



Clinical trial results:

A Randomized, Double-blind, Placebo-controlled Study to Evaluate the Clinical Outcomes, Antiviral Activity, Safety, Tolerability, Pharmacokinetics, and Pharmacokinetics/Pharmacodynamics of JNJ-53718678 in Adult and Adolescent Hematopoietic Stem Cell Transplant Recipients with Respiratory Syncytial Virus Infection of the Upper Respiratory Tract

Summary

EudraCT number	2019-001551-39
Trial protocol	FR GB DE ES SE BE BG IT
Global end of trial date	04 February 2022

Results information

Result version number	v1 (current)
This version publication date	09 February 2023
First version publication date	09 February 2023

Trial information

Trial identification

Sponsor protocol code	53718678RSV2005
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04056611
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Janssen Sciences Ireland UC
Sponsor organisation address	Barnahely, Cork, Ringaskiddy, Ireland, P43 FA46
Public contact	Clinical Registry Group, Janssen Sciences Ireland UC, ClinicalTrialsEU@its.jnj.com
Scientific contact	Clinical Registry Group, Janssen Sciences Ireland UC, 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	04 February 2022
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	04 February 2022
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The main objective of this trial was to evaluate the effect of JNJ-53718678 on the development of respiratory syncytial virus (RSV) lower respiratory tract infection (LRTI) in adult hematopoietic stem cell transplant recipients with RSV upper respiratory tract infection (URTI).

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.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	26 December 2019
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	France: 1
Country: Number of subjects enrolled	Brazil: 1
Country: Number of subjects enrolled	Israel: 1
Worldwide total number of subjects	3
EEA total number of subjects	1

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)	3
From 65 to 84 years	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Randomised subjects received rilematovir treatment. The dose of rilematovir was dependent upon coadministration without/with cytochrome P450 3A4 inhibitors or with posaconazole.

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

Arm title	JNJ-53718678
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Arm description:

Subjects with age of greater than or equal to (\geq) 18 to less than or equal to (\leq) 75 years received rilematovir 125 milligrams (mg) twice daily (bid) for 21 days.

Arm type	Experimental
Investigational medicinal product name	JNJ-53718678
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received JNJ-53718678 125 mg bid for 21 days.

Number of subjects in period 1	JNJ-53718678
Started	3
Completed	2
Not completed	1
Physician decision	1

Baseline characteristics

Reporting groups

Reporting group title	JNJ-53718678
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Reporting group description:

Subjects with age of greater than or equal to (\geq) 18 to less than or equal to (\leq) 75 years received rilematovir 125 milligrams (mg) twice daily (bid) for 21 days.

Reporting group values	JNJ-53718678	Total	
Number of subjects	3	3	
Age categorical			
Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	3	3	
From 65-84 years	0	0	
85 years and over	0	0	
Age continuous			
Units: years			
arithmetic mean	47		
standard deviation	± 13.89	-	
Sex: Female, Male			
Units: subjects			
Female	1	1	
Male	2	2	

End points

End points reporting groups

Reporting group title	JNJ-53718678
Reporting group description:	
Subjects with age of greater than or equal to (\geq) 18 to less than or equal to (\leq) 75 years received rilematovir 125 milligrams (mg) twice daily (bid) for 21 days.	

Primary: Percentage of Subjects Who Developed Respiratory Syncytial Virus (RSV) Lower Respiratory Tract Infection (LRTI)

End point title	Percentage of Subjects Who Developed Respiratory Syncytial Virus (RSV) Lower Respiratory Tract Infection (LRTI) ^[1]
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End point description:

RSV LRTI: defined as development of lower respiratory sign/symptom (eg, decrease in oxygen (O₂) saturation/increase in supplemental O₂ to maintain O₂ saturation, wheezing, rhonchi, rales, dyspnea, tachypnea, worsening cough) & positive RSV test from lower respiratory tract (LRT) sample (eg, sputum [S], induced sputum [IS], bronchoalveolar lavage [BAL], lung biopsy [LB]/ autopsy specimen [AS]) within ± 4 days of new chest image finding, compared to baseline, consistent with LRTI; OR positive RSV test from LRT sample (eg, S, IS, BAL, LB/AS) only; OR positive RSV test from upper respiratory tract sample within ± 4 days of new chest image finding, compared to baseline, consistent with RSV LRTI determined by Endpoint Adjudication Committee. Efficacy analysis set: all subjects randomised, treated (had at least 1 dose) & had RSV infection confirmed by central laboratory analysis, excluding subjects infected with co-pathogen at baseline not identified during screening, analysed as randomised.

End point type	Primary
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End point timeframe:

Up to Day 28

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: No inferential statistics was planned for this primary endpoint.

End point values	JNJ-53718678			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: Percentage of subjects				
number (not applicable)	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Who Developed RSV-associated Lower Respiratory Tract Complication (LRTC)

End point title	Percentage of Subjects Who Developed RSV-associated Lower Respiratory Tract Complication (LRTC)
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End point description:

Percentage of subjects who developed RSV-associated LRTC was assessed. RSV-associated LRTC: development of a lower respiratory sign or symptom (including decrease in oxygen saturation or increase in supplemental oxygen to maintain oxygen saturation, wheezing, rhonchi, rales, dyspnea, tachypnea, and worsening cough) and met one of following subcategories determined by Endpoint Adjudication Committee (EAC): a) RSV LRTI, b) secondary bacterial LRTI, c) secondary LRTI due to

unusual pathogens, d) secondary LRTC of unknown etiology (new chest image finding than baseline, consistent with LRTI, inflammatory process/ some other clinically significant pulmonary process which were absent within 4 days of new chest image finding). Efficacy analysis set: all subjects who were randomised, treated (took at least 1 dose), and had RSV infection confirmed by central laboratory analysis, excluding subjects infected with a co-pathogen at baseline not identified during screening, analyzed as randomised.

End point type	Secondary
End point timeframe:	
Up to Day 28	

End point values	JNJ-53718678			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: Percentage of subjects				
number (not applicable)	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Treatment-emergent Adverse Events (TEAEs)

End point title	Number of Subjects with Treatment-emergent Adverse Events (TEAEs)
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End point description:

An AE is any untoward medical occurrence in a clinical study participant administered a medicinal (investigational or non investigational) product. An AE did not necessarily have a causal relationship with the intervention. Any AE which occurred post 1st dose administration of study drug up to the end of study (i.e., Day 49) was considered as treatment-emergent. The safety analysis set included all randomised subjects who took at least 1 dose of study intervention and were analysed 'as treated'.

End point type	Secondary
End point timeframe:	
Up to Day 49	

End point values	JNJ-53718678			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: Subjects	2			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with Treatment-emergent Abnormal (Grade

>=3) Clinical Laboratory Findings

End point title	Percentage of Subjects with Treatment-emergent Abnormal (Grade >=3) Clinical Laboratory Findings
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End point description:

Percentage of subjects with greater than or equal to (>=) Grade 3 treatment-emergent clinical laboratory abnormalities (platelet count decreased, glucose increase) was assessed in this outcome measure. Treatment-emergent: any abnormality occurred post 1st dose of study drug up to end of study (i.e., Day 49). The safety analysis set included all randomised subjects who took at least 1 dose of study intervention and were analysed 'as treated'.

End point type	Secondary
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End point timeframe:

Up to Day 49

End point values	JNJ-53718678			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: Percentage of subjects				
number (not applicable)				
Platelet count decreased	33.33			
Glucose increase	33.33			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with Clinically Significant Abnormalities in Electrocardiogram (ECG) Findings

End point title	Percentage of Subjects with Clinically Significant Abnormalities in Electrocardiogram (ECG) Findings
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End point description:

Percentage of subjects with clinically significant abnormalities in ECG findings was assessed in this endpoint. Various ECG variables assessed were heart rate: abnormally low (<= 45 beats per minute [bpm]), abnormally high (>= 120 bpm); PR interval: abnormally high (>=210 milliseconds [msec]); QRS interval: abnormally high (>=120 msec), QT interval and corrected QT (QTcF; according to Fridericia's formula) interval (>450 msec, >480 msec, or >500 msec, increases from baseline >30 msec or >60 msec). The safety analysis set included all randomised subjects who took at least 1 dose of study intervention and were analysed 'as treated'.

End point type	Secondary
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End point timeframe:

Up to Day 49

End point values	JNJ-53718678			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: Percentage of subjects				
number (not applicable)				
Heart rate	0			
PR interval	0			
QRS interval	0			
QTcF	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with Treatment-emergent Abnormal Vital Signs Findings

End point title	Percentage of Subjects with Treatment-emergent Abnormal Vital Signs Findings
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End point description:

Percentage of subjects with abnormal vital signs findings was assessed. Abnormal vital parameters included pulse rate: abnormally low ≤ 45 bpm, abnormally high ≥ 120 bpm; SBP: abnormally low ≤ 90 Millimeter of mercury (mmHg), Grade 1 (mild): > 90 mmHg - < 100 mmHg, Grade 2 (moderate): ≥ 100 mmHg to < 110 mmHg, Grade 3 (severe): ≥ 110 mmHg; DBP: abnormally low ≤ 50 mmHg, Grade 1: > 90 mmHg to < 100 mmHg, Grade 2: ≥ 100 mmHg to < 110 mmHg, Grade 3: ≥ 110 mmHg; Respiratory rate-Grade 1 (mild): 17-20 breaths per minute (bpm), Grade 2 (moderate): 21-25 bpm, Grade 3 (severe): > 25 bpm, Grade 4 (potentially life threatening): intubation; Temperature: abnormally high > 38.0 degree celsius. Treatment-emergent: any abnormality occurred post 1st dose of study drug up to EOS (Day 49). Vital signs abnormalities reported for at least 1 subject were reported in this endpoint. The safety analysis set: all randomised subjects who took at least 1 dose of study intervention and were analysed 'as treated'.

End point type	Secondary
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End point timeframe:

Up to Day 49

End point values	JNJ-53718678			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: Percentage of subjects				
number (not applicable)				
Respiratory rate: Grade 2	67.67			
DBP: Grade 1	33.33			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects who Progressed to Respiratory Failure (of any Cause) Requiring Mechanical Ventilation (Invasive or Noninvasive) and/or Death Among Those Who Developed RSV LRTI or RSV-associated LRTC per the EAC's Assessment

End point title	Percentage of Subjects who Progressed to Respiratory Failure (of any Cause) Requiring Mechanical Ventilation (Invasive or Noninvasive) and/or Death Among Those Who Developed RSV LRTI or RSV-associated LRTC per the EAC's Assessment
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End point description:

Percentage of subjects who progressed to respiratory failure (of any cause) requiring mechanical ventilation (invasive or noninvasive) and/or death among those who developed RSV LRTI or RSV-associated LRTC per the EAC's assessment was assessed. Efficacy analysis set included all subjects who were randomised, treated (took at least 1 dose), and had a RSV infection confirmed by central laboratory analysis, excluding subjects infected with a co-pathogen at baseline not identified during screening, analysed as randomised. Here, '0' in the 'number of subjects analysed' field (N=0) signifies that no subjects were available for the analysis because none of the subjects developed RSV LRTI or RSV-associated LRTC per the EAC's assessment.

End point type	Secondary
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End point timeframe:

Up to Day 49

End point values	JNJ-53718678			
Subject group type	Reporting group			
Number of subjects analysed	0 ^[2]			
Units: Percentage of subjects				
number (not applicable)				

Notes:

[2] - No subject was available for analysis as none of subject developed RSV LRTI or RSV-associated LRTC.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects who Progressed to Respiratory Failure (of any Cause) Requiring Mechanical Ventilation (Invasive or Noninvasive) and/or Death (all-cause Mortality)

End point title	Percentage of Subjects who Progressed to Respiratory Failure (of any Cause) Requiring Mechanical Ventilation (Invasive or Noninvasive) and/or Death (all-cause Mortality)
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End point description:

Percentage of subjects who progressed to respiratory failure (of any cause) requiring mechanical ventilation (invasive or noninvasive) and/or death (all-cause mortality) was assessed. Efficacy analysis set included all subjects who were randomised, treated (took at least 1 dose), and had a RSV infection confirmed by central laboratory analysis, excluding subjects infected with a co-pathogen at baseline not identified during screening, analysed as randomised.

End point type	Secondary
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End point timeframe:

Up to Day 49

End point values	JNJ-53718678			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: Percentage of subjects				
number (not applicable)	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects who Progressed to Death (All-cause Mortality) Among Those Who Developed RSV LRTI or RSV-associated LRTC per the EAC's Assessment

End point title	Percentage of Subjects who Progressed to Death (All-cause Mortality) Among Those Who Developed RSV LRTI or RSV-associated LRTC per the EAC's Assessment
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End point description:

Percentage of subjects who progressed to death (all-cause mortality) among those who developed RSV LRTI or RSV-associated LRTC per the EAC's assessment was assessed. Efficacy analysis set included all subjects who were randomised, treated (took at least 1 dose), and had a RSV infection confirmed by central laboratory analysis, excluding subjects infected with a co-pathogen at baseline not identified during screening, analyzed as randomised. Here, '0' in the 'number of subjects analysed' field (N=0) signifies that no subjects were available for the analysis because none of the subjects developed RSV LRTI or RSV-associated LRTC per the EAC's Assessment.

End point type	Secondary
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End point timeframe:

Up to Day 49

End point values	JNJ-53718678			
Subject group type	Reporting group			
Number of subjects analysed	0 ^[3]			
Units: Percentage of subjects				
number (not applicable)				

Notes:

[3] - No subject was available for analysis as none of subject developed RSV LRTI or RSV-associated LRTC.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Who Progressed to Death (All-cause Mortality)

End point title	Percentage of Subjects Who Progressed to Death (All-cause Mortality)
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End point description:

Percentage of subjects who progressed to death (All-cause mortality) was assessed. Efficacy analysis set included all subjects who were randomised, treated (took at least 1 dose), and had a RSV infection confirmed by central laboratory analysis, excluding subjects infected with a co-pathogen at baseline not identified during screening, analysed as randomised.

End point type	Secondary
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End point timeframe:

Up to Day 49

End point values	JNJ-53718678			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: Percentage of subjects				
number (not applicable)	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects who Progressed to Respiratory Failure (of any Cause) Requiring Mechanical Ventilation (Invasive or Noninvasive) Among Those who Developed RSV LRTI or RSV-associated LRTC per the EAC's Assessment

End point title	Percentage of Subjects who Progressed to Respiratory Failure (of any Cause) Requiring Mechanical Ventilation (Invasive or Noninvasive) Among Those who Developed RSV LRTI or RSV-associated LRTC per the EAC's Assessment
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End point description:

Percentage of subjects who progressed to respiratory failure (of any cause) requiring mechanical ventilation (invasive or noninvasive) among those who developed RSV LRTI or RSV-associated LRTC per the EAC's assessment was assessed. Efficacy analysis set included all subjects who were randomised, treated (took at least 1 dose), and had a RSV infection confirmed by central laboratory analysis, excluding subjects infected with a co-pathogen at baseline not identified during screening, analysed as randomised. Here, '0' in the 'number of subjects analysed' field (N=0) signifies that no subjects were available for the analysis because none of the subjects developed RSV LRTI or RSV-associated LRTC per the EAC's Assessment.

End point type	Secondary
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End point timeframe:

Up to Day 49

End point values	JNJ-53718678			
Subject group type	Reporting group			
Number of subjects analysed	0 ^[4]			
Units: Percentage of subjects				
number (not applicable)				

Notes:

[4] - No subject was available for analysis as none of subject developed RSV LRTI or RSV-associated LRTC.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects who Progressed to Respiratory Failure (of any Cause) Requiring Mechanical Ventilation (Invasive or Noninvasive)

End point title	Percentage of Subjects who Progressed to Respiratory Failure (of any Cause) Requiring Mechanical Ventilation (Invasive or Noninvasive)
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End point description:

Percentage of subjects who progressed to respiratory failure (of any cause) requiring mechanical ventilation (invasive or noninvasive) was assessed. Efficacy analysis set included all subjects who were randomised, treated (took at least 1 dose), and had a RSV infection confirmed by central laboratory analysis, excluding subjects infected with a co-pathogen at baseline not identified during screening, analysed as randomised.

End point type	Secondary
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End point timeframe:

Up to Day 49

End point values	JNJ-53718678			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: Percentage of subjects				
number (not applicable)	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Supplemental Oxygen Free Days

End point title	Number of Supplemental Oxygen Free Days
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End point description:

Number of supplemental oxygen free days was reported. The number of supplemental oxygen free days was the number of days the subjects did not receive/require supplemental oxygen during the first 28 days post treatment. Efficacy analysis set included all subjects who were randomised, treated (took at least 1 dose), and had a RSV infection confirmed by central laboratory analysis, excluding subjects infected with a co-pathogen at baseline not identified during screening, analyzed as randomised. Here, "n" (number analyzed)" is defined as number of subjects analysed for each specified category.

End point type	Secondary
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End point timeframe:

Through Day 28

End point values	JNJ-53718678			
Subject group type	Reporting group			
Number of subjects analysed	3 ^[5]			
Units: Days				
Subject 1 (n=1)	25			
Subject 2 (n=1)	28			
Subject 3 (n=1)	28			

Notes:

[5] - Planned analysis was not performed as study terminated prematurely due to low subject recruitment.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with Treatment-emergent Oxygen Supplementation

End point title	Percentage of Subjects with Treatment-emergent Oxygen Supplementation
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End point description:

Percentage of subjects who required treatment-emergent oxygen supplementation (e.g., supplemental oxygen, noninvasive pressure ventilation, invasive mechanical ventilation [tracheal tube, laryngeal mask or tracheostomy]). Any AE which occurred post 1st dose administration of study drug up to the end of study (i.e., Day 49) were considered as treatment-emergent. Efficacy analysis set included all subjects who were randomised, treated (took at least 1 dose), and had a RSV infection confirmed by central laboratory analysis, excluding subjects infected with a co-pathogen at baseline not identified during screening and were analysed as randomised.

End point type	Secondary
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End point timeframe:

Up to Day 49

End point values	JNJ-53718678			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: Percentage of subjects				
number (not applicable)	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Respiratory Rate Over Time

End point title	Respiratory Rate Over Time
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End point description:

Respiratory rate over time was assessed by investigator. The safety analysis set included all randomised subjects who took at least 1 dose of study intervention and were analysed 'as treated'. Here, 'N' (number of subjects analysed) signifies number of subjects who were evaluable for this endpoint and 'n' (number analysed) represent number of subjects with available data for each specified timepoint. Here, '99999' indicates that data was not collected for this time point because sample collection was not performed as prespecified in the protocol.

End point type	Secondary
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End point timeframe:

Baseline (Day 1), Days 15, 28, and 35

End point values	JNJ-53718678			
Subject group type	Reporting group			
Number of subjects analysed	2			
Units: Breaths per minute				
number (not applicable)				
Subject 1: Baseline (n=1)	99999			
Subject 1: Day 15 (n=1)	20			
Subject 1: Day 28 (n=1)	20			
Subject 1: Day 35 (n=1)	20			
Subject 2: Baseline (n=1)	16			
Subject 2: Day 15 (n=1)	20			
Subject 2: Day 28 (n=1)	16			
Subject 2: Day 35 (n=1)	99999			

Statistical analyses

No statistical analyses for this end point

Secondary: Heart Rate Over Time

End point title	Heart Rate Over Time
End point description:	Heart rate over time was reported by investigator. The safety analysis set included all randomised subjects who took at least 1 dose of study intervention and were analysed 'as treated'. Here, 'n' (number analysed) represent number of subjects with available data for each specified timepoints. Here, '99999' indicates that data was not collected for this time point because sample collection was not performed as prespecified in the protocol.
End point type	Secondary
End point timeframe:	Baseline (Day 1), Days 15, 28, and 35

End point values	JNJ-53718678			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: Beats per minute				
number (not applicable)				
Subject 1: Baseline (n=1)	83			
Subject 1: Day 15 (n=1)	99999			
Subject 1: Day 28 (n=1)	99999			
Subject 1: Day 35 (n=1)	99999			
Subject 2: Baseline (n=1)	72			
Subject 2: Day 15 (n=1)	79			
Subject 2: Day 28 (n=1)	99999			
Subject 2: Day 35 (n=1)	70			

Subject 3: Baseline (n=1)	70			
Subject 3: Day 15 (n=1)	73			
Subject 3: Day 28 (n=1)	78			
Subject 3: Day 35 (n=1)	99999			

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
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End point description:

Peripheral capillary oxygen saturation (SpO2) over time was reported by investigator. The safety analysis set included all randomised subjects who took at least 1 dose of study intervention and were analysed 'as treated'. Here, 'n' (number analysed) represent number of subjects with available data for each specified timepoint. Here, '99999' indicates that data was not collected for this time point because sample collection was not performed as prespecified in the protocol.

End point type	Secondary
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End point timeframe:

Baseline, Days 15, 28, and 35

End point values	JNJ-53718678			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: Percentage (%) of Spo2				
number (not applicable)				
Subject 1: Baseline (n=1)	96			
Subject 1: Day 15 (n=1)	99999			
Subject 1: Day 28 (n=1)	99999			
Subject 1: Day 35 (n=1)	99999			
Subject 2: Baseline (n=1)	98			
Subject 2: Day 15 (n=1)	97			
Subject 2: Day 28 (n=1)	100			
Subject 2: Day 35 (n=1)	96			
Subject 3: Baseline (n=1)	96			
Subject 3: Day 15 (n=1)	97			
Subject 3: Day 28 (n=1)	95			
Subject 3: Day 35 (n=1)	99999			

Statistical analyses

No statistical analyses for this end point

Secondary: Body Temperature Over Time

End point title	Body Temperature Over Time
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End point description:

Body temperature (in degrees celsius) over time was reported. The safety analysis set included all randomised subjects who took at least 1 dose of study intervention and were analysed 'as treated'. Here, 'n' (number analysed) represent number of subjects with available data for each specified timepoint. Here, '99999' indicates that data was not collected for this time point because sample collection was not performed as prespecified in the protocol.

End point type Secondary

End point timeframe:

Baseline, Days 15, 28, and 35

End point values	JNJ-53718678			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: Degree Celsius				
number (not applicable)				
Subject 1: Baseline (n=1)	36.3			
Subject 1: Day 15 (n=1)	99999			
Subject 1: Day 28 (n=1)	99999			
Subject 1: Day 35 (n=1)	99999			
Subject 2: Baseline (n=1)	36.8			
Subject 2: Day 15 (n=1)	36.8			
Subject 2: Day 28 (n=1)	36.5			
Subject 2: Day 35 (n=1)	36.7			
Subject 3: Baseline (n=1)	35.9			
Subject 3: Day 15 (n=1)	36.1			
Subject 3: Day 28 (n=1)	36.2			
Subject 3: Day 35 (n=1)	99999			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Hospitalised (of Subjects Who Were not Hospitalised at Baseline)

End point title Percentage of Subjects Hospitalised (of Subjects Who Were not Hospitalised at Baseline)

End point description:

Percentage of subjects who were not hospitalised at baseline and required hospitalisation during the study was assessed. Efficacy analysis set included all subjects who were randomised, treated (took at least 1 dose), and had a RSV infection confirmed by central laboratory analysis, excluding subjects infected with a co-pathogen at baseline not identified during screening, analysed as randomised.

End point type Secondary

End point timeframe:

Up to Day 49

End point values	JNJ-53718678			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: Percentage of subjects				
number (not applicable)	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Who were Re-hospitalised

End point title	Percentage of Subjects Who were Re-hospitalised
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End point description:

Percentage of subjects who were re-hospitalised (of subjects who were hospitalised at baseline and discharged during the study and of subjects who were not hospitalised at baseline and required hospitalisation and were discharged during the study) were assessed in this endpoint. Efficacy analysis set included all subjects who were randomised, treated (took at least 1 dose), and had a RSV infection confirmed by central laboratory analysis, excluding subjects infected with a co-pathogen at baseline not identified during screening, analysed as randomised.

End point type	Secondary
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End point timeframe:

Up to Day 49

End point values	JNJ-53718678			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: Percentage of subjects				
number (not applicable)	33.33			

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Hospital Stay

End point title	Duration of Hospital Stay
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End point description:

Duration (in days) of hospital stay was assessed. Efficacy analysis set included all subjects who were randomised, treated (took at least 1 dose), and had a RSV infection confirmed by central laboratory analysis, excluding subjects infected with a co-pathogen at baseline not identified during screening, analysed as randomised. Here, 'N' (number of subjects analysed) signifies number of subjects who were evaluable for this endpoint.

End point type	Secondary
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End point timeframe:

Up to Day 49

End point values	JNJ-53718678			
Subject group type	Reporting group			
Number of subjects analysed	1			
Units: Days				
number (not applicable)	4			

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Intensive Care Unit (ICU) Stay

End point title	Duration of Intensive Care Unit (ICU) Stay
End point description:	Duration of ICU stay was reported. Duration (in hours) was defined as total number of hours a subjects was in ICU from first dose of study drug until study termination. Efficacy analysis set included all subjects who were randomised, treated (took at least 1 dose), and had a RSV infection confirmed by central laboratory analysis, excluding subjects infected with a co-pathogen at baseline not identified during screening, analysed as randomised.
End point type	Secondary
End point timeframe:	Up to Day 49

End point values	JNJ-53718678			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: Hours				
median (full range (min-max))	0 (0 to 0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Grade 3 and Grade 4 Treatment-emergent Adverse Events (TEAEs) in the Infections and Infestations System Organ Class

End point title	Number of Subjects with Grade 3 and Grade 4 Treatment-emergent Adverse Events (TEAEs) in the Infections and Infestations System Organ Class
End point description:	An AE is any untoward medical occurrence in a clinical study subject administered a medicinal (investigational or non investigational) product. An AE did not necessarily had a causal relationship with the intervention. Subjects with Grade 3 or Grade 4 AE were assessed in this endpoint. Any AE which occurred post 1st dose administration of study drug up to the end of study (i.e., Day 49) were

considered as treatment-emergent. The safety analysis set included all randomised subjects who took at least 1 dose of study intervention and were analysed 'as treated'.

End point type	Secondary
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End point timeframe:

Up to Day 49

End point values	JNJ-53718678			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: Subjects	1			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Respiratory Related AEs

End point title	Number of Subjects with Respiratory Related AEs
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End point description:

Number of subjects with respiratory related AEs (respiratory infections) was assessed. The safety analysis set included all randomised subjects who took at least 1 dose of study intervention and were analysed 'as treated'.

End point type	Secondary
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End point timeframe:

Up to Day 49

End point values	JNJ-53718678			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: Subjects	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Thoracic-related AEs

End point title	Number of Subjects with Thoracic-related AEs
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End point description:

Number of subjects with thoracic-related AEs was assessed. The safety analysis set included all randomised subjects who took at least 1 dose of study intervention and were analysed 'as treated'.

End point type	Secondary
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End point timeframe:

Up to Day 49

End point values	JNJ-53718678			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: Subjects	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Antibiotic Use Among Those Who Developed RSV LRTI or RSV-Associated LRTC per the EAC's Assessment

End point title	Number of Subjects with Antibiotic Use Among Those Who Developed RSV LRTI or RSV-Associated LRTC per the EAC's Assessment
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End point description:

Number of subjects with antibiotic use among those who developed RSV LRTI or RSV-associated LRTC per the EAC's assessment was assessed. Efficacy analysis set included all subjects who were randomised, treated (took at least 1 dose), and had a RSV infection confirmed by central laboratory analysis, excluding subjects infected with a co-pathogen at baseline not identified during screening, analysed as randomised. Here, '0' in the 'number of subjects analysed' field (N=0) signifies that no subjects were available for the analysis because none of the subjects developed RSV LRTI or RSV-associated LRTC per the EAC's Assessment.

End point type	Secondary
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End point timeframe:

Up to Day 49

End point values	JNJ-53718678			
Subject group type	Reporting group			
Number of subjects analysed	0 ^[6]			
Units: Subjects				

Notes:

[6] - No subject was available for analysis as none of subject developed RSV LRTI or RSV-associated LRTC.

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma Concentration of JNJ-53718678

End point title	Plasma Concentration of JNJ-53718678
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End point description:

Plasma Concentration of JNJ-53718678 was reported. PK analysis set included all subjects who received JNJ-53718678 and for whom at least one PK concentration was reported. Here, 'n' (number analyzed)

represents number of subjects with available data for each specified timepoints. Here, '99999' indicates that data was not collected for this time point because sample collection was not performed as prespecified in the protocol.

End point type	Secondary
End point timeframe:	
Days 1, 3, 8, 15 and 22	

End point values	JNJ-53718678			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: nanograms per millilitre (ng/mL)				
number (not applicable)				
Subject 1: Day 1 (n=1)	1380			
Subject 1: Day 3 (n=1)	99999			
Subject 1: Day 8 (n=1)	99999			
Subject 1: Day 15 (n=1)	99999			
Subject 1: Day 22 (n=1)	99999			
Subject 2: Day 1 (n=1)	653			
Subject 2: Day 3 (n=1)	99999			
Subject 2: Day 8 (n=1)	1780			
Subject 2: Day 15 (n=1)	1680			
Subject 2: Day 22 (n=1)	802			
Subject 3: Day 1 (n=1)	155			
Subject 3: Day 3 (n=1)	1680			
Subject 3: Day 8 (n=1)	2290			
Subject 3: Day 15 (n=1)	2510			
Subject 3: Day 22 (n=1)	812			

Statistical analyses

No statistical analyses for this end point

Secondary: RSV Viral Load Over Time

End point title	RSV Viral Load Over Time
End point description:	
<p>RSV viral (RSV B) load was measured over time by quantitative reverse transcription polymerase chain reaction in the nasal swab specimens collected at the clinic visits and at home. Efficacy analysis set included all subjects who were randomised, treated (took at least 1 dose), and had a RSV infection confirmed by central laboratory analysis, excluding subjects infected with a co-pathogen at baseline not identified during screening, analysed as randomised. Here, 'n' (number analysed) represent number of subjects with available data for each specified timepoints. Here, '99999' indicates that data was not collected for this time point because sample collection was not performed as prespecified in the protocol.</p>	
End point type	Secondary
End point timeframe:	
Baseline, Days 15, 28, and 35	

End point values	JNJ-53718678			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: log10 copies per millilitre (mL)				
number (not applicable)				
Subject 1: RSV B: Baseline (n=1)	3.85			
Subject 1: RSV B: Day 15 (n=1)	99999			
Subject 1: RSV B: Day 28 (n=1)	0			
Subject 1: RSV B: Day 35 (n=1)	99999			
Subject 2: RSV B: Baseline (n=1)	8.01			
Subject 2: RSV B: Day 15 (n=1)	5.95			
Subject 2: RSV B: Day 28 (n=1)	5.16			
Subject 2: RSV B: Day 35 (n=1)	5.63			
Subject 3: RSV B: Baseline (n=1)	8.73			
Subject 3: RSV B: Day 15 (n=1)	5.36			
Subject 3: RSV B: Day 28 (n=1)	0			
Subject 3: RSV B: Day 35 (n=1)	99999			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to Day 49

Adverse event reporting additional description:

The safety analysis set included all randomised subjects who took at least 1 dose of study intervention and were analysed 'as treated'.

Assessment type	Non-systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	24.1
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Reporting groups

Reporting group title	JNJ-53718678
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Reporting group description:

Subjects with age of greater than or equal to (\geq) 18 to less than or equal to (\leq) 75 years received rilematovir 125 milligrams (mg) twice daily (bid) for 21 days.

Serious adverse events	JNJ-53718678		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 3 (33.33%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Infections and infestations			
Sepsis			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	JNJ-53718678		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	2 / 3 (66.67%)		
Vascular disorders			
Hot Flush			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Nervous system disorders			

Dysgeusia subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1		
Blood and lymphatic system disorders Thrombocytopenia subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1		
Infections and infestations Cytomegalovirus Infection Reactivation subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
21 June 2019	The purpose of this amendment was to correct an inconsistency regarding the classification of Cytochrome P450 3A4 (CYP3A4) inhibitors and CYP3A4 inducers in the concomitant therapy section and to update the exclusion criteria to clarify that enrollment of subjects during the follow-up phase of another clinical study was allowed.
11 December 2019	The purpose of this amendment was to ensure consistency between different sections, to clarify, and make minor corrections to different parts of the protocol. In addition, regulatory feedback from competent authorities was incorporated.
03 June 2020	The purpose of this amendment was to implement a risk mitigation plan (including dose modifications) following an exposure (C _{max})-related important potential risk of QT interval prolongation identified in the thorough QT Study 53718678RSV1009 in healthy adult subjects.
10 July 2020	The purpose of this amendment was to implement recommendations regarding cardiac safety and concomitant medications by Health Authorities.
03 August 2020	The purpose of this amendment was to implement recommendations regarding cardiac safety and concomitant medications by Health Authorities.
07 May 2021	The purpose of this amendment was to replace the oral suspension formulations of rilematovir and placebo by oral film-coated tablets, to specify the clinical management of laboratory-confirmed SARS-CoV-2 infection, diagnosed during the study and to add specifics on the administration of a locally approved (including emergency use-authorized) coronavirus disease 2019 (COVID-19) vaccine during the study.

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.

As the study was terminated early due to low number of subjects enrolled, some efficacy analyses were not performed as per change in the planned analysis. Hence, data was collected and analyzed for safety and selected efficacy parameters only.

Notes: