Clinical trial results:
A Phase 3, Randomized, Double-blind, Placebo-controlled Study to Evaluate the Efficacy and Safety of Rilematovir in Infants and Children (>=28 Days to <=5 Years of Age) and Subsequently in Neonates (<28 Days of Age), Hospitalized With Acute Respiratory Tract Infection Due to Respiratory Syncytial Virus (RSV)

Summary

EudraCT number	2020-002023-11
Trial protocol	BG DE SE CZ HU BE PL Outside EU/EEA EE LV SK IT
Global end of trial date	18 March 2022

Results information

Result version number	v1 (current)
This version publication date	04 October 2022
First version publication date	04 October 2022

Trial information

Trial identification

Sponsor protocol code	53718678RSV3001

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04583280
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Janssen Research & Development LLC
Sponsor organisation address	920 Route 202, South Raritan New Jersey, United States, 08869
Public contact	Clinical Registry Group, Janssen Research & Development LLC, ClinicalTrialsEU@its.jnj.com
Scientific contact	Clinical Registry Group, Janssen Research & Development LLC, ClinicalTrialsEU@its.jnj.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-001838-PIP01-15
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	01 June 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	18 March 2022
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

Main objective of the trial was to evaluate the superiority of rilematovir compared to placebo treatment with respect to the clinical outcome on the respiratory syncytial virus (RSV) Recovery Scale (RRS).

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 Practice (GCP) and applicable regulatory requirements.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	06 September 2021
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Argentina: 7
Country: Number of subjects enrolled	Brazil: 2
Country: Number of subjects enrolled	Czechia: 1
Country: Number of subjects enrolled	Spain: 5
Country: Number of subjects enrolled	Hungary: 1
Country: Number of subjects enrolled	Japan: 2
Country: Number of subjects enrolled	Malaysia: 1
Country: Number of subjects enrolled	Ukraine: 9
Worldwide total number of subjects	28
EEA total number of subjects	7

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)	20

Children (2-11 years)	8
Adolescents (12-17 years)	0
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 28 subjects with acute respiratory tract infection due to RSV were randomised and treated (8 subjects in Placebo arm and 20 subjects in rilematovir arm). Of these, 27 subjects completed the study.

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	Investigator, Subject

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Subjects aged greater than or equal to (>=) 28 days to less than (<) 3 months, >=3 to <6 months, and >=6 months to less than or equal to (<=) 5 years received placebo matching to rilematovir as oral suspension twice daily (BID) from Days 1 to 7 (14 consecutive doses).

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

Dosage and administration details:

Subjects received placebo matching to rilematovir BID from Days 1 to 7.

Arm title	Rilematovir

Arm description:

Subjects aged >=28 days to <3 months, >=3 to <6 months, and >=6 months to <=5 years received rilematovir 2.5 milligram per kilogram (mg/kg), 3 mg/kg and 4.5 mg/kg respectively, as oral suspension BID from Days 1 to 7 (14 consecutive doses).

Arm type	Experimental
Investigational medicinal product name	Rilematovir 2.5 mg/kg
Investigational medicinal product code	JNJ-53718678
Other name	
Pharmaceutical forms	Oral suspension
Routes of administration	Oral use

Dosage and administration details:

Subjects aged >=28 days to <3 months received rilematovir 2.5 mg/kg orally as 20 mg/mL suspension BID from Days 1 to 7.

Investigational medicinal product name	Rilematovir 4.5 mg/kg
Investigational medicinal product code	JNJ-53718678
Other name	
Pharmaceutical forms	Oral suspension
Routes of administration	Oral use

Dosage and administration details:

Subjects aged >=6 months to <=5 years received rilematovir 4.5 mg/kg orally as 20 mg/mL suspension BID from Days 1 to 7.

Investigational medicinal product name	Rilematovir 3 mg/kg
Investigational medicinal product code	JNJ-53718678
Other name	
Pharmaceutical forms	Oral suspension
Routes of administration	Oral use

Dosage and administration details:

Subjects aged >=3 to <6 months received rilematovir 3 mg/kg orally as 20 mg/mL suspension BID from Days 1 to 7.

Number of subjects in period 1	Placebo	Rilematovir
Started	8	20
Completed	8	19
Not completed	0	1
Consent withdrawn parent/caregiver	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Subjects aged greater than or equal to (>=) 28 days to less than (<) 3 months, >=3 to <6 months, and >=6 months to less than or equal to (<=) 5 years received placebo matching to rilematovir as oral suspension twice daily (BID) from Days 1 to 7 (14 consecutive doses).	
Reporting group title	Rilematovir
Reporting group description:	
Subjects aged >=28 days to <3 months, >=3 to <6 months, and >=6 months to <=5 years received rilematovir 2.5 milligram per kilogram (mg/kg), 3 mg/kg and 4.5 mg/kg respectively, as oral suspension BID from Days 1 to 7 (14 consecutive doses).	

Reporting group values	Placebo	Rilematovir	Total
Number of subjects	8	20	28
Title for AgeCategorical			
Units: subjects			
Children (2-11 years)	2	6	8
Infants and toddlers(28 days-23 months)	6	14	20
Title for AgeContinuous			
Units: months			
arithmetic mean	15.3	16.2	
standard deviation	± 19.4	± 13.67	-
Title for Gender			
Units: subjects			
Female	6	12	18
Male	2	8	10

End points

End points reporting groups

Reporting group title	Placebo

Reporting group description:

Subjects aged greater than or equal to (>=) 28 days to less than (<) 3 months, >=3 to <6 months, and >=6 months to less than or equal to (<=) 5 years received placebo matching to rilematovir as oral suspension twice daily (BID) from Days 1 to 7 (14 consecutive doses).

Reporting group title	Rilematovir

Reporting group description:

Subjects aged >=28 days to <3 months, >=3 to <6 months, and >=6 months to <=5 years received rilematovir 2.5 milligram per kilogram (mg/kg), 3 mg/kg and 4.5 mg/kg respectively, as oral suspension BID from Days 1 to 7 (14 consecutive doses).

Primary: Percentage of Subjects by Respiratory Syncytial Virus (RSV) Recovery Scale (RRS) Category

End point title	Percentage of Subjects by Respiratory Syncytial Virus (RSV) Recovery Scale (RRS) Category[1]

End point description:

RRS was an ordinal scale to assess a subject's clinical status. The RRS provided 7 mutually exclusive categories ordered from best to worst where 1 =home without signs/symptoms, 2 =home with sign/symptoms, 3 =ward without supplemental oxygen (O2) or feeding/hydration, 4 =ward with supplemental O2 or feeding/hydration, 5 =intensive care unit (ICU) without mechanical ventilation (included both invasive and non-invasive mechanical ventilation), 6 =required mechanical ventilation and 7=worst (death). Higher category indicated worst condition. With or without signs/symptoms was defined as the key RSV signs/symptoms resolved (absent or mild) or not resolved assessed by parent/caregiver. Intent-to-Treat-infected (ITT-i) analysis set was analysed. Due to the early termination of study, last day of RRS treatment (Day 8) was considered instead of the original planned day defined as when 50% subjects would have been discharged.

End point type	Primary

End point timeframe:

Baseline to Day 8

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 analysis was performed.

End point values	Placebo	Rilematovir		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8	19		
Units: Percentage of subjects				
number (not applicable)				
Home without symptoms	25.0	31.6		
Home with symptoms	50.0	26.3		
Ward without supplemental oxygen/feeding/hydration	25.0	36.8		
Ward with supplemental or feeding/hydration	0	5.3		
ICU without mechanical ventilation	0	0		
Requiring mechanical ventilation	0	0		
Death	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Clinically Resolved From RSV Disease Based on the Clinician Reported Outcome (ClinRO) Sign/Symptoms Questionnaire at Day 8

End point title	Percentage of Subjects Clinically Resolved From RSV Disease Based on the Clinician Reported Outcome (ClinRO) Sign/Symptoms Questionnaire at Day 8

End point description:

Clinically resolved was defined as subject required no oxygen supplementation, no supplemental feeding/hydration, no need for ICU and had Key RSV signs/symptoms resolved to absent or mild as per ClinRO signs/symptoms questionnaire. Clinically resolved Key RSV signs/symptoms were assessed based on clinician's observations as resolved if subject had no retractions, tachypnea, tachycardia, breathing problems (nasal flaring, head bobbing, grunting); cough (resolved if little or no coughing or occasional strong cough or sometimes productive) and wheezing (resolved if no wheezing or terminal expiratory wheezing or only with stethoscope). ITT-i analysis set included all randomised subjects who received at least 1 dose of study intervention and had an RSV infection confirmed by central laboratory analysis.

End point type	Secondary

End point timeframe:

Day 8

End point values	Placebo	Rilematovir		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8	19		
Units: Percentage of subjects				
number (not applicable)	37.5	31.6		

Statistical analyses

No statistical analyses for this end point

Secondary: Time From First Study Dose to Resolution of key RSV Signs/Symptoms Based on Observer Reported Outcome (ObsRO) Questionnaire After Free of Supplementation (Oxygen/Feeding/Hydration) for at Least 24 Hours

End point title	Time From First Study Dose to Resolution of key RSV Signs/Symptoms Based on Observer Reported Outcome (ObsRO) Questionnaire After Free of Supplementation (Oxygen/Feeding/Hydration) for at Least 24 Hours

End point description:

Time from first dose of study intervention to first resolution of Key RSV signs/symptoms was evaluated based on ObsRO assessment after free of supplementation (O2/feeding/hydration) for at least 24 hours. Clinically resolved was defined as subject required no oxygen supplementation, no supplemental

feeding/hydration, no need for ICU and had Key RSV signs/symptoms resolved to absent or mild as per ObsRO signs/symptoms questionnaire. Resolution of key Signs/Symptoms assessment was based on observations of child's parent/caregiver as resolved if no retractions, tachypnea, tachycardia, breathing problems (gasping for air nostrils, flaring when breathing, head bobbed back and forth when breathing), no breathing sound; cough (no coughing, little coughing without problems). Kaplan-Meier method was used for estimation. ITT-i analysis set was analysed. 99999 indicated upper limit of 95% confidence interval (CI) in placebo arm could not be estimated due to low number of subjects with events.

End point type	Secondary

End point timeframe:

up to Day 21

End point values	Placebo	Rilematovir		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8	19		
Units: Hours				
median (confidence interval 95%)	237.0 (114.38 to 99999)	144.8 (96.09 to 210.93)		

Statistical analyses

No statistical analyses for this end point

Secondary: Time From Discharge to Resolution of key RSV Signs/Symptoms Based on ObsRO Sign/Symptoms Questionnaire

End point title	Time From Discharge to Resolution of key RSV Signs/Symptoms Based on ObsRO Sign/Symptoms Questionnaire

End point description:

Time (hours) from discharge from the hospital to resolution of key RSV Signs/Symptoms (breathing problems, retractions, tachypnea, cough, wheezing/breathing sounds, and tachycardia) was planned to be reported. ObsRO Signs/Symptoms questionnaire was based on observations by child's parent/caregiver to assess resolution of key Signs/symptoms of RSV disease as resolved: if no retractions, tachypnea, tachycardia, breathing problems (gasping for air nostrils, flaring when breathing, head bobbed back and forth when breathing), no breathing sound; cough (no coughing, a little coughing without problems caused by coughing). Data for this endpoint was not analysed as the study was terminated early.

End point type	Secondary

End point timeframe:

Up to 21 Days

End point values	Placebo	Rilematovir		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[2]	0[3]		
Units: hours				
median (confidence interval 95%)	(to)	(to)		

Notes:

[2] - Data for this endpoint was not analysed as the study was terminated early.

[3] - Data for this endpoint was not analysed as the study was terminated early.

Statistical analyses

No statistical analyses for this end point

Secondary: Time From First Dosing to end of Oxygen Supplementation

End point title	Time From First Dosing to end of Oxygen Supplementation

End point description:

Time from first dosing to end of oxygen supplementation was planned to be analysed. Data for this endpoint was not analysed as the study was terminated early.

End point type	Secondary

End point timeframe:

Up to Day 35

End point values	Placebo	Rilematovir		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[4]	0[5]		
Units: hours				
median (confidence interval 95%)	(to)	(to)		

Notes:

[4] - Data for this endpoint was not analysed as the study was terminated early.

[5] - Data for this endpoint was not analysed as the study was terminated early.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Post-baseline RSV-Related Complications

End point title	Number of Subjects with Post-baseline RSV-Related Complications

End point description:

RSV related complications included respiratory complications (respiratory failure, apnoeic attacks, bronchiolitis, bronchial obstruction, pneumonia and asthmatic crisis), infectious complications (otitis media, bacterial respiratory tract infections and sepsis), cardiovascular complications (arrhythmia, cardiogenic shock, hemodynamic instability, congestive cardiac failure), acid-base or electrolyte complications (metabolic acidosis, metabolic alkalosis, hyponatremia, hypokalemia, hyperkalemia, hypocalcemia, hypercalcemia, hypoglycemia and hyperglycemia). Subjects were counted only once for any given event, regardless of the number of times they actually experienced the event. ITT-i analysis set included all randomised subjects who received at least 1 dose of study intervention and had an RSV infection confirmed by central laboratory analysis. Subjects were counted only once for any given event, regardless of the number of times they actually experienced the event.

End point type	Secondary

End point timeframe:

Up to Day 35

End point values	Placebo	Rilematovir		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8	19		
Units: Subjects	1	3		

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)

End point description:

An adverse event (AE) is any untoward medical occurrence in a clinical study subject administered a medicinal (investigational or non-investigational) product and did not necessarily have a causal relationship with the treatment. A TEAE was defined as an AE with an onset after the initiation study drug (Day 1) up to end of study (Day 35). Safety analysis set included all subjects who received at least 1 dose of study intervention.

End point type	Secondary

End point timeframe:

Up to Day 35

End point values	Placebo	Rilematovir		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8	20		
Units: Subjects	5	11		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Abnormalities in Clinical Laboratory Values

End point title	Number of Subjects with Abnormalities in Clinical Laboratory Values

End point description:

Number of subjects with abnormally low (AL) and abnormally high (AH) values of bicarbonate, direct bilirubin, urea nitrogen, basophils, eosinophils, erythrocyte (Ery). mean corpuscular hemoglobin (HGB) concentration (conc), Ery. mean corpuscular hemoglobin, erythrocytes, leukocytes, lymphocytes, monocytes, neutrophils and reticulocytes compared to baseline as assessed based on the investigator's discretion were reported. Safety analysis set included all subjects who received at least 1 dose of study intervention. Here, N (number of subjects analysed) signifies subjects evaluated for this endpoint and 'n' (number analysed) signifies number of subjects with available data at each specified category.

End point type	Secondary

End point timeframe:
Up to Day 35

End point values	Placebo	Rilematovir		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8	18		
Units: Subjects				
Bicarbonate- Abnormally low (n =8, 17)	1	3		
Bicarbonate- Abnormally high (n =8, 17)	0	0		
Direct bilirubin- Abnormally low (n =7, 16)	2	9		
Direct bilirubin- Abnormally high (n =7, 16)	0	0		
Urea nitrogen- Abnormally low (n =8, 17)	1	3		
Urea nitrogen- Abnormally high (n =8, 17)	0	0		
Basophils- Abnormally low (n =7, 17)	0	0		
Basophils- Abnormally high(n =7, 17)	0	1		
Eosinophils- Abnormally low (n =7, 17)	0	0		
Eosinophils- Abnormally high (n =7, 17)	5	12		
Ery. mean corpuscular HGB conc.-AL (n =7, 17)	1	3		
Ery. mean corpuscular HGB conc.-AH (n =7, 17)	0	0		
Ery. mean corpuscular hemoglobin-AL (n =7, 18)	0	3		
Ery. mean corpuscular hemoglobin-AH (n =7, 18)	0	0		
Erythrocytes- Abnormally low (n =7, 18)	0	0		
Erythrocytes- Abnormally high (n =7, 18)	0	2		
Leukocytes- Abnormally low (n =7, 18)	1	1		
Leukocytes- Abnormally high (n =7, 18)	0	5		
Lymphocytes- Abnormally low (n =7, 17)	0	0		
Lymphocytes- Abnormally high (n =7, 17)	0	3		
Monocytes- Abnormally low (n =7, 17)	1	4		
Monocytes- Abnormally high (n =7, 17)	0	0		
Neutrophils- Abnormally low (n =7, 17)	4	10		
Neutrophils- Abnormally high(n =7, 17)	0	0		
Reticulocytes- Abnormally low (n =7, 18)	0	0		
Reticulocytes- Abnormally high (n =7, 18)	1	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Abnormalities in Electrocardiograms (ECG)

End point title	Number of Subjects with Abnormalities in Electrocardiograms (ECG)

End point description:

Number of subjects with abnormally low and abnormally high values of ECG Abnormalities (PR Interval and RR Interval) as assessed based on the investigator's discretion were reported. Safety analysis set included all subjects who received at least 1 dose of study intervention.

End point type	Secondary

End point timeframe:

Up to Day 35

End point values	Placebo	Rilematovir		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8	20		
Units: Subjects				
PR Interval- Abnormally low	0	0		
PR Interval- Abnormally high	0	1		
RR Interval- Abnormally low	1	7		
RR Interval- Abnormally high	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Abnormalities in Vital Signs

End point title	Number of Subjects with Abnormalities in Vital Signs

End point description:

Number of subjects with abnormally low and abnormally high vital signs as assessed based on the investigator's discretion were reported. Abnormal vital signs included systolic blood pressure (SBP) (millimeter of mercury [mmHg]), diastolic blood pressure (DBP) (mmHg), pulse rate (Beats per minute), respiratory rate (Breaths per minute), temperature (Celsius) and oxygen saturation (%). Safety analysis set included all subjects who received at least 1 dose of study intervention. Here, 'n' (number analysed) signifies number of subjects with available data at specified categories.

End point type	Secondary

End point timeframe:

Up to Day 35

End point values	Placebo	Rilematovir		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8	20		
Units: Subjects				
SBP- Abnormally low (n=8,20)	0	0		
SBP- Abnormally high (n=8,20)	0	4		
DBP- Abnormally low (n=8,20)	0	0		
DBP- Abnormally high (n=8,20)	1	3		
Pulse Rate- Abnormally low (n=8,20)	0	0		
Pulse Rate- Abnormally high (n=8,20)	1	2		
Respiratory Rate- Abnormally low (n=8,20)	0	0		
Respiratory Rate- Abnormally high (n=8,20)	0	3		
Temperature - Abnormally low (n=8,20)	0	0		
Temperature - Abnormally high (n=8,20)	1	0		
Oxygen Saturation- Abnormally low (n=8,19)	0	1		
Oxygen Saturation- Abnormally high (n=8,19)	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Resolution of Signs/symptoms of RSV Disease as Assessed by ObsRO Signs/Symptoms Questionnaire

End point title	Time to Resolution of Signs/symptoms of RSV Disease as Assessed by ObsRO Signs/Symptoms Questionnaire

End point description:

Time to resolution of signs/symptoms of RSV disease symptoms was planned to be reported. Resolution of signs/symptoms assessment was based on observations of child's parent/caregiver as per ObsRO signs/symptoms questionnaire as resolved if general illness behavior appeared well, less active, less interested in playing/toys, tired more easily; sleep disturbance(as usual, little more restless, disturbed); crying: resolved if subject cried(as usual/cried more than usual but calmed if held/soothed);feeding problems: as usual/little less than usual; no dehydration(dark yellow urine/less urine/soft spot on top of head sunk in/sunken eyes/dry skin or lips);retractions (belly sucked in when breathing in/ribs more visible than usual when breathing in/skin at base of throat sucked in when breathing in),no tachypnea/tachycardia; no nasal signs; no breathing problems. Data for this endpoint was not analysed as study was terminated early.

End point type	Secondary

End point timeframe:

Up to Day 21

End point values	Placebo	Rilematovir		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[6]	0[7]		
Units: Hours				
median (confidence interval 95%)	(to)	(to)		

Notes:

[6] - Data for this endpoint was not analysed as the study was terminated early.

[7] - Data for this endpoint was not analysed as the study was terminated early.

Statistical analyses

No statistical analyses for this end point

Secondary: ObsRO Signs/Symptoms Questionnaire Scores

End point title	ObsRO Signs/Symptoms Questionnaire Scores

End point description:

ObsRO Signs/Symptoms questionnaire was used to monitor specific signs/symptoms of RSV disease based on observations by child's parent/caregiver. It consisted of 9 items, each item was scored as follows: sleep disturbance =0,1,2,3; crying =0,1,2,3; illness behavior =0,1,2,3; nasal signs =0,1,2; breathing problems [tachypnea, tachycardia, retractions] =0,2,3; breathing sounds =0,3; cough =0,1,2,3; feeding problems =0,1,2,3; and dehydration =0,1,2,3. In each item score of 0 and 1 indicated signs/symptoms resolved and score of 2 and 3 indicated signs/symptoms not resolved. A summary score was derived (mean of the item scores) and rated on a 4-point scale, with scores ranging from 0 to 3, higher score indicated, worse/higher severity of sign/symptom. Data for this endpoint was not analysed as the study was terminated early.

End point type	Secondary

End point timeframe:

Up to Day 21

End point values	Placebo	Rilematovir		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[8]	0[9]		
Units: Score on a scale				
arithmetic mean (standard deviation)	()	()		

Notes:

[8] - Data for this endpoint was not analysed as the study was terminated early.

[9] - Data for this endpoint was not analysed as the study was terminated early.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in ObsRO Signs/Symptoms Questionnaire Scores Over Time

End point title	Change From Baseline in ObsRO Signs/Symptoms Questionnaire Scores Over Time

End point description:

ObsRO Signs/Symptoms questionnaire was used to monitor specific signs/symptoms of RSV disease based on observations by child's parent/caregiver. It consisted of 9 items, each item was scored as follows: sleep disturbance =0,1,2,3; crying =0,1,2,3; illness behavior =0,1,2,3; nasal signs =0,1,2; breathing problems [tachypnea, tachycardia, retractions] =0,2,3; breathing sounds =0,3; cough =0,1,2,3; feeding problems =0,1,2,3; and dehydration =0,1,2,3. In each item score of 0 and 1 indicated signs/symptoms resolved and score of 2 and 3 indicated signs/symptoms not resolved. A summary

score was derived (mean of the item scores) and rated on a 4-point scale, with scores ranging from 0 to 3, higher score indicated, worse/higher severity of sign/symptom. Data for this endpoint was not analysed as the study was terminated early.

End point type	Secondary

End point timeframe:

Up to Day 21

End point values	Placebo	Rilematovir		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[10]	0[11]		
Units: Score on a scale				
arithmetic mean (standard deviation)	()	()		

Notes:

[10] - Data for this endpoint was not analysed as the study was terminated early.

[11] - Data for this endpoint was not analysed as the study was terminated early.

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Improvement in RSV disease Based on ObsRO General Health Questions (GHQ)

End point title	Time to Improvement in RSV disease Based on ObsRO General Health Questions (GHQ)

End point description:

ObsRO GHQ was a 5-item questionnaire to evaluate parent/caregiver's general impression of child's RSV disease severity, change in RSV disease, and overall health status. Subject had to choose one answer from multiple options for each question i.e. how would you rate child's RSV now: recovered, very mild, mild, moderate, severe, very severe); would you say child's RSV had improved is about same or is worse than when child entered study: very much improved, much improved, a little improved, about the same, a little worse, much worse, very much worse); overall, how is the child's health now: excellent, very good, good, fair, poor, very poor; has the child's health returned to normal how the child was before RSV: Yes, No); which of these did you use to decide your answers: what I saw myself, what I saw and what another caregiver told me, what another caregiver told me. Data for this endpoint was not analysed as the study was terminated early.

End point type	Secondary

End point timeframe:

Up to Day 21

End point values	Placebo	Rilematovir		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[12]	0[13]		
Units: Hours				
median (confidence interval 95%)	(to)	(to)		

Notes:

[12] - Data for this endpoint was not analysed as the study was terminated early.

[13] - Data for this endpoint was not analysed as the study was terminated early.

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Resolution of Signs/Symptoms of RSV Disease as Assessed by ClinRO Signs/Symptoms Questionnaire

End point title	Time to Resolution of Signs/Symptoms of RSV Disease as Assessed by ClinRO Signs/Symptoms Questionnaire

End point description:

Time to resolution from first dose of study drug until first time of resolution of all RSV Symptoms was planned to be reported. Clinically resolved RSV signs/symptoms were assessed based on clinician's observations by ClinRO signs/symptoms questionnaire as activity level (resolved if subject was alert and active or irritable), sleep disturbance (resolved if subject was normal or occasional restlessness/disturbed), feeding problems (resolved if subject took >75% of normal amount of feeds via usual route), resolved if subject had no dehydration, retractions, tachypnea and tachycardia, nasal secretions (resolved if subjects had none or minimal/moderate nasal secretions), had no breathing problems, cough (resolved if little or no coughing/occasional strong cough/sometimes productive) and wheezing (resolved if no wheezing/terminal expiratory wheezing/only with stethoscope). Data for this endpoint was not analysed as the study was terminated early.

End point type	Secondary

End point timeframe:

Up to Day 21

End point values	Placebo	Rilematovir		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[14]	0[15]		
Units: Hours				
median (confidence interval 95%)	(to)	(to)		

Notes:

[14] - Data for this endpoint was not analysed as the study was terminated early.

[15] - Data for this endpoint was not analysed as the study was terminated early.

Statistical analyses

No statistical analyses for this end point

Secondary: ClinRO Signs/Symptoms Questionnaire Scores

End point title	ClinRO Signs/Symptoms Questionnaire Scores

End point description:

ClinRO Signs/Symptoms questionnaire was based on observations by clinician and it consisted of 12 items, each item was scored as follows: activity level =0,1,2,3; sleep disturbance =0,1,2,3; retractions =2,3; tachypnea =2; breathing problems =0,2,3; tachycardia =0,2; feeding problems =0,2,3; cough =0,1,3; nasal secretions =0,1,2; wheezing =0,1,2,3; and dehydration =0,3. In each item score of 0 and 1 indicated signs/symptoms were resolved and score of 2 and 3 indicated signs/symptoms were not resolved. A summary score was derived =mean of the item scores) and rated on a 4-point scale, with scores ranging from 0 to 3, higher score indicated, worse/higher severity of sign/symptom. Data for this endpoint was not analysed as the study was terminated early.

End point type	Secondary

End point timeframe:

Up to Day 21

End point values	Placebo	Rilematovir		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[16]	0[17]		
Units: Score on a scale				
arithmetic mean (standard deviation)	()	()		

Notes:

[16] - Data for this endpoint was not analysed as the study was terminated early.

[17] - Data for this endpoint was not analysed as the study was terminated early.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in ClinRO Signs/Symptoms Questionnaire Scores

End point title	Change From Baseline in ClinRO Signs/Symptoms Questionnaire Scores

End point description:

ClinRO Signs/Symptoms questionnaire was based on observations by clinician and it consisted of 12 items, each item was scored as follows: activity level =0,1,2,3; sleep disturbance =0,1,2,3; retractions =2,3; tachypnea =2; breathing problems =0,2,3; tachycardia =0,2; feeding problems =0,2,3; cough =0,1,3; nasal secretions =0,1,2; wheezing =0,1,2,3; and dehydration =0,3. In each item score of 0 and 1 indicated signs/symptoms were resolved and score of 2 and 3 indicated signs/symptoms were not resolved. A summary score was derived =mean of the item scores) and rated on a 4-point scale, with scores ranging from 0 to 3, higher score indicated, worse/higher severity of sign/symptom. Data for this endpoint was not analysed as the study was terminated early.

End point type	Secondary

End point timeframe:

Up to Day 21

End point values	Placebo	Rilematovir		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[18]	0[19]		
Units: Score on a scale				
arithmetic mean (standard deviation)	()	()		

Notes:

[18] - Data for this endpoint was not analysed as the study was terminated early.

[19] - Data for this endpoint was not analysed as the study was terminated early.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in ClinRO GHQ Over Time

End point title	Change From Baseline in ClinRO GHQ Over Time

End point description:

ClinRO GHQ was a 3 items questionnaire to evaluate the clinician’s general impression of the child’s RSV severity, change in RSV disease, and overall health status. Subject had to choose one answer from multiple options for each question i.e. do you have any concerns relating to the subject’s overall condition (no concerns [condition is stable or improving], some concerns [may become unstable/requires close observation], extremely concerned [unstable, requires immediate medical review]; overall, how would you rate the subject’s current health status (excellent, good, fair, poor); with respect to the child’s RSV infection, how would you describe the child’s health now compared to the baseline assessment (very much worse, much worse, a little worse, unchanged a little improved, much

very improved, much improved. Data for this endpoint was not analysed as the study was terminated early.

End point type	Secondary

End point timeframe:

Up to Day 21

End point values	Placebo	Rilematovir		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[20]	0[21]		
Units: Score on a scale				
arithmetic mean (standard deviation)	()	()		

Notes:

[20] - Data for this endpoint was not analysed as the study was terminated early.

[21] - Data for this endpoint was not analysed as the study was terminated early.

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Hospital Discharge From Start of Dosing

End point title	Time to Hospital Discharge From Start of Dosing

End point description:

Time (in hours) from first dose of study intervention to first hospital discharge was planned to be analysed. Data for this endpoint was not analysed as the study was terminated early.

End point type	Secondary

End point timeframe:

Up to Day 35

End point values	Placebo	Rilematovir		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[22]	0[23]		
Units: hours				
median (confidence interval 95%)	(to)	(to)		

Notes:

[22] - Data for this endpoint was not analysed as the study was terminated early.

[23] - Data for this endpoint was not analysed as the study was terminated early.

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Readiness for Hospital Discharge

End point title	Time to Readiness for Hospital Discharge

End point description:

Hospital discharge readiness referred to a subject having improved respiratory effort (example: improved retractions, stable respiratory rate), improved O2 saturation to greater than or equal to (>=) 92 percent (%) without need for supplemental oxygen, fever control, adequate hydration/feeding

without supplementation, stable and/or baseline mental status. Data for this endpoint was not analysed as the study was terminated early.

End point type	Secondary

End point timeframe:

Up to Day 35

End point values	Placebo	Rilematovir		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[24]	0[25]		
Units: hours				
median (confidence interval 95%)	(to)	(to)		

Notes:

[24] - Data for this endpoint was not analysed as the study was terminated early.

[25] - Data for this endpoint was not analysed as the study was terminated early.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Required Intensive Care Unit (ICU) Stay After First Dose of Rilematovir

End point title	Percentage of Subjects Required Intensive Care Unit (ICU) Stay After First Dose of Rilematovir

End point description:

Percentage of subjects required ICU stay were analysed and reported. ITT-i analysis set included all randomized subjects who received at least 1 dose of study intervention and had an RSV infection confirmed by central laboratory analysis. Here, N (number of subjects analysed) signifies subjects with no ICU stay before first dose of rilematovir.

End point type	Secondary

End point timeframe:

Up to Day 35

End point values	Placebo	Rilematovir		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	17		
Units: Percentage of subjects				
number (not applicable)	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Requiring ICU Stay

End point title	Duration of Requiring ICU Stay

End point description:

Duration (in hours) of requiring ICU stay was defined as total number of hours a subject experienced an ICU stay from first dose of rilematovir until study termination, calculated as the sum of all separate records of ICU stay. ITT-i analysis set included all randomized subjects who received at least 1 dose of study intervention and had an RSV infection confirmed by central laboratory analysis. Here, N (number of subjects analysed) signifies subjects who required ICU stay before first dose of rilematovir and continued after first dose plus subjects who required ICU stay after first dose of drug without prior ICU stay.

End point type	Secondary

End point timeframe:

Up to Day 35

End point values	Placebo	Rilematovir		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2	2		
Units: hours				
arithmetic mean (standard deviation)	66.46 (± 24.145)	40.83 (± 22.822)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Requiring Re-hospitalization for Respiratory/other Reasons

End point title	Percentage of Subjects Requiring Re-hospitalization for Respiratory/other Reasons

End point description:

Percentage of subjects requiring re-hospitalization (subjects re-hospitalized [ward or ICU] after been discharged from hospital) for respiratory/other reasons were reported. ITT-i analysis set included all randomised subjects who received at least 1 dose of study intervention and had an RSV infection confirmed by central laboratory analysis.

End point type	Secondary

End point timeframe:

Up to Day 35

End point values	Placebo	Rilematovir		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8	19		
Units: Percentage of subjects				
number (not applicable)	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Requiring Oxygen Supplementation After First Dose of Rilematovir

End point title	Percentage of Subjects Requiring Oxygen Supplementation After First Dose of Rilematovir

End point description:

Percentage of subjects requiring any type of oxygen supplementation (invasive mechanical ventilation, non-invasive mechanical ventilation and non-invasive non-mechanical ventilation) were reported. ITT-i analysis set included all randomised subjects who received at least 1 dose of study intervention and had an RSV infection confirmed by central laboratory analysis. Here, N (number of subjects analysed) signifies subjects with no use of oxygen supplementation before first dose of rilematovir.

End point type	Secondary

End point timeframe:

Up to Day 35

End point values	Placebo	Rilematovir		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	13		
Units: Percentage of subjects				
number (not applicable)	16.7	30.8		

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Oxygen Supplementation

End point title	Duration of Oxygen Supplementation

End point description:

Duration (in hours) of oxygen supplementation was defined as total number of hours a subject used supplemental oxygen from first dose of rilematovir until study termination, calculated as the sum of all separate records of supplementation. ITT-i analysis set included all randomised subjects who received at least 1 dose of study intervention and had an RSV infection confirmed by central laboratory analysis. Here, N (number of subjects analysed) signifies subjects required oxygen supplementation before first dose of rilematovir and continued after first dose plus subjects who required oxygen supplementation after first dose of rilematovir without prior oxygen supplementation.

End point type	Secondary

End point timeframe:

Up to Day 35

End point values	Placebo	Rilematovir		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	10		
Units: Hours				
arithmetic mean (standard deviation)	39.91 (± 26.146)	66.59 (± 51.956)		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to end of Supplemental Feeding/hydration

End point title	Time to end of Supplemental Feeding/hydration

End point description:

Time (in hours) to end of supplemental feeding/hydration was planned to be reported. Data for this endpoint was not analysed as the study was terminated early.

End point type	Secondary

End point timeframe:

Up to Day 35

End point values	Placebo	Rilematovir		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[26]	0[27]		
Units: Hours				
median (confidence interval 95%)	(to)	(to)		

Notes:

[26] - Data for this endpoint was not analysed as the study was terminated early.

[27] - Data for this endpoint was not analysed as the study was terminated early.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Requiring Hydration and/or Feeding by Intravenous (IV) Administration or Nasogastric Tube After First Dose of Rilematovir

End point title	Percentage of Subjects Requiring Hydration and/or Feeding by Intravenous (IV) Administration or Nasogastric Tube After First Dose of Rilematovir

End point description:

Percentage of subjects requiring any type of hydration and/or feeding by intravenous (IV) administration or nasogastric tube or percutaneous endoscopic gastrostomy were reported. ITT-i analysis set included all randomized subjects who received at least 1 dose of study intervention and had an RSV infection confirmed by central laboratory analysis. Here, N (number of subjects analysed) signifies subjects with no use of feeding/hydration supplementation before 1st dose of study drug.

End point type	Secondary

End point timeframe:

Up to Day 35

End point values	Placebo	Rilematovir		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	15		
Units: Percentage of subjects				
number (not applicable)	33.3	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Supplemental Feeding/hydration

End point title	Duration of Supplemental Feeding/hydration

End point description:

Duration (in hours) of supplemental feeding/hydration was defined as total number of hours a subject was administered feeding/hydration supplementation from first dose of rilematovir until study termination, calculated as the sum all separate records of supplementation use per subject. ITT-i analysis set included all randomized subjects who received at least 1 dose of study intervention and had an RSV infection confirmed by central laboratory analysis. Here, N (number of subjects analysed) signifies subjects required supplemental feeding/hydration before first dose of rilematovir and continued after first dose plus subjects required supplemental feeding/hydration after first dose of rilematovir without prior supplemental feeding/hydration.

End point type	Secondary

End point timeframe:

Up to Day 35

End point values	Placebo	Rilematovir		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	4		
Units: Hours				
arithmetic mean (standard deviation)	43.13 (± 41.526)	31.96 (± 21.311)		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to end of Supplemental Oxygen and/or Feeding/hydration

End point title	Time to end of Supplemental Oxygen and/or Feeding/hydration

End point description:

Time to end of supplemental oxygen and/or feeding/hydration was planned to be analysed. Data for this endpoint was not analysed as the study was terminated early.

End point type	Secondary

End point timeframe:

Up to Day 35

End point values	Placebo	Rilematovir		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[28]	0[29]		
Units: Hours				
arithmetic mean (confidence interval 95%)	(to)	(to)		

Notes:

[28] - Data for this endpoint was not analysed as the study was terminated early.

[29] - Data for this endpoint was not analysed as the study was terminated early.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Medical Encounters and Treatments

End point title	Number of Subjects with Medical Encounters and Treatments

End point description:

Medical resource utilization was assessed by number of medical care encounters. Medical encounters referred as physician or emergency room visits, tests and procedures, and medications, surgeries and other selected procedures, inpatient and outpatient. ITT-i analysis set included all randomised subjects who received at least 1 dose of study intervention and had an RSV infection confirmed by central laboratory analysis.

End point type	Secondary

End point timeframe:

Up to Day 35

End point values	Placebo	Rilematovir		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8	19		
Units: Subjects	1	3		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Antibiotic Treatment Episodes

End point title	Number of Subjects with Antibiotic Treatment Episodes

End point description:

Number of subjects with antibiotic treatment episodes were planned to be reported. Data for this endpoint was not analysed as the study was terminated early.

End point type	Secondary

End point timeframe:

Up to Day 35

End point values	Placebo	Rilematovir		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[30]	0[31]		
Units: Subjects				

Notes:

[30] - Data for this endpoint was not analysed as the study was terminated early.

[31] - Data for this endpoint was not analysed as the study was terminated early.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Systemic or Inhaled Corticosteroids and Bronchodilators use

End point title	Number of Subjects with Systemic or Inhaled Corticosteroids and Bronchodilators use

End point description:

Number of subjects with systemic or inhaled corticosteroids and bronchodilators use were planned to be reported. Data for this endpoint was not analysed as the study was terminated early.

End point type	Secondary

End point timeframe:

Up to Day 35

End point values	Placebo	Rilematovir		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[32]	0[33]		
Units: Subjects				

Notes:

[32] - Data for this endpoint was not analysed as the study was terminated early.

[33] - Data for this endpoint was not analysed as the study was terminated early.

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the RSV Viral Load-time Curve [AUC]) From Immediately Prior to First Dose of Study Intervention (Baseline) Through Day 8

End point title	Area Under the RSV Viral Load-time Curve [AUC]) From Immediately Prior to First Dose of Study Intervention (Baseline) Through Day 8

End point description:

Area under the RSV viral load-time curve was planned to be analysed. RSV viral load was planned to be measured by quantitative reverse transcription (qRT)- polymerase chain reaction (PCR) in the mid-turbinate (MT) nasal swab specimens. Data for this endpoint was not analysed as the study was terminated early.

End point type	Secondary

End point timeframe:

Baseline up to Day 8

End point values	Placebo	Rilematovir		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[34]	0[35]		
Units: nanogram*hour per millilitre				
arithmetic mean (standard deviation)	()	()		

Notes:

[34] - Data for this endpoint was not analysed as the study was terminated early.

[35] - Data for this endpoint was not analysed as the study was terminated early.

Statistical analyses

No statistical analyses for this end point

Secondary: RSV Viral Load at Baseline, Days 2, 3, 5, 8, 14 and 21

End point title	RSV Viral Load at Baseline, Days 2, 3, 5, 8, 14 and 21

End point description:

Antiviral activity was determined based on measurements of RSV viral load which was measured by quantitative reverse transcription polymerase chain reaction (qRT-PCR) in the mid-turbinate (MT) nasal swab specimens. ITT-i analysis set included all randomized subjects who received at least 1 dose of study intervention and had an RSV infection confirmed by central laboratory analysis. Here, 'n' (number analysed) signifies number of subjects with data evaluable at each specified time points.

End point type	Secondary

End point timeframe:

Baseline, Days 2, 3, 5, 8, 14 and 21

End point values	Placebo	Rilematovir		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8	19		
Units: log10 copies per millilitre				
arithmetic mean (standard deviation)				
Baseline (n =8,18)	7.031 (± 1.9995)	6.286 (± 1.3671)		
Day 2 (n =8,19)	6.000 (± 1.5678)	5.579 (± 1.5668)		
Day 3 (n =8,19)	5.465 (± 1.7454)	4.981 (± 1.9530)		
Day 5 (n =8,19)	4.066 (± 1.5565)	4.132 (± 1.5199)		
Day 8 (n =8,18)	1.373 (± 2.0865)	2.156 (± 2.1681)		
Day 14 (n =7,17)	1.217 (± 2.1478)	0.709 (± 1.3389)		
Day 21 (n =7,17)	0.414 (± 1.0961)	0.464 (± 1.4547)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in RSV Viral Load at Days 2, 3, 5, 8, 14 and 21

End point title	Change From Baseline in RSV Viral Load at Days 2, 3, 5, 8, 14 and 21

End point description:

Antiviral activity was determined based on measurements of RSV viral load which was measured by qRT-PCR, in the MT nasal swab specimens. ITT-i analysis set included all randomized subjects who received at least 1 dose of study intervention and had an RSV infection confirmed by central laboratory analysis. Here, N (number of subjects analysed) signifies subjects evaluated for this endpoint and 'n' (number analysed) signifies number of subjects evaluable at specified time points.

End point type	Secondary

End point timeframe:

Baseline, Days 2, 3, 5, 8, 14 and 21

End point values	Placebo	Rilematovir		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8	18		
Units: log10 copies per millitre				
arithmetic mean (standard deviation)				
Day 2 (n =8, 18)	-1.031 (± 0.6091)	-0.825 (± 1.2906)		
Day 3 (n =8, 18)	-1.566 (± 2.2167)	-1.436 (± 1.5185)		
Day 5 (n =8, 18)	-2.965 (± 1.9154)	-2.241 (± 1.3393)		
Day 8 (n =8, 17)	-5.658 (± 1.9872)	-4.126 (± 1.8461)		
Day 14 (n =7, 17)	-5.693 (± 2.2654)	-5.640 (± 2.0261)		
Day 21 (n =7, 16)	-7.207 (± 1.3201)	-5.789 (± 1.9560)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with Undetectable RSV Viral Load

End point title	Percentage of Subjects with Undetectable RSV Viral Load

End point description:

Percentage of subjects with undetectable RSV viral load was analysed. ITT-i analysis set included all

randomized subjects who received at least 1 dose of study intervention and had an RSV infection confirmed by central laboratory analysis. Here, 'n' (number analysed) signifies number of subjects evaluable at specified time points.

End point type	Secondary

End point timeframe:

Baseline, Days 2, 3, 5, 8, 14 and 21

End point values	Placebo	Rilematovir		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8	19		
Units: Percentage of subjects				
number (not applicable)				
Baseline (n= 8,18)	0	0		
Day 2 (n= 8,19)	0	0		
Day 3 (n= 8,19)	0	5.3		
Day 5 (n= 8,19)	0	0		
Day 8 (n= 8,18)	62.5	44.4		
Day 14 (n= 7,17)	71.4	76.5		
Day 21 (n= 7,17)	85.7	88.2		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Post-baseline Changes in the RSV F-gene Compared with Baseline Sequences

End point title	Number of Subjects with Post-baseline Changes in the RSV F-gene Compared with Baseline Sequences

End point description:

Number of subjects with post-baseline changes in the RSV F-gene compared with baseline sequences was planned to be reported. Data for this endpoint was not analysed as the study was terminated early.

End point type	Secondary

End point timeframe:

Baseline up to Day 21

End point values	Placebo	Rilematovir		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[36]	0[37]		
Units: Subjects				

Notes:

[36] - Data for this endpoint was not analysed as the study was terminated early.

[37] - Data for this endpoint was not analysed as the study was terminated early.

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma Concentrations of Rilematovir

End point title	Plasma Concentrations of Rilematovir[38]

End point description:

Plasma concentrations of rilematovir was analysed. Subject wise data were reported for this endpoint. Pharmacokinetics analysis set (PKAS) included subjects who had received at least 1 dose of rilematovir and had at least 1 valid blood sample drawn for Pharmacokinetics analysis. No summary analysis was done as study was terminated early and subject wise data were reported. Here, "n" signifies specific subject with data available at specified timepoint.

End point type	Secondary

End point timeframe:

1 hour Post-dose (Day 1) and pre-dose (Day 2)

Notes:

[38] - 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 analysed for specified arms only.

End point values	Rilematovir			
Subject group type	Reporting group			
Number of subjects analysed	18			
Units: nanogram per millilitre				
number (not applicable)				
Subject 1 Day 1 (n=1)	1450			
Subject 2 Day 1 (n=1)	1750			
Subject 3 Day 1 (n=1)	72.5			
Subject 4 Day 1 (n=1)	656			
Subject 5 Day 1 (n=1)	918			
Subject 6 Day 1 (n=1)	1050			
Subject 7 Day 1 (n=1)	135			
Subject 8 Day 1 (n=1)	1730			
Subject 9 Day 1 (n=1)	602			
Subject 10 Day 1 (n=1)	1810			
Subject 11 Day 1 (n=1)	1640			
Subject 12 Day 1 (n=1)	3760			
Subject 13 Day 1 (n=1)	561			
Subject 14 Day 1 (n=1)	127			
Subject 15 Day 1 (n=1)	787			
Subject 16 Day 1 (n=1)	2020			
Subject 17 Day 1 (n=1)	157			
Subject 18 Day 1 (n=1)	1260			
Subject 1 Day 2 (n=1)	134			
Subject 2 Day 2 (n=1)	281			
Subject 3 Day 2 (n=1)	5.74			
Subject 5 Day 2 (n=1)	417			
Subject 6 Day 2 (n=1)	828			
Subject 7 Day 2 (n=1)	1030			
Subject 8 Day 2 (n=1)	339			
Subject 9 Day 2 (n=1)	186			
Subject 10 Day 2 (n=1)	687			
Subject 11 Day 2 (n=1)	1750			
Subject 12 Day 2 (n=1)	4650			

Subject 13 Day 2 (n=1)	311			
Subject 14 Day 2 (n=1)	77.3			
Subject 15 Day 2 (n=1)	749			
Subject 16 Day 2 (n=1)	457			
Subject 17 Day 2 (n=1)	493			
Subject 18 Day 2 (n=1)	2930			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Acceptability and Palatability of the Rilematovir Formulation as Assessed by Parent(s)/Caregiver(s)

End point title	Percentage of Subjects With Acceptability and Palatability of the Rilematovir Formulation as Assessed by Parent(s)/Caregiver(s)

End point description:

Acceptability and palatability were assessed by clinician electronic clinical outcome assessment (eCOA) questionnaire which consisted of 7 questions, 1- child took medicine easily, 2- disgusted expressions after tasting medicine, 3- cried after tasting medicine, 4- would not open mouth or turned head away to avoid medicine, 5- spit out or coughed out medicine, 6- gagged, 7- vomited (within 2 minutes of swallowing medicine). ITT-i analysis set included all randomized subjects who received at least 1 dose of study intervention and had an RSV infection confirmed by central laboratory analysis. Here, N (number of subjects analysed) signifies subjects evaluated for this endpoint. Reported only those categories which had data for at least one reporting arm.

End point type	Secondary

End point timeframe:

Day 8

End point values	Placebo	Rilematovir		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7	15		
Units: Percentage of subjects				
number (not applicable)				
Child took medicine easily	85.7	86.7		
Disgusted expressions after tasting medicine	0	13.3		
Did not open mouth or turned head away	14.3	6.7		
Spit out or coughed out medicine	14.3	0		
Gagged	0	6.7		

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum Observed Plasma Concentration (Cmax) of Rilematovir

End point title	Maximum Observed Plasma Concentration (Cmax) of Rilematovir[39]

End point description:

Cmax of rilematovir was planned to be analysed. Data for this endpoint was not analysed as the study was terminated early.

End point type	Secondary

End point timeframe:

Up to Day 35

Notes:

[39] - 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 analysed for specified arms only.

End point values	Rilematovir			
Subject group type	Reporting group			
Number of subjects analysed	0[40]			
Units: nanogram per milliliter				
arithmetic mean (standard deviation)	()			

Notes:

[40] - Data for this endpoint was not analysed as the study was terminated early.

Statistical analyses

No statistical analyses for this end point

Secondary: Pre dose Plasma Concentration (Ctrough) of Rilematovir

End point title	Pre dose Plasma Concentration (Ctrough) of Rilematovir[41]

End point description:

Ctrough of rilematovir was planned to be analysed. Data for this endpoint was not analysed as the study was terminated early.

End point type	Secondary

End point timeframe:

Pre-dose on Day 1

Notes:

[41] - 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 analysed for specified arms only.

End point values	Rilematovir			
Subject group type	Reporting group			
Number of subjects analysed	0[42]			
Units: nanogram per milliliter				
arithmetic mean (standard deviation)	()			

Notes:

[42] - Data for this endpoint was not analysed as the study was terminated early.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: Up to Day 35	
Assessment type	Non-systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	24.1
Reporting groups	
Reporting group title	Placebo
Reporting group description: Subjects aged >=28 days to <3 months, >=3 to <6 months and >=6 months to <=5 years received placebo matching to rilematovir BID from Days 1 to 7 (14 consecutive doses).	
Reporting group title	Rilematovir
Reporting group description: Subjects aged >=28 days to <3 months, >=3 to <6 months and >=6 months to <=5 years received 2.5, 3 and 4.5 mg/kg rilematovir respectively as 20 mg/mL suspension BID from Days 1 to 7 (14 consecutive doses).	

Serious adverse events	Placebo	Rilematovir	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 8 (0.00%)	1 / 20 (5.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Infections and infestations			
Parainfluenzae Virus Infection			
subjects affected / exposed	0 / 8 (0.00%)	1 / 20 (5.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Placebo	Rilematovir	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 8 (62.50%)	10 / 20 (50.00%)	
Investigations			
Eosinophil Count Increased			
subjects affected / exposed	1 / 8 (12.50%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Blood Magnesium Decreased			

subjects affected / exposed	1 / 8 (12.50%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Oxygen Saturation Decreased			
subjects affected / exposed	0 / 8 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Cardiac disorders			
Ventricular Extrasystoles			
subjects affected / exposed	0 / 8 (0.00%)	2 / 20 (10.00%)	
occurrences (all)	0	2	
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 8 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Blood and lymphatic system disorders			
Neutrophilia			
subjects affected / exposed	0 / 8 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Thrombocytosis			
subjects affected / exposed	1 / 8 (12.50%)	1 / 20 (5.00%)	
occurrences (all)	1	1	
General disorders and administration site conditions			
Hyperthermia			
subjects affected / exposed	1 / 8 (12.50%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Infusion Site Extravasation			
subjects affected / exposed	1 / 8 (12.50%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Pyrexia			
subjects affected / exposed	1 / 8 (12.50%)	2 / 20 (10.00%)	
occurrences (all)	1	2	
Gastrointestinal disorders			
Abdominal Pain			
subjects affected / exposed	0 / 8 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Diarrhoea			

subjects affected / exposed	0 / 8 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Faeces Discoloured			
subjects affected / exposed	0 / 8 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Vomiting			
subjects affected / exposed	1 / 8 (12.50%)	0 / 20 (0.00%)	
occurrences (all)	2	0	
Respiratory, thoracic and mediastinal disorders			
Epistaxis			
subjects affected / exposed	0 / 8 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Respiratory Distress			
subjects affected / exposed	0 / 8 (0.00%)	2 / 20 (10.00%)	
occurrences (all)	0	2	
Skin and subcutaneous tissue disorders			
Eczema Infantile			
subjects affected / exposed	1 / 8 (12.50%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Onychomadesis			
subjects affected / exposed	0 / 8 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Rash			
subjects affected / exposed	0 / 8 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Skin Exfoliation			
subjects affected / exposed	0 / 8 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Urticaria			
subjects affected / exposed	0 / 8 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Infections and infestations			
Covid-19			
subjects affected / exposed	0 / 8 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Laryngitis			

subjects affected / exposed	0 / 8 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Pneumonia			
subjects affected / exposed	0 / 8 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Rhinitis			
subjects affected / exposed	0 / 8 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	2	
Upper Respiratory Tract Infection			
subjects affected / exposed	0 / 8 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Metabolism and nutrition disorders			
Hyperkalaemia			
subjects affected / exposed	0 / 8 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Hypermagnesaemia			
subjects affected / exposed	0 / 8 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
04 May 2021	Amendment 1 included the following changes: addition of estimand language for the primary endpoint, revised assessments for follow-up of subjects who prematurely discontinued the study intervention/the study, inclusion criterion was updated to clarify correction of gestational age applied only to subjects born preterm, inclusion criterion 5 was updated to ensure enrollment of subjects with at least moderate RSV disease severity who were more likely to benefit from RSV treatment, protocol-defined RRS categories were further specified, additional laboratory assessments were added to further evaluate hepatobiliary effects, values for vital sign abnormalities for age group 3 to less than or equal to (<=) 5 years of age were updated, and PRESORS timing and instructions were clarified and minor changes were incorporated.

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.

Data collection and analysis was not performed for few secondary endpoints.

Notes: