Clinical trial results:
A Phase 2a, randomized, double-blinded, placebo-controlled study to evaluate the antiviral activity, safety, and pharmacokinetics of repeated doses of orally administered JNJ-53718678 against Respiratory Syncytial Virus (RSV) infection in the virus challenge model in healthy adult subjects.

Summary

EudraCT number	2014-005041-41
Trial protocol	GB
Global end of trial date	02 October 2015

Results information

Result version number	v1 (current)
This version publication date	11 November 2016
First version publication date	11 November 2016

Trial information

Trial identification

Sponsor protocol code	53718678RSV2001

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02387606
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Janssen Sciences Ireland UC
Sponsor organisation address	Eastgate Village, Eastgate Little Island, Co. Cork, Ireland,
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 October 2015
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	02 October 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective was to evaluate the antiviral effect (nasal wash respiratory syncytial virus [RSV] area under the viral load-time curve [VL AUC] by quantitative reverse transcriptase-polymerase chain reaction [qRT-PCR]) assay of repeated oral dosing of JNJ-53718678 compared to placebo in healthy adult subjects infected through inoculation with RSV-A Memphis 37b virus.

Protection of trial subjects:

Safety assessments included adverse event (AE) analysis, clinical laboratory tests, electrocardiogram (ECG), vital sign assessments, and physical examination. Special events of interest were the coagulation system (prothrombin [PT] and activated partial thromboplastin time [aPTT]) as well as liver/gall bladder toxicities (alanine aminotransferase [ALT], aspartate aminotransferase [AST], bilirubin).

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	11 May 2015
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	United Kingdom: 66
Worldwide total number of subjects	66
EEA total number of subjects	66

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)	66
From 65 to 84 years	0

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted from 11 May 2015 to 02 October 2015.

Pre-assignment

Screening details:

Total 69 subjects were inoculated out of which 66 subjects were randomised and dosed in this study.

Period 1

Period 1 title	Overall (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:

Placebo was administered as 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:

Placebo was administered as oral solution once daily

Arm title	JNJ-53718678 75 milligram (mg) once daily

Arm description:

JNJ-53718678 75 mg was administered as 7.5 milliliter (ml) once daily as oral solution for 7 days in cohort 2.

Arm type	Experimental
Investigational medicinal product name	JNJ-53718678 75 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral solution
Routes of administration	Oral use

Dosage and administration details:

JNJ-53718678 75 mg was administered as 7.5 ml as oral solution once daily for 7 days

Arm title	JNJ-53718678 200 mg once daily

Arm description:

JNJ-53718678 200 mg was administered as 20 ml oral solution once daily for 7 days in both cohort 1 and cohort 2.

Arm type	Experimental

Investigational medicinal product name	JNJ-53718678 200 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral solution
Routes of administration	Oral use

Dosage and administration details:

JNJ-53718678 200 mg was administered as 20 ml oral solution once daily for 7 days in both cohort 1 and cohort 2.

Arm title	JNJ-53718678 500 mg once daily

Arm description:

JNJ-53718678 500 mg was administered as 50 ml oral solution once daily for 7 days in both cohort 1 and cohort 2

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:

JNJ-53718678 500 mg was administered as 50 ml oral solution once daily for 7 days in both cohort 1 and cohort 2

Number of subjects in period 1	Placebo	JNJ-53718678 75 milligram (mg) once daily	JNJ-53718678 200 mg once daily
Started	16	15	17
Completed	15	13	16
Not completed	1	2	1
Adverse event, non-fatal	1	1	1
Other	-	1	-

Number of subjects in period 1	JNJ-53718678 500 mg once daily
Started	18
Completed	17
Not completed	1
Adverse event, non-fatal	-
Other	1

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Placebo was administered as oral solution once daily for 7 days.	
Reporting group title	JNJ-53718678 75 milligram (mg) once daily
Reporting group description:	
JNJ-53718678 75 mg was administered as 7.5 milliliter (ml) once daily as oral solution for 7 days in cohort 2.	
Reporting group title	JNJ-53718678 200 mg once daily
Reporting group description:	
JNJ-53718678 200 mg was administered as 20 ml oral solution once daily for 7 days in both cohort 1 and cohort 2.	
Reporting group title	JNJ-53718678 500 mg once daily
Reporting group description:	
JNJ-53718678 500 mg was administered as 50 ml oral solution once daily for 7 days in both cohort 1 and cohort 2	

Reporting group values	Placebo	JNJ-53718678 75 milligram (mg) once daily	JNJ-53718678 200 mg once daily
Number of subjects	16	15	17
Title for AgeCategorical			
Units: subjects			
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	16	15	17
From 65 to 84 years	0	0	0
85 years and over	0	0	0
Title for AgeContinuous			
Units: years			
arithmetic mean	24.3	24	21.7
standard deviation	± 4.06	± 5.55	± 2.52
Title for Gender			
Units: subjects			
Male	16	15	17

Reporting group values	JNJ-53718678 500 mg once daily	Total	
Number of subjects	18	66	
Title for AgeCategorical			
Units: subjects			
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	18	66	
From 65 to 84 years	0	0	
85 years and over	0	0	
Title for AgeContinuous			
Units: years			
arithmetic mean	22.1		

standard deviation	± 2.8	-	

Title for Gender Units: subjects			
Male	18	66	

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Placebo was administered as oral solution once daily for 7 days.	
Reporting group title	JNJ-53718678 75 milligram (mg) once daily
Reporting group description:	
JNJ-53718678 75 mg was administered as 7.5 milliliter (ml) once daily as oral solution for 7 days in cohort 2.	
Reporting group title	JNJ-53718678 200 mg once daily
Reporting group description:	
JNJ-53718678 200 mg was administered as 20 ml oral solution once daily for 7 days in both cohort 1 and cohort 2.	
Reporting group title	JNJ-53718678 500 mg once daily
Reporting group description:	
JNJ-53718678 500 mg was administered as 50 ml oral solution once daily for 7 days in both cohort 1 and cohort 2	

Primary: Area Under the Viral Load-time Curve (VL AUC) Over Time Measured With Quantitative Reverse Transcriptase –Polymerase Chain Reaction (qRT-PCR) Assay

End point title	Area Under the Viral Load-time Curve (VL AUC) Over Time Measured With Quantitative Reverse Transcriptase –Polymerase Chain Reaction (qRT-PCR) Assay

End point description:

VL for RSV-A Memphis 37b was determined by quantitative reverse transcriptase -polymerase chain reaction (qRT-PCR) assay of nasal wash. The VL AUC was calculated based on the viral load values measured 2 times per day, starting with the last value prior to first dosing, and ending with the last available value before discharge (day 13). Here, intent-to-treat-infected (ITT-I) population was defined as all subjects who were challenged by virus inoculation with a positive viral load value (measured with qRT-PCR assay) immediately prior to first dosing or with 2 or more positive viral load values (measured with qRT-PCR assay) after the first administration of study medication and who received at least one dose of JNJ-53718678 or placebo.

End point type	Primary

End point timeframe:

Baseline up to discharge (Day 13)

End point values	Placebo	JNJ-53718678 75 milligram (mg) once daily	JNJ-53718678 200 mg once daily	JNJ-53718678 500 mg once daily
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	12	9	12	12
Units: log10 PFUe*hour per ml				
least squares mean (confidence interval 95%)	432.8 (272.4 to 593.2)	240.3 (42.3 to 438.4)	203.8 (96.7 to 310.8)	253.8 (135.4 to 372.2)

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v JNJ-53718678 75 milligram (mg) once daily
Number of subjects included in analysis	21
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.105
Method	Least Squares Estimates
Parameter estimate	Mean difference (net)
Point estimate	-192.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-429.6
upper limit	44.7

Statistical analysis title	Statistical Analysis 2
Comparison groups	JNJ-53718678 200 mg once daily v Placebo
Number of subjects included in analysis	24
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0167
Method	Least Squares Estimates
Parameter estimate	Mean difference (net)
Point estimate	-229
Confidence interval	
level	95 %
sides	2-sided
lower limit	-411.8
upper limit	-46.2

Statistical analysis title	Statistical Analysis 3
Comparison groups	Placebo v JNJ-53718678 500 mg once daily

Number of subjects included in analysis	24
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0629
Method	Least Squares Estimates
Parameter estimate	Mean difference (net)
Point estimate	-179
Confidence interval	
level	95 %
sides	2-sided
lower limit	-368.6
upper limit	10.6

Secondary: Area Under Curve of Viral Load From Time 0 to 7 Days After First Dose Measured With qRT-PCR Assay

End point title	Area Under Curve of Viral Load From Time 0 to 7 Days After First Dose Measured With qRT-PCR Assay

End point description:

VL for RSV-A Memphis 37b was determined by quantitative reverse transcriptase -polymerase chain reaction (qRT-PCR) assay of nasal wash. The VL AUC was calculated based on the viral load values measured 2 times per day, starting with the last value prior to first dosing, and ending with the last available value on dosing day 7. Here, intent-to-treat-infected (ITT-I) population was defined as all subjects who were challenged by virus inoculation with a positive viral load value (measured with qRT-PCR assay) immediately prior to first dosing or with 2 or more positive viral load values (measured with qRT-PCR assay) after the first administration of study medication and who received at least one dose of JNJ-53718678 or placebo.

End point type	Secondary

End point timeframe:

Baseline through day 7 of dose.

End point values	Placebo	JNJ-53718678 75 milligram (mg) once daily	JNJ-53718678 200 mg once daily	JNJ-53718678 500 mg once daily
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	12	9	12	12
Units: log10 PFUe * hour per ml				
least squares mean (confidence interval 95%)	390.5 (265.7 to 515.4)	205.5 (61.3 to 349.7)	192.9 (68 to 317.7)	268.1 (143.2 to 392.9)

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under Curve of Viral Load-Time From Time 0 to 24 Hours After First Dose Measured With qRT-PCR Assay

End point title	Area Under Curve of Viral Load-Time From Time 0 to 24 Hours

	After First Dose Measured With qRT-PCR Assay

End point description:

VL for RSV-A Memphis 37b was determined by quantitative reverse transcriptase -polymerase chain reaction (qRT-PCR) assay of nasal wash. The VL AUC was calculated based on the viral load values measured 2 times per day, starting with the last value prior to first dosing, and ending with the value 24 hours after start of dosing. Here, intent-to-treat-infected (ITT-I) population was defined as all subjects who were challenged by virus inoculation with a positive viral load value (measured with qRT-PCR assay) immediately prior to first dosing or with 2 or more positive viral load values (measured with qRT-PCR assay) after the first administration of study medication and who received at least one dose of JNJ-53718678 or placebo.

End point type	Secondary

End point timeframe:

Baseline to 24 hours after first dose

End point values	Placebo	JNJ-53718678 75 milligram (mg) once daily	JNJ-53718678 200 mg once daily	JNJ-53718678 500 mg once daily
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	12	9	12	12
Units: log10 PFUe*hour per ml				
least squares mean (confidence interval 95%)	43 (25.4 to 60.5)	35.8 (15.4 to 56.1)	54.5 (36.9 to 72.1)	65 (47.4 to 82.6)

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under Curve of Viral Load-Time From Time 0 to 48 Hours After First Dose Measured With qRT-PCR Assay

End point title	Area Under Curve of Viral Load-Time From Time 0 to 48 Hours After First Dose Measured With qRT-PCR Assay

End point description:

VL for RSV-A Memphis 37b was determined by quantitative reverse transcriptase -polymerase chain reaction (qRT-PCR) assay of nasal wash. The VL AUC was calculated based on the viral load values measured 2 times per day, starting with the last value prior to first dosing, and ending with the value 48 hours after start of dosing. Here, intent-to-treat-infected (ITT-I) population was defined as all subjects who were challenged by virus inoculation with a positive viral load value (measured with qRT-PCR assay) immediately prior to first dosing or with 2 or more positive viral load values (measured with qRT-PCR assay) after the first administration of study medication and who received at least one dose of JNJ-53718678 or placebo.

End point type	Secondary

End point timeframe:

Baseline to 48 hours after first dose

End point values	Placebo	JNJ-53718678 75 milligram (mg) once daily	JNJ-53718678 200 mg once daily	JNJ-53718678 500 mg once daily
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	12	9	12	12
Units: log10 PFUe*hour per ml				
least squares mean (confidence interval 95%)	112.2 (71.7 to 152.7)	83.5 (36.8 to 130.3)	100.9 (60.4 to 141.4)	125.9 (85.4 to 166.4)

Statistical analyses

No statistical analyses for this end point

Secondary: Peak Viral Load Measured With qRT-PCR Assay

End point title	Peak Viral Load Measured With qRT-PCR Assay

End point description:

Peak viral load is defined as the maximum viral load value from baseline up to discharge. Here, intent-to-treat-infected (ITT-I) population was defined as all subjects who were challenged by virus inoculation with a positive viral load value (measured with qRT-PCR assay) immediately prior to first dosing or with 2 or more positive viral load values (measured with qRT-PCR assay) after the first administration of study medication and who received at least one dose of JNJ-53718678 or placebo.

End point type	Secondary

End point timeframe:

Baseline up to discharge (Day 13)

End point values	Placebo	JNJ-53718678 75 milligram (mg) once daily	JNJ-53718678 200 mg once daily	JNJ-53718678 500 mg once daily
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	12	9	12	12
Units: log10 PFUe				
least squares mean (confidence interval 95%)	4.7 (3.7 to 5.7)	3.2 (2 to 4.3)	3.4 (2.4 to 4.4)	4 (3 to 5)

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Total Clinical Symptom Score

End point title	Overall Total Clinical Symptom Score

End point description:

Total (i.e sum) clinical symptom score was assessed using a composite of 10 self-reported symptoms on the Symptom Diary Card (SDC). Every Symptom Score ranges from 0 to 3. The overall total Clinical Symptom Score is the sum of all total Clinical Symptom Scores across all days. Here, intent-to-treat-infected (ITT-I) population was defined as all subjects who were challenged by virus inoculation with a positive viral load value (measured with qRT-PCR assay) immediately prior to first dosing or with 2 or

more positive viral load values (measured with qRT-PCR assay) after the first administration of study medication and who received at least one dose of JNJ-53718678 or placebo.

End point type	Secondary
End point timeframe:	
Baseline up to discharge (Day 13)	

End point values	Placebo	JNJ-53718678 75 milligram (mg) once daily	JNJ-53718678 200 mg once daily	JNJ-53718678 500 mg once daily
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	12	9	12	12
Units: Units on a scale				
least squares mean (confidence interval 95%)	36.6 (20.4 to 52.8)	6.4 (-12.3 to 25.2)	23.1 (6.9 to 39.3)	14.8 (-1.4 to 31.1)

Statistical analyses

No statistical analyses for this end point

Secondary: Peak Total Clinical Symptom Score

End point title	Peak Total Clinical Symptom Score
End point description:	
The peak total symptom score was the maximum of the total symptom score values for 1 subject. Here, intent-to-treat-infected (ITT-I) population was defined as all subjects who were challenged by virus inoculation with a positive viral load value (measured with qRT-PCR assay) immediately prior to first dosing or with 2 or more positive viral load values (measured with qRT-PCR assay) after the first administration of study medication and who received at least one dose of JNJ-53718678 or placebo.	
End point type	Secondary
End point timeframe:	
Baseline up to discharge (Day 13)	

End point values	Placebo	JNJ-53718678 75 milligram (mg) once daily	JNJ-53718678 200 mg once daily	JNJ-53718678 500 mg once daily
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	12	9	12	12
Units: Units on a scale				
least squares mean (confidence interval 95%)	5 (2.9 to 7.1)	1.3 (-1 to 3.7)	2.6 (0.5 to 4.6)	1.9 (-0.1 to 4)

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Tissues Used

End point title	Number of Tissues Used

End point description:

Here, intent-to-treat-infected (ITT-I) population was defined as all subjects who were challenged by virus inoculation with a positive viral load value (measured with qRT-PCR assay) immediately prior to first dosing or with 2 or more positive viral load values (measured with qRT-PCR assay) after the first administration of study medication and who received at least one dose of JNJ-53718678 or placebo.

End point type	Secondary

End point timeframe:

Baseline up to discharge (Day 13)

End point values	Placebo	JNJ-53718678 75 milligram (mg) once daily	JNJ-53718678 200 mg once daily	JNJ-53718678 500 mg once daily
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	12	9	12	12
Units: Number				
arithmetic mean (standard deviation)	25.3 (± 25.99)	14.9 (± 28.31)	6.8 (± 6.31)	11.3 (± 8.41)

Statistical analyses

No statistical analyses for this end point

Secondary: Weight of Mucus

End point title	Weight of Mucus

End point description:

Here, intent-to-treat-infected (ITT-I) population was defined as all subjects who were challenged by virus inoculation with a positive viral load value (measured with qRT-PCR assay) immediately prior to first dosing or with 2 or more positive viral load values (measured with qRT-PCR assay) after the first administration of study medication and who received at least one dose of JNJ-53718678 or placebo.

End point type	Secondary

End point timeframe:

Baseline up to discharge (Day 13)

End point values	Placebo	JNJ-53718678 75 milligram (mg) once daily	JNJ-53718678 200 mg once daily	JNJ-53718678 500 mg once daily
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	12	9	12	12
Units: Grams				
arithmetic mean (standard deviation)	10.111 (±	7.014 (±	2.994 (±	4.798 (±

14.9639)	15.5249)	3.7404)	5.1623)

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under Curve of Viral Load Over Time Measured With Plaque Assay

End point title	Area Under Curve of Viral Load Over Time Measured With Plaque Assay

End point description:

VL for RSV-A Memphis 37b was determined by plaque forming unit (PFU) assay of nasal wash. The VL AUC was calculated based on the VL values measured 2 times per day, starting with the last value prior to first dosing, and ending with the last available value before discharge (day 13). Here, intent-to-treat-infected (ITT-I) population was defined as all subjects who were challenged by virus inoculation with a positive viral load value (measured with qRT-PCR assay) immediately prior to first dosing or with 2 or more positive viral load values (measured with qRT-PCR assay) after the first administration of study medication and who received at least one dose of JNJ-53718678 or placebo.

End point type	Secondary

End point timeframe:

Baseline up to discharge (Day 13)

End point values	Placebo	JNJ-53718678 75 milligram (mg) once daily	JNJ-53718678 200 mg once daily	JNJ-53718678 500 mg once daily
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	12	9	12	12
Units: log10 PFU*hour per ml				
least squares mean (confidence interval 95%)	282.1 (183.2 to 380.9)	206.6 (92.4 to 320.7)	150.6 (51.7 to 249.5)	256 (157.1 to 354.9)

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under Curve of Viral Load-Time From Time 0 to 24 Hours After First Dose Measured With Plaque Assay

End point title	Area Under Curve of Viral Load-Time From Time 0 to 24 Hours After First Dose Measured With Plaque Assay

End point description:

VL for RSV-A Memphis 37b was determined by plaque forming unit (PFU) assay of nasal wash. The VL AUC was calculated based on the VL values measured 2 times per day, starting with the last available value prior to first dosing, and ending with the value 24 hours after start of dosing. Here, intent-to-treat-infected (ITT-I) population was defined as all subjects who were challenged by virus inoculation with a positive viral load value (measured with qRT-PCR assay) immediately prior to first dosing or with 2 or more positive viral load values (measured with qRT-PCR assay) after the first administration of study medication and who received at least one dose of JNJ-53718678 or placebo.

End point type	Secondary

End point timeframe:

Baseline up to 24 hours after first dose

End point values	Placebo	JNJ-53718678 75 milligram (mg) once daily	JNJ-53718678 200 mg once daily	JNJ-53718678 500 mg once daily
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	12	9	12	12
Units: log10 PFU*hour per ml				
least squares mean (confidence interval 95%)	20.4 (4 to 36.8)	27 (8 to 45.9)	27.3 (10.9 to 43.8)	48.5 (32.1 to 64.9)

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under Curve of Viral Load-Time From Time 0 to 48 Hours After First Dose Measured With Plaque Assay

End point title	Area Under Curve of Viral Load-Time From Time 0 to 48 Hours After First Dose Measured With Plaque Assay

End point description:

VL for RSV-A Memphis 37b was determined by plaque forming unit (PFU) assay of nasal wash. The VL AUC was calculated based on the VL values measured 2 times per day, starting with the last value prior to first dosing, and ending with the last available value prior to first dosing, and ending with the value 48 hours after start of dosing. Here, intent-to-treat-infected (ITT-I) population was defined as all subjects who were challenged by virus inoculation with a positive viral load value (measured with qRT-PCR assay) immediately prior to first dosing or with 2 or more positive viral load values (measured with qRT-PCR assay) after the first administration of study medication and who received at least one dose of JNJ-53718678 or placebo.

End point type	Secondary

End point timeframe:

Baseline up to 48 hours after first dose

End point values	Placebo	JNJ-53718678 75 milligram (mg) once daily	JNJ-53718678 200 mg once daily	JNJ-53718678 500 mg once daily
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	12	9	12	12
Units: log10 PFUe*hour per ml				
least squares mean (confidence interval 95%)	72.7 (37.5 to 108)	63.5 (22.8 to 104.2)	59 (23.8 to 94.3)	103.6 (68.4 to 138.8)

Statistical analyses

No statistical analyses for this end point

Secondary: Peak Viral Load Measured With Plaque Assay

End point title	Peak Viral Load Measured With Plaque Assay

End point description:

Here, intent-to-treat-infected (ITT-I) population was defined as all subjects who were challenged by virus inoculation with a positive viral load value (measured with qRT-PCR assay) immediately prior to first dosing or with 2 or more positive viral load values (measured with qRT-PCR assay) after the first administration of study medication and who received at least one dose of JNJ-53718678 or placebo.

End point type	Secondary

End point timeframe:

Baseline up to discharge (Day 13)

End point values	Placebo	JNJ-53718678 75 milligram (mg) once daily	JNJ-53718678 200 mg once daily	JNJ-53718678 500 mg once daily
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	12	9	12	12
Units: log10 PFU				
least squares mean (confidence interval 95%)	4.2 (3.3 to 5.2)	2.7 (1.6 to 3.8)	2.9 (2 to 3.9)	3.7 (2.7 to 4.6)

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under Curve of Viral Load From Time 0 to 7 Days After First Dose Measured With Plaque Assay

End point title	Area Under Curve of Viral Load From Time 0 to 7 Days After First Dose Measured With Plaque Assay

End point description:

VL for RSV-A Memphis 37b was determined by plaque forming unit (PFU) assay of nasal wash. The VL AUC was calculated based on the VL values measured 2 times per day, starting with the last value prior to first dosing, and ending with the last available value 7 days after start of dosing. Here, intent-to-treat-infected (ITT-I) population was defined as all subjects who were challenged by virus inoculation with a positive viral load value (measured with qRT-PCR assay) immediately prior to first dosing or with 2 or more positive viral load values (measured with qRT-PCR assay) after the first administration of study medication and who received at least one dose of JNJ-53718678 or placebo.

End point type	Secondary

End point timeframe:

Baseline through 7 days after first dose

End point values	Placebo	JNJ-53718678 75 milligram (mg) once daily	JNJ-53718678 200 mg once daily	JNJ-53718678 500 mg once daily
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	12	9	12	12
Units: log10 PFU*hour per ml				
least squares mean (confidence interval 95%)	265 (174.8 to 355.2)	170.3 (66.2 to 274.5)	130.9 (40.7 to 221.1)	215 (124.8 to 305.2)

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: Baseline through Day 28	
Assessment type	Non-systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	17.1
Reporting groups	
Reporting group title	Placebo
Reporting group description: JNJ-53718678 500 mg was administered as 50 ml oral solution once daily for 7 days in both cohort 1 and cohort 2	
Reporting group title	JNJ-53718678 75 mg qd
Reporting group description: JNJ-53718678 75 mg is administered as 7.5 milliliter (ml) once daily as oral solution for 7 days in cohort 2	
Reporting group title	JNJ-53718678 200 mg qd
Reporting group description: JNJ-53718678 200 mg was administered as 20 ml oral solution once daily for 7 days in both cohort 1 and cohort 2	
Reporting group title	JNJ-53718678 500 mg qd
Reporting group description: JNJ-53718678 500 mg was administered as 50 ml oral solution once daily for 7 days in both cohort 1 and cohort 2	

Serious adverse events	Placebo	JNJ-53718678 75 mg qd	JNJ-53718678 200 mg qd
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 17 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			

Serious adverse events	JNJ-53718678 500 mg qd		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 18 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			

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

Non-serious adverse events	Placebo	JNJ-53718678 75 mg qd	JNJ-53718678 200 mg qd
Total subjects affected by non-serious adverse events			
subjects affected / exposed	9 / 16 (56.25%)	8 / 15 (53.33%)	13 / 17 (76.47%)
Vascular disorders			
Haematoma			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Vessel Puncture Site Bruise			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Respiratory, thoracic and mediastinal disorders			
Epistaxis			
subjects affected / exposed	0 / 16 (0.00%)	2 / 15 (13.33%)	6 / 17 (35.29%)
occurrences (all)	0	2	7
Investigations			
Activated Partial Thromboplastin Time Prolonged			
subjects affected / exposed	2 / 16 (12.50%)	2 / 15 (13.33%)	1 / 17 (5.88%)
occurrences (all)	2	2	1
Alanine Aminotransferase Increased			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Bilirubin Conjugated Increased			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Blood Cholesterol Increased			
subjects affected / exposed	0 / 16 (0.00%)	4 / 15 (26.67%)	0 / 17 (0.00%)
occurrences (all)	0	4	0
Blood Creatinine Increased			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Blood Fibrinogen Decreased			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Electrocardiogram Pr Prolongation			

subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
C-Reactive Protein Increased			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Electrocardiogram QRS Complex Prolonged			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
Low Density Lipoprotein Increased			
subjects affected / exposed	0 / 16 (0.00%)	3 / 15 (20.00%)	0 / 17 (0.00%)
occurrences (all)	0	3	0
Electrocardiogram Change			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	1 / 17 (5.88%)
occurrences (all)	0	1	1
Neutrophil Count Decreased			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Spirometry Abnormal			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
Limb Injury			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Cardiac disorders			
Tachycardia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Palpitations			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			

Dizziness			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Eye disorders			
Ocular Hyperaemia			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	4 / 16 (25.00%)	0 / 15 (0.00%)	3 / 17 (17.65%)
occurrences (all)	4	0	3
Abdominal Pain			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Toothache			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Skin and subcutaneous tissue disorders			
Dermatitis Contact			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Dermatitis Allergic			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Erythema			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	2 / 17 (11.76%)
occurrences (all)	0	0	2
Rash Erythematous			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Rash Macular			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1

Urticaria			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Groin Pain			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal Chest Pain			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Decreased Appetite			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	JNJ-53718678 500 mg qd		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	13 / 18 (72.22%)		
Vascular disorders			
Haematoma			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
General disorders and administration site conditions			
Vessel Puncture Site Bruise			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Respiratory, thoracic and mediastinal disorders			
Epistaxis			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Investigations			
Activated Partial Thromboplastin Time Prolonged			

subjects affected / exposed	0 / 18 (0.00%)			
occurrences (all)	0			
Alanine Aminotransferase Increased				
subjects affected / exposed	0 / 18 (0.00%)			
occurrences (all)	0			
Bilirubin Conjugated Increased				
subjects affected / exposed	0 / 18 (0.00%)			
occurrences (all)	0			
Blood Cholesterol Increased				
subjects affected / exposed	1 / 18 (5.56%)			
occurrences (all)	1			
Blood Creatinine Increased				
subjects affected / exposed	1 / 18 (5.56%)			
occurrences (all)	1			
Blood Fibrinogen Decreased				
subjects affected / exposed	0 / 18 (0.00%)			
occurrences (all)	0			
Electrocardiogram Pr Prolongation				
subjects affected / exposed	0 / 18 (0.00%)			
occurrences (all)	0			
C-Reactive Protein Increased				
subjects affected / exposed	0 / 18 (0.00%)			
occurrences (all)	0			
Electrocardiogram QRS Complex Prolonged				
subjects affected / exposed	0 / 18 (0.00%)			
occurrences (all)	0			
Low Density Lipoprotein Increased				
subjects affected / exposed	0 / 18 (0.00%)			
occurrences (all)	0			
Electrocardiogram Change				
subjects affected / exposed	0 / 18 (0.00%)			
occurrences (all)	0			
Neutrophil Count Decreased				
subjects affected / exposed	0 / 18 (0.00%)			
occurrences (all)	0			

Spirometry Abnormal			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Limb Injury			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Cardiac disorders			
Tachycardia			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Palpitations			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Eye disorders			
Ocular Hyperaemia			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	9 / 18 (50.00%)		
occurrences (all)	10		
Abdominal Pain			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Toothache			

subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0		
Skin and subcutaneous tissue disorders Dermatitis Contact subjects affected / exposed occurrences (all) Dermatitis Allergic subjects affected / exposed occurrences (all) Erythema subjects affected / exposed occurrences (all) Rash Erythematous subjects affected / exposed occurrences (all) Rash Macular subjects affected / exposed occurrences (all) Urticaria subjects affected / exposed occurrences (all)	 0 / 18 (0.00%) 0 0 / 18 (0.00%) 0 0 / 18 (0.00%) 0 0 / 18 (0.00%) 0 0 / 18 (0.00%) 0 0 / 18 (0.00%) 0		
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) Groin Pain subjects affected / exposed occurrences (all) Musculoskeletal Chest Pain subjects affected / exposed occurrences (all)	 0 / 18 (0.00%) 0 1 / 18 (5.56%) 1 1 / 18 (5.56%) 1		
Metabolism and nutrition disorders Decreased Appetite subjects affected / exposed occurrences (all)	 1 / 18 (5.56%) 1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
02 June 2015	Amendment was created to make the time window for start of dosing after a positive RSV-detection test in Cohort 2 flexible, in line with other dosing decisions for Cohort 2 which were also determined based upon the emerging data from Cohort 1. In addition, some updates occured: for consistency between the protocol body text and the Time and Events Schedule, the Time and Events Schedule was updated to indicate that (1) nasal wash samples for the RSV positivity assay were collected from Study Day 2 onwards and that (2) the SDC also had to be completed on Study Day 1. To make the differences between Cohort 1 and Cohort 2 clearer, the time and events schedule was split up in 2 separate tables (1 for each cohort). Due to a company name change, Retroscreen Virology Limited was replaced by hVIVO. For consistency within the protocol, the limit for the PR-interval was changed from <220 millisecound (msec) to <210 msec, in line with the determination of values greater than or equal to (>=) 210 msec as "abnormally high". Minor errors were corrected.
28 August 2015	The protocol was updated to include a third cohort of 8 or 12 subjects (randomized 3:1 to JNJ-53718678 75 mg or placebo, respectively), depending on the combined infection rate for Cohort 1 and Cohort 2, to supplement the number of subjects dosed with 75 mg in Cohort 2 with the purpose of having overall an approximately equal number of infected subjects (in the ITT-I population which was used for the efficacy analysis) on each dose level evaluated (ie, JNJ-53718678 75 mg, 200 mg, and 500 mg). As a result of the decision on the doses in Cohort 2, for Cohorts 1 and 2 combined, 18 subjects were planned to be randomized to either the JNJ-53718678 200-mg or 500-mg dose level, whereas only 12 subjects were planned to be randomized to the JNJ-53718678 75-mg dose. In line with the decisions for Cohort 2, the duration of dosing in Cohort 3 was to be 7 days, the dosing regimen qd, and the start of treatment approximately 12 hours after positive PCR or in the morning of Day 6 for non-infected subjects, while the assessment schedule was to be the same as for Cohort 1. In view of the addition of Cohort 3, the final analysis including data from all cohorts was to be performed after completion of Cohort 3. However, in view of further development activities, an unblinded interim analysis on the combined data from Cohort 1 and Cohort 2 was planned after completion of Cohort 2. It was clarified that additional subjects could be recruited in case of a dropout after receiving the first dose of study for reasons other than safety. If a subject dropped out of the study due to safety concerns, no additional subject could be recruited to replace this subject. Cohort 3 was not performed and the final analysis was performed after completion of cohort 2.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported