subjects			
Hispanic or Latino	12	12	23
Not Hispanic or Latino	90	88	281
Unknown or Not Reported	0	0	0
Race (NIH/OMB)			
Race of all patients included in the study. ITT population was used for this assessment.			
Units: Subjects			
American Indian or Alaska Native	2	2	7
Asian	28	22	86
Native Hawaiian or Other Pacific Islander	0	1	1
Black or African American	1	1	10
White	71	74	200

More than one race	0	0	0
Unknown or Not Reported	0	0	0

Reporting group values	Total		
Number of subjects	506		
Age categorical Units: Subjects			

Age Continuous			
Age of all patients included in the study. Intent-to-treat (ITT) population: All participants who were randomized at Week 0.			
Units: years arithmetic mean standard deviation	- -		
Sex: Female, Male			
Gender distribution of all patients included in the study. ITT population was used for this assessment.			
Units: Subjects			
Female	145		
Male	361		
Ethnicity (NIH/OMB)			
Ethnicity of all patients included in the study. ITT population was used for this assessment.			
Units: Subjects			
Hispanic or Latino	47		
Not Hispanic or Latino	459		
Unknown or Not Reported	0		
Race (NIH/OMB)			
Race of all patients included in the study. ITT population was used for this assessment.			
Units: Subjects			
American Indian or Alaska Native	11		
Asian	136		
Native Hawaiian or Other Pacific Islander	2		
Black or African American	12		
White	345		
More than one race	0		
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 milligram (mg) 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	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. Nonresponder imputation (NRI) was used for missing data. ITT population (Intent-to-treat (ITT): All participants who were randomized at Week 0) was used for this assessment.

End point type	Primary

End point timeframe:

Baseline and 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	102[2]	304[3]		
Units: percentage of participants				
number (not applicable)	4.9	75.3		

Notes:

[2] - ITT

[3] - ITT

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Cochran-Mantel-Haenszel test adjusted for strata (baseline weight [≤100 kilo gram (kg) versus (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.

Comparison groups	Placebo (Part A) v Risankizumab (Part A)
Number of subjects included in analysis	406
Analysis specification	Pre-specified
Analysis type	other[4]
P-value	< 0.001
Method	Cochran-Mantel-Haenszel
Parameter estimate	adjusted difference in percentage
Point estimate	70.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	64
upper limit	76.7

Notes:

[4] - 95% confedence interval (CI) for adjusted difference of 2 treatment groups, calculated by subtracting % of patients in placebo group from % of patients in Risankizumab group using Cochran-Mantel-Haenszel test adjusted for strata.

Primary: Percentage of Participants Achieving 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 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. ITT population was used for this assessment.

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	102[6]	304[7]		
Units: percentage of participants				
number (not applicable)	7.8	87.8		

Notes:

[6] - ITT

[7] - ITT

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Cochran-Mantel-Haenszel test adjusted for strata (baseline weight [≤100 kg vs >100 kg] and prior exposure to TNF antagonists [0 vs ≥1]). 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	406
Analysis specification	Pre-specified
Analysis type	other[8]
P-value	< 0.001
Method	Cochran-Mantel-Haenszel
Parameter estimate	adjusted difference in percentage
Point estimate	79.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	73.5
upper limit	86.3

Notes:

[8] - 95% confedence interval (CI) for adjusted difference of 2 treatment groups, calculated by subtracting % of patients in placebo group from % of patients in Risankizumab group using Cochran-Mantel-Haenszel test adjusted for strata.

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. ITT population was used for this assessment.

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	102[10]	304[11]		
Units: percentage of participants				
number (not applicable)	2.0	36.8		

Notes:

[10] - ITT

[11] - ITT

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Cochran-Mantel-Haenszel test adjusted for strata (baseline weight [≤100 kg vs >100 kg] and prior exposure to TNF antagonists [0 vs ≥1]). 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	406
Analysis specification	Pre-specified
Analysis type	other[12]
P-value	< 0.001
Method	Cochran-Mantel-Haenszel
Parameter estimate	adjusted difference in percentage
Point estimate	34.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	28.6
upper limit	40.8

Notes:

[12] - 95% confedence interval (CI) for adjusted difference of 2 treatment groups, calculated by subtracting % of patients in placebo group from % of patients in Risankizumab group using Cochran-Mantel-Haenszel test adjusted for strata.

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. ITT population was used for this assessment.

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	102[14]	304[15]		
Units: percentage of participants				
number (not applicable)	0.0	35.9		

Notes:

[14] - ITT

[15] - ITT

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Cochran-Mantel-Haenszel test adjusted for strata (baseline weight [≤100 kg vs >100 kg] and prior exposure to TNF antagonists [0 vs ≥1]). 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	406
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	Cochran-Mantel-Haenszel
Parameter estimate	adjusted difference in percentage
Point estimate	35.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	30
upper limit	41

Secondary: Percentage of Participants Achieving 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 Dermatology Life Quality Index (DLQI) score of 0 or 1 at Week 16 in Participants Who Received Risankizumab Compared With Placebo (Part A)[16]

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. ITT population was used for this assessment.

End point type	Secondary

End point timeframe:

Week 16

Notes:

[16] - 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	102[17]	304[18]		
Units: percentage of participants				
number (not applicable)	7.8	65.8		

Notes:

[17] - ITT

[18] - ITT

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Cochran-Mantel-Haenszel test adjusted for strata (baseline weight [≤100 kg vs >100 kg] and prior exposure to TNF antagonists [0 vs ≥1]). 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	406
Analysis specification	Pre-specified
Analysis type	other[19]
P-value	< 0.001
Method	Cochran-Mantel-Haenszel
Parameter estimate	adjusted difference in percentage
Point estimate	57.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	50.4
upper limit	65.3

Notes:

[19] - 95% confedence interval (CI) for adjusted difference of 2 treatment groups, calculated by subtracting % of patients in placebo group from % of patients in Risankizumab group using Cochran-Mantel-Haenszel test adjusted for strata.

Secondary: Percentage of Participants Achieving Psoriasis Symptoms Scale (PSS) Total Score of 0 at Week 16 in Participants Who Received Risankizumab Compared With Placebo (Part A)

End point title	Percentage of Participants Achieving Psoriasis Symptoms Scale (PSS) Total Score of 0 at Week 16 in Participants Who Received Risankizumab Compared With Placebo (Part A)[20]

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 total score 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. ITT population was used for this assessment.

End point type	Secondary

End point timeframe:

Week 16

Notes:

[20] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: 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	102[21]	304[22]		
Units: percentage of participants				
number (not applicable)	2.0	29.3		

Notes:

[21] - ITT

[22] - ITT

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Cochran-Mantel-Haenszel test adjusted for strata (baseline weight [≤100 kg vs >100 kg] and prior exposure to TNF antagonists [0 vs ≥1]). 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	406
Analysis specification	Pre-specified
Analysis type	other[23]
P-value	< 0.001
Method	Cochran-Mantel-Haenszel
Parameter estimate	adjusted difference in percentage
Point estimate	27.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	21.2
upper limit	32.9

Notes:

[23] - 95% confedence interval (CI) for adjusted difference of 2 treatment groups, calculated by subtracting % of patients in placebo group from % of patients in Risankizumab group using Cochran-Mantel-Haenszel test adjusted for strata.

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)[24]

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. Nonresponder imputation (NRI) was used for missing data. ITT population was used for this assessment.

End point type	Secondary

End point timeframe:

Week 16

Notes:

[24] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: 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	100[25]	304[26]		
Units: percentage of participants				
number (not applicable)	42.0	75.3		

Notes:

[25] - ITT

[26] - ITT

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Cochran-Mantel-Haenszel test adjusted for strata (baseline weight [≤100 kg vs >100 kg] and prior exposure to TNF antagonists [0 vs ≥1]). 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	404
Analysis specification	Pre-specified
Analysis type	other[27]
P-value	< 0.001
Method	Cochran-Mantel-Haenszel
Parameter estimate	adjusted difference in percentage
Point estimate	33.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	22.7
upper limit	44.3

Notes:

[27] - 95% confedence interval (CI) for adjusted difference of 2 treatment groups, calculated by subtracting % of patients in Ustekinumab group from % of patients in Risankizumab group using Cochran-Mantel-Haenszel test adjusted for strata.

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)[28]

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. ITT population was used for this assessment.

End point type	Secondary

End point timeframe:

Week 16

Notes:

[28] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: 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	100[29]	304[30]		
Units: percentage of participants				
number (not applicable)	63.0	87.8		

Notes:

[29] - ITT

[30] - ITT

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Cochran-Mantel-Haenszel test adjusted for strata (baseline weight [≤100 kg vs >100 kg] and prior exposure to TNF antagonists [0 vs ≥1]). 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	404
Analysis specification	Pre-specified
Analysis type	other[31]
P-value	< 0.001
Method	Cochran-Mantel-Haenszel
Parameter estimate	adjusted difference in percentage
Point estimate	25.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	15.2
upper limit	35

Notes:

[31] - 95% confedence interval (CI) for adjusted difference of 2 treatment groups, calculated by subtracting % of patients in Ustekinumab group from % of patients in Risankizumab group using Cochran-Mantel-Haenszel test adjusted for strata.

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)[32]

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. ITT population was used for this assessment.

End point type	Secondary

End point timeframe:

Week 16

Notes:

[32] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: 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	100[33]	304[34]		
Units: percentage of participants				
number (not applicable)	12.0	35.9		

Notes:

[33] - ITT

[34] - ITT

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Cochran-Mantel-Haenszel test adjusted for strata (baseline weight [≤100 kg vs >100 kg] and prior exposure to TNF antagonists [0 vs ≥1]). 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	404
Analysis specification	Pre-specified
Analysis type	other[35]
P-value	< 0.001
Method	Cochran-Mantel-Haenszel
Parameter estimate	adjusted difference in percentage
Point estimate	23.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	15.5
upper limit	32.1

Notes:

[35] - 95% confedence interval (CI) for adjusted difference of 2 treatment groups, calculated by subtracting % of patients in Ustekinumab group from % of patients in Risankizumab group using Cochran-Mantel-Haenszel test adjusted for strata.

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)[36]

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. ITT population was used for this assessment.

End point type	Secondary

End point timeframe:

Week 16

Notes:

[36] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: 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	100[37]	304[38]		
Units: percentage of participants				
number (not applicable)	14.0	36.8		

Notes:

[37] - ITT

[38] - ITT

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Cochran-Mantel-Haenszel test adjusted for strata (baseline weight [≤100 kg vs >100 kg] and prior exposure to TNF antagonists [0 vs ≥1]). 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	404
Analysis specification	Pre-specified
Analysis type	other[39]
P-value	< 0.001
Method	Cochran-Mantel-Haenszel
Parameter estimate	adjusted difference in percentage
Point estimate	22.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	14.3
upper limit	31.6

Notes:

[39] - 95% confedence interval (CI) for adjusted difference of 2 treatment groups, calculated by subtracting % of patients in Ustekinumab group from % of patients in Risankizumab group using Cochran-Mantel-Haenszel test adjusted for strata.

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. Nonresponder imputation (NRI) was used for missing data. ITT population was used for this assessment. Non-responder imputation. Analysis performed on all participants randomized to ustekinumab or risankizumab treatment in Part A.

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	100[40]	304[41]		
Units: percentage of participants				
number (not applicable)	44.0	81.9		

Notes:

[40] - ITT

[41] - ITT

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Cochran-Mantel-Haenszel test adjusted for strata (baseline weight [≤100 kg vs >100 kg] and prior exposure to TNF antagonists [0 vs ≥1]). 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	404
Analysis specification	Pre-specified
Analysis type	other[42]
P-value	< 0.001
Method	Cochran-Mantel-Haenszel
Parameter estimate	adjusted difference in percentage
Point estimate	38.3

Confidence interval	
level	95 %
sides	2-sided
lower limit	27.9
upper limit	48.6

Notes:

[42] - 95% confedence interval (CI) for adjusted difference of 2 treatment groups, calculated by subtracting % of patients in Ustekinumab group from % of patients in Risankizumab group using Cochran-Mantel-Haenszel test adjusted for strata.

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. 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. Nonresponder imputation (NRI) was used for missing data. ITT population was used for this assessment. Analysis performed on all participants randomized to ustekinumab or risankizumab treatment in Part A.

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	100[43]	304[44]		
Units: percentage of participants				
number (not applicable)	21.0	56.3		

Notes:

[43] - ITT

[44] - ITT

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Cochran-Mantel-Haenszel test adjusted for strata (baseline weight [≤100 kg vs >100 kg] and prior exposure to TNF] antagonists [0 vs ≥1]). 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	404
Analysis specification	Pre-specified
Analysis type	other[45]
P-value	< 0.001
Method	Cochran-Mantel-Haenszel
Parameter estimate	adjusted difference in percentage
Point estimate	35.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	25.7
upper limit	44.6

Notes:

[45] - 95% confedence interval (CI) for adjusted difference of 2 treatment groups, calculated by subtracting % of patients in Ustekinumab group from % of patients in Risankizumab group using Cochran-Mantel-Haenszel test adjusted for strata.

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. ITT population was used for this assessment. Non-responder imputation. Analysis performed on all participants randomized to ustekinumab or risankizumab treatment in Part A.

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	100[46]	304[47]		
Units: percentage of participants				
number (not applicable)	21.0	57.6		

Notes:

[46] - ITT

[47] - ITT

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Cochran-Mantel-Haenszel test adjusted for strata (baseline weight [≤100 kg vs >100 kg] and prior exposure to TNF] antagonists [0 vs ≥1]). 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	404
Analysis specification	Pre-specified
Analysis type	other[48]
P-value	< 0.001
Method	Cochran-Mantel-Haenszel
Parameter estimate	adjusted difference in percentage
Point estimate	36.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	27
upper limit	45.9

Notes:

[48] - 95% confedence interval (CI) for adjusted difference of 2 treatment groups, calculated by subtracting % of patients in Ustekinumab group from % of patients in Risankizumab group using Cochran-Mantel-Haenszel test adjusted for strata.

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)[49]

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 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. ITT population was used for this assessment.

End point type	Secondary

End point timeframe:

Week 12

Notes:

[49] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: 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	100[50]	304[51]		
Units: percentage of participants				
number (not applicable)	70.0	86.8		

Notes:

[50] - ITT

[51] - ITT

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Cochran-Mantel-Haenszel test adjusted for strata (baseline weight [≤100 kg vs >100 kg] and prior exposure to TNF antagonists [0 vs ≥1]). 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	404
Analysis specification	Pre-specified
Analysis type	other[52]
P-value	< 0.001
Method	Cochran-Mantel-Haenszel
Parameter estimate	adjusted difference in percentage
Point estimate	17
Confidence interval	
level	95 %
sides	2-sided
lower limit	7.4
upper limit	26.6

Notes:

[52] - 95% confedence interval (CI) for adjusted difference of 2 treatment groups, calculated by subtracting % of patients in Ustekinumab group from % of patients in Risankizumab group using Cochran-Mantel-Haenszel test adjusted for strata.

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)[53]

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. ITT population was used for this assessment.

End point type	Secondary

End point timeframe:

Week 12

Notes:

[53] - 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	100[54]	304[55]		
Units: percentage of participants				
number (not applicable)	65.0	82.2		

Notes:

[54] - ITT

[55] - ITT

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Cochran-Mantel-Haenszel test adjusted for strata (baseline weight [≤100 kg vs >100 kg] and prior exposure to TNF] antagonists [0 vs ≥1]). 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	404
Analysis specification	Pre-specified
Analysis type	other[56]
P-value	< 0.001
Method	Cochran-Mantel-Haenszel
Parameter estimate	adjusted difference in percentage
Point estimate	17.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	7.3
upper limit	27.3

Notes:

[56] - 95% confedence interval (CI) for adjusted difference of 2 treatment groups, calculated by subtracting % of patients in Ustekinumab group from % of patients in Risankizumab group using Cochran-Mantel-Haenszel test adjusted for strata.

Secondary: Percentage of Participants Achieving 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 DLQI score of 0 or 1 at Week 16 in Participants Who Received Risankizumab Compared With Ustekinumab (Part A)[57]

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. ITT population was used for this assessment.

End point type	Secondary

End point timeframe:

Week 16

Notes:

[57] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: 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	100[58]	304[59]		
Units: percentage of participants				
number (not applicable)	43.0	65.8		

Notes:

[58] - ITT

[59] - ITT

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Cochran-Mantel-Haenszel test adjusted for strata (baseline weight [≤100 kg vs >100 kg] and prior exposure to TNF] antagonists [0 vs ≥1]). 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	404
Analysis specification	Pre-specified
Analysis type	other[60]
P-value	< 0.001
Method	Cochran-Mantel-Haenszel
Parameter estimate	adjusted difference in percentage
Point estimate	23
Confidence interval	
level	95 %
sides	2-sided
lower limit	11.9
upper limit	34

Notes:

[60] - 95% confedence interval (CI) for adjusted difference of 2 treatment groups, calculated by subtracting % of patients in Ustekinumab group from % of patients in Risankizumab group using Cochran-Mantel-Haenszel test adjusted for strata.

Secondary: PSS Total Score: Change from Baseline to Week 16 in Participants Who Received Risankizumab Compared With Placebo (Part A)

End point title	PSS Total Score: Change from Baseline to Week 16 in Participants Who Received Risankizumab Compared With Placebo (Part A)[61]

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 total score 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. A negative change from Baseline indicates improvement. Last observation carried forward (LOCF) imputation was used for missing data. ITT population was used for this assessment. Last observation carried forward. Participants randomized to placebo or risankizumab with an observed baseline PSS and at least one postbaseline PSS observation on or prior to Week 16.

End point type	Secondary

End point timeframe:

Baseline and Week 16

Notes:

[61] - 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	83[62]	251[63]		
Units: units on a scale				
least squares mean (standard error)	0.157 (± 0.3476)	-5.608 (± 0.2254)		

Notes:

[62] - ITT

[63] - ITT

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Placebo (Part A) v Risankizumab (Part A)
Number of subjects included in analysis	334
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001 [64]
Method	van Elteren test
Parameter estimate	Mean difference (final values)
Point estimate	-5.765
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.496
upper limit	-5.035

Notes:

[64] - 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).

Adverse events

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:

TES/AEs in Part A are defined as events from first dose of study drug in Part A until prior to first dose in Part B or up to 105 days after last dose of study drug if the participant discontinued in Part A; TEAEs and TESAEs in Part B are defined as events from first dose of study drug in Part B 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 mg 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	3 / 102 (2.94%)	8 / 100 (8.00%)	7 / 304 (2.30%)
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)			

Basal cell carcinoma			
subjects affected / exposed	0 / 102 (0.00%)	0 / 100 (0.00%)	0 / 304 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Squamous cell carcinoma of skin			
subjects affected / exposed	1 / 102 (0.98%)	0 / 100 (0.00%)	1 / 304 (0.33%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 102 (0.00%)	0 / 100 (0.00%)	1 / 304 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombophlebitis			
subjects affected / exposed	0 / 102 (0.00%)	0 / 100 (0.00%)	0 / 304 (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 / 102 (0.00%)	0 / 100 (0.00%)	0 / 304 (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 / 102 (0.00%)	0 / 100 (0.00%)	1 / 304 (0.33%)
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			
Chest pain			
subjects affected / exposed	0 / 102 (0.00%)	0 / 100 (0.00%)	0 / 304 (0.00%)
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			

Female genital tract fistula			
subjects affected / exposed	0 / 102 (0.00%)	0 / 100 (0.00%)	0 / 304 (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
Ovarian cyst			
subjects affected / exposed	1 / 102 (0.98%)	0 / 100 (0.00%)	0 / 304 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Pulmonary sarcoidosis			
subjects affected / exposed	0 / 102 (0.00%)	0 / 100 (0.00%)	0 / 304 (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
Sleep apnoea syndrome			
subjects affected / exposed	0 / 102 (0.00%)	0 / 100 (0.00%)	0 / 304 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Acute psychosis			
subjects affected / exposed	0 / 102 (0.00%)	0 / 100 (0.00%)	0 / 304 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Schizoaffective disorder			
subjects affected / exposed	0 / 102 (0.00%)	0 / 100 (0.00%)	0 / 304 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Suicidal ideation			
subjects affected / exposed	0 / 102 (0.00%)	1 / 100 (1.00%)	0 / 304 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Wound complication			

subjects affected / exposed	0 / 102 (0.00%)	0 / 100 (0.00%)	0 / 304 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wrist fracture			
subjects affected / exposed	0 / 102 (0.00%)	0 / 100 (0.00%)	0 / 304 (0.00%)
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			
Angina pectoris			
subjects affected / exposed	0 / 102 (0.00%)	1 / 100 (1.00%)	0 / 304 (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
Angina unstable			
subjects affected / exposed	0 / 102 (0.00%)	0 / 100 (0.00%)	0 / 304 (0.00%)
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 / 102 (0.00%)	0 / 100 (0.00%)	0 / 304 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Left ventricular failure			
subjects affected / exposed	0 / 102 (0.00%)	0 / 100 (0.00%)	0 / 304 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mitral valve incompetence			
subjects affected / exposed	0 / 102 (0.00%)	0 / 100 (0.00%)	0 / 304 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Prinzmetal angina			
subjects affected / exposed	0 / 102 (0.00%)	0 / 100 (0.00%)	0 / 304 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Supraventricular tachycardia			

subjects affected / exposed	0 / 102 (0.00%)	0 / 100 (0.00%)	0 / 304 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Post herpetic neuralgia			
subjects affected / exposed	0 / 102 (0.00%)	1 / 100 (1.00%)	0 / 304 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			
Hypoacusis			
subjects affected / exposed	0 / 102 (0.00%)	0 / 100 (0.00%)	0 / 304 (0.00%)
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			
Enteritis			
subjects affected / exposed	0 / 102 (0.00%)	0 / 100 (0.00%)	1 / 304 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 102 (0.00%)	0 / 100 (0.00%)	0 / 304 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis acute			
subjects affected / exposed	0 / 102 (0.00%)	0 / 100 (0.00%)	0 / 304 (0.00%)
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 stone			
subjects affected / exposed	1 / 102 (0.98%)	0 / 100 (0.00%)	0 / 304 (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
Cholecystitis acute			

subjects affected / exposed	1 / 102 (0.98%)	0 / 100 (0.00%)	0 / 304 (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
Cholelithiasis			
subjects affected / exposed	0 / 102 (0.00%)	0 / 100 (0.00%)	0 / 304 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Drug-induced liver injury			
subjects affected / exposed	0 / 102 (0.00%)	1 / 100 (1.00%)	1 / 304 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Liver injury			
subjects affected / exposed	0 / 102 (0.00%)	1 / 100 (1.00%)	0 / 304 (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
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 102 (0.00%)	0 / 100 (0.00%)	1 / 304 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intervertebral disc protrusion			
subjects affected / exposed	0 / 102 (0.00%)	0 / 100 (0.00%)	0 / 304 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lumbar spinal stenosis			
subjects affected / exposed	1 / 102 (0.98%)	0 / 100 (0.00%)	0 / 304 (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
Psoriatic arthropathy			
subjects affected / exposed	0 / 102 (0.00%)	0 / 100 (0.00%)	0 / 304 (0.00%)
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			

Anal abscess			
subjects affected / exposed	0 / 102 (0.00%)	1 / 100 (1.00%)	0 / 304 (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
Cellulitis			
subjects affected / exposed	0 / 102 (0.00%)	0 / 100 (0.00%)	1 / 304 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	0 / 102 (0.00%)	0 / 100 (0.00%)	0 / 304 (0.00%)
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 / 102 (0.00%)	0 / 100 (0.00%)	0 / 304 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis			
subjects affected / exposed	0 / 102 (0.00%)	0 / 100 (0.00%)	0 / 304 (0.00%)
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 / 102 (0.00%)	0 / 100 (0.00%)	0 / 304 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sinusitis			
subjects affected / exposed	0 / 102 (0.00%)	1 / 100 (1.00%)	0 / 304 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tonsillitis			
subjects affected / exposed	0 / 102 (0.00%)	0 / 100 (0.00%)	0 / 304 (0.00%)
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/Risankizum	Ustekinumab/Usteki	Risankizumab/Risan

	ab (Part B)	numab (Part B)	kizumab (Part B)
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 97 (3.09%)	4 / 99 (4.04%)	16 / 297 (5.39%)
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)			
Basal cell carcinoma			
subjects affected / exposed	1 / 97 (1.03%)	0 / 99 (0.00%)	0 / 297 (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
Squamous cell carcinoma of skin			
subjects affected / exposed	1 / 97 (1.03%)	0 / 99 (0.00%)	0 / 297 (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
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 97 (0.00%)	0 / 99 (0.00%)	0 / 297 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombophlebitis			
subjects affected / exposed	0 / 97 (0.00%)	0 / 99 (0.00%)	1 / 297 (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
Surgical and medical procedures			
Abortion induced			
subjects affected / exposed	0 / 97 (0.00%)	0 / 99 (0.00%)	1 / 297 (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
Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous			
subjects affected / exposed	0 / 97 (0.00%)	0 / 99 (0.00%)	1 / 297 (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
General disorders and administration site conditions			

Chest pain			
subjects affected / exposed	0 / 97 (0.00%)	0 / 99 (0.00%)	1 / 297 (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			
Female genital tract fistula			
subjects affected / exposed	0 / 97 (0.00%)	0 / 99 (0.00%)	1 / 297 (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
Ovarian cyst			
subjects affected / exposed	0 / 97 (0.00%)	0 / 99 (0.00%)	0 / 297 (0.00%)
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			
Pulmonary sarcoidosis			
subjects affected / exposed	0 / 97 (0.00%)	0 / 99 (0.00%)	1 / 297 (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
Sleep apnoea syndrome			
subjects affected / exposed	0 / 97 (0.00%)	1 / 99 (1.01%)	0 / 297 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Acute psychosis			
subjects affected / exposed	0 / 97 (0.00%)	1 / 99 (1.01%)	0 / 297 (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
Schizoaffective disorder			
subjects affected / exposed	0 / 97 (0.00%)	1 / 99 (1.01%)	0 / 297 (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
Suicidal ideation			

subjects affected / exposed	0 / 97 (0.00%)	0 / 99 (0.00%)	0 / 297 (0.00%)
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			
Wound complication			
subjects affected / exposed	1 / 97 (1.03%)	0 / 99 (0.00%)	0 / 297 (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
Wrist fracture			
subjects affected / exposed	0 / 97 (0.00%)	0 / 99 (0.00%)	1 / 297 (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 disorders			
Angina pectoris			
subjects affected / exposed	0 / 97 (0.00%)	0 / 99 (0.00%)	0 / 297 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angina unstable			
subjects affected / exposed	0 / 97 (0.00%)	0 / 99 (0.00%)	1 / 297 (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	0 / 97 (0.00%)	0 / 99 (0.00%)	1 / 297 (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
Left ventricular failure			
subjects affected / exposed	0 / 97 (0.00%)	0 / 99 (0.00%)	1 / 297 (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
Mitral valve incompetence			
subjects affected / exposed	0 / 97 (0.00%)	0 / 99 (0.00%)	1 / 297 (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

Prinzmetal angina			
subjects affected / exposed	0 / 97 (0.00%)	0 / 99 (0.00%)	1 / 297 (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
Supraventricular tachycardia			
subjects affected / exposed	0 / 97 (0.00%)	0 / 99 (0.00%)	1 / 297 (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			
Post herpetic neuralgia			
subjects affected / exposed	0 / 97 (0.00%)	0 / 99 (0.00%)	0 / 297 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			
Hypoacusis			
subjects affected / exposed	0 / 97 (0.00%)	0 / 99 (0.00%)	1 / 297 (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			
Enteritis			
subjects affected / exposed	0 / 97 (0.00%)	0 / 99 (0.00%)	0 / 297 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 97 (0.00%)	0 / 99 (0.00%)	1 / 297 (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
Pancreatitis acute			
subjects affected / exposed	0 / 97 (0.00%)	0 / 99 (0.00%)	1 / 297 (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
Hepatobiliary disorders			
Bile duct stone			

subjects affected / exposed	0 / 97 (0.00%)	0 / 99 (0.00%)	0 / 297 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis acute			
subjects affected / exposed	0 / 97 (0.00%)	0 / 99 (0.00%)	0 / 297 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholelithiasis			
subjects affected / exposed	1 / 97 (1.03%)	1 / 99 (1.01%)	0 / 297 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Drug-induced liver injury			
subjects affected / exposed	0 / 97 (0.00%)	0 / 99 (0.00%)	0 / 297 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Liver injury			
subjects affected / exposed	0 / 97 (0.00%)	0 / 99 (0.00%)	0 / 297 (0.00%)
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 / 97 (0.00%)	0 / 99 (0.00%)	0 / 297 (0.00%)
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 / 97 (0.00%)	0 / 99 (0.00%)	1 / 297 (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
Lumbar spinal stenosis			
subjects affected / exposed	0 / 97 (0.00%)	0 / 99 (0.00%)	0 / 297 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psoriatic arthropathy			

subjects affected / exposed	0 / 97 (0.00%)	0 / 99 (0.00%)	1 / 297 (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
Infections and infestations			
Anal abscess			
subjects affected / exposed	0 / 97 (0.00%)	0 / 99 (0.00%)	0 / 297 (0.00%)
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			
subjects affected / exposed	1 / 97 (1.03%)	0 / 99 (0.00%)	0 / 297 (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
Gastroenteritis			
subjects affected / exposed	0 / 97 (0.00%)	0 / 99 (0.00%)	1 / 297 (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
Osteomyelitis			
subjects affected / exposed	1 / 97 (1.03%)	0 / 99 (0.00%)	0 / 297 (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
Pyelonephritis			
subjects affected / exposed	0 / 97 (0.00%)	0 / 99 (0.00%)	1 / 297 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	0 / 97 (0.00%)	0 / 99 (0.00%)	1 / 297 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sinusitis			
subjects affected / exposed	0 / 97 (0.00%)	0 / 99 (0.00%)	0 / 297 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tonsillitis			

subjects affected / exposed	0 / 97 (0.00%)	1 / 99 (1.01%)	0 / 297 (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

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	16 / 102 (15.69%)	16 / 100 (16.00%)	45 / 304 (14.80%)
Nervous system disorders			
Headache			
subjects affected / exposed	2 / 102 (1.96%)	2 / 100 (2.00%)	9 / 304 (2.96%)
occurrences (all)	2	2	9
Skin and subcutaneous tissue disorders			
Psoriasis			
subjects affected / exposed	6 / 102 (5.88%)	1 / 100 (1.00%)	0 / 304 (0.00%)
occurrences (all)	6	1	0
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	2 / 102 (1.96%)	6 / 100 (6.00%)	17 / 304 (5.59%)
occurrences (all)	2	6	20
Urinary tract infection			
subjects affected / exposed	1 / 102 (0.98%)	2 / 100 (2.00%)	1 / 304 (0.33%)
occurrences (all)	1	2	1
Viral upper respiratory tract infection			
subjects affected / exposed	6 / 102 (5.88%)	6 / 100 (6.00%)	20 / 304 (6.58%)
occurrences (all)	7	8	24

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	25 / 97 (25.77%)	36 / 99 (36.36%)	75 / 297 (25.25%)
Nervous system disorders			
Headache			
subjects affected / exposed	3 / 97 (3.09%)	5 / 99 (5.05%)	5 / 297 (1.68%)
occurrences (all)	3	5	5
Skin and subcutaneous tissue disorders			

Psoriasis			
subjects affected / exposed	0 / 97 (0.00%)	1 / 99 (1.01%)	1 / 297 (0.34%)
occurrences (all)	0	1	1
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	8 / 97 (8.25%)	11 / 99 (11.11%)	30 / 297 (10.10%)
occurrences (all)	10	14	32
Urinary tract infection			
subjects affected / exposed	0 / 97 (0.00%)	5 / 99 (5.05%)	3 / 297 (1.01%)
occurrences (all)	0	5	4
Viral upper respiratory tract infection			
subjects affected / exposed	15 / 97 (15.46%)	18 / 99 (18.18%)	40 / 297 (13.47%)
occurrences (all)	17	20	45

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
13 May 2016	Anti-drug antibody sampling added to Week 4. Line item biologic therapy changed to psoriasis therapy. % Body surface area involvement added as line item. Remove Week 0. Remove Interactive Response Technology call from Follow-Up 3 Visit. Patient with a positive or suspected history of Psoriatic Arthritis (PsA) will be evaluated via ClASsification of Psoriatic Arthritis. Revised text to specify timing of vital sign measurements and hypersensitivity monitoring at dosing visits. Replaced criteria for eligibility in Open Label Extension study of without having missed more than one study treatment with without early treatment discontinuation. Removed prior to receiving BI 655066. Clarification on how efficacy data will be used on submission as well as additional information on unblinding. Added thrombotic events. Patients that discontinue study medication should complete all study visits and procedures as initially planned. Added region and instructions for injections. Added that dosing injections should be performed within approximately 5 minutes. Added tofacitinib Xeljanz® and apremilast Otezla® Removed efalizumab Raptiva®. Additional medications requiring washout Medication not available. Added absolute PASI of <3 at all visits collected. Revised text to specify the timing of vital sign measurements and hypersensitivity monitoring at dosing visits. Added absolute count to the Differential Manual. Added Activated to Partial Thromboplastin Time. Added test done in clinic for urine pregnancy. Moved creatinine from dipstick urinalysis to urine section. Added albumin/creatinine ratio to urine section. Specified Purified Protein Derivative skin test is not provided or performed by central laboratory. Removed For Japan only, the reason for the decision on causal relationship for unlisted AEs needs to be provided in the eCRF. Removed At visit 2 these questionnaires should be obtained after having the patient randomised. Removed maximum of 2 visits for screening.
11 October 2016	Changed BI drug or BI investigational product or BI 655066 to refer to either names for this compound: BI 655066/ ABBV-066/risankizumab. Changed sponsor from Boehringer Ingelheim (BI) to AbbVie in the US and BI for all other participating countries. Changed text to specify Statistical Evaluation will be done by AbbVie according to their SOPs. Updated text to "AbbVie/Boehringer Ingelheim reserves the right to discontinue the trial overall or at a particular trial site at any time for the following reasons". Changed DNA banking sample storage from Boehringer Ingelheim to AbbVie or a third party delegate (e.g. Boehringer Ingelheim Pharma GmbH & Co. KG; Birkendorfer Str. 65, 88397 Biberach, Germany). Changed text to specify that AbbVie summary tables and listings will be produced and analyses based on AbbVie standards.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported