Clinical trial results:
A Phase 2b, Randomized, Double-blind, Placebo-controlled Study to Evaluate the Antiviral Activity, Clinical Outcomes, Safety, Tolerability, and Pharmacokinetics of Orally Administered ALS-008176 Regimens in Adult Subjects Hospitalized with Respiratory Syncytial Virus

Summary

EudraCT number	2016-001653-40
Trial protocol	GB BE ES PL SE NL BG
Global end of trial date	17 October 2018

Results information

Result version number	v1 (current)
This version publication date	28 October 2019
First version publication date	28 October 2019

Trial information

Trial identification

Sponsor protocol code	64041575RSV2003

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02935673
WHO universal trial number (UTN)	-

Notes:

Sponsors

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

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	17 October 2018
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	17 October 2018
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The main objectives of this study were to characterize the pharmacokinetics (PK) and to confirm the population PK (popPK) model derived from healthy volunteers in hospitalized adults infected with respiratory syncytial virus (RSV) (Part 1) and to determine in hospitalized adults infected with RSV the dose response relationship of multiple regimens of lumicitabine on antiviral activity based on nasal RSV shedding using quantitative reverse transcriptase-polymerase chain reaction (qRT-PCR) assay (Part 2).

Protection of trial subjects:

This study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and that are consistent with Good Clinical Practices and applicable regulatory requirements. Safety was evaluated throughout the study and included monitoring of adverse events (AEs), clinical laboratory tests, vital signs/peripheral capillary oxygen saturation (SpO2) measurements, physical examinations, and electrocardiograms (ECGs).

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	08 November 2016
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: 2
Country: Number of subjects enrolled	Australia: 7
Country: Number of subjects enrolled	Spain: 3
Country: Number of subjects enrolled	France: 7
Country: Number of subjects enrolled	United Kingdom: 1
Country: Number of subjects enrolled	Japan: 9
Country: Number of subjects enrolled	Korea, Republic of: 4
Country: Number of subjects enrolled	Malaysia: 2
Country: Number of subjects enrolled	Poland: 2
Country: Number of subjects enrolled	Sweden: 7
Country: Number of subjects enrolled	Taiwan: 3
Country: Number of subjects enrolled	United States: 2
Worldwide total number of subjects	49
EEA total number of subjects	20

Notes:

Subjects enrolled per age group	
In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	20
From 65 to 84 years	22
85 years and over	7

Subject disposition

Recruitment

Recruitment details:

Sponsor halted screening and enrollment in study on 22 June 2018 due to emerging lumicitabine nonclinical data. On 17 October 2018, study was stopped prematurely by Sponsor as a precautionary measure, to allow further evaluation of new nonclinical pharmacokinetic (PK) and safety findings and determine their relevance to human studies.

Pre-assignment

Screening details:

A total of 49 subjects were randomized and treated (2 subjects in Part 0, 36 subjects in Part 1 and 11 subjects in Part 2). Analyses were conducted on pooled groups across the 3 study parts.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Subjects received a single loading dose (LD) (Dose 1) of matching placebo tablet orally on Day 1 followed by nine maintenance doses (MD) (Doses 2 to 10) of matching placebo tablets orally twice daily (bid) from Day 1/2 to Day 5/6 (depending on the timing of the LD administration).

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

Dosage and administration details:

Subjects received a single LD followed by nine MDs (Doses 2 to 10) of matched placebo bid.

Arm title	750 mg LD / 250 mg MD Lumicitabine

Arm description:

Subjects received a single 750 milligram (mg) LD (Dose 1) of lumicitabine tablet orally followed by nine MD (Doses 2 to 10) of 250 mg lumicitabine tablets orally bid from Day 1/2 to Day 5/6 (depending on the timing of the LD administration).

Arm type	Experimental
Investigational medicinal product name	Lumicitabine 250 mg
Investigational medicinal product code	
Other name	JNJ-64041575, ALS-008176
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received nine 250 mg MDs (Doses 2 to 10) of lumicitabine bid.

Investigational medicinal product name	Lumicitabine 750 mg
Investigational medicinal product code	
Other name	JNJ-64041575, ALS-008176
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received a single 750 mg LD of lumicitabine.

Arm title	1000 mg LD / 500 mg MD Lumicitabine

Arm description:

Subjects received a single 1000 mg LD (Dose 1) of lumicitabine tablet orally followed by nine MD (Doses 2 to 10) of 500 mg lumicitabine tablets orally bid from Day 1/2 to Day 5/6 (depending on the timing of the LD administration).

Arm type	Experimental
Investigational medicinal product name	Lumicitabine 1000 mg
Investigational medicinal product code	
Other name	JNJ-64041575, ALS-008176
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received a single 1000 mg LD of lumicitabine.

Investigational medicinal product name	Lumicitabine 500 mg
Investigational medicinal product code	
Other name	JNJ-64041575, ALS-008176
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received nine 500 mg MDs (Doses 2 to 10) of lumicitabine bid.

Number of subjects in period 1	Placebo	750 mg LD / 250 mg MD Lumicitabine	1000 mg LD / 500 mg MD Lumicitabine
Started	16	27	6
Completed	15	24	6
Not completed	1	3	0
Adverse event, non-fatal	-	1	-
Withdrawal by subject	1	2	-

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Subjects received a single loading dose (LD) (Dose 1) of matching placebo tablet orally on Day 1 followed by nine maintenance doses (MD) (Doses 2 to 10) of matching placebo tablets orally twice daily (bid) from Day 1/2 to Day 5/6 (depending on the timing of the LD administration).	
Reporting group title	750 mg LD / 250 mg MD Lumicitabine
Reporting group description:	
Subjects received a single 750 milligram (mg) LD (Dose 1) of lumicitabine tablet orally followed by nine MD (Doses 2 to 10) of 250 mg lumicitabine tablets orally bid from Day 1/2 to Day 5/6 (depending on the timing of the LD administration).	
Reporting group title	1000 mg LD / 500 mg MD Lumicitabine
Reporting group description:	
Subjects received a single 1000 mg LD (Dose 1) of lumicitabine tablet orally followed by nine MD (Doses 2 to 10) of 500 mg lumicitabine tablets orally bid from Day 1/2 to Day 5/6 (depending on the timing of the LD administration).	

Reporting group values	Placebo	750 mg LD / 250 mg MD Lumicitabine	1000 mg LD / 500 mg MD Lumicitabine
Number of subjects	16	27	6
Title for AgeCategorical			
Units: subjects			
Adults (18-64 years)	8	10	2
From 65 to 84 years	5	13	4
85 years and over	3	4	0
Title for AgeContinuous			
Units: months			
arithmetic mean	65.5	66.3	68.7
standard deviation	± 17.94	± 17.75	± 18.46
Title for Gender			
Units: subjects			
Female	5	9	5
Male	11	18	1

Reporting group values	Total		
Number of subjects	49		
Title for AgeCategorical			
Units: subjects			
Adults (18-64 years)	20		
From 65 to 84 years	22		
85 years and over	7		
Title for AgeContinuous			
Units: months			
arithmetic mean			
standard deviation	-		
Title for Gender			
Units: subjects			
Female	19		
Male	30		

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Subjects received a single loading dose (LD) (Dose 1) of matching placebo tablet orally on Day 1 followed by nine maintenance doses (MD) (Doses 2 to 10) of matching placebo tablets orally twice daily (bid) from Day 1/2 to Day 5/6 (depending on the timing of the LD administration).	
Reporting group title	750 mg LD / 250 mg MD Lumicitabine
Reporting group description:	
Subjects received a single 750 milligram (mg) LD (Dose 1) of lumicitabine tablet orally followed by nine MD (Doses 2 to 10) of 250 mg lumicitabine tablets orally bid from Day 1/2 to Day 5/6 (depending on the timing of the LD administration).	
Reporting group title	1000 mg LD / 500 mg MD Lumicitabine
Reporting group description:	
Subjects received a single 1000 mg LD (Dose 1) of lumicitabine tablet orally followed by nine MD (Doses 2 to 10) of 500 mg lumicitabine tablets orally bid from Day 1/2 to Day 5/6 (depending on the timing of the LD administration).	

Primary: Maximum Observed Plasma Concentration (Cmax) of JNJ-63549109 at Day 1

End point title	Maximum Observed Plasma Concentration (Cmax) of JNJ-63549109 at Day 1[1][2]
End point description:	
Cmax is the maximum observed plasma concentration of JNJ-63549109. JNJ-63549109 is the metabolized product of lumicitabine. Pharmacokinetic (PK) analysis was performed on safety population which included all subjects who received at least 1 dose of study drug, analyzed as treated. Here 'N' (number of subjects analyzed) signifies number of subjects evaluable for this endpoint. Analyses were conducted on pooled groups across the 3 study parts.	
End point type	Primary
End point timeframe:	
Day 1	

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 were done, no inferential statistical analyses were performed.

[2] - 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	750 mg LD / 250 mg MD Lumicitabine	1000 mg LD / 500 mg MD Lumicitabine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	26	4		
Units: nanogram per milliliter (ng/mL)				
arithmetic mean (standard deviation)	1845 (± 545.2)	2801 (± 1509)		

Statistical analyses

No statistical analyses for this end point

Primary: Maximum Observed Plasma Concentration of JNJ-63549109 at Day 5

End point title	Maximum Observed Plasma Concentration of JNJ-63549109 at Day 5[3][4]

End point description:

Cmax is the maximum observed plasma concentration of JNJ-63549109. JNJ-63549109 is the metabolized product of lumicitabine. PK analysis was performed on safety population which included all subjects who received at least 1 dose of study drug, analyzed as treated. Here 'N' (number of subjects analyzed) signifies number of subjects evaluable for this endpoint. Analyses were conducted on pooled groups across the 3 study parts.

End point type	Primary

End point timeframe:

Day 5

Notes:

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

[4] - 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	750 mg LD / 250 mg MD Lumicitabine	1000 mg LD / 500 mg MD Lumicitabine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22	2		
Units: ng/mL				
arithmetic mean (standard deviation)	745.4 (± 164.2)	1145 (± 440.8)		

Statistical analyses

No statistical analyses for this end point

Primary: Area Under the Plasma Concentration-time Curve from Time 0 to 24 Hours After Dosing (AUC[0-24h]) of JNJ-63549109 at Day 1

End point title	Area Under the Plasma Concentration-time Curve from Time 0 to 24 Hours After Dosing (AUC[0-24h]) of JNJ-63549109 at Day 1[5][6]

End point description:

AUC (0-24h) is the area under the plasma concentration-time curve from time 0 to 24 hours after dosing of JNJ-63549109. JNJ-63549109 is the metabolized product of lumicitabine. PK analysis was performed on safety population which included all subjects who received at least 1 dose of study drug, analyzed as treated. Here 'N' (number of subjects analyzed) signifies number of subjects evaluable for this endpoint. Analyses were conducted on pooled groups across the 3 study parts.

End point type	Primary

End point timeframe:

Day 1

Notes:

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

[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	750 mg LD / 250 mg MD Lumicitabine	1000 mg LD / 500 mg MD Lumicitabine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	26	4		
Units: nanogram*hour per milliliter (ng*h/mL)				
arithmetic mean (standard deviation)	9936 (± 2090)	17120 (± 4330)		

Statistical analyses

No statistical analyses for this end point

Primary: Area Under the Plasma Concentration-time Curve from Time 0 to 24 Hours After Dosing (AUC[0-24h]) of JNJ-63549109 at Day 5

End point title	Area Under the Plasma Concentration-time Curve from Time 0 to 24 Hours After Dosing (AUC[0-24h]) of JNJ-63549109 at Day 5[7][8]

End point description:

AUC(0-24h) is the area under the plasma concentration-time curve from time 0 to 24 hours after dosing of JNJ-63549109. JNJ-63549109 is the metabolized product of lumicitabine. PK analysis was performed on safety population which included all subjects who received at least 1 dose of study drug, analyzed as treated. Here 'N' (number of subjects analyzed) signifies number of subjects evaluable for this endpoint. Analyses were conducted on pooled groups across the 3 study parts.

End point type	Primary

End point timeframe:

Day 5

Notes:

[7] - 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 were done, no inferential statistical analyses were performed.

[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	750 mg LD / 250 mg MD Lumicitabine	1000 mg LD / 500 mg MD Lumicitabine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22	2		
Units: ng*h/mL				
arithmetic mean (standard deviation)	7557 (± 1525)	13300 (± 4603)		

Statistical analyses

No statistical analyses for this end point

Primary: Trough Observed Plasma Concentration (Ctrough) of JNJ-63549109 at Day 1

End point title	Trough Observed Plasma Concentration (Ctrough) of JNJ-63549109 at Day 1[9][10]

End point description:

Ctrough is the trough observed plasma concentration of JNJ-63549109. JNJ-63549109 is the metabolized product of lumicitabine. PK analysis was performed on safety population which included all subjects who received at least 1 dose of study drug, analyzed as treated. Here 'N' (number of subjects analyzed) signifies number of subjects evaluable for this endpoint. Analyses were conducted on pooled groups across the 3 study parts.

End point type	Primary

End point timeframe:

Day 1

Notes:

[9] - 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 were done, no inferential statistical analyses were performed.

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

End point values	750 mg LD / 250 mg MD Lumicitabine	1000 mg LD / 500 mg MD Lumicitabine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	26	4		
Units: ng/mL				
arithmetic mean (standard deviation)	93.7 (± 44.16)	184.4 (± 184.4)		

Statistical analyses

No statistical analyses for this end point

Primary: Trough Observed Plasma Concentration of JNJ-63549109 at Day 5

End point title	Trough Observed Plasma Concentration of JNJ-63549109 at Day 5[11][12]

End point description:

Ctrough is the trough observed plasma concentration of JNJ-63549109. JNJ-63549109 is the metabolized product of lumicitabine. PK analysis was performed on safety population which included all subjects who received at least 1 dose of study drug, analyzed as treated. Here 'N' (number of subjects analyzed) signifies number of subjects evaluable for this endpoint. Analyses were conducted on pooled groups across the 3 study parts.

End point type	Primary

End point timeframe:

Day 5

Notes:

[11] - 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 were done, no inferential statistical analyses were performed.

[12] - 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	750 mg LD / 250 mg MD Lumicitabine	1000 mg LD / 500 mg MD Lumicitabine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22	2		
Units: ng/mL				
arithmetic mean (standard deviation)	148.3 (± 60.41)	281.3 (± 156.6)		

Statistical analyses

No statistical analyses for this end point

Primary: Least Square Mean Difference (Low and High Dose Lumicitabine Versus Placebo) of Respiratory Syncytial Virus (RSV) Ribonucleic Acid (RNA) Viral Load Area Under the Concentration-time Curve From Day 0 to 7 (AUC[0-7])

End point title	Least Square Mean Difference (Low and High Dose Lumicitabine Versus Placebo) of Respiratory Syncytial Virus (RSV) Ribonucleic Acid (RNA) Viral Load Area Under the Concentration-time Curve From Day 0 to 7 (AUC[0-7])[13][14]

End point description:

RSV RNA viral load in log10 copies/milliliter/day (log10 copies/mL/day) was measured in mid-turbinate nasal swabs and in endotracheal samples (obtained from intubated subjects or via suction through tracheostomy or other sampling methods) using quantitative reverse transcription-polymerase chain reaction (qRT-PCR). Intent-to-treat-infected (ITT-i) set included all randomly assigned subjects who received at least 1 dose of study drug and who had an RSV infection confirmed by a PCR-based assay at the central laboratory at baseline, analyzed as randomized. Analyses were conducted on pooled groups across the 3 study parts.

End point type	Primary

End point timeframe:

Day 0 to 7

Notes:

[13] - 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 were done, no inferential statistical analyses were performed.

[14] - 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	750 mg LD / 250 mg MD Lumicitabine	1000 mg LD / 500 mg MD Lumicitabine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21	5		
Units: log10 copies/mL/day				
least squares mean (confidence interval 95%)	-0.32 (-0.89 to 0.24)	-0.36 (-1.33 to 0.62)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Adverse Events (AEs)

End point title	Number of Subjects with Adverse Events (AEs)

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 set included all subjects who received at least 1 dose of study drug, analyzed as treated. Analyses were conducted on pooled groups across the 3 study parts.

End point type	Secondary

End point timeframe:

Up to 28 days

End point values	Placebo	750 mg LD / 250 mg MD Lumicitabine	1000 mg LD / 500 mg MD Lumicitabine	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	16	27	6	
Units: Subjects	7	22	5	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Vital Sign Abnormalities

End point title	Number of Subjects with Vital Sign Abnormalities

End point description:

Number of subjects with vital sign (systolic and diastolic blood pressure [BP], pulse rate, respiratory rate, temperature and oxygen saturation) abnormalities were reported. For systolic BP: abnormally low refers to less than or equal to (<=) 90 millimeter of mercury (mmHg); for diastolic BP: abnormally low refers to <=50 mmHg; for pulse rate abnormally low refers to less than (<) 45 beats per minutes (bpm) and abnormally high refers to greater than or equal to (>=) 120 bpm; for temperature in degree Celsius abnormally high refers to greater than (>) 37.8 (tympanic), >38.0 (forehead), >38.0 (oral), >37.2 (rectal), >38.0 (axillary); for oxygen saturation in % abnormally low refers to <95. Grade 1=mild; grade 2=moderate; grade 3=severe. Safety set included all subjects who received at least 1 dose of study drug, analyzed as treated. Here 'n' (number analyzed) signifies number of subjects evaluable for specified categories. Analyses were conducted on pooled groups across 3 study parts.

End point type	Secondary

End point timeframe:

Up to 28 Days

End point values	Placebo	750 mg LD / 250 mg MD Lumicitabine	1000 mg LD / 500 mg MD Lumicitabine	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	16	27	6	
Units: Subjects				
Systolic BP (Abnormally Low) (n=16,27,6)	1	0	0	
Systolic BP (Grade 1 or mild) (n=16,27,6)	2	6	2	
Systolic BP (Grade 2 or moderate) (n=16,27,6)	5	4	0	
Systolic BP (Grade 3 or severe) (n=16,27,6)	1	1	1	
Diastolic BP (Abnormally low) (n=16,27,6)	2	2	1	
Diastolic BP (Grade 1 or mild) (n=16,27,6)	5	8	1	
Diastolic BP (Grade 2 or moderate) (n=16,27,6)	3	1	0	
Diastolic BP (Grade 3 or severe) (n=16,27,6)	0	1	0	
Pulse Rate (Abnormally high (n=16,27,6)	2	1	0	
Respiratory Rate (Grade 1 or mild) (n=16,26,6)	2	0	1	
Respiratory Rate (Grade 2 or moderate) (n=16,26,6)	4	6	1	
Respiratory Rate (Grade 3 or severe) (n=16,26,6)	3	2	0	
Temperature (Abnormally high) (n=16,27,6)	4	2	0	
Oxygen Saturation (Abnormally low) (n=16,27,6)	7	9	2	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with QT Interval Abnormalities

End point title	Number of Subjects with QT Interval Abnormalities

End point description:

Number of subjects with QT interval abnormalities (prolonged) were reported. Safety set included all subjects who received at least 1 dose of study drug, analyzed as treated. Here 'N' (number of subjects analyzed) signifies number of subjects evaluable for this endpoint. Analyses were conducted on pooled groups across the 3 study parts.

End point type	Secondary

End point timeframe:

Up to 28 Days

End point values	Placebo	750 mg LD / 250 mg MD Lumicitabine	1000 mg LD / 500 mg MD Lumicitabine	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	15	24	5	
Units: Subjects	0	1	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Clinical Laboratory Abnormalities

End point title	Number of Subjects with Clinical Laboratory Abnormalities

End point description:

Number of subjects with clinical laboratory (serum chemistry and hematology) abnormalities were reported. Safety set included all subjects who received at least 1 dose of study drug, analyzed as treated. Here 'n' (number analyzed) signifies number of subjects evaluable for specified categories. Analyses were conducted on pooled groups across the 3 study parts. Abbreviations; Erythrocyte MCHC = Erythrocyte Mean Corpuscular Hemoglobin Concentration; Erythrocyte MCH = Erythrocyte Mean Corpuscular Hemoglobin; Ery. = Erythrocyte

End point type	Secondary

End point timeframe:

Up to 28 Days

End point values	Placebo	750 mg LD / 250 mg MD Lumicitabine	1000 mg LD / 500 mg MD Lumicitabine	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	16	27	6	
Units: Subjects				
Bicarbonate : Low (n=9,17,2)	0	2	0	
Bicarbonate: High (n=9,17,2)	3	5	0	
Chloride : Low (n=15,25,6)	0	3	0	
Chloride : High (n=15,25,6)	0	2	0	
Creatine Kinase : Low (n=13,19,6)	4	2	3	
Creatine Kinase ; High (n=13,19,6)	0	0	1	
Direct Bilirubin : High (n=7,15,4)	0	1	0	
Indirect Bilirubin : Low (n=7,12,4)	1	0	2	
Basophils : High (n=16,27,6)	0	0	1	
Eosinophils : High (n=16,27,6)	3	1	1	
Erythrocyte MCHC : Low (n=16,27,6)	1	1	0	
Erythrocyte MCH : Low (n=16,27,6)	1	0	0	
Erythrocyte MCH : High (n=16,27,6)	0	3	1	
Erythrocytes : Low (n=16,27,6)	5	3	1	

Ery. Distribution Width : Low (n=11,20,4)	0	1	0	
Ery. Distribution Width : High (n=11,20,4)	2	5	3	
Hematocrit : Low (n=16,26,6)	4	5	0	
Hematocrit : High (n=16,26,6)	1	0	0	
Lymphocytes : Low (n=16,27,6)	0	4	0	
Lymphocytes : High (n=16,27,6)	4	3	2	
Monocyte : Low (n=16,27,6)	0	2	1	
Monocyte : High (n=16,27,6)	5	5	3	
Reticulocytes : Low (n=8,11,6)	0	1	2	
Reticulocytes : High (n=8,11,6)	4	2	4	
Reticulocytes/Erythrocytes : Low (n=6,14,4)	1	0	1	
Reticulocytes/Erythrocytes : High (n=6,14,4)	4	9	3	

Statistical analyses

No statistical analyses for this end point

Secondary: Time of Hospital Stay From Study Treatment Initiation to Discharge

End point title	Time of Hospital Stay From Study Treatment Initiation to Discharge

End point description:

It is the time from treatment initiation to hospital discharge in hours. ITT-i set included all randomly assigned subjects who received at least 1 dose of study drug and who had an RSV infection confirmed by a PCR-based assay at the central laboratory at baseline, analyzed as randomized. Analyses were conducted on pooled groups across the 3 study parts.

End point type	Secondary

End point timeframe:

From study treatment initiation to discharge (Up to 28 Days)

End point values	Placebo	750 mg LD / 250 mg MD Lumicitabine	1000 mg LD / 500 mg MD Lumicitabine	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	15	21	5	
Units: Hours				
arithmetic mean (standard deviation)	183.91 (± 217.020)	146.72 (± 94.910)	405.24 (± 294.771)	

Statistical analyses

No statistical analyses for this end point

Secondary: Time of Hospital Stay From Admission to Discharge

End point title	Time of Hospital Stay From Admission to Discharge

End point description:

It is the time from hospital admission to hospital discharge in hours. ITT-i set included all randomly assigned subjects who received at least 1 dose of study drug and who had an RSV infection confirmed by a PCR-based assay at the central laboratory at baseline, analyzed as randomized. Here 'N' (number of subjects analyzed) signifies number of subjects evaluable for this endpoint. Analyses were conducted on pooled groups across the 3 study parts.

End point type	Secondary

End point timeframe:

From admission to discharge (Up to 28 days)

End point values	Placebo	750 mg LD / 250 mg MD Lumicitabine	1000 mg LD / 500 mg MD Lumicitabine	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	10	17	3	
Units: Hours				
arithmetic mean (standard deviation)	192.40 (± 199.363)	181.97 (± 107.938)	297.53 (± 348.729)	

Statistical analyses

No statistical analyses for this end point

Secondary: Time of Hospital Stay from Study Treatment Initiation to Readiness for Discharge

End point title	Time of Hospital Stay from Study Treatment Initiation to Readiness for Discharge

End point description:

It is the time from study treatment initiation to readiness for discharge in hours, with readiness for discharge defined by the investigator. ITT-i set included all randomly assigned subjects who received at least 1 dose of study drug and who had an RSV infection confirmed by a PCR-based assay at the central laboratory at baseline, analyzed as randomized. Analyses were conducted on pooled groups across the 3 study parts.

End point type	Secondary

End point timeframe:

From study treatment initiation to readiness for discharge on Day 2 or up to Day 6 if hospitalization is prolonged

End point values	Placebo	750 mg LD / 250 mg MD Lumicitabine	1000 mg LD / 500 mg MD Lumicitabine	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	15	21	5	
Units: Hours				
arithmetic mean (standard deviation)	111.05 (± 78.237)	144.17 (± 96.019)	197.60 (± 256.702)	

Statistical analyses

No statistical analyses for this end point

Secondary: Time of Hospital Stay from Admission to Readiness for Discharge

End point title	Time of Hospital Stay from Admission to Readiness for Discharge

End point description:

It is the time from hospital admission to readiness for discharge in hours, with readiness for discharge defined by the investigator. ITT-i set included all randomly assigned subjects who received at least 1 dose of study drug and who had an RSV infection confirmed by a PCR-based assay at the central laboratory at baseline, analyzed as randomized. Here 'N' (number of subjects analyzed) signifies number of subjects evaluable for this endpoint. Analyses were conducted on pooled groups across the 3 study parts.

End point type	Secondary

End point timeframe:

Up to 28 Days

End point values	Placebo	750 mg LD / 250 mg MD Lumicitabine	1000 mg LD / 500 mg MD Lumicitabine	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	10	17	3	
Units: Hours				
arithmetic mean (standard deviation)	133.41 (± 83.057)	178.82 (± 108.522)	297.13 (± 349.159)	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects Who Required to be Admitted to the Intensive Care Unit (ICU) Since Initiation of Treatment

End point title	Number of Subjects Who Required to be Admitted to the Intensive Care Unit (ICU) Since Initiation of Treatment

End point description:

Number of subjects who required to be admitted to the ICU after the initiation of treatment were reported. ITT-i set included all randomly assigned subjects who received at least 1 dose of study drug and who had an RSV infection confirmed by a PCR-based assay at the central laboratory at baseline, analyzed as randomized. Analyses were conducted on pooled groups across the 3 study parts.

End point type	Secondary

End point timeframe:

Up to 28 Days

End point values	Placebo	750 mg LD / 250 mg MD Lumicitabine	1000 mg LD / 500 mg MD Lumicitabine	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	15	21	5	
Units: Subjects	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Intensive Care Unit Stay

End point title	Duration of Intensive Care Unit Stay

End point description:

In the event that a subject required ICU since initiation of treatment, the duration for how long the subject remained in the ICU was measured. ITT-i set included all randomly assigned subjects who received at least 1 dose of study drug and who had an RSV infection confirmed by a PCR-based assay at the central laboratory at baseline, analyzed as randomized.

End point type	Secondary

End point timeframe:

Up to 28 Days

End point values	Placebo	750 mg LD / 250 mg MD Lumicitabine	1000 mg LD / 500 mg MD Lumicitabine	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[15]	0[16]	0[17]	
Units: Hours				
arithmetic mean (standard deviation)	()	()	()	

Notes:

[15] - Overall subjects analyzed is 0 as none of subjects admitted to ICU since initiation of treatment.

[16] - Overall subjects analyzed is 0 as none of subjects admitted to ICU since initiation of treatment.

[17] - Overall subjects analyzed is 0 as none of subjects admitted to ICU since initiation of treatment.

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:

Number of subjects who required supplemental oxygen were reported. ITT-i set included all randomly assigned subjects who received at least 1 dose of study drug and who had an RSV infection confirmed by a PCR-based assay at the central laboratory at baseline, analyzed as randomized. Analyses were conducted on pooled groups across the 3 study parts.

End point type	Secondary

End point timeframe:

Up to 28 Days

End point values	Placebo	750 mg LD / 250 mg MD Lumicitabine	1000 mg LD / 500 mg MD Lumicitabine	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	15	21	5	
Units: Subjects	14	18	4	

Statistical analyses

No statistical analyses for this end point

Secondary: Time to End of Oxygen Supplementation

End point title	Time to End of Oxygen Supplementation

End point description:

It is the time from first dose of study drug to the last end date and time of any oxygen supplementation in hours. Population included ITT-i set who required supplemental oxygen. Analyses were conducted on pooled groups across the 3 study parts.

End point type	Secondary

End point timeframe:

Up to 28 Days

End point values	Placebo	750 mg LD / 250 mg MD Lumicitabine	1000 mg LD / 500 mg MD Lumicitabine	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	14	18	4	
Units: Hours				
arithmetic mean (standard error)	83.92 (± 168.125)	139.38 (± 237.584)	132.40 (± 288.568)	

Statistical analyses

No statistical analyses for this end point

Secondary: Time (Number of Hours) 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 the Onset of Respiratory Symptoms

End point title	Time (Number of Hours) 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 the Onset of Respiratory Symptoms

End point description:

Time (number of hours) 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	750 mg LD / 250 mg MD Lumicitabine	1000 mg LD / 500 mg MD Lumicitabine	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[18]	0[19]	0[20]	
Units: Hours				
arithmetic mean (standard deviation)	()	()	()	

Notes:

[18] - Data was not collected and analyzed because this study was stopped prematurely.

[19] - Data was not collected and analyzed because this study was stopped prematurely.

[20] - Data was not collected and analyzed because this study was stopped prematurely.

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Return to Pre-respiratory Syncytial Virus (Pre-RSV) Disease Level for Respiratory Rate

End point title	Time to Return to Pre-respiratory Syncytial Virus (Pre-RSV) Disease Level for Respiratory Rate

End point description:

It is the time from first dose of study drug until the time to return to pre-RSV disease level for respiratory rate. The return to pre-RSV disease level occurred when the observed value of the parameter was indicated by the investigator as normal, and no later observed values were indicated by the investigator as abnormal. ITT-i set included all randomly assigned subjects who received at least 1 dose of study drug and who had an RSV infection confirmed by a PCR-based assay at the central laboratory at baseline, analyzed as randomized. Analyses were conducted on pooled groups across the 3 study parts.

End point type	Secondary

End point timeframe:

Up to 28 Days

End point values	Placebo	750 mg LD / 250 mg MD Lumicitabine	1000 mg LD / 500 mg MD Lumicitabine	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	15	21	5	
Units: Hours				
arithmetic mean (standard deviation)	64.72 (± 180.542)	47.75 (± 153.293)	196.96 (± 290.694)	

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Return to Pre-RSV Disease Level for Oxygen Saturation

End point title	Time to Return to Pre-RSV Disease Level for Oxygen Saturation

End point description:

It is the time from first dose of study drug until the time to return to pre-RSV disease level for oxygen saturation. The return to pre-RSV disease level occurred when the observed value of the parameter was indicated by the investigator as normal, and no later observed values were indicated by the investigator as abnormal. ITT-i set included all randomly assigned subjects who received at least 1 dose of study drug and who had an RSV infection confirmed by a PCR-based assay at the central laboratory at baseline, analyzed as randomized. Analyses were conducted on pooled groups across the 3 study parts.

End point type	Secondary

End point timeframe:

Up to 28 Days

End point values	Placebo	750 mg LD / 250 mg MD Lumicitabine	1000 mg LD / 500 mg MD Lumicitabine	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	15	21	5	
Units: Hours				
arithmetic mean (standard deviation)	55.55 (± 85.915)	33.85 (± 57.703)	47.56 (± 106.347)	

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Return to Pre-RSV Disease Level for Body Temperature

End point title	Time to Return to Pre-RSV Disease Level for Body Temperature

End point description:

It is the time from first dose of study drug until the time to return to pre-RSV disease level for body temperature. The return to pre-RSV disease level occurred when the observed value of the parameter was indicated by the investigator as normal, and no later observed values were indicated by the investigator as abnormal.

End point type	Secondary

End point timeframe:

Up to 28 Days

End point values	Placebo	750 mg LD / 250 mg MD Lumicitabine	1000 mg LD / 500 mg MD Lumicitabine	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[21]	0[22]	0[23]	
Units: Degree Celsius				
arithmetic mean (standard deviation)	()	()	()	

Notes:

[21] - Data was not collected and analyzed because this study was stopped prematurely.

[22] - Data was not collected and analyzed because this study was stopped prematurely.

[23] - Data was not collected and analyzed because this study was stopped prematurely.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects Who Required Noninvasive Mechanical Ventilation Support

End point title	Number of Subjects Who Required Noninvasive Mechanical Ventilation Support

End point description:

Number of subjects who required noninvasive mechanical ventilation support (that is supplemental oxygen [excluding mechanical ventilation]) were reported. ITT-i set included all randomly assigned subjects who received at least 1 dose of study drug and who had an RSV infection confirmed by a PCR-based assay at the central laboratory at baseline, analyzed as randomized. Analyses were conducted on pooled groups across the 3 study parts.

End point type	Secondary

End point timeframe:

Up to 28 Days

End point values	Placebo	750 mg LD / 250 mg MD Lumicitabine	1000 mg LD / 500 mg MD Lumicitabine	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	15	21	5	
Units: Subjects	14	18	4	

Statistical analyses

No statistical analyses for this end point

Secondary: Time to End of Noninvasive Mechanical Ventilation Support

End point title	Time to End of Noninvasive Mechanical Ventilation Support

End point description:

It is the time from first dose of study drug to the last end date and time of noninvasive mechanical ventilation in hours. Population included ITT-i set who required noninvasive mechanical ventilation support. Analyses were conducted on pooled groups across the 3 study parts.

End point type	Secondary

End point timeframe:

Up to 28 Days

End point values	Placebo	750 mg LD / 250 mg MD Lumicitabine	1000 mg LD / 500 mg MD Lumicitabine	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	14	18	4	
Units: Hours				
arithmetic mean (standard deviation)	83.92 (± 168.125)	139.38 (± 237.584)	132.40 (± 288.568)	

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:

Number of subjects who required invasive mechanical ventilation support were reported. ITT-i set included all randomly assigned subjects who received at least 1 dose of study drug and who had an RSV infection confirmed by a PCR-based assay at the central laboratory at baseline, analyzed as randomized. Analyses were conducted on pooled groups across the 3 study parts.

End point type	Secondary

End point timeframe:

Up to 28 Days

End point values	Placebo	750 mg LD / 250 mg MD Lumicitabine	1000 mg LD / 500 mg MD Lumicitabine	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	15	21	5	
Units: Subjects	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Time to End of Invasive Mechanical Ventilation Support

End point title	Time to End of Invasive Mechanical Ventilation Support

End point description:

It is the time from first dose of study drug to the last end date and time of invasive mechanical ventilation support in hours. ITT-i set included all randomly assigned subjects who received at least 1 dose of study drug and who had an RSV infection confirmed by a PCR-based assay at the central laboratory at baseline, analyzed as randomized. Zero subjects were analysed for this endpoint as none

of subjects required invasive ventilation support. Analyses were conducted on pooled groups across the 3 study parts.

End point type	Secondary

End point timeframe:

Up to 28 Days

End point values	Placebo	750 mg LD / 250 mg MD Lumicitabine	1000 mg LD / 500 mg MD Lumicitabine	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[24]	0[25]	0[26]	
Units: Hours				
arithmetic mean (standard deviation)	()	()	()	

Notes:

[24] - 0 subjects analysed for this endpoint as none of subjects required invasive ventilation support.

[25] - 0 subjects analysed for this endpoint as none of subjects required invasive ventilation support.

[26] - 0 subjects analysed for this endpoint as none of subjects required invasive ventilation support.

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Return to Pre-RSV Functional Status as Assessed by KATZ Activities of Daily Living (ADL) Score

End point title	Time to Return to Pre-RSV Functional Status as Assessed by KATZ Activities of Daily Living (ADL) Score

End point description:

It is the time from first dose of study drug until the time to return to pre-RSV functional status. Functional status is total points on KATZ index of independence in activities of daily living (KATZ ADL score). Katz activities of daily living assessed questions related to bathing, dressing, toileting, transferring, continence and feeding components. Total score was calculated by adding scores for all 6 activities which ranges from 0 high (subject independent) to 6 low (subject very dependent). Return to pre-RSV functional status occurs at timepoint where for first time KATZ ADL score is equal or higher than pre-RSV KATZ ADL score and after which no scores lower than pre-RSV KATZ ADL score occur anymore. ITT-i set included all randomly assigned subjects who received at least 1 dose of study drug and who had an RSV infection confirmed by a PCR-based assay at the central laboratory at baseline, analyzed as randomized. Analyses were conducted on pooled groups across the 3 study parts.

End point type	Secondary

End point timeframe:

Up to 28 Days

End point values	Placebo	750 mg LD / 250 mg MD Lumicitabine	1000 mg LD / 500 mg MD Lumicitabine	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	15	21	5	
Units: Days				
arithmetic mean (standard deviation)	3.60 (± 7.434)	4.48 (± 6.961)	6.00 (± 11.203)	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects Who Required Hydration or Feeding by Intravenous (IV) Catheter or Nasogastric Tube

End point title	Number of Subjects Who Required Hydration or Feeding by Intravenous (IV) Catheter or Nasogastric Tube

End point description:

Number of subjects who required hydration or feeding by IV catheter or nasogastric tube were reported. ITT-i set included all randomly assigned subjects who received at least 1 dose of study drug and who had an RSV infection confirmed by a PCR-based assay at the central laboratory at baseline, analyzed as randomized. Analyses were conducted on pooled groups across the 3 study parts.

End point type	Secondary

End point timeframe:

Up to 28 Days

End point values	Placebo	750 mg LD / 250 mg MD Lumicitabine	1000 mg LD / 500 mg MD Lumicitabine	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	15	21	5	
Units: Subjects	3	5	1	

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 is defined as the time from first dose of study drug until the time at which the following criteria were all met: normalization of blood oxygen level (return to baseline; by pulse oximetry) without requirement of supplemental oxygen beyond baseline level, normalization of oral feeding, normalization of respiratory rate and normalization of heart rate. ITT-i set included all randomly assigned subjects who received at least 1 dose of study drug and who had an RSV infection confirmed by a PCR-based assay at the central laboratory at baseline, analyzed as randomized. Analyses were conducted on pooled groups across the 3 study parts.

End point type	Secondary

End point timeframe:

Up to 28 Days

End point values	Placebo	750 mg LD / 250 mg MD Lumicitabine	1000 mg LD / 500 mg MD Lumicitabine	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	15	21	5	
Units: Hours				
arithmetic mean (standard deviation)	151.21 (± 266.460)	171.74 (± 261.384)	207.00 (± 282.955)	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects in Each Ordinal Scale Category

End point title	Number of Subjects in Each Ordinal Scale Category

End point description:

Number of subjects in each ordinal scale category were reported. Ordinal scale consists of 6 categories or clinical states that are exhaustive, mutually exclusive, and ordered: category 1) death; category 2) admitted to ICU; category 3) non-ICU hospitalization requiring supplemental oxygen; category 4) non-ICU hospitalization not requiring supplemental oxygen; category 5) not hospitalized, unable to resume normal activities; category 6) not hospitalized, resumption of normal activities. ITT-i set included all randomly assigned subjects who received at least 1 dose of study drug and who had an RSV infection confirmed by a PCR-based assay at central laboratory at baseline, analyzed as randomized. Analyses were conducted on pooled groups across the 3 study parts.

End point type	Secondary

End point timeframe:

Day 5/6 (Day of last study treatment)

End point values	Placebo	750 mg LD / 250 mg MD Lumicitabine	1000 mg LD / 500 mg MD Lumicitabine	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	15	21	5	
Units: Subjects				
Category 1	0	0	0	
Category 2	0	1	0	
Category 3	2	5	1	
Category 4	6	8	1	
Category 5	5	2	1	
Category 6	2	5	2	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with All-Cause Mortality

End point title	Number of Subjects with All-Cause Mortality

End point description:

All-cause mortality included all deaths of subjects due to any cause. Safety set included all subjects who received at least 1 dose of study drug, analyzed as treated. Analyses were conducted on pooled groups across the 3 study parts.

End point type	Secondary

End point timeframe:

Up to 28 Days

End point values	Placebo	750 mg LD / 250 mg MD Lumicitabine	1000 mg LD / 500 mg MD Lumicitabine	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	16	27	6	
Units: Subjects	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: RSV RNA Viral Load Over Time

End point title	RSV RNA Viral Load Over Time

End point description:

Antiviral activity RSV RNA viral load was measured in mid-turbinate nasal swabs (obtained from non-intubated subjects) or in mid-turbinate nasal swabs and endotracheal samples (obtained from intubated subjects or via suction through tracheostomy or other sampling methods) using qRT-PCR performed at the central laboratory. ITT-i set included all randomly assigned subjects who received at least 1 dose of study drug and who had an RSV infection confirmed by a PCR-based assay at the central laboratory at baseline, analyzed as randomized. Here 'n' (number analyzed) signifies number of subjects evaluable for each time point. Analyses were conducted on pooled groups across the 3 study parts.

End point type	Secondary

End point timeframe:

Days 2, 3, 4, 5, 6, 7, 10, 14 and 28

End point values	Placebo	750 mg LD / 250 mg MD Lumicitabine	1000 mg LD / 500 mg MD Lumicitabine	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	15	21	5	
Units: log10 copies/mL				
arithmetic mean (standard deviation)				
Day 2 (n=15,21,4)	5.9257 (± 1.95951)	4.7208 (± 1.60154)	3.4242 (± 1.10867)	

Day 3 (n=15,19,3)	4.8255 (± 1.84651)	4.3515 (± 1.97633)	4.3129 (± 0.99078)	
Day 4 (n=15,21,3)	4.0608 (± 1.57493)	3.9345 (± 1.64600)	4.0729 (± 1.15419)	
Day 5 (n=15,20,3)	3.6463 (± 1.44056)	3.6206 (± 1.71515)	4.5344 (± 0.97473)	
Day 6 (n=15,19,3)	3.6996 (± 1.98383)	3.4313 (± 1.57700)	3.2163 (± 1.30083)	
Day 7 (n=15,19,5)	3.4044 (± 1.75773)	3.2306 (± 1.58432)	2.6147 (± 0.89779)	
Day 10 (n=15,15,4)	2.5966 (± 1.04644)	2.7516 (± 1.72825)	2.5792 (± 1.00954)	
Day 14 (n=15,21,4)	2.3605 (± 1.00220)	2.3010 (± 1.03732)	2.1512 (± 0.50236)	
Day 28 (n=14,21,4)	1.9179 (± 0.06682)	1.9714 (± 0.22559)	1.9000 (± 0.00000)	

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 is the highest value of log10 viral load at or after the baseline measurement. Peak viral load over time was measured by qRT-PCR.

End point type	Secondary

End point timeframe:

Up to 28 Days

End point values	Placebo	750 mg LD / 250 mg MD Lumicitabine	1000 mg LD / 500 mg MD Lumicitabine	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[27]	0[28]	0[29]	
Units: Copies/mL				
arithmetic mean (standard deviation)	()	()	()	

Notes:

[27] - Data was not collected and analyzed because this study was stopped prematurely.

[28] - Data was not collected and analyzed because this study was stopped prematurely.

[29] - Data was not collected and analyzed because this study was stopped prematurely.

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 is the time from initiation of study treatment until the first time point with the

peak viral load.

End point type	Secondary

End point timeframe:

Up to 28 Days

End point values	Placebo	750 mg LD / 250 mg MD Lumicitabine	1000 mg LD / 500 mg MD Lumicitabine	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[30]	0[31]	0[32]	
Units: Hours				
arithmetic mean (standard deviation)	()	()	()	

Notes:

[30] - Data was not collected and analyzed because this study was stopped prematurely.

[31] - Data was not collected and analyzed because this study was stopped prematurely.

[32] - Data was not collected and analyzed because this study was stopped prematurely.

Statistical analyses

No statistical analyses for this end point

Secondary: Rate of Decline of Viral Load

End point title	Rate of Decline of Viral Load

End point description:

Rate of decline of viral load over the first 24 hours calculated as a log decline/24 hours defined as: 24-hour log viral load after first dose of study drug minus (–) log viral load at baseline divided by (/) date/time of 24-hour viral load sample – date/time of baseline viral load.

End point type	Secondary

End point timeframe:

Up to 28 Days

End point values	Placebo	750 mg LD / 250 mg MD Lumicitabine	1000 mg LD / 500 mg MD Lumicitabine	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[33]	0[34]	0[35]	
Units: copies/ml				
arithmetic mean (standard deviation)	()	()	()	

Notes:

[33] - Data was not collected and analyzed because this study was stopped prematurely.

[34] - Data was not collected and analyzed because this study was stopped prematurely.

[35] - Data was not collected and analyzed because this study was stopped prematurely.

Statistical analyses

No statistical analyses for this end point

Secondary: Time to RSV RNA Viral Load Being Undetectable

End point title	Time to RSV RNA Viral Load Being Undetectable

End point description:

It is the time in hours from initiation of study treatment until the first post baseline time point at which the virus is undetectable in an assessment and after which time no detectable virus assessment follows as measured by qRT-PCR.

End point type	Secondary

End point timeframe:

Up to 28 Days

End point values	Placebo	750 mg LD / 250 mg MD Lumicitabine	1000 mg LD / 500 mg MD Lumicitabine	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[36]	0[37]	0[38]	
Units: Hours				
arithmetic mean (standard deviation)	()	()	()	

Notes:

[36] - Data was not collected and analyzed because this study was stopped prematurely.

[37] - Data was not collected and analyzed because this study was stopped prematurely.

[38] - Data was not collected and analyzed because this study was stopped prematurely.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Undetectable Viral Load

End point title	Number of Subjects with Undetectable Viral Load

End point description:

Number of subjects with undetectable viral load up to 28 days were reported. ITT-i set included all randomly assigned subjects who received at least 1 dose of study drug and who had an RSV infection confirmed by a PCR-based assay at the central laboratory at baseline, analyzed as randomized. Analyses were conducted on pooled groups across the 3 study parts.

End point type	Secondary

End point timeframe:

Up to 28 Days

End point values	Placebo	750 mg LD / 250 mg MD Lumicitabine	1000 mg LD / 500 mg MD Lumicitabine	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	15	21	5	
Units: Subjects	14	19	5	

Statistical analyses

No statistical analyses for this end point

Secondary: RSV RNA Viral Load AUC up to Day 14

End point title	RSV RNA Viral Load AUC up to Day 14

End point description:

RSV RNA viral load was measured in midturbinate nasal swabs and in endotracheal samples (obtained from intubated subjects or via suction through tracheostomy or other sampling.

End point type	Secondary

End point timeframe:

Up to Day 14

End point values	Placebo	750 mg LD / 250 mg MD Lumicitabine	1000 mg LD / 500 mg MD Lumicitabine	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[39]	0[40]	0[41]	
Units: Log10 copies/mL/day				
arithmetic mean (standard deviation)	()	()	()	

Notes:

[39] - Data was not collected and analyzed because this study was stopped prematurely.

[40] - Data was not collected and analyzed because this study was stopped prematurely.

[41] - Data was not collected and analyzed because this study was stopped prematurely.

Statistical analyses

No statistical analyses for this end point

Secondary: RSV RNA Viral Load AUC in Subjects Assigned to a Longer Dosing Duration

End point title	RSV RNA Viral Load AUC in Subjects Assigned to a Longer Dosing Duration

End point description:

RSV RNA viral load was measured in midturbinate nasal swabs and in endotracheal samples (obtained from intubated subjects or via suction through tracheostomy or other sampling. ITT-i set included all randomly assigned subjects who received at least 1 dose of study drug and who had an RSV infection confirmed by a PCR-based assay at the central laboratory at baseline, analyzed as randomized.

End point type	Secondary

End point timeframe:

Up to 1 Day after the last dose of study drug

End point values	Placebo	750 mg LD / 250 mg MD Lumicitabine	1000 mg LD / 500 mg MD Lumicitabine	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[42]	0[43]	0[44]	
Units: log10 copies/mL/day				
arithmetic mean (standard deviation)	()	()	()	

Notes:

[42] - No subject received extended treatment, therefore data was not analyzed.

[43] - No subject received extended treatment, therefore data was not analyzed.

[44] - No subject received extended treatment, therefore data was not analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with 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 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 with postbaseline changes in the RSV polymerase L gene and other regions of the RSV genome compared with baseline sequences were reported. ITT-i set included all randomly assigned subjects who received at least 1 dose of study drug and who had an RSV infection confirmed by a PCR-based assay at the central laboratory at baseline, analyzed as randomized. Here 'N' (number of subjects analyzed) signifies number of subjects evaluable for this endpoint. Analyses were conducted on pooled groups across the 3 study parts.

End point type	Secondary

End point timeframe:

Baseline up to 28 Days

End point values	Placebo	750 mg LD / 250 mg MD Lumicitabine	1000 mg LD / 500 mg MD Lumicitabine	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	10	12	4	
Units: Subjects	0	0	0	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Up to 28 Days	
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 loading dose (LD) (Dose 1) of matching placebo tablet orally on Day 1 followed by nine maintenance doses (MD) (Doses 2 to 10) of matching placebo tablets orally twice daily (bid) from Day 1/2 to Day 5/6 (depending on the timing of the LD administration).	
Reporting group title	750 mg LD / 250 mg MD Lumicitabine
Reporting group description:	
Subjects received a single 750 milligram (mg) LD (Dose 1) of lumicitabine tablet orally followed by nine MD (Doses 2 to 10) of 250 mg lumicitabine tablets orally bid from Day 1/2 to Day 5/6 (depending on the timing of the LD administration).	
Reporting group title	1000 mg LD / 500 mg MD Lumicitabine
Reporting group description:	
Subjects received a single 1000 mg LD (Dose 1) of lumicitabine tablet orally followed by nine MD (Doses 2 to 10) of 500 mg lumicitabine tablets orally bid from Day 1/2 to Day 5/6 (depending on the timing of the LD administration).	

Serious adverse events	Placebo	750 mg LD / 250 mg MD Lumicitabine	1000 mg LD / 500 mg MD Lumicitabine
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 16 (12.50%)	4 / 27 (14.81%)	1 / 6 (16.67%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Thermal Burn			
subjects affected / exposed	1 / 16 (6.25%)	0 / 27 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Cardiac Failure			
subjects affected / exposed	1 / 16 (6.25%)	0 / 27 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			

Pancytopenia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 27 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Intestinal Obstruction			
subjects affected / exposed	0 / 16 (0.00%)	1 / 27 (3.70%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Chronic Obstructive Pulmonary Disease			
subjects affected / exposed	0 / 16 (0.00%)	1 / 27 (3.70%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	0 / 16 (0.00%)	1 / 27 (3.70%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Influenza			
subjects affected / exposed	0 / 16 (0.00%)	1 / 27 (3.70%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	1 / 16 (6.25%)	0 / 27 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	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	750 mg LD / 250 mg MD Lumicitabine	1000 mg LD / 500 mg MD Lumicitabine
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 16 (37.50%)	17 / 27 (62.96%)	5 / 6 (83.33%)
Vascular disorders			
Deep Vein Thrombosis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 27 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Hypertension			
subjects affected / exposed	1 / 16 (6.25%)	1 / 27 (3.70%)	0 / 6 (0.00%)
occurrences (all)	4	1	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 16 (6.25%)	0 / 27 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Chest Pain			
subjects affected / exposed	2 / 16 (12.50%)	2 / 27 (7.41%)	0 / 6 (0.00%)
occurrences (all)	3	2	0
Oedema Peripheral			
subjects affected / exposed	1 / 16 (6.25%)	0 / 27 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Pyrexia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 27 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 16 (0.00%)	2 / 27 (7.41%)	0 / 6 (0.00%)
occurrences (all)	0	2	0
Chronic Obstructive Pulmonary Disease			
subjects affected / exposed	0 / 16 (0.00%)	0 / 27 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Haemoptysis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 27 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	2
Psychiatric disorders			

Insomnia			
subjects affected / exposed	2 / 16 (12.50%)	0 / 27 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Investigations			
Alanine Aminotransferase Increased			
subjects affected / exposed	1 / 16 (6.25%)	2 / 27 (7.41%)	1 / 6 (16.67%)
occurrences (all)	1	2	1
Aspartate Aminotransferase Increased			
subjects affected / exposed	0 / 16 (0.00%)	1 / 27 (3.70%)	1 / 6 (16.67%)
occurrences (all)	0	1	1
Blood Creatine Phosphokinase Increased			
subjects affected / exposed	0 / 16 (0.00%)	2 / 27 (7.41%)	0 / 6 (0.00%)
occurrences (all)	0	2	0
Blood Fibrinogen Increased			
subjects affected / exposed	1 / 16 (6.25%)	0 / 27 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
C-Reactive Protein Increased			
subjects affected / exposed	1 / 16 (6.25%)	0 / 27 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Eosinophil Count Increased			
subjects affected / exposed	1 / 16 (6.25%)	0 / 27 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Gamma-Glutamyltransferase Increased			
subjects affected / exposed	1 / 16 (6.25%)	1 / 27 (3.70%)	0 / 6 (0.00%)
occurrences (all)	1	1	0
Hepatic Enzyme Increased			
subjects affected / exposed	0 / 16 (0.00%)	0 / 27 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Occult Blood Positive			
subjects affected / exposed	0 / 16 (0.00%)	0 / 27 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Injury, poisoning and procedural complications			
Overdose			

subjects affected / exposed	1 / 16 (6.25%)	3 / 27 (11.11%)	0 / 6 (0.00%)
occurrences (all)	1	3	0
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 16 (0.00%)	2 / 27 (7.41%)	0 / 6 (0.00%)
occurrences (all)	0	2	0
Somnolence			
subjects affected / exposed	0 / 16 (0.00%)	0 / 27 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Blood and lymphatic system disorders			
Eosinophilia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 27 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Febrile Neutropenia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 27 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
Abdominal Pain Upper			
subjects affected / exposed	0 / 16 (0.00%)	2 / 27 (7.41%)	1 / 6 (16.67%)
occurrences (all)	0	2	1
Diarrhoea			
subjects affected / exposed	1 / 16 (6.25%)	1 / 27 (3.70%)	0 / 6 (0.00%)
occurrences (all)	1	1	0
Gastritis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 27 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Hepatobiliary disorders			
Hepatic Function Abnormal			
subjects affected / exposed	0 / 16 (0.00%)	2 / 27 (7.41%)	0 / 6 (0.00%)
occurrences (all)	0	2	0
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	1 / 16 (6.25%)	0 / 27 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Alopecia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 27 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1

Erythema			
subjects affected / exposed	0 / 16 (0.00%)	0 / 27 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Haemorrhage Subcutaneous			
subjects affected / exposed	0 / 16 (0.00%)	0 / 27 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Hyperhidrosis			
subjects affected / exposed	0 / 16 (0.00%)	2 / 27 (7.41%)	0 / 6 (0.00%)
occurrences (all)	0	2	0
Rash			
subjects affected / exposed	1 / 16 (6.25%)	3 / 27 (11.11%)	1 / 6 (16.67%)
occurrences (all)	1	3	1
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	1 / 16 (6.25%)	0 / 27 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Renal Impairment			
subjects affected / exposed	0 / 16 (0.00%)	0 / 27 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			
Myalgia			
subjects affected / exposed	0 / 16 (0.00%)	2 / 27 (7.41%)	0 / 6 (0.00%)
occurrences (all)	0	2	0
Infections and infestations			
Acarodermatitis			
subjects affected / exposed	1 / 16 (6.25%)	0 / 27 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Respiratory Tract Infection Bacterial			
subjects affected / exposed	1 / 16 (6.25%)	0 / 27 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Urinary Tract Infection			
subjects affected / exposed	0 / 16 (0.00%)	0 / 27 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Metabolism and nutrition disorders			
Hyperglycaemia			

subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 2	0 / 27 (0.00%) 0	0 / 6 (0.00%) 0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
19 July 2016	The overall reason for the amendment 1 was to add an inclusion criteria for female subjects to assure that woman agree not to donate eggs, and to add a section on rash management.
13 January 2017	The overall reason for the amendment 2 was to create a new Part 1 of the study protocol to characterize the pharmacokinetics (PK), to confirm the population pharmacokinetic (popPK) model derived from healthy volunteers in hospitalized adults with respiratory syncytial virus (RSV) infection, and to more clearly define the study eligibility criteria to ensure subject safety. Furthermore, changes requested by health authorities were made: women of childbearing potential were allowed to participate in the study, the age limit for subjects was lowered, the endpoints of the study were updated, subjects on extracorporeal membrane oxygenation were excluded, the guidelines concerning corticosteroid use were adjusted, clarifications regarding the use of the electronic clinical outcome assessment (eCOA) device were added single electrocardiogram (ECG) measurements were changed to triplicate ECGs and the dose dispensing instructions were deleted.
05 September 2017	The overall reason for the amendment 3 was to remove furosemide, ibuprofen, and trimethoprim/sulfametoxazole from the list of prohibited moderate/strong inhibitors of organic anion transporter (OAT) 3.
20 March 2018	The overall reason for the amendment 4 was for Part 2 of the study (1) to include additional safety samples for biochemistry, (2) to lift the requirement for triplicate electrocardiograms (ECGs) and reduce the ECG timepoints, (3) to prohibit the use of P-glycoprotein (P-gp) inhibitors and inducers, and (4) to optimize the PK sampling scheme.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

As the study was stopped prematurely the planned final analyses were adapted. Due to small number of subjects in Part 2, it was decided to pool the data from the 3 parts of the study to perform an evaluation of selected planned analyses only.

Notes: