Clinical trial results:
A Phase 2 Single-Arm Open-Label Extension Study to Investigate Safety With Risankizumab in Psoriatic Arthritis Subjects Who Have Completed Week 24 Visit of Study M16¬002 (1311.5)

Summary

EudraCT number	2016-003113-94
Trial protocol	CZ DE FI ES BE FR
Global end of trial date	30 July 2018

Results information

Result version number	v1 (current)
This version publication date	13 July 2019
First version publication date	13 July 2019

Trial information

Trial identification

Sponsor protocol code	M16-244

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02986373
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	AbbVie Deutschland GmbH & Co. KG
Sponsor organisation address	AbbVie House, Vanwall Business Park, Vanwall Road, Maidenhead, Berkshire, United Kingdom, SL6-4UB
Public contact	Global Medical Services, AbbVie, 001 800-633-9110,
Scientific contact	Maureen Kelly, MD, AbbVie, maureen.kelly@abbvie.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	30 July 2018
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	30 July 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

This is an open-label extension (OLE) study to assess the efficacy, safety and tolerability of risankizumab in participants with psoriatic arthritis (PsA).

Participants who had completed all doses of study drug and the Week 24 visit of M16-002 (1311.5; the lead-in study) were eligible to enroll in M16-244 (this study). Participants were allowed to either finish the Week 24 visit of the lead-in study and take the first dose of study drug for this study on the same day, or delay the start of this study up to 8 weeks if needed.

Protection of trial subjects:

Subject or his or her representative read and understood the information provided about the study and gave written permission.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	15 December 2016
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Belgium: 5
Country: Number of subjects enrolled	Canada: 6
Country: Number of subjects enrolled	Czech Republic: 13
Country: Number of subjects enrolled	Finland: 15
Country: Number of subjects enrolled	France: 4
Country: Number of subjects enrolled	Japan: 14
Country: Number of subjects enrolled	Poland: 38
Country: Number of subjects enrolled	Spain: 9
Country: Number of subjects enrolled	Taiwan: 5
Country: Number of subjects enrolled	United States: 36
Worldwide total number of subjects	145
EEA total number of subjects	84

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)	121
From 65 to 84 years	24
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Participants who had completed all doses of study drug and the Week 24 visit of M16-002 (NCT02719171; lead-in study) were eligible to enroll in M16-244 (this study).

Period 1

Period 1 title	Overall Trial (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Risankizumab

Arm description:

Participants received open-label risankizumab 150 mg by subcutaneous injection at Weeks 0, 12, 24, and 36.

Arm type	Experimental
Investigational medicinal product name	Risankizumab
Investigational medicinal product code	
Other name	ABBV-066, BI 655066
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Risankizumab administered by subcutaneous injection.

Number of subjects in period 1	Risankizumab
Started	145
Completed	106
Not completed	39
Adverse Event	4
Not specified	24
Withdrawal by Subject	10
Lost to follow-up	1

Baseline characteristics

Reporting groups	
Reporting group title	Overall Trial (overall period)

Reporting group description: -

Reporting group values	Overall Trial (overall period)	Total	
Number of subjects	145	145	
Age categorical Units: Subjects			
In utero		0	
Preterm newborn infants (gestational age < 37 wks)		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)		0	
From 65-84 years		0	
85 years and over		0	
Age continuous Units: years			
arithmetic mean	50.4		
standard deviation	± 12.52	-	
Gender categorical Units: Subjects			
Female	61	61	
Male	84	84	
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	3	3	
Not Hispanic or Latino	138	138	
Unknown or Not Reported	4	4	
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	1	1	
Asian	21	21	
Native Hawaiian or Other Pacific Islander	0	0	
Black or African American	0	0	
White	119	119	
More than one race	0	0	
Unknown or Not Reported	4	4	

End points

End points reporting groups

Reporting group title	Risankizumab

Reporting group description:

Participants received open-label risankizumab 150 mg by subcutaneous injection at Weeks 0, 12, 24, and 36.

Primary: Number of Participants With Adverse Events

End point title	Number of Participants With Adverse Events[1]

End point description:

An adverse event (AE) is defined as any untoward medical occurrence in a patient or clinical investigation subject administered a pharmaceutical product and which does not necessarily have a causal relationship with this treatment. The investigator assessed the relationship of each event to the use of study drug as either probably related, possibly related, probably not related or not related. A serious adverse event (SAE) is an event that results in death, is life-threatening, requires or prolongs hospitalization, results in a congenital anomaly, persistent or significant disability/incapacity or is an important medical event that, based on medical judgment, may jeopardize the subject and may require medical or surgical intervention to prevent any of the outcomes listed above. Treatment-emergent events (TEAEs) are defined as an AE that began or worsened in severity after initiation of study drug and 20 weeks (140 days) after last dose. Abbreviations: NMSC=non-melanoma skin cancer.

End point type	Primary

End point timeframe:

From the first dose of study drug in this study until 20 weeks after the last dose of study drug (up to 56 weeks).

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Descriptive data are summarized for this end point per protocol.

End point values	Risankizumab			
Subject group type	Reporting group			
Number of subjects analysed	145[2]			
Units: Participants				
Any AE	87			
Any AE possibly drug related	22			
Any SAE at least possibly drug related	1			
Any severe AE	7			
Any SAE	5			
Any AE leading to discontinuation of study drug	5			
Any major adverse cardiac events (adjudicated)	2			
Any serious infections events	2			
Any tuberculosis events	2			
Any malignant tumor events	1			
Any malignancies excluding NMSC events	1			

Notes:

[2] - Safety Analysis Set: all participants that received at least 1 dose of study drug in this study.

Statistical analyses

No statistical analyses for this end point

Secondary: Modified Total Sharp Score (mTSS): Change From Baseline (in the Lead-in Study) to Week 24 in the Lead-in Study

End point title	Modified Total Sharp Score (mTSS): Change From Baseline (in the Lead-in Study) to Week 24 in the Lead-in Study

End point description:

The mTSS is a measure of change in joint health. X-rays of hands, wrists, and feet (including distal interphalangeal joints) were obtained at Week 24 and Week 48. Totals for hands and feet for erosion scores (range 0 to 320) and joint space narrowing scores (range 0 to 208) were calculated and added to obtain the mTSS (range = 0 [normal] to 528 [maximal disease]). An increase in mTSS from Baseline represents disease progression and/or joint worsening; no progression was defined as a change of ≤0.5. Analysis based on derivation method #1 per the lead-in study. Baseline is defined as baseline in the lead-in study.

End point type	Secondary

End point timeframe:

Baseline (Lead-in Study), Week 24 (Lead-in Study)

End point values	Risankizumab			
Subject group type	Reporting group			
Number of subjects analysed	118[3]			
Units: units on a scale				
arithmetic mean (confidence interval 95%)	0.12 (-0.16 to 0.40)			

Notes:

[3] - Safety Analysis Set

Statistical analyses

No statistical analyses for this end point

Secondary: mTSS: Change From Baseline (in the Lead-in Study) to Week 24

End point title	mTSS: Change From Baseline (in the Lead-in Study) to Week 24

End point description:

The mTSS is a measure of change in joint health. X-rays of hands, wrists, and feet (including distal interphalangeal joints) were obtained at Week 24 and Week 48. Totals for hands and feet for erosion scores (range 0 to 320) and joint space narrowing scores (range 0 to 208) were calculated and added to obtain the mTSS (range = 0 [normal] to 528 [maximal disease]). An increase in mTSS from Baseline represents disease progression and/or joint worsening; no progression was defined as a change of ≤0.5. Analysis based on derivation method #1 per the lead-in study. Baseline is defined as baseline in the lead-in study.

End point type	Secondary

End point timeframe:

Baseline (Lead-in Study), Week 24

End point values	Risankizumab			
Subject group type	Reporting group			
Number of subjects analysed	118[4]			
Units: units on a scale				
arithmetic mean (confidence interval 95%)	0.38 (0.06 to 0.71)			

Notes:

[4] - Safety Analysis Set

Statistical analyses

No statistical analyses for this end point

Secondary: mTSS: Change From Baseline (in the Lead-in Study) to Week 48

End point title	mTSS: Change From Baseline (in the Lead-in Study) to Week 48

End point description:

The mTSS is a measure of change in joint health. X-rays of hands, wrists, and feet (including distal interphalangeal joints) were obtained at Week 24 and Week 48. Totals for hands and feet for erosion scores (range 0 to 320) and joint space narrowing scores (range 0 to 208) were calculated and added to obtain the mTSS (range = 0 [normal] to 528 [maximal disease]). An increase in mTSS from Baseline represents disease progression and/or joint worsening; no progression was defined as a change of ≤0.5. Analysis based on derivation method #1 per the lead-in study. Baseline is defined as baseline in the lead-in study.

End point type	Secondary

End point timeframe:

Baseline (Lead-in Study), Week 48

End point values	Risankizumab			
Subject group type	Reporting group			
Number of subjects analysed	102[5]			
Units: units on a scale				
arithmetic mean (confidence interval 95%)	0.34 (-0.07 to 0.75)			

Notes:

[5] - Safety Analysis Set

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Achieving American College of Rheumatology 20% (ACR20) Response at Week 0

End point title	Percentage of Participants Achieving American College of Rheumatology 20% (ACR20) Response at Week 0

End point description:

Response defined by ACR20 criteria (improvement from baseline) at Week 0: ≥20% improvement in tender joint count; ≥20% improvement in swollen joint count; and ≥20% improvement in at least 3 out of the following 5 parameters: Patient's Assessment of Pain Intensity visual analog scale (VAS), Patient's Global Assessment of Disease Activity, Investigator's Global Assessment of Disease Activity, Health Assessment Questionnaire Disability Index (HAQ-DI), and acute phase reactant value (C-reactive protein). Baseline is defined as the last non missing pre-treatment observation prior to first dose in the

lead-in study.

End point type	Secondary

End point timeframe:

Week 0

End point values	Risankizumab			
Subject group type	Reporting group			
Number of subjects analysed	145[6]			
Units: Percentage of Participants				
number (confidence interval 95%)	43.4 (35.2 to 51.9)			

Notes:

[6] - Safety Analysis Set

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Achieving ACR20 Response at Week 4

End point title	Percentage of Participants Achieving ACR20 Response at Week 4

End point description:

Response defined by ACR20 criteria (improvement from baseline) at Week 4: ≥20% improvement in tender joint count; ≥20% improvement in swollen joint count; and ≥20% improvement in at least 3 out of the following 5 parameters: Patient's Assessment of Pain Intensity VAS, Patient's Global Assessment of Disease Activity, Investigator's Global Assessment of Disease Activity, HAQ-DI, and acute phase reactant value (C-reactive protein). Baseline is defined as the last non missing pre-treatment observation prior to first dose in the lead-in study.

End point type	Secondary

End point timeframe:

Week 4

End point values	Risankizumab			
Subject group type	Reporting group			
Number of subjects analysed	144[7]			
Units: percentage of participants				
number (confidence interval 95%)	55.6 (47.1 to 63.8)			

Notes:

[7] - Safety Analysis Set

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Achieving ACR20 Response at Week 12

End point title	Percentage of Participants Achieving ACR20 Response at Week

	12

End point description:

Response defined by ACR20 criteria (improvement from baseline) at Week 12: ≥20% improvement in tender joint count; ≥20% improvement in swollen joint count; and ≥20% improvement in at least 3 out of the following 5 parameters: Patient's Assessment of Pain Intensity VAS, Patient's Global Assessment of Disease Activity, Investigator's Global Assessment of Disease Activity, HAQ-DI, and acute phase reactant value (C-reactive protein). Baseline is defined as baseline in the lead-in study.

End point type	Secondary

End point timeframe:

Week 12

End point values	Risankizumab			
Subject group type	Reporting group			
Number of subjects analysed	142[8]			
Units: percentage of participants				
number (confidence interval 95%)	57.0 (48.5 to 65.3)			

Notes:

[8] - Safety Analysis Set

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Achieving ACR20 Response at Week 24

End point title	Percentage of Participants Achieving ACR20 Response at Week 24

End point description:

Response defined by ACR20 criteria (improvement from baseline) at Week 24: ≥20% improvement in tender joint count; ≥20% improvement in swollen joint count; and ≥20% improvement in at least 3 out of the following 5 parameters: Patient's Assessment of Pain Intensity VAS, Patient's Global Assessment of Disease Activity, Investigator's Global Assessment of Disease Activity, HAQ-DI, and acute phase reactant value (C-reactive protein). Baseline is defined as the last non missing pre-treatment observation prior to first dose in the lead-in study.

End point type	Secondary

End point timeframe:

Week 24

End point values	Risankizumab			
Subject group type	Reporting group			
Number of subjects analysed	134[9]			
Units: percentage of participants				
number (confidence interval 95%)	62.7 (53.9 to 70.9)			

Notes:

[9] - Safety Analysis Set

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Achieving ACR20 Response at Week 36

End point title	Percentage of Participants Achieving ACR20 Response at Week 36

End point description:

Response defined by ACR20 criteria (improvement from baseline) at Week 36: ≥20% improvement in tender joint count; ≥20% improvement in swollen joint count; and ≥20% improvement in at least 3 out of the following 5 parameters: Patient's Assessment of Pain Intensity VAS, Patient's Global Assessment of Disease Activity, Investigator's Global Assessment of Disease Activity, HAQ-DI, and acute phase reactant value (C-reactive protein). Baseline is defined as the last non missing pre-treatment observation prior to first dose in the lead-in study.

End point type	Secondary

End point timeframe:

Week 36

End point values	Risankizumab			
Subject group type	Reporting group			
Number of subjects analysed	115[10]			
Units: percentage of participants				
number (confidence interval 95%)	68.7 (59.4 to 77.0)			

Notes:

[10] - Safety Analysis Set

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Achieving ACR20 Response at Week 48

End point title	Percentage of Participants Achieving ACR20 Response at Week 48

End point description:

Response defined by ACR20 criteria (improvement from baseline) at Week 48: ≥20% improvement in tender joint count; ≥20% improvement in swollen joint count; and ≥20% improvement in at least 3 out of the following 5 parameters: Patient's Assessment of Pain Intensity VAS, Patient's Global Assessment of Disease Activity, Investigator's Global Assessment of Disease Activity, HAQ-DI, and acute phase reactant value (C-reactive protein). Baseline is defined as the last non missing pre-treatment observation prior to first dose in the lead-in study.

End point type	Secondary

End point timeframe:

Week 48

End point values	Risankizumab			
Subject group type	Reporting group			
Number of subjects analysed	109[11]			
Units: percentage of participants				
number (confidence interval 95%)	69.7 (60.2 to 78.2)			

Notes:

[11] - Safety Analysis Set

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Achieving ACR20 Response at Week 52

End point title	Percentage of Participants Achieving ACR20 Response at Week 52

End point description:

Response defined by ACR20 criteria (improvement from baseline) at Week 52: ≥20% improvement in tender joint count; ≥20% improvement in swollen joint count; and ≥20% improvement in at least 3 out of the following 5 parameters: Patient's Assessment of Pain Intensity VAS, Patient's Global Assessment of Disease Activity, Investigator's Global Assessment of Disease Activity, HAQ-DI, and acute phase reactant value (C-reactive protein). Baseline is defined as the last non missing pre-treatment observation prior to first dose in the lead-in study.

End point type	Secondary

End point timeframe:

Week 52

End point values	Risankizumab			
Subject group type	Reporting group			
Number of subjects analysed	101[12]			
Units: percentage of participants				
number (confidence interval 95%)	75.2 (65.7 to 83.3)			

Notes:

[12] - Safety Analysis Set

Statistical analyses

No statistical analyses for this end point

Secondary: Health Assessment Questionnaire Disability Index (HAQ-DI): Change From Baseline (in the Lead-in Study) to Week 0

End point title	Health Assessment Questionnaire Disability Index (HAQ-DI): Change From Baseline (in the Lead-in Study) to Week 0

End point description:

The HAQ-DI is a patient-reported questionnaire specific for rheumatoid arthritis that consists of 20 questions referring to 8 domains: dressing/grooming, arising, eating, walking, hygiene, reach, grip, and daily activities. Participants assessed their ability to do each task over the past week using the following response categories: without any difficulty (0); with some difficulty (1); with much difficulty (2); and unable to do (3). Scores on each task were summed and averaged to provide an overall score ranging from 0 to 3, where 0 represents no disability and 3 very severe, high-dependency disability. HAQ remission indicating normal physical function is defined by HAQ-DI score of < 0.5. Negative change from Baseline indicates improvement. Baseline is defined as baseline in the lead-in study.

End point type	Secondary

End point timeframe:

Baseline (Lead-in Study), Week 0

End point values	Risankizumab			
Subject group type	Reporting group			
Number of subjects analysed	143[13]			
Units: units on a scale				
arithmetic mean (confidence interval 95%)	-0.176 (-0.249 to -0.102)			

Notes:

[13] - Safety Analysis Set

Statistical analyses

No statistical analyses for this end point

Secondary: HAQ-DI: Change From Baseline (in the Lead-in Study) to Week 4

End point title	HAQ-DI: Change From Baseline (in the Lead-in Study) to Week 4

End point description:

The HAQ-DI is a patient-reported questionnaire specific for rheumatoid arthritis that consists of 20 questions referring to 8 domains: dressing/grooming, arising, eating, walking, hygiene, reach, grip, and daily activities. Participants assessed their ability to do each task over the past week using the following response categories: without any difficulty (0); with some difficulty (1); with much difficulty (2); and unable to do (3). Scores on each task were summed and averaged to provide an overall score ranging from 0 to 3, where 0 represents no disability and 3 very severe, high-dependency disability. HAQ remission indicating normal physical function is defined by HAQ-DI score of < 0.5. Negative change from Baseline indicates improvement. Baseline is defined as baseline in the lead-in study.

End point type	Secondary

End point timeframe:

Baseline (Lead-in Study), Week 4

End point values	Risankizumab			
Subject group type	Reporting group			
Number of subjects analysed	143[14]			
Units: units on a scale				
arithmetic mean (confidence interval 95%)	-0.258 (-0.332 to -0.183)			

Notes:

[14] - Safety Analysis Set

Statistical analyses

No statistical analyses for this end point

Secondary: HAQ-DI: Change From Baseline (in the Lead-in Study) to Week 12

End point title	HAQ-DI: Change From Baseline (in the Lead-in Study) to Week 12

End point description:

The HAQ-DI is a patient-reported questionnaire specific for rheumatoid arthritis that consists of 20 questions referring to 8 domains: dressing/grooming, arising, eating, walking, hygiene, reach, grip, and daily activities. Participants assessed their ability to do each task over the past week using the following response categories: without any difficulty (0); with some difficulty (1); with much difficulty (2); and unable to do (3). Scores on each task were summed and averaged to provide an overall score ranging from 0 to 3, where 0 represents no disability and 3 very severe, high-dependency disability. HAQ remission indicating normal physical function is defined by HAQ-DI score of < 0.5. Negative change from Baseline indicates improvement. Baseline is defined as the last non missing pre-treatment observation prior to first dose in the lead-in study.

End point type	Secondary

End point timeframe:

Baseline (Lead-in Study), Week 12

End point values	Risankizumab			
Subject group type	Reporting group			
Number of subjects analysed	140[15]			
Units: units on a scale				
arithmetic mean (confidence interval 95%)	-0.261 (-0.336 to -0.186)			

Notes:

[15] - Safety Analysis Set

Statistical analyses

No statistical analyses for this end point

Secondary: HAQ-DI: Change From Baseline (in the Lead-in Study) to Week 24

End point title	HAQ-DI: Change From Baseline (in the Lead-in Study) to Week 24

End point description:

The HAQ-DI is a patient-reported questionnaire specific for rheumatoid arthritis that consists of 20 questions referring to 8 domains: dressing/grooming, arising, eating, walking, hygiene, reach, grip, and daily activities. Participants assessed their ability to do each task over the past week using the following response categories: without any difficulty (0); with some difficulty (1); with much difficulty (2); and unable to do (3). Scores on each task were summed and averaged to provide an overall score ranging from 0 to 3, where 0 represents no disability and 3 very severe, high-dependency disability. HAQ remission indicating normal physical function is defined by HAQ-DI score of < 0.5. Negative change from Baseline indicates improvement. Baseline is defined as baseline in the lead-in study.

End point type	Secondary

End point timeframe:

Baseline (Lead-in Study), Week 24

End point values	Risankizumab			
Subject group type	Reporting group			
Number of subjects analysed	133[16]			
Units: units on a scale				
arithmetic mean (confidence interval 95%)	-0.296 (-0.374 to -0.217)			

Notes:

[16] - Safety Analysis Set

Statistical analyses

No statistical analyses for this end point

Secondary: HAQ-DI: Change From Baseline (in the Lead-in Study) to Week 36

End point title	HAQ-DI: Change From Baseline (in the Lead-in Study) to Week 36

End point description:

The HAQ-DI is a patient-reported questionnaire specific for rheumatoid arthritis that consists of 20 questions referring to 8 domains: dressing/grooming, arising, eating, walking, hygiene, reach, grip, and daily activities. Participants assessed their ability to do each task over the past week using the following response categories: without any difficulty (0); with some difficulty (1); with much difficulty (2); and unable to do (3). Scores on each task were summed and averaged to provide an overall score ranging from 0 to 3, where 0 represents no disability and 3 very severe, high-dependency disability. HAQ remission indicating normal physical function is defined by HAQ-DI score of < 0.5. Negative change from Baseline indicates improvement. Baseline is defined as baseline in the lead-in study.

End point type	Secondary

End point timeframe:

Baseline (Lead-in Study), Week 36

End point values	Risankizumab			
Subject group type	Reporting group			
Number of subjects analysed	114[17]			
Units: units on a scale				
arithmetic mean (confidence interval 95%)	-0.294 (-0.384 to -0.204)			

Notes:

[17] - Safety Analysis Set

Statistical analyses

No statistical analyses for this end point

Secondary: HAQ-DI: Change From Baseline (in the Lead-in Study) to Week 48

End point title	HAQ-DI: Change From Baseline (in the Lead-in Study) to Week 48

End point description:

The HAQ-DI is a patient-reported questionnaire specific for rheumatoid arthritis that consists of 20 questions referring to 8 domains: dressing/grooming, arising, eating, walking, hygiene, reach, grip, and daily activities. Participants assessed their ability to do each task over the past week using the following response categories: without any difficulty (0); with some difficulty (1); with much difficulty (2); and unable to do (3). Scores on each task were summed and averaged to provide an overall score ranging from 0 to 3, where 0 represents no disability and 3 very severe, high-dependency disability. HAQ remission indicating normal physical function is defined by HAQ-DI score of < 0.5. Negative change from Baseline indicates improvement. Baseline is defined as baseline in the lead-in study.

End point type	Secondary

End point timeframe:

Baseline (Lead-in Study), Week 48

End point values	Risankizumab			
Subject group type	Reporting group			
Number of subjects analysed	107[18]			
Units: units on a scale				
arithmetic mean (confidence interval 95%)	-0.298 (-0.381 to -0.215)			

Notes:

[18] - Safety Analysis Set

Statistical analyses

No statistical analyses for this end point

Secondary: HAQ-DI: Change From Baseline (in the Lead-in Study) to Week 52

End point title	HAQ-DI: Change From Baseline (in the Lead-in Study) to Week 52

End point description:

The HAQ-DI is a patient-reported questionnaire specific for rheumatoid arthritis that consists of 20 questions referring to 8 domains: dressing/grooming, arising, eating, walking, hygiene, reach, grip, and daily activities. Participants assessed their ability to do each task over the past week using the following response categories: without any difficulty (0); with some difficulty (1); with much difficulty (2); and unable to do (3). Scores on each task were summed and averaged to provide an overall score ranging from 0 to 3, where 0 represents no disability and 3 very severe, high-dependency disability. HAQ remission indicating normal physical function is defined by HAQ-DI score of < 0.5. Negative change from Baseline indicates improvement. Baseline is defined as baseline in the lead-in study.

End point type	Secondary

End point timeframe:

Baseline (Lead-in Study), Week 52

End point values	Risankizumab			
Subject group type	Reporting group			
Number of subjects analysed	99[19]			
Units: units on a scale				
arithmetic mean (confidence interval 95%)	-0.318 (-0.405 to -0.231)			

Notes:

[19] - Safety Analysis Set

Statistical analyses

No statistical analyses for this end point

Secondary: Short Form Health Survey 36 (SF-36) Physical Component Summary (PCS) Score: Change From Baseline (in the Lead-in Study) to Week 0

End point title	Short Form Health Survey 36 (SF-36) Physical Component Summary (PCS) Score: Change From Baseline (in the Lead-in Study) to Week 0

End point description:

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

End point type	Secondary

End point timeframe:

Baseline (Lead-in Study), Week 0

End point values	Risankizumab			
Subject group type	Reporting group			
Number of subjects analysed	144[20]			
Units: units on a scale				
median (confidence interval 95%)	2.11 (0.89 to 3.34)			

Notes:

[20] - Safety Analysis Set

Statistical analyses

No statistical analyses for this end point

Secondary: SF-36 PCS Score: Change From Baseline (in the Lead-in Study) to Week 4

End point title	SF-36 PCS Score: Change From Baseline (in the Lead-in Study) to Week 4

End point description:

The SF-36 Health determined participants' overall quality of life by assessing 1) limitations in physical functioning due to health problems; 2) limitations in usual role because of physical health problems; 3) bodily pain; 4) general health perceptions; 5) vitality; 6) limitations in social functioning because of physical or emotional problems; 7) limitations in usual role due to emotional problems; and 8) general

mental health. Items 1-4 comprise the physical component of the SF-36. Scores on each item were summed and averaged (range = 0-100); a positive change from Baseline indicates improvement. Baseline is defined as baseline in the lead-in study.

End point type	Secondary

End point timeframe:

Baseline (Lead-in Study), Week 4

End point values	Risankizumab			
Subject group type	Reporting group			
Number of subjects analysed	143[21]			
Units: units on a scale				
median (confidence interval 95%)	3.63 (2.41 to 4.85)			

Notes:

[21] - Safety Analysis Set

Statistical analyses

No statistical analyses for this end point

Secondary: SF-36 PCS Score: Change From Baseline (in the Lead-in Study) to Week 12

End point title	SF-36 PCS Score: Change From Baseline (in the Lead-in Study) to Week 12

End point description:

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

End point type	Secondary

End point timeframe:

Baseline (Lead-in Study), Week 12

End point values	Risankizumab			
Subject group type	Reporting group			
Number of subjects analysed	140[22]			
Units: units on a scale				
median (confidence interval 95%)	3.63 (2.32 to 4.94)			

Notes:

[22] - Safety Analysis Set

Statistical analyses

No statistical analyses for this end point

Secondary: SF-36 PCS Score: Change From Baseline (in the Lead-in Study) to Week 24

End point title	SF-36 PCS Score: Change From Baseline (in the Lead-in Study) to Week 24

End point description:

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

End point type	Secondary

End point timeframe:

Baseline (Lead-in Study), Week 24

End point values	Risankizumab			
Subject group type	Reporting group			
Number of subjects analysed	134[23]			
Units: units on a scale				
median (confidence interval 95%)	3.76 (2.50 to 5.02)			

Notes:

[23] - Safety Analysis Set

Statistical analyses

No statistical analyses for this end point

Secondary: SF-36 PCS Score: Change From Baseline (in the Lead-in Study) to Week 36

End point title	SF-36 PCS Score: Change From Baseline (in the Lead-in Study) to Week 36

End point description:

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

End point type	Secondary

End point timeframe:

Baseline (Lead-in Study), Week 36

End point values	Risankizumab			
Subject group type	Reporting group			
Number of subjects analysed	115[24]			
Units: units on a scale				
median (confidence interval 95%)	4.27 (2.97 to 5.57)			

Notes:

[24] - Safety Analysis Set

Statistical analyses

No statistical analyses for this end point

Secondary: SF-36 PCS Score: Change From Baseline (in the Lead-in Study) to Week 48

End point title	SF-36 PCS Score: Change From Baseline (in the Lead-in Study) to Week 48

End point description:

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

End point type	Secondary

End point timeframe:

Baseline (Lead-in Study), Week 48

End point values	Risankizumab			
Subject group type	Reporting group			
Number of subjects analysed	108[25]			
Units: units on a scale				
median (confidence interval 95%)	5.08 (3.66 to 6.50)			

Notes:

[25] - Safety Analysis Set

Statistical analyses

No statistical analyses for this end point

Secondary: SF-36 PCS Score: Change From Baseline (in the Lead-in Study) to Week 52

End point title	SF-36 PCS Score: Change From Baseline (in the Lead-in Study) to Week 52

End point description:

The SF-36 Health determined participants' overall quality of life by assessing 1) limitations in physical functioning due to health problems; 2) limitations in usual role because of physical health problems; 3) bodily pain; 4) general health perceptions; 5) vitality; 6) limitations in social functioning because of physical or emotional problems; 7) limitations in usual role due to emotional problems; and 8) general mental health. Items 1-4 comprise the physical component of the SF-36. Scores on each item were

summed and averaged (range = 0-100); a positive change from Baseline indicates improvement. Baseline is defined as baseline in the lead-in study.

End point type	Secondary

End point timeframe:

Baseline (Lead-in Study), Week 52

End point values	Risankizumab			
Subject group type	Reporting group			
Number of subjects analysed	100[26]			
Units: units on a scale				
median (confidence interval 95%)	4.47 (3.11 to 5.84)			

Notes:

[26] - Safety Analysis Set

Statistical analyses

No statistical analyses for this end point

Secondary: SF-36 Mental Component Summary (MCS) Score: Change From Baseline (in the Lead-in Study) to Week 0

End point title	SF-36 Mental Component Summary (MCS) Score: Change From Baseline (in the Lead-in Study) to Week 0

End point description:

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

End point type	Secondary

End point timeframe:

Baseline (Lead-in Study), Week 0

End point values	Risankizumab			
Subject group type	Reporting group			
Number of subjects analysed	144[27]			
Units: units on a scale				
median (confidence interval 95%)	0.86 (-0.64 to 2.35)			

Notes:

[27] - Safety Analysis Set

Statistical analyses

No statistical analyses for this end point

Secondary: SF-36 MCS Score: Change From Baseline (in the Lead-in Study) to Week 4

End point title	SF-36 MCS Score: Change From Baseline (in the Lead-in Study) to Week 4

End point description:

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

End point type	Secondary

End point timeframe:

Baseline (Lead-in Study), Week 4

End point values	Risankizumab			
Subject group type	Reporting group			
Number of subjects analysed	143[28]			
Units: units on a scale				
median (confidence interval 95%)	2.79 (1.27 to 4.31)			

Notes:

[28] - Safety Analysis Set

Statistical analyses

No statistical analyses for this end point

Secondary: SF-36 MCS Score: Change From Baseline (in the Lead-in Study) to Week 12

End point title	SF-36 MCS Score: Change From Baseline (in the Lead-in Study) to Week 12

End point description:

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

End point type	Secondary

End point timeframe:

Baseline (Lead-in Study), Week 12

End point values	Risankizumab			
Subject group type	Reporting group			
Number of subjects analysed	140[29]			
Units: units on a scale				
median (confidence interval 95%)	2.22 (0.49 to 3.96)			

Notes:

[29] - Safety Analysis Set

Statistical analyses

No statistical analyses for this end point

Secondary: SF-36 MCS Score: Change From Baseline (in the Lead-in Study) to Week 24

End point title	SF-36 MCS Score: Change From Baseline (in the Lead-in Study) to Week 24

End point description:

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

End point type	Secondary

End point timeframe:

Baseline (Lead-in Study), Week 24

End point values	Risankizumab			
Subject group type	Reporting group			
Number of subjects analysed	134[30]			
Units: units on a scale				
median (confidence interval 95%)	4.08 (2.39 to 5.77)			

Notes:

[30] - Safety Analysis Set

Statistical analyses

No statistical analyses for this end point

Secondary: SF-36 MCS Score: Change From Baseline (in the Lead-in Study) to Week 36

End point title	SF-36 MCS Score: Change From Baseline (in the Lead-in Study) to Week 36

End point description:

The SF-36 determined participants' overall quality of life by assessing 1) limitations in physical functioning due to health problems; 2) limitations in usual role because of physical health problems; 3) bodily pain; 4) general health perceptions; 5) vitality; 6) limitations in social functioning because of physical or emotional problems; 7) limitations in usual role due to emotional problems; and 8) general mental health. Items 5-8 comprise the mental component of the SF-36. Scores on each item were

summed and averaged (range = 0-100); a positive change from Baseline indicates improvement. Baseline is defined as baseline in the lead-in study.

End point type	Secondary

End point timeframe:

Baseline (Lead-in Study), Week 36

End point values	Risankizumab			
Subject group type	Reporting group			
Number of subjects analysed	115[31]			
Units: units on a scale				
median (confidence interval 95%)	3.44 (1.60 to 5.28)			

Notes:

[31] - Safety Analysis Set

Statistical analyses

No statistical analyses for this end point

Secondary: SF-36 MCS Score: Change From Baseline (in the Lead-in Study) to Week 48

End point title	SF-36 MCS Score: Change From Baseline (in the Lead-in Study) to Week 48

End point description:

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

End point type	Secondary

End point timeframe:

Baseline (Lead-in Study), Week 48

End point values	Risankizumab			
Subject group type	Reporting group			
Number of subjects analysed	108[32]			
Units: units on a scale				
median (confidence interval 95%)	3.36 (1.40 to 5.31)			

Notes:

[32] - Safety Analysis Set

Statistical analyses

No statistical analyses for this end point

Secondary: SF-36 MCS Score: Change From Baseline (in the Lead-in Study) to Week 52

End point title	SF-36 MCS Score: Change From Baseline (in the Lead-in Study) to Week 52

End point description:

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

End point type	Secondary

End point timeframe:

Baseline (Lead-in Study), Week 52

End point values	Risankizumab			
Subject group type	Reporting group			
Number of subjects analysed	100[33]			
Units: units on a scale				
median (confidence interval 95%)	4.33 (2.56 to 6.10)			

Notes:

[33] - Safety Analysis Set

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Treatment-emergent adverse events (TEAEs) and serious adverse events (TESAEs) were collected from the first dose of study drug in this study until 20 weeks after the last dose of study drug (up to 56 weeks).

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	20.0

Reporting groups

Reporting group title	RISANKIZUMAB

Reporting group description: -

Serious adverse events	RISANKIZUMAB		
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 145 (3.45%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Investigations			
GLOMERULAR FILTRATION RATE ABNORMAL			
subjects affected / exposed	1 / 145 (0.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
COLORECTAL CANCER			
subjects affected / exposed	1 / 145 (0.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
ACUTE CORONARY SYNDROME			
subjects affected / exposed	1 / 145 (0.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
ANGINA PECTORIS			

subjects affected / exposed	1 / 145 (0.69%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
ISCHAEMIC CARDIOMYOPATHY				
subjects affected / exposed	1 / 145 (0.69%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Nervous system disorders				
ISCHAEMIC STROKE				
subjects affected / exposed	1 / 145 (0.69%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
ACUTE RESPIRATORY DISTRESS SYNDROME				
subjects affected / exposed	1 / 145 (0.69%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
PNEUMONIA HAEMOPHILUS				
subjects affected / exposed	1 / 145 (0.69%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
PNEUMONIA PSEUDOMONAL				
subjects affected / exposed	1 / 145 (0.69%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
STAPHYLOCOCCAL INFECTION				
subjects affected / exposed	1 / 145 (0.69%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
UROSEPSIS				

subjects affected / exposed	1 / 145 (0.69%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	RISANKIZUMAB		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	16 / 145 (11.03%)		
Infections and infestations			
VIRAL UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	16 / 145 (11.03%)		
occurrences (all)	21		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
23 May 2018	Revisions to the protocol included extending the adverse event collection period and contraception requirement duration from 16 weeks after the last dose of study drug to 20 weeks after the last dose of study drug and adding a follow-up phone call 20 weeks after the last dose of study drug. These changes were made based on the availability of additional data clarifying the risankizumab terminal half-life (t1/2) from 16 weeks to 20 weeks in Investigator's Brochure Edition 3.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported