Clinical trial results:
A Phase 1/2, randomized, observer-blind, controlled, multi-center, dose-escalation study to evaluate safety, reactogenicity and immunogenicity of GSK Biologicals' respiratory syncytial virus (RSV) investigational vaccine based on the RSV viral proteins F, N and M2-1 encoded by chimpanzee-derived adenovector (ChAd155-RSV) (GSK3389245A), when administered intramuscularly according to a 0, 1-month schedule to RSV-seropositive infants aged 12 to 23 months.

Summary

EudraCT number	2016-000117-76
Trial protocol	ES PL IT
Global end of trial date	31 March 2021

Results information

Result version number	v1 (current)
This version publication date	14 October 2021
First version publication date	14 October 2021

Trial information

Trial identification

Sponsor protocol code	204838

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02927873
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	GlaxoSmithKline Biologicals
Sponsor organisation address	Rue de l'Institut 89, Rixensart, Belgium, B-1330
Public contact	GSK Response Center, GlaxoSmithKline, 044 8664357343, GSKClinicalSupportHD@gsk.com
Scientific contact	GSK Response Center, GlaxoSmithKline, 044 8664357343, GSKClinicalSupportHD@gsk.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	13 August 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	19 February 2019
Global end of trial reached?	Yes
Global end of trial date	31 March 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the safety and reactogenicity of three dose levels of the RSV investigational vaccine when administered as two IM doses according to a 0, 1-month schedule, up to 30 days after Dose 2 (i.e. Day 61) in RSV-seropositive infants aged 12 to 23 months.

Protection of trial subjects:

All subjects were supervised for at least 60 min after vaccination with appropriate medical treatment readily available. As requested by Italian health authorities, in addition to the 60 minutes supervision after vaccination, the first 8 infants have completed a period of observation of at least 48 hours following administration of dose 1 prior to continuing to immunize the rest of the subjects (i.e. from the ninth subject and beyond) with dose 1 in the step 1. The same process has been applied following the administration of dose 2 in step 1 and further applied in step 2 and step 3 of the trial. Vaccines were administered by qualified and trained personnel. Vaccines were administered only to eligible subjects that had no contraindications to any components of the vaccines. Subjects were followed-up for 2 years after the last vaccination.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	17 January 2017
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	Canada: 1
Country: Number of subjects enrolled	Italy: 7
Country: Number of subjects enrolled	Mexico: 4
Country: Number of subjects enrolled	Panama: 31
Country: Number of subjects enrolled	Poland: 1
Country: Number of subjects enrolled	Spain: 26
Country: Number of subjects enrolled	Taiwan: 12
Country: Number of subjects enrolled	United States: 25
Worldwide total number of subjects	107
EEA total number of subjects	34

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)	107
Children (2-11 years)	0
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:

The study was conducted at 32 centers in 8 countries (Canada, Italy, Mexico, Panama, Poland, Spain, Taiwan and United States).

Pre-assignment

Screening details:

Out of 107 participants enrolled in the study, 21 participants were not assigned to any study group and 4 participants did not receive any study treatment. 82 subjects were vaccinated and included in the Exposed Set.

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, Monitor, Carer, Data analyst, Assessor

Blinding implementation details:

Observer-blind

Arms

Are arms mutually exclusive?	Yes
Arm title	RSV LD Group

Arm description:

RSV-seropositive infants, aged 12 to 23 months at the time of first vaccination, received 2 doses (0.5 mL each) of the RSV low dose (LD) vaccine, administered intramuscularly, one each at Day 1 and Day 31.

Arm type	Experimental
Investigational medicinal product name	RSV (GSK3389245A) low dose formulation vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

2 doses of 0.5 ml each of RSV (GSK3389245A) low dose formulation vaccine administered intramuscularly in the left anterolateral thigh or deltoid, at Day 1 and Day 31.

Arm title	RSV MD Group

Arm description:

RSV-seropositive infants, aged 12 to 23 months at the time of first vaccination, received 2 doses (0.15 mL each) of the RSV middle dose (MD) vaccine, administered intramuscularly, one each at Day 1 and Day 31.

Arm type	Experimental
Investigational medicinal product name	RSV (GSK3389245A) middle dose formulation vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

2 doses of 0.15 ml each of RSV (GSK3389245A) middle dose formulation vaccine administered intramuscularly in the left anterolateral thigh or deltoid, at Day 1 and Day 31.

Arm title	RSV HD Group

Arm description:

RSV-seropositive infants, aged 12 to 23 months at the time of first vaccination, received 2 doses (0.5 mL each) of the RSV high dose (HD) vaccine, administered intramuscularly, one each at Day 1 and Day 31.

Arm type	Experimental
Investigational medicinal product name	RSV (GSK3389245A) high dose formulation vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

2 doses of 0.5 ml each of RSV (GSK3389245A) high dose formulation vaccine administered intramuscularly in the left anterolateral thigh or deltoid, at Day 1 and Day 31.

Arm title	Placebo LD group

Arm description:

RSV-seropositive infants, aged 12 to 23 months at the time of first vaccination, received 2 doses (0.5 mL each) of placebo, administered intramuscularly, one each at Day 1 and Day 31.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

2 doses (0.5 mL each for Placebo LD and Placebo HD groups and 0.15 mL for Placebo MD group) of Placebo administered intramuscularly in the left anterolateral thigh or deltoid, at Day 1 and Day 31.

Arm title	Placebo MD group

Arm description:

RSV-seropositive infants, aged 12 to 23 months at the time of first vaccination, received 2 doses (0.15 mL each) of placebo, administered intramuscularly, one each at Day 1 and Day 31.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

2 doses (0.5 mL each for Placebo LD and Placebo HD groups and 0.15 mL for Placebo MD group) of Placebo administered intramuscularly in the left anterolateral thigh or deltoid, at Day 1 and Day 31.

Arm title	Placebo HD group

Arm description:

RSV-seropositive infants, aged 12 to 23 months at the time of first vaccination, received 2 doses (0.5 mL each) of placebo, administered intramuscularly, one each at Day 1 and Day 31.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

2 doses (0.5 mL each for Placebo LD and Placebo HD groups and 0.15 mL for Placebo MD group) of Placebo administered intramuscularly in the left anterolateral thigh or deltoid, at Day 1 and Day 31.

Number of subjects in period 1[1]	RSV LD Group	RSV MD Group	RSV HD Group
Started	11	14	18
Completed	9	11	18
Not completed	2	3	0
PARENTS REFUSED SAFETY FOLLOW-UP	1	-	-
PARENTS NOT ABLE TO COME TO SITE	-	1	-
WITHDRAWN, ACCEPTED CALLS FOR SAFETY SURVEILLANCE	1	-	-
MIGRATED / MOVED FROM THE STUDY AREA	-	-	-
Lost to follow-up	-	1	-
CONSENT WITHDRAWAL NOT DUE TO ADV. EVENT	-	1	-

Number of subjects in period 1[1]	Placebo LD group	Placebo MD group	Placebo HD group
Started	11	11	17
Completed	11	11	16
Not completed	0	0	1
PARENTS REFUSED SAFETY FOLLOW-UP	-	-	-
PARENTS NOT ABLE TO COME TO SITE	-	-	-
WITHDRAWN, ACCEPTED CALLS FOR SAFETY SURVEILLANCE	-	-	-
MIGRATED / MOVED FROM THE STUDY AREA	-	-	1
Lost to follow-up	-	-	-
CONSENT WITHDRAWAL NOT DUE TO ADV. EVENT	-	-	-

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: Out of 107 participants enrolled in the study, 21 participants were not assigned to any study group and 4 participants did not receive any study treatment. 82 subjects were vaccinated and included in the Exposed Set.

Baseline characteristics

Reporting groups	
Reporting group title	RSV LD Group
Reporting group description:	
RSV-seropositive infants, aged 12 to 23 months at the time of first vaccination, received 2 doses (0.5 mL each) of the RSV low dose (LD) vaccine, administered intramuscularly, one each at Day 1 and Day 31.	
Reporting group title	RSV MD Group
Reporting group description:	
RSV-seropositive infants, aged 12 to 23 months at the time of first vaccination, received 2 doses (0.15 mL each) of the RSV middle dose (MD) vaccine, administered intramuscularly, one each at Day 1 and Day 31.	
Reporting group title	RSV HD Group
Reporting group description:	
RSV-seropositive infants, aged 12 to 23 months at the time of first vaccination, received 2 doses (0.5 mL each) of the RSV high dose (HD) vaccine, administered intramuscularly, one each at Day 1 and Day 31.	
Reporting group title	Placebo LD group
Reporting group description:	
RSV-seropositive infants, aged 12 to 23 months at the time of first vaccination, received 2 doses (0.5 mL each) of placebo, administered intramuscularly, one each at Day 1 and Day 31.	
Reporting group title	Placebo MD group
Reporting group description:	
RSV-seropositive infants, aged 12 to 23 months at the time of first vaccination, received 2 doses (0.15 mL each) of placebo, administered intramuscularly, one each at Day 1 and Day 31.	
Reporting group title	Placebo HD group
Reporting group description:	
RSV-seropositive infants, aged 12 to 23 months at the time of first vaccination, received 2 doses (0.5 mL each) of placebo, administered intramuscularly, one each at Day 1 and Day 31.	

Reporting group values	RSV LD Group	RSV MD Group	RSV HD Group
Number of subjects	11	14	18
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	11	14	18
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous Units: months			
arithmetic mean	15.4	15.6	16.3
standard deviation	± 1.6	± 3.3	± 4.0

Sex: Female, Male Units: Subjects			
FEMALE	4	7	10
MALE	7	7	8
Race/Ethnicity, Customized Units: Subjects			
AFRICAN HERITAGE / AFRICAN AMERICAN	0	0	0
ASIAN - EAST ASIAN HERITAGE	0	0	3
ASIAN - SOUTH EAST ASIAN HERITAGE	0	0	1
NATIVE HAWAIIAN OR OTHER PACIFIC ISLANDER	0	1	0
OTHER, NOT SPECIFIED	0	7	12
WHITE - CAUCASIAN / EUROPEAN HERITAGE	11	6	2

Reporting group values	Placebo LD group	Placebo MD group	Placebo HD group
Number of subjects	11	11	17
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	11	11	17
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous Units: months			
arithmetic mean	15.0	16.2	17.4
standard deviation	± 1.9	± 2.7	± 3.8
Sex: Female, Male Units: Subjects			
FEMALE	5	3	12
MALE	6	8	5
Race/Ethnicity, Customized Units: Subjects			
AFRICAN HERITAGE / AFRICAN AMERICAN	0	1	0
ASIAN - EAST ASIAN HERITAGE	0	1	3
ASIAN - SOUTH EAST ASIAN HERITAGE	0	1	0
NATIVE HAWAIIAN OR OTHER PACIFIC ISLANDER	0	0	0
OTHER, NOT SPECIFIED	2	4	9
WHITE - CAUCASIAN / EUROPEAN HERITAGE	9	4	5

Reporting group values	Total		
Number of subjects	82		

Age categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	0		
Newborns (0-27 days)	0		
Infants and toddlers (28 days-23 months)	82		
Children (2-11 years)	0		
Adolescents (12-17 years)	0		
Adults (18-64 years)	0		
From 65-84 years	0		
85 years and over	0		
Age continuous Units: months			
arithmetic mean			
standard deviation	-		
Sex: Female, Male Units: Subjects			
FEMALE	41		
MALE	41		
Race/Ethnicity, Customized Units: Subjects			
AFRICAN HERITAGE / AFRICAN AMERICAN	1		
ASIAN - EAST ASIAN HERITAGE	7		
ASIAN - SOUTH EAST ASIAN HERITAGE	2		
NATIVE HAWAIIAN OR OTHER PACIFIC ISLANDER	1		
OTHER, NOT SPECIFIED	34		
WHITE - CAUCASIAN / EUROPEAN HERITAGE	37		

End points

End points reporting groups

Reporting group title	RSV LD Group
Reporting group description: RSV-seropositive infants, aged 12 to 23 months at the time of first vaccination, received 2 doses (0.5 mL each) of the RSV low dose (LD) vaccine, administered intramuscularly, one each at Day 1 and Day 31.	
Reporting group title	RSV MD Group
Reporting group description: RSV-seropositive infants, aged 12 to 23 months at the time of first vaccination, received 2 doses (0.15 mL each) of the RSV middle dose (MD) vaccine, administered intramuscularly, one each at Day 1 and Day 31.	
Reporting group title	RSV HD Group
Reporting group description: RSV-seropositive infants, aged 12 to 23 months at the time of first vaccination, received 2 doses (0.5 mL each) of the RSV high dose (HD) vaccine, administered intramuscularly, one each at Day 1 and Day 31.	
Reporting group title	Placebo LD group
Reporting group description: RSV-seropositive infants, aged 12 to 23 months at the time of first vaccination, received 2 doses (0.5 mL each) of placebo, administered intramuscularly, one each at Day 1 and Day 31.	
Reporting group title	Placebo MD group
Reporting group description: RSV-seropositive infants, aged 12 to 23 months at the time of first vaccination, received 2 doses (0.15 mL each) of placebo, administered intramuscularly, one each at Day 1 and Day 31.	
Reporting group title	Placebo HD group
Reporting group description: RSV-seropositive infants, aged 12 to 23 months at the time of first vaccination, received 2 doses (0.5 mL each) of placebo, administered intramuscularly, one each at Day 1 and Day 31.	

Primary: Number of subjects with any solicited local adverse events (AEs)

End point title	Number of subjects with any solicited local adverse events (AEs)[1]
End point description: Assessed solicited local symptoms are pain, redness and swelling at injection site. Any = occurrence of the symptom regardless of intensity grade. Any redness and swelling symptom = symptom reported with a surface diameter greater than 0 millimeters.	
End point type	Primary
End point timeframe: During a 7-day follow-up period after each vaccination (vaccine/placebo administered at Day 1 and Day 31)	

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: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

End point values	RSV LD Group	RSV MD Group	RSV HD Group	Placebo LD group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11	13	18	11
Units: Subjects				
DOSE 1, Any Pain (N=11,13,18,11,11,17)	1	2	0	2
DOSE 1, Any Redness (N=11,13,18,11,11,17)	2	1	3	3
DOSE 1, Any Swelling (N=11,13,18,11,11,17)	0	0	1	1
DOSE 2, Any Pain (N=10,12,17,11,11,17)	2	2	2	1
DOSE 2, Any Redness (N=10,12,17,11,11,17)	2	1	2	3
DOSE 2, Any Swelling (N=10,12,17,11,11,17)	0	0	0	1

End point values	Placebo MD group	Placebo HD group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	17		
Units: Subjects				
DOSE 1, Any Pain (N=11,13,18,11,11,17)	0	2		
DOSE 1, Any Redness (N=11,13,18,11,11,17)	0	3		
DOSE 1, Any Swelling (N=11,13,18,11,11,17)	1	2		
DOSE 2, Any Pain (N=10,12,17,11,11,17)	0	3		
DOSE 2, Any Redness (N=10,12,17,11,11,17)	0	2		
DOSE 2, Any Swelling (N=10,12,17,11,11,17)	0	2		

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with any solicited general AEs

End point title	Number of subjects with any solicited general AEs[2]

End point description:

Assessed solicited general symptoms are drowsiness, fever [defined as temperature equal to or above (≥) 37.5 degrees Celsius (°C)/99.5 degrees Fahrenheit (°F) for oral, axillary or tympanic route, or ≥ 38.0°C/100.4°F for rectal route, the preferred route for recording temperature in this study being axillary], irritability/fussiness and loss of appetite. Any = occurrence of the symptom regardless of intensity grade or relation to study vaccination.

End point type	Primary

End point timeframe:

During a 7-day follow-up period after each vaccination (vaccine/placebo administered at Day 1 and Day 31)

Notes:

[2] - 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: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

End point values	RSV LD Group	RSV MD Group	RSV HD Group	Placebo LD group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11	13	18	11
Units: Subjects				
DOSE 1, Any Drowsiness (N=11,13,18,11,11,17)	4	2	4	5
DOSE 1, Any Irritability (N=11,13,18,11,11,17)	3	3	4	4
DOSE 1, Any Loss Of Appetite (N=11,13,18,11,11,17)	3	3	4	2
DOSE 1, Any Fever (N=11,13,18,11,11,17)	3	3	10	3
DOSE 2, Any Drowsiness (N=10, 12,17,11,11,17)	2	1	5	3
DOSE 2, Any Irritability (N=10,12,17,11,11,17)	3	1	5	3
DOSE 2, Any Loss Of Appetite (N=10,12,17,11,11,17)	3	0	6	3
DOSE 2, Any Fever (N=10,12,17,11,11,17)	2	2	5	1

End point values	Placebo MD group	Placebo HD group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	17		
Units: Subjects				
DOSE 1, Any Drowsiness (N=11,13,18,11,11,17)	3	4		
DOSE 1, Any Irritability (N=11,13,18,11,11,17)	2	2		
DOSE 1, Any Loss Of Appetite (N=11,13,18,11,11,17)	2	3		
DOSE 1, Any Fever (N=11,13,18,11,11,17)	2	0		
DOSE 2, Any Drowsiness (N=10, 12,17,11,11,17)	2	5		
DOSE 2, Any Irritability (N=10,12,17,11,11,17)	1	6		
DOSE 2, Any Loss Of Appetite (N=10,12,17,11,11,17)	2	5		
DOSE 2, Any Fever (N=10,12,17,11,11,17)	2	1		

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with any unsolicited AEs

End point title	Number of subjects with any unsolicited AEs[3]

End point description:

An unsolicited AE covers any untoward medical occurrence in a clinical investigation subject temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. Unsolicited AEs are reported in addition to those solicited during the clinical study and any solicited symptom with onset outside the specified period of follow-up for solicited symptoms. Any is defined as the occurrence of any unsolicited AE regardless of intensity grade or relation to study vaccination.

End point type	Primary

End point timeframe:

During a 30-day follow-up period after each vaccination (vaccine/placebo administered at Day 1 and Day 31)

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: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

End point values	RSV LD Group	RSV MD Group	RSV HD Group	Placebo LD group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11	14	18	11
Units: Subjects	9	9	13	7

End point values	Placebo MD group	Placebo HD group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	17		
Units: Subjects	10	13		

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with any serious adverse events (SAEs) from Day 1 up to Day 61

End point title	Number of subjects with any serious adverse events (SAEs) from Day 1 up to Day 61[4]

End point description:

Assessed SAEs include any untoward medical occurrences that resulted in death, were life-threatening, required hospitalization or prolongation of hospitalization or resulted in disability/incapacity. Any = occurrence of SAE regardless of intensity grade or relation to study vaccination.

End point type	Primary

End point timeframe:

From Day 1 up to Day 61

Notes:

[4] - 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: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

End point values	RSV LD Group	RSV MD Group	RSV HD Group	Placebo LD group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11	14	18	11
Units: Subjects	0	0	1	1

End point values	Placebo MD group	Placebo HD group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	17		
Units: Subjects	0	2		

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with episode of spontaneous or excessive bleeding (AE of specific interest)

End point title	Number of subjects with episode of spontaneous or excessive bleeding (AE of specific interest)[5]

End point description:

Any episode of spontaneous or excessive bleeding if occurring after vaccination was to be fully investigated with a full range of hematological tests to identify the underlying cause and reported as an AE of specific interest.

End point type	Primary

End point timeframe:

During a 30-day follow-up period after each vaccination (vaccine/placebo administered at Day 1 and Day 31)

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: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

End point values	RSV LD Group	RSV MD Group	RSV HD Group	Placebo LD group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11	14	18	11
Units: Subjects	0	0	0	0

End point values	Placebo MD group	Placebo HD group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	17		
Units: Subjects	0	0		

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with hematological laboratory results change with respect to normal laboratory ranges and versus baseline, at Day 2

End point title	Number of subjects with hematological laboratory results change with respect to normal laboratory ranges and versus baseline, at Day 2[6]

End point description:

Assessed hematological laboratory parameters include hemoglobin level [HgL] white blood cells [WBC] and platelet count [PLC]. Hematological abnormalities refer to range indicator at timing, categorized as Below, Within or Above normal ranges, and compared to baseline range indicator of the same parameter, at Screening (Day-29 to Day 1) i.e. Unknown, Below, Within or Above. [e.g. HgL, Below, Below = HgL below normal ranges at baseline versus below normal ranges at Day 2].

End point type	Primary

End point timeframe:

At Day 2

Notes:

[6] - 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: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

End point values	RSV LD Group	RSV MD Group	RSV HD Group	Placebo LD group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11	14	15	11
Units: Subjects				
HgL, Below, Below (N = 3, 2, 1, 1, 0, 0)	3	2	1	1
HgL, Within, Unknown (N = 8, 12, 15, 10, 11, 16)	0	1	0	0
HgL, Within, Below (N = 8, 12, 15, 10, 11, 16)	0	2	0	0
HgL, Within, Within (N = 8, 12, 15, 10, 11, 16)	8	9	15	10
HgL, Within, Above (N = 8, 12, 15, 10, 11, 16)	0	0	0	0
HgL, Above, Within (N = 0, 0, 1, 0, 0, 1)	0	0	0	0
HgL, Above, Above (N = 0, 0, 1, 0, 0, 1)	0	0	1	0
WBC, Below, Below (N = 0, 0, 1, 0, 0, 1)	0	0	1	0
WBC, Below, Within (N = 0, 0, 1, 0, 0, 1)	0	0	0	0
WBC, Within, Unknown (N = 11, 14, 14, 11, 7, 16)	0	1	0	0
WBC, Within, Below (N = 11, 14, 14, 11, 7, 16)	0	2	1	0
WBC, Within, Within (N = 11, 14, 14, 11, 7, 16)	11	11	13	11

WBC, Within, Above (N = 11, 14, 14, 11, 7, 16)	0	0	0	0
WBC, Above, Within (N = 0, 0, 2, 0, 4, 0)	0	0	1	0
WBC, Above, Above (N = 0, 0, 2, 0, 4, 0)	0	0	1	0
PLC, Within, Unknown (N = 10, 12, 15, 9, 6, 15)	0	1	0	0
PLC, Within, Below (N = 10, 12, 15, 9, 6, 15)	0	0	1	0
PLC, Within, Within (N = 10, 12, 15, 9, 6, 15)	10	10	12	9
PLC, Within, Above (N = 10, 12, 15, 9, 6, 15)	0	1	2	0
PLC, Above, Within (N = 1, 1, 2, 2, 5, 2)	1	1	2	1
PLC, Above, Above (N = 1, 1, 2, 2, 5, 2)	0	0	0	1

End point values	Placebo MD group	Placebo HD group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	16		
Units: Subjects				
HgL, Below, Below (N = 3, 2, 1, 1, 0, 0)	0	0		
HgL, Within, Unknown (N = 8, 12, 15, 10, 11, 16)	0	0		
HgL, Within, Below (N = 8, 12, 15, 10, 11, 16)	2	2		
HgL, Within, Within (N = 8, 12, 15, 10, 11, 16)	9	13		
HgL, Within, Above (N = 8, 12, 15, 10, 11, 16)	0	1		
HgL, Above, Within (N = 0, 0, 1, 0, 0, 1)	0	1		
HgL, Above, Above (N = 0, 0, 1, 0, 0, 1)	0	0		
WBC, Below, Below (N = 0, 0, 1, 0, 0, 1)	0	0		
WBC, Below, Within (N = 0, 0, 1, 0, 0, 1)	0	1		
WBC, Within, Unknown (N = 11, 14, 14, 11, 7, 16)	0	0		
WBC, Within, Below (N = 11, 14, 14, 11, 7, 16)	0	2		
WBC, Within, Within (N = 11, 14, 14, 11, 7, 16)	6	13		
WBC, Within, Above (N = 11, 14, 14, 11, 7, 16)	1	1		
WBC, Above, Within (N = 0, 0, 2, 0, 4, 0)	2	0		
WBC, Above, Above (N = 0, 0, 2, 0, 4, 0)	2	0		
PLC, Within, Unknown (N = 10, 12, 15, 9, 6, 15)	0	0		
PLC, Within, Below (N = 10, 12, 15, 9, 6, 15)	0	0		
PLC, Within, Within (N = 10, 12, 15, 9, 6, 15)	4	12		

PLC, Within, Above (N = 10, 12, 15, 9, 6, 15)	2	3		
PLC, Above, Within (N = 1, 1, 2, 2, 5, 2)	2	0		
PLC, Above, Above (N = 1, 1, 2, 2, 5, 2)	3	2		

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with hematological laboratory results change with respect to normal laboratory ranges and versus baseline, at Day 8

End point title	Number of subjects with hematological laboratory results change with respect to normal laboratory ranges and versus baseline, at Day 8[7]

End point description:

Assessed hematological laboratory parameters include hemoglobin level [HgL] white blood cells [WBC] and platelet count [PLC]. Hematological abnormalities refer to range indicator at timing, categorized as Below, Within or Above normal ranges, and compared to baseline range indicator of the same parameter, at Screening (Day-29 to Day 1) i.e. Below, Within or Above. [e.g. HgL, Below, Below = HgL below normal ranges at baseline versus below normal ranges at Day 8].

End point type	Primary

End point timeframe:

At Day 8

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: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

End point values	RSV LD Group	RSV MD Group	RSV HD Group	Placebo LD group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9	3	2	8
Units: Subjects				
HgL, Below, Below (N = 2, 1, 0, 1, 0,0)	2	1	0	1
HgL, Within, Within (N = 7, 2, 2, 7, 5, 2)	7	2	2	7
HgL, Above, Above (N = 0, 0, 0, 0, 0, 1)	0	0	0	0
WBC, Within, Within (N = 9, 3, 2, 8, 2, 3)	8	2	2	8
WBC, Within, Above (N = 9, 3, 2, 8, 2, 3)	1	1	0	0
WBC, Above, Within (N = 0, 0, 0, 0, 3, 0)	0	0	0	0
PLC, Within, Within (N = 8, 3, 2, 8, 3, 3)	7	3	1	8
PLC, Within, Above (N = 8, 3, 2, 8, 3, 3)	1	0	1	0
PLC, Above, Within (N = 1, 0 0, 0, 2, 0)	1	0	0	0
PLC, Above, Above (N = 1, 0 0, 0, 2, 0)	0	0	0	0

End point values	Placebo MD group	Placebo HD group		

Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	3		
Units: Subjects				
HgL, Below, Below (N = 2, 1, 0, 1, 0,0)	0	0		
HgL, Within, Within (N = 7, 2, 2, 7, 5, 2)	5	2		
HgL, Above, Above (N = 0, 0, 0, 0, 0, 1)	0	1		
WBC, Within, Within (N = 9, 3, 2, 8, 2, 3)	2	3		
WBC, Within, Above (N = 9, 3, 2, 8, 2, 3)	0	0		
WBC, Above, Within (N = 0, 0, 0, 0, 3, 0)	3	0		
PLC, Within, Within (N = 8, 3, 2, 8, 3, 3)	0	3		
PLC, Within, Above (N = 8, 3, 2, 8, 3, 3)	3	0		
PLC, Above, Within (N = 1, 0 0, 0, 2, 0)	1	0		
PLC, Above, Above (N = 1, 0 0, 0, 2, 0)	1	0		

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with hematological laboratory results change with respect to normal laboratory ranges and versus baseline, at Day 31

End point title	Number of subjects with hematological laboratory results change with respect to normal laboratory ranges and versus baseline, at Day 31[8]

End point description:

Assessed hematological laboratory parameters include hemoglobin level [HgL] white blood cells [WBC] and platelet count [PLC]. Hematological abnormalities refer to range indicator at timing, categorized as Below, Within or Above normal ranges, and compared to baseline range indicator of the same parameter, at Screening (Day-29 to Day 1) i.e. Unknown, Below, Within or Above. [e.g. HgL, Below, Below = HgL below normal ranges at baseline versus below normal ranges at Day 31].

End point type	Primary

End point timeframe:

At Day 31

Notes:

[8] - 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: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

End point values	RSV LD Group	RSV MD Group	RSV HD Group	Placebo LD group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10	12	16	10
Units: Subjects				
HgL, Below, Below (N = 3, 2, 1, 1, 0, 0)	3	1	1	1
HgL, Below, Within (N = 3, 2, 1, 1, 0, 0)	0	1	0	0
HgL, Within, Unknown (N = 7, 10, 16, 9, 9, 16)	0	1	0	0
HgL, Within, Below (N = 7, 10, 16, 9, 9, 16)	0	0	0	0

HgL, Within, Within (N = 7, 10, 16, 9, 9, 16)	7	9	15	9
HgL, Within, Above (N = 7, 10, 16, 9, 9, 16)	0	0	1	0
HgL, Above, Within (N = 0, 0, 1, 0, 0, 1)	0	0	1	0
WBC, Below, Within (N = 0, 0, 1, 0, 0, 1)	0	0	1	0
WBC, Within, Unknown (N = 10, 12, 15, 10, 5, 16)	0	1	0	0
WBC, Within, Below (N = 10, 12, 15, 10, 5, 16)	0	0	0	0
WBC, Within, Within (N = 10, 12, 15, 10, 5, 16)	10	9	13	10
WBC, Within, Above (N = 10, 12, 15, 10, 5, 16)	0	2	2	0
WBC, Above, Within (N = 0, 0, 2, 0, 4, 0)	0	0	1	0
WBC, Above, Above (N = 0, 0, 2, 0, 4, 0)	0	0	1	0
PLC, Within, Unknown (N = 10, 11, 16, 8, 5, 15)	0	1	0	0
PLC, Within, Within (N = 10, 11, 16, 8, 5, 15)	9	8	15	8
PLC, Within, Above (N = 10, 11, 16, 8, 5, 15)	1	2	1	0
PLC, Above, Within (N = 0, 1, 2, 2, 4, 2)	0	1	2	2
PLC, Above, Above (N = 0, 1, 2, 2, 4, 2)	0	0	0	0

End point values	Placebo MD group	Placebo HD group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	16		
Units: Subjects				
HgL, Below, Below (N = 3, 2, 1, 1, 0, 0)	0	0		
HgL, Below, Within (N = 3, 2, 1, 1, 0, 0)	0	0		
HgL, Within, Unknown (N = 7, 10, 16, 9, 9, 16)	0	0		
HgL, Within, Below (N = 7, 10, 16, 9, 9, 16)	1	2		
HgL, Within, Within (N = 7, 10, 16, 9, 9, 16)	8	14		
HgL, Within, Above (N = 7, 10, 16, 9, 9, 16)	0	0		
HgL, Above, Within (N = 0, 0, 1, 0, 0, 1)	0	1		
WBC, Below, Within (N = 0, 0, 1, 0, 0, 1)	0	1		
WBC, Within, Unknown (N = 10, 12, 15, 10, 5, 16)	0	0		
WBC, Within, Below (N = 10, 12, 15, 10, 5, 16)	0	1		
WBC, Within, Within (N = 10, 12, 15, 10, 5, 16)	4	15		
WBC, Within, Above (N = 10, 12, 15, 10, 5, 16)	1	0		

WBC, Above, Within (N = 0, 0, 2, 0, 4, 0)	3	0		
WBC, Above, Above (N = 0, 0, 2, 0, 4, 0)	1	0		
PLC, Within, Unknown (N = 10, 11, 16, 8, 5, 15)	0	0		
PLC, Within, Within (N = 10, 11, 16, 8, 5, 15)	4	13		
PLC, Within, Above (N = 10, 11, 16, 8, 5, 15)	1	2		
PLC, Above, Within (N = 0, 1, 2, 2, 4, 2)	2	1		
PLC, Above, Above (N = 0, 1, 2, 2, 4, 2)	2	1		

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with hematological laboratory results change with respect to normal laboratory ranges and versus baseline, at Day 32

End point title	Number of subjects with hematological laboratory results change with respect to normal laboratory ranges and versus baseline, at Day 32[9]

End point description:

Assessed hematological laboratory parameters include hemoglobin level [HgL] white blood cells [WBC] and platelet count [PLC]. Hematological abnormalities refer to range indicator at timing, categorized as Below, Within or Above normal ranges, and compared to baseline range indicator of the same parameter, at Screening (Day-29 to Day 1) i.e. Unknown, Below, Within or Above. [e.g. HgL, Below, Below = HgL below normal ranges at baseline versus below normal ranges at Day 32].

End point type	Primary

End point timeframe:

At Day 32

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: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

End point values	RSV LD Group	RSV MD Group	RSV HD Group	Placebo LD group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10	10	15	11
Units: Subjects				
HgL, Below, Below (N = 3, 2, 1, 1, 0, 0)	2	2	1	1
HgL, Below, Within (N = 3, 2, 1, 1, 0, 0)	1	0	0	0
HgL, Within, Unknown (N = 7, 8, 15, 10, 10, 16)	0	0	0	1
HgL, Within, Below (N = 7, 8, 15, 10, 10, 16)	1	1	0	0
HgL, Within, Within (N = 7, 8, 15, 10, 10, 16)	6	7	14	9
HgL, Within, Above (N = 7, 8, 15, 10, 10, 16)	0	0	1	0
HgL, Above, Within (N = 0, 0, 1, 0, 0, 1)	0	0	0	0
HgL, Above, Above (N = 0, 0, 1, 0, 0, 1)	0	0	1	0

WBC, Below, Within (N = 0, 0, 1, 0, 0, 1)	0	0	1	0
WBC, Within, Unknown (N = 10, 10, 14, 11, 7, 16)	0	0	0	1
WBC, Within, Below (N = 10, 10, 14, 11, 7, 16)	1	2	3	0
WBC, Within, Within (N = 10, 10, 14, 11, 7, 16)	9	7	11	10
WBC, Within, Above (N = 10, 10, 14, 11, 7, 16)	0	1	0	0
WBC, Above, Within (N = 0, 0, 2, 0, 3, 0)	0	0	1	0
WBC, Above, Above (N = 0, 0, 2, 0, 3, 0)	0	0	1	0
PLC, Within, Unknown (N = 10, 9, 15, 9, 5, 15)	0	0	0	1
PLC, Within, Below (N = 10, 9, 15, 9, 5, 15)	0	1	0	0
PLC, Within, Within (N = 10, 9, 15, 9, 5, 15)	10	7	15	7
PLC, Within, Above (N = 10, 9, 15, 9, 5, 15)	0	1	0	1
PLC, Above, Within (N = 0, 1, 2, 2, 5, 2)	0	1	2	2
PLC, Above, Above (N = 0, 1, 2, 2, 5, 2)	0	0	0	0

End point values	Placebo MD group	Placebo HD group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	16		
Units: Subjects				
HgL, Below, Below (N = 3, 2, 1, 1, 0, 0)	0	0		
HgL, Below, Within (N = 3, 2, 1, 1, 0, 0)	0	0		
HgL, Within, Unknown (N = 7, 8, 15, 10, 10, 16)	0	0		
HgL, Within, Below (N = 7, 8, 15, 10, 10, 16)	1	2		
HgL, Within, Within (N = 7, 8, 15, 10, 10, 16)	8	14		
HgL, Within, Above (N = 7, 8, 15, 10, 10, 16)	1	0		
HgL, Above, Within (N = 0, 0, 1, 0, 0, 1)	0	1		
HgL, Above, Above (N = 0, 0, 1, 0, 0, 1)	0	0		
WBC, Below, Within (N = 0, 0, 1, 0, 0, 1)	0	1		
WBC, Within, Unknown (N = 10, 10, 14, 11, 7, 16)	0	0		
WBC, Within, Below (N = 10, 10, 14, 11, 7, 16)	1	2		
WBC, Within, Within (N = 10, 10, 14, 11, 7, 16)	5	14		
WBC, Within, Above (N = 10, 10, 14, 11, 7, 16)	1	0		
WBC, Above, Within (N = 0, 0, 2, 0, 3, 0)	2	0		
WBC, Above, Above (N = 0, 0, 2, 0, 3, 0)	1	0		

PLC, Within, Unknown (N = 10, 9, 15, 9, 5, 15)	0	0		
PLC, Within, Below (N = 10, 9, 15, 9, 5, 15)	0	0		
PLC, Within, Within (N = 10, 9, 15, 9, 5, 15)	4	14		
PLC, Within, Above (N = 10, 9, 15, 9, 5, 15)	1	1		
PLC, Above, Within (N = 0, 1, 2, 2, 5, 2)	4	1		
PLC, Above, Above (N = 0, 1, 2, 2, 5, 2)	1	1		

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with hematological laboratory results change with respect to normal laboratory ranges and versus baseline, at Day 38

End point title	Number of subjects with hematological laboratory results change with respect to normal laboratory ranges and versus baseline, at Day 38[10]

End point description:

Assessed hematological laboratory parameters include hemoglobin level [HgL] white blood cells [WBC] and platelet count [PLC]. Hematological abnormalities refer to range indicator at timing, categorized as Below, Within or Above normal ranges, and compared to baseline range indicator of the same parameter, at Screening (Day-29 to Day 1) i.e. Below, Within or Above. [e.g. HgL, Below, Below = HgL below normal ranges at baseline versus below normal ranges at Day 38].
Note: As per Protocol, hematology testing for RSV HD group on Day 38 was not performed since no platelet decrease (i.e., less than 150000 cells/cubic millimeter) was detected on Day 32.

End point type	Primary

End point timeframe:

At Day 38

Notes:

[10] - 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: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

End point values	RSV LD Group	RSV MD Group	RSV HD Group	Placebo LD group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	1	0[11]	6
Units: Subjects				
HgL, Below, Below (N = 2, 0, 0, 1, 0, 0)	2	0		1
HgL, Within, Within (N = 6, 1, 0, 5, 2, 1)	6	1		5
HgL, Above, Above (N = 0, 0, 0, 0, 0, 1)	0	0		0
WBC, Within, Within (N = 8, 1, 0, 6, 1, 2)	8	1		4
WBC, Within, Above (N = 8, 1, 0, 6, 1, 2)	0	0		2
WBC, Above, Above (N = 0, 0, 0, 0, 1, 0)	0	0		0
PLC, Within, Within (N = 8, 1, 0, 6, 1, 2)	7	1		5
PLC, Within, Above (N = 8, 1, 0, 6, 1, 2)	1	0		1

PLC, Above, Above (N = 0, 0, 0, 0, 1, 0,)	0	0		0

Notes:

[11] - No data collected for this study group at this time point.

End point values	Placebo MD group	Placebo HD group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2	2		
Units: Subjects				
HgL, Below, Below (N = 2, 0, 0, 1, 0, 0)	0	0		
HgL, Within, Within (N = 6, 1, 0, 5, 2, 1)	2	1		
HgL, Above, Above (N = 0, 0, 0, 0, 0, 1)	0	1		
WBC, Within, Within (N = 8, 1, 0, 6, 1, 2)	1	2		
WBC, Within, Above (N = 8, 1, 0, 6, 1, 2)	0	0		
WBC, Above, Above (N = 0, 0, 0, 0, 1, 0)	1	0		
PLC, Within, Within (N = 8, 1, 0, 6, 1, 2)	0	1		
PLC, Within, Above (N = 8, 1, 0, 6, 1, 2)	1	1		
PLC, Above, Above (N = 0, 0, 0, 0, 1, 0,)	1	0		

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with hematological laboratory results change with respect to normal laboratory ranges and versus baseline, at Day 61

End point title	Number of subjects with hematological laboratory results change with respect to normal laboratory ranges and versus baseline, at Day 61[12]

End point description:

Assessed hematological laboratory parameters include hemoglobin level [HgL] white blood cells [WBC] and platelet count [PLC]. Hematological abnormalities refer to range indicator at timing, categorized as Below, Within or Above normal ranges, and compared to baseline range indicator of the same parameter, at Screening (Day-29 to Day 1) i.e. Unknown, Below, Within or Above. [e.g. HgL, Below, Below = HgL below normal ranges at baseline versus below normal ranges at Day 61].

End point type	Primary

End point timeframe:

At Day 61

Notes:

[12] - 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: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

End point values	RSV LD Group	RSV MD Group	RSV HD Group	Placebo LD group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10	12	16	9
Units: Subjects				
HgL, Below, Below (N = 3, 1, 1, 0, 0, 0)	2	1	0	0
HgL, Below, Within (N = 3, 1, 1, 0, 0, 0)	1	0	1	0
HgL, Within, Unknown (N = 7, 11, 16, 9, 11, 15)	0	0	0	1
HgL, Within, Below (N = 7, 11, 16, 9, 11, 15)	0	1	0	0
HgL, Within, Within (N = 7, 11, 16, 9, 11, 15)	7	10	16	8
HgL, Above, Within (N = 0, 0, 1, 0, 0, 1)	0	0	0	0
HgL, Above, Above (N = 0, 0, 1, 0, 0, 1)	0	0	1	0
WBC, Below, Within (N = 0, 0, 1, 0, 0, 1)	0	0	1	0
WBC, Within, Unknown (N = 10, 12, 15, 9, 7, 15)	0	0	0	1
WBC, Within, Below (N = 10, 12, 15, 9, 7, 15)	1	0	0	0
WBC, Within, Within (N = 10, 12, 15, 9, 7, 15)	9	11	14	8
WBC, Within, Above (N = 10, 12, 15, 9, 7, 15)	0	1	1	0
WBC, Above, Within (N = 0, 0, 2, 0, 4, 0)	0	0	1	0
WBC, Above, Above (N = 0, 0, 2, 0, 4, 0)	0	0	1	0
PLC, Within, Unknown (N = 10, 11, 16, 6, 6, 14)	0	0	0	1
PLC, Within, Below (N = 10, 11, 16, 6, 6, 14)	0	0	0	0
PLC, Within, Within (N = 10, 11, 16, 6, 6, 14)	9	8	15	4
PLC, Within, Above (N = 10, 11, 16, 6, 6, 14)	1	3	1	1
PLC, Above, Within (N = 0, 1, 2, 2, 5, 2)	0	1	2	2
PLC, Above, Above (N = 0, 1, 2, 2, 5, 2)	0	0	0	0

End point values	Placebo MD group	Placebo HD group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	15		
Units: Subjects				
HgL, Below, Below (N = 3, 1, 1, 0, 0, 0)	0	0		
HgL, Below, Within (N = 3, 1, 1, 0, 0, 0)	0	0		
HgL, Within, Unknown (N = 7, 11, 16, 9, 11, 15)	0	0		
HgL, Within, Below (N = 7, 11, 16, 9, 11, 15)	0	2		
HgL, Within, Within (N = 7, 11, 16, 9, 11, 15)	11	13		
HgL, Above, Within (N = 0, 0, 1, 0, 0, 1)	0	1		

HgL, Above, Above (N = 0, 0, 1, 0, 0, 1)	0	0		
WBC, Below, Within (N = 0, 0, 1, 0, 0, 1)	0	1		
WBC, Within, Unknown (N = 10, 12, 15, 9, 7, 15)	0	0		
WBC, Within, Below (N = 10, 12, 15, 9, 7, 15)	0	3		
WBC, Within, Within (N = 10, 12, 15, 9, 7, 15)	6	10		
WBC, Within, Above (N = 10, 12, 15, 9, 7, 15)	1	2		
WBC, Above, Within (N = 0, 0, 2, 0, 4, 0)	4	0		
WBC, Above, Above (N = 0, 0, 2, 0, 4, 0)	0	0		
PLC, Within, Unknown (N = 10, 11, 16, 6, 6, 14)	0	0		
PLC, Within, Below (N = 10, 11, 16, 6, 6, 14)	0	1		
PLC, Within, Within (N = 10, 11, 16, 6, 6, 14)	5	8		
PLC, Within, Above (N = 10, 11, 16, 6, 6, 14)	1	5		
PLC, Above, Within (N = 0, 1, 2, 2, 5, 2)	4	1		
PLC, Above, Above (N = 0, 1, 2, 2, 5, 2)	1	1		

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with biochemical laboratory results change with respect to normal laboratory ranges and versus baseline, at Day 31

End point title	Number of subjects with biochemical laboratory results change with respect to normal laboratory ranges and versus baseline, at Day 31[13]

End point description:

Assessed biochemical laboratory parameters include alanine aminotransferase [ALT], aspartate aminotransferase [AST] and creatinine [CREA]. Biochemical abnormalities refer to range indicator at timing, categorized as Below, Within or Above normal ranges, and compared to baseline range indicator of the same parameter, at Screening (Day-29 to Day 1) i.e. Unknown, Below, Within or Above. [e.g. ALT, Below, Below = ALT below normal ranges at baseline versus below normal ranges at Day 31].

End point type	Primary

End point timeframe:

At Day 31

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: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

End point values	RSV LD Group	RSV MD Group	RSV HD Group	Placebo LD group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9	11	16	11
Units: Subjects				
ALT, Below, Below (N = 2, 0, 0, 0, 0, 1)	1	0	0	0
ALT, Below, Within (N = 2, 0, 0, 0, 0, 1)	1	0	0	0
ALT, Below, Above (N = 2, 0, 0, 0, 0, 1)	0	0	0	0
ALT, Within, Unknown (N = 8, 11, 16, 11, 9, 13)	0	1	0	0
ALT, Within, Below (N = 8, 11, 16, 11, 9, 13)	1	0	0	0
ALT, Within, Within (N = 8, 11, 16, 11, 9, 13)	7	10	15	11
ALT, Within, Above (N = 8, 11, 16, 11, 9, 13)	0	0	1	0
ALT, Above, Within (N = 0, 1, 2, 0, 0, 3)	0	1	1	0
ALT, Above, Above (N = 0, 1, 2, 0, 0, 3)	0	0	1	0
AST, Within, Unknown (N = 9, 9, 15, 10, 8, 14)	0	1	0	0
AST, Within, Within (N = 9, 9, 15, 10, 8, 14)	9	7	13	9
AST, Within, Above (N = 9, 9, 15, 10, 8, 14)	0	1	2	1
AST, Above, Below (N = 1, 3, 3, 1, 1, 3)	0	0	0	0
AST, Above, Within (N = 1, 3, 3, 1, 1, 3)	1	1	1	1
AST, Above, Above (N = 1, 3, 3, 1, 1, 3)	0	2	2	0
CREA, Below, Unknown (N = 7, 4, 4, 8, 1, 0)	0	1	0	0
CREA, Below, Below (N = 7, 4, 4, 8, 1, 0)	4	3	1	7
CREA, Below, Within (N = 7, 4, 4, 8, 1, 0)	3	0	3	1
CREA, Within, Below (N = 3, 8, 14, 3, 7, 17)	3	1	4	0
CREA, Within, Within (N = 3, 8, 14, 3, 7, 17)	0	7	10	3
CREA, Within, Above(N = 3, 8, 14, 3, 7, 17)	0	0	0	0
CREA, Above, Within (N = 0, 0, 0, 0, 1, 0)	0	0	0	0

End point values	Placebo MD group	Placebo HD group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	17		
Units: Subjects				
ALT, Below, Below (N = 2, 0, 0, 0, 0, 1)	0	0		
ALT, Below, Within (N = 2, 0, 0, 0, 0, 1)	0	0		
ALT, Below, Above (N = 2, 0, 0, 0, 0, 1)	0	1		
ALT, Within, Unknown (N = 8, 11, 16, 11, 9, 13)	0	0		
ALT, Within, Below (N = 8, 11, 16, 11, 9, 13)	0	0		

ALT, Within, Within (N = 8, 11, 16, 11, 9, 13)	7	13		
ALT, Within, Above (N = 8, 11, 16, 11, 9, 13)	2	0		
ALT, Above, Within (N = 0, 1, 2, 0, 0, 3)	0	2		
ALT, Above, Above (N = 0, 1, 2, 0, 0, 3)	0	1		
AST, Within, Unknown (N = 9, 9, 15, 10, 8, 14)	0	0		
AST, Within, Within (N = 9, 9, 15, 10, 8, 14)	7	14		
AST, Within, Above (N = 9, 9, 15, 10, 8, 14)	1	0		
AST, Above, Below (N = 1, 3, 3, 1, 1, 3)	0	1		
AST, Above, Within (N = 1, 3, 3, 1, 1, 3)	0	0		
AST, Above, Above (N = 1, 3, 3, 1, 1, 3)	1	2		
CREA, Below, Unknown (N = 7, 4, 4, 8, 1, 0)	0	0		
CREA, Below, Below (N = 7, 4, 4, 8, 1, 0)	1	0		
CREA, Below, Within (N = 7, 4, 4, 8, 1, 0)	0	0		
CREA, Within, Below (N = 3, 8, 14, 3, 7, 17)	0	4		
CREA, Within, Within (N = 3, 8, 14, 3, 7, 17)	7	12		
CREA, Within, Above(N = 3, 8, 14, 3, 7, 17)	0	1		
CREA, Above, Within (N = 0, 0, 0, 0, 1, 0)	1	0		

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with biochemical laboratory results change with respect to normal laboratory ranges and versus baseline, at Day 61

End point title	Number of subjects with biochemical laboratory results change with respect to normal laboratory ranges and versus baseline, at Day 61[14]

End point description:

Assessed biochemical laboratory parameters include alanine aminotransferase [ALT], aspartate aminotransferase [AST] and creatinine [CREA]. Biochemical abnormalities refer to range indicator at timing, categorized as Below, Within or Above normal ranges, and compared to baseline range indicator of the same parameter, at Screening (Day-29 to Day 1) i.e. Below, Within or Above. [e.g. ALT, Below, Below = ALT below normal ranges at baseline versus below normal ranges at Day 61].

End point type	Primary

End point timeframe:

At Day 61

Notes:

[14] - 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: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

End point values	RSV LD Group	RSV MD Group	RSV HD Group	Placebo LD group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9	11	16	11
Units: Subjects				
ALT, Below, Below (N = 2, 0, 0, 0, 0, 1)	1	0	0	0
ALT, Below, Within (N = 2, 0, 0, 0, 0, 1)	1	0	0	0
ALT, Within, Within (N = 8, 11, 16, 11, 10, 12)	8	10	15	10
ALT, Within, Above (N = 8, 11, 16, 11, 10, 12)	0	1	1	1
ALT, Above, Within (N = 0, 1, 2, 0, 1, 2)	0	1	2	0
ALT, Above, Above (N = 0, 1, 2, 0, 1, 2)	0	0	0	0
AST, Within, Within (N = 9, 10, 15, 10, 9, 13)	9	9	15	10
AST, Within, Above (N = 9, 10, 15, 10, 9, 13)	0	1	0	0
AST, Above, Within (N = 1, 2, 3, 1, 2, 3)	1	1	1	0
AST, Above, Above (N = 1, 2, 3, 1, 2, 3)	0	1	2	1
CREA, Below, Below (N = 7, 3, 4, 8, 2, 0)	4	2	2	7
CREA, Below, Within (N = 7, 3, 4, 8, 2, 0)	3	1	2	1
CREA, Within, Below (N = 3, 9, 14, 3, 8, 16)	3	1	3	0
CREA, Within, Within (N = 3, 9, 14, 3, 8, 16)	0	8	10	3
CREA, Within, Above (N = 3, 9, 14, 3, 8, 16)	0	0	1	0
CREA, Above, Within (N = 0, 0, 0, 0, 1, 0)	0	0	0	0

End point values	Placebo MD group	Placebo HD group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	16		
Units: Subjects				
ALT, Below, Below (N = 2, 0, 0, 0, 0, 1)	0	0		
ALT, Below, Within (N = 2, 0, 0, 0, 0, 1)	0	1		
ALT, Within, Within (N = 8, 11, 16, 11, 10, 12)	9	12		
ALT, Within, Above (N = 8, 11, 16, 11, 10, 12)	1	0		
ALT, Above, Within (N = 0, 1, 2, 0, 1, 2)	1	1		
ALT, Above, Above (N = 0, 1, 2, 0, 1, 2)	0	1		
AST, Within, Within (N = 9, 10, 15, 10, 9, 13)	8	13		
AST, Within, Above (N = 9, 10, 15, 10, 9, 13)	1	0		
AST, Above, Within (N = 1, 2, 3, 1, 2, 3)	0	1		
AST, Above, Above (N = 1, 2, 3, 1, 2, 3)	2	2		
CREA, Below, Below (N = 7, 3, 4, 8, 2, 0)	1	0		

CREA, Below, Within (N = 7, 3, 4, 8, 2, 0)	1	0		
CREA, Within, Below (N = 3, 9, 14, 3, 8, 16)	0	1		
CREA, Within, Within (N = 3, 9, 14, 3, 8, 16)	8	15		
CREA, Within, Above (N = 3, 9, 14, 3, 8, 16)	0	0		
CREA, Above, Within (N = 0, 0, 0, 0, 1, 0)	1	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any SAEs from Day 1 up to Day 366

End point title	Number of subjects with any SAEs from Day 1 up to Day 366

End point description:

Assessed SAEs include any untoward medical occurrences that resulted in death, were life-threatening, required hospitalization or prolongation of hospitalization or resulted in disability/incapacity. Any = occurrence of SAE regardless of intensity grade or relation to study vaccination.

End point type	Secondary

End point timeframe:

From Day 1 up to Day 366

End point values	RSV LD Group	RSV MD Group	RSV HD Group	Placebo LD group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11	14	18	11
Units: Subjects	1	1	1	3

End point values	Placebo MD group	Placebo HD group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	17		
Units: Subjects	1	2		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with lower respiratory tract infection associated with RSV infection (RSV-LRTI) (AE of specific interest) from Dose 1 administration (Day 1) up to Day 366

End point title	Number of subjects with lower respiratory tract infection associated with RSV infection (RSV-LRTI) (AE of specific interest) from Dose 1 administration (Day 1) up to Day 366

End point description:

Subjects experiencing an LRTI associated with RSV infection were reported as AE of specific interest. To identify RSV-LRTI for the purpose of AE of specific interest, the diagnosis was based on the investigators' clinical judgment taking into account the clinical history, the examination, relevant medical investigations and locally-available diagnostic test for RSV.

End point type	Secondary

End point timeframe:

From Dose 1 administration (Day 1) up to Day 366

End point values	RSV LD Group	RSV MD Group	RSV HD Group	Placebo LD group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11	14	18	11
Units: Subjects	0	1	0	3

End point values	Placebo MD group	Placebo HD group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	17		
Units: Subjects	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with respiratory tract infection associated with RSV infection (RSV-RTI), RSV-LRTI, severe RSV-LRTI (according to standardized case definitions) from Dose 1 administration (Day 1) up to Day 366

End point title	Number of subjects with respiratory tract infection associated with RSV infection (RSV-RTI), RSV-LRTI, severe RSV-LRTI (according to standardized case definitions) from Dose 1 administration (Day 1) up to Day 366

End point description:

RSV-RTI refers to subject having runny nose OR blocked nose OR cough AND confirmed RSV infection [RSV infection confirmed on nasal swab positive for RSV A or B by quantitative Reverse Transcription Polymerase Chain Reaction (qRT-PCR) performed at sponsor level]. RSV-LRTI refers to subject with history of cough OR difficulty breathing [based on history reported by parents/legally acceptable representatives (LARs) and includes difficulty breathing (e.g. showing signs of wheezing or stridor, tachypnoea, flaring of nostrils, chest in-drawing, apnoea) associated with nasal obstruction] AND Blood Oxygen Saturation (SpO2) lower than (<) 95 percent (%), OR respiratory rate (RR) increase [defined as ≥ 40/minute (12 months of age or above)] AND confirmed RSV infection. RSV-severe LRTI are cases meeting the case definition of RSV-LRTI AND SpO2 < 93%, OR lower chest wall in-drawing.

End point type	Secondary

End point timeframe:

From Dose 1 administration (Day 1) up to Day 366

End point values	RSV LD Group	RSV MD Group	RSV HD Group	Placebo LD group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11	14	18	11
Units: Subjects				
RSV-RTI	1	3	1	4
RSV-LRTI	0	0	0	1
RSV-severe LRTI	0	0	0	1

End point values	Placebo MD group	Placebo HD group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	17		
Units: Subjects				
RSV-RTI	3	3		
RSV-LRTI	0	0		
RSV-severe LRTI	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any SAEs from Day 1 up to study conclusion at Day 731

End point title	Number of subjects with any SAEs from Day 1 up to study conclusion at Day 731

End point description:

Assessed SAEs include any untoward medical occurrences that resulted in death, were life-threatening, required hospitalization or prolongation of hospitalization or resulted in disability/incapacity. Any = occurrence of SAE regardless of intensity grade or relation to study vaccination.

End point type	Secondary

End point timeframe:

From Day 1 up to study conclusion at Day 731

End point values	RSV LD Group	RSV MD Group	RSV HD Group	Placebo LD group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11	14	18	11
Units: Subjects	1	1	2	3

End point values	Placebo MD group	Placebo HD group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	17		
Units: Subjects	1	2		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with RSV-LRTI (AE of specific interest) from Dose 1 administration (Day 1) up to study conclusion at Day 731

End point title	Number of subjects with RSV-LRTI (AE of specific interest) from Dose 1 administration (Day 1) up to study conclusion at Day 731

End point description:

Subjects experiencing an LRTI associated with RSV infection were reported as AE of specific interest. To identify RSV-LRTI for the purpose of AE of specific interest, the diagnosis was based on the investigators' clinical judgment taking into account the clinical history, the examination, relevant medical investigations and locally-available diagnostic test for RSV.

End point type	Secondary

End point timeframe:

From Dose 1 administration (Day 1) up to study conclusion at Day 731

End point values	RSV LD Group	RSV MD Group	RSV HD Group	Placebo LD group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11	14	18	11
Units: Subjects	0	1	0	3

End point values	Placebo MD group	Placebo HD group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	17		
Units: Subjects	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with RSV-RTI, RSV-LRTI, severe RSV-LRTI (according to standardized case definitions) from Dose 1 administration (Day 1) up to study conclusion at Day 731

End point title	Number of subjects with RSV-RTI, RSV-LRTI, severe RSV-LRTI (according to standardized case definitions) from Dose 1 administration (Day 1) up to study conclusion at Day 731

End point description:

RSV-RTI refers to subject having runny nose OR blocked nose OR cough AND confirmed RSV infection (RSV infection confirmed on nasal swab positive for RSV A or B by qRT-PCR performed at sponsor level). RSV-LRTI refers to subject with history of cough OR difficulty breathing [based on history reported by parents/LARs and includes difficulty breathing (e.g. showing signs of wheezing or stridor, tachypnoea, flaring of nostrils, chest in-drawing, apnoea) associated with nasal obstruction] AND Sp02 < 95% OR respiratory rate (RR) increase [defined as ≥ 40/minute (12 months of age or above)] AND confirmed RSV infection. RSV-severe LRTI are cases meeting the case definition of RSV-LRTI AND SpO2 < 93%, OR lower chest wall in-drawing.

End point type	Secondary

End point timeframe:

From Dose 1 administration (Day 1) up to study conclusion at Day 731

End point values	RSV LD Group	RSV MD Group	RSV HD Group	Placebo LD group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11	14	18	11
Units: Subjects				
RSV-RTI	2	6	2	5
RSV-LRTI	0	0	0	1
RSV-severe LRTI	0	0	0	1

End point values	Placebo MD group	Placebo HD group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	17		
Units: Subjects				
RSV-RTI	4	4		
RSV-LRTI	0	0		
RSV-severe LRTI	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Frequency of RSV-specific CD4+ T-cells expressing at least two markers upon stimulation with F, N and M2-1 peptide pools

End point title	Frequency of RSV-specific CD4+ T-cells expressing at least two markers upon stimulation with F, N and M2-1 peptide pools

End point description:

Magnitude of cell mediated immunity (CMI) response to the investigational RSV vaccine was measured in terms of frequency of RSV-specific CD4+ T-cells expressing at least two markers upon stimulation

with F, N and M2-1 peptide pools and expressed in RSV-specific CD4+ T-cells/million cells. Assessed markers were CD40-L, IL-2, TNF-α and IFN-.

End point type	Secondary

End point timeframe:

At Pre-vaccination (Screening), Day 31, Day 61 and Day 366

End point values	RSV LD Group	RSV MD Group	RSV HD Group	Placebo LD group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9	3	1	10
Units: RSV-specific CD4+ T-cells/million cells				
median (inter-quartile range (Q1-Q3))				
RSV F pool 15/11 Ag, Screening (N=8,3,1,9,1,0)	169.5 (85 to 218)	123 (32 to 268)	1 (1 to 1)	176 (120 to 336)
RSV F pool 15/11 Ag, Day 31 (N=9,2,1,7,2,0)	291 (231 to 469)	546 (484 to 608)	1086 (1086 to 1086)	234 (48 to 350)
RSV F pool 15/11 Ag, Day 61 (N =8,3,1,10,2,0)	214 (74.5 to 331.5)	451 (93 to 495)	394 (394 to 394)	105.5 (1 to 193)
RSV F pool 15/11 Ag, Day 366 (N=4,2,1,4,2,1)	206 (71 to 288.5)	108.5 (1 to 216)	1164 (1164 to 1164)	252.5 (169.5 to 495)
RSV N pool 15/11 Ag, Screening (N=8,3,1,8,1,0)	51 (1 to 121)	54 (1 to 369)	140 (140 to 140)	104 (27 to 174)
RSV N pool 15/11 Ag, Day 31 (N=8,2,1,9,2,0)	129.5 (23.5 to 226.5)	229 (1 to 457)	289 (289 to 289)	58 (1 to 102)
RSV N pool 15/11 Ag, Day 61 (N=7,3,1,10,2, 0)	70 (1 to 165)	144 (34 to 426)	1 (1 to 1)	71 (50 to 117)
RSV N pool 15/11 Ag, Day 366 (N=6,2,1,6,2,1)	56 (1 to 269)	41.5 (1 to 82)	82 (82 to 82)	89 (42 to 113)
RSV M2-1 pool 15/11 Ag, Screening (N=5,3,1,5,1,0)	1 (1 to 9)	1 (1 to 10)	56 (56 to 56)	1 (1 to 1)
RSV M2-1 pool 15/11 Ag, Day 31 (N=5,2,1,8,2,0)	1 (1 to 34)	21.5 (1 to 42)	229 (229 to 229)	1 (1 to 13)
RSV M2-1 pool 15/11 Ag, Day 61 (N=6,3,1,9,2,0)	8 (1 to 57)	2 (1 to 55)	46 (46 to 46)	30 (1 to 33)
RSV M2-1 pool 15/11 Ag, Day 366 (N=6,2,1,5,2,1)	7 (1 to 81)	2.5 (1 to 4)	13 (13 to 13)	23 (6 to 27)

End point values	Placebo MD group	Placebo HD group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2	1		
Units: RSV-specific CD4+ T-cells/million cells				
median (inter-quartile range (Q1-Q3))				
RSV F pool 15/11 Ag, Screening (N=8,3,1,9,1,0)	1813 (1813 to 1813)	0 (0 to 0)		
RSV F pool 15/11 Ag, Day 31 (N=9,2,1,7,2,0)	1129.5 (379 to 1880)	0 (0 to 0)		
RSV F pool 15/11 Ag, Day 61 (N =8,3,1,10,2,0)	759 (218 to 1300)	0 (0 to 0)		
RSV F pool 15/11 Ag, Day 366 (N=4,2,1,4,2,1)	664.5 (252 to 1077)	229 (229 to 229)		

RSV N pool 15/11 Ag, Screening (N=8,3,1,8,1,0)	253 (253 to 253)	0 (0 to 0)		
RSV N pool 15/11 Ag, Day 31 (N=8,2,1,9,2,0)	193 (180 to 206)	0 (0 to 0)		
RSV N pool 15/11 Ag, Day 61 (N=7,3,1,10,2, 0)	64.5 (52 to 77)	0 (0 to 0)		
RSV N pool 15/11 Ag, Day 366 (N=6,2,1,6,2,1)	78 (27 to 129)	91 (91 to 91)		
RSV M2-1 pool 15/11 Ag, Screening (N=5,3,1,5,1,0)	214 (214 to 214)	0 (0 to 0)		
RSV M2-1 pool 15/11 Ag, Day 31 (N=5,2,1,8,2,0)	145.5 (100 to 191)	0 (0 to 0)		
RSV M2-1 pool 15/11 Ag, Day 61 (N=6,3,1,9,2,0)	1 (1 to 1)	0 (0 to 0)		
RSV M2-1 pool 15/11 Ag, Day 366 (N=6,2,1,5,2,1)	48 (1 to 95)	56 (56 to 56)		

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-RSV-A neutralizing antibody titers

End point title	Anti-RSV-A neutralizing antibody titers

End point description:

Humoral response to the investigational RSV vaccine was measured in terms of anti-RSV-A neutralizing antibody titers and expressed as geometric mean titers (GMTs) in Estimated Dilution 60 (ED60) titers.

End point type	Secondary

End point timeframe:

At Pre-vaccination (Screening), Day 31, Day 61 and Day 366

End point values	RSV LD Group	RSV MD Group	RSV HD Group	Placebo LD group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10	13	18	11
Units: Titers				
geometric mean (confidence interval 95%)				
Screening (N = 10, 13, 17, 10, 11, 16)	127.4 (44 to 368.5)	179.4 (99.2 to 324.5)	495.7 (242.5 to 1013.1)	376.5 (89.3 to 1587.5)
Day 31 (N = 10, 12, 18, 10, 9, 17)	711.7 (229.7 to 2204.9)	1646 (815.8 to 3321)	2203.9 (1383.7 to 3510.3)	645.9 (266.3 to 1566.5)
Day 61 (N = 10, 12, 17, 11, 11, 15)	1081.3 (648.3 to 1803.3)	1809 (1022.6 to 3200.2)	1974.9 (1356.9 to 2874.3)	421.5 (178.9 to 993.1)
Day 366 (N = 9, 11, 16, 11, 11, 16)	236.9 (105.7 to 531)	837 (546.6 to 1281.6)	1038 (629.3 to 1712.3)	398.5 (163.5 to 971.7)

End point values	Placebo MD	Placebo HD		

	group	group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	17		
Units: Titers				
geometric mean (confidence interval 95%)				
Screening (N = 10, 13, 17, 10, 11, 16)	214.6 (80.8 to 569.9)	332 (158.5 to 695.4)		
Day 31 (N = 10, 12, 18, 10, 9, 17)	703.9 (244.3 to 2028.4)	295 (149.6 to 581.8)		
Day 61 (N = 10, 12, 17, 11, 11, 15)	316.4 (169 to 592.3)	307.1 (148.5 to 634.9)		
Day 366 (N = 9, 11, 16, 11, 11, 16)	545.4 (269.4 to 1104.3)	493.8 (216 to 1129.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-RSV-F antibody concentrations

End point title	Anti-RSV-F antibody concentrations

End point description:

Humoral response to the investigational RSV vaccine was measured as anti-RSV F antibody concentrations and expressed as geometric mean concentrations (GMCs) in enzyme-linked immunosorbent assay (ELISA) units per milliliter (EU/mL).

End point type	Secondary

End point timeframe:

At Pre-vaccination (Screening), Day 31, Day 61 and Day 366

End point values	RSV LD Group	RSV MD Group	RSV HD Group	Placebo LD group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10	13	17	11
Units: EU/mL				
geometric mean (confidence interval 95%)				
Screening (N = 9, 13, 17, 10, 9, 16)	2082 (864.3 to 5015.5)	2061.6 (1343.6 to 3163.4)	3686.4 (1964.5 to 6917.5)	3933.2 (1789.1 to 8646.7)
Day 31 (N = 10, 11, 17, 9, 9, 17)	4807.2 (1738.5 to 13292.8)	10810.9 (4062.2 to 28771.1)	17419 (11639.6 to 26068.2)	6134.2 (2752 to 13673)
Day 61 (N = 9, 12, 15, 11, 11, 15)	6167.5 (3701.3 to 10277.1)	15577.4 (8012.9 to 30283.2)	15083.8 (10555 to 21555.7)	2983.3 (1612.8 to 5518.3)
Day 366 (N = 9, 11, 17, 11, 11, 16)	3988.5 (1789.4 to 8890.1)	6521.1 (3702.5 to 11485.4)	6490.7 (4509.7 to 9341.8)	3591.3 (1472.8 to 8756.9)

End point values	Placebo MD group	Placebo HD group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	17		
Units: EU/mL				
geometric mean (confidence interval 95%)				
Screening (N = 9, 13, 17, 10, 9, 16)	1216.3 (472.9 to 3128.7)	2988.6 (1420.9 to 6286)		
Day 31 (N = 10, 11, 17, 9, 9, 17)	7911.6 (3187.7 to 19636)	2350.6 (1235.9 to 4470.7)		
Day 61 (N = 9, 12, 15, 11, 11, 15)	3182 (1737.1 to 5828.8)	2101.3 (1038.3 to 4252.6)		
Day 366 (N = 9, 11, 17, 11, 11, 16)	3047.5 (1577.7 to 5886.6)	4487.9 (1936.8 to 10398.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Palivizumab-competing antibody concentrations

End point title	Palivizumab-competing antibody concentrations

End point description:

Humoral response to the investigational RSV vaccine was measured as Palivizumab-competing antibody concentrations and expressed as geometric mean concentrations (GMCs) in microgram/milliliter (µg/mL).

End point type	Secondary

End point timeframe:

At Pre-vaccination (Screening), Day 31 and Day 61

End point values	RSV LD Group	RSV MD Group	RSV HD Group	Placebo LD group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10	13	17	11
Units: µg/mL				
geometric mean (confidence interval 95%)				
Screening (N = 9, 13, 17, 10, 9, 16)	5.2 (4.3 to 6.3)	4.8 (4.8 to 4.8)	6.6 (5 to 8.6)	6.2 (4.2 to 9.2)
Day 31 (N = 10, 11, 17, 9, 9, 17)	7.9 (5.3 to 11.7)	11.1 (6.2 to 19.8)	17.5 (13 to 23.6)	8 (4.4 to 14.5)
Day 61 (N = 9, 12, 15, 11, 11, 15)	6.3 (4.6 to 8.6)	15.2 (9.2 to 25.1)	14 (10.1 to 19.4)	6.1 (4.3 to 8.6)

End point values	Placebo MD group	Placebo HD group		

Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	17		
Units: µg/mL				
geometric mean (confidence interval 95%)				
Screening (N = 9, 13, 17, 10, 9, 16)	4.8 (4.8 to 4.8)	7.2 (4.8 to 10.9)		
Day 31 (N = 10, 11, 17, 9, 9, 17)	12.5 (6.2 to 25.5)	6.8 (4.8 to 9.6)		
Day 61 (N = 9, 12, 15, 11, 11, 15)	7 (4.5 to 10.8)	6.6 (4.8 to 9)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Solicited adverse events were collected during the 7-day follow-up period and unsolicited adverse events during the 30-day follow-up period after any vaccination. Serious adverse events were collected from Day 1 up to Day 731.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23.1

Reporting groups

Reporting group title	RSV LD Group

Reporting group description:

RSV-seropositive infants, aged 12 to 23 months at the time of first vaccination, received 2 doses (0.5 mL each) of the RSV low dose (LD) vaccine, administered intramuscularly, one each at Day 1 and Day 31.

Reporting group title	RSV MD Group

Reporting group description:

RSV-seropositive infants, aged 12 to 23 months at the time of first vaccination, received 2 doses (0.15 mL each) of the RSV middle dose (MD) vaccine, administered intramuscularly, one each at Day 1 and Day 31.

Reporting group title	Placebo MD group

Reporting group description:

RSV-seropositive infants, aged 12 to 23 months at the time of first vaccination, received 2 doses (0.15 mL each) of placebo, administered intramuscularly, one each at Day 1 and Day 31.

Reporting group title	Placebo LD group

Reporting group description:

RSV-seropositive infants, aged 12 to 23 months at the time of first vaccination, received 2 doses (0.5 mL each) of placebo, administered intramuscularly, one each at Day 1 and Day 31.

Reporting group title	Placebo HD group

Reporting group description:

RSV-seropositive infants, aged 12 to 23 months at the time of first vaccination, received 2 doses (0.5 mL each) of placebo, administered intramuscularly, one each at Day 1 and Day 31.

Reporting group title	RSV HD Group

Reporting group description:

RSV-seropositive infants, aged 12 to 23 months at the time of first vaccination, received 2 doses (0.5 mL each) of the RSV high dose (HD) vaccine, administered intramuscularly, one each at Day 1 and Day 31.

Serious adverse events	RSV LD Group	RSV MD Group	Placebo MD group
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 11 (9.09%)	1 / 14 (7.14%)	1 / 11 (9.09%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Nervous system disorders			
Unresponsive to stimuli			

subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	1 / 11 (9.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile convulsion			
subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	1 / 11 (9.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Respiratory syncytial virus infection			
subjects affected / exposed	0 / 11 (0.00%)	1 / 14 (7.14%)	0 / 11 (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
Coronavirus infection			
subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	1 / 11 (9.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enterovirus infection			
subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	1 / 11 (9.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Escherichia urinary tract infection			
subjects affected / exposed	1 / 11 (9.09%)	0 / 14 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory syncytial virus bronchiolitis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rhinovirus infection			
subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	1 / 11 (9.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tonsillitis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpangina			
subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Placebo LD group	Placebo HD group	RSV HD Group
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 11 (27.27%)	2 / 17 (11.76%)	2 / 18 (11.11%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Nervous system disorders			
Unresponsive to stimuli			

subjects affected / exposed	0 / 11 (0.00%)	0 / 17 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile convulsion			
subjects affected / exposed	0 / 11 (0.00%)	0 / 17 (0.00%)	1 / 18 (5.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 17 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Respiratory syncytial virus infection			
subjects affected / exposed	2 / 11 (18.18%)	0 / 17 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronavirus infection			
subjects affected / exposed	1 / 11 (9.09%)	0 / 17 (0.00%)	0 / 18 (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
Gastroenteritis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 17 (0.00%)	2 / 18 (11.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis			
subjects affected / exposed	1 / 11 (9.09%)	0 / 17 (0.00%)	0 / 18 (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
Enterovirus infection			
subjects affected / exposed	0 / 11 (0.00%)	0 / 17 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Escherichia urinary tract infection			
subjects affected / exposed	0 / 11 (0.00%)	0 / 17 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory syncytial virus bronchiolitis			
subjects affected / exposed	1 / 11 (9.09%)	0 / 17 (0.00%)	0 / 18 (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
Rhinovirus infection			
subjects affected / exposed	0 / 11 (0.00%)	0 / 17 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tonsillitis			
subjects affected / exposed	1 / 11 (9.09%)	0 / 17 (0.00%)	0 / 18 (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
Herpangina			
subjects affected / exposed	0 / 11 (0.00%)	1 / 17 (5.88%)	0 / 18 (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	0 / 11 (0.00%)	1 / 17 (5.88%)	0 / 18 (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

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

Non-serious adverse events	RSV LD Group	RSV MD Group	Placebo MD group
Total subjects affected by non-serious adverse events			
subjects affected / exposed	10 / 11 (90.91%)	11 / 14 (78.57%)	10 / 11 (90.91%)
Injury, poisoning and procedural complications			
Face injury			

subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Head injury			
subjects affected / exposed	1 / 11 (9.09%)	0 / 14 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Procedural pain			
subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Arthropod bite			
subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	5 / 11 (45.45%)	5 / 14 (35.71%)	4 / 11 (36.36%)
occurrences (all)	7	5	6
Injection site erythema			
subjects affected / exposed	2 / 11 (18.18%)	2 / 14 (14.29%)	0 / 11 (0.00%)
occurrences (all)	4	2	0
Injection site pain			
subjects affected / exposed	3 / 11 (27.27%)	3 / 14 (21.43%)	0 / 11 (0.00%)
occurrences (all)	3	4	0
Injection site swelling			
subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			
Tympanic membrane perforation			
subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0

Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	2 / 11 (18.18%)	2 / 14 (14.29%)	2 / 11 (18.18%)
occurrences (all)	2	3	3
Teething			
subjects affected / exposed	1 / 11 (9.09%)	0 / 14 (0.00%)	1 / 11 (9.09%)
occurrences (all)	1	0	1
Vomiting			
subjects affected / exposed	1 / 11 (9.09%)	0 / 14 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Constipation			
subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal inflammation			
subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Stomatitis			
subjects affected / exposed	0 / 11 (0.00%)	1 / 14 (7.14%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	2 / 11 (18.18%)
occurrences (all)	0	0	2
Rhinorrhoea			
subjects affected / exposed	0 / 11 (0.00%)	1 / 14 (7.14%)	1 / 11 (9.09%)
occurrences (all)	0	1	1
Catarrh			
subjects affected / exposed	0 / 11 (0.00%)	1 / 14 (7.14%)	1 / 11 (9.09%)
occurrences (all)	0	1	1
Rhinitis allergic			
subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Nasal congestion			
subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			

Rash			
subjects affected / exposed	1 / 11 (9.09%)	0 / 14 (0.00%)	1 / 11 (9.09%)
occurrences (all)	2	0	1
Eczema			
subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Dermatitis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Dermatitis diaper			
subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Miliaria			
subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Rash macular			
subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Erythema			
subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Irritability			
subjects affected / exposed	1 / 11 (9.09%)	1 / 14 (7.14%)	0 / 11 (0.00%)
occurrences (all)	1	1	0
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	2 / 11 (18.18%)	6 / 14 (42.86%)	4 / 11 (36.36%)
occurrences (all)	2	10	5
Gastroenteritis			
subjects affected / exposed	0 / 11 (0.00%)	1 / 14 (7.14%)	3 / 11 (27.27%)
occurrences (all)	0	1	3
Conjunctivitis			
subjects affected / exposed	3 / 11 (27.27%)	0 / 14 (0.00%)	0 / 11 (0.00%)
occurrences (all)	3	0	0
Upper respiratory tract infection			

subjects affected / exposed	1 / 11 (9.09%)	1 / 14 (7.14%)	1 / 11 (9.09%)
occurrences (all)	1	2	1
Pharyngotonsillitis			
subjects affected / exposed	1 / 11 (9.09%)	0 / 14 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Influenza			
subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Tonsillitis streptococcal			
subjects affected / exposed	1 / 11 (9.09%)	0 / 14 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Otitis media			
subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Varicella			
subjects affected / exposed	0 / 11 (0.00%)	1 / 14 (7.14%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Impetigo			
subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Bronchiolitis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Croup infectious			
subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Gastroenteritis viral			
subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Hand-foot-and-mouth disease			
subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Paronychia			
subjects affected / exposed	1 / 11 (9.09%)	0 / 14 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Pharyngitis			

subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Tonsillitis			
subjects affected / exposed	1 / 11 (9.09%)	0 / 14 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Acarodermatitis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Bronchitis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Pharyngitis streptococcal			
subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 11 (9.09%)	0 / 14 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0

Non-serious adverse events	Placebo LD group	Placebo HD group	RSV HD Group
Total subjects affected by non-serious adverse events			
subjects affected / exposed	11 / 11 (100.00%)	14 / 17 (82.35%)	17 / 18 (94.44%)
Injury, poisoning and procedural complications			
Face injury			
subjects affected / exposed	1 / 11 (9.09%)	0 / 17 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Head injury			
subjects affected / exposed	0 / 11 (0.00%)	0 / 17 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Procedural pain			
subjects affected / exposed	1 / 11 (9.09%)	0 / 17 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Arthropod bite			
subjects affected / exposed	0 / 11 (0.00%)	1 / 17 (5.88%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
General disorders and administration site conditions			

Pyrexia			
subjects affected / exposed	5 / 11 (45.45%)	2 / 17 (11.76%)	11 / 18 (61.11%)
occurrences (all)	5	2	15
Injection site erythema			
subjects affected / exposed	3 / 11 (27.27%)	4 / 17 (23.53%)	4 / 18 (22.22%)
occurrences (all)	6	5	5
Injection site pain			
subjects affected / exposed	2 / 11 (18.18%)	4 / 17 (23.53%)	2 / 18 (11.11%)
occurrences (all)	3	5	2
Injection site swelling			
subjects affected / exposed	1 / 11 (9.09%)	3 / 17 (17.65%)	1 / 18 (5.56%)
occurrences (all)	2	4	1
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 11 (0.00%)	1 / 17 (5.88%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Ear and labyrinth disorders			
Tympanic membrane perforation			
subjects affected / exposed	0 / 11 (0.00%)	0 / 17 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	1 / 11 (9.09%)	0 / 17 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	2 / 11 (18.18%)	3 / 17 (17.65%)	0 / 18 (0.00%)
occurrences (all)	3	3	0
Teething			
subjects affected / exposed	1 / 11 (9.09%)	1 / 17 (5.88%)	0 / 18 (0.00%)
occurrences (all)	1	1	0
Vomiting			
subjects affected / exposed	1 / 11 (9.09%)	0 / 17 (0.00%)	2 / 18 (11.11%)
occurrences (all)	1	0	2
Constipation			
subjects affected / exposed	1 / 11 (9.09%)	0 / 17 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0

Gastrointestinal inflammation			
subjects affected / exposed	0 / 11 (0.00%)	0 / 17 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Stomatitis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 17 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 11 (0.00%)	1 / 17 (5.88%)	2 / 18 (11.11%)
occurrences (all)	0	1	2
Rhinorrhoea			
subjects affected / exposed	0 / 11 (0.00%)	1 / 17 (5.88%)	1 / 18 (5.56%)
occurrences (all)	0	1	2
Catarrh			
subjects affected / exposed	0 / 11 (0.00%)	0 / 17 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Rhinitis allergic			
subjects affected / exposed	0 / 11 (0.00%)	1 / 17 (5.88%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Nasal congestion			
subjects affected / exposed	0 / 11 (0.00%)	0 / 17 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	1 / 11 (9.09%)	1 / 17 (5.88%)	0 / 18 (0.00%)
occurrences (all)	1	1	0
Eczema			
subjects affected / exposed	1 / 11 (9.09%)	1 / 17 (5.88%)	0 / 18 (0.00%)
occurrences (all)	1	1	0
Dermatitis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 17 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Dermatitis diaper			
subjects affected / exposed	0 / 11 (0.00%)	0 / 17 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Miliaria			

subjects affected / exposed	1 / 11 (9.09%)	0 / 17 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Rash macular			
subjects affected / exposed	0 / 11 (0.00%)	1 / 17 (5.88%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Erythema			
subjects affected / exposed	0 / 11 (0.00%)	0 / 17 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Psychiatric disorders			
Irritability			
subjects affected / exposed	0 / 11 (0.00%)	1 / 17 (5.88%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	0 / 11 (0.00%)	5 / 17 (29.41%)	7 / 18 (38.89%)
occurrences (all)	0	7	8
Gastroenteritis			
subjects affected / exposed	0 / 11 (0.00%)	1 / 17 (5.88%)	3 / 18 (16.67%)
occurrences (all)	0	1	3
Conjunctivitis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 17 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection			
subjects affected / exposed	0 / 11 (0.00%)	0 / 17 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Pharyngotonsillitis			
subjects affected / exposed	0 / 11 (0.00%)	1 / 17 (5.88%)	1 / 18 (5.56%)
occurrences (all)	0	1	1
Influenza			
subjects affected / exposed	0 / 11 (0.00%)	0 / 17 (0.00%)	2 / 18 (11.11%)
occurrences (all)	0	0	2
Tonsillitis streptococcal			
subjects affected / exposed	1 / 11 (9.09%)	0 / 17 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Otitis media			

subjects affected / exposed	1 / 11 (9.09%)	0 / 17 (0.00%)	1 / 18 (5.56%)
occurrences (all)	1	0	1
Varicella			
subjects affected / exposed	0 / 11 (0.00%)	1 / 17 (5.88%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Impetigo			
subjects affected / exposed	0 / 11 (0.00%)	0 / 17 (0.00%)	2 / 18 (11.11%)
occurrences (all)	0	0	2
Bronchiolitis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 17 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Croup infectious			
subjects affected / exposed	0 / 11 (0.00%)	0 / 17 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis viral			
subjects affected / exposed	0 / 11 (0.00%)	0 / 17 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Hand-foot-and-mouth disease			
subjects affected / exposed	0 / 11 (0.00%)	0 / 17 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Paronychia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 17 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Pharyngitis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 17 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Tonsillitis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 17 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Acarodermatitis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 17 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Bronchitis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 17 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	2
Pharyngitis streptococcal			

subjects affected / exposed	0 / 11 (0.00%)	0 / 17 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 11 (0.00%)	3 / 17 (17.65%)	2 / 18 (11.11%)
occurrences (all)	0	3	2

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
16 January 2017	• The Spanish competent authorities requested the Sponsor to extend the long term medical follow-up for one additional year. The purpose of this amendment was to respond to this request by increasing the follow-up of the subjects from one year to two years. This included the collection of adverse events of specific interest [RSV-LRTI] and serious adverse events, the surveillance for respiratory tract infection, difficulty of breathing and wheezing. • The Italian competent authorities requested that, in addition to the 60 minutes observation planned per protocol between each infant receiving ChAd155-RSV vaccination, the Sponsor monitors potential hypersensitivity reactions for a longer period following both vaccine administrations in a sufficient number of infants before another one could be vaccinated with the same dose. The Sponsor agreed to put in place a 48-hour observation period after the first and second doses administered to the first eight infants enrolled in each step, before continuing vaccination of more infants with a minimum interval of 60 minutes. • Following the request from investigators, the screening period has been increased from 15 days (Day -14 to Day 0) to 30 days (Day -29 to Day 0) in order to improve recruitment of subjects. • Following the request from investigators, the following exclusion criteria have been clarified: History of wheezing; History of chronic cough. • The satisfactory outcome of the review by an Independent Data Monitoring Committee (IDMC) of safety data from study 201974 (RSV PED-001) in healthy adults has been added to the rationale for the choice of study population. • The holding rule for hospitalization due to any local or general solicited AE has been restricted to any local or general solicited AE that could not reasonably be attributed to a cause other than vaccination in order to exclude irrelevant cases. • In addition, possibility to assess RSV infection using WHO case definition, has been added to this protocol.
08 June 2017	• During initial implementation of this study, parents have given feedback that the number of visits and blood tests were challenging to accommodate with busy family schedules and were demanding for young children. This amendment reduced the burden on families whilst maintaining the intended close oversight of the potential risk of thrombocytopenia, by reducing the number and frequency of required blood tests and visits unless clinically required. • It has been clarified that blood samples for CMI and for humoral immunogenicity may be postponed until after the RSV serostatus was known and eligibility was confirmed up to or on Day 0 (but before vaccination). • The age range for enrolment has been expanded an additional 6 months, from 12 to 17 months initially, to 12 to 23 months. • The following inclusion criterion has been removed, to be able to include those infants who despite being mildly underweight or premature have had normal subsequent courses: "Born full-term (i.e. after a gestation period of 37 to less than 42 completed weeks) with a minimum birth weight of 2.5 kg". Other criteria pertaining to current weight, health status of the child, and Synagis administration excluded infants who have experienced prematurity and its associated complications. • Because enrolment in the trial was slower than anticipated, the safety monitoring oversight plan of the IDMC was adapted to provide regular review of accumulating safety data every four weeks in addition to the currently planned review at end of each dose level. • To allow the extension of the recruitment network, some investigational sites without a laboratory in proximity capable to perform the whole blood stimulation (WBS) necessary for the CMI assay was allowed to participate. Therefore, blood sampling for the assessment of CMI was only performed for subjects recruited in sites with a WBS capable laboratory in proximity.

12 September 2017	• The Spanish competent authorities (Agencia Española de Medicamentos y Productos Sanitarios [AEMPS]) requested the Sponsor to add the inclusion criterion of being born full-term, which was removed for Protocol Amendment 2. This inclusion criterion was required for Spain. • The collection of birth weight and gestation at birth in weeks at the screening visit has been added to the list of study procedures. This procedure was applicable to all participating countries and permitted the identification of pre-term infants recruited in the study.
10 December 2017	• An Independent Data Monitoring Committee (IDMC) reviewed all accumulating unblinded safety and reactogenicity data on a monthly basis for this study to ensure that there was a timely identification of any safety signal. As safety data accumulated, it may have been that there was sufficient evidence of safety of the current dose level to allow progression to the next dose level. For instance, taking the a priori safety concern of thrombocytopenia, this amendment applied both Frequentist and Bayesian approaches to the existing data, to show the likelihood of observing more extreme values. The number of subjects evaluated by the IDMC for the two-step dose escalation to steps 2 and 3 after administration of two doses of study vaccine could continue to be 32 subjects at steps 1 and 2 as before. However, in the absence of a significant safety concern detected in the regular monitoring of all parameters of accumulating safety data, the IDMC agreed to recommend that dose escalation could potentially proceed on at least 16 subjects, without requiring the enrolment and evaluation of the full group size of 32 subjects.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported