



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 |
|-----------------|---|

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. 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:

[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. 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 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 (\pm 0.3316) | -6.402 (\pm 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

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 occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 98 (0.00%) 0 / 0 0 / 0 | 0 / 99 (0.00%) 0 / 0 0 / 0 | 1 / 294 (0.34%) 0 / 1 0 / 0 |
| Diverticulitis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 98 (0.00%) 0 / 0 0 / 0 | 0 / 99 (0.00%) 0 / 0 0 / 0 | 1 / 294 (0.34%) 0 / 1 0 / 0 |
| Herpes zoster subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 98 (0.00%) 0 / 0 0 / 0 | 1 / 99 (1.01%) 1 / 1 0 / 0 | 1 / 294 (0.34%) 1 / 1 0 / 0 |
| Osteomyelitis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 98 (0.00%) 0 / 0 0 / 0 | 0 / 99 (0.00%) 0 / 0 0 / 0 | 1 / 294 (0.34%) 0 / 1 0 / 0 |
| Pneumonia subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 98 (0.00%) 0 / 0 0 / 0 | 0 / 99 (0.00%) 0 / 0 0 / 0 | 0 / 294 (0.00%) 0 / 0 0 / 0 |
| Sepsis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 98 (0.00%) 0 / 0 0 / 0 | 0 / 99 (0.00%) 0 / 0 0 / 0 | 1 / 294 (0.34%) 0 / 1 0 / 0 |
| Metabolism and nutrition disorders Dehydration subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 98 (0.00%) 0 / 0 0 / 0 | 0 / 99 (0.00%) 0 / 0 0 / 0 | 0 / 294 (0.00%) 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