



Clinical trial results:

A Randomized, Double-Blind, Placebo-Controlled, Multicenter, Phase 2 Proof-of-Concept Study to Evaluate Safety, Tolerability, and Efficacy of GS-9876 in Subjects with Active Rheumatoid Arthritis on Background Therapy with Methotrexate

Summary

EudraCT number	2016-001496-75
Trial protocol	CZ PL
Global end of trial date	20 September 2017

Results information

Result version number	v2 (current)
This version publication date	18 May 2019
First version publication date	06 September 2018
Version creation reason	<ul style="list-style-type: none">• Correction of full data setAdding text to "Limitations and Caveats" section

Trial information

Trial identification

Sponsor protocol code	GS-US-379-1582
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02885181
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Gilead Sciences
Sponsor organisation address	333 Lakeside Drive, Foster City, 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	20 September 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	22 August 2017
Global end of trial reached?	Yes
Global end of trial date	20 September 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study is to evaluate the effect of GS-9876 versus placebo for the treatment of signs and symptoms of rheumatoid arthritis (RA) in participants with active RA as measured by change from baseline in Disease Activity Score for 28 joint count using C-reactive protein (CRP) (DAS28 (CRP)) at Week 12.

Protection of trial subjects:

The protocol and consent/assent forms were submitted by 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/assent forms (if applicable) after initial IEC/IRB approval were submitted by 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:

Participants received background therapy with methotrexate administered orally or parenterally once weekly.

Evidence for comparator: -

Actual start date of recruitment	21 September 2016
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Poland: 6
Country: Number of subjects enrolled	Bulgaria: 7
Country: Number of subjects enrolled	Czech Republic: 3
Country: Number of subjects enrolled	United States: 33
Country: Number of subjects enrolled	Moldova, Republic of: 18
Country: Number of subjects enrolled	Georgia: 10
Country: Number of subjects enrolled	Ukraine: 6
Worldwide total number of subjects	83
EEA total number of subjects	16

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)	64
From 65 to 84 years	19
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 21 September 2016. The last study visit occurred on 20 September 2017.

Pre-assignment

Screening details:

140 participants were screened.

Period 1

Period 1 title	Overall study (overall 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	GS-9876 30 mg

Arm description:

GS-9876 30 mg + filgotinib placebo for 12 weeks

Arm type	Experimental
Investigational medicinal product name	GS-9876 30 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

GS-9876 30 mg tablet administered 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:

Filgotinib placebo 2 tablets administered once daily

Arm title	GS-9876 10 mg
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Arm description:

GS-9876 10 mg + filgotinib placebo for 12 weeks

Arm type	Experimental
Investigational medicinal product name	GS-9876 10 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

GS-9876 10 mg administered 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:	
Filgotinib placebo 2 tablets administered once daily	
Arm title	Filgotinib
Arm description:	
Filgotinib + GS-9876 placebo for 12 weeks	
Arm type	Experimental
Investigational medicinal product name	Filgotinib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
2 X 100 mg tablets administered once daily	
Investigational medicinal product name	GS-9876 Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
GS-9876 placebo tablet administered once daily	
Arm title	Placebo
Arm description:	
GS-9876 placebo + filgotinib placebo for 12 weeks	
Arm type	Placebo
Investigational medicinal product name	GS-9876 Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
GS-9876 placebo 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:	
Filgotinib placebo (2 tablets) administered orally once daily	

Number of subjects in period 1	GS-9876 30 mg	GS-9876 10 mg	Filgotinib
Started	20	20	21
Completed	20	19	21
Not completed	0	1	0
Consent withdrawn by subject	-	-	-
Adverse event, non-fatal	-	-	-
Investigator's discretion	-	1	-

Number of subjects in period 1	Placebo
Started	22
Completed	19
Not completed	3
Consent withdrawn by subject	1
Adverse event, non-fatal	1
Investigator's discretion	1

Baseline characteristics

Reporting groups

Reporting group title	GS-9876 30 mg
Reporting group description: GS-9876 30 mg + filgotinib placebo for 12 weeks	
Reporting group title	GS-9876 10 mg
Reporting group description: GS-9876 10 mg + filgotinib placebo for 12 weeks	
Reporting group title	Filgotinib
Reporting group description: Filgotinib + GS-9876 placebo for 12 weeks	
Reporting group title	Placebo
Reporting group description: GS-9876 placebo + filgotinib placebo for 12 weeks	

Reporting group values	GS-9876 30 mg	GS-9876 10 mg	Filgotinib
Number of subjects	20	20	21
Age categorical Units: Subjects			

Age continuous Units: years arithmetic mean standard deviation	58 ± 7.0	56 ± 11.4	53 ± 15.4
Gender categorical Units: Subjects			
Female	15	16	17
Male	5	4	4
Race Units: Subjects			
American Indian or Alaska Native	0	1	0
Asian	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	2	0
White	20	17	21
Ethnicity Units: Subjects			
Hispanic or Latino	1	1	2
Not Hispanic or Latino	19	19	19
Disease Activity Score 28 C- Reactive Protein (DAS28 CRP)			
Disease Activity Score 28 C-Reactive Protein (DAS28 (CRP)) is a measure of the participant's disease activity calculated using the tender joint counts (28 joints), swollen joint counts (28 joints), participant's global assessment of disease activity (visual analog scale: 0 = no disease activity to 100 = maximum disease activity) and C-Reactive Protein (CRP) for a total possible score of 1 to 9.4.			
Units: units on a scale arithmetic mean	5.78	5.65	6.09

standard deviation	± 0.691	± 0.941	± 1.112
Health Assessment Questionnaire Disease Index (HAQ-DI)			
The Health Assessment Questionnaire – Disability Index (HAQ-DI) is a self-reported tool used to assess the ability to perform tasks in 8 functional categories: dressing and grooming, arising, eating, walking, hygiene, reach, grip, and common daily activities. Responses in each functional category were collected as 0 (without any difficulty) to 3 (unable to do a task in that area). The HAQ-DI score ranges from 0 (no disability) to 3 (completely disabled), when 6 or more categories are non-missing.			
Units: units on a scale			
arithmetic mean	1.38	1.47	1.61
standard deviation	± 0.650	± 0.425	± 0.591

Reporting group values	Placebo	Total	
Number of subjects	22	83	
Age categorical			
Units: Subjects			

Age continuous			
Units: years			
arithmetic mean	54		
standard deviation	± 10.9	-	
Gender categorical			
Units: Subjects			
Female	21	69	
Male	1	14	
Race			
Units: Subjects			
American Indian or Alaska Native	0	1	
Asian	1	1	
Native Hawaiian or Other Pacific Islander	0	0	
Black or African American	2	4	
White	19	77	
Ethnicity			
Units: Subjects			
Hispanic or Latino	0	4	
Not Hispanic or Latino	22	79	
Disease Activity Score 28 C- Reactive Protein (DAS28 CRP)			
Disease Activity Score 28 C-Reactive Protein (DAS28 (CRP)) is a measure of the participant's disease activity calculated using the tender joint counts (28 joints), swollen joint counts (28 joints), participant's global assessment of disease activity (visual analog scale: 0 = no disease activity to 100 = maximum disease activity) and C-Reactive Protein (CRP) for a total possible score of 1 to 9.4.			
Units: units on a scale			
arithmetic mean	5.51		
standard deviation	± 1.003	-	
Health Assessment Questionnaire Disease Index (HAQ-DI)			
The Health Assessment Questionnaire – Disability Index (HAQ-DI) is a self-reported tool used to assess the ability to perform tasks in 8 functional categories: dressing and grooming, arising, eating, walking, hygiene, reach, grip, and common daily activities. Responses in each functional category were collected as 0 (without any difficulty) to 3 (unable to do a task in that area). The HAQ-DI score ranges from 0 (no disability) to 3 (completely disabled), when 6 or more categories are non-missing.			
Units: units on a scale			
arithmetic mean	1.51		
standard deviation	± 0.577	-	

End points

End points reporting groups

Reporting group title	GS-9876 30 mg
Reporting group description: GS-9876 30 mg + filgotinib placebo for 12 weeks	
Reporting group title	GS-9876 10 mg
Reporting group description: GS-9876 10 mg + filgotinib placebo for 12 weeks	
Reporting group title	Filgotinib
Reporting group description: Filgotinib + GS-9876 placebo for 12 weeks	
Reporting group title	Placebo
Reporting group description: GS-9876 placebo + filgotinib placebo for 12 weeks	

Primary: Change From Baseline in Disease Activity Score 28 C-Reactive Protein (DAS28 (CRP)) at Week 12

End point title	Change From Baseline in Disease Activity Score 28 C-Reactive Protein (DAS28 (CRP)) at Week 12
End point description: Disease Activity Score 28 C-Reactive Protein (DAS28 (CRP)) is a measure of the participant's disease activity calculated using the tender joint counts (28 joints), swollen joint counts (28 joints), participant's global assessment of disease activity (visual analog scale: 0 = no disease activity to 100 = maximum disease activity) and C-Reactive Protein (CRP) for a total possible score of 1 to 9.4. Higher values indicate higher disease activity. A negative change from baseline indicates improvement. Participants in the Full Analysis Set (participants who received at least 1 dose of study drug) with available data were analyzed.	
End point type	Primary
End point timeframe: Baseline; Week 12	

End point values	GS-9876 30 mg	GS-9876 10 mg	Filgotinib	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	20	17	21	19
Units: units on a scale				
arithmetic mean (standard deviation)	-1.26 (± 1.276)	-0.78 (± 1.119)	-2.46 (± 1.242)	-1.36 (± 1.044)

Statistical analyses

Statistical analysis title	GS-9876 30 mg vs. Placebo
Comparison groups	GS-9876 30 mg v Placebo

Number of subjects included in analysis	39
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.978
Method	Cochran-Mantel-Haenszel
Parameter estimate	Least Squares (LS) Means of Differences
Point estimate	0.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.74
upper limit	0.76

Statistical analysis title	GS-9876 10 mg vs. Placebo
Comparison groups	GS-9876 10 mg v Placebo
Number of subjects included in analysis	36
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3
Method	Cochran-Mantel-Haenszel
Parameter estimate	LS Means of Differences
Point estimate	0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.36
upper limit	1.16

Statistical analysis title	Filgotinib vs. Placebo
Comparison groups	Filgotinib v Placebo
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.002
Method	Cochran-Mantel-Haenszel
Parameter estimate	LS Means of Differences]
Point estimate	-1.18
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.92
upper limit	-0.43

Secondary: Percentage of Participants Who Achieved American College of

Rheumatology (ACR)20 Improvement at Week 12

End point title	Percentage of Participants Who Achieved American College of Rheumatology (ACR)20 Improvement at Week 12
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End point description:

American College of Rheumatology (ACR)20 response was defined as having $\geq 20\%$ improvement from baseline in the number of tender and the number of swollen joints, and a 20% improvement in at least 3 of the following 5 criteria: Physician's Global Assessment of Disease Activity (PhGA), Participant's Global Assessment of Disease Activity (PtGA), Participant's pain assessment, Participant's assessment of physical function (HAQ-DI) score, and C-reactive protein (CRP). Participants in the Full Analysis Set were analyzed.

End point type	Secondary
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End point timeframe:

Week 12

End point values	GS-9876 30 mg	GS-9876 10 mg	Filgotinib	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	20	20	21	22
Units: percentage of participants				
number (not applicable)	35.0	25.0	81.0	40.9

Statistical analyses

Statistical analysis title	GS-9876 30 mg vs. Placebo
Comparison groups	GS-9876 30 mg v Placebo
Number of subjects included in analysis	42
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.66
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in Response Rates
Point estimate	-5.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-36
upper limit	24

Statistical analysis title	GS-9876 10 mg vs. Placebo
Comparison groups	GS-9876 10 mg v Placebo

Number of subjects included in analysis	42
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.277
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in Response Rates
Point estimate	-15.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-44.7
upper limit	13.8

Statistical analysis title	Filgotinib vs. Placebo
Comparison groups	Filgotinib v Placebo
Number of subjects included in analysis	43
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.009
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in Response Rates
Point estimate	40
Confidence interval	
level	95 %
sides	2-sided
lower limit	10.7
upper limit	65.6

Secondary: Percentage of Participants Who Achieved ACR50 Improvement at Week 12

End point title	Percentage of Participants Who Achieved ACR50 Improvement at Week 12
End point description:	
ACR50 response was defined as having $\geq 50\%$ improvement from baseline in the number of tender and the number of swollen joints, and a 50% improvement in at least 3 of the following 5 criteria: PhGA, PtGA, Participant's pain assessment, HAQ-DI score, and CRP. Participants in the Full Analysis Set were analyzed.	
End point type	Secondary
End point timeframe:	
Week 12	

End point values	GS-9876 30 mg	GS-9876 10 mg	Filgotinib	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	20	20	21	22
Units: percentage of participants				
number (not applicable)	20.0	20.0	47.6	22.7

Statistical analyses

Statistical analysis title	Gs-9876 30 mg vs. Placebo
Comparison groups	GS-9876 30 mg v Placebo
Number of subjects included in analysis	42
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.853
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in Response Rates
Point estimate	-2.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-32
upper limit	27.5

Statistical analysis title	GS-9876 10 mg vs. Placebo
Comparison groups	Placebo v GS-9876 10 mg
Number of subjects included in analysis	42
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.852
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in Response Rates
Point estimate	-2.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-32
upper limit	27.5

Statistical analysis title	Filgotinib vs. Placebo
Comparison groups	Filgotinib v Placebo

Number of subjects included in analysis	43
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.092
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in Response Rates
Point estimate	24.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.6
upper limit	51.5

Secondary: Percentage of Participants Who Achieved ACR70 Improvement at Week 12

End point title	Percentage of Participants Who Achieved ACR70 Improvement at Week 12
End point description:	
ACR70 response was defined as having $\geq 70\%$ improvement from baseline in the number of tender and the number of swollen joints, and a 70% improvement in at least 3 of the following 5 criteria: PhGA, PtGA, Participant's pain assessment, HAQ-DI score, and CRP. Participants in the Full Analysis Set were analyzed.	
End point type	Secondary
End point timeframe:	
Week 12	

End point values	GS-9876 30 mg	GS-9876 10 mg	Filgotinib	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	20	20	21	22
Units: percentage of participants				
number (not applicable)	5.0	15.0	38.1	13.6

Statistical analyses

Statistical analysis title	GS-9876 30 mg vs. Placebo
Comparison groups	GS-9876 30 mg v Placebo
Number of subjects included in analysis	42
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.36
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in Response Rates
Point estimate	-8.6

Confidence interval	
level	95 %
sides	2-sided
lower limit	-37.9
upper limit	22.5

Statistical analysis title	GS-9876 10 mg va. Placebo
Comparison groups	GS-9876 10 mg v Placebo
Number of subjects included in analysis	42
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.896
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in Response Rates
Point estimate	1.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-28
upper limit	31.7

Statistical analysis title	Filgotinib vs. Placebo
Comparison groups	Filgotinib v Placebo
Number of subjects included in analysis	43
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.072
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in Response Rates
Point estimate	24.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.6
upper limit	50.1

Secondary: Change From Baseline in The Health Assessment Questionnaire - Disability Index (HAQ-DI) Score at Week 12

End point title	Change From Baseline in The Health Assessment Questionnaire - Disability Index (HAQ-DI) Score at Week 12
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End point description:

The Health Assessment Questionnaire – Disability Index (HAQ-DI) is a self-reported tool used to assess the ability to perform tasks in 8 functional categories: dressing and grooming, arising, eating, walking, hygiene, reach, grip, and other activities. Responses in each functional category were collected as 0 (without any difficulty) to 3 (unable to do a task in that area). The HAQ-DI score ranges from 0 (no

disability) to 3 (completely disabled), when 6 or more categories are non-missing. Participants in the Full Analysis Set with available data were analyzed.

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

End point values	GS-9876 30 mg	GS-9876 10 mg	Filgotinib	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	20	19	21	19
Units: units on a scale				
arithmetic mean (standard deviation)	-0.46 (± 0.480)	-0.18 (± 0.800)	-0.70 (± 0.649)	-0.39 (± 0.389)

Statistical analyses

Statistical analysis title	GS-9876 30 mg vs. Placebo
Comparison groups	GS-9876 30 mg v Placebo
Number of subjects included in analysis	39
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.528
Method	Cochran-Mantel-Haenszel
Parameter estimate	LS Means of Differences
Point estimate	-0.12
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.49
upper limit	0.25

Statistical analysis title	GS9876 10 mg vs. Placebo
Comparison groups	GS-9876 10 mg v Placebo
Number of subjects included in analysis	38
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.293
Method	Cochran-Mantel-Haenszel
Parameter estimate	LS Means of Differences
Point estimate	0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.17
upper limit	0.57

Statistical analysis title	Filfotinib vs. Placebo
Comparison groups	Filgotinib v Placebo
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.072
Method	Cochran-Mantel-Haenszel
Parameter estimate	LS Means of Differences
Point estimate	-0.33
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.7
upper limit	0.03

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to 12 weeks + 30 days

Adverse event reporting additional description:

Safety Analysis Set: participants who received at least 1 dose of study drug.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	20.0
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Reporting groups

Reporting group title	GS-9876 30 mg
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Reporting group description:

GS-9876 30 mg tablet orally once daily + filgotinib placebo 2 tablets orally once daily for 12 weeks and background therapy with methotrexate orally or parenterally once weekly

Reporting group title	GS-9876 10 mg
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Reporting group description:

GS-9876 10 mg tablet orally once daily + filgotinib placebo 2 tablets orally once daily for 12 weeks and background therapy with methotrexate orally or parenterally once weekly

Reporting group title	Filgotinib
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Reporting group description:

Filgotinib 2 x 100 mg tablets orally once daily + GS-9876 placebo tablet orally once daily for 12 weeks and background therapy with methotrexate orally or parenterally once weekly

Reporting group title	Placebo
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Reporting group description:

GS-9876 placebo tablet orally once daily + filgotinib placebo 2 tablets orally once daily for 12 weeks and background therapy with methotrexate orally or parenterally once weekly

Serious adverse events	GS-9876 30 mg	GS-9876 10 mg	Filgotinib
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	0 / 21 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			

Serious adverse events	Placebo		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 22 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			

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

Non-serious adverse events	GS-9876 30 mg	GS-9876 10 mg	Filgotinib
Total subjects affected by non-serious adverse events			
subjects affected / exposed	7 / 20 (35.00%)	8 / 20 (40.00%)	4 / 21 (19.05%)
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	0 / 21 (0.00%)
occurrences (all)	1	0	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	2 / 21 (9.52%)
occurrences (all)	0	0	2
Condition aggravated			
subjects affected / exposed	0 / 20 (0.00%)	2 / 20 (10.00%)	0 / 21 (0.00%)
occurrences (all)	0	2	0
Oedema peripheral			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	0 / 21 (0.00%)
occurrences (all)	1	0	0
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	0 / 21 (0.00%)
occurrences (all)	1	0	0
Psychiatric disorders			
Depression			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	0 / 21 (0.00%)
occurrences (all)	1	0	0
Investigations			
Blood creatine phosphokinase increased			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	1 / 21 (4.76%)
occurrences (all)	1	0	1
Blood pressure increased			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	0 / 21 (0.00%)
occurrences (all)	1	0	0
Liver function test increased			

subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1	0 / 20 (0.00%) 0	0 / 21 (0.00%) 0
Cardiac disorders Angina unstable subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1	0 / 20 (0.00%) 0	0 / 21 (0.00%) 0
Nervous system disorders Amnesia subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1	0 / 20 (0.00%) 0	0 / 21 (0.00%) 0
Blood and lymphatic system disorders Lymphopenia subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	1 / 20 (5.00%) 1	0 / 21 (0.00%) 0
Ear and labyrinth disorders Meniere's disease subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	1 / 20 (5.00%) 1	0 / 21 (0.00%) 0
Eye disorders Hypermetropia subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1	0 / 20 (0.00%) 0	0 / 21 (0.00%) 0
Gastrointestinal disorders Dyspepsia subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	2 / 20 (10.00%) 2	1 / 21 (4.76%) 1
Epigastric discomfort subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1	0 / 20 (0.00%) 0	0 / 21 (0.00%) 0
Abdominal discomfort subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	1 / 20 (5.00%) 1	0 / 21 (0.00%) 0
Nausea subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	1 / 20 (5.00%) 1	0 / 21 (0.00%) 0
Skin and subcutaneous tissue disorders			

Rash subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1	0 / 20 (0.00%) 0	0 / 21 (0.00%) 0
Renal and urinary disorders Haematuria subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	1 / 20 (5.00%) 1	0 / 21 (0.00%) 0
Endocrine disorders Hypothyroidism subjects affected / exposed occurrences (all)	2 / 20 (10.00%) 2	0 / 20 (0.00%) 0	0 / 21 (0.00%) 0
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1	0 / 20 (0.00%) 0	0 / 21 (0.00%) 0
Muscular weakness subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1	0 / 20 (0.00%) 0	0 / 21 (0.00%) 0
Spinal osteoarthritis subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	1 / 20 (5.00%) 1	0 / 21 (0.00%) 0
Infections and infestations Urinary tract infection subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	1 / 20 (5.00%) 1	0 / 21 (0.00%) 0

Non-serious adverse events	Placebo		
Total subjects affected by non-serious adverse events subjects affected / exposed	1 / 22 (4.55%)		
Vascular disorders Hypertension subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0		
General disorders and administration site conditions Asthenia subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0		

Condition aggravated subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0		
Oedema peripheral subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0		
Respiratory, thoracic and mediastinal disorders Oropharyngeal pain subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0		
Psychiatric disorders Depression subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0		
Investigations Blood creatine phosphokinase increased subjects affected / exposed occurrences (all) Blood pressure increased subjects affected / exposed occurrences (all) Liver function test increased subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0 0 / 22 (0.00%) 0 0 / 22 (0.00%) 0		
Cardiac disorders Angina unstable subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0		
Nervous system disorders Amnesia subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0		
Blood and lymphatic system disorders Lymphopenia subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0		
Ear and labyrinth disorders			

Meniere's disease subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0		
Eye disorders Hypermetropia subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0		
Gastrointestinal disorders Dyspepsia subjects affected / exposed occurrences (all) Epigastric discomfort subjects affected / exposed occurrences (all) Abdominal discomfort subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0 1 / 22 (4.55%) 1 0 / 22 (0.00%) 0 0 / 22 (0.00%) 0		
Skin and subcutaneous tissue disorders Rash subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0		
Renal and urinary disorders Haematuria subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0		
Endocrine disorders Hypothyroidism subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0		
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) Muscular weakness	0 / 22 (0.00%) 0		

subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
Spinal osteoarthritis			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
27 June 2016	<ul style="list-style-type: none">• Addition of filgotinib treatment arm for exploratory objectives• Other changes to correct discrepancies between different sections of the protocol and/or to provide further clarification

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: