Clinical trial results:
A Pilot Phase 2a, Randomized, Double-blind, Placebo-controlled Study to Explore the Antiviral Activity, Clinical Outcomes, Safety, Tolerability, and Pharmacokinetics of JNJ-53718678 at Two Dose Levels in Non-hospitalized Adult Subjects Infected With Respiratory Syncytial Virus

Summary

EudraCT number	2017-003252-24
Trial protocol	BE ES SE PL BG
Global end of trial date	26 December 2019

Results information

Result version number	v1 (current)
This version publication date	06 January 2021
First version publication date	06 January 2021

Trial information

Trial identification

Sponsor protocol code	53718678RSV2004

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03379675
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Janssen Research and Development LLC
Sponsor organisation address	920 US, Route 202, P.O. Box 300, Raritan, United States, 08869
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	02 July 2020
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	26 December 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of this study was to explore the antiviral effect of JNJ-53718678 at 2 dose levels (80 milligrams [mg] and 500 mg) once daily for 7 days in adults with Respiratory Syncytial Virus (RSV) infection, as measured by RSV viral load in nasal secretions by quantitative reverse transcription polymerase chain reaction (qRT-PCR) assay.

Protection of trial subjects:

This study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and that are consistent with Good Clinical Practices and applicable regulatory requirements. Safety and tolerability were evaluated throughout the study from signing of the informed consent form (ICF) until the last study-related activity. Safety evaluations included monitoring of adverse events (AEs), clinical laboratory tests, vital signs measurements, physical examinations, electrocardiograms (ECGs), and assessment of specific toxicities.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	26 February 2018
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	Argentina: 12
Country: Number of subjects enrolled	Belgium: 1
Country: Number of subjects enrolled	Bulgaria: 7
Country: Number of subjects enrolled	Brazil: 5
Country: Number of subjects enrolled	Canada: 10
Country: Number of subjects enrolled	Germany: 6
Country: Number of subjects enrolled	Spain: 2
Country: Number of subjects enrolled	France: 1
Country: Number of subjects enrolled	Mexico: 6
Country: Number of subjects enrolled	Poland: 8
Country: Number of subjects enrolled	Russian Federation: 1
Country: Number of subjects enrolled	Sweden: 2
Country: Number of subjects enrolled	Taiwan: 2
Country: Number of subjects enrolled	Ukraine: 3
Country: Number of subjects enrolled	United States: 6

Worldwide total number of subjects	72
EEA total number of subjects	27

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)	54
From 65 to 84 years	18
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 79 subjects were screened for this study, but only 72 subjects were randomized and received intervention. Out of the 72, 66 were RSV positive and thus included in the intent-to-treat infected (ITT-i) analysis.

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	Placebo

Arm description:

Subjects received matching placebo as an oral solution once daily for 7 days.

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

Dosage and administration details:

Subjects were administered matching placebo once daily for 7 days.

Arm title	JNJ-53718678 80 mg

Arm description:

Subjects received JNJ-53718678 80 mg as an oral solution once daily for 7 days. In addition, subjects received matching placebo to maintain the blinding.

Arm type	Experimental
Investigational medicinal product name	JNJ-53718678 80 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral solution
Routes of administration	Oral use

Dosage and administration details:

Subjects were administered JNJ-53718678 80 mg once daily for 7 days.

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral solution
Routes of administration	Oral use

Dosage and administration details:

Subjects were administered JNJ-53718678 80 mg once daily for 7 days. In addition, subjects received matching placebo to maintain the blinding.

Arm title	JNJ-53718678 500 mg

Arm description:

Subjects received JNJ-53718678 500 mg as an oral solution once daily for 7 days.

Arm type	Experimental
Investigational medicinal product name	JNJ-53718678 500 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral solution
Routes of administration	Oral use

Dosage and administration details:

Subjects were administered JNJ-53718678 500 mg once daily for 7 days.

Number of subjects in period 1	Placebo	JNJ-53718678 80 mg	JNJ-53718678 500 mg
Started	24	24	24
Completed	22	22	20
Not completed	2	2	4
Consent withdrawn by subject	2	1	2
Adverse event, non-fatal	-	-	2
Lost to follow-up	-	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Subjects received matching placebo as an oral solution once daily for 7 days.	
Reporting group title	JNJ-53718678 80 mg
Reporting group description:	
Subjects received JNJ-53718678 80 mg as an oral solution once daily for 7 days. In addition, subjects received matching placebo to maintain the blinding.	
Reporting group title	JNJ-53718678 500 mg
Reporting group description:	
Subjects received JNJ-53718678 500 mg as an oral solution once daily for 7 days.	

Reporting group values	Placebo	JNJ-53718678 80 mg	JNJ-53718678 500 mg
Number of subjects	24	24	24
Title for AgeCategorical			
Units: subjects			
Adults (18-64 years)	17	22	15
From 65 to 84 years	7	2	9
85 years and over	0	0	0
Title for AgeContinuous			
Units: years			
arithmetic mean	58.9	48.4	51.7
standard deviation	± 14.16	± 17.39	± 17.89
Title for Gender			
Units: subjects			
Female	14	11	12
Male	10	13	12

Reporting group values	Total		
Number of subjects	72		
Title for AgeCategorical			
Units: subjects			
Adults (18-64 years)	54		
From 65 to 84 years	18		
85 years and over	0		
Title for AgeContinuous			
Units: years			
arithmetic mean			
standard deviation	-		
Title for Gender			
Units: subjects			
Female	37		
Male	35		

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Subjects received matching placebo as an oral solution once daily for 7 days.	
Reporting group title	JNJ-53718678 80 mg
Reporting group description:	
Subjects received JNJ-53718678 80 mg as an oral solution once daily for 7 days. In addition, subjects received matching placebo to maintain the blinding.	
Reporting group title	JNJ-53718678 500 mg
Reporting group description:	
Subjects received JNJ-53718678 500 mg as an oral solution once daily for 7 days.	

Primary: Area Under the Respiratory Syncytial Virus (RSV) Viral Load-time Curve (AUC) Over Time

End point title	Area Under the Respiratory Syncytial Virus (RSV) Viral Load-time Curve (AUC) Over Time[1]
End point description:	
Area under the RSV Viral Load (VL)-time curve was determined as log10 copies*hour per milliliter (Log10 copies*hr/mL) by quantitative reverse transcription polymerase chain reaction (qRT-PCR) assay of mid turbine nasal swabs. The intent-to-treat-infected (ITT-i) population consisted of all randomized subjects who received at least 1 dose of study drug and who had a central lab-confirmed RSV infection. Here, 'n' (number analyzed) signifies number of subjects who were analyzed at specified timepoints.	
End point type	Primary
End point timeframe:	
Baseline through Days 3, 5, 8 and 14	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Descriptive statistics was done, no inferential statistical analyses was performed.

End point values	Placebo	JNJ-53718678 80 mg	JNJ-53718678 500 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	21	21	21	
Units: Log10 copies*hr/mL				
arithmetic mean (standard deviation)				
Day 3 (n=21,21,21)	203.4 (± 87.63)	246.3 (± 67.39)	207.3 (± 89.55)	
Day 5 (n=21,21,20)	340.4 (± 148.30)	424.2 (± 145.73)	344.5 (± 189.40)	
Day 8 (n=21,21,20)	486.1 (± 254.15)	612.3 (± 253.29)	470.7 (± 305.38)	
Day 14 (n=20,19,20)	619.9 (± 394.15)	747.1 (± 352.25)	534.4 (± 379.92)	

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline in RSV Viral Load Over Time

End point title	Change from Baseline in RSV Viral Load Over Time[2]

End point description:

Change from baseline in RSV viral load over time was measured as log10 copies per milliliter (Log10 copies/mL) by qRT-PCR assay in the mid-turbinate nasal swab specimens. The ITT-i population consisted of all randomized subjects who received at least 1 dose of study drug and who had a central lab-confirmed RSV infection. Here, 'n' (number analyzed) signifies number of subjects who were analyzed at specified timepoints.

End point type	Primary

End point timeframe:

Baseline up to Day 21

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Descriptive statistics was done, no inferential statistical analyses was performed.

End point values	Placebo	JNJ-53718678 80 mg	JNJ-53718678 500 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	22	21	23	
Units: Log10 copies/mL				
arithmetic mean (standard deviation)				
Day 2 (n=19,20,22)	-0.865 (± 1.0917)	-0.373 (± 1.2557)	-0.862 (± 1.9590)	
Day 3 (n=20,20,21)	-2.221 (± 1.7093)	-1.436 (± 1.6165)	-2.210 (± 1.7185)	
Day 4 (n=20,21,20)	-2.325 (± 2.1919)	-2.300 (± 1.8980)	-2.670 (± 1.8937)	
Day 5 (n=20,21,20)	-3.031 (± 1.5010)	-2.324 (± 1.6727)	-3.156 (± 2.2887)	
Day 6 (n=20,21,20)	-3.169 (± 1.3263)	-3.149 (± 1.6325)	-3.448 (± 2.1068)	
Day 7 (n=19,21,20)	-3.312 (± 1.3333)	-3.093 (± 1.8236)	-3.746 (± 1.9299)	
Day 8 (n=21,20,18)	-3.953 (± 1.5674)	-3.983 (± 1.3928)	-4.960 (± 1.7804)	
Day 9 (n=12,11,8)	-4.095 (± 1.8738)	-5.236 (± 2.1955)	-4.227 (± 3.2780)	
Day 10 (n=10,10,9)	-3.861 (± 1.3354)	-5.207 (± 1.6821)	-5.186 (± 1.9710)	
Day 11 (n=7,8,7)	-5.267 (± 1.7261)	-5.108 (± 1.8076)	-4.824 (± 2.3663)	
Day 12 (n=7,7,7)	-5.553 (± 2.2298)	-5.248 (± 1.7249)	-5.488 (± 2.0944)	
Day 13 (n=6,6,7)	-6.629 (± 1.6551)	-5.454 (± 1.7934)	-5.488 (± 2.0944)	
Day 14 (n=19,18,19)	-4.858 (± 1.7419)	-5.777 (± 1.6183)	-5.135 (± 1.6444)	
Day 21 (n=20,19,20)	-5.129 (± 1.6513)	-5.898 (± 1.6421)	-5.433 (± 2.1416)	

Statistical analyses

No statistical analyses for this end point

Primary: RSV Viral Load Over Time

End point title	RSV Viral Load Over Time[3]

End point description:

RSV viral load over time was measured as log10 copies/mL by qRT-PCR assay in the mid-turbinate nasal swab specimens. The ITT-i population consisted of all randomized subjects who received at least 1 dose of study drug and who had a central lab-confirmed RSV infection. Here, 'n' (number analyzed) signifies number of subjects who were analyzed at specified timepoints.

End point type	Primary

End point timeframe:

Baseline up to Day 21

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Descriptive statistics was done, no inferential statistical analyses was performed.

End point values	Placebo	JNJ-53718678 80 mg	JNJ-53718678 500 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	22	21	23	
Units: Log10 copies/mL				
arithmetic mean (standard deviation)				
Baseline	5.285 (± 1.7158)	5.851 (± 1.6777)	5.523 (± 1.7911)	
Day 2 (n=19,20,22)	4.495 (± 2.2524)	5.511 (± 1.2844)	4.626 (± 2.0161)	
Day 3 (n=20,20,21)	3.160 (± 2.2603)	4.448 (± 1.9513)	3.267 (± 2.5490)	
Day 4 (n=20,21,20)	3.057 (± 1.7489)	3.551 (± 2.1392)	2.870 (± 2.5162)	
Day 5 (n=20,21,20)	2.351 (± 2.1302)	3.528 (± 1.9824)	2.384 (± 2.4214)	
Day 6 (n=20,21,20)	2.213 (± 1.7570)	2.703 (± 2.1637)	2.092 (± 2.3186)	
Day 7 (n=19,21,20)	2.152 (± 2.0668)	2.758 (± 1.6277)	1.795 (± 2.0617)	
Day 8 (n=21,20,18)	1.398 (± 1.5958)	1.804 (± 1.7888)	0.661 (± 1.5572)	
Day 9 (n=12,11,8)	1.413 (± 1.6205)	0.960 (± 1.7302)	1.647 (± 1.9728)	
Day 10 (n=10,10,9)	1.569 (± 1.7910)	0.818 (± 1.7313)	0.619 (± 1.2299)	
Day 11 (n=7,8,7)	1.910 (± 1.5213)	0.579 (± 1.6379)	0.664 (± 1.1385)	
Day 12 (n=7,7,7)	0.905 (± 1.5454)	0.470 (± 1.2425)	0.000 (± 0.0000)	
Day 13 (n=6,6,7)	0.000 (± 0.0000)	0.000 (± 0.0000)	0.000 (± 0.0000)	
Day 14 (n=19,18,19)	0.492 (± 0.9910)	0.290 (± 0.8579)	0.421 (± 1.2601)	
Day 21 (n=20,19,20)	0.253 (± 0.7866)	0.113 (± 0.4932)	0.108 (± 0.4808)	

Statistical analyses

No statistical analyses for this end point

Primary: Time to Undetectable RSV Viral Load

End point title	Time to Undetectable RSV Viral Load[4]

End point description:

The time to undetectable nasal RSV RNA viral load was defined as the time to the first post-baseline time point at which RSV RNA was undetectable and after which time there were no more detectable virus assessments. The ITT-i population consisted of all randomized subjects who received at least 1 dose of study drug and who had a central lab-confirmed RSV infection.

End point type	Primary

End point timeframe:

Up to Day 21

Notes:

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Descriptive statistics was done, no inferential statistical analyses was performed.

End point values	Placebo	JNJ-53718678 80 mg	JNJ-53718678 500 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	22	21	23	
Units: days				
median (confidence interval 90%)	9.7 (7.03 to 11.74)	8.0 (6.86 to 12.80)	7.0 (5.92 to 9.90)	

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects with Undetectable RSV Viral Load

End point title	Number of Subjects with Undetectable RSV Viral Load[5]

End point description:

The number of subjects with undetectable RSV viral load over time were reported. The ITT-i population consisted of all randomized subjects who received at least 1 dose of study drug and who had a central lab-confirmed RSV infection. Here, n (subjects analyzed) signifies the number of subjects analyzed at specified timepoints.

End point type	Primary

End point timeframe:

Baseline up to Day 21

Notes:

[5] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Descriptive statistics was done, no inferential statistical analyses was performed.

End point values	Placebo	JNJ-53718678 80 mg	JNJ-53718678 500 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	22	21	23	
Units: subjects				
Baseline	0	0	0	
Day 2 (n=19,20,22)	1	0	1	
Day 3 (n=20,20,21)	4	1	6	

Day 4 (n=20,21,20)	3	3	6	
Day 5 (n=20,21,20)	7	3	8	
Day 6 (n=20,21,20)	6	7	9	
Day 7 (n=19,21,20)	7	4	10	
Day 8 (n=21,20,18)	11	9	15	
Day 9 (n=12,11,8)	6	8	4	
Day 10 (n=10,10,9)	5	8	7	
Day 11 (n=7,8,7)	4	7	5	
Day 12 (n=7,7,7)	5	6	7	
Day 13 (n=6,6,7)	6	6	7	
Day 14 (n=19,18,19)	15	16	17	
Day 21 (n=20,19,20)	18	18	19	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with Adverse Events (AEs) as a Measure of Safety and Tolerability

End point title	Number of subjects with Adverse Events (AEs) as a Measure of Safety and Tolerability

End point description:

An adverse event is any untoward medical event that occurs in a subject administered an investigational product, and it does not necessarily indicate only events with clear causal relationship with the relevant investigational product. The safety population included randomized subjects who received at least one dose of study drug.

End point type	Secondary

End point timeframe:

Up to Day 28

End point values	Placebo	JNJ-53718678 80 mg	JNJ-53718678 500 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	24	24	24	
Units: subjects	15	18	9	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Clinically Significant Laboratory Abnormalities

End point title	Number of Subjects with Clinically Significant Laboratory Abnormalities

End point description:

Number of subjects with clinically significant laboratory (serum chemistry, hematology and urinalyses) abnormalities were reported. The safety population included randomized subjects who received at least

one dose of study drug.

End point type	Secondary

End point timeframe:

Up to Day 28

End point values	Placebo	JNJ-53718678 80 mg	JNJ-53718678 500 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	24	24	24	
Units: subjects	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Treatment Emergent Vital Sign Abnormalities

End point title	Number of Subjects with Treatment Emergent Vital Sign Abnormalities

End point description:

The subjects were analyzed for abnormalities in vital sign parameters like diastolic blood pressure (DBP), oxygen saturation, pulse rate, respiratory rate (RR), systolic blood pressure (SBP) and temperature. The classification was based on division of microbiology and infectious diseases (DMID) scale. The ITT-i population consisted of all randomized subjects who received at least 1 dose of study drug and who had a central lab-confirmed RSV infection. Here, n (subjects analyzed) signifies the number of subjects analyzed at specified categories.

End point type	Secondary

End point timeframe:

Up to Day 28

End point values	Placebo	JNJ-53718678 80 mg	JNJ-53718678 500 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	24	24	24	
Units: subjects				
Abnormally low DBP (n=21,21,22)	2	0	0	
Mild increased DBP (n=21,21,22)	0	3	0	
Moderate increased DBP (n=21,21,22)	0	0	1	
Abnormally low oxygen saturation (n=21,21,22)	2	1	2	
Abnormally high pulse rate (n=21,21,22)	1	0	0	
Mild increased RR (n=21,21,22)	3	3	0	
Moderate increased RR (n=21,21,22)	2	1	1	
Severe increased RR (n=21,21,22)	0	1	0	
Abnormally low SBP (n=21,21,22)	1	1	0	
Mild increased SBP (n=21,21,22)	3	4	1	

Moderate increased SBP (n=21,21,22)	1	0	0	
Severe increased SBP (n=21,21,22)	0	0	1	
Abnormally high temperature (n=22,21,22)	1	1	1	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Worst Treatment Emergent Electrocardiograms (ECGs) Abnormalities

End point title	Number of Subjects with Worst Treatment Emergent Electrocardiograms (ECGs) Abnormalities

End point description:

The number of subjects with ECG abnormalities were reported. The ECG variables that were analyzed are heart rate, PR interval, QRS interval, QT interval, and corrected QT (QTc) interval. The safety population included randomized subjects who received at least one dose of study drug. Here, 'n' (subjects analyzed) signifies number of subjects analyzed for specified categories.

End point type	Secondary

End point timeframe:

Up to Day 28

End point values	Placebo	JNJ-53718678 80 mg	JNJ-53718678 500 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	24	24	24	
Units: subjects				
Abnormally low heart rate (n=23,24,22)	1	1	0	
Abnormally high PR interval (n=21,24,22)	0	0	1	
Abnormally high QRS interval (n=23,24,22)	0	0	1	
QTcB Increase 30 and 60ms (Bazett) (n=23,24,22)	1	2	5	
QTcF Increase 30 and 60ms (Fridericia)(n=23,24,22)	0	1	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Abnormalities in Physical Examination

End point title	Number of Subjects With Abnormalities in Physical Examination

End point description:

A physical examination (including height [only at screening] and body weight measurements) and skin examination were performed. A skin examination included an examination of the mucous membranes, but not a vaginal or rectal examination. The safety population included randomized subjects who received at least one dose of study drug.

End point type	Secondary

End point timeframe:

Up to Day 28

End point values	Placebo	JNJ-53718678 80 mg	JNJ-53718678 500 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[6]	0[7]	0[8]	
Units: subjects				

Notes:

[6] - Clinically relevant treatment emergent abnormalities were reported as adverse events.

[7] - Clinically relevant treatment emergent abnormalities were reported as adverse events.

[8] - Clinically relevant treatment emergent abnormalities were reported as adverse events.

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Resolution of Selected RSV Symptoms as Assessed by RI-PRO

End point title	Time to Resolution of Selected RSV Symptoms as Assessed by RI-PRO

End point description:

Resolution of RSV symptoms was defined as a score of 'Not at all' (score = 0) or 'A little bit' (score = 1) for at least 24 hours for symptoms of the RI-PRO questionnaire. RI-PRO is a 32 items questionnaire computed in six domain scores, representing symptom severity. Selected RSV symptoms include symptoms in the following domains: Nose, Throat, Chest/respiratory and Body/systemic. The ITT-i population consisted of all randomized subjects who received at least 1 dose of study drug and who had a central lab-confirmed RSV infection.

End point type	Secondary

End point timeframe:

Up to Day 21

End point values	Placebo	JNJ-53718678 80 mg	JNJ-53718678 500 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	22	21	23	
Units: days				
median (confidence interval 90%)	10.6 (6.40 to 15.90)	7.4 (5.05 to 9.52)	7.7 (6.36 to 18.92)	

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Return to Usual Activity/Health Based on RI-PRO

End point title	Time to Return to Usual Activity/Health Based on RI-PRO

End point description:

Time from the first dose of study drug until the time of return to usual activity/health was determined. Return to usual activity/health when the response is 'Yes' on RI-PRO additional question 7 ('Have you returned to your usual activity/health today?') for at least 24 hours. The ITT-i population consisted of all randomized subjects who received at least 1 dose of study drug and who had a central lab-confirmed RSV infection.

End point type	Secondary

End point timeframe:

Up to Day 21

End point values	Placebo	JNJ-53718678 80 mg	JNJ-53718678 500 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	22	21	23	
Units: days				
median (confidence interval 90%)				
Time to return to usual activity	5.6 (4.62 to 10.62)	3.0 (1.39 to 7.88)	6.0 (2.99 to 8.33)	
Time to return to usual health	9.1 (5.62 to 10.64)	8.6 (5.57 to 10.81)	8.3 (5.51 to 11.87)	

Statistical analyses

No statistical analyses for this end point

Secondary: Peripheral Capillary Oxygen Saturation (SpO2) Over Time

End point title	Peripheral Capillary Oxygen Saturation (SpO2) Over Time

End point description:

Oxygen saturation was measured by the investigator over time. The ITT-i population consisted of all randomized subjects who received at least 1 dose of study drug and who had a central lab-confirmed RSV infection. Here, 'n' (subjects analyzed) signifies number of subjects analyzed at specified timepoints.

End point type	Secondary

End point timeframe:

Baseline, Days 3, 8, 14 and 21

End point values	Placebo	JNJ-53718678 80 mg	JNJ-53718678 500 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	21	21	22	
Units: Percentage of SpO2 (%)				
arithmetic mean (standard deviation)				
Baseline (n=21,21,22)	95.8 (± 2.74)	96.0 (± 2.60)	95.6 (± 2.72)	
Day 3 (n=20,21,21)	95.7 (± 3.57)	96.8 (± 2.17)	95.8 (± 2.62)	
Day 8 (n=21,21,19)	96.9 (± 2.26)	96.5 (± 2.23)	97.2 (± 1.69)	
Day 14 (n=20,19,20)	96.7 (± 1.81)	96.6 (± 2.14)	97.4 (± 0.99)	
Day 21 (n=20,19,20)	96.6 (± 2.41)	97.1 (± 1.47)	97.1 (± 1.23)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Peripheral Capillary Oxygen saturation

End point title	Change from Baseline in Peripheral Capillary Oxygen saturation

End point description:

Change from baseline in oxygen saturation levels was calculated by the investigator. The ITT-i population consisted of all randomized subjects who received at least 1 dose of study drug and who had a central lab-confirmed RSV infection. Here, 'n' (subjects analyzed) signifies number of subjects analyzed at specified timepoints.

End point type	Secondary

End point timeframe:

Days 3, 8, 14 and 21

End point values	Placebo	JNJ-53718678 80 mg	JNJ-53718678 500 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	22	21	23	
Units: % of SpO2				
arithmetic mean (standard deviation)				
Day 3 (n=19,21,20)	0.2 (± 2.44)	0.9 (± 1.73)	0.5 (± 2.21)	
Day 8 (n=20,21,18)	1.1 (± 2.07)	0.5 (± 1.29)	1.3 (± 2.72)	
Day 14 (n=19,19,19)	1.2 (± 2.09)	0.7 (± 1.73)	1.2 (± 2.10)	
Day 21 (n=19,19,19)	1.1 (± 2.21)	1.2 (± 2.22)	1.3 (± 3.11)	

Statistical analyses

No statistical analyses for this end point

Secondary: Pulse Rate Over Time

End point title	Pulse Rate Over Time

End point description:

Pulse rate was measured by the investigator over time. The ITT-i population consisted of all randomized subjects who received at least 1 dose of study drug and who had a central lab-confirmed RSV infection. Here, 'n' (subjects analyzed) signifies number of subjects analyzed at specified timepoints.

End point type	Secondary

End point timeframe:

Baseline, Days 3, 8, 14 and 21

End point values	Placebo	JNJ-53718678 80 mg	JNJ-53718678 500 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	22	21	23	
Units: beats/min				
arithmetic mean (standard deviation)				
Baseline (n=22,21,23)	77.8 (± 13.05)	78.0 (± 12.16)	76.9 (± 10.86)	
Day 3 (n=20,21,21)	78.7 (± 15.64)	76.6 (± 13.20)	76.4 (± 11.88)	
Day 8 (n=21,21,19)	71.8 (± 10.58)	74.5 (± 12.74)	70.7 (± 8.22)	
Day 14 (n=20,19,20)	73.3 (± 6.27)	71.4 (± 13.09)	73.0 (± 12.62)	
Day 21 (n=20,19,20)	71.7 (± 10.00)	71.9 (± 9.76)	69.4 (± 7.13)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Pulse Rate

End point title	Change from Baseline in Pulse Rate

End point description:

Change from baseline in pulse rate was calculated by the investigator. The ITT-i population consisted of all randomized subjects who received at least 1 dose of study drug and who had a central lab-confirmed RSV infection. Here, 'n' (subjects analyzed) signifies number of subjects analyzed at specified timepoints.

End point type	Secondary

End point timeframe:

Days 3, 8, 14 and 21

End point values	Placebo	JNJ-53718678 80 mg	JNJ-53718678 500 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	22	21	23	
Units: beats/min				
arithmetic mean (standard deviation)				
Day 3 (n=20,21,21)	0.2 (± 11.80)	-1.4 (± 10.17)	0.0 (± 10.27)	
Day 8 (n=21,21,19)	-6.4 (± 11.61)	-3.5 (± 14.03)	-5.4 (± 13.17)	
Day 14 (n=20,19,20)	-5.3 (± 10.29)	-7.4 (± 13.76)	-4.3 (± 13.16)	
Day 21 (n=20,19,20)	-6.9 (± 12.85)	-6.8 (± 12.11)	-6.9 (± 9.11)	

Statistical analyses

No statistical analyses for this end point

Secondary: Respiratory Rate Over Time

End point title	Respiratory Rate Over Time

End point description:

Respiratory rate was measured by the investigator over time. The ITT-i population consisted of all randomized subjects who received at least 1 dose of study drug and who had a central lab-confirmed RSV infection. Here, 'n' (subjects analyzed) signifies number of subjects analyzed at specified timepoints.

End point type	Secondary

End point timeframe:

Baseline, Days 3, 8, 14 and 21

End point values	Placebo	JNJ-53718678 80 mg	JNJ-53718678 500 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	21	21	23	
Units: breaths/min				
arithmetic mean (standard deviation)				
Baseline (n=21,21,23)	19.2 (± 3.52)	18.0 (± 3.08)	18.2 (± 3.55)	
Day 3 (n=19,21,21)	18.3 (± 3.06)	16.7 (± 3.02)	17.1 (± 2.64)	
Day 8 (n=21,21,19)	18.0 (± 2.48)	17.4 (± 4.15)	16.9 (± 1.82)	
Day 14 (n=20,19,20)	18.1 (± 2.44)	16.4 (± 3.10)	16.6 (± 2.11)	
Day 21 (n=20,19,20)	17.6 (± 2.82)	15.7 (± 3.41)	16.6 (± 2.23)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Respiratory Rate

End point title	Change from Baseline in Respiratory Rate

End point description:

Change from baseline in respiratory rate was calculated by the investigator. The ITT-i population consisted of all randomized subjects who received at least 1 dose of study drug and who had a central lab-confirmed RSV infection. Here, 'n' (subjects analyzed) signifies number of subjects analyzed at specified timepoints.

End point type	Secondary

End point timeframe:

Days 3, 8, 14 and 21

End point values	Placebo	JNJ-53718678 80 mg	JNJ-53718678 500 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	22	21	23	
Units: breaths/min				
arithmetic mean (standard deviation)				
Day 3 (n=19,21,21)	-0.8 (± 2.25)	-1.3 (± 3.52)	-0.9 (± 2.10)	

Day 8 (n=21,21,19)	-1.1 (± 3.51)	0.6 (± 4.17)	-1.4 (± 2.34)	
Day 14 (n=20,19,20)	-1.3 (± 3.33)	-1.7 (± 3.59)	-1.8 (± 2.83)	
Day 21 (n=20,19,20)	-1.8 (± 3.33)	-2.4 (± 4.34)	-1.8 (± 2.73)	

Statistical analyses

No statistical analyses for this end point

Secondary: Body Temperature Over Time

End point title	Body Temperature Over Time

End point description:

Body temperature was measured over time. Subjects were provided a thermometer and asked to record body temperature in the electronic device on the non-visit days. The ITT-i population consisted of all randomized subjects who received at least 1 dose of study drug and who had a central lab-confirmed RSV infection. Here, 'n' (subjects analyzed) signifies number of subjects analyzed at specified timepoints.

End point type	Secondary

End point timeframe:

Baseline up to Day 21

End point values	Placebo	JNJ-53718678 80 mg	JNJ-53718678 500 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	22	21	23	
Units: degree celsius				
arithmetic mean (standard deviation)				
Baseline (n=22,21,23)	36.75 (± 0.561)	36.73 (± 0.601)	36.83 (± 0.622)	
Day 2 (n=19,20,17)	36.60 (± 0.593)	36.62 (± 0.733)	36.57 (± 0.585)	
Day 3 (n=21,20,21)	36.69 (± 0.446)	36.65 (± 0.574)	36.57 (± 0.572)	
Day 4 (n=19,21,19)	36.58 (± 0.430)	36.35 (± 0.647)	36.05 (± 0.939)	
Day 5 (n=19,21,19)	36.55 (± 0.485)	36.32 (± 0.543)	36.24 (± 0.665)	
Day 6 (n=18,21,19)	36.33 (± 0.659)	36.29 (± 0.389)	36.39 (± 0.735)	
Day 7 (n=17,20,20)	36.40 (± 0.571)	36.33 (± 0.495)	36.28 (± 0.656)	
Day 8 (n=20,21,18)	36.55 (± 0.404)	36.44 (± 0.527)	36.26 (± 0.396)	
Day 9 (n=1,0,1)	36.60 (± 0.00)	0.00 (± 0.00)	36.30 (± 0.00)	
Day 10 (n=0,0,2)	0.00 (± 0.00)	0.00 (± 0.00)	36.20 (± 0.424)	
Day 11 (n=0,0,1)	0.00 (± 0.00)	0.00 (± 0.00)	36.30 (± 0.00)	
Day 12 (n=0,0,1)	0.00 (± 0.00)	0.00 (± 0.00)	36.30 (± 0.00)	
Day 14 (n=20,19,20)	36.50 (± 0.291)	36.38 (± 0.346)	36.37 (± 0.389)	
Day 21 (n=20,19,20)	36.46 (± 0.299)	36.40 (± 0.380)	36.32 (± 0.380)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Body Temperature

End point title	Change from Baseline in Body Temperature

End point description:

Change from baseline in body temperature was calculated. Subjects were provided a thermometer and asked to record body temperature in the electronic device on the non-visit days. The ITT-i population consisted of all randomized subjects who received at least 1 dose of study drug and who had a central lab-confirmed RSV infection. Here, 'n' (subjects analyzed) signifies number of subjects analyzed at specified timepoints.

End point type	Secondary

End point timeframe:

Day 2 up to Day 21

End point values	Placebo	JNJ-53718678 80 mg	JNJ-53718678 500 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	22	21	23	
Units: degree celcius				
arithmetic mean (standard deviation)				
Day 2 (n=19,20,17)	-0.19 (± 0.573)	-0.14 (± 0.720)	-0.34 (± 0.433)	
Day 3 (n=21,20,21)	-0.01 (± 0.595)	-0.11 (± 0.621)	-0.27 (± 0.390)	
Day 4 (n=19,21,19)	-0.15 (± 0.485)	-0.38 (± 0.589)	-0.82 (± 0.808)	
Day 5 (n=19,21,19)	-0.17 (± 0.650)	-0.41 (± 0.645)	-0.63 (± 0.667)	
Day 6 (n=18,21,19)	-0.42 (± 0.866)	-0.45 (± 0.530)	-0.48 (± 0.785)	
Day 7 (n=17,20,20)	-0.39 (± 0.799)	-0.42 (± 0.653)	-0.57 (± 0.715)	
Day 8 (n=20,21,18)	-0.11 (± 0.477)	-0.29 (± 0.652)	-0.55 (± 0.465)	
Day 9 (n=1,0,1)	-0.80 (± 0.00)	0.00 (± 0.00)	-0.10 (± 0.00)	
Day 10 (n=0,0,2)	0.00 (± 0.00)	0.00 (± 0.00)	-0.25 (± 0.354)	
Day 11 (n=0,0,1)	0.00 (± 0.00)	0.00 (± 0.00)	-0.10 (± 0.00)	
Day 12 (n=0,0,1)	0.00 (± 0.00)	0.00 (± 0.00)	-0.10 (± 0.00)	
Day 14 (n=20,19,20)	-0.20 (± 0.411)	-0.40 (± 0.624)	-0.48 (± 0.402)	
Day 21 (n=20,19,20)	-0.24 (± 0.503)	-0.37 (± 0.615)	-0.52 (± 0.537)	

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Plasma Concentration-Time Curve From Time Point 0 Hours Until 24 Hours Post dose

End point title	Area Under the Plasma Concentration-Time Curve From Time Point 0 Hours Until 24 Hours Post dose[9]

End point description:

AUC (0-24) is defined as area under the plasma concentration-time curve from time point 0 hours until 24 hours post dose. Pharmacokinetic analysis set included all subjects who received JNJ-53718678 and for whom at least one pharmacokinetic (PK) concentration was reported. Here 'N' (number of subjects analyzed) signifies number of subjects analyzed for this endpoint and 'n' (number analyzed) signifies number of subjects analyzed for this endpoint at specified timepoints.

End point type	Secondary

End point timeframe:

Days 1 and 7 up to 24 hours post dose

Notes:

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Endpoint was planned to be analyzed for specified arms only.

End point values	JNJ-53718678 80 mg	JNJ-53718678 500 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20	17		
Units: nanogram hours per milliliter (ng*h/mL)				
arithmetic mean (standard deviation)				
Day 1 (n=17,15)	4530 (± 1560)	29800 (± 9180)		
Day 7 (n=18,16)	5470 (± 1620)	41200 (± 15300)		

Statistical analyses

No statistical analyses for this end point

Secondary: Predose Plasma Concentration (Ctrough) of JNJ-53718678

End point title	Predose Plasma Concentration (Ctrough) of JNJ-53718678[10]

End point description:

Ctrough is the trough observed plasma concentration of JNJ-53718678. Pharmacokinetic analysis set included all subjects who received JNJ-53718678 and for whom at least one pharmacokinetic (PK) concentration was reported. Here 'N' (number of subjects analyzed) signifies number of subjects analyzed for this endpoint and 'n' (number analyzed) signifies number of subjects analyzed for this endpoint at specified timepoints.

End point type	Secondary

End point timeframe:

Days 1 and 7

Notes:

[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Endpoint was planned to be analyzed for specified arms only.

End point values	JNJ-53718678 80 mg	JNJ-53718678 500 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20	17		
Units: nanogram per milliliter (ng/mL)				
arithmetic mean (standard deviation)				
Day 1 (n=17,15)	68.2 (± 36.2)	514 (± 249)		
Day 7 (n=18,16)	84.4 (± 39.4)	774 (± 451)		

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum Observed Plasma Concentration (Cmax) of JNJ-53718678

End point title	Maximum Observed Plasma Concentration (Cmax) of JNJ-53718678[11]

End point description:

Cmax is the maximum observed plasma concentration of JNJ-53718678. Pharmacokinetic analysis set included all subjects who received JNJ-53718678 and for whom at least one pharmacokinetic (PK) concentration was reported. Here 'N' (number of subjects analyzed) signifies number of subjects analyzed for this endpoint and 'n' (number analyzed) signifies number of subjects analyzed for this endpoint at specified timepoints.

End point type	Secondary

End point timeframe:

Days 1 and 7

Notes:

[11] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Endpoint was planned to be analyzed for specified arms only.

End point values	JNJ-53718678 80 mg	JNJ-53718678 500 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20	17		
Units: ng/mL				
arithmetic mean (standard deviation)				
Day 1 (n=20,17)	490 (± 150)	2870 (± 802)		
Day 7 (n=18,16)	552 (± 131)	3540 (± 1050)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Up to 29 days	
Adverse event reporting additional description:	
Safety analysis set included all randomized subjects who received at least one dose of study drug.	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	22.1

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Subjects received matching placebo as an oral solution once daily for 7 days.	
Reporting group title	JNJ-53718678 80 mg
Reporting group description:	
Subjects received JNJ-53718678 80 mg as an oral solution once daily for 7 days. In addition, subjects received matching placebo to maintain the blinding.	
Reporting group title	JNJ-53718678 500 mg
Reporting group description:	
Subjects received JNJ-53718678 500 mg as an oral solution once daily for 7 days.	

Serious adverse events	Placebo	JNJ-53718678 80 mg	JNJ-53718678 500 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 24 (0.00%)	0 / 24 (0.00%)	0 / 24 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			

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

Non-serious adverse events	Placebo	JNJ-53718678 80 mg	JNJ-53718678 500 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	11 / 24 (45.83%)	13 / 24 (54.17%)	6 / 24 (25.00%)
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 24 (0.00%)	2 / 24 (8.33%)	0 / 24 (0.00%)
occurrences (all)	0	2	0
Headache			

subjects affected / exposed	3 / 24 (12.50%)	2 / 24 (8.33%)	0 / 24 (0.00%)
occurrences (all)	3	2	0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	9 / 24 (37.50%)	9 / 24 (37.50%)	5 / 24 (20.83%)
occurrences (all)	10	14	5
Vomiting			
subjects affected / exposed	1 / 24 (4.17%)	3 / 24 (12.50%)	0 / 24 (0.00%)
occurrences (all)	1	3	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	3 / 24 (12.50%)	0 / 24 (0.00%)	0 / 24 (0.00%)
occurrences (all)	3	0	0
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	2 / 24 (8.33%)	1 / 24 (4.17%)	0 / 24 (0.00%)
occurrences (all)	3	1	0
Rash			
subjects affected / exposed	1 / 24 (4.17%)	2 / 24 (8.33%)	0 / 24 (0.00%)
occurrences (all)	1	2	0
Infections and infestations			
Urinary Tract Infection			
subjects affected / exposed	0 / 24 (0.00%)	2 / 24 (8.33%)	1 / 24 (4.17%)
occurrences (all)	0	2	1

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
24 April 2019	The amendment 1 included the following changes: some other minor editorial changes, corrections, and clarifications: replaced the RI-PRO questionnaire by the RiiQ questionnaire for the assessment of the duration and severity of signs and symptoms of RSV infection as reported by the subject, for all newly enrolled subjects after approval of the amendment.

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.

The RiiQ Scale that replaced RI-PRO questionnaire was only evaluated in the 5 subjects who were enrolled after implementation of protocol amendment 1. This sample size was too small to draw conclusions on comparison between RiiQ and RI-PRO results.

Notes: