



Clinical trial results:

A Randomised, Phase 2, Double-blind, Placebo-controlled Study to Assess the Safety and Efficacy of Filgotinib, GS-9876 and GS-4059 in Adult Subjects with Active Sjogren's Syndrome

Summary

EudraCT number	2016-003558-34
Trial protocol	GB ES PL
Global end of trial date	02 October 2019

Results information

Result version number	v2 (current)
This version publication date	17 October 2020
First version publication date	04 January 2020
Version creation reason	• New data added to full data set Updated the record to post final results.

Trial information

Trial identification

Sponsor protocol code	GS-US-445-4189
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03100942
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Gilead Sciences
Sponsor organisation address	333 Lakeside Drive, Foster City, CA, United States, 94404
Public contact	Gilead Clinical Study Information Center, Gilead Sciences, GileadClinicalTrials@gilead.com
Scientific contact	Gilead Clinical Study Information Center, Gilead Sciences, GileadClinicalTrials@gilead.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	02 October 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	10 January 2019
Global end of trial reached?	Yes
Global end of trial date	02 October 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study was to assess the efficacy of filgotinib, lanraplenib, and tirabrutinib in adults with active Sjogren's Syndrome (SjS).

Protection of trial subjects:

The protocol and consent forms were submitted for each investigator to a duly constituted Independent Ethics Committee (IEC) or Institutional Review Board (IRB) for review and approval before study initiation. All revisions to the consent forms (if applicable) after initial IEC/IRB approval were submitted on behalf of the investigator to the IEC/IRB for review and approval before implementation in accordance with regulatory requirements.

This study was conducted in accordance with recognized international scientific and ethical standards, including but not limited to the International Conference on Harmonization guideline for Good Clinical Practice (ICH GCP) and the original principles embodied in the Declaration of Helsinki.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 May 2017
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	Spain: 15
Country: Number of subjects enrolled	United Kingdom: 9
Country: Number of subjects enrolled	United States: 106
Country: Number of subjects enrolled	Poland: 22
Worldwide total number of subjects	152
EEA total number of subjects	46

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	0

months)	
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	130
From 65 to 84 years	22
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were enrolled at study sites in the United States and Europe. The first participant was screened on 01 May 2017. The last study visit occurred on 02 October 2019.

Pre-assignment

Screening details:

348 participants were screened.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Lanraplenib

Arm description:

Lanraplenib (1 x 30 mg tablet) + filgotinib placebo (1 x tablet) + tirabrutinib placebo (1 x tablet) orally once daily for up to 49.4 weeks

Arm type	Experimental
Investigational medicinal product name	Lanraplenib
Investigational medicinal product code	
Other name	GS-9876
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

1 x 30 mg tablet administered orally once daily

Investigational medicinal product name	Filgotinib placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

1 tablet administered orally once daily

Investigational medicinal product name	Tirabrutinib placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

1 tablet administered orally once daily

Arm title	Filgotinib
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Arm description:

Filgotinib (1 x 200 mg tablet) + lanraplenib placebo (1 x tablet) + tirabrutinib placebo (1 x tablet) orally once daily for up to 50.4 weeks.

Arm type	Experimental
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Investigational medicinal product name	Filgotinib
Investigational medicinal product code	
Other name	GS-6034
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

1 x 200 mg tablet administered orally once daily

Investigational medicinal product name	Lanraplenib placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

1 tablet administered orally once daily

Investigational medicinal product name	Tirabrutinib placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

1 tablet administered orally once daily

Arm title	Tirabrutinib
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Arm description:

Tirabrutinib (1 × 40 mg tablet) + filgotinib placebo (1 × tablet) + lanraplenib placebo (1 × tablet) orally once daily for up to 50.3 weeks.

Arm type	Experimental
Investigational medicinal product name	Tirabrutinib
Investigational medicinal product code	
Other name	GS-4059
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

1 x 40 mg tablet administered orally once daily

Investigational medicinal product name	Filgotinib placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

1 tablet administered orally once daily

Investigational medicinal product name	Lanraplenib placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

1 tablet administered orally once daily

Arm title	Placebo
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Arm description:

Participants received filgotinib placebo + lanraplenib placebo + tirabrutinib placebo tablets orally once daily for 24 weeks.

At Week 24 visit, participants were re-randomized 1:1:1, in a blinded fashion and receive either of the

following study drugs through Week 48:

- filgotinib + lanraplenib placebo + tirabrutinib placebo
- lanraplenib + filgotinib placebo + tirabrutinib placebo
- tirabrutinib + filgotinib placebo + lanraplenib placebo

Arm type	Placebo
Investigational medicinal product name	Filgotinib placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

1 tablet administered orally once daily

Investigational medicinal product name	Lanraplenib placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

1 tablet administered orally once daily

Investigational medicinal product name	Tirabrutinib placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

1 tablet administered orally once daily

Investigational medicinal product name	Filgotinib
Investigational medicinal product code	
Other name	GS-6034
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

1 x 200 mg tablet administered orally once daily

Investigational medicinal product name	Lanraplenib
Investigational medicinal product code	
Other name	GS-9876
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

1 x 30 mg tablet administered orally once daily

Investigational medicinal product name	Tirabrutinib
Investigational medicinal product code	
Other name	GS-4059
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

1 x 40 mg tablet administered orally once daily

Number of subjects in period 1 ^[1]	Lanraplenib	Filgotinib	Tirabrutinib
Started	37	38	39
Completed	26	29	33
Not completed	11	9	6
Withdrew Consent	4	5	3
Adverse Event	5	2	1
Protocol Violation	-	1	1
Lost to follow-up	-	-	1
Investigator`s Discretion	2	1	-

Number of subjects in period 1 ^[1]	Placebo
Started	36
Completed	32
Not completed	4
Withdrew Consent	3
Adverse Event	-
Protocol Violation	1
Lost to follow-up	-
Investigator`s Discretion	-

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: Two participants who were randomized but did not receive the study drug are not included in the subject disposition table.

Period 2

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo to Lanraplenib

Arm description:

Participants who received placebo for 24 weeks were re-randomized at the Week 24 visit and received lanraplenib (1 × 30 mg tablet) + filgotinib placebo (1 × tablet) + tirabrutinib placebo (1 × tablet) orally once daily for up to 25.1 weeks.

Arm type	Experimental
Investigational medicinal product name	Lanraplenib
Investigational medicinal product code	
Other name	GS-9876
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details: 1 x 30 mg tablet administered orally once daily	
Investigational medicinal product name	Filgotinib placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: 1 tablet administered orally once daily	
Investigational medicinal product name	Tirabrutinib placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: 1 tablet administered orally once daily	
Arm title	Placebo to Filgotinib
Arm description: Participants who received placebo for 24 weeks were re-randomized at the Week 24 visit and received filgotinib (1 x 200 mg tablet) + lanraplenib placebo (1 x tablet) + tirabrutinib placebo (1 x tablet) orally once daily for up to 24.4 weeks.	
Arm type	Experimental
Investigational medicinal product name	Filgotinib
Investigational medicinal product code	
Other name	GS-6034
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: 1 x 200 mg tablet administered orally once daily	
Investigational medicinal product name	Lanraplenib placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: 1 tablet administered orally once daily	
Investigational medicinal product name	Tirabrutinib placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: 1 tablet administered orally once daily	
Arm title	Placebo to Tirabrutinib
Arm description: Participants who received placebo for 24 weeks were re-randomized at the Week 24 visit and received tirabrutinib (1 x 40 mg tablet) + filgotinib placebo (1 x tablet) + lanraplenib placebo (1 x tablet) orally once daily for up to 24.9 weeks.	
Arm type	Experimental

Investigational medicinal product name	Tirabrutinib
Investigational medicinal product code	
Other name	GS-4059
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

1 x 40 mg tablet administered orally once daily

Investigational medicinal product name	Filgotinib placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

1 tablet administered orally once daily

Investigational medicinal product name	Lanraplenib placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

1 tablet administered orally once daily

Number of subjects in period 2^[2]	Placebo to Lanraplenib	Placebo to Filgotinib	Placebo to Tirabrutinib
Started	10	12	10
Completed	10	12	9
Not completed	0	0	1
Withdrew Consent	-	-	1

Notes:

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

Justification: Period 2 (Placebo Arm Re-randomized) includes participants who completed 24 weeks of placebo treatment and were re-randomized to receive lanraplenib or filgotinib or tirabrutinib.

Baseline characteristics

Reporting groups

Reporting group title	Lanraplenib
Reporting group description: Lanraplenib (1 x 30 mg tablet) + filgotinib placebo (1 x tablet) + tirabrutinib placebo (1 x tablet) orally once daily for up to 49.4 weeks	
Reporting group title	Filgotinib
Reporting group description: Filgotinib (1 x 200 mg tablet) + lanraplenib placebo (1 x tablet) + tirabrutinib placebo (1 x tablet) orally once daily for up to 50.4 weeks.	
Reporting group title	Tirabrutinib
Reporting group description: Tirabrutinib (1 x 40 mg tablet) + filgotinib placebo (1 x tablet) + lanraplenib placebo (1 x tablet) orally once daily for up to 50.3 weeks.	
Reporting group title	Placebo
Reporting group description: Participants received filgotinib placebo + lanraplenib placebo + tirabrutinib placebo tablets orally once daily for 24 weeks. At Week 24 visit, participants were re-randomized 1:1:1, in a blinded fashion and receive either of the following study drugs through Week 48:	
• filgotinib + lanraplenib placebo + tirabrutinib placebo • lanraplenib + filgotinib placebo + tirabrutinib placebo • tirabrutinib + filgotinib placebo + lanraplenib placebo	

Reporting group values	Lanraplenib	Filgotinib	Tirabrutinib
Number of subjects	37	38	39
Age categorical			
Units: Subjects			

Age continuous			
Units: years			
arithmetic mean	56.2	52.2	55.8
standard deviation	± 9.72	± 10.54	± 10.06
Gender categorical			
Units: Subjects			
Female	36	38	37
Male	1	0	2
Race			
Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	1	1
Black	5	5	4
White	31	32	34
Other	1	0	0
Ethnicity			
Units: Subjects			
Hispanic or Latino	6	4	1
Not Hispanic or Latino	31	34	38

European League Against Rheumatism (EULAR) Sjogren's Syndrome Disease Activity Index (ESSDAI)			
Overall score (ranged from 0 (best) to 123 (worst activity)) was calculated as sum of all individual weighted domain scores . For additional details on this index, please see Endpoints section.			
Units: Score on a scale			
arithmetic mean	10.5	10.2	10.4
standard deviation	± 4.89	± 6.23	± 5.36
EULAR Sjogren's syndrome patient reported index (ESSPRI)			
The ESSPRI is a patient-reported questionnaire to assess subjective patient symptoms and includes 3 domains (dryness, pain, and fatigue). Each domain scored on scale of 0-10 (0 =no symptoms at all and 10 = worst symptoms imaginable), and an overall score is calculated as the mean of the three individual domain scores where all domains carry the same weight. Minimum score can be 0 and maximum score can be 10.			
Units: Score on a scale			
arithmetic mean	6.6	6.3	5.9
standard deviation	± 1.90	± 2.31	± 2.39

Reporting group values	Placebo	Total	
Number of subjects	36	150	
Age categorical			
Units: Subjects			

Age continuous			
Units: years			
arithmetic mean	53.2		
standard deviation	± 10.28	-	
Gender categorical			
Units: Subjects			
Female	35	146	
Male	1	4	
Race			
Units: Subjects			
American Indian or Alaska Native	1	1	
Asian	0	2	
Black	5	19	
White	30	127	
Other	0	1	
Ethnicity			
Units: Subjects			
Hispanic or Latino	6	17	
Not Hispanic or Latino	30	133	
European League Against Rheumatism (EULAR) Sjogren's Syndrome Disease Activity Index (ESSDAI)			
Overall score (ranged from 0 (best) to 123 (worst activity)) was calculated as sum of all individual weighted domain scores . For additional details on this index, please see Endpoints section.			
Units: Score on a scale			
arithmetic mean	9.3		
standard deviation	± 3.96	-	
EULAR Sjogren's syndrome patient reported index (ESSPRI)			
The ESSPRI is a patient-reported questionnaire to assess subjective patient symptoms and includes 3 domains (dryness, pain, and fatigue). Each domain scored on scale of 0-10 (0 =no symptoms at all and			

10 = worst symptoms imaginable), and an overall score is calculated as the mean of the three individual domain scores where all domains carry the same weight. Minimum score can be 0 and maximum score can be 10.

Units: Score on a scale			
arithmetic mean	5.9		
standard deviation	± 2.24	-	

End points

End points reporting groups

Reporting group title	Lanraplenib
Reporting group description: Lanraplenib (1 × 30 mg tablet) + filgotinib placebo (1 × tablet) + tirabrutinib placebo (1 × tablet) orally once daily for up to 49.4 weeks	
Reporting group title	Filgotinib
Reporting group description: Filgotinib (1 × 200 mg tablet) + lanraplenib placebo (1 × tablet) + tirabrutinib placebo (1 × tablet) orally once daily for up to 50.4 weeks.	
Reporting group title	Tirabrutinib
Reporting group description: Tirabrutinib (1 × 40 mg tablet) + filgotinib placebo (1 × tablet) + lanraplenib placebo (1 × tablet) orally once daily for up to 50.3 weeks.	
Reporting group title	Placebo
Reporting group description: Participants received filgotinib placebo + lanraplenib placebo + tirabrutinib placebo tablets orally once daily for 24 weeks. At Week 24 visit, participants were re-randomized 1:1:1, in a blinded fashion and receive either of the following study drugs through Week 48: • filgotinib + lanraplenib placebo + tirabrutinib placebo • lanraplenib + filgotinib placebo + tirabrutinib placebo • tirabrutinib + filgotinib placebo + lanraplenib placebo	
Reporting group title	Placebo to Lanraplenib
Reporting group description: Participants who received placebo for 24 weeks were re-randomized at the Week 24 visit and received lanraplenib (1 × 30 mg tablet) + filgotinib placebo (1 × tablet) + tirabrutinib placebo (1 × tablet) orally once daily for up to 25.1 weeks.	
Reporting group title	Placebo to Filgotinib
Reporting group description: Participants who received placebo for 24 weeks were re-randomized at the Week 24 visit and received filgotinib (1 × 200 mg tablet) + lanraplenib placebo (1 × tablet) + tirabrutinib placebo (1 × tablet) orally once daily for up to 24.4 weeks.	
Reporting group title	Placebo to Tirabrutinib
Reporting group description: Participants who received placebo for 24 weeks were re-randomized at the Week 24 visit and received tirabrutinib (1 × 40 mg tablet) + filgotinib placebo (1 × tablet) + lanraplenib placebo (1 × tablet) orally once daily for up to 24.9 weeks.	

Primary: Percentage of Participants Fulfilling Protocol-Specified Response Criteria at Week 12, as Compared to Baseline

End point title	Percentage of Participants Fulfilling Protocol-Specified Response Criteria at Week 12, as Compared to Baseline
End point description: Response was defined as: Improvement $\geq 20\%$ in ≥ 3 of 5 participant-reported Sjogren's syndrome (SjS) related visual analogue score (VAS) measures (participant's assessment of global disease, pain, oral dryness, ocular dryness and fatigue), with no increase defined as > 30 mm from baseline (Day 1) in any of the above 5 VAS measures, AND either $\geq 20\%$ improvement in high sensitivity C-reactive protein (hsCRP) (if hsCRP $\geq 1.5 \times$ upper limit of normal [ULN] on Day 1) or no increase in hsCRP to $\geq 1.5 \times$ ULN (if hsCRP $< 1.5 \times$ ULN on Day 1). The Full Analysis Set included all randomized participants who received at least one dose of study drug.	
End point type	Primary

End point timeframe:

Week 12

End point values	Lanraplenib	Filgotinib	Tirabrutinib	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	35	37	37	34
Units: Percentage of participants				
number (confidence interval 95%)	42.9 (25.0 to 60.7)	43.2 (25.9 to 60.6)	35.1 (18.4 to 51.9)	26.5 (10.2 to 42.8)

Statistical analyses

Statistical analysis title	Lanraplenib vs Placebo
Statistical analysis description: For the analysis of the difference in response rates, the data with missing response values were imputed by multiple imputation method with logistic regression.	
Comparison groups	Lanraplenib v Placebo
Number of subjects included in analysis	69
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1597 ^[1]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in Response Rates
Point estimate	15.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.3
upper limit	37.6

Notes:

[1] - P-values were obtained from Cochran-Mantel-Haenszel (CMH) test stratified by randomization stratification factors.

Statistical analysis title	Filgotinib vs Placebo
Statistical analysis description: For the analysis of the difference in response rates, the data with missing response values were imputed by multiple imputation method with logistic regression.	
Comparison groups	Filgotinib v Placebo
Number of subjects included in analysis	71
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1694 ^[2]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in Response Rates
Point estimate	16.6

Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.1
upper limit	38.3

Notes:

[2] - P-values were obtained from CMH test stratified by randomization stratification factors.

Statistical analysis title	Tirabrutinib vs Placebo
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Statistical analysis description:

For the analysis of the difference in response rates, the data with missing response values were imputed by multiple imputation method with logistic regression.

Comparison groups	Tirabrutinib v Placebo
Number of subjects included in analysis	71
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3309 ^[3]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in Response Rates
Point estimate	8.1

Confidence interval

level	95 %
sides	2-sided
lower limit	-13.2
upper limit	29.4

Notes:

[3] - P-values were obtained from CMH test stratified by randomization stratification factors.

Secondary: Change From Baseline in European League Against Rheumatism (EULAR) Sjogren's Syndrome Disease Activity Index (ESSDAI) at Week 12

End point title	Change From Baseline in European League Against Rheumatism (EULAR) Sjogren's Syndrome Disease Activity Index (ESSDAI) at Week 12
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End point description:

The ESSDAI is a physician-administered tool designed to measure disease activity. It consists of 12 organ-specific 'domains' contributing to disease activity associated with the participant's Sjogren's Syndrome only (constitutional, lymphadenopathy, articular, muscular, cutaneous, glandular, pulmonary, renal, peripheral nervous system, central nervous system, hematological, biological). Each domain is assessed for activity level (i.e., no, low, moderate, high) and assigned a numerical score based on pre-determined weighting of each individual domain. Overall score (ranges from 0 (no activity) to 123 (worst activity)) is calculated as sum of all individual weighted domain scores. A negative change from baseline value indicates improvement. Participants in the Full Analysis Set were analyzed.

End point type	Secondary
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End point timeframe:

Baseline; Week 12

End point values	Lanraplenib	Filgotinib	Tirabrutinib	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	37	38	39	36
Units: Score on a scale				
least squares mean (standard error)	-2.5 ($\pm$ 0.76)	-4.7 ($\pm$ 0.72)	-3.2 ($\pm$ 0.73)	-3.9 ($\pm$ 0.76)

Statistical analyses

Statistical analysis title	Lanraplenib vs Placebo
Statistical analysis description:	
Least Squares (LS) Means, 95% confidence interval (CI), and P-values were obtained from Mixed Effects Model for Repeated Measures (MMRM) with the terms for baseline value, treatment, stratification factors, visit, and treatment-by-visit interaction.	
Comparison groups	Lanraplenib v Placebo
Number of subjects included in analysis	73
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2066
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	1.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.7
upper limit	3.4
Variability estimate	Standard error of the mean
Dispersion value	1.05

Statistical analysis title	Filgotinib vs Placebo
Statistical analysis description:	
LS Means, 95% CI, and P-values were obtained from MMRM with the terms for baseline value, treatment, stratification factors, visit, and treatment-by-visit interaction.	
Comparison groups	Filgotinib v Placebo
Number of subjects included in analysis	74
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3998
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.9
upper limit	1.2

Variability estimate	Standard error of the mean
Dispersion value	1.04

Statistical analysis title	Tirabrutinib vs Placebo
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Statistical analysis description:

LS Means, 95% CI, and P-values were obtained from MMRM with the terms for baseline value, treatment, stratification factors, visit, and treatment-by-visit interaction.

Comparison groups	Tirabrutinib v Placebo
Number of subjects included in analysis	75
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5113
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.4
upper limit	2.7
Variability estimate	Standard error of the mean
Dispersion value	1.04

Secondary: Change From Baseline in EULAR Sjogren's Syndrome Patient Reported Index (ESSPRI) at Week 12

End point title	Change From Baseline in EULAR Sjogren's Syndrome Patient Reported Index (ESSPRI) at Week 12
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End point description:

The ESSPRI is a participant-reported questionnaire to assess subjective participant symptoms and includes 3 domains (dryness, pain, and fatigue). Each domain is scored on scale of 0-10 (0 = no symptom at all and 10 = worst symptom imaginable), and an overall score is calculated as the mean of the three individual domains where all domains carry the same weight. Minimum score can be 0 and maximum score can be 10. A negative change from baseline value indicates improvement. Participants in the Full Analysis Set were analyzed.

End point type	Secondary
End point timeframe:	
Baseline; Week 12	

End point values	Lanraplenib	Filgotinib	Tirabrutinib	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	37	38	39	36
Units: Score on a scale				
least squares mean (standard error)	-1.0 (± 0.34)	-1.4 (± 0.33)	-1.4 (± 0.33)	-1.0 (± 0.34)

Statistical analyses

Statistical analysis title	Lanraplenib vs Placebo
Statistical analysis description: LS Means, 95% CI, and P-values were obtained from MMRM with the terms for baseline value, treatment, stratification factors, visit, and treatment-by-visit interaction.	
Comparison groups	Lanraplenib v Placebo
Number of subjects included in analysis	73
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9446
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.9
upper limit	1
Variability estimate	Standard error of the mean
Dispersion value	0.47

Statistical analysis title	Filgotinib vs Placebo
Statistical analysis description: LS Means, 95% CI, and P-values were obtained from MMRM with the terms for baseline value, treatment, stratification factors, visit, and treatment-by-visit interaction.	
Comparison groups	Filgotinib v Placebo
Number of subjects included in analysis	74
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3977
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.3
upper limit	0.5
Variability estimate	Standard error of the mean
Dispersion value	0.47

Statistical analysis title	Tirabrutinib vs Placebo
Statistical analysis description: LS Means, 95% CI, and P-values were obtained from MMRM with the terms for baseline value, treatment, stratification factors, visit, and treatment-by-visit interaction.	
Comparison groups	Tirabrutinib v Placebo
Number of subjects included in analysis	75
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4966
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.2
upper limit	0.6
Variability estimate	Standard error of the mean
Dispersion value	0.47

Secondary: Change From Baseline in ESSDAI at Week 24

End point title	Change From Baseline in ESSDAI at Week 24
End point description: The ESSDAI is a physician-administered tool designed to measure disease activity. It consists of 12 organ-specific 'domains' contributing to disease activity associated with the participant's Sjogren's Syndrome only (constitutional, lymphadenopathy, articular, muscular, cutaneous, glandular, pulmonary, renal, peripheral nervous system, central nervous system, hematological, biological). Each domain is assessed for activity level (i.e., no, low, moderate, high) and assigned a numerical score based on pre-determined weighting of each individual domain. Overall score (ranges from 0 (no activity) to 123 (worst activity)) is calculated as sum of all individual weighted domain scores. A negative change from baseline value indicates improvement. Participants in the Full Analysis Set were analyzed.	
End point type	Secondary
End point timeframe: Baseline; Week 24	

End point values	Lanraplenib	Filgotinib	Tirabrutinib	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	37	38	39	36
Units: Score on a scale				
least squares mean (standard error)	-4.3 (± 0.81)	-5.4 (± 0.75)	-4.0 (± 0.75)	-4.2 (± 0.78)

Statistical analyses

Statistical analysis title	Lanraplenib vs Placebo
Statistical analysis description: LS Means, 95% CI, and P-values were obtained from MMRM with the terms for baseline value, treatment, stratification factors, visit, and treatment-by-visit interaction.	
Comparison groups	Lanraplenib v Placebo
Number of subjects included in analysis	73
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9564
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.2
upper limit	2.1
Variability estimate	Standard error of the mean
Dispersion value	1.1

Statistical analysis title	Filgotinib vs Placebo
Statistical analysis description: LS Means, 95% CI, and P-values were obtained from MMRM with the terms for baseline value, treatment, stratification factors, visit, and treatment-by-visit interaction.	
Comparison groups	Filgotinib v Placebo
Number of subjects included in analysis	74
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2788
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-1.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.3
upper limit	0.9
Variability estimate	Standard error of the mean
Dispersion value	1.07

Statistical analysis title	Tirabrutinib vs Placebo
Statistical analysis description: LS Means, 95% CI, and P-values were obtained from MMRM with the terms for baseline value, treatment, stratification factors, visit, and treatment-by-visit interaction.	
Comparison groups	Tirabrutinib v Placebo

Number of subjects included in analysis	75
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8047
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.8
upper limit	2.3
Variability estimate	Standard error of the mean
Dispersion value	1.06

Secondary: Change From Baseline in ESSPRI at Week 24

End point title	Change From Baseline in ESSPRI at Week 24
End point description:	
The ESSPRI is a participant-reported questionnaire to assess subjective participant symptoms and includes 3 domains (dryness, pain, and fatigue). Each domain is scored on scale of 0-10 (0 = no symptom at all and 10 = worst symptom imaginable), and an overall score is calculated as the mean of the three individual domains where all domains carry the same weight. Minimum score can be 0 and maximum score can be 10. A negative change from baseline value indicates improvement. Participants in the Full Analysis Set were analyzed.	
End point type	Secondary
End point timeframe:	
Baseline; Week 24	

End point values	Lanraplenib	Filgotinib	Tirabrutinib	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	37	38	39	36
Units: Score on a scale				
least squares mean (standard error)	-1.1 (± 0.34)	-0.8 (± 0.31)	-1.2 (± 0.31)	-0.9 (± 0.33)

Statistical analyses

Statistical analysis title	Lanraplenib vs Placebo
Statistical analysis description:	
LS Means, 95% CI, and P-values were obtained from MMRM with the terms for baseline value, treatment, stratification factors, visit, and treatment-by-visit interaction.	
Comparison groups	Lanraplenib v Placebo

Number of subjects included in analysis	73
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6782
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.1
upper limit	0.7
Variability estimate	Standard error of the mean
Dispersion value	0.46

Statistical analysis title	Filgotinib vs Placebo
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Statistical analysis description:

LS Means, 95% CI, and P-values were obtained from MMRM with the terms for baseline value, treatment, stratification factors, visit, and treatment-by-visit interaction.

Comparison groups	Filgotinib v Placebo
Number of subjects included in analysis	74
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9171
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.8
upper limit	0.9
Variability estimate	Standard error of the mean
Dispersion value	0.45

Statistical analysis title	Tirabrutinib vs Placebo
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Statistical analysis description:

LS Means, 95% CI, and P-values were obtained from MMRM with the terms for baseline value, treatment, stratification factors, visit, and treatment-by-visit interaction.

Comparison groups	Tirabrutinib v Placebo
Number of subjects included in analysis	75
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4641
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-0.3

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.2
upper limit	0.5
Variability estimate	Standard error of the mean
Dispersion value	0.45

Adverse events

Adverse events information

Timeframe for reporting adverse events:

First dose date up to last dose date (Maximum: 50.4 weeks) plus 30 days

Adverse event reporting additional description:

The Safety Analysis Set included participants who received at least one dose of study drug.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	22.0
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Reporting groups

Reporting group title	Lanraplenib
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Reporting group description:

Lanraplenib (1 × 30 mg tablet) + filgotinib placebo (1 × tablet) + tirabrutinib placebo (1 × tablet) orally once daily for up to 49.4 weeks.

Reporting group title	Filgotinib
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Reporting group description:

Filgotinib (1 × 200 mg tablet) + lanraplenib placebo (1 × tablet) + tirabrutinib placebo (1 × tablet) orally once daily for up to 50.4 weeks.

Reporting group title	Tirabrutinib
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Reporting group description:

Tirabrutinib (1 × 40 mg tablet) + filgotinib placebo (1 × tablet) + lanraplenib placebo (1 × tablet) orally once daily for up to 50.3 weeks.

Reporting group title	Placebo to Lanraplenib
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Reporting group description:

Participants who received placebo for 24 weeks were re-randomized at the Week 24 visit and received lanraplenib (1 × 30 mg tablet) + filgotinib placebo (1 × tablet) + tirabrutinib placebo (1 × tablet) orally once daily for up to 25.1 weeks.

Reporting group title	Placebo to Filgotinib
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Reporting group description:

Participants who received placebo for 24 weeks were re-randomized at the Week 24 visit and received filgotinib (1 × 200 mg tablet) + lanraplenib placebo (1 × tablet) + tirabrutinib placebo (1 × tablet) orally once daily for up to 24.4 weeks.

Reporting group title	Placebo to Tirabrutinib
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Reporting group description:

Participants who received placebo for 24 weeks were rerandomized at the Week 24 visit and received tirabrutinib (1 × 40 mg tablet) + filgotinib placebo (1 × tablet) + lanraplenib placebo (1 × tablet) orally once daily for up to 24.9 weeks.

Reporting group title	Placebo on Placebo Controlled Period
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Reporting group description:

Participants received filgotinib placebo + lanraplenib placebo + tirabrutinib placebo tablets orally once daily for 24 weeks in placebo controlled period.

At Week 24 visit, participants were re-randomized 1:1:1, in a blinded fashion and receive either of the following study drugs through Week 48:

- filgotinib + lanraplenib placebo + tirabrutinib placebo
- lanraplenib + filgotinib placebo + tirabrutinib placebo
- tirabrutinib + filgotinib placebo + lanraplenib placebo

Serious adverse events	Lanraplenib	Filgotinib	Tirabrutinib
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 37 (8.11%)	5 / 38 (13.16%)	1 / 39 (2.56%)
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)			
Breast cancer			
subjects affected / exposed	0 / 37 (0.00%)	0 / 38 (0.00%)	0 / 39 (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			
Acute coronary syndrome			
subjects affected / exposed	1 / 37 (2.70%)	0 / 38 (0.00%)	0 / 39 (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			
Migraine			
subjects affected / exposed	0 / 37 (0.00%)	1 / 38 (2.63%)	0 / 39 (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
Gastrointestinal disorders			
Gastroesophageal reflux disease			
subjects affected / exposed	0 / 37 (0.00%)	0 / 38 (0.00%)	0 / 39 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis			
subjects affected / exposed	0 / 37 (0.00%)	1 / 38 (2.63%)	0 / 39 (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
Pancreatitis acute			
subjects affected / exposed	1 / 37 (2.70%)	0 / 38 (0.00%)	0 / 39 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Interstitial lung disease			

subjects affected / exposed	0 / 37 (0.00%)	1 / 38 (2.63%)	0 / 39 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Suicidal ideation			
subjects affected / exposed	1 / 37 (2.70%)	0 / 38 (0.00%)	0 / 39 (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
Renal and urinary disorders			
Renal failure			
subjects affected / exposed	0 / 37 (0.00%)	1 / 38 (2.63%)	0 / 39 (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
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 37 (0.00%)	0 / 38 (0.00%)	1 / 39 (2.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rheumatoid arthritis			
subjects affected / exposed	0 / 37 (0.00%)	0 / 38 (0.00%)	0 / 39 (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			
Diverticulitis			
subjects affected / exposed	0 / 37 (0.00%)	1 / 38 (2.63%)	0 / 39 (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

Serious adverse events	Placebo to Lanraplenib	Placebo to Filgotinib	Placebo to Tirabrutinib
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 10 (0.00%)	1 / 12 (8.33%)	0 / 10 (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)			

Breast cancer			
subjects affected / exposed	0 / 10 (0.00%)	1 / 12 (8.33%)	0 / 10 (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
Cardiac disorders			
Acute coronary syndrome			
subjects affected / exposed	0 / 10 (0.00%)	0 / 12 (0.00%)	0 / 10 (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			
Migraine			
subjects affected / exposed	0 / 10 (0.00%)	0 / 12 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 10 (0.00%)	0 / 12 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 12 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis acute			
subjects affected / exposed	0 / 10 (0.00%)	0 / 12 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Interstitial lung disease			
subjects affected / exposed	0 / 10 (0.00%)	0 / 12 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Suicidal ideation			

subjects affected / exposed	0 / 10 (0.00%)	0 / 12 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Renal failure			
subjects affected / exposed	0 / 10 (0.00%)	0 / 12 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 12 (0.00%)	0 / 10 (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
Rheumatoid arthritis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 12 (0.00%)	0 / 10 (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			
Diverticulitis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 12 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Placebo on Placebo Controlled Period		
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 36 (5.56%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast cancer			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			

Acute coronary syndrome			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Migraine			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Gastroesophageal reflux disease			
subjects affected / exposed	1 / 36 (2.78%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pancreatitis			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pancreatitis acute			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Interstitial lung disease			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Suicidal ideation			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Renal failure			

subjects affected / exposed	0 / 36 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Rheumatoid arthritis			
subjects affected / exposed	1 / 36 (2.78%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Diverticulitis			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Lanraplenib	Filgotinib	Tirabrutinib
Total subjects affected by non-serious adverse events			
subjects affected / exposed	30 / 37 (81.08%)	31 / 38 (81.58%)	32 / 39 (82.05%)
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 37 (0.00%)	3 / 38 (7.89%)	3 / 39 (7.69%)
occurrences (all)	0	3	3
Vasculitis			
subjects affected / exposed	0 / 37 (0.00%)	0 / 38 (0.00%)	0 / 39 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	4 / 37 (10.81%)	0 / 38 (0.00%)	3 / 39 (7.69%)
occurrences (all)	4	0	4
Immune system disorders			

Seasonal allergy subjects affected / exposed occurrences (all)	1 / 37 (2.70%) 1	1 / 38 (2.63%) 1	2 / 39 (5.13%) 2
Respiratory, thoracic and mediastinal disorders			
Cough subjects affected / exposed occurrences (all)	0 / 37 (0.00%) 0	1 / 38 (2.63%) 1	3 / 39 (7.69%) 3
Oropharyngeal pain subjects affected / exposed occurrences (all)	0 / 37 (0.00%) 0	2 / 38 (5.26%) 2	0 / 39 (0.00%) 0
Epistaxis subjects affected / exposed occurrences (all)	0 / 37 (0.00%) 0	0 / 38 (0.00%) 0	1 / 39 (2.56%) 1
Allergic sinusitis subjects affected / exposed occurrences (all)	0 / 37 (0.00%) 0	0 / 38 (0.00%) 0	0 / 39 (0.00%) 0
Psychiatric disorders			
Insomnia subjects affected / exposed occurrences (all)	1 / 37 (2.70%) 1	1 / 38 (2.63%) 1	2 / 39 (5.13%) 2
Investigations			
Alanine aminotransferase increased subjects affected / exposed occurrences (all)	4 / 37 (10.81%) 5	1 / 38 (2.63%) 1	2 / 39 (5.13%) 2
Aspartate aminotransferase increased subjects affected / exposed occurrences (all)	4 / 37 (10.81%) 5	1 / 38 (2.63%) 1	1 / 39 (2.56%) 1
Light chain analysis increased subjects affected / exposed occurrences (all)	0 / 37 (0.00%) 0	0 / 38 (0.00%) 0	1 / 39 (2.56%) 1
Blood creatine phosphokinase increased subjects affected / exposed occurrences (all)	0 / 37 (0.00%) 0	0 / 38 (0.00%) 0	0 / 39 (0.00%) 0
Blood potassium increased			

subjects affected / exposed occurrences (all)	0 / 37 (0.00%) 0	0 / 38 (0.00%) 0	0 / 39 (0.00%) 0
Liver function test abnormal subjects affected / exposed occurrences (all)	0 / 37 (0.00%) 0	0 / 38 (0.00%) 0	0 / 39 (0.00%) 0
Transaminases increased subjects affected / exposed occurrences (all)	0 / 37 (0.00%) 0	0 / 38 (0.00%) 0	0 / 39 (0.00%) 0
Injury, poisoning and procedural complications			
Fall subjects affected / exposed occurrences (all)	1 / 37 (2.70%) 1	2 / 38 (5.26%) 2	2 / 39 (5.13%) 2
Contusion subjects affected / exposed occurrences (all)	0 / 37 (0.00%) 0	2 / 38 (5.26%) 2	2 / 39 (5.13%) 2
Arthropod bite subjects affected / exposed occurrences (all)	0 / 37 (0.00%) 0	0 / 38 (0.00%) 0	0 / 39 (0.00%) 0
Nervous system disorders			
Headache subjects affected / exposed occurrences (all)	0 / 37 (0.00%) 0	3 / 38 (7.89%) 3	3 / 39 (7.69%) 4
Dizziness subjects affected / exposed occurrences (all)	3 / 37 (8.11%) 3	1 / 38 (2.63%) 1	1 / 39 (2.56%) 1
Migraine subjects affected / exposed occurrences (all)	1 / 37 (2.70%) 1	1 / 38 (2.63%) 1	0 / 39 (0.00%) 0
Sciatica subjects affected / exposed occurrences (all)	0 / 37 (0.00%) 0	3 / 38 (7.89%) 3	0 / 39 (0.00%) 0
Blood and lymphatic system disorders			
Neutropenia subjects affected / exposed occurrences (all)	2 / 37 (5.41%) 2	2 / 38 (5.26%) 2	0 / 39 (0.00%) 0
Anaemia			

subjects affected / exposed	1 / 37 (2.70%)	0 / 38 (0.00%)	2 / 39 (5.13%)
occurrences (all)	1	0	2
Lymphadenopathy			
subjects affected / exposed	2 / 37 (5.41%)	0 / 38 (0.00%)	0 / 39 (0.00%)
occurrences (all)	2	0	0
Lymphopenia			
subjects affected / exposed	0 / 37 (0.00%)	0 / 38 (0.00%)	0 / 39 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Vision blurred			
subjects affected / exposed	0 / 37 (0.00%)	1 / 38 (2.63%)	1 / 39 (2.56%)
occurrences (all)	0	1	1
Corneal erosion			
subjects affected / exposed	0 / 37 (0.00%)	0 / 38 (0.00%)	0 / 39 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	3 / 37 (8.11%)	3 / 38 (7.89%)	3 / 39 (7.69%)
occurrences (all)	3	3	3
Nausea			
subjects affected / exposed	2 / 37 (5.41%)	4 / 38 (10.53%)	2 / 39 (5.13%)
occurrences (all)	2	5	2
Vomiting			
subjects affected / exposed	2 / 37 (5.41%)	3 / 38 (7.89%)	2 / 39 (5.13%)
occurrences (all)	2	3	2
Abdominal pain upper			
subjects affected / exposed	0 / 37 (0.00%)	1 / 38 (2.63%)	1 / 39 (2.56%)
occurrences (all)	0	1	1
Constipation			
subjects affected / exposed	0 / 37 (0.00%)	0 / 38 (0.00%)	3 / 39 (7.69%)
occurrences (all)	0	0	3
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 37 (0.00%)	0 / 38 (0.00%)	1 / 39 (2.56%)
occurrences (all)	0	0	1
Dental caries			

subjects affected / exposed	2 / 37 (5.41%)	0 / 38 (0.00%)	0 / 39 (0.00%)
occurrences (all)	2	0	0
Food poisoning			
subjects affected / exposed	0 / 37 (0.00%)	1 / 38 (2.63%)	0 / 39 (0.00%)
occurrences (all)	0	1	0
Lip blister			
subjects affected / exposed	0 / 37 (0.00%)	2 / 38 (5.26%)	0 / 39 (0.00%)
occurrences (all)	0	2	0
Pyrexia			
subjects affected / exposed	3 / 37 (8.11%)	0 / 38 (0.00%)	0 / 39 (0.00%)
occurrences (all)	3	0	0
Asthenia			
subjects affected / exposed	0 / 37 (0.00%)	1 / 38 (2.63%)	0 / 39 (0.00%)
occurrences (all)	0	1	0
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	4 / 37 (10.81%)	2 / 38 (5.26%)	3 / 39 (7.69%)
occurrences (all)	4	2	3
Alopecia			
subjects affected / exposed	0 / 37 (0.00%)	2 / 38 (5.26%)	2 / 39 (5.13%)
occurrences (all)	0	2	2
Hyperhidrosis			
subjects affected / exposed	1 / 37 (2.70%)	2 / 38 (5.26%)	0 / 39 (0.00%)
occurrences (all)	1	2	0
Rash papular			
subjects affected / exposed	1 / 37 (2.70%)	0 / 38 (0.00%)	2 / 39 (5.13%)
occurrences (all)	1	0	2
Rash pruritic			
subjects affected / exposed	1 / 37 (2.70%)	0 / 38 (0.00%)	1 / 39 (2.56%)
occurrences (all)	1	0	1
Pruritus generalised			
subjects affected / exposed	2 / 37 (5.41%)	0 / 38 (0.00%)	0 / 39 (0.00%)
occurrences (all)	2	0	0
Rash macular			
subjects affected / exposed	0 / 37 (0.00%)	0 / 38 (0.00%)	2 / 39 (5.13%)
occurrences (all)	0	0	2

Pruritus			
subjects affected / exposed	0 / 37 (0.00%)	0 / 38 (0.00%)	0 / 39 (0.00%)
occurrences (all)	0	0	0
Skin lesion			
subjects affected / exposed	0 / 37 (0.00%)	0 / 38 (0.00%)	0 / 39 (0.00%)
occurrences (all)	0	0	0
Urticaria			
subjects affected / exposed	0 / 37 (0.00%)	0 / 38 (0.00%)	0 / 39 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	4 / 37 (10.81%)	4 / 38 (10.53%)	6 / 39 (15.38%)
occurrences (all)	4	4	7
Myalgia			
subjects affected / exposed	2 / 37 (5.41%)	0 / 38 (0.00%)	1 / 39 (2.56%)
occurrences (all)	2	0	1
Osteoarthritis			
subjects affected / exposed	1 / 37 (2.70%)	2 / 38 (5.26%)	0 / 39 (0.00%)
occurrences (all)	1	2	0
Back pain			
subjects affected / exposed	1 / 37 (2.70%)	1 / 38 (2.63%)	1 / 39 (2.56%)
occurrences (all)	1	2	1
Muscle spasms			
subjects affected / exposed	0 / 37 (0.00%)	2 / 38 (5.26%)	2 / 39 (5.13%)
occurrences (all)	0	2	2
Neck pain			
subjects affected / exposed	0 / 37 (0.00%)	1 / 38 (2.63%)	1 / 39 (2.56%)
occurrences (all)	0	1	1
Musculoskeletal pain			
subjects affected / exposed	1 / 37 (2.70%)	1 / 38 (2.63%)	0 / 39 (0.00%)
occurrences (all)	1	1	0
Pain in extremity			
subjects affected / exposed	0 / 37 (0.00%)	3 / 38 (7.89%)	0 / 39 (0.00%)
occurrences (all)	0	3	0
Rheumatoid arthritis			

subjects affected / exposed	1 / 37 (2.70%)	1 / 38 (2.63%)	0 / 39 (0.00%)
occurrences (all)	1	1	0
Temporomandibular joint syndrome			
subjects affected / exposed	0 / 37 (0.00%)	1 / 38 (2.63%)	0 / 39 (0.00%)
occurrences (all)	0	1	0
Exostosis			
subjects affected / exposed	0 / 37 (0.00%)	0 / 38 (0.00%)	0 / 39 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	4 / 37 (10.81%)	6 / 38 (15.79%)	9 / 39 (23.08%)
occurrences (all)	4	7	11
Nasopharyngitis			
subjects affected / exposed	3 / 37 (8.11%)	6 / 38 (15.79%)	4 / 39 (10.26%)
occurrences (all)	3	7	5
Urinary tract infection			
subjects affected / exposed	1 / 37 (2.70%)	2 / 38 (5.26%)	4 / 39 (10.26%)
occurrences (all)	1	2	4
Sinusitis			
subjects affected / exposed	2 / 37 (5.41%)	1 / 38 (2.63%)	5 / 39 (12.82%)
occurrences (all)	2	1	5
Bronchitis			
subjects affected / exposed	2 / 37 (5.41%)	3 / 38 (7.89%)	1 / 39 (2.56%)
occurrences (all)	2	3	1
Gastroenteritis viral			
subjects affected / exposed	3 / 37 (8.11%)	2 / 38 (5.26%)	3 / 39 (7.69%)
occurrences (all)	3	2	3
Influenza			
subjects affected / exposed	1 / 37 (2.70%)	0 / 38 (0.00%)	3 / 39 (7.69%)
occurrences (all)	1	0	3
Oral herpes			
subjects affected / exposed	2 / 37 (5.41%)	3 / 38 (7.89%)	0 / 39 (0.00%)
occurrences (all)	2	3	0
Pharyngitis			
subjects affected / exposed	0 / 37 (0.00%)	2 / 38 (5.26%)	0 / 39 (0.00%)
occurrences (all)	0	2	0

Furuncle			
subjects affected / exposed	1 / 37 (2.70%)	0 / 38 (0.00%)	1 / 39 (2.56%)
occurrences (all)	1	0	1
Lower respiratory tract infection			
subjects affected / exposed	2 / 37 (5.41%)	0 / 38 (0.00%)	1 / 39 (2.56%)
occurrences (all)	2	0	1
Pneumonia			
subjects affected / exposed	0 / 37 (0.00%)	2 / 38 (5.26%)	1 / 39 (2.56%)
occurrences (all)	0	2	1
Helicobacter infection			
subjects affected / exposed	0 / 37 (0.00%)	0 / 38 (0.00%)	0 / 39 (0.00%)
occurrences (all)	0	0	0
Herpes zoster			
subjects affected / exposed	0 / 37 (0.00%)	2 / 38 (5.26%)	0 / 39 (0.00%)
occurrences (all)	0	2	0
Laryngitis			
subjects affected / exposed	2 / 37 (5.41%)	0 / 38 (0.00%)	0 / 39 (0.00%)
occurrences (all)	2	0	0
Otitis media			
subjects affected / exposed	0 / 37 (0.00%)	1 / 38 (2.63%)	0 / 39 (0.00%)
occurrences (all)	0	1	0
Vulvovaginal mycotic infection			
subjects affected / exposed	0 / 37 (0.00%)	0 / 38 (0.00%)	2 / 39 (5.13%)
occurrences (all)	0	0	2
Conjunctivitis viral			
subjects affected / exposed	0 / 37 (0.00%)	0 / 38 (0.00%)	0 / 39 (0.00%)
occurrences (all)	0	0	0
Fungal skin infection			
subjects affected / exposed	0 / 37 (0.00%)	0 / 38 (0.00%)	0 / 39 (0.00%)
occurrences (all)	0	0	0
Vaginal infection			
subjects affected / exposed	0 / 37 (0.00%)	0 / 38 (0.00%)	0 / 39 (0.00%)
occurrences (all)	0	0	0
Viral pharyngitis			
subjects affected / exposed	0 / 37 (0.00%)	0 / 38 (0.00%)	0 / 39 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Placebo to Lanraplenib	Placebo to Filgotinib	Placebo to Tirabrutinib
Total subjects affected by non-serious adverse events			
subjects affected / exposed	10 / 10 (100.00%)	10 / 12 (83.33%)	7 / 10 (70.00%)
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 10 (0.00%)	1 / 12 (8.33%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Vasculitis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 12 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	2 / 10 (20.00%)	1 / 12 (8.33%)	0 / 10 (0.00%)
occurrences (all)	2	1	0
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	0 / 10 (0.00%)	1 / 12 (8.33%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 10 (0.00%)	0 / 12 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Oropharyngeal pain			
subjects affected / exposed	0 / 10 (0.00%)	0 / 12 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Epistaxis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 12 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Allergic sinusitis			
subjects affected / exposed	0 / 10 (0.00%)	1 / 12 (8.33%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Psychiatric disorders			
Insomnia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 12 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Investigations			

Alanine aminotransferase increased subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 12 (0.00%) 0	0 / 10 (0.00%) 0
Aspartate aminotransferase increased subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 12 (0.00%) 0	0 / 10 (0.00%) 0
Light chain analysis increased subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1	0 / 12 (0.00%) 0	0 / 10 (0.00%) 0
Blood creatine phosphokinase increased subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	1 / 12 (8.33%) 1	0 / 10 (0.00%) 0
Blood potassium increased subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	1 / 12 (8.33%) 1	0 / 10 (0.00%) 0
Liver function test abnormal subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 3	0 / 12 (0.00%) 0	0 / 10 (0.00%) 0
Transaminases increased subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1	0 / 12 (0.00%) 0	0 / 10 (0.00%) 0
Injury, poisoning and procedural complications Fall subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	1 / 12 (8.33%) 1	0 / 10 (0.00%) 0
Contusion subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 12 (0.00%) 0	0 / 10 (0.00%) 0
Arthropod bite subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 12 (0.00%) 0	1 / 10 (10.00%) 1
Nervous system disorders Headache subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1	1 / 12 (8.33%) 1	1 / 10 (10.00%) 1

Dizziness subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 12 (0.00%) 0	0 / 10 (0.00%) 0
Migraine subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	1 / 12 (8.33%) 1	0 / 10 (0.00%) 0
Sciatica subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 12 (0.00%) 0	0 / 10 (0.00%) 0
Blood and lymphatic system disorders			
Neutropenia subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	1 / 12 (8.33%) 1	0 / 10 (0.00%) 0
Anaemia subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 12 (0.00%) 0	0 / 10 (0.00%) 0
Lymphadenopathy subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 12 (0.00%) 0	1 / 10 (10.00%) 1
Lymphopenia subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	1 / 12 (8.33%) 1	0 / 10 (0.00%) 0
Eye disorders			
Vision blurred subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	1 / 12 (8.33%) 1	0 / 10 (0.00%) 0
Corneal erosion subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1	0 / 12 (0.00%) 0	0 / 10 (0.00%) 0
Gastrointestinal disorders			
Diarrhoea subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1	2 / 12 (16.67%) 2	0 / 10 (0.00%) 0
Nausea subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 12 (0.00%) 0	0 / 10 (0.00%) 0
Vomiting			

subjects affected / exposed	0 / 10 (0.00%)	0 / 12 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Abdominal pain upper			
subjects affected / exposed	0 / 10 (0.00%)	0 / 12 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Constipation			
subjects affected / exposed	0 / 10 (0.00%)	0 / 12 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 10 (0.00%)	1 / 12 (8.33%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Dental caries			
subjects affected / exposed	0 / 10 (0.00%)	0 / 12 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Food poisoning			
subjects affected / exposed	0 / 10 (0.00%)	1 / 12 (8.33%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Lip blister			
subjects affected / exposed	0 / 10 (0.00%)	0 / 12 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Pyrexia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 12 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Asthenia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 12 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	0 / 10 (0.00%)	0 / 12 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Alopecia			
subjects affected / exposed	0 / 10 (0.00%)	1 / 12 (8.33%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Hyperhidrosis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 12 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0

Rash papular			
subjects affected / exposed	0 / 10 (0.00%)	0 / 12 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Rash pruritic			
subjects affected / exposed	1 / 10 (10.00%)	0 / 12 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Pruritus generalised			
subjects affected / exposed	0 / 10 (0.00%)	0 / 12 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Rash macular			
subjects affected / exposed	0 / 10 (0.00%)	0 / 12 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Pruritus			
subjects affected / exposed	1 / 10 (10.00%)	0 / 12 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Skin lesion			
subjects affected / exposed	0 / 10 (0.00%)	0 / 12 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Urticaria			
subjects affected / exposed	1 / 10 (10.00%)	0 / 12 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 12 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Myalgia			
subjects affected / exposed	1 / 10 (10.00%)	0 / 12 (0.00%)	1 / 10 (10.00%)
occurrences (all)	1	0	1
Osteoarthritis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 12 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	2
Back pain			
subjects affected / exposed	0 / 10 (0.00%)	0 / 12 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Muscle spasms			

subjects affected / exposed	0 / 10 (0.00%)	0 / 12 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Neck pain			
subjects affected / exposed	2 / 10 (20.00%)	0 / 12 (0.00%)	0 / 10 (0.00%)
occurrences (all)	2	0	0
Musculoskeletal pain			
subjects affected / exposed	0 / 10 (0.00%)	1 / 12 (8.33%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Pain in extremity			
subjects affected / exposed	0 / 10 (0.00%)	0 / 12 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Rheumatoid arthritis			
subjects affected / exposed	1 / 10 (10.00%)	0 / 12 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Temporomandibular joint syndrome			
subjects affected / exposed	2 / 10 (20.00%)	0 / 12 (0.00%)	0 / 10 (0.00%)
occurrences (all)	2	0	0
Exostosis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 12 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	0 / 10 (0.00%)	1 / 12 (8.33%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Nasopharyngitis			
subjects affected / exposed	1 / 10 (10.00%)	1 / 12 (8.33%)	2 / 10 (20.00%)
occurrences (all)	2	2	3
Urinary tract infection			
subjects affected / exposed	2 / 10 (20.00%)	2 / 12 (16.67%)	0 / 10 (0.00%)
occurrences (all)	3	3	0
Sinusitis			
subjects affected / exposed	1 / 10 (10.00%)	0 / 12 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Bronchitis			
subjects affected / exposed	0 / 10 (0.00%)	1 / 12 (8.33%)	0 / 10 (0.00%)
occurrences (all)	0	1	0

Gastroenteritis viral			
subjects affected / exposed	2 / 10 (20.00%)	0 / 12 (0.00%)	0 / 10 (0.00%)
occurrences (all)	2	0	0
Influenza			
subjects affected / exposed	0 / 10 (0.00%)	1 / 12 (8.33%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Oral herpes			
subjects affected / exposed	0 / 10 (0.00%)	0 / 12 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Pharyngitis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 12 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Furuncle			
subjects affected / exposed	0 / 10 (0.00%)	1 / 12 (8.33%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Lower respiratory tract infection			
subjects affected / exposed	0 / 10 (0.00%)	0 / 12 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Pneumonia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 12 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Helicobacter infection			
subjects affected / exposed	0 / 10 (0.00%)	0 / 12 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Herpes zoster			
subjects affected / exposed	0 / 10 (0.00%)	0 / 12 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Laryngitis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 12 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Otitis media			
subjects affected / exposed	0 / 10 (0.00%)	1 / 12 (8.33%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Vulvovaginal mycotic infection			
subjects affected / exposed	0 / 10 (0.00%)	0 / 12 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0

Conjunctivitis viral subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	1 / 12 (8.33%) 1	0 / 10 (0.00%) 0
Fungal skin infection subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	1 / 12 (8.33%) 1	0 / 10 (0.00%) 0
Vaginal infection subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1	0 / 12 (0.00%) 0	0 / 10 (0.00%) 0
Viral pharyngitis subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 12 (0.00%) 0	1 / 10 (10.00%) 1

Non-serious adverse events	Placebo on Placebo Controlled Period		
Total subjects affected by non-serious adverse events subjects affected / exposed	23 / 36 (63.89%)		
Vascular disorders Hypertension subjects affected / exposed occurrences (all)	0 / 36 (0.00%) 0		
Vasculitis subjects affected / exposed occurrences (all)	0 / 36 (0.00%) 0		
General disorders and administration site conditions Fatigue subjects affected / exposed occurrences (all)	2 / 36 (5.56%) 2		
Immune system disorders Seasonal allergy subjects affected / exposed occurrences (all)	0 / 36 (0.00%) 0		
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)	3 / 36 (8.33%) 3		
Oropharyngeal pain			

subjects affected / exposed occurrences (all)	0 / 36 (0.00%) 0		
Epistaxis subjects affected / exposed occurrences (all)	0 / 36 (0.00%) 0		
Allergic sinusitis subjects affected / exposed occurrences (all)	0 / 36 (0.00%) 0		
Psychiatric disorders Insomnia subjects affected / exposed occurrences (all)	1 / 36 (2.78%) 1		
Investigations Alanine aminotransferase increased subjects affected / exposed occurrences (all)	0 / 36 (0.00%) 0		
Aspartate aminotransferase increased subjects affected / exposed occurrences (all)	0 / 36 (0.00%) 0		
Light chain analysis increased subjects affected / exposed occurrences (all)	0 / 36 (0.00%) 0		
Blood creatine phosphokinase increased subjects affected / exposed occurrences (all)	0 / 36 (0.00%) 0		
Blood potassium increased subjects affected / exposed occurrences (all)	0 / 36 (0.00%) 0		
Liver function test abnormal subjects affected / exposed occurrences (all)	0 / 36 (0.00%) 0		
Transaminases increased subjects affected / exposed occurrences (all)	0 / 36 (0.00%) 0		
Injury, poisoning and procedural complications			

Fall			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Contusion			
subjects affected / exposed	1 / 36 (2.78%)		
occurrences (all)	1		
Arthropod bite			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 36 (2.78%)		
occurrences (all)	1		
Dizziness			
subjects affected / exposed	3 / 36 (8.33%)		
occurrences (all)	4		
Migraine			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Sciatica			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Anaemia			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Lymphadenopathy			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Lymphopenia			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Eye disorders			

Vision blurred			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Corneal erosion			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	1 / 36 (2.78%)		
occurrences (all)	1		
Nausea			
subjects affected / exposed	1 / 36 (2.78%)		
occurrences (all)	1		
Vomiting			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Abdominal pain upper			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Constipation			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 36 (2.78%)		
occurrences (all)	1		
Dental caries			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Food poisoning			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Lip blister			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Pyrexia			

subjects affected / exposed	1 / 36 (2.78%)		
occurrences (all)	1		
Asthenia			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	2 / 36 (5.56%)		
occurrences (all)	2		
Alopecia			
subjects affected / exposed	2 / 36 (5.56%)		
occurrences (all)	2		
Hyperhidrosis			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Rash papular			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Rash pruritic			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Pruritus generalised			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Rash macular			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Pruritus			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Skin lesion			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Urticaria			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		

Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Myalgia			
subjects affected / exposed	1 / 36 (2.78%)		
occurrences (all)	1		
Osteoarthritis			
subjects affected / exposed	1 / 36 (2.78%)		
occurrences (all)	1		
Back pain			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Muscle spasms			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Neck pain			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Musculoskeletal pain			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Pain in extremity			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Rheumatoid arthritis			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Temporomandibular joint syndrome			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Exostosis			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Infections and infestations			

Upper respiratory tract infection			
subjects affected / exposed	4 / 36 (11.11%)		
occurrences (all)	5		
Nasopharyngitis			
subjects affected / exposed	4 / 36 (11.11%)		
occurrences (all)	5		
Urinary tract infection			
subjects affected / exposed	6 / 36 (16.67%)		
occurrences (all)	6		
Sinusitis			
subjects affected / exposed	3 / 36 (8.33%)		
occurrences (all)	3		
Bronchitis			
subjects affected / exposed	3 / 36 (8.33%)		
occurrences (all)	3		
Gastroenteritis viral			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Influenza			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Oral herpes			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Pharyngitis			
subjects affected / exposed	2 / 36 (5.56%)		
occurrences (all)	2		
Furuncle			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Lower respiratory tract infection			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Pneumonia			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		

Helicobacter infection			
subjects affected / exposed	1 / 36 (2.78%)		
occurrences (all)	1		
Herpes zoster			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Laryngitis			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Otitis media			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Vulvovaginal mycotic infection			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Conjunctivitis viral			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Fungal skin infection			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Vaginal infection			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Viral pharyngitis			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
12 July 2018	- Protocol Amendment included: 1) Addition of biomarker sample collection at Day 1 and Week 18 visits. 2) Addition of a primary and secondary analysis to be conducted after all participants either complete Week 24 visit or prematurely discontinued from the study. 3) Assembly of an internal unblinded team independent of the blinded study team to closely monitor study progress and drug safety.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

An unplanned review of unblinded clinical trial data was performed in this study that was not prospectively specified in the protocol. There was no impact on the overall integrity or conclusions of the study.

Notes: