



Clinical trial results:

A Phase 2b Randomized, Double-blind, Multicenter, Placebo controlled, Parallel-group, Dose Range Finding Study of JNJ-38518168 in Participants with Active Rheumatoid Arthritis Despite Concomitant Methotrexate Therapy

Due to a system error, the data reported in v1 is not correct and has been removed from public view.

Summary

EudraCT number	2011-002840-29
Trial protocol	HU CZ LV RO
Global end of trial date	03 July 2014

Results information

Result version number	v2 (current)
This version publication date	15 July 2016
First version publication date	16 August 2015
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	38518168ARA2002
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01679951
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Janssen-Cilag International NV
Sponsor organisation address	Antwerpseweg 15-17, Beerse, Belgium, B-2340
Public contact	Clinical Registry Group, Janssen Research and Development, ClinicalTrialsEU@its.jnj.com
Scientific contact	Clinical Registry Group, Janssen Research and Development, ClinicalTrialsEU@its.jnj.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	03 July 2014
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	03 July 2014
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The primary objective is to assess the efficacy {as measured by the reduction of the signs and symptoms of rheumatoid arthritis (RA)} of JNJ-38518168 at doses of 3, 10, and 30 milligram/day (mg/d) compared with placebo in subjects with active RA despite concomitant methotrexate (MTX) therapy.

Protection of trial subjects:

Safety assessments include vital signs, general physical examination, adverse events, concomitant medication review, electrocardiograms (ECGs), pregnancy testing, routine laboratory testing, ferritin test, and fasting lipid measurements.

Background therapy:

Stable dose of MTX.

Evidence for comparator: -

Actual start date of recruitment	31 October 2012
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Argentina: 4
Country: Number of subjects enrolled	Chile: 13
Country: Number of subjects enrolled	Colombia: 20
Country: Number of subjects enrolled	Czech Republic: 11
Country: Number of subjects enrolled	Hungary: 25
Country: Number of subjects enrolled	Japan: 31
Country: Number of subjects enrolled	Latvia: 13
Country: Number of subjects enrolled	Mexico: 42
Country: Number of subjects enrolled	Poland: 23
Country: Number of subjects enrolled	Romania: 2
Country: Number of subjects enrolled	Russian Federation: 42
Country: Number of subjects enrolled	Thailand: 16
Country: Number of subjects enrolled	Taiwan: 1
Country: Number of subjects enrolled	Ukraine: 19
Country: Number of subjects enrolled	United States: 10
Worldwide total number of subjects	272
EEA total number of subjects	74

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)	236
From 65 to 84 years	36
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted from 31 October 2012 to 03 July 2014.

Pre-assignment

Screening details:

A total of 649 participants were screened, of which, 272 subjects were randomized.

Period 1

Period 1 title	24 weeks Placebo Controlled Period (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	Placebo

Arm description:

Daily Placebo from Week 0 to Week 24 (unless early escape at week 16); if early escape, 30 mg/day JNJ-38518168 from Week 16 up to Week 24.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Participants administered with two placebo tablets, one matching the 3 and 10 mg size, one matching the 30 mg size, daily with or without food.

Arm title	JNJ-38518168 3 mg
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Arm description:

JNJ-38518168 3 mg/day from Week 0 to Week 24 (unless early escape at week 16); if early escape, 30 mg/day JNJ-38518168 from Week 16 up to Week 24.

Arm type	Experimental
Investigational medicinal product name	JNJ-38518168 3 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Participants administered with one JNJ-38518168 3 mg tablet and one placebo tablet daily with or without food.

Arm title	JNJ-38518168 10 mg
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Arm description:

JNJ-38518168 10 mg/day from Week 0 to Week 24 (unless early escape at week 16); if early escape, 30 mg/day JNJ-38518168 from Week 16 up to Week 24.

Arm type	Experimental
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Investigational medicinal product name	JNJ-38518168 10 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Participant administered with one JNJ-38518168 10 mg tablet and one placebo tablet daily with or without food.

Arm title	JNJ-38518168 30 mg
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Arm description:

JNJ-38518168 30 mg/day from Week 0 to Week 24.

Arm type	Experimental
Investigational medicinal product name	JNJ-38518168 30 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Participants administered with one JNJ-38518168 30 mg tablet, one placebo tablet daily with or without food.

Number of subjects in period 1	Placebo	JNJ-38518168 3 mg	JNJ-38518168 10 mg
Started	68	68	68
Completed	57	50	57
Not completed	11	18	11
Consent withdrawn by subject	-	2	-
Physician decision	-	-	-
Adverse event, non-fatal	5	7	3
Other	4	6	5
Lost to follow-up	-	-	-
Lack of efficacy	2	3	3

Number of subjects in period 1	JNJ-38518168 30 mg
Started	68
Completed	53
Not completed	15
Consent withdrawn by subject	2
Physician decision	1
Adverse event, non-fatal	3
Other	3
Lost to follow-up	1
Lack of efficacy	5

Baseline characteristics

Reporting groups

Reporting group title	Placebo
Reporting group description: Daily Placebo from Week 0 to Week 24 (unless early escape at week 16); if early escape, 30 mg/day JNJ-38518168 from Week 16 up to Week 24.	
Reporting group title	JNJ-38518168 3 mg
Reporting group description: JNJ-38518168 3 mg/day from Week 0 to Week 24 (unless early escape at week 16); if early escape, 30 mg/day JNJ-38518168 from Week 16 up to Week 24.	
Reporting group title	JNJ-38518168 10 mg
Reporting group description: JNJ-38518168 10 mg/day from Week 0 to Week 24 (unless early escape at week 16); if early escape, 30 mg/day JNJ-38518168 from Week 16 up to Week 24.	
Reporting group title	JNJ-38518168 30 mg
Reporting group description: JNJ-38518168 30 mg/day from Week 0 to Week 24.	

Reporting group values	Placebo	JNJ-38518168 3 mg	JNJ-38518168 10 mg
Number of subjects	68	68	68
Title for AgeCategorical Units: subjects			
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	62	59	60
From 65 to 84 years	6	9	8
85 years and over	0	0	0
Title for AgeContinuous Units: Years			
arithmetic mean	51.5	52.8	49.5
standard deviation	± 11.44	± 11.39	± 13.24
Title for Gender Units: subjects			
Female	57	60	52
Male	11	8	16

Reporting group values	JNJ-38518168 30 mg	Total	
Number of subjects	68	272	
Title for AgeCategorical Units: subjects			
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	55	236	
From 65 to 84 years	13	36	
85 years and over	0	0	
Title for AgeContinuous Units: Years			
arithmetic mean	53.8		

standard deviation	± 12.55	-	
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Title for Gender			
Units: subjects			
Female	51	220	
Male	17	52	

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description: Daily Placebo from Week 0 to Week 24 (unless early escape at week 16); if early escape, 30 mg/day JNJ-38518168 from Week 16 up to Week 24.	
Reporting group title	JNJ-38518168 3 mg
Reporting group description: JNJ-38518168 3 mg/day from Week 0 to Week 24 (unless early escape at week 16); if early escape, 30 mg/day JNJ-38518168 from Week 16 up to Week 24.	
Reporting group title	JNJ-38518168 10 mg
Reporting group description: JNJ-38518168 10 mg/day from Week 0 to Week 24 (unless early escape at week 16); if early escape, 30 mg/day JNJ-38518168 from Week 16 up to Week 24.	
Reporting group title	JNJ-38518168 30 mg
Reporting group description: JNJ-38518168 30 mg/day from Week 0 to Week 24.	
Subject analysis set title	Modified intent to treat (m-ITT) population
Subject analysis set type	Modified intention-to-treat
Subject analysis set description: Modified intent-to-treat (m-ITT) population included all the randomized participants who received at least 1 dose of study drug.	

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

End point title	Change From Baseline in Disease Activity Index Score (DAS28) Using C-Reactive Protein (CRP) at Week 12
End point description: The Disease Activity Index Score (DAS28) based on C-Reactive Protein (CRP) is a statistically derived index combining tender joints (28 joints), swollen joints (28 joints), CRP (mg/L) and participant's global assessment of disease activity (participant rated arthritis activity assessment with transformed scores ranging 0 to 100 mm; higher scores indicated greater affectation due to disease activity). The set of 28 joint count is based on evaluation of the shoulder, elbow, wrist, metacarpophalangeal (MCP) MCP1 to MCP5, proximal interphalangeal (PIP) PIP1 to PIP5 joints of both the upper right extremity and the upper left extremity as well as the knee joints of lower right and lower left extremities. Modified intent-to-treat (m-ITT) population included all the randomized participants who received at least 1 dose of study drug.	
End point type	Primary
End point timeframe: Week 12	

End point values	Placebo	JNJ-38518168 3 mg	JNJ-38518168 10 mg	JNJ-38518168 30 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	67	67	68	66
Units: Units on a scale				
arithmetic mean (standard deviation)	-1.346 (± 1.45853)	-1.2108 (± 1.03667)	-1.0509 (± 1.24138)	-1.2933 (± 1.20112)

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	JNJ-38518168 3 mg v Placebo
Number of subjects included in analysis	134
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.537
Method	ANOVA

Statistical analysis title	Statistical analysis 2
Comparison groups	JNJ-38518168 10 mg v Placebo
Number of subjects included in analysis	135
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.207
Method	ANOVA

Statistical analysis title	Statistical Analysis 3
Comparison groups	JNJ-38518168 30 mg v Placebo
Number of subjects included in analysis	133
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.82
Method	ANCOVA

Secondary: Change From Baseline in Disease Activity Index Score (DAS28) Using C-Reactive Protein (CRP) at Week 24

End point title	Change From Baseline in Disease Activity Index Score (DAS28) Using C-Reactive Protein (CRP) at Week 24
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End point description:

The Disease Activity Index Score (DAS28) based on C-Reactive Protein (CRP) is a statistically derived index combining tender joints (28 joints), swollen joints (28 joints), CRP (mg/L) and participant's global assessment of disease activity (participant rated arthritis activity assessment with transformed scores ranging 0 to 100 mm; higher scores indicated greater affectation due to disease activity). The set of 28 joint count is based on evaluation of the shoulder, elbow, wrist, metacarpophalangeal (MCP) MCP1 to MCP5, proximal interphalangeal (PIP) PIP1 to PIP5 joints of both the upper right extremity and the upper left extremity as well as the knee joints of lower right and lower left extremities. Modified intent-to-treat (m-ITT) population included all the randomized participants who received at least 1 dose of study drug.

End point type	Secondary
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End point timeframe:

Week 24

End point values	Placebo	JNJ-38518168 3 mg	JNJ-38518168 10 mg	JNJ-38518168 30 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	64	62	64	63
Units: Units on a scale				
arithmetic mean (standard deviation)	-1.4856 (\pm 1.37984)	-1.3912 (\pm 1.26788)	-1.2642 (\pm 1.32334)	-1.3581 (\pm 1.30176)

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	JNJ-38518168 3 mg v Placebo
Number of subjects included in analysis	126
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.69
Method	ANCOVA

Statistical analysis title	Statistical Analysis 2
Comparison groups	JNJ-38518168 10 mg v Placebo
Number of subjects included in analysis	128
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.356
Method	ANCOVA

Statistical analysis title	Statistical Analysis 3
Comparison groups	JNJ-38518168 30 mg v Placebo
Number of subjects included in analysis	127
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.593
Method	ANCOVA

Secondary: Change from baseline in DAS28 (using Erythrocyte Sedimentation Rate [ESR]) at Week 12 and Week 24

End point title	Change from baseline in DAS28 (using Erythrocyte Sedimentation Rate [ESR]) at Week 12 and Week 24
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End point description:

The Disease Activity Index Score (DAS28) based on ESR is a statistically derived index combining tender joints (28 joints), swollen joints (28 joints), ESR (mm/hour) and participant's global assessment of disease activity (participant rated arthritis activity assessment with transformed scores ranging 0 to 100 mm; higher scores indicated greater affectation due to disease activity). The set of 28 joint count is based on evaluation of the shoulder, elbow, wrist, metacarpophalangeal (MCP) MCP1 to MCP5, proximal

interphalangeal (PIP) PIP1 to PIP5 joints of both the upper right extremity and the upper left extremity as well as the knee joints of lower right and lower left extremities. The m-ITT population included all the randomized participants who received at least 1 dose of study drug. Here, 'N' (number of participants analyzed) signifies those participants who were evaluated for this measure & 'n' signifies those participants who were evaluated for this measure at given time points.

End point type	Secondary
End point timeframe:	
Week 12 and Week 24	

End point values	Placebo	JNJ-38518168 3 mg	JNJ-38518168 10 mg	JNJ-38518168 30 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	68	67	68	68
Units: Unit on a scale				
least squares mean (standard error)				
Change at Week 12 (n=66, 65, 66, 63)	-1.4075 (± 0.14945)	-1.2149 (± 0.15092)	-1.205 (± 0.15018)	-1.3545 (± 0.15341)
Change at Week 24 (n=63, 60, 62, 61)	-1.6447 (± 0.16111)	-1.567 (± 0.1655)	-1.5501 (± 0.16369)	-1.5638 (± 0.16431)

Statistical analyses

No statistical analyses for this end point

Secondary: DAS28 (using CRP) response rates at Week 12 and Week 24

End point title	DAS28 (using CRP) response rates at Week 12 and Week 24
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End point description:

The Disease Activity Index Score (DAS28) response using C-Reactive Protein (CRP) is a statistically derived index based on both DAS28 score at the visit and improvement from baseline. When DAS28 is ≤ 3.2 and improvement is > 1.2 , it is considered as "good response". A "moderate" response is defined as improvement > 1.2 or improvement is between 0.6 to 1.2 but DAS28 score is < 5.1 . Otherwise, it is considered as "no response". The m-ITT population included all the randomized participants who received at least 1 dose of study drug. Here, 'N' (number of participants analyzed) signifies those participants who were evaluable for this measure & 'n' signifies those participants who were evaluable for this measure at given time points.

End point type	Secondary
End point timeframe:	
Week 12 and Week 24	

End point values	Placebo	JNJ-38518168 3 mg	JNJ-38518168 10 mg	JNJ-38518168 30 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	68	67	68	68
Units: percentage of participants				
number (not applicable)				
Week 12 (n=67, 67, 68, 66)	56.7	61.2	52.9	66.7
Week 24 (n=64, 62, 64, 63)	67.2	58.1	62.5	58.7

Statistical analyses

No statistical analyses for this end point

Secondary: DAS28 (using ESR) response rates at Week 12 and Week 24

End point title	DAS28 (using ESR) response rates at Week 12 and Week 24
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End point description:

The Disease Activity Index Score (DAS28) response using ESR is a statistically derived index based on both DAS28 score at the visit and improvement from baseline. When DAS28 is ≤ 3.2 and improvement is > 1.2 , it is considered as "good response". A "moderate" response is defined as improvement > 1.2 or improvement is between 0.6 to 1.2 but DAS28 score is < 5.1 . Otherwise, it is considered as "no response". The m-ITT population included all the randomized participants who received at least 1 dose of study drug. Here, 'N' (number of participants analyzed) signifies those participants who were evaluable for this measure & 'n' signifies those participants who were evaluable for this measure at given time points.

End point type	Secondary
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End point timeframe:

Week 12 and Week 24

End point values	Placebo	JNJ-38518168 3 mg	JNJ-38518168 10 mg	JNJ-38518168 30 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	68	67	68	68
Units: Percentage of participants				
number (not applicable)				
Week 12 (n=66, 65, 66, 63)	53	49.2	57.6	63.5
Week 24 (n=63, 60, 62, 61)	66.7	61.7	67.7	60.7

Statistical analyses

No statistical analyses for this end point

Secondary: DAS28 (using CRP) remission rates at Week 12 and Week 24

End point title	DAS28 (using CRP) remission rates at Week 12 and Week 24
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End point description:

DAS28 remission is defined as a DAS28 value of < 2.6 at a visit. The m-ITT population included all the randomized participants who received at least 1 dose of study drug. Here, 'N' (number of participants analyzed) signifies those participants who were evaluable for this measure & 'n' signifies those participants who were evaluable for this measure at given time points.

End point type	Secondary
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End point timeframe:

Week 12 and Week 24

End point values	Placebo	JNJ-38518168 3 mg	JNJ-38518168 10 mg	JNJ-38518168 30 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	68	67	68	68
Units: percentage of participants				
number (not applicable)				
Week 12 (n=68, 67, 68, 68)	5.9	11.9	10.3	5.9
Week 24 (n=64, 62, 64, 65)	7.8	9.7	12.5	10.8

Statistical analyses

No statistical analyses for this end point

Secondary: DAS28 (using ESR) remission rates at Week 12 and Week 24

End point title	DAS28 (using ESR) remission rates at Week 12 and Week 24
End point description:	
DAS28 remission is defined as a DAS28 value of < 2.6 at a visit. The m-ITT population included all the randomized participants who received at least 1 dose of study drug. Here, 'N' (number of participants analyzed) signifies those participants who were evaluable for this measure & 'n' signifies those participants who were evaluable for this measure at given time points.	
End point type	Secondary
End point timeframe:	
Week 12 and Week 24	

End point values	Placebo	JNJ-38518168 3 mg	JNJ-38518168 10 mg	JNJ-38518168 30 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	68	67	68	68
Units: percentage of participants				
number (not applicable)				
Week 12 (n=68, 67, 68, 67)	4.4	4.5	4.4	1.5
Week 24 (n=64, 62, 64, 64)	4.7	6.5	7.8	3.1

Statistical analyses

No statistical analyses for this end point

Secondary: American College of Rheumatology (ACR) 20/50/70 response rates at Week 12 and Week 24

End point title	American College of Rheumatology (ACR) 20/50/70 response rates at Week 12 and Week 24
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End point description:

An ACR 20/50/70 response is defined as a greater than or equal to 20/50/70 percentage improvement from baseline in: 1. Swollen joint count (66 joints) and tender joint count (68 joints) 2. greater than or equal to 20/50/70 percentage improvement in 3 of the following 5 assessments: a. Patient's assessment of pain (VAS) (0-10 cm) b. Patient's Global Assessment of Disease activity (VAS) (0-10 cm) c. Physician's Global Assessment of Disease Activity (VAS) (0-10 cm) d. Patient's assessment of physical function as measured by the Health Assessment Questionnaire (HAQ) e. C- reactive protein (CRP). The m-ITT population included all the randomized participants who received at least 1 dose of study drug. Here, 'N' (number of participants analyzed) signifies those participants who were evaluable for this measure & 'n' signifies those participants who were evaluable for this measure at given time points.

End point type	Secondary
End point timeframe:	
Week 12 and Week 24	

End point values	Placebo	JNJ-38518168 3 mg	JNJ-38518168 10 mg	JNJ-38518168 30 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	68	67	68	68
Units: percentage of participants				
number (not applicable)				
Week 12: ACR 20 (n=68, 67, 68, 68)	36.8	35.8	47.1	36.8
Week 12: ACR 50 (n=68, 67, 68, 68)	22.1	11.9	16.2	14.7
Week 12: ACR 70 (n=68, 67, 68, 68)	8.8	6	2.9	5.9
Week 24: ACR 20 (n=64, 62, 64, 65)	50	48.4	51.6	43.1
Week 24: ACR 50 (n=64, 62, 64, 65)	23.4	22.6	20.3	13.8
Week 24: ACR 70 (n=64, 62, 64, 65)	7.8	11.3	12.5	4.6

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description:	
Statistical analysis for Week 12: ACR 20	
Comparison groups	JNJ-38518168 3 mg v Placebo
Number of subjects included in analysis	135
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.909
Method	Cochran-Mantel-Haenszel

Statistical analysis title	Statistical Analysis 2
Statistical analysis description:	
Statistical analysis for Week 12: ACR 20	
Comparison groups	JNJ-38518168 10 mg v Placebo

Number of subjects included in analysis	136
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.224
Method	Cochran-Mantel-Haenszel

Statistical analysis title	Statistical Analysis 3
Statistical analysis description:	
Statistical analysis for Week 12: ACR 20	
Comparison groups	JNJ-38518168 30 mg v Placebo
Number of subjects included in analysis	136
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 1
Method	Cochran-Mantel-Haenszel

Secondary: Hybrid ACR response at Week 12 and Week 24

End point title	Hybrid ACR response at Week 12 and Week 24
End point description:	
The hybrid ACR response is a continuous variable of mean % change in ACR response measures that is limited to an overall score of -100 (maximal worsening) to +100 (maximal improvement) after taking into consideration of ACR20/50/70 response. The m-ITT population included all the randomized participants who received at least 1 dose of study drug. Here, 'N' (number of participants analyzed) signifies those participants who were evaluable for this measure & 'n' signifies those participants who were evaluable for this measure at given time points.	
End point type	Secondary
End point timeframe:	
Week 12 and Week 24	

End point values	Placebo	JNJ-38518168 3 mg	JNJ-38518168 10 mg	JNJ-38518168 30 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	68	67	68	68
Units: unit on a scale				
arithmetic mean (standard deviation)				
Week 12 (n=67, 60, 65, 64)	22.33 (± 32.341)	25.72 (± 25.824)	23.52 (± 30.933)	25.5 (± 27.57)
Week 24 (n=61, 53, 61, 57)	29.82 (± 29.112)	31.76 (± 33.49)	25.54 (± 35.877)	24.04 (± 31.905)

Statistical analyses

No statistical analyses for this end point

Secondary: ACR/European League Against Rheumatism (EULAR) remission rates at Week 12 and Week 24

End point title	ACR/European League Against Rheumatism (EULAR) remission rates at Week 12 and Week 24
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End point description:

ACR/EULAR remission is defined as scores on the tender joint count, swollen joint count, CRP (in mg/dL), and patient global assessment (0-10 scale) are all less than or equal to 1 . The m-ITT population included all the randomized participants who received at least 1 dose of study drug. Here, 'N' (number of participants analyzed) signifies those participants who were evaluable for this measure & 'n' signifies those participants who were evaluable for this measure at given time points.

End point type	Secondary
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End point timeframe:

Week 12 and Week 24

End point values	Placebo	JNJ-38518168 3 mg	JNJ-38518168 10 mg	JNJ-38518168 30 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	68	67	68	68
Units: percentage of participants				
number (not applicable)				
Week 12 (n=68, 67, 68, 68)	0	1.5	2.9	2.9
Week 12 (n=64, 62, 64, 65)	1.6	3.2	4.7	3.1

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in Simplified Disease Activity Index (SDAI) at Week 12 and Week 24

End point title	Change from baseline in Simplified Disease Activity Index (SDAI) at Week 12 and Week 24
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End point description:

The SDAI is the numerical sum of 5 outcome parameters: tender joint count (TJC) and swollen joint count (SJC) based on a 28-joint assessment, patient global assessment of disease activity (PGA VAS in cm), physician global assessment of disease activity (MDGA VAS in cm) and C-reactive protein (CRP in mg/dL). The m-ITT population included all the randomized participants who received at least 1 dose of study drug. Here, 'N' (number of participants analyzed) signifies those participants who were evaluable for this measure & 'n' signifies those participants who were evaluable for this measure at given time points.

End point type	Secondary
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End point timeframe:

Week 12 and Week 24

End point values	Placebo	JNJ-38518168 3 mg	JNJ-38518168 10 mg	JNJ-38518168 30 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	68	67	68	68
Units: units on a scale				
arithmetic mean (standard deviation)				
Week 12 (n=66, 65, 68, 62)	-18.0532 (± 18.07508)	-15.5735 (± 11.46746)	-13.5475 (± 13.89626)	-17.1179 (± 15.04138)
Week 24 (n=63, 60, 64, 59)	-19.0301 (± 16.63858)	-17.9037 (± 15.00419)	-15.4572 (± 15.4755)	-17.7375 (± 14.65954)

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in Clinical Disease Activity Index (CDAI) at Week 12 and Week 24

End point title	Change from baseline in Clinical Disease Activity Index (CDAI) at Week 12 and Week 24
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End point description:

The CDAI is the numerical sum of 4 outcome parameters: TJC and SJC based on a 28-joint assessment, PGA, and MDGA. The m-ITT population included all the randomized participants who received at least 1 dose of study drug. Here, 'N' (number of participants analyzed) signifies those participants who were evaluable for this measure & 'n' signifies those participants who were evaluable for this measure at given time points.

End point type	Secondary
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End point timeframe:

Week 12 and Week 24

End point values	Placebo	JNJ-38518168 3 mg	JNJ-38518168 10 mg	JNJ-38518168 30 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	68	67	68	68
Units: unit on a scale				
arithmetic mean (standard deviation)				
Week 12 (n=66, 65, 68, 62)	-17.84 (± 17.798)	-15.06 (± 11.485)	-13.31 (± 13.174)	-16.9 (± 14.61)
Week 24 (n=63, 60, 64, 59)	-18.78 (± 16.04)	-17.43 (± 14.511)	-15.36 (± 15.165)	-17.33 (± 14.177)

Statistical analyses

No statistical analyses for this end point

Secondary: Health Assessment Questionnaire - Disability Index (HAQ-DI) response rate at Week 12 and Week 24

End point title	Health Assessment Questionnaire - Disability Index (HAQ-DI) response rate at Week 12 and Week 24
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End point description:

The HAQ-DI is a 20-question instrument that assesses the degree of difficulty a person has in accomplishing tasks in 8 functional areas (dressing, arising, eating, walking, hygiene, reaching, gripping, and activities of daily living). Responses in each functional area are scored from 0 (no difficulty), to 3 (inability to perform a task in that area). HAQ responders are those subjects who achieve a > 0.22 improvement in HAQ from baseline. The m-ITT population included all the randomized participants who received at least 1 dose of study drug. Here, 'N' (number of participants analyzed) signifies those participants who were evaluable for this measure & 'n' signifies those participants who were evaluable for this measure at given time points.

End point type	Secondary
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End point timeframe:

Week 12 and Week 24

End point values	Placebo	JNJ-38518168 3 mg	JNJ-38518168 10 mg	JNJ-38518168 30 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	68	67	68	68
Units: Percentage of participants				
number (not applicable)				
Week 12 (n=67, 67, 68, 66)	53.7	49.3	52.9	60.6
Week 24 (n=64, 63, 64, 63)	62.5	57.1	57.8	49.2

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in HAQ-DI score at Week 12 and Week 24

End point title	Change from baseline in HAQ-DI score at Week 12 and Week 24
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End point description:

The HAQ-DI is a 20-question instrument that assesses the degree of difficulty a person has in accomplishing tasks in 8 functional areas (dressing, arising, eating, walking, hygiene, reaching, gripping, and activities of daily living). Responses in each functional area are scored from 0 (no difficulty), to 3 (inability to perform a task in that area). The m-ITT population included all the randomized participants who received at least 1 dose of study drug. Here, 'N' (number of participants analyzed) signifies those participants who were evaluable for this measure & 'n' signifies those participants who were evaluable for this measure at given time points.

End point type	Secondary
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End point timeframe:

Week 12 and Week 24

End point values	Placebo	JNJ-38518168 3 mg	JNJ-38518168 10 mg	JNJ-38518168 30 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	67	67	68	66
Units: unit on scale				
least squares mean (standard error)				

Week 12 (n=67, 67, 68, 66)	-0.2322 (± 0.06359)	-0.2338 (± 0.06352)	-0.2466 (± 0.06329)	-0.3674 (± 0.06424)
Week 24 (n=64, 63, 64, 63)	-0.2892 (± 0.06969)	-0.3167 (± 0.07043)	-0.2823 (± 0.07023)	-0.2516 (± 0.07068)

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description: Statistical analysis for Week 12	
Comparison groups	JNJ-38518168 3 mg v Placebo
Number of subjects included in analysis	134
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.988
Method	ANCOVA

Statistical analysis title	Statistical Analysis 2
Statistical analysis description: Statistical analysis for Week 12	
Comparison groups	JNJ-38518168 10 mg v Placebo
Number of subjects included in analysis	135
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.874
Method	ANCOVA

Statistical analysis title	Statistical Analysis 3
Statistical analysis description: Statistical analysis for Week 12	
Comparison groups	JNJ-38518168 30 mg v Placebo
Number of subjects included in analysis	133
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.136
Method	ANCOVA

Secondary: Percent change from baseline in ESR levels at Week 12 and Week 24

End point title	Percent change from baseline in ESR levels at Week 12 and Week 24
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End point description:

Erythrocyte sedimentation rate (ESR) is a lab test that measures overall inflammation level. The m-ITT population included all the randomized participants who received at least 1 dose of study drug. Here, 'N'

(number of participants analyzed) signifies those participants who were evaluable for this measure & 'n' signifies those participants who were evaluable for this measure at given time points.

End point type	Secondary
End point timeframe:	
Week 12 and Week 24	

End point values	Placebo	JNJ-38518168 3 mg	JNJ-38518168 10 mg	JNJ-38518168 30 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	68	67	68	68
Units: percent change				
arithmetic mean (standard deviation)				
Week 12 (n=67, 65, 66, 64)	-2.65 (± 61.922)	-0.51 (± 60.462)	-12.1 (± 42.836)	-15.11 (± 34.324)
Week 24 (n=63, 61, 62, 62)	-6.83 (± 61.901)	-16.98 (± 42.513)	-4.12 (± 111.822)	-12.37 (± 46.144)

Statistical analyses

No statistical analyses for this end point

Secondary: Percent change from baseline in ACR components at Week 12 and Week 24

End point title	Percent change from baseline in ACR components at Week 12 and Week 24
End point description:	
<p>The ACR components include tender (of 68 joints) and swollen (of 66 joints) joint counts, patient's assessment of pain (PAP) (0-10 cm VAS), patient's global assessment of disease activity (Patients GADA) (0-10 cm VAS), physician's global assessment of disease activity (Physicians GADA) (0-10 cm VAS), Health Assessment Questionnaire-Disability Index (HAQ-DI), and C-reactive protein (CRP). The m-ITT population included all the randomized participants who received at least 1 dose of study drug. Here, 'N' (number of participants analyzed) signifies those participants who were evaluable for this measure & 'n' signifies those participants who were evaluable for this measure at given time points.</p>	
End point type	Secondary
End point timeframe:	
Week 12 and Week 24	

End point values	Placebo	JNJ-38518168 3 mg	JNJ-38518168 10 mg	JNJ-38518168 30 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	68	67	68	68
Units: percent change				
arithmetic mean (standard deviation)				
W-12: Swollen Joints (n=68, 67, 68, 68)	-47.09 (± 41.962)	-42.61 (± 38.549)	-38.45 (± 42.792)	-49.16 (± 36.086)
W-24: Swollen Joints (n=64, 63, 64, 65)	-46.57 (± 46.368)	-47.18 (± 44.745)	-43.83 (± 50.12)	-49.19 (± 40.676)

W-12: Tender Joint (n=68, 67, 68, 68)	-42.01 (± 38.653)	-39.34 (± 40.908)	-34.08 (± 52.916)	-42.8 (± 46.532)
W-24: Tender Joint (n=64, 63, 64, 65)	-49.16 (± 37.893)	-43.63 (± 45.341)	-42.85 (± 57.755)	-37.6 (± 59.481)
W-12: PAP (67, 67,68,66)	-3.77 (± 69.675)	-20.87 (± 68.219)	-11.05 (± 90.822)	-14.34 (± 86.633)
W-24: PAP (64,63,64,63)	-18.68 (± 58.988)	-25.35 (± 62.807)	-12.09 (± 87.988)	-9.75 (± 84.198)
W-12: Patients-GADA (67, 67,68,66)	-6.83 (± 65.368)	5.34 (± 163.888)	-21.56 (± 41.004)	-24.48 (± 43.78)
W-24: Patients-GADA (64,63,64,63)	-19.22 (± 64.002)	1.64 (± 157.848)	-19.39 (± 52.087)	-19.42 (± 59.116)
W-12: Physicians-GADA (66, 65,68,62)	-35.76 (± 40.718)	-37.16 (± 37.12)	-38.5 (± 35.633)	-42.83 (± 34.837)
W-24: Physicians-GADA (63,61,64,59)	-38 (± 38.64)	-39.91 (± 40.962)	-39.91 (± 40.301)	-40.86 (± 39.112)
W-12: HAQ-DI (67,65,66,64)	-6.56 (± 53.466)	-9.1 (± 66.147)	-19.01 (± 39.831)	-21.13 (± 40.729)
W-24: HAQ-DI (64,61,62,61)	-6.23 (± 92.169)	-11.73 (± 100.462)	-18.22 (± 55.337)	-12.31 (± 47.954)
W-12: CRP (68,67,68,68)	89.62 (± 447.216)	44.41 (± 356.124)	83.54 (± 477.163)	4.61 (± 86.846)
W-24: CRP (64,63,64,65)	50.11 (± 393.99)	44.48 (± 360.594)	52.03 (± 309.206)	0.92 (± 74.172)

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Baseline through week 28

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	17.0
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Reporting groups

Reporting group title	JNJ-38518168 3 mg
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Reporting group description:

Participants received JNJ-38518168 3 mg/day from Week 0 to Week 24 (unless early escape at week 16).

Reporting group title	JNJ-38518168 10 mg
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Reporting group description:

Participants received JNJ-38518168 10 mg once daily from week 0 to week 24 (unless early escape at week 16).

Reporting group title	Placebo
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Reporting group description:

Participants received placebo daily from Week 0 to Week 24 (unless early escape at week 16).

Reporting group title	Early escape to JNJ- 38518168 30 mg
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Reporting group description:

Subjects who entered early escape at week 16 and received JNJ-38518168 dose of 30 mg per day from week 16 to week 24.

Reporting group title	JNJ-38518168 30 mg
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Reporting group description:

Participants received JNJ-38518168 30 mg once daily from week 0 to week 24.

Serious adverse events	JNJ-38518168 3 mg	JNJ-38518168 10 mg	Placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 67 (4.48%)	5 / 68 (7.35%)	5 / 68 (7.35%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Investigations			
Lipase Increased			
subjects affected / exposed	0 / 67 (0.00%)	1 / 68 (1.47%)	0 / 68 (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
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Papilloma			

subjects affected / exposed	0 / 67 (0.00%)	1 / 68 (1.47%)	0 / 68 (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
Injury, poisoning and procedural complications			
Ankle Fracture			
subjects affected / exposed	1 / 67 (1.49%)	0 / 68 (0.00%)	0 / 68 (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
Fibula Fracture			
subjects affected / exposed	0 / 67 (0.00%)	0 / 68 (0.00%)	1 / 68 (1.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hip Fracture			
subjects affected / exposed	0 / 67 (0.00%)	1 / 68 (1.47%)	0 / 68 (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
Joint Dislocation			
subjects affected / exposed	1 / 67 (1.49%)	0 / 68 (0.00%)	0 / 68 (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
Tibia Fracture			
subjects affected / exposed	0 / 67 (0.00%)	0 / 68 (0.00%)	1 / 68 (1.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Hypertensive Crisis			
subjects affected / exposed	1 / 67 (1.49%)	0 / 68 (0.00%)	0 / 68 (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
Thrombophlebitis Superficial			
subjects affected / exposed	0 / 67 (0.00%)	0 / 68 (0.00%)	1 / 68 (1.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 67 (1.49%)	0 / 68 (0.00%)	1 / 68 (1.47%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 67 (0.00%)	1 / 68 (1.47%)	0 / 68 (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			
Abdominal Pain Lower			
subjects affected / exposed	0 / 67 (0.00%)	1 / 68 (1.47%)	0 / 68 (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
Gastric Ulcer Haemorrhage			
subjects affected / exposed	0 / 67 (0.00%)	0 / 68 (0.00%)	0 / 68 (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
Hepatobiliary disorders			
Cholecystitis Chronic			
subjects affected / exposed	0 / 67 (0.00%)	1 / 68 (1.47%)	0 / 68 (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
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 67 (0.00%)	0 / 68 (0.00%)	1 / 68 (1.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epistaxis			
subjects affected / exposed	1 / 67 (1.49%)	0 / 68 (0.00%)	0 / 68 (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
Musculoskeletal and connective tissue disorders			

Arthralgia			
subjects affected / exposed	0 / 67 (0.00%)	1 / 68 (1.47%)	0 / 68 (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
Osteoarthritis			
subjects affected / exposed	0 / 67 (0.00%)	0 / 68 (0.00%)	0 / 68 (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			
Gastroenteritis			
subjects affected / exposed	0 / 67 (0.00%)	1 / 68 (1.47%)	0 / 68 (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
Postoperative Wound Infection			
subjects affected / exposed	1 / 67 (1.49%)	0 / 68 (0.00%)	0 / 68 (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
Metabolism and nutrition disorders			
Diabetic Ketoacidosis			
subjects affected / exposed	0 / 67 (0.00%)	0 / 68 (0.00%)	1 / 68 (1.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Serious adverse events	Early escape to JNJ-38518168 30 mg	JNJ-38518168 30 mg	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 19 (0.00%)	2 / 68 (2.94%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Investigations			
Lipase Increased			
subjects affected / exposed	0 / 19 (0.00%)	0 / 68 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Papilloma			

subjects affected / exposed	0 / 19 (0.00%)	0 / 68 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Ankle Fracture			
subjects affected / exposed	0 / 19 (0.00%)	0 / 68 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fibula Fracture			
subjects affected / exposed	0 / 19 (0.00%)	0 / 68 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hip Fracture			
subjects affected / exposed	0 / 19 (0.00%)	0 / 68 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Joint Dislocation			
subjects affected / exposed	0 / 19 (0.00%)	0 / 68 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tibia Fracture			
subjects affected / exposed	0 / 19 (0.00%)	0 / 68 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Hypertensive Crisis			
subjects affected / exposed	0 / 19 (0.00%)	0 / 68 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombophlebitis Superficial			
subjects affected / exposed	0 / 19 (0.00%)	0 / 68 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 19 (0.00%)	0 / 68 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 19 (0.00%)	0 / 68 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal Pain Lower			
subjects affected / exposed	0 / 19 (0.00%)	0 / 68 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric Ulcer Haemorrhage			
subjects affected / exposed	0 / 19 (0.00%)	1 / 68 (1.47%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholecystitis Chronic			
subjects affected / exposed	0 / 19 (0.00%)	0 / 68 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 19 (0.00%)	0 / 68 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epistaxis			
subjects affected / exposed	0 / 19 (0.00%)	0 / 68 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			

Arthralgia			
subjects affected / exposed	0 / 19 (0.00%)	0 / 68 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteoarthritis			
subjects affected / exposed	0 / 19 (0.00%)	1 / 68 (1.47%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Gastroenteritis			
subjects affected / exposed	0 / 19 (0.00%)	0 / 68 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postoperative Wound Infection			
subjects affected / exposed	0 / 19 (0.00%)	0 / 68 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Diabetic Ketoacidosis			
subjects affected / exposed	0 / 19 (0.00%)	0 / 68 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 3 %

Non-serious adverse events	JNJ-38518168 3 mg	JNJ-38518168 10 mg	Placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	22 / 67 (32.84%)	22 / 68 (32.35%)	24 / 68 (35.29%)
Injury, poisoning and procedural complications			
Tendon Rupture			
subjects affected / exposed	0 / 67 (0.00%)	0 / 68 (0.00%)	0 / 68 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Headache			

subjects affected / exposed occurrences (all)	1 / 67 (1.49%) 1	6 / 68 (8.82%) 6	2 / 68 (2.94%) 2
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all)	1 / 67 (1.49%) 1	3 / 68 (4.41%) 3	3 / 68 (4.41%) 3
Gastrointestinal disorders Constipation subjects affected / exposed occurrences (all) Diarrhoea subjects affected / exposed occurrences (all)	1 / 67 (1.49%) 1 2 / 67 (2.99%) 2	2 / 68 (2.94%) 2 1 / 68 (1.47%) 1	1 / 68 (1.47%) 1 1 / 68 (1.47%) 1
Skin and subcutaneous tissue disorders Eczema subjects affected / exposed occurrences (all) Rash subjects affected / exposed occurrences (all)	0 / 67 (0.00%) 0 0 / 67 (0.00%) 0	0 / 68 (0.00%) 0 0 / 68 (0.00%) 0	0 / 68 (0.00%) 0 0 / 68 (0.00%) 0
Renal and urinary disorders Haematuria subjects affected / exposed occurrences (all)	0 / 67 (0.00%) 0	0 / 68 (0.00%) 0	0 / 68 (0.00%) 0
Musculoskeletal and connective tissue disorders Muscle Spasms subjects affected / exposed occurrences (all) Rheumatoid Arthritis subjects affected / exposed occurrences (all) Rheumatoid Nodule subjects affected / exposed occurrences (all)	2 / 67 (2.99%) 2 3 / 67 (4.48%) 3 0 / 67 (0.00%) 0	0 / 68 (0.00%) 0 4 / 68 (5.88%) 4 0 / 68 (0.00%) 0	0 / 68 (0.00%) 0 2 / 68 (2.94%) 2 0 / 68 (0.00%) 0
Infections and infestations			

Bronchitis			
subjects affected / exposed	4 / 67 (5.97%)	3 / 68 (4.41%)	2 / 68 (2.94%)
occurrences (all)	4	3	2
Influenza			
subjects affected / exposed	1 / 67 (1.49%)	1 / 68 (1.47%)	1 / 68 (1.47%)
occurrences (all)	1	1	1
Nasopharyngitis			
subjects affected / exposed	2 / 67 (2.99%)	5 / 68 (7.35%)	7 / 68 (10.29%)
occurrences (all)	2	5	7
Pharyngitis			
subjects affected / exposed	3 / 67 (4.48%)	1 / 68 (1.47%)	1 / 68 (1.47%)
occurrences (all)	3	1	1
Respiratory Tract Infection			
subjects affected / exposed	0 / 67 (0.00%)	0 / 68 (0.00%)	3 / 68 (4.41%)
occurrences (all)	0	0	3
Upper Respiratory Tract Infection			
subjects affected / exposed	5 / 67 (7.46%)	4 / 68 (5.88%)	3 / 68 (4.41%)
occurrences (all)	5	4	3
Urinary Tract Infection			
subjects affected / exposed	4 / 67 (5.97%)	4 / 68 (5.88%)	2 / 68 (2.94%)
occurrences (all)	4	4	2
Viral Pharyngitis			
subjects affected / exposed	0 / 67 (0.00%)	0 / 68 (0.00%)	0 / 68 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Diabetes Mellitus			
subjects affected / exposed	0 / 67 (0.00%)	0 / 68 (0.00%)	1 / 68 (1.47%)
occurrences (all)	0	0	1

Non-serious adverse events	Early escape to JNJ-38518168 30 mg	JNJ-38518168 30 mg	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 19 (31.58%)	27 / 68 (39.71%)	
Injury, poisoning and procedural complications			
Tendon Rupture			
subjects affected / exposed	1 / 19 (5.26%)	0 / 68 (0.00%)	
occurrences (all)	1	0	

Nervous system disorders Headache subjects affected / exposed occurrences (all)	0 / 19 (0.00%) 0	1 / 68 (1.47%) 1	
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all)	0 / 19 (0.00%) 0	1 / 68 (1.47%) 1	
Gastrointestinal disorders Constipation subjects affected / exposed occurrences (all) Diarrhoea subjects affected / exposed occurrences (all)	1 / 19 (5.26%) 1 0 / 19 (0.00%) 0	3 / 68 (4.41%) 1 8 / 68 (11.76%) 8	
Skin and subcutaneous tissue disorders Eczema subjects affected / exposed occurrences (all) Rash subjects affected / exposed occurrences (all)	1 / 19 (5.26%) 1 1 / 19 (5.26%) 1	0 / 68 (0.00%) 0 0 / 68 (0.00%) 0	
Renal and urinary disorders Haematuria subjects affected / exposed occurrences (all)	1 / 19 (5.26%) 1	0 / 68 (0.00%) 0	
Musculoskeletal and connective tissue disorders Muscle Spasms subjects affected / exposed occurrences (all) Rheumatoid Arthritis subjects affected / exposed occurrences (all) Rheumatoid Nodule subjects affected / exposed occurrences (all)	0 / 19 (0.00%) 0 0 / 19 (0.00%) 0 1 / 19 (5.26%) 1	3 / 68 (4.41%) 3 2 / 68 (2.94%) 2 0 / 68 (0.00%) 0	
Infections and infestations			

Bronchitis			
subjects affected / exposed	0 / 19 (0.00%)	4 / 68 (5.88%)	
occurrences (all)	0	4	
Influenza			
subjects affected / exposed	1 / 19 (5.26%)	0 / 68 (0.00%)	
occurrences (all)	1	0	
Nasopharyngitis			
subjects affected / exposed	0 / 19 (0.00%)	8 / 68 (11.76%)	
occurrences (all)	0	8	
Pharyngitis			
subjects affected / exposed	0 / 19 (0.00%)	2 / 68 (2.94%)	
occurrences (all)	0	2	
Respiratory Tract Infection			
subjects affected / exposed	0 / 19 (0.00%)	1 / 68 (1.47%)	
occurrences (all)	0	1	
Upper Respiratory Tract Infection			
subjects affected / exposed	0 / 19 (0.00%)	1 / 68 (1.47%)	
occurrences (all)	0	1	
Urinary Tract Infection			
subjects affected / exposed	0 / 19 (0.00%)	5 / 68 (7.35%)	
occurrences (all)	0	5	
Viral Pharyngitis			
subjects affected / exposed	1 / 19 (5.26%)	0 / 68 (0.00%)	
occurrences (all)	1	0	
Metabolism and nutrition disorders			
Diabetes Mellitus			
subjects affected / exposed	1 / 19 (5.26%)	1 / 68 (1.47%)	
occurrences (all)	1	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
08 March 2013	The amendment updated information regarding drug-drug interactions (DDIs), criteria for subject enrollment, and the list of prohibited medications, based on preliminary PK results from the 38518168ARA1003 DDI study with ketoconazole. In addition, editorial changes were also made for clarity throughout the protocol.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
03 July 2014	The decision was made to prematurely discontinue this trial due to lack of efficacy.	-

Notes:

Limitations and caveats

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

The trial was discontinued due to lack of efficacy.

Notes: