Clinical trial results:
A Multicenter, Randomized, Double-Blind, Placebo-Controlled, Dose-Finding, Clinical Trial in Subjects with Active Psoriatic Arthritis to Investigate Efficacy, Tolerability, Safety, Pharmacokinetics and Immunogenicity of Izokibep (ABY-035)

Summary

EudraCT number	2019-003405-94
Trial protocol	AT HU CZ DE ES BE
Global end of trial date	20 April 2022

Results information

Result version number	v2 (current)
This version publication date	13 December 2024
First version publication date	09 August 2023
Version creation reason	• New data added to full data set Added pharmacokinetic (PK) endpoint.

Trial information

Trial identification

Sponsor protocol code	ABY-035-202

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04713072
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	ACELYRIN, INC.
Sponsor organisation address	4149 Liberty Canyon Rd, Agoura Hills, United States, CA 91301
Public contact	Clinical Trial Information Desk, ACELYRIN, INC., +1 805-456-4393, clinicaltrials@acelyrin.com
Scientific contact	Clinical Trial Information Desk, ACELYRIN, INC., +1 805-456-4393, clinicaltrials@acelyrin.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	20 April 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	20 April 2022
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study was to evaluate efficacy of different dose regimens of ABY-035 compared with placebo in subjects with active psoriatic arthritis (PsA).

Protection of trial subjects:

This study was conducted in accordance with International Council on Harmonization (ICH) Good Clinical Practice, and the principles of the Declaration of Helsinki, in addition to following the laws and regulations of the country or countries in which a study is conducted.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	04 August 2020
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: 1
Country: Number of subjects enrolled	Czechia: 33
Country: Number of subjects enrolled	Spain: 15
Country: Number of subjects enrolled	Germany: 17
Country: Number of subjects enrolled	Poland: 46
Country: Number of subjects enrolled	Belgium: 2
Country: Number of subjects enrolled	Hungary: 21
Worldwide total number of subjects	135
EEA total number of subjects	135

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)	122
From 65 to 84 years	13
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This study was conducted at 28 trial centres in 7 European countries (Austria, Belgium, Czech Republic, Germany, Hungary, Poland, Spain) from 04 August 2020 to 20 April 2022.

Pre-assignment

Screening details:

One-hundred ninety-seven subjects with confirmed PsA were screened, of which 135 subjects were found eligible and were randomized in a 1:1:1 ratio to 1 of the 3 treatment arms in period 1. The trial was prematurely terminated during Treatment Period II via Amendment 2 by sponsor decision to accelerate clinical development.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Treatment Period 1: izokibep 40 mg Q2W

Arm description:

Subjects received lower dose izokibep 40 mg subcutaneously (SC) every 2 weeks (Q2W) during treatment period 1 which spanned weeks 0 to 16.

Arm type	Experimental
Investigational medicinal product name	INN: izokibep
Investigational medicinal product code	ABY-035
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subject received izokibep 40 mg SC injection Q2W.

Arm title	Treatment Period 1: izokibep 80 mg Q2W

Arm description:

Subjects received higher dose izokibep 80 mg SC injection Q2W during treatment period 1 which spanned weeks 0 to 16.

Arm type	Experimental
Investigational medicinal product name	INN: izokibep
Investigational medicinal product code	ABY-035
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subject received izokibep 80 mg SC injection Q2W.

Arm title	Treatment Period 1: Placebo

Arm description:

Subject received matched placebo SC injection Q2W from Week 0 through Week 14.

Arm type	Placebo

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

Dosage and administration details:

Subject received matched placebo solution for SC injection Q2W.

Number of subjects in period 1	Treatment Period 1: izokibep 40 mg Q2W	Treatment Period 1: izokibep 80 mg Q2W	Treatment Period 1: Placebo
Started	44	47	44
Completed	42	46	43
Not completed	2	1	1
Adverse event, non-fatal	2	1	1

Period 2

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Treatment Period 2: izokibep 40mg Q2W

Arm description:

Subject who completed izokibep 40 mg in treatment period 1 continued to receive lower dose izokibep 40mg SC injection Q2W from Week 16 to Week 44 in treatment period 2.

Arm type	Experimental
Investigational medicinal product name	INN: izokibep
Investigational medicinal product code	ABY-035
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subject received lower dose izokibep 40 mg SC injection Q2W.

Arm title	Treatment Period 2: izokibep 80 mg Q2W

Arm description:

Subject who completed izokibep 80 mg in treatment period 1 continued to receive higher dose izokibep 80 mg Q2W from Week 16 to Week 44 in treatment period 2.

Arm type	Experimental

Investigational medicinal product name	INN: izokibep
Investigational medicinal product code	ABY-035
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subject received higher dose izokibep 80 mg SC injection Q2W.

Arm title	Treatment Period 2: Placebo/izokibep 80 mg

Arm description:

Subject who received placebo in treatment period 1 switched to higher dose izokibep 80 mg Q2W from Week 16 to Week 44 in treatment period 2.

Arm type	Experimental
Investigational medicinal product name	INN: izokibep
Investigational medicinal product code	ABY-035
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subject received placebo in treatment period 1 switched to higher dose izokibep 80 mg Q2W from Week 16 to Week 44 in treatment period 2.

Number of subjects in period 2	Treatment Period 2: izokibep 40mg Q2W	Treatment Period 2: izokibep 80 mg Q2W	Treatment Period 2: Placebo/izokibep 80 mg
Started	42	46	43
Completed	39	44	40
Not completed	3	2	3
Consent withdrawn by subject	1	-	1
Others	-	-	1
Adverse event	-	1	1
Unspecified	2	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Treatment Period 1: izokibep 40 mg Q2W
Reporting group description:	
Subjects received lower dose izokibep 40 mg subcutaneously (SC) every 2 weeks (Q2W) during treatment period 1 which spanned weeks 0 to 16.	
Reporting group title	Treatment Period 1: izokibep 80 mg Q2W
Reporting group description:	
Subjects received higher dose izokibep 80 mg SC injection Q2W during treatment period 1 which spanned weeks 0 to 16.	
Reporting group title	Treatment Period 1: Placebo
Reporting group description:	
Subject received matched placebo SC injection Q2W from Week 0 through Week 14.	

Reporting group values	Treatment Period 1: izokibep 40 mg Q2W	Treatment Period 1: izokibep 80 mg Q2W	Treatment Period 1: Placebo
Number of subjects	44	47	44
Age categorical			
Units: Subjects			
Age continuous			
Units: years			
arithmetic mean	47.6	50.1	47.6
standard deviation	± 12.5	± 10.9	± 12.6
Gender categorical			
Units: Subjects			
Female	23	28	22
Male	21	19	22
Ethnicity			
Units: Subjects			
Hispanic or Latino	1	1	0
Not Hispanic or Latino	43	46	44
Race			
Units: Subjects			
White	44	47	44

Reporting group values	Total		
Number of subjects	135		
Age categorical			
Units: Subjects			
Age continuous			
Units: years			
arithmetic mean			
standard deviation	-		
Gender categorical			
Units: Subjects			
Female	73		
Male	62		

Ethnicity Units: Subjects			
Hispanic or Latino	2		
Not Hispanic or Latino	133		
Race Units: Subjects			
White	135		

End points

End points reporting groups

Reporting group title	Treatment Period 1: izokibep 40 mg Q2W
Reporting group description:	
Subjects received lower dose izokibep 40 mg subcutaneously (SC) every 2 weeks (Q2W) during treatment period 1 which spanned weeks 0 to 16.	
Reporting group title	Treatment Period 1: izokibep 80 mg Q2W
Reporting group description:	
Subjects received higher dose izokibep 80 mg SC injection Q2W during treatment period 1 which spanned weeks 0 to 16.	
Reporting group title	Treatment Period 1: Placebo
Reporting group description:	
Subject received matched placebo SC injection Q2W from Week 0 through Week 14.	
Reporting group title	Treatment Period 2: izokibep 40mg Q2W
Reporting group description:	
Subject who completed izokibep 40 mg in treatment period 1 continued to receive lower dose izokibep 40mg SC injection Q2W from Week 16 to Week 44 in treatment period 2.	
Reporting group title	Treatment Period 2: izokibep 80 mg Q2W
Reporting group description:	
Subject who completed izokibep 80 mg in treatment period 1 continued to receive higher dose izokibep 80 mg Q2W from Week 16 to Week 44 in treatment period 2.	
Reporting group title	Treatment Period 2: Placebo/izokibep 80 mg
Reporting group description:	
Subject who received placebo in treatment period 1 switched to higher dose izokibep 80 mg Q2W from Week 16 to Week 44 in treatment period 2.	

Primary: American College of Rheumatology Criteria (ACR50) Response Rate at Visit 9 (Week 16) for Izokibep 80 mg vs Placebo

End point title	American College of Rheumatology Criteria (ACR50) Response Rate at Visit 9 (Week 16) for Izokibep 80 mg vs Placebo[1]
End point description:	
ACR 50 responders are subjects with at least 50% improvement from baseline in tender joint count, swollen joint count, and at least 3 of the 5 remaining core set measures: Health Assessment Questionnaire-Disability Index which measures subjects perceived degree of difficulty performing daily activities, acute phase reactant as measured by high-sensitivity C-reactive protein (hsCRP), Subject's Assessment of Pain-Visual Analog Scale (VAS), Subject's Global Assessment of Disease Activity, and Physician's Global Assessment of Disease Activity. Full analysis set (FAS) cohort included all randomized subjects with at least 1 documented application of the investigational medical product (IMP) and at least one post-Baseline ACR efficacy data available for the clinical trial. Number of subjects (responders) who achieved 50% improvement based on ACR50 response rate for Izokibep 80 mg vs placebo were reported.	
End point type	Primary
End point timeframe:	
At 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: Data was planned to be reported only for Higher dose vs Placebo arms for this endpoint.

End point values	Treatment Period 1: izokibep 80 mg Q2W	Treatment Period 1: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	47	44		
Units: Subjects				
At Week 16	22	6		

Statistical analyses

Statistical analysis title	Higher Dose (80 mg) vs Placebo
Comparison groups	Treatment Period 1: izokibep 80 mg Q2W v Treatment Period 1: Placebo
Number of subjects included in analysis	91
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0006
Method	Regression, Cox
Parameter estimate	Odds ratio (OR)
Point estimate	6.96
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.31
upper limit	20.91

Primary: ACR50 Response Rate at Visit 7 (Week 12) for Izokibep 80 mg vs Placebo

End point title	ACR50 Response Rate at Visit 7 (Week 12) for Izokibep 80 mg vs Placebo[2]

End point description:

ACR50 responders are subjects with at least 50% improvement from baseline in tender joint count swollen joint count , and at least 3 of the 5 remaining core set measures: Health Assessment Questionnaire-Disability Index which measures subjects perceived degree of difficulty performing daily activities, acute phase reactant as measured by hsCRP, subjects Assessment of Pain-Visual Analog Scale, subjects Global Assessment of Disease Activity, and Physician's Global Assessment of Disease Activity. FAS cohort included all randomized subjects with at least 1 documented application of the IMP and at least one post-Baseline ACR efficacy data available for the clinical trial. Number of subjects (responders) who achieved 50% improvement based on ACR50 response rate at V7 (Week 12) for izokibep 80 mg vs Placebo were reported.

End point type	Primary

End point timeframe:

At Week 12

Notes:

[2] - 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: Data was planned to be reported only for Higher dose vs Placebo arms for this endpoint.

End point values	Treatment Period 1: izokibep 80 mg Q2W	Treatment Period 1: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	47	44		
Units: Subjects				
At Week 12	21	3		

Statistical analyses

Statistical analysis title	Higher Dose (80 mg) vs Placebo
Comparison groups	Treatment Period 1: izokibep 80 mg Q2W v Treatment Period 1: Placebo
Number of subjects included in analysis	91
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Regression, Cox
Parameter estimate	Odds ratio (OR)
Point estimate	14.85
Confidence interval	
level	95 %
sides	2-sided
lower limit	4.17
upper limit	52.92

Secondary: ACR20/70 Response Rate at Visit 9/Visit 7 (Week 16/12) for Izokibep 80 mg vs Placebo

End point title	ACR20/70 Response Rate at Visit 9/Visit 7 (Week 16/12) for Izokibep 80 mg vs Placebo[3]

End point description:

ACR20/70 responders are subjects with at least 20% and 70% improvement from baseline in tender joint count, swollen joint count, and at least 3 of the 5 remaining core set measures: Health Assessment Questionnaire-Disability Index which measures subjects perceived degree of difficulty performing daily activities, acute phase reactant as measured by hsCRP, Subject's Assessment of Pain-VAS, Subject's Global Assessment of Disease Activity, and Physician's Global Assessment of Disease Activity. FAS cohort included all randomized subjects with at least one documented application of the IMP and at least one post-Baseline ACR efficacy data available for the clinical trial. Number of subjects (responders) who achieved 20% and 70% improvement in ACR 20/70 response rate for izokibep 80 mg vs Placebo was reported.

End point type	Secondary

End point timeframe:

At Week 12 and 16

Notes:

[3] - 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: Data was planned to be reported only for Higher dose vs Placebo arms for this endpoint.

End point values	Treatment Period 1: izokibep 80 mg Q2W	Treatment Period 1: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	47	44		
Units: Subjects				
At Week 12: ACR 20	37	17		
At Week 16: ACR 20	34	13		
At Week 12: ACR 70	7	2		
At Week 16: ACR 70	8	2		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects who Achieved Minimal Disease Activity (MDA) at Visit 9/Visit 7 (Week 16/12) for Izokibep 80 mg vs Placebo

End point title	Percentage of Subjects who Achieved Minimal Disease Activity (MDA) at Visit 9/Visit 7 (Week 16/12) for Izokibep 80 mg vs Placebo[4]

End point description:

MDA is considered achieved when 5 of the following 7 criteria are met: <=1 tender joint in the TJC68; <=1 swollen joint in the SJC66; PASI <=1 or BSA-PsO <=3%; Subject's pain assessment <=15 mm VAS; Subject's global assessment of DA <=20 mm VAS; and HAQ-DI <=0.5; Tender entheseal points <=1 site out of six sites included in the LEI. FAS cohort included all randomized subjects with at least one documented application of the IMP and at least one post-Baseline ACR efficacy data available for the clinical trial. Here, "number of subjects analysed" signifies subjects who were evaluable for this endpoint. n=number analysed signifies subjects who were evaluable at specific timepoint. Percentage of subjects who achieved MDA at Visit 9/Visit 7 (Week 16/12) for Izokibep 80 mg vs Placebo were reported.

End point type	Secondary

End point timeframe:

At Week 12 and 16

Notes:

[4] - 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: Data was planned to be reported only for Higher dose vs Placebo arms for this endpoint.

End point values	Treatment Period 1: izokibep 80 mg Q2W	Treatment Period 1: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	46	43		
Units: Percentage of Subjects				
number (not applicable)				
At Week 12 (n=46,42)	17.4	2.4		
At Week 16 (n=46,43)	34.8	4.7		

Statistical analyses

No statistical analyses for this end point

Secondary: ACR20/50/70 Response Rate at Visit 9/Visit 7 (Week 16/12) for Izokibep 40 mg vs Placebo

End point title	ACR20/50/70 Response Rate at Visit 9/Visit 7 (Week 16/12) for Izokibep 40 mg vs Placebo[5]

End point description:

ACR20/50/70 responders are subjects with at least 20%, 50% and 70% improvement from baseline in tender joint count, swollen joint count, and at least 3 of the 5 remaining core set measures: Health Assessment Questionnaire-Disability Index which measures subjects perceived degree of difficulty performing daily activities, acute phase reactant as measured by hsCRP, Patient's Assessment of Pain-VAS, Patient's Global Assessment of Disease Activity, and Physician's Global Assessment of Disease Activity. FAS cohort included all randomized subjects with at least one documented application of the IMP and at least one post-Baseline ACR efficacy data available for the clinical trial. Here, "number of subjects analysed" signifies subjects who were evaluable for this endpoint. Number of subjects (responders) who achieved 20%, 50% and 70% improvement in ACR20/50/70 response rate at Week 12 and 16 for Izokibep 40 mg vs Placebo was reported.

End point type	Secondary

End point timeframe:

At Week 12 and 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: Data was planned to be reported only for Lower dose vs Placebo arms for this endpoint.

End point values	Treatment Period 1: izokibep 40 mg Q2W	Treatment Period 1: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	44	44		
Units: Subjects				
At Week 12: ACR 20	29	17		
At Week 16: ACR 20	27	13		
At Week 12: ACR 50	17	3		
At Week 16: ACR 50	19	6		
At Week 12: ACR 70	10	2		
At Week 16: ACR 70	12	2		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects who Achieved MDA at Visit 9/Visit 7 (Week 16/12) for Izokibep 40 mg vs Placebo

End point title	Percentage of Subjects who Achieved MDA at Visit 9/Visit 7 (Week 16/12) for Izokibep 40 mg vs Placebo[6]

End point description:

MDA is considered achieved when 5 of the following 7 criteria are met: <=1 tender joint in the TJC68; <=1 swollen joint in the SJC66; PASI <=1 or BSA-PsO <=3%; Subject's entheseal points <=1 site out of six sites included in the LEI. FAS cohort included all randomized subjects with at least one documented application of the IMP and at least one post-Baseline ACR efficacy data available for the clinical trial. Here, "number of subjects analysed" signifies subjects who were evaluable for this endpoint. Percentage of subjects who achieved MDA at Week 12 and 16 for Izokibep 40 mg vs Placebo was reported.

End point type	Secondary

End point timeframe:

At Week 12 and Week 16

Notes:

[6] - 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: Data was planned to be reported only for Lower dose vs Placebo arms for this endpoint.

End point values	Treatment Period 1: izokibep 40 mg Q2W	Treatment Period 1: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	43	43		
Units: Percentage of Subjects				
number (not applicable)				
At Week 12 (n= 43, 42)	20.9	2.4		
At Week 16 (n=42, 43)	38.1	4.7		

Statistical analyses

No statistical analyses for this end point

Secondary: ACR20/50/70 Response Rate at Visit 5 (Week 8) for Izokibep 80 mg vs Placebo

End point title	ACR20/50/70 Response Rate at Visit 5 (Week 8) for Izokibep 80 mg vs Placebo[7]

End point description:

ACR20/50/70 responders are subjects with at least 20%, 50% and 70% improvement from baseline in for tender joint count, swollen joint count, and at least 3 of the 5 remaining core set measures: Health Assessment Questionnaire-Disability Index which measures subjects perceived degree of difficulty performing daily activities, acute phase reactant as measured by hsCRP, Subject's Assessment of Pain-VAS, Subject's Global Assessment of Disease Activity, and Physician's Global Assessment of Disease Activity. FAS cohort included all randomized subjects with at least one documented application of the IMP and at least one post-Baseline ACR efficacy data available for the clinical trial. Number of subjects (responders) who achieved 20%, 50% and 70% improvement in ACR20/50/70 response rate at Week 8 for izokibep 80 mg vs Placebo were reported.

End point type	Secondary

End point timeframe:

At Week 8

Notes:

[7] - 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: Data was planned to be reported only for Higher dose vs Placebo arms for this endpoint.

End point values	Treatment Period 1: izokibep 80 mg Q2W	Treatment Period 1: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	47	44		
Units: Subjects				
At Week 8: ACR 20	31	16		
At Week 8: ACR 50	17	2		

At Week 8: ACR 70	3	1		

Statistical analyses

No statistical analyses for this end point

Secondary: ACR20/50/70 Response Rate at Visit 5 (Week 8) for Izokibep 40 mg vs Placebo

End point title	ACR20/50/70 Response Rate at Visit 5 (Week 8) for Izokibep 40 mg vs Placebo[8]

End point description:

ACR20/50/70 responders are subjects with at least 20%, 50% and 70% improvement from baseline in for tender joint count, swollen joint count, and at least 3 of the 5 remaining core set measures: Health Assessment Questionnaire-Disability Index which measures subjects perceived degree of difficulty performing daily activities, acute phase reactant as measured by hsCRP, Subject's Assessment of Pain-VAS, Subject's Global Assessment of Disease Activity, and Physician's Global Assessment of Disease Activity. FAS cohort included all randomized subjects with at least one documented application of the IMP and at least one post-Baseline ACR efficacy data available for the clinical trial. Number of subjects (responders) who achieved 20%, 50% and 70% improvement in ACR20/50/70 response rate at Week 8 for izokibep 40 mg vs Placebo were reported.

End point type	Secondary

End point timeframe:

At Week 8

Notes:

[8] - 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: Data was planned to be reported only for Lower dose vs Placebo arms for this endpoint.

End point values	Treatment Period 1: izokibep 40 mg Q2W	Treatment Period 1: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	44	44		
Units: Subjects				
At Week 8: ACR 20	27	16		
At Week 8: ACR 50	13	2		
At Week 8: ACR 70	9	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects who Achieved MDA at Visit 5 (Week 8) for Izokibep 80 mg, Izokibep 40 mg and Placebo

End point title	Percentage of Subjects who Achieved MDA at Visit 5 (Week 8) for Izokibep 80 mg, Izokibep 40 mg and Placebo

End point description:

MDA is considered achieved when 5 of the following 7 criteria are met: <=1 tender joint in the TJC68;

<=1 swollen joint in the SJC66; PASI <=1 or BSA-PsO <=3%; Subject's pain assessment <=15 mm VAS; Subject's global assessment of DA <=20 mm VAS; and HAQ-DI <=0.5; Tender entheseal points <=1 site out of six sites included in the LEI. FAS cohort included all randomized subjects with at least one documented application of the IMP and at least one post-Baseline ACR efficacy data available for the clinical trial. Here, "number of subjects analysed" signifies subjects who were evaluable for this endpoint. Percentage of subjects who achieved MDA at Week 8 for Izokibep 80 mg, Izokibep 40 mg and Placebo were reported.

End point type	Secondary

End point timeframe:

At Week 8

End point values	Treatment Period 1: izokibep 40 mg Q2W	Treatment Period 1: izokibep 80 mg Q2W	Treatment Period 1: Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	42	46	41	
Units: Percentage of Subjects				
number (not applicable)	26.2	19.6	2.4	

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma Concentration of Izokibep

End point title	Plasma Concentration of Izokibep[9]

End point description:

Plasma concentration of izokibep was reported. Pharmacokinetic (PK) Population (PhP) included all subjects with at least one PK assessment with valid data. Here, "number of subjects analysed" signifies subjects who were evaluable for this endpoint and "n" signifies subjects who were evaluable at specified timepoints. "99999" means data was not available because no subjects were available for analysis at timepoint specified in categories.

End point type	Secondary

End point timeframe:

Treatment Period I: At Weeks 0, 2, 4, 8, 12 and 16; Treatment Period II: At Weeks 18, 32 and 44

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: Descriptive data was reported as per plan.

End point values	Treatment Period 1: izokibep 40 mg Q2W	Treatment Period 2: izokibep 40mg Q2W	Treatment Period 1: izokibep 80 mg Q2W	Treatment Period 2: izokibep 80 mg Q2W
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	44	24	47	22
Units: nanogram per milliliter (ng/mL)				
geometric mean (geometric coefficient of variation)				
Week 0 (n=44,0,47,0,0)	0.0 (± 0.0)	99999 (± 99999)	0.0 (± 0.0)	99999 (± 99999)

Week 2 (n=41,0,41,0,0)	1891.568 (± 77.83)	99999 (± 99999)	4057.993 (± 36.14)	99999 (± 99999)
Week 4 (n=44,0,41,0,0)	2499.924 (± 62.79)	99999 (± 99999)	5639.367 (± 34.02)	99999 (± 99999)
Week 8 (n=21,0,20,0,0)	3429.037 (± 49.80)	99999 (± 99999)	6836.772 (± 43.51)	99999 (± 99999)
Week 12 (n=41,0,41,0,0)	3452.024 (± 57.69)	99999 (± 99999)	6699.973 (± 36.14)	99999 (± 99999)
Week 16 (n=41,0,41,0,0)	3266.782 (± 46.93)	99999 (± 99999)	6310.016 (± 32.36)	99999 (± 99999)
Week 18 (n=0,24,0,22,22)	99999 (± 99999)	3700.224 (± 46.92)	99999 (± 99999)	6886.234 (± 31.19)
Week 32 (n=0,18,0,16,14)	99999 (± 99999)	3680.908 (± 47.02)	99999 (± 99999)	7132.319 (± 37.55)
Week 44 (n=0,9,0,5,6)	99999 (± 99999)	2940.559 (± 73.20)	99999 (± 99999)	4698.114 (± 19.75)

End point values	Treatment Period 2: Placebo/izokibep 80 mg			
Subject group type	Reporting group			
Number of subjects analysed	22			
Units: nanogram per milliliter (ng/mL)				
geometric mean (geometric coefficient of variation)				
Week 0 (n=44,0,47,0,0)	99999 (± 99999)			
Week 2 (n=41,0,41,0,0)	99999 (± 99999)			
Week 4 (n=44,0,41,0,0)	99999 (± 99999)			
Week 8 (n=21,0,20,0,0)	99999 (± 99999)			
Week 12 (n=41,0,41,0,0)	99999 (± 99999)			
Week 16 (n=41,0,41,0,0)	99999 (± 99999)			
Week 18 (n=0,24,0,22,22)	4265.863 (± 40.51)			
Week 32 (n=0,18,0,16,14)	6355.536 (± 43.51)			
Week 44 (n=0,9,0,5,6)	6399.956 (± 37.72)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: Treatment Period 1: Week 0 to Week 16: Treatment Period 2: After Week 16 up to Week 48	
Assessment type	Non-systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	22.1
Reporting groups	
Reporting group title	Treatment Period 1: izokibep 40 mg Q2W
Reporting group description: Subjects received lower dose izokibep 40 mg SC injection Q2W from Week 0 to Week 16 in treatment period 1.	
Reporting group title	Treatment Period 1: izokibep 80 mg Q2W
Reporting group description: Subjects received higher dose izokibep 80 mg SC injection Q2W from Week 0 to Week 16 treatment period 1.	
Reporting group title	Treatment Period 1: Placebo
Reporting group description: Subject received matched placebo SC injection Q2W from Week 0 through Week 14 in treatment period 1.	
Reporting group title	Treatment Period 2: izokibep 40 mg Q2W
Reporting group description: Subject who completed izokibep 40 mg in treatment period 1 continued to receive lower dose izokibep 40 mg SC injection Q2W from Week 16 to Week 44 in treatment period 2.	
Reporting group title	Treatment Period 2: izokibep 80 mg Q2W
Reporting group description: Subject who completed izokibep 80 mg in treatment period 1 continued to receive higher dose of izokibep 80 mg SC injection Q2W from Week 16 to Week 44 in treatment period 2.	
Reporting group title	Treatment Period 2: Placebo/izokibep 80 mg
Reporting group description: Subject who received placebo in treatment period 1 switched to higher dose izokibep 80 mg Q2W from Week 16 to Week 44 in treatment period 2.	

Serious adverse events	Treatment Period 1: izokibep 40 mg Q2W	Treatment Period 1: izokibep 80 mg Q2W	Treatment Period 1: Placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 44 (0.00%)	0 / 47 (0.00%)	0 / 44 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Vulval cancer			
subjects affected / exposed	0 / 44 (0.00%)	0 / 47 (0.00%)	0 / 44 (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			
Concussion			
subjects affected / exposed	0 / 44 (0.00%)	0 / 47 (0.00%)	0 / 44 (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
Ligament injury			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 44 (0.00%)	0 / 47 (0.00%)	0 / 44 (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
Ulna fracture			
subjects affected / exposed	0 / 44 (0.00%)	0 / 47 (0.00%)	0 / 44 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Angina unstable			
subjects affected / exposed	0 / 44 (0.00%)	0 / 47 (0.00%)	0 / 44 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Intercostal neuralgia			
subjects affected / exposed	0 / 44 (0.00%)	0 / 47 (0.00%)	0 / 44 (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			
Hepatitis E			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 44 (0.00%)	0 / 47 (0.00%)	0 / 44 (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 viral			
alternative assessment type: Systematic			

subjects affected / exposed	0 / 44 (0.00%)	0 / 47 (0.00%)	0 / 44 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Treatment Period 2: izokibep 40 mg Q2W	Treatment Period 2: izokibep 80 mg Q2W	Treatment Period 2: Placebo/izokibep 80 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 42 (2.38%)	3 / 46 (6.52%)	3 / 43 (6.98%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Vulval cancer			
subjects affected / exposed	0 / 42 (0.00%)	1 / 46 (2.17%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Concussion			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	1 / 43 (2.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ligament injury			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 42 (0.00%)	1 / 46 (2.17%)	0 / 43 (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
Ulna fracture			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	1 / 43 (2.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Angina unstable			
subjects affected / exposed	1 / 42 (2.38%)	0 / 46 (0.00%)	0 / 43 (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			

Intercostal neuralgia			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	1 / 43 (2.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Hepatitis E			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	1 / 43 (2.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia viral			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 42 (0.00%)	1 / 46 (2.17%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Treatment Period 1: izokibep 40 mg Q2W	Treatment Period 1: izokibep 80 mg Q2W	Treatment Period 1: Placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	29 / 44 (65.91%)	26 / 47 (55.32%)	23 / 44 (52.27%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Uterine leiomyoma			
subjects affected / exposed	0 / 44 (0.00%)	0 / 47 (0.00%)	1 / 44 (2.27%)
occurrences (all)	0	0	1
Vascular disorders			
Hypertension			
subjects affected / exposed	2 / 44 (4.55%)	0 / 47 (0.00%)	4 / 44 (9.09%)
occurrences (all)	2	0	4
Phlebitis			
subjects affected / exposed	0 / 44 (0.00%)	0 / 47 (0.00%)	0 / 44 (0.00%)
occurrences (all)	0	0	0
Thrombophlebitis superficial			
subjects affected / exposed	0 / 44 (0.00%)	0 / 47 (0.00%)	0 / 44 (0.00%)
occurrences (all)	0	0	0

Hypertensive crisis			
subjects affected / exposed	1 / 44 (2.27%)	0 / 47 (0.00%)	0 / 44 (0.00%)
occurrences (all)	1	0	0
Thrombosis			
subjects affected / exposed	0 / 44 (0.00%)	0 / 47 (0.00%)	0 / 44 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Chills			
subjects affected / exposed	0 / 44 (0.00%)	0 / 47 (0.00%)	1 / 44 (2.27%)
occurrences (all)	0	0	1
Fatigue			
subjects affected / exposed	0 / 44 (0.00%)	1 / 47 (2.13%)	0 / 44 (0.00%)
occurrences (all)	0	2	0
Influenza like illness			
subjects affected / exposed	1 / 44 (2.27%)	0 / 47 (0.00%)	0 / 44 (0.00%)
occurrences (all)	1	0	0
Injection site discolouration			
subjects affected / exposed	0 / 44 (0.00%)	1 / 47 (2.13%)	0 / 44 (0.00%)
occurrences (all)	0	1	0
Injection site erythema			
subjects affected / exposed	8 / 44 (18.18%)	5 / 47 (10.64%)	0 / 44 (0.00%)
occurrences (all)	13	9	0
Injection site pruritus			
subjects affected / exposed	0 / 44 (0.00%)	1 / 47 (2.13%)	0 / 44 (0.00%)
occurrences (all)	0	1	0
Injection site reaction			
subjects affected / exposed	12 / 44 (27.27%)	12 / 47 (25.53%)	0 / 44 (0.00%)
occurrences (all)	41	36	0
Peripheral swelling			
subjects affected / exposed	0 / 44 (0.00%)	1 / 47 (2.13%)	0 / 44 (0.00%)
occurrences (all)	0	1	0
Pyrexia			
subjects affected / exposed	0 / 44 (0.00%)	0 / 47 (0.00%)	2 / 44 (4.55%)
occurrences (all)	0	0	2
Vaccination site pain			

subjects affected / exposed	0 / 44 (0.00%)	1 / 47 (2.13%)	0 / 44 (0.00%)
occurrences (all)	0	1	0
Asthenia			
subjects affected / exposed	0 / 44 (0.00%)	0 / 47 (0.00%)	0 / 44 (0.00%)
occurrences (all)	0	0	0
Drug intolerance			
subjects affected / exposed	0 / 44 (0.00%)	0 / 47 (0.00%)	0 / 44 (0.00%)
occurrences (all)	0	0	0
Injection site bruising			
subjects affected / exposed	0 / 44 (0.00%)	0 / 47 (0.00%)	0 / 44 (0.00%)
occurrences (all)	0	0	0
Injection site pain			
subjects affected / exposed	0 / 44 (0.00%)	0 / 47 (0.00%)	0 / 44 (0.00%)
occurrences (all)	0	0	0
Discomfort			
subjects affected / exposed	0 / 44 (0.00%)	0 / 47 (0.00%)	0 / 44 (0.00%)
occurrences (all)	0	0	0
Injection site urticaria			
subjects affected / exposed	0 / 44 (0.00%)	0 / 47 (0.00%)	0 / 44 (0.00%)
occurrences (all)	0	0	0
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	0 / 44 (0.00%)	0 / 47 (0.00%)	0 / 44 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
Ovarian cyst			
subjects affected / exposed	0 / 44 (0.00%)	0 / 47 (0.00%)	0 / 44 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 44 (0.00%)	1 / 47 (2.13%)	0 / 44 (0.00%)
occurrences (all)	0	1	0
Oropharyngeal pain			
subjects affected / exposed	0 / 44 (0.00%)	0 / 47 (0.00%)	1 / 44 (2.27%)
occurrences (all)	0	0	1
Rhinitis allergic			

subjects affected / exposed	0 / 44 (0.00%)	0 / 47 (0.00%)	1 / 44 (2.27%)
occurrences (all)	0	0	1
Paranasal cyst			
subjects affected / exposed	0 / 44 (0.00%)	0 / 47 (0.00%)	0 / 44 (0.00%)
occurrences (all)	0	0	0
Pleurisy			
subjects affected / exposed	0 / 44 (0.00%)	0 / 47 (0.00%)	0 / 44 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Adjustment disorder with depressed mood			
subjects affected / exposed	0 / 44 (0.00%)	1 / 47 (2.13%)	0 / 44 (0.00%)
occurrences (all)	0	1	0
Depression			
subjects affected / exposed	0 / 44 (0.00%)	0 / 47 (0.00%)	1 / 44 (2.27%)
occurrences (all)	0	0	1
Insomnia			
subjects affected / exposed	0 / 44 (0.00%)	1 / 47 (2.13%)	0 / 44 (0.00%)
occurrences (all)	0	1	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 44 (0.00%)	1 / 47 (2.13%)	0 / 44 (0.00%)
occurrences (all)	0	1	0
Blood cholesterol increased			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 44 (0.00%)	1 / 47 (2.13%)	0 / 44 (0.00%)
occurrences (all)	0	1	0
Blood creatine phosphokinase increased			
subjects affected / exposed	1 / 44 (2.27%)	0 / 47 (0.00%)	0 / 44 (0.00%)
occurrences (all)	1	0	0
Blood pressure increased			
subjects affected / exposed	1 / 44 (2.27%)	0 / 47 (0.00%)	0 / 44 (0.00%)
occurrences (all)	2	0	0
Dehydroepiandrosterone decreased			
alternative assessment type: Systematic			

subjects affected / exposed	1 / 44 (2.27%)	0 / 47 (0.00%)	0 / 44 (0.00%)
occurrences (all)	1	0	0
Gamma-glutamyltransferase increased			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 44 (0.00%)	0 / 47 (0.00%)	1 / 44 (2.27%)
occurrences (all)	0	0	1
Low density lipoprotein increased			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 44 (0.00%)	1 / 47 (2.13%)	0 / 44 (0.00%)
occurrences (all)	0	1	0
Mean cell volume increased			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 44 (2.27%)	2 / 47 (4.26%)	0 / 44 (0.00%)
occurrences (all)	1	2	0
C-reactive protein increased			
subjects affected / exposed	0 / 44 (0.00%)	0 / 47 (0.00%)	0 / 44 (0.00%)
occurrences (all)	0	0	0
Amylase increased			
subjects affected / exposed	0 / 44 (0.00%)	0 / 47 (0.00%)	0 / 44 (0.00%)
occurrences (all)	0	0	0
Lipase increased			
subjects affected / exposed	0 / 44 (0.00%)	0 / 47 (0.00%)	1 / 44 (2.27%)
occurrences (all)	0	0	2
Red blood cell count increased			
subjects affected / exposed	0 / 44 (0.00%)	0 / 47 (0.00%)	0 / 44 (0.00%)
occurrences (all)	0	0	0
Hepatic enzyme increased			
subjects affected / exposed	1 / 44 (2.27%)	0 / 47 (0.00%)	0 / 44 (0.00%)
occurrences (all)	1	0	0
Body temperature increased			
subjects affected / exposed	1 / 44 (2.27%)	0 / 47 (0.00%)	0 / 44 (0.00%)
occurrences (all)	1	0	0
Transaminases increased			

subjects affected / exposed	0 / 44 (0.00%)	0 / 47 (0.00%)	0 / 44 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Meniscus injury			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 44 (2.27%)	0 / 47 (0.00%)	0 / 44 (0.00%)
occurrences (all)	1	0	0
Thermal burn			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 44 (0.00%)	0 / 47 (0.00%)	1 / 44 (2.27%)
occurrences (all)	0	0	1
Vaccination complication			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 44 (0.00%)	1 / 47 (2.13%)	2 / 44 (4.55%)
occurrences (all)	0	3	3
Arthropod sting			
subjects affected / exposed	0 / 44 (0.00%)	0 / 47 (0.00%)	0 / 44 (0.00%)
occurrences (all)	0	0	0
Ligament sprain			
subjects affected / exposed	0 / 44 (0.00%)	1 / 47 (2.13%)	0 / 44 (0.00%)
occurrences (all)	0	1	0
Ligament injury			
subjects affected / exposed	0 / 44 (0.00%)	0 / 47 (0.00%)	0 / 44 (0.00%)
occurrences (all)	0	0	0
Ulna fracture			
subjects affected / exposed	0 / 44 (0.00%)	0 / 47 (0.00%)	0 / 44 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	0 / 44 (0.00%)	0 / 47 (0.00%)	0 / 44 (0.00%)
occurrences (all)	0	0	0
Palpitations			
subjects affected / exposed	0 / 44 (0.00%)	0 / 47 (0.00%)	0 / 44 (0.00%)
occurrences (all)	0	0	0
Tachycardia			

subjects affected / exposed	0 / 44 (0.00%)	0 / 47 (0.00%)	0 / 44 (0.00%)
occurrences (all)	0	0	0
Tricuspid valve incompetence			
subjects affected / exposed	0 / 44 (0.00%)	0 / 47 (0.00%)	0 / 44 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Ataxia			
subjects affected / exposed	0 / 44 (0.00%)	1 / 47 (2.13%)	0 / 44 (0.00%)
occurrences (all)	0	1	0
Post herpetic neuralgia			
subjects affected / exposed	1 / 44 (2.27%)	0 / 47 (0.00%)	0 / 44 (0.00%)
occurrences (all)	1	0	0
Headache			
subjects affected / exposed	0 / 44 (0.00%)	4 / 47 (8.51%)	4 / 44 (9.09%)
occurrences (all)	0	6	4
Sciatica			
subjects affected / exposed	0 / 44 (0.00%)	0 / 47 (0.00%)	1 / 44 (2.27%)
occurrences (all)	0	0	1
Tension headache			
subjects affected / exposed	0 / 44 (0.00%)	0 / 47 (0.00%)	0 / 44 (0.00%)
occurrences (all)	0	0	0
Intercostal neuralgia			
subjects affected / exposed	0 / 44 (0.00%)	0 / 47 (0.00%)	0 / 44 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Anaemia of chronic disease			
subjects affected / exposed	0 / 44 (0.00%)	0 / 47 (0.00%)	1 / 44 (2.27%)
occurrences (all)	0	0	1
Leukopenia			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 44 (2.27%)	0 / 47 (0.00%)	0 / 44 (0.00%)
occurrences (all)	1	0	0
Lymphadenopathy			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 44 (2.27%)	0 / 47 (0.00%)	0 / 44 (0.00%)
occurrences (all)	1	0	0

Neutropenia			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 44 (0.00%)	1 / 47 (2.13%)	0 / 44 (0.00%)
occurrences (all)	0	1	0
Thrombocytopenia			
subjects affected / exposed	0 / 44 (0.00%)	0 / 47 (0.00%)	0 / 44 (0.00%)
occurrences (all)	0	0	0
Lymphopenia			
subjects affected / exposed	0 / 44 (0.00%)	1 / 47 (2.13%)	1 / 44 (2.27%)
occurrences (all)	0	2	1
Poikilocytosis			
subjects affected / exposed	0 / 44 (0.00%)	0 / 47 (0.00%)	0 / 44 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	1 / 44 (2.27%)	0 / 47 (0.00%)	0 / 44 (0.00%)
occurrences (all)	1	0	0
Vertigo			
subjects affected / exposed	0 / 44 (0.00%)	1 / 47 (2.13%)	0 / 44 (0.00%)
occurrences (all)	0	1	0
Vertigo positional			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 44 (2.27%)	0 / 47 (0.00%)	0 / 44 (0.00%)
occurrences (all)	1	0	0
Eye disorders			
Blepharitis			
subjects affected / exposed	0 / 44 (0.00%)	0 / 47 (0.00%)	0 / 44 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	1 / 44 (2.27%)	0 / 47 (0.00%)	0 / 44 (0.00%)
occurrences (all)	1	0	0
Diarrhoea			
subjects affected / exposed	0 / 44 (0.00%)	2 / 47 (4.26%)	3 / 44 (6.82%)
occurrences (all)	0	2	3
Flatulence			

subjects affected / exposed	1 / 44 (2.27%)	0 / 47 (0.00%)	0 / 44 (0.00%)
occurrences (all)	1	0	0
Abdominal hernia			
subjects affected / exposed	0 / 44 (0.00%)	0 / 47 (0.00%)	0 / 44 (0.00%)
occurrences (all)	0	0	0
Abdominal pain			
subjects affected / exposed	0 / 44 (0.00%)	0 / 47 (0.00%)	0 / 44 (0.00%)
occurrences (all)	0	0	0
Dyspepsia			
subjects affected / exposed	0 / 44 (0.00%)	0 / 47 (0.00%)	0 / 44 (0.00%)
occurrences (all)	0	0	0
Hepatobiliary disorders			
Hepatic steatosis			
subjects affected / exposed	0 / 44 (0.00%)	0 / 47 (0.00%)	1 / 44 (2.27%)
occurrences (all)	0	0	1
Hypertransaminasaemia			
subjects affected / exposed	0 / 44 (0.00%)	0 / 47 (0.00%)	0 / 44 (0.00%)
occurrences (all)	0	0	0
Steatohepatitis			
subjects affected / exposed	0 / 44 (0.00%)	0 / 47 (0.00%)	0 / 44 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Madarosis			
subjects affected / exposed	0 / 44 (0.00%)	1 / 47 (2.13%)	0 / 44 (0.00%)
occurrences (all)	0	1	0
Papule			
subjects affected / exposed	1 / 44 (2.27%)	0 / 47 (0.00%)	0 / 44 (0.00%)
occurrences (all)	1	0	0
Rash pruritic			
subjects affected / exposed	1 / 44 (2.27%)	0 / 47 (0.00%)	0 / 44 (0.00%)
occurrences (all)	1	0	0
Skin lesion inflammation			
subjects affected / exposed	0 / 44 (0.00%)	0 / 47 (0.00%)	0 / 44 (0.00%)
occurrences (all)	0	0	0
Acne			

subjects affected / exposed	0 / 44 (0.00%)	0 / 47 (0.00%)	1 / 44 (2.27%)
occurrences (all)	0	0	1
Nail fold inflammation			
subjects affected / exposed	0 / 44 (0.00%)	0 / 47 (0.00%)	0 / 44 (0.00%)
occurrences (all)	0	0	0
Pruritus			
subjects affected / exposed	0 / 44 (0.00%)	0 / 47 (0.00%)	0 / 44 (0.00%)
occurrences (all)	0	0	0
Skin maceration			
subjects affected / exposed	0 / 44 (0.00%)	0 / 47 (0.00%)	1 / 44 (2.27%)
occurrences (all)	0	0	1
Renal and urinary disorders			
Cystitis noninfective			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 44 (0.00%)	0 / 47 (0.00%)	1 / 44 (2.27%)
occurrences (all)	0	0	1
Pollakiuria			
subjects affected / exposed	1 / 44 (2.27%)	0 / 47 (0.00%)	0 / 44 (0.00%)
occurrences (all)	1	0	0
Dysuria			
subjects affected / exposed	0 / 44 (0.00%)	0 / 47 (0.00%)	0 / 44 (0.00%)
occurrences (all)	0	0	0
Haematuria			
subjects affected / exposed	0 / 44 (0.00%)	0 / 47 (0.00%)	0 / 44 (0.00%)
occurrences (all)	0	0	0
Endocrine disorders			
Autoimmune thyroiditis			
subjects affected / exposed	0 / 44 (0.00%)	0 / 47 (0.00%)	0 / 44 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Bursitis			
subjects affected / exposed	0 / 44 (0.00%)	0 / 47 (0.00%)	1 / 44 (2.27%)
occurrences (all)	0	0	1
Neck pain			
alternative assessment type: Systematic			

subjects affected / exposed	0 / 44 (0.00%)	1 / 47 (2.13%)	1 / 44 (2.27%)
occurrences (all)	0	1	1
Intervertebral disc disorder			
subjects affected / exposed	1 / 44 (2.27%)	0 / 47 (0.00%)	0 / 44 (0.00%)
occurrences (all)	1	0	0
Osteoarthritis			
subjects affected / exposed	1 / 44 (2.27%)	0 / 47 (0.00%)	0 / 44 (0.00%)
occurrences (all)	1	0	0
Muscle contracture			
subjects affected / exposed	0 / 44 (0.00%)	0 / 47 (0.00%)	0 / 44 (0.00%)
occurrences (all)	0	0	0
Spinal pain			
subjects affected / exposed	0 / 44 (0.00%)	0 / 47 (0.00%)	0 / 44 (0.00%)
occurrences (all)	0	0	0
Tendonitis			
subjects affected / exposed	0 / 44 (0.00%)	0 / 47 (0.00%)	0 / 44 (0.00%)
occurrences (all)	0	0	0
Back pain			
subjects affected / exposed	0 / 44 (0.00%)	0 / 47 (0.00%)	0 / 44 (0.00%)
occurrences (all)	0	0	0
Arthralgia			
subjects affected / exposed	0 / 44 (0.00%)	0 / 47 (0.00%)	1 / 44 (2.27%)
occurrences (all)	0	0	1
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 44 (0.00%)	0 / 47 (0.00%)	1 / 44 (2.27%)
occurrences (all)	0	0	1
Conjunctivitis			
subjects affected / exposed	0 / 44 (0.00%)	1 / 47 (2.13%)	0 / 44 (0.00%)
occurrences (all)	0	1	0
Cystitis			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 44 (2.27%)	0 / 47 (0.00%)	0 / 44 (0.00%)
occurrences (all)	1	0	0
Herpes zoster			

subjects affected / exposed	1 / 44 (2.27%)	0 / 47 (0.00%)	0 / 44 (0.00%)
occurrences (all)	1	0	0
Laryngitis			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 44 (0.00%)	0 / 47 (0.00%)	1 / 44 (2.27%)
occurrences (all)	0	0	1
Nasopharyngitis			
subjects affected / exposed	1 / 44 (2.27%)	2 / 47 (4.26%)	0 / 44 (0.00%)
occurrences (all)	1	2	0
Oral herpes			
subjects affected / exposed	2 / 44 (4.55%)	0 / 47 (0.00%)	0 / 44 (0.00%)
occurrences (all)	2	0	0
Pulpitis dental			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 44 (2.27%)	0 / 47 (0.00%)	0 / 44 (0.00%)
occurrences (all)	1	0	0
Respiratory tract infection			
subjects affected / exposed	0 / 44 (0.00%)	0 / 47 (0.00%)	1 / 44 (2.27%)
occurrences (all)	0	0	1
Upper respiratory tract infection			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 44 (4.55%)	3 / 47 (6.38%)	1 / 44 (2.27%)
occurrences (all)	2	3	1
Vulvovaginal candidiasis			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 44 (2.27%)	0 / 47 (0.00%)	0 / 44 (0.00%)
occurrences (all)	1	0	0
Corona virus infection			
subjects affected / exposed	1 / 44 (2.27%)	1 / 47 (2.13%)	2 / 44 (4.55%)
occurrences (all)	1	1	2
Gastroenteritis viral			
subjects affected / exposed	0 / 44 (0.00%)	0 / 47 (0.00%)	0 / 44 (0.00%)
occurrences (all)	0	0	0
Pharyngitis			

subjects affected / exposed	0 / 44 (0.00%)	0 / 47 (0.00%)	0 / 44 (0.00%)
occurrences (all)	0	0	0
Erysipelas			
subjects affected / exposed	0 / 44 (0.00%)	0 / 47 (0.00%)	0 / 44 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal infection			
subjects affected / exposed	0 / 44 (0.00%)	0 / 47 (0.00%)	0 / 44 (0.00%)
occurrences (all)	0	0	0
Groin abscess			
subjects affected / exposed	0 / 44 (0.00%)	0 / 47 (0.00%)	0 / 44 (0.00%)
occurrences (all)	0	0	0
Sinusitis			
subjects affected / exposed	0 / 44 (0.00%)	0 / 47 (0.00%)	0 / 44 (0.00%)
occurrences (all)	0	0	0
Tonsillitis			
subjects affected / exposed	0 / 44 (0.00%)	0 / 47 (0.00%)	0 / 44 (0.00%)
occurrences (all)	0	0	0
Urinary tract infection			
subjects affected / exposed	1 / 44 (2.27%)	2 / 47 (4.26%)	0 / 44 (0.00%)
occurrences (all)	1	2	0
Metabolism and nutrition disorders			
Hyperglycaemia			
subjects affected / exposed	0 / 44 (0.00%)	2 / 47 (4.26%)	2 / 44 (4.55%)
occurrences (all)	0	2	2
Hyperkalaemia			
alternative assessment type: Systematic			
subjects affected / exposed	3 / 44 (6.82%)	2 / 47 (4.26%)	2 / 44 (4.55%)
occurrences (all)	3	2	2
Hypocalcaemia			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 44 (0.00%)	0 / 47 (0.00%)	1 / 44 (2.27%)
occurrences (all)	0	0	1
Impaired fasting glucose			
subjects affected / exposed	0 / 44 (0.00%)	0 / 47 (0.00%)	1 / 44 (2.27%)
occurrences (all)	0	0	1
Dyslipidaemia			

subjects affected / exposed	0 / 44 (0.00%)	0 / 47 (0.00%)	0 / 44 (0.00%)
occurrences (all)	0	0	0
Iron deficiency			
subjects affected / exposed	0 / 44 (0.00%)	0 / 47 (0.00%)	0 / 44 (0.00%)
occurrences (all)	0	0	0
Hypercholesterolaemia			
subjects affected / exposed	0 / 44 (0.00%)	0 / 47 (0.00%)	0 / 44 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Treatment Period 2: izokibep 40 mg Q2W	Treatment Period 2: izokibep 80 mg Q2W	Treatment Period 2: Placebo/izokibep 80 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	24 / 42 (57.14%)	27 / 46 (58.70%)	22 / 43 (51.16%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Uterine leiomyoma			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	0 / 43 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 42 (0.00%)	2 / 46 (4.35%)	1 / 43 (2.33%)
occurrences (all)	0	2	1
Phlebitis			
subjects affected / exposed	1 / 42 (2.38%)	0 / 46 (0.00%)	0 / 43 (0.00%)
occurrences (all)	1	0	0
Thrombophlebitis superficial			
subjects affected / exposed	1 / 42 (2.38%)	0 / 46 (0.00%)	0 / 43 (0.00%)
occurrences (all)	1	0	0
Hypertensive crisis			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	0 / 43 (0.00%)
occurrences (all)	0	0	0
Thrombosis			
subjects affected / exposed	0 / 42 (0.00%)	1 / 46 (2.17%)	0 / 43 (0.00%)
occurrences (all)	0	1	0
General disorders and administration site conditions			
Chills			

subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	0 / 43 (0.00%)
occurrences (all)	0	0	0
Fatigue			
subjects affected / exposed	1 / 42 (2.38%)	0 / 46 (0.00%)	1 / 43 (2.33%)
occurrences (all)	1	0	1
Influenza like illness			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	0 / 43 (0.00%)
occurrences (all)	0	0	0
Injection site discolouration			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	0 / 43 (0.00%)
occurrences (all)	0	0	0
Injection site erythema			
subjects affected / exposed	6 / 42 (14.29%)	5 / 46 (10.87%)	5 / 43 (11.63%)
occurrences (all)	15	11	13
Injection site pruritus			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	0 / 43 (0.00%)
occurrences (all)	0	0	0
Injection site reaction			
subjects affected / exposed	5 / 42 (11.90%)	7 / 46 (15.22%)	7 / 43 (16.28%)
occurrences (all)	42	34	39
Peripheral swelling			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	0 / 43 (0.00%)
occurrences (all)	0	0	0
Pyrexia			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	1 / 43 (2.33%)
occurrences (all)	0	0	2
Vaccination site pain			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	1 / 43 (2.33%)
occurrences (all)	0	0	2
Asthenia			
subjects affected / exposed	0 / 42 (0.00%)	1 / 46 (2.17%)	0 / 43 (0.00%)
occurrences (all)	0	1	0
Drug intolerance			
subjects affected / exposed	1 / 42 (2.38%)	0 / 46 (0.00%)	0 / 43 (0.00%)
occurrences (all)	1	0	0
Injection site bruising			

subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	1 / 43 (2.33%)
occurrences (all)	0	0	1
Injection site pain			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	1 / 43 (2.33%)
occurrences (all)	0	0	1
Discomfort			
subjects affected / exposed	0 / 42 (0.00%)	1 / 46 (2.17%)	0 / 43 (0.00%)
occurrences (all)	0	1	0
Injection site urticaria			
subjects affected / exposed	0 / 42 (0.00%)	1 / 46 (2.17%)	0 / 43 (0.00%)
occurrences (all)	0	1	0
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	0 / 42 (0.00%)	1 / 46 (2.17%)	0 / 43 (0.00%)
occurrences (all)	0	2	0
Reproductive system and breast disorders			
Ovarian cyst			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	1 / 43 (2.33%)
occurrences (all)	0	0	1
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 42 (2.38%)	0 / 46 (0.00%)	1 / 43 (2.33%)
occurrences (all)	1	0	1
Oropharyngeal pain			
subjects affected / exposed	1 / 42 (2.38%)	0 / 46 (0.00%)	1 / 43 (2.33%)
occurrences (all)	1	0	1
Rhinitis allergic			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	0 / 43 (0.00%)
occurrences (all)	0	0	0
Paranasal cyst			
subjects affected / exposed	0 / 42 (0.00%)	1 / 46 (2.17%)	0 / 43 (0.00%)
occurrences (all)	0	1	0
Pleurisy			
subjects affected / exposed	1 / 42 (2.38%)	0 / 46 (0.00%)	0 / 43 (0.00%)
occurrences (all)	1	0	0
Psychiatric disorders			

Adjustment disorder with depressed mood			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	0 / 43 (0.00%)
occurrences (all)	0	0	0
Depression			
subjects affected / exposed	0 / 42 (0.00%)	1 / 46 (2.17%)	0 / 43 (0.00%)
occurrences (all)	0	1	0
Insomnia			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	0 / 43 (0.00%)
occurrences (all)	0	0	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 42 (2.38%)	0 / 46 (0.00%)	1 / 43 (2.33%)
occurrences (all)	1	0	1
Blood cholesterol increased			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	0 / 43 (0.00%)
occurrences (all)	0	0	0
Blood creatine phosphokinase increased			
subjects affected / exposed	2 / 42 (4.76%)	2 / 46 (4.35%)	2 / 43 (4.65%)
occurrences (all)	2	2	3
Blood pressure increased			
subjects affected / exposed	2 / 42 (4.76%)	0 / 46 (0.00%)	1 / 43 (2.33%)
occurrences (all)	2	0	1
Dehydroepiandrosterone decreased			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	0 / 43 (0.00%)
occurrences (all)	0	0	0
Gamma-glutamyltransferase increased			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 42 (0.00%)	3 / 46 (6.52%)	2 / 43 (4.65%)
occurrences (all)	0	3	2
Low density lipoprotein increased			
alternative assessment type: Systematic			

subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	0 / 43 (0.00%)
occurrences (all)	0	0	0
Mean cell volume increased			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	0 / 43 (0.00%)
occurrences (all)	0	0	0
C-reactive protein increased			
subjects affected / exposed	1 / 42 (2.38%)	0 / 46 (0.00%)	0 / 43 (0.00%)
occurrences (all)	1	0	0
Amylase increased			
subjects affected / exposed	0 / 42 (0.00%)	1 / 46 (2.17%)	0 / 43 (0.00%)
occurrences (all)	0	1	0
Lipase increased			
subjects affected / exposed	0 / 42 (0.00%)	1 / 46 (2.17%)	1 / 43 (2.33%)
occurrences (all)	0	2	1
Red blood cell count increased			
subjects affected / exposed	0 / 42 (0.00%)	1 / 46 (2.17%)	0 / 43 (0.00%)
occurrences (all)	0	1	0
Hepatic enzyme increased			
subjects affected / exposed	1 / 42 (2.38%)	0 / 46 (0.00%)	0 / 43 (0.00%)
occurrences (all)	1	0	0
Body temperature increased			
subjects affected / exposed	1 / 42 (2.38%)	0 / 46 (0.00%)	1 / 43 (2.33%)
occurrences (all)	1	0	1
Transaminases increased			
subjects affected / exposed	1 / 42 (2.38%)	0 / 46 (0.00%)	0 / 43 (0.00%)
occurrences (all)	1	0	0
Injury, poisoning and procedural complications			
Meniscus injury			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	0 / 43 (0.00%)
occurrences (all)	0	0	0
Thermal burn			
alternative assessment type: Systematic			

subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	0 / 43 (0.00%)
occurrences (all)	0	0	0
Vaccination complication			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 42 (0.00%)	1 / 46 (2.17%)	0 / 43 (0.00%)
occurrences (all)	0	1	0
Arthropod sting			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	1 / 43 (2.33%)
occurrences (all)	0	0	1
Ligament sprain			
subjects affected / exposed	1 / 42 (2.38%)	0 / 46 (0.00%)	0 / 43 (0.00%)
occurrences (all)	1	0	0
Ligament injury			
subjects affected / exposed	0 / 42 (0.00%)	1 / 46 (2.17%)	0 / 43 (0.00%)
occurrences (all)	0	1	0
Ulna fracture			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	1 / 43 (2.33%)
occurrences (all)	0	0	1
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	1 / 42 (2.38%)	0 / 46 (0.00%)	0 / 43 (0.00%)
occurrences (all)	1	0	0
Palpitations			
subjects affected / exposed	0 / 42 (0.00%)	1 / 46 (2.17%)	0 / 43 (0.00%)
occurrences (all)	0	1	0
Tachycardia			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	1 / 43 (2.33%)
occurrences (all)	0	0	1
Tricuspid valve incompetence			
subjects affected / exposed	1 / 42 (2.38%)	0 / 46 (0.00%)	0 / 43 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			
Ataxia			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	0 / 43 (0.00%)
occurrences (all)	0	0	0
Post herpetic neuralgia			

subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	0 / 43 (0.00%)
occurrences (all)	0	0	0
Headache			
subjects affected / exposed	1 / 42 (2.38%)	4 / 46 (8.70%)	2 / 43 (4.65%)
occurrences (all)	1	4	2
Sciatica			
subjects affected / exposed	0 / 42 (0.00%)	1 / 46 (2.17%)	0 / 43 (0.00%)
occurrences (all)	0	1	0
Tension headache			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	1 / 43 (2.33%)
occurrences (all)	0	0	1
Intercostal neuralgia			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	1 / 43 (2.33%)
occurrences (all)	0	0	1
Blood and lymphatic system disorders			
Anaemia of chronic disease			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	0 / 43 (0.00%)
occurrences (all)	0	0	0
Leukopenia			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 42 (2.38%)	0 / 46 (0.00%)	1 / 43 (2.33%)
occurrences (all)	1	0	1
Lymphadenopathy			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	0 / 43 (0.00%)
occurrences (all)	0	0	0
Neutropenia			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	0 / 43 (0.00%)
occurrences (all)	0	0	0
Thrombocytopenia			
subjects affected / exposed	0 / 42 (0.00%)	1 / 46 (2.17%)	0 / 43 (0.00%)
occurrences (all)	0	1	0
Lymphopenia			

subjects affected / exposed	1 / 42 (2.38%)	0 / 46 (0.00%)	0 / 43 (0.00%)
occurrences (all)	1	0	0
Poikilocytosis			
subjects affected / exposed	1 / 42 (2.38%)	0 / 46 (0.00%)	0 / 43 (0.00%)
occurrences (all)	1	0	0
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	0 / 43 (0.00%)
occurrences (all)	0	0	0
Vertigo			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	0 / 43 (0.00%)
occurrences (all)	0	0	0
Vertigo positional			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	0 / 43 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Blepharitis			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	1 / 43 (2.33%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	0 / 43 (0.00%)
occurrences (all)	0	0	0
Diarrhoea			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	1 / 43 (2.33%)
occurrences (all)	0	0	1
Flatulence			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	0 / 43 (0.00%)
occurrences (all)	0	0	0
Abdominal hernia			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	1 / 43 (2.33%)
occurrences (all)	0	0	1
Abdominal pain			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	1 / 43 (2.33%)
occurrences (all)	0	0	1

Dyspepsia			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	1 / 43 (2.33%)
occurrences (all)	0	0	1
Hepatobiliary disorders			
Hepatic steatosis			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	1 / 43 (2.33%)
occurrences (all)	0	0	1
Hypertransaminasaemia			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	2 / 43 (4.65%)
occurrences (all)	0	0	2
Steatohepatitis			
subjects affected / exposed	1 / 42 (2.38%)	0 / 46 (0.00%)	0 / 43 (0.00%)
occurrences (all)	1	0	0
Skin and subcutaneous tissue disorders			
Madarosis			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	0 / 43 (0.00%)
occurrences (all)	0	0	0
Papule			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	0 / 43 (0.00%)
occurrences (all)	0	0	0
Rash pruritic			
subjects affected / exposed	0 / 42 (0.00%)	1 / 46 (2.17%)	0 / 43 (0.00%)
occurrences (all)	0	1	0
Skin lesion inflammation			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	1 / 43 (2.33%)
occurrences (all)	0	0	2
Acne			
subjects affected / exposed	0 / 42 (0.00%)	1 / 46 (2.17%)	0 / 43 (0.00%)
occurrences (all)	0	1	0
Nail fold inflammation			
subjects affected / exposed	0 / 42 (0.00%)	1 / 46 (2.17%)	0 / 43 (0.00%)
occurrences (all)	0	1	0
Pruritus			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	1 / 43 (2.33%)
occurrences (all)	0	0	1
Skin maceration			

subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	0 / 43 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Cystitis noninfective			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	0 / 43 (0.00%)
occurrences (all)	0	0	0
Pollakiuria			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	0 / 43 (0.00%)
occurrences (all)	0	0	0
Dysuria			
subjects affected / exposed	0 / 42 (0.00%)	1 / 46 (2.17%)	0 / 43 (0.00%)
occurrences (all)	0	1	0
Haematuria			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	2 / 43 (4.65%)
occurrences (all)	0	0	2
Endocrine disorders			
Autoimmune thyroiditis			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	1 / 43 (2.33%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			
Bursitis			
subjects affected / exposed	0 / 42 (0.00%)	1 / 46 (2.17%)	0 / 43 (0.00%)
occurrences (all)	0	1	0
Neck pain			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	0 / 43 (0.00%)
occurrences (all)	0	0	0
Intervertebral disc disorder			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	0 / 43 (0.00%)
occurrences (all)	0	0	0
Osteoarthritis			
subjects affected / exposed	0 / 42 (0.00%)	2 / 46 (4.35%)	0 / 43 (0.00%)
occurrences (all)	0	2	0
Muscle contracture			

subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	2 / 43 (4.65%)
occurrences (all)	0	0	2
Spinal pain			
subjects affected / exposed	0 / 42 (0.00%)	1 / 46 (2.17%)	0 / 43 (0.00%)
occurrences (all)	0	1	0
Tendonitis			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	1 / 43 (2.33%)
occurrences (all)	0	0	1
Back pain			
subjects affected / exposed	3 / 42 (7.14%)	2 / 46 (4.35%)	2 / 43 (4.65%)
occurrences (all)	3	2	3
Arthralgia			
subjects affected / exposed	3 / 42 (7.14%)	1 / 46 (2.17%)	1 / 43 (2.33%)
occurrences (all)	3	1	1
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 42 (0.00%)	1 / 46 (2.17%)	0 / 43 (0.00%)
occurrences (all)	0	1	0
Conjunctivitis			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	0 / 43 (0.00%)
occurrences (all)	0	0	0
Cystitis			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	0 / 43 (0.00%)
occurrences (all)	0	0	0
Herpes zoster			
subjects affected / exposed	1 / 42 (2.38%)	0 / 46 (0.00%)	1 / 43 (2.33%)
occurrences (all)	1	0	1
Laryngitis			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	0 / 43 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	3 / 42 (7.14%)	4 / 46 (8.70%)	2 / 43 (4.65%)
occurrences (all)	3	4	2
Oral herpes			

subjects affected / exposed	0 / 42 (0.00%)	2 / 46 (4.35%)	0 / 43 (0.00%)
occurrences (all)	0	2	0
Pulpitis dental			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	0 / 43 (0.00%)
occurrences (all)	0	0	0
Respiratory tract infection			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	1 / 43 (2.33%)
occurrences (all)	0	0	1
Upper respiratory tract infection			
alternative assessment type: Systematic			
subjects affected / exposed	3 / 42 (7.14%)	1 / 46 (2.17%)	0 / 43 (0.00%)
occurrences (all)	3	1	0
Vulvovaginal candidiasis			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	0 / 43 (0.00%)
occurrences (all)	0	0	0
Corona virus infection			
subjects affected / exposed	2 / 42 (4.76%)	3 / 46 (6.52%)	2 / 43 (4.65%)
occurrences (all)	2	3	2
Gastroenteritis viral			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	1 / 43 (2.33%)
occurrences (all)	0	0	1
Pharyngitis			
subjects affected / exposed	1 / 42 (2.38%)	1 / 46 (2.17%)	2 / 43 (4.65%)
occurrences (all)	1	1	2
Erysipelas			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	1 / 43 (2.33%)
occurrences (all)	0	0	1
Gastrointestinal infection			
subjects affected / exposed	0 / 42 (0.00%)	1 / 46 (2.17%)	0 / 43 (0.00%)
occurrences (all)	0	1	0
Groin abscess			
subjects affected / exposed	0 / 42 (0.00%)	1 / 46 (2.17%)	0 / 43 (0.00%)
occurrences (all)	0	1	0

Sinusitis			
subjects affected / exposed	1 / 42 (2.38%)	0 / 46 (0.00%)	1 / 43 (2.33%)
occurrences (all)	1	0	1
Tonsillitis			
subjects affected / exposed	0 / 42 (0.00%)	1 / 46 (2.17%)	0 / 43 (0.00%)
occurrences (all)	0	1	0
Urinary tract infection			
subjects affected / exposed	1 / 42 (2.38%)	0 / 46 (0.00%)	0 / 43 (0.00%)
occurrences (all)	1	0	0
Metabolism and nutrition disorders			
Hyperglycaemia			
subjects affected / exposed	0 / 42 (0.00%)	2 / 46 (4.35%)	0 / 43 (0.00%)
occurrences (all)	0	4	0
Hyperkalaemia			
alternative assessment type: Systematic			
subjects affected / exposed	4 / 42 (9.52%)	1 / 46 (2.17%)	0 / 43 (0.00%)
occurrences (all)	10	2	0
Hypocalcaemia			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	0 / 43 (0.00%)
occurrences (all)	0	0	0
Impaired fasting glucose			
subjects affected / exposed	0 / 42 (0.00%)	1 / 46 (2.17%)	0 / 43 (0.00%)
occurrences (all)	0	1	0
Dyslipidaemia			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	1 / 43 (2.33%)
occurrences (all)	0	0	1
Iron deficiency			
subjects affected / exposed	0 / 42 (0.00%)	1 / 46 (2.17%)	0 / 43 (0.00%)
occurrences (all)	0	1	0
Hypercholesterolaemia			
subjects affected / exposed	1 / 42 (2.38%)	1 / 46 (2.17%)	0 / 43 (0.00%)
occurrences (all)	1	1	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
25 November 2020	Protocol amendment 1: Optimization of dosing regimen in Treatment Period II The bi-weekly dosing frequency was maintained after trial Week 16 and was not changed to four-weekly dosing administration. This Amendment was based on the data analysis of the clinical trial ABY-035-002 (EudraCT No. 2017-001615-36) and the updated ABY-035 PK/PD model. In consequence, the following aspects also changed: To allow for bi-weekly IMP administration, 7 additional trial visits were introduced. Visit 9a (Week 18) was added with IMP administration and one-hour supervision period. In addition, two weeks after the main visits (visit 10, 11, 12, 13, 14, 15 and 16) 6 additional visits (visits 10a, 11a, 12a, 13a, 14a and 15a) were performed to record IMP administration, adverse events, adverse events of special interest and concomitant medication. The one-hour supervision period after IMP administration at V11 (Week 24) was removed as subjects had already – as for the first 4 trial weeks – 3 one-hour supervision periods. It was therefore ensured that subjects who switched from Placebo to ABY-035 at Week 16 had the same level of safety surveillance as subjects exposed to ABY-035 from trial start. Because the End of Study (EoT) Visit occurred 2 weeks after the last IMP administration, the EoT was changed from Week 48 to Week 46. At Week 48 was an additional safety follow-up via a phone call (FUS).
24 September 2021	Protocol Amendment 2: Premature termination of Treatment Period II: - The clinical trial was prematurely terminated because a detailed analysis of the data from the recently completed phase II psoriasis trial with izokibep and data from other IL-17 inhibitors in psoriatic arthritis and other diseases with inflammatory joint conditions suggest that higher doses/dosing regimens than currently being studied in the protocol may be necessary to improve patient outcomes. Thus, the premature treatment termination during Treatment Period II had the consequence of omissions of trial visits during Treatment Period II and changes in the timing of one trial visit during the follow-up period for patients still ongoing at the timepoint of the amendment. - Modification of trial analyses due to premature study termination. - Change in imputation method. - Pharmacokinetic (PK) analysis. - Update of Patient Information and Informed Consent Form.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported