Clinical trial results:
A Phase 2, Randomized, Double-blind, Placebo-controlled Study to Evaluate the Antiviral Activity, Clinical Outcomes, Safety, Tolerability, and Pharmacokinetics of Orally Administered Lumicitabine (JNJ-64041575) Regimens in Hospitalized Infants and Children Aged 28 Days to 36 Months Infected With Respiratory Syncytial Virus

Summary

EudraCT number	2017-001862-56
Trial protocol	GB DE BE FI SK ES IE PT FR IT
Global end of trial date	23 March 2018

Results information

Result version number	v2 (current)
This version publication date	31 October 2019
First version publication date	26 April 2019
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	CR108367

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03333317
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Janssen- Cilag International NV
Sponsor organisation address	Turnhoutseweg 30, Beerse, Belgium, B-2340
Public contact	Clinical Registry Group, Janssen- Cilag International NV, ClinicalTrialsEU@its.jnj.com
Scientific contact	Clinical Registry Group, Janssen- Cilag International NV, 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-001758-PIP01-15
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	Yes
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	23 March 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	23 March 2018
Global end of trial reached?	Yes
Global end of trial date	23 March 2018
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The purpose of this study was to determine in hospitalized infants and children who were infected with respiratory syncytial virus (RSV) the dose-response relationship of multiple regimens of lumicitabine on antiviral activity based on nasal RSV shedding using quantitative real-time reverse transcriptase polymerase chain reaction (qRT-PCR).

Protection of trial subjects:

The study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and that are consistent with Good Clinical Practices and applicable regulatory requirements. Safety evaluations were based upon the type, incidence, and severity of treatment-emergent adverse events (TEAEs) and adverse events (AEs) of special interest reported throughout the study, and on changes in vital sign measurements, clinical laboratory test results, physical examinations and 12-lead electrocardiograms (ECGs).

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	24 November 2017
Long term follow-up planned	Yes
Long term follow-up rationale	Efficacy, Safety
Long term follow-up duration	2 Years
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Japan: 7
Worldwide total number of subjects	7
EEA total number of subjects	0

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)	6
Children (2-11 years)	1
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:

On 17 October 2018, the study was stopped prematurely by the sponsor as a precautionary measure, to allow further evaluation and assessment of the new nonclinical pharmacokinetics (PK) and safety findings and determine their relevance to human studies.

Pre-assignment

Screening details:

Total 8 subjects that met all the eligibility criteria and had signed an ICF were enrolled, of which 7 subjects were randomized to receive lumicitabine or placebo. One eligible subject was not randomized and treated due to a lack of availability of study drug at the clinical site.

Period 1

Period 1 title	Treatment and Follow-up (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Subjects received a single dose of lumicitabine-40 milligrams/kilogram (mg/kg) matched placebo as a loading dose (LD) (Dose 1) followed by 9 maintenance dose (MD) of lumicitabine-20 mg/kg matched placebo twice a day or a single dose of lumicitabine-60 mg/kg matched placebo LD (Dose 1) followed by nine lumicitabine-40 mg/kg matched placebo MD (Dose 2 to 10).

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

Dosage and administration details:

Subjects received oral administration of matching placebo.

Arm title	Lumicitabine 40/20 mg/kg LD/MD

Arm description:

Subjects received a single dose of lumicitabine-40 mg/kg as LD (Dose 1) followed by 9 MD doses of lumicitabine 20 mg/kg twice a day.

Arm type	Experimental
Investigational medicinal product name	Lumicitabine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for oral suspension
Routes of administration	Oral use

Dosage and administration details:

Subjects received a single dose of lumicitabine-40 mg/kg as LD (Dose 1) followed by 9 MD doses of lumicitabine-20 mg/kg
twice a day.

Arm title	Lumicitabine 60/40 mg/kg LD/MD

Arm description:

Subjects received a single dose of lumicitabine-60 mg/kg as LD (Dose 1) followed by 9 MD doses of

lumicitabine 40 mg/kg twice a day.

Arm type	Experimental
Investigational medicinal product name	Lumicitabine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for oral suspension
Routes of administration	Oral use

Dosage and administration details:

Subjects received a single dose of lumicitabine-60 mg/kg as LD (Dose 1) followed by 9 MD doses of lumicitabine-40mg/kg
twice a day.

Number of subjects in period 1	Placebo	Lumicitabine 40/20 mg/kg LD/MD	Lumicitabine 60/40 mg/kg LD/MD
Started	3	1	3
Completed	3	1	3

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Subjects received a single dose of lumicitabine-40 milligrams/kilogram (mg/kg) matched placebo as a loading dose (LD) (Dose 1) followed by 9 maintenance dose (MD) of lumicitabine-20 mg/kg matched placebo twice a day or a single dose of lumicitabine-60 mg/kg matched placebo LD (Dose 1) followed by nine lumicitabine-40 mg/kg matched placebo MD (Dose 2 to 10).	
Reporting group title	Lumicitabine 40/20 mg/kg LD/MD
Reporting group description:	
Subjects received a single dose of lumicitabine-40 mg/kg as LD (Dose 1) followed by 9 MD doses of lumicitabine 20 mg/kg twice a day.	
Reporting group title	Lumicitabine 60/40 mg/kg LD/MD
Reporting group description:	
Subjects received a single dose of lumicitabine-60 mg/kg as LD (Dose 1) followed by 9 MD doses of lumicitabine 40 mg/kg twice a day.	

Reporting group values	Placebo	Lumicitabine 40/20 mg/kg LD/MD	Lumicitabine 60/40 mg/kg LD/MD
Number of subjects	3	1	3
Title for AgeCategorical Units: subjects			
In utero	0	0	0
Preterm newborn - gestational age < 37 wk	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	2	1	3
Children (2-11 years)	1	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	0	0	0
From 65 to 84 years	0	0	0
85 years and over	0	0	0
Title for AgeContinuous			
Here '99999' indicates that the data was not estimated due to only single subject was analyzed.			
Units: months			
arithmetic mean	16.0	17.0	6.3
standard deviation	± 13.08	± 99999	± 2.52
Title for Gender Units: subjects			
Female	0	0	1
Male	3	1	2

Reporting group values	Total		
Number of subjects	7		
Title for AgeCategorical Units: subjects			
In utero	0		
Preterm newborn - gestational age < 37 wk	0		
Newborns (0-27 days)	0		

Infants and toddlers (28 days-23 months)	6		
Children (2-11 years)	1		
Adolescents (12-17 years)	0		
Adults (18-64 years)	0		
From 65 to 84 years	0		
85 years and over	0		
Title for AgeContinuous			
Here '99999' indicates that the data was not estimated due to only single subject was analyzed.			
Units: months			
arithmetic mean			
standard deviation	-		
Title for Gender			
Units: subjects			
Female	1		
Male	6		

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Subjects received a single dose of lumicitabine-40 milligrams/kilogram (mg/kg) matched placebo as a loading dose (LD) (Dose 1) followed by 9 maintenance dose (MD) of lumicitabine-20 mg/kg matched placebo twice a day or a single dose of lumicitabine-60 mg/kg matched placebo LD (Dose 1) followed by nine lumicitabine-40 mg/kg matched placebo MD (Dose 2 to 10).	
Reporting group title	Lumicitabine 40/20 mg/kg LD/MD
Reporting group description:	
Subjects received a single dose of lumicitabine-40 mg/kg as LD (Dose 1) followed by 9 MD doses of lumicitabine 20 mg/kg twice a day.	
Reporting group title	Lumicitabine 60/40 mg/kg LD/MD
Reporting group description:	
Subjects received a single dose of lumicitabine-60 mg/kg as LD (Dose 1) followed by 9 MD doses of lumicitabine 40 mg/kg twice a day.	

Primary: Area Under the Curve (AUC) of Respiratory Syncytial Virus (RSV) Viral Load

End point title	Area Under the Curve (AUC) of Respiratory Syncytial Virus (RSV) Viral Load[1]
End point description:	
AUC of RSV viral load was measured by quantitative reverse transcriptase-polymerase chain reaction (qRT-PCR) assay of the mid-turbinate nasal swab.	
End point type	Primary
End point timeframe:	
Day 1 to 7: Predose, 0.25 and 2 hours postdose	

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 formal statistical hypothesis testing was planned for this study due to the descriptive nature of this study.

End point values	Placebo	Lumicitabine 40/20 mg/kg LD/MD	Lumicitabine 60/40 mg/kg LD/MD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[2]	0[3]	0[4]	
Units: Copies*Day/milliliters				
arithmetic mean (standard deviation)	()	()	()	

Notes:

[2] - As study was terminated early with fewer subjects, result for this endpoint could not be determined.
[3] - As study was terminated early with fewer subjects, result for this endpoint could not be determined.
[4] - As study was terminated early with fewer subjects, result for this endpoint could not be determined.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Emergent Adverse Event (AE)

End point title	Number of Subjects with Emergent Adverse Event (AE)

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 does not necessarily have a causal relationship with the treatment. An AE can, therefore, be any unfavorable and unintended sign (including an abnormal finding), symptom, or disease temporally associated with the use of a medicinal (investigational or non-investigational) product, whether or not related to that medicinal (investigational or non-investigational) product. Safety analysis set was defined as all subjects who received at least 1 dose of study drug, analyzed as treated.

End point type	Secondary

End point timeframe:

Approximately up to 28 days

End point values	Placebo	Lumicitabine 40/20 mg/kg LD/MD	Lumicitabine 60/40 mg/kg LD/MD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	3	1	3	
Units: Subjects				
number (not applicable)	3	1	3	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Clinically Significant Physical Examinations Abnormalities

End point title	Number of Subjects with Clinically Significant Physical Examinations Abnormalities

End point description:

Number of subjects with clinically significant physical examination (respiratory system, nose, ear, throat, facial and neck lymph nodes, and skin examination) abnormalities that emerged after treatment initiation was reported. Randomized or Treated set was defined as all subjects who were in the Randomized Analysis Set (all randomized subjects with a randomization date at or before the date of the first intake of medication, or with a randomization date and a missing date for first medication intake, analyzed as randomized) and/or all subjects treated (AST) set.

End point type	Secondary

End point timeframe:

Up to 28 days

End point values	Placebo	Lumicitabine 40/20 mg/kg LD/MD	Lumicitabine 60/40 mg/kg LD/MD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	3	1	3	
Units: Subjects	2	1	1	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Emergent Clinical Relevant Vital Signs Abnormalities

End point title	Number of Subjects with Emergent Clinical Relevant Vital Signs Abnormalities

End point description:

The number of subjects with emergent clinically relevant vital signs (temperature, pulse rate, respiratory rate, diastolic blood pressure, systolic blood pressure, oxygen saturation) abnormalities that emerged after treatment initiation was reported. Safety analysis set was defined as all subjects who received at least 1 dose of study drug, analyzed as treated.

End point type	Secondary

End point timeframe:

Up to 28 days

End point values	Placebo	Lumicitabine 40/20 mg/kg LD/MD	Lumicitabine 60/40 mg/kg LD/MD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	3	1	3	
Units: Subjects				
number (not applicable)				
Systolic Blood Pressure (Abnormally high)	2	1	1	
Diastolic Blood Pressure (Abnormally high)	1	1	0	
Pulse Rate (Abnormally high)	1	1	1	
Respiratory Rate (Abnormally high)	1	0	0	
Temperature (High)	1	0	1	
Oxygen Saturation (Abnormally low)	1	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Electrocardiogram (ECG) Abnormalities

End point title	Number of Subjects with Electrocardiogram (ECG) Abnormalities

End point description:

The number of subjects with ECG (PR, QT, QRS, QTc intervals, and heart rate) abnormalities reported. Safety analysis set was defined as all subjects who received at least 1 dose of study drug, analyzed as

treated.

End point type	Secondary

End point timeframe:

Up to 28 days

End point values	Placebo	Lumicitabine 40/20 mg/kg LD/MD	Lumicitabine 60/40 mg/kg LD/MD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	3	1	3	
Units: Subjects				
number (not applicable)				
QT Duration	1	0	0	
QTcB: Bazett's Correction Formula	0	0	0	
QTcF: Fridericia's Correction Formula	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Worst Emergent Laboratory Abnormalities (Division of Microbiology and Infectious Diseases [DMID] Toxicity Grades)

End point title	Number of Subjects with Worst Emergent Laboratory Abnormalities (Division of Microbiology and Infectious Diseases [DMID] Toxicity Grades)

End point description:

The number of subjects with Laboratory (hematology, serum chemistry, and urinalysis) abnormalities reported based on the DMID toxicity grading scale. Safety analysis set was defined as all subjects who received at least 1 dose of study drug, analyzed as treated.

End point type	Secondary

End point timeframe:

Up to 28 days

End point values	Placebo	Lumicitabine 40/20 mg/kg LD/MD	Lumicitabine 60/40 mg/kg LD/MD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	3	1	3	
Units: Subjects				
number (not applicable)				
Alanine transaminase (ALT): Grade 0	3	0	3	
ALT: Grade 1	0	1	0	
Aspartate Aminotransferase (AST): Grade 0	3	1	3	
Bilirubin: Grade 0	3	1	3	
Creatinine: Grade 0	3	1	2	

Creatinine: Grade 2	0	0	1	
Hypoglycemia: Grade 0	3	1	3	
Hyperglycemia: Grade 0	3	1	3	
Hypokalemia: Grade 0	3	1	3	
Hyperkalemia: Grade 0	1	1	1	
Hyperkalemia: Grade 1	2	0	2	
Hyponatremia: Grade 0	3	1	3	
Hypernatremia: Grade 0	3	1	3	
Hemoglobin: Grade 0	2	1	2	
Hemoglobin: Grade 1	1	0	0	
Hemoglobin: Grade 2	0	0	1	
Absolute neutrophil count: Grade 0	2	1	0	
Absolute neutrophil count: Grade 1	1	0	1	
Absolute neutrophil count: Grade 3	0	0	1	
Absolute neutrophil count: Grade 4	0	0	1	
Platelets: Grade 0	3	1	2	
Platelets: Grade 3	0	0	1	

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum Observed Plasma Concentration (Cmax) of JNJ-63549109 (Metabolite of Lumicitabine)

End point title	Maximum Observed Plasma Concentration (Cmax) of JNJ-63549109 (Metabolite of Lumicitabine)[5]

End point description:

The Cmax is the maximum observed plasma concentration. Intent to Treat (ITT) set was defined as all randomized subjects who receive at least 1 dose of study. Here, "99999" indicates that the data was not estimable as only one subject was analyzed in the specified arm.

End point type	Secondary

End point timeframe:

Day 1 and Day 5

Notes:

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

End point values	Lumicitabine 40/20 mg/kg LD/MD	Lumicitabine 60/40 mg/kg LD/MD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1	3		
Units: nano-gram/milliliter (ng/ml)				
arithmetic mean (standard deviation)				
Day 1	6184 (± 99999)	7003 (± 3806)		
Day 5	3261 (± 99999)	5112 (± 1665)		

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under Plasma Concentration-time Curve (AUC) of JNJ-63549109 (Metabolite of Lumicitabine)

End point title	Area Under Plasma Concentration-time Curve (AUC) of JNJ-63549109 (Metabolite of Lumicitabine)[6]

End point description:

AUC is the area under the plasma concentration-time curve. ITT set was defined as all randomized subjects who receive at least 1 dose of study. Here, "99999" indicates that the data was not estimable as only one subject was analyzed in the specified arm.

End point type	Secondary

End point timeframe:

Day 1 and Day 5

Notes:

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

End point values	Lumicitabine 40/20 mg/kg LD/MD	Lumicitabine 60/40 mg/kg LD/MD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1	3		
Units: nanogram hour per milliliters (ng*h/ml)				
arithmetic mean (standard deviation)				
Day 1	12700 (± 99999)	17800 (± 713.9)		
Day 5	11840 (± 99999)	20500 (± 655.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Trough Observed Analyte Concentration (C[trough]) of JNJ-63549109 (Metabolite of Lumicitabine)

End point title	Trough Observed Analyte Concentration (C[trough]) of JNJ-63549109 (Metabolite of Lumicitabine)[7]

End point description:

C(trough) is the plasma concentration before dosing or at the end of the dosing interval of any dose other than the first dose in a multiple dosing regimen of JNJ-63549109 (Metabolite of Lumicitabine). ITT set was defined as all randomized subjects who receive at least 1 dose of study Here, "99999" indicates that the data was not estimable as only one subject was analyzed in the specified arm.

End point type	Secondary

End point timeframe:

Day 1 and Day 5

Notes:

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

End point values	Lumicitabine 40/20 mg/kg LD/MD	Lumicitabine 60/40 mg/kg LD/MD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1	3		
Units: ng/ml				
arithmetic mean (standard deviation)				
Day 1	91.16 (± 99999)	187.8 (± 52.97)		
Day 5	189.8 (± 99999)	358.3 (± 37.42)		

Statistical analyses

No statistical analyses for this end point

Secondary: Predicted Concentration of JNJ-63549109 (Metabolite of Lumicitabine) at 12 hours Postdose (C12h)

End point title	Predicted Concentration of JNJ-63549109 (Metabolite of Lumicitabine) at 12 hours Postdose (C12h)[8]

End point description:

C12h is the predicted concentration of JNJ-63549109 at 12 hours Postdose. C12h is a model-based prediction. It was determined using a population pharmacokinetic (PK) model and based on the individual model predicted concentration-time profiles.

End point type	Secondary

End point timeframe:

12 hours postdose

Notes:

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

End point values	Lumicitabine 40/20 mg/kg LD/MD	Lumicitabine 60/40 mg/kg LD/MD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[9]	0[10]		
Units: ng/ml				
arithmetic mean (standard deviation)	()	()		

Notes:

[9] - As study was terminated early with fewer subjects, result for this endpoint could not be determined.
[10] - As study was terminated early with fewer subjects, result for this endpoint could not be determined.

Statistical analyses

No statistical analyses for this end point

Secondary: Length of Hospital Stay

End point title	Length of Hospital Stay

End point description:

Length of hospital stay is defined as the time from hospitalization to actual hospital discharge. Randomized or Treated (RT) set was defined as subjects who were in the Randomized Analysis Set (all randomized subjects with a randomization date at or before the date of the first intake of medication, or with a randomization date and a missing date for first medication intake, analyzed as randomized) and/or the all subjects treated (AST) set. Here '99999' indicates that the subject was not analyzed for the respective arm.

End point type	Secondary

End point timeframe:

Up to 28 days

End point values	Placebo	Lumicitabine 40/20 mg/kg LD/MD	Lumicitabine 60/40 mg/kg LD/MD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	3	1	3	
Units: Hours				
number (not applicable)				
Subject 1	143.5	99999	99999	
Subject 2	167.8	99999	99999	
Subject 3	179.4	99999	99999	
Subject 4	99999	167.8	99999	
Subject 5	99999	99999	120	
Subject 6	99999	99999	239.5	
Subject 7	99999	99999	149.3	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects Admitted to the Intensive Care Unit (ICU)

End point title	Number of Subjects Admitted to the Intensive Care Unit (ICU)

End point description:

Number of subjects who were admitted to the ICU was reported. Randomized or Treated set was defined as all subjects who were in the Randomized Analysis Set (all randomized subjects with a randomization date at or before the date of the first intake of medication, or with a randomization date and a missing date for first medication intake, analyzed as randomized) and/or the AST set.

End point type	Secondary

End point timeframe:

Up to 28 days

End point values	Placebo	Lumicitabine 40/20 mg/kg LD/MD	Lumicitabine 60/40 mg/kg LD/MD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	3	1	3	
Units: Subjects				
number (not applicable)	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of ICU Stay

End point title	Duration of ICU Stay

End point description:

In the event that a subject required ICU, the duration for how long the subject remained in the ICU was reported.

End point type	Secondary

End point timeframe:

Up to 28 days

End point values	Placebo	Lumicitabine 40/20 mg/kg LD/MD	Lumicitabine 60/40 mg/kg LD/MD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[11]	0[12]	0[13]	
Units: Hours				
number (not applicable)				

Notes:

[11] - No subject was admitted to ICU hence results could not be determined for this end point.

[12] - No subject was admitted to ICU hence results could not be determined for this end point.

[13] - No subject was admitted to ICU hence results could not be determined for this end point.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects who Required Supplemental Oxygen

End point title	Number of Subjects who Required Supplemental Oxygen

End point description:

The number of subjects who required supplemental oxygen above pre-RSV infection status was reported. Randomized or Treated set was defined as all subjects who were in the Randomized Analysis Set (all randomized subjects with a randomization date at or before the date of the first intake of medication, or with a randomization date and a missing date for first medication intake, analyzed as randomized) and/or the AST set.

End point type	Secondary

End point timeframe:

Up to 28 days

End point values	Placebo	Lumicitabine 40/20 mg/kg LD/MD	Lumicitabine 60/40 mg/kg LD/MD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	3	1	3	
Units: Subjects	1	1	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects who Required Non-invasive Mechanical Ventilation Support

End point title	Number of Subjects who Required Non-invasive Mechanical Ventilation Support

End point description:

The number of subjects who required non-invasive mechanical ventilation support (that is, continuous positive airway pressure) above pre-RSV infection status was reported. Randomized or Treated set was defined as all subjects who were in the Randomized Analysis Set (all randomized subjects with a randomization date at or before the date of the first intake of medication, or with a randomization date and a missing date for first medication intake, analyzed as randomized) and/or the AST set.

End point type	Secondary

End point timeframe:

Up to 28 days

End point values	Placebo	Lumicitabine 40/20 mg/kg LD/MD	Lumicitabine 60/40 mg/kg LD/MD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	3	1	3	
Units: Subjects	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects who Required Invasive Mechanical Ventilation Support

End point title	Number of Subjects who Required Invasive Mechanical Ventilation Support

End point description:

The number of subjects who required invasive mechanical ventilation support (for example, endotracheal-mechanical ventilation or mechanical ventilation via tracheostomy) above pre-RSV infection status was reported. Randomized or Treated set was defined as all subjects who were in the

Randomized Analysis Set (all randomized subjects with a randomization date at or before the date of the first intake of medication, or with a randomization date and a missing date for first medication intake, analyzed as randomized) and/or the AST set.

End point type	Secondary

End point timeframe:

Up to 28 days

End point values	Placebo	Lumicitabine 40/20 mg/kg LD/MD	Lumicitabine 60/40 mg/kg LD/MD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	3	1	3	
Units: Subjects	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Supplemental Oxygen

End point title	Duration of Supplemental Oxygen

End point description:

Duration of supplemental oxygen above pre-RSV infection status was assessed. Population included Randomized or Treated set who received who received supplemental oxygen.

End point type	Secondary

End point timeframe:

Up to 28 days

End point values	Placebo	Lumicitabine 40/20 mg/kg LD/MD	Lumicitabine 60/40 mg/kg LD/MD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	1	1	0[14]	
Units: Hours				
number (not applicable)	59.4	0.5		

Notes:

[14] - No subject received supplemental oxygen hence results could not be determined for this end point.

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Non-invasive Mechanical Ventilation Support

End point title	Duration of Non-invasive Mechanical Ventilation Support

End point description:

Duration of non-invasive mechanical ventilation support (that is, continuous positive airway pressure) to

deliver oxygen above pre-RSV infection status was measured.

End point type	Secondary

End point timeframe:

Up to 28 days

End point values	Placebo	Lumicitabine 40/20 mg/kg LD/MD	Lumicitabine 60/40 mg/kg LD/MD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[15]	0[16]	0[17]	
Units: Hours				
number (not applicable)				

Notes:

[15] - No subject received non-invasive mechanical ventilation support, result was not drawn for endpoint.
[16] - No subject received non-invasive mechanical ventilation support, result was not drawn for endpoint.
[17] - No subject received non-invasive mechanical ventilation support, result was not drawn for endpoint.

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Invasive Mechanical Ventilation Support

End point title	Duration of Invasive Mechanical Ventilation Support

End point description:

Duration of invasive mechanical ventilation support (for example, endotracheal-mechanical ventilation or mechanical ventilation via tracheostomy) to deliver oxygen above pre-RSV infection status was measured.

End point type	Secondary

End point timeframe:

Up to 28 days

End point values	Placebo	Lumicitabine 40/20 mg/kg LD/MD	Lumicitabine 60/40 mg/kg LD/MD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[18]	0[19]	0[20]	
Units: Hours				
number (not applicable)				

Notes:

[18] - No subject received invasive mechanical ventilation support, result was not determined for endpoint.
[19] - No subject received invasive mechanical ventilation support, result was not determined for endpoint.
[20] - No subject received invasive mechanical ventilation support, result was not determined for endpoint.

Statistical analyses

No statistical analyses for this end point

Secondary: Time to no Longer Requiring Supplemental Oxygen

End point title	Time to no Longer Requiring Supplemental Oxygen

End point description:

Time to no longer requiring supplemental oxygen above pre-RSV infection status was reported. Population included Randomized or Treated set who received who received supplemental oxygen.

End point type	Secondary

End point timeframe:

Up to 28 days

End point values	Placebo	Lumicitabine 40/20 mg/kg LD/MD	Lumicitabine 60/40 mg/kg LD/MD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	1	1	0[21]	
Units: Hours				
number (not applicable)	59.4	0.5		

Notes:

[21] - No subject received supplemental oxygen hence results could not be determined for this end point.

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Clinical Stability

End point title	Time to Clinical Stability

End point description:

Time to clinical stability was defined as the time at which the following criteria are all met: normalization of blood oxygen level (return to baseline, by pulse oximetry) without the requirement of supplemental oxygen beyond baseline level, normalization of oral feeding, normalization of respiratory rate, and normalization of heart rate. Randomized or Treated set was defined as all subjects who were in the Randomized Analysis Set (all randomized subjects with a randomization date at or before the date of the first intake of medication, or with a randomization date and a missing date for first medication intake, analyzed as randomized) and/or the AST set. As study was terminated early with fewer subjects than planned, collected data could not be summarized. Hence, individual data for each subject was reported. Here '99999' indicates that the subject was not analyzed for respective arm.

End point type	Secondary

End point timeframe:

Up to 28 days

End point values	Placebo	Lumicitabine 40/20 mg/kg LD/MD	Lumicitabine 60/40 mg/kg LD/MD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	3	1	3	
Units: Hours				
number (not applicable)				
Subject 1	63.8	99999	99999	

Subject 2	39.5	99999	99999	
Subject 3	191.2	99999	99999	
Subject 4	99999	63.3	99999	
Subject 5	99999	99999	71.3	
Subject 6	99999	99999	646.4	
Subject 7	99999	99999	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Time From Initiation of Study Treatment Until Peripheral Capillary Oxygen Saturation (SpO2) Greater Than or Equal to (>=)93 Percent (%) on Room Air Among Subjects who were not on Supplemental Oxygen Prior to Onset of Respiratory Symptoms

End point title	Time From Initiation of Study Treatment Until Peripheral Capillary Oxygen Saturation (SpO2) Greater Than or Equal to (>=)93 Percent (%) on Room Air Among Subjects who were not on Supplemental Oxygen Prior to Onset of Respiratory Symptoms

End point description:

Time from initiation of study treatment until SpO2 >=93% on room air among subjects who were not on supplemental oxygen prior to the onset of respiratory symptoms was reported.

End point type	Secondary

End point timeframe:

Up to 28 days

End point values	Placebo	Lumicitabine 40/20 mg/kg LD/MD	Lumicitabine 60/40 mg/kg LD/MD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[22]	0[23]	0[24]	
Units: Days				
number (not applicable)				

Notes:

[22] - As study was terminated early with fewer subjects, result for this endpoint could not be determined.

[23] - As study was terminated early with fewer subjects, result for this endpoint could not be determined.

[24] - As study was terminated early with fewer subjects, result for this endpoint could not be determined.

Statistical analyses

No statistical analyses for this end point

Secondary: Time for Respiratory Rate to Return to Pre-RSV Infection Status

End point title	Time for Respiratory Rate to Return to Pre-RSV Infection Status

End point description:

Time for the respiratory rate to return to pre-RSV infection status was measured. Randomized or

Treated set was defined as all subjects who were in the Randomized Analysis Set (all randomized subjects with a randomization date at or before the date of the first intake of medication, or with a randomization date and a missing date for first medication intake, analyzed as randomized) and/or the AST set. As the study was terminated early with fewer subjects than planned, collected data were not summarized. Hence, individual data for each subject was reported. Here '99999' indicates that the subject was not analyzed for respective arm.

End point type	Secondary

End point timeframe:

Up to 28 days

End point values	Placebo	Lumicitabine 40/20 mg/kg LD/MD	Lumicitabine 60/40 mg/kg LD/MD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	3	1	3	
Units: Hours				
number (not applicable)				
Subject 1	0	99999	99999	
Subject 2	39.5	99999	99999	
Subject 3	46.4	99999	99999	
Subject 4	99999	0	99999	
Subject 5	99999	99999	71.3	
Subject 6	99999	99999	646.4	
Subject 7	99999	99999	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Time for SpO2 to Return to Pre-RSV Infection Status

End point title	Time for SpO2 to Return to Pre-RSV Infection Status

End point description:

Time for SpO2 to return to pre-RSV infection status was measured. Randomized or Treated set was defined as all subjects who were in the Randomized Analysis Set (all randomized subjects with a randomization date at or before the date of the first intake of medication, or with a randomization date and a missing date for first medication intake, analyzed as randomized) and/or the AST set. As the study was terminated early with fewer subjects than planned, collected data was not summarized. Hence, individual data for each subject was reported. Here '99999' indicates that the subject was not analyzed for respective arm.

End point type	Secondary

End point timeframe:

Up to 28 days

End point values	Placebo	Lumicitabine 40/20 mg/kg LD/MD	Lumicitabine 60/40 mg/kg LD/MD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	3	1	3	
Units: Hours				
number (not applicable)				
Subject 1	0	99999	99999	
Subject 2	0	99999	99999	
Subject 3	70	99999	99999	
Subject 4	99999	33.7	99999	
Subject 5	99999	99999	0	
Subject 6	99999	99999	0	
Subject 7	99999	99999	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Time for Body Temperature to Return To Pre-RSV Infection Status

End point title	Time for Body Temperature to Return To Pre-RSV Infection Status

End point description:

Time for body temperature to return to pre-RSV infection status was measured. Randomized or Treated set was defined as all subjects who were in the Randomized Analysis Set (all randomized subjects with a randomization date at or before the date of the first intake of medication, or with a randomization date and a missing date for first medication intake, analyzed as randomized) and/or the AST set. As the study was terminated early with fewer subjects than planned, collected data was not summarized. Hence, individual data for each subject was reported. Here '99999' indicates that the subject was not analyzed for respective arm.

End point type	Secondary

End point timeframe:

Up to 28 days

End point values	Placebo	Lumicitabine 40/20 mg/kg LD/MD	Lumicitabine 60/40 mg/kg LD/MD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	3	1	3	
Units: Days				
number (not applicable)				
Subject 1	0	99999	99999	
Subject 2	643.5	99999	99999	
Subject 3	37.4	99999	99999	
Subject 4	99999	16.7	99999	
Subject 5	99999	99999	0	
Subject 6	99999	99999	0	
Subject 7	99999	99999	641.6	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Acute Otitis Media

End point title	Number of Subjects With Acute Otitis Media

End point description:

Number of subjects with acute otitis media was reported. Randomized or Treated set was defined as all subjects who were in the Randomized Analysis Set (all randomized subjects with a randomization date at or before the date of the first intake of medication, or with a randomization date and a missing date for first medication intake, analyzed as randomized) and/or the AST set.

End point type	Secondary

End point timeframe:

Up to 28 days

End point values	Placebo	Lumicitabine 40/20 mg/kg LD/MD	Lumicitabine 60/40 mg/kg LD/MD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	3	1	3	
Units: Subjects	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Signs and Symptoms of RSV Infection

End point title	Duration of Signs and Symptoms of RSV Infection

End point description:

Duration of signs and symptoms of RSV infection was assessed.

End point type	Secondary

End point timeframe:

Up to 28 days

End point values	Placebo	Lumicitabine 40/20 mg/kg LD/MD	Lumicitabine 60/40 mg/kg LD/MD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[25]	0[26]	0[27]	
Units: Hours				
number (not applicable)				

Notes:

[25] - As study was terminated early with fewer subjects, result for this endpoint could not be determined.
[26] - As study was terminated early with fewer subjects, result for this endpoint could not be determined.
[27] - As study was terminated early with fewer subjects, result for this endpoint could not be determined.

Statistical analyses

No statistical analyses for this end point

Secondary: Severity of Signs and Symptoms of RSV Infection Assessed by the Pediatric RSV Electronic Severity and Outcome Rating System (PRESORS)

End point title	Severity of Signs and Symptoms of RSV Infection Assessed by the Pediatric RSV Electronic Severity and Outcome Rating System (PRESORS)

End point description:

The severity of signs and symptoms of RSV infection were assessed by the PRESORS. PRESORS questions were answered by means of the following response scale: a lot less than usual, a little less than usual, about as much as usual, a little more than usual, a lot more than usual.

End point type	Secondary

End point timeframe:

Up to 28 Days

End point values	Placebo	Lumicitabine 40/20 mg/kg LD/MD	Lumicitabine 60/40 mg/kg LD/MD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[28]	0[29]	0[30]	
Units: Score on scale				
arithmetic mean (standard deviation)	()	()	()	

Notes:

[28] - As study was terminated early with fewer subjects, result for this endpoint could not be determined.
[29] - As study was terminated early with fewer subjects, result for this endpoint could not be determined.
[30] - As study was terminated early with fewer subjects, result for this endpoint could not be determined.

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:

RSV viral load over time was measured by qRT-PCR in the mid-turbinate nasal swab specimens.

Intention-To-Treat-infected (ITT-i) set was defined as all randomly assigned subjects who receive at least 1 dose of study drug and who have an RSV infection confirmed by a polymerase chain reaction (PCR)-based assay at baseline or within 1 hour after the first study medication intake at the central laboratory.

End point type	Secondary

End point timeframe:

On Day 2, 3, 4, 5, 6, 7, 10, 14 and 28

End point values	Placebo	Lumicitabine 40/20 mg/kg LD/MD	Lumicitabine 60/40 mg/kg LD/MD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	3	1	3	
Units: log10 per milliliters (log10/mL)				
arithmetic mean (standard deviation)				
Day 2	5.817 (± 2.2087)	6.809 (± 99999)	6.660 (± 0.9732)	
Day 3	5.443 (± 1.4645)	6.000 (± 99999)	5.351 (± 0.5794)	
Day 4	4.674 (± 2.4209)	2.900 (± 99999)	4.190 (± 1.4190)	
Day 5	3.808 (± 1.0049)	5.949 (± 99999)	4.521 (± 1.7506)	
Day 6	3.137 (± 1.9306)	6.514 (± 99999)	4.110 (± 1.6980)	
Day 7	2.994 (± 1.4450)	4.584 (± 99999)	2.754 (± 1.2688)	
Day 10	2.821 (± 1.5950)	1.900 (± 99999)	3.573 (± 0.7610)	
Day 14	1.900 (± 0.0000)	2.900 (± 99999)	1.983 (± 0.1443)	
Day 28	1.900 (± 0.0000)	1.900 (± 00000)	1.900 (± 0.0000)	

Statistical analyses

No statistical analyses for this end point

Secondary: Peak Viral Load

End point title	Peak Viral Load

End point description:

Peak viral load was measured by qRT-PCR in the mid-turbinate nasal swab specimens.

End point type	Secondary

End point timeframe:

Up to 28 days

End point values	Placebo	Lumicitabine 40/20 mg/kg LD/MD	Lumicitabine 60/40 mg/kg LD/MD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[31]	0[32]	0[33]	
Units: log10 copies/mL				
arithmetic mean (standard deviation)	()	()	()	

Notes:

[31] - As study was terminated early with fewer subjects, result for this endpoint could not be determined.
[32] - As study was terminated early with fewer subjects, result for this endpoint could not be determined.
[33] - As study was terminated early with fewer subjects, result for this endpoint could not be determined.

Statistical analyses

No statistical analyses for this end point

Secondary: Time To Peak Viral Load

End point title	Time To Peak Viral Load

End point description:

Time to peak viral load was reported.

End point type	Secondary

End point timeframe:

Up to 28 days

End point values	Placebo	Lumicitabine 40/20 mg/kg LD/MD	Lumicitabine 60/40 mg/kg LD/MD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[34]	0[35]	0[36]	
Units: Hours				
number (not applicable)				

Notes:

[34] - As study was terminated early with fewer subjects, result for this endpoint could not be determined.
[35] - As study was terminated early with fewer subjects, result for this endpoint could not be determined.
[36] - As study was terminated early with fewer subjects, result for this endpoint could not be determined.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with Decline of Viral Load

End point title	Percentage of Subjects with Decline of Viral Load

End point description:

Percentage of subjects with decline in viral load during treatment as measured by qRT-PCR was reported. ITT-i set was defined as all randomly assigned subjects who receive at least 1 dose of study drug and who have an RSV infection confirmed by a polymerase chain reaction (PCR)-based assay at baseline or within 1 hour after the first study medication intake at the central laboratory.

End point type	Secondary

End point timeframe:

Up to 28 days

End point values	Placebo	Lumicitabine 40/20 mg/kg LD/MD	Lumicitabine 60/40 mg/kg LD/MD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	3	1	3	
Units: Percentage of subjects				
number (not applicable)	100	100	100	

Statistical analyses

No statistical analyses for this end point

Secondary: Time to RSV Ribonucleic Acid (RNA) Being Undetectable

End point title	Time to RSV Ribonucleic Acid (RNA) Being Undetectable

End point description:

Time to RSV RNA being undetectable (the time from initiation of study treatment until the time at which it is observed that the virus is undetectable in an assessment and after which time no virus positive assessment follows) was assessed as measured by qRT-PCR.

End point type	Secondary

End point timeframe:

Up to 28 days

End point values	Placebo	Lumicitabine 40/20 mg/kg LD/MD	Lumicitabine 60/40 mg/kg LD/MD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[37]	0[38]	0[39]	
Units: Hours				
number (not applicable)				

Notes:

[37] - As study was terminated early with fewer subjects, result for this endpoint could not be determined.

[38] - As study was terminated early with fewer subjects, result for this endpoint could not be determined.

[39] - As study was terminated early with fewer subjects, result for this endpoint could not be determined.

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 the undetectable viral load was reported.

End point type	Secondary

End point timeframe:

Up to 28 days

End point values	Placebo	Lumicitabine 40/20 mg/kg LD/MD	Lumicitabine 60/40 mg/kg LD/MD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[40]	0[41]	0[42]	
Units: Percentage of Subjects				
arithmetic mean (standard deviation)	()	()	()	

Notes:

[40] - As study was terminated early with fewer subjects, result for this endpoint could not be determined.
[41] - As study was terminated early with fewer subjects, result for this endpoint could not be determined.
[42] - As study was terminated early with fewer subjects, result for this endpoint could not be determined.

Statistical analyses

No statistical analyses for this end point

Secondary: AUC of RSV RNA Viral Load From Baseline up to Day 10

End point title	AUC of RSV RNA Viral Load From Baseline up to Day 10[43]

End point description:

AUC of RSV RNA viral load was measured in mid-turbinate nasal swabs and in the endotracheal sample.

End point type	Secondary

End point timeframe:

Baseline up to Day 10

Notes:

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

End point values	Lumicitabine 40/20 mg/kg LD/MD	Lumicitabine 60/40 mg/kg LD/MD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[44]	0[45]		
Units: ng*h/ml				
arithmetic mean (standard deviation)	()	()		

Notes:

[44] - As study was terminated early with fewer subjects, result for this endpoint could not be determined.
[45] - As study was terminated early with fewer subjects, result for this endpoint could not be determined.

Statistical analyses

No statistical analyses for this end point

Secondary: AUC of RSV RNA Viral Load From Baseline up to Day 14

End point title	AUC of RSV RNA Viral Load From Baseline up to Day 14[46]

End point description:

AUC of RSV RNA viral load was measured in midturbinate nasal swabs and in endotracheal samples.

End point type	Secondary

End point timeframe:

Baseline up to Day 14

Notes:

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

End point values	Lumicitabine 40/20 mg/kg LD/MD	Lumicitabine 60/40 mg/kg LD/MD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[47]	0[48]		
Units: ng*h/ml				
arithmetic mean (standard deviation)	()	()		

Notes:

[47] - As study was terminated early with fewer subjects, result for this endpoint could not be determined.
[48] - As study was terminated early with fewer subjects, result for this endpoint could not be determined.

Statistical analyses

No statistical analyses for this end point

Secondary: AUC of RSV Viral Load From Baseline Until 1 day (+2 Days) After the Last Dose of Study Drug

End point title	AUC of RSV Viral Load From Baseline Until 1 day (+2 Days) After the Last Dose of Study Drug[49]

End point description:

AUC of RSV viral load was measured in midturbinate nasal swabs and in endotracheal samples.

End point type	Secondary

End point timeframe:

Baseline Until 1 day (+2 Days) After the Last Dose of Study Drug (approximately up to 10 days)

Notes:

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

End point values	Lumicitabine 40/20 mg/kg LD/MD	Lumicitabine 60/40 mg/kg LD/MD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[50]	0[51]		
Units: ng*h/ml				
arithmetic mean (standard deviation)	()	()		

Notes:

[50] - As study was terminated early with fewer subjects, result for this endpoint could not be determined.
[51] - As study was terminated early with fewer subjects, result for this endpoint could not be determined.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Emergent Postbaseline Changes in the RSV Polymerase L-gene and Other Regions of the RSV Genome Compared With Baseline Sequences

End point title	Number of Subjects With Emergent Postbaseline Changes in the RSV Polymerase L-gene and Other Regions of the RSV Genome Compared With Baseline Sequences

End point description:

Number of subjects were assessed for changes in the RSV polymerase L-gene (only if no mutations are seen in the L-gene) and other regions of the RSV genome compared with baseline sequences. Population included randomized or treated set and those who received supplemental oxygen. As study was terminated early with fewer participants than planned, results for this endpoint could not be drawn. Hence, individual data for each participant was reported. Here, n (number analyzed) signifies specific participant evaluated in respective arm.

End point type	Secondary

End point timeframe:

Baseline up to 28 days

End point values	Placebo	Lumicitabine 40/20 mg/kg LD/MD	Lumicitabine 60/40 mg/kg LD/MD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	3	1	3	
Units: Subjects				
number (not applicable)	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Acceptability of the Lumicitabine Formulation as Assessed by Parent(s)/Caregiver(s) electronic clinical outcome assessment (eCOA)

End point title	Acceptability of the Lumicitabine Formulation as Assessed by Parent(s)/Caregiver(s) electronic clinical outcome assessment (eCOA)

End point description:

Acceptability of the lumicitabine formulation was assessed by parent(s)/caregiver(s) eCOA.

End point type	Secondary

End point timeframe:

Up to Day 6

End point values	Placebo	Lumicitabine 40/20 mg/kg LD/MD	Lumicitabine 60/40 mg/kg LD/MD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[52]	0[53]	0[54]	
Units: Units on scale				
arithmetic mean (standard deviation)	()	()	()	

Notes:

[52] - As study was terminated early with fewer subjects, result for this endpoint could not be determined.
[53] - As study was terminated early with fewer subjects, result for this endpoint could not be determined.
[54] - As study was terminated early with fewer subjects, result for this endpoint could not be determined.

Statistical analyses

No statistical analyses for this end point

Secondary: Palatability of the Lumicitabine Formulation as Assessed by Parent(s)/Caregiver(s) eCOA

End point title	Palatability of the Lumicitabine Formulation as Assessed by Parent(s)/Caregiver(s) eCOA

End point description:

Palatability (taste and texture) of the lumicitabine formulation was assessed by parent(s)/caregiver(s) eCOA.

End point type	Secondary

End point timeframe:

Up to Day 6

End point values	Placebo	Lumicitabine 40/20 mg/kg LD/MD	Lumicitabine 60/40 mg/kg LD/MD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[55]	0[56]	0[57]	
Units: Units on scale				
arithmetic mean (standard deviation)	()	()	()	

Notes:

[55] - As study was terminated early with fewer subjects, result for this endpoint could not be determined.
[56] - As study was terminated early with fewer subjects, result for this endpoint could not be determined.
[57] - As study was terminated early with fewer subjects, result for this endpoint could not be determined.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to 28 days

Adverse event reporting additional description:

Safety analysis set was defined as all subjects who received at least 1 dose of study drug, analyzed as treated.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	20.0

Reporting groups

Reporting group title	Placebo

Reporting group description:

Subjects received a single dose of lumicitabine-40 milligrams/kilogram (mg/kg) matched placebo as a loading dose (LD) (Dose 1) followed by 9 maintenance dose (MD) of lumicitabine-20 mg/kg matched placebo twice a day or a single dose of lumicitabine-60 mg/kg matched placebo LD (Dose 1) followed by nine lumicitabine-40 mg/kg matched placebo MD (Dose 2 to 10).

Reporting group title	60/40 mg/kg LD/MD

Reporting group description:

Subjects received a single dose of lumicitabine-60 mg/kg as LD (Dose 1) followed by 9 MD doses of lumicitabine 40 mg/kg twice a day.

Reporting group title	40/20 mg/kg LD/MD

Reporting group description:

Subjects received a single dose of lumicitabine-40 mg/kg as LD (Dose 1) followed by 9 MD doses of lumicitabine 20 mg/kg twice a day.

Serious adverse events	Placebo	60/40 mg/kg LD/MD	40/20 mg/kg LD/MD
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 1 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Blood and lymphatic system disorders			
Febrile Neutropenia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Placebo	60/40 mg/kg LD/MD	40/20 mg/kg LD/MD
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 3 (100.00%)	3 / 3 (100.00%)	1 / 1 (100.00%)
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	0 / 3 (0.00%)	2 / 3 (66.67%)	0 / 1 (0.00%)
occurrences (all)	0	2	0
Thrombocytopenia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Respiratory, thoracic and mediastinal disorders			
Rhinorrhoea			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Skin and subcutaneous tissue disorders			
Dermatitis Diaper			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Erythema			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 1 (0.00%)
occurrences (all)	2	0	0
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 1 (100.00%)
occurrences (all)	0	0	1
Pharyngitis			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Pneumonia Bacterial			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
17 August 2017	This amendment was to remove furosemide, ibuprofen, and trimethoprim/sulfamethoxazole from the list of prohibited moderate/strong inhibitors of organic anion transporter 3. In addition, no food intake information with regard to study drug administration was collected for discharged subjects due to the minimal impact of food intake on trough levels (PK sample at Day 7). Furthermore, it was clarified that leftover samples from nasal swabs and PK testing only (not safety testing) could be used for exploratory biomarker analysis.

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.

Only 7 subjects were treated before the study was prematurely terminated. Due to this small number of treated subjects, statistical analysis was not conducted as planned. Hence it was not possible to evaluate the primary or secondary objectives.

Notes: