Clinical trial results:
A Phase 2, Open-label, Uncontrolled, Single-dose Study to Evaluate the Safety and Tolerability, Pharmacokinetics, and Occurrence of Antidrug Antibody for Nirsevimab in Immunocompromised Children <=24 Months of Age

Summary

EudraCT number	2021-003221-30
Trial protocol	ES BE PL
Global end of trial date	17 February 2023

Results information

Result version number	v1
This version publication date	11 August 2023
First version publication date	11 August 2023

Trial information

Trial identification

Sponsor protocol code	D5290C00008

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04484935
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	AstraZeneca
Sponsor organisation address	Karlebyhusentren, B674 Astraallen, Södertälje, Sweden, 151 85
Public contact	Global Clinical Lead, AstraZeneca, +1 877-240-9479, information.center@astrazeneca.com
Scientific contact	Global Clinical Lead, AstraZeneca, +1 877-240-9479, information.center@astrazeneca.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	17 February 2023
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	17 February 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the safety and tolerability of nirsevimab when administered to immunocompromised children <=24 months of age.

Protection of trial subjects:

This study was performed in accordance with the ethical principles that have their origin in the Declaration of Helsinki and that are consistent with International Council for Harmonisation/Good Clinical Practice, applicable regulatory requirements, and the AstraZeneca policy on Bioethics.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	19 August 2020
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	Belgium: 6
Country: Number of subjects enrolled	Japan: 26
Country: Number of subjects enrolled	Poland: 3
Country: Number of subjects enrolled	South Africa: 14
Country: Number of subjects enrolled	Spain: 10
Country: Number of subjects enrolled	Ukraine: 21
Country: Number of subjects enrolled	United Kingdom: 1
Country: Number of subjects enrolled	United States: 19
Worldwide total number of subjects	100
EEA total number of subjects	19

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)	94

Children (2-11 years)	6
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:

This Phase 2, open-label, uncontrolled, single-dose study was conducted at 28 investigational sites in immunocompromised children who were <=24 months of age at the time of dose administration.

Pre-assignment

Screening details:

This study consisted of a screening period (Visit 1, Day -30 to Day -1); a dosing visit (Visit 2, Day 1) where participants received treatment with nirsevimab and a follow-up period up to Day 361 (Visit 3 to 7). A total of 100 children were enrolled in this study.

Period 1

Period 1 title	Overall study (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Nirsevimab

Arm description:

Participants in their first year of life with a body weight <5 kilogram (kg) received a single fixed intramuscular (IM) dose of 50 milligram (mg) nirsevimab and those with body weight >=5 kg received a single fixed IM dose of 100 mg nirsevimab. Participants in their second year of life received a single fixed IM dose of 200 mg (2 × 100 mg) of nirsevimab.

Arm type	Experimental
Investigational medicinal product name	Nirsevimab
Investigational medicinal product code	
Other name	MEDI8897
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Nirsevimab was administered as an intramuscular injection in the anterolateral aspect of the thigh. Participants receiving the 200 mg dose (administered as 2 injections) received 1 injection in each thigh. The maximum volume administered with each injection was 1.0 milliliter (mL).

Number of subjects in period 1	Nirsevimab
Started	100
Completed	94
Not completed	6
Death	3
Withdrawal	1
Unspecified	1
Lost to follow-up	1

Baseline characteristics

Reporting groups	
Reporting group title	Nirsevimab
Reporting group description:	
Participants in their first year of life with a body weight <5 kilogram (kg) received a single fixed intramuscular (IM) dose of 50 milligram (mg) nirsevimab and those with body weight >=5 kg received a single fixed IM dose of 100 mg nirsevimab. Participants in their second year of life received a single fixed IM dose of 200 mg (2 × 100 mg) of nirsevimab.	

Reporting group values	Nirsevimab	Total	
Number of subjects	100	100	
Age Categorical Units: Subjects			
Age Continuous Units: months			
arithmetic mean	12.97		
standard deviation	± 6.232	-	
Gender Categorical Units: Subjects			
Female	35	35	
Male	65	65	
Race Units: Subjects			
Asian	28	28	
American Indian or Alaskan Native	1	1	
Black or African American	20	20	
Native Hawaiian or Other Pacific Islander	0	0	
White	45	45	
Other	4	4	
Multiple categories checked	2	2	
Ethnicity Units: Subjects			
Not Hispanic or Latino	93	93	
Hispanic or Latino	7	7	

End points

End points reporting groups

Reporting group title	Nirsevimab

Reporting group description:

Participants in their first year of life with a body weight <5 kilogram (kg) received a single fixed intramuscular (IM) dose of 50 milligram (mg) nirsevimab and those with body weight >=5 kg received a single fixed IM dose of 100 mg nirsevimab. Participants in their second year of life received a single fixed IM dose of 200 mg (2 × 100 mg) of nirsevimab.

Subject analysis set title	Nirsevimab 50 mg/100 mg
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants in their first year of life with a body weight <5 kg received a single fixed IM dose of 50 mg nirsevimab and those with body weight >=5 kg received a single fixed IM dose of 100 mg nirsevimab.

Subject analysis set title	Nirsevimab 200 mg
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants in their second year of life received a single fixed IM dose of 200 mg (2 × 100 mg) of nirsevimab.

Primary: Number of Participants With Treatment-Emergent Adverse Events (TEAEs), Treatment-emergent serious AEs (TESAEs), AEs of Special Interest (AESIs), and New Onset Chronic Disease (NOCDs)

End point title	Number of Participants With Treatment-Emergent Adverse Events (TEAEs), Treatment-emergent serious AEs (TESAEs), AEs of Special Interest (AESIs), and New Onset Chronic Disease (NOCDs)[1]

End point description:

An AE was any untoward medical occurrence in a clinical study participant, temporally associated with the use of study treatment,whether or not considered related to the treatment. TEAEs were AEs whose onset occurred after receiving nirsevimab and within 360 days post dose. A TESAE was any AE that resulted in death, was life-threatening, required inpatient hospitalization, resulted in persistent or significant disability/incapacity, was a congenital abnormality, or was medically significant. AESIs were defined as AEs of immediate (type I) hypersensitivity (including anaphylaxis), thrombocytopenia, and immune complex disease following the administration of nirsevimab based on investigator assessment and Medical Dictionary for Regulatory Activities (MedDRA) preferred term (PT) codes. An NOCD was a newly diagnosed medical condition of a chronic, ongoing nature post administration of treatment. As treated population: All participants who were enrolled and received any dose of nirsevimab.

End point type	Primary

End point timeframe:

TEAEs were collected from the first dose administration (Day 1) up to 360 days post dose

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis was pre-specified for this endpoint.

End point values	Nirsevimab			
Subject group type	Reporting group			
Number of subjects analysed	100			
Units: participants				
number (not applicable)				
Any TEAE	81			
TESAE	32			
AESI based on investigator assessment	5			
AESI based on selected MedDRA PT codes	29			

NOCD	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Serum Concentrations of Nirsevimab

End point title	Serum Concentrations of Nirsevimab

End point description:

Serum concentrations of nirsevimab at selected time points were evaluated to confirm that adequate exposures for protection from respiratory syncitial virus (RSV) lower respiratory tract infection (LRTI) are maintained for at least 5 months after dosing. As treated population: All participants who were enrolled and received any dose of nirsevimab. 99999 = data was below the lower limit of quantification (0.5 microgram [mcg]/mL).

End point type	Secondary

End point timeframe:

Baseline (Day 1) and on Days 8 (for Japanese participants), 31, 151 and 361

End point values	Nirsevimab 50 mg/100 mg	Nirsevimab 200 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	48	52		
Units: mcg/mL				
geometric mean (geometric coefficient of variation)				
Baseline (Day 1), n = 48, 52	99999 (± 99999)	99999 (± 99999)		
Day 8, n = 15, 11	139.24 (± 22.26)	206.79 (± 16.58)		
Day 31, n = 47, 50	66.00 (± 141.06)	109.77 (± 91.74)		
Day 151, n = 39, 44	19.80 (± 101.19)	24.14 (± 121.54)		
Day 361, n = 29, 38	1.86 (± 119.96)	1.93 (± 158.95)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Anti-Drug Antibody (ADA) Response to Nirsevimab

End point title	Number of Participants With Anti-Drug Antibody (ADA) Response to Nirsevimab

End point description:

Blood samples were analyzed for the presence of ADAs for nirsevimab using validated assays. ADA

prevalence was defined as ADA positive at baseline and/or post baseline. ADA incidence was defined as the percentage of treatment-emergent ADA positive participants in a population. Treatment induced ADA positive was defined as ADA negative at baseline and post-baseline ADA positive. Treatment-boosted ADA positive was defined as baseline positive ADA titre that was boosted to a 4-fold or higher level following study dose administration. Treatment-emergent ADA positive was defined as either treatment-induced ADA positive or treatment-boosted ADA positive. Here n=only those participants with data available were analyzed. As treated population: All participants who were enrolled and received any dose of nirsevimab.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and on Days 31, 151 and 361

End point values	Nirsevimab			
Subject group type	Reporting group			
Number of subjects analysed	100			
Units: participants				
number (not applicable)				
ADA prevalence, n=100	11			
ADA incidence, n=97	11			
Both Baseline and post-baseline ADA positive, n=95	0			
Treatment-induced ADA positive, n=97	11			
Only Baseline ADA positive, n=98	0			
Treatment-boosted ADA positive, n=95	0			
ADA persistently positive, n=95	9			
ADA transiently positive, n=95	2			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Medically Attended (MA) RSV LRTI (Inpatient and Outpatient) and Hospitalizations

End point title	Number of Participants With Medically Attended (MA) RSV LRTI (Inpatient and Outpatient) and Hospitalizations

End point description:

Number of participants with LRTI and hospitalizations due to reverse transcriptase-polymerase chain reaction (RT-PCR)-confirmed RSV was assessed. MA RSV LRTI consisted of participants with protocol-defined LRTI, positive central RT-PCR RSV test result, Investigator assessed LRTI at an inpatient or outpatient setting. MA RSV LRTI with hospitalization consisted of participants with protocol-defined LRTI, positive central RT-PCR RSV test result, Investigator assessed LRTI at an inpatient setting.

End point type	Secondary

End point timeframe:

Through 150 days post dose

End point values	Nirsevimab			
Subject group type	Reporting group			
Number of subjects analysed	100			
Units: participants				
number (not applicable)				
MA RSV LRTI	0			
MA RSV LRTI with hospitalization	0			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Includes TEAEs with an onset on or after dosing of nirsevimab and within 361 days post dose.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	25.0

Reporting groups	
Reporting group title	Nirsevimab 200mg
Reporting group description: -	
Reporting group title	Nirsevimab 50mg/100mg
Reporting group description: -	

Serious adverse events	Nirsevimab 200mg	Nirsevimab 50mg/100mg	
Total subjects affected by serious adverse events			
subjects affected / exposed	20 / 52 (38.46%)	12 / 48 (25.00%)	
number of deaths (all causes)	1	2	
number of deaths resulting from adverse events	1	2	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumour haemorrhage			
subjects affected / exposed	0 / 52 (0.00%)	1 / 48 (2.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 52 (1.92%)	2 / 48 (4.17%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Complication associated with device			
subjects affected / exposed	1 / 52 (1.92%)	0 / 48 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Graft versus host disease			

subjects affected / exposed	1 / 52 (1.92%)	0 / 48 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemophagocytic lymphohistiocytosis			
subjects affected / exposed	0 / 52 (0.00%)	1 / 48 (2.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transplant rejection			
subjects affected / exposed	1 / 52 (1.92%)	0 / 48 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Respiratory distress			
subjects affected / exposed	0 / 52 (0.00%)	1 / 48 (2.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Adenoidal hypertrophy			
subjects affected / exposed	1 / 52 (1.92%)	0 / 48 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tonsillar hypertrophy			
subjects affected / exposed	1 / 52 (1.92%)	0 / 48 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Gastrostomy failure			
subjects affected / exposed	1 / 52 (1.92%)	0 / 48 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Iatrogenic injury			

subjects affected / exposed	1 / 52 (1.92%)	0 / 48 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Congenital, familial and genetic disorders			
Sickle cell disease			
subjects affected / exposed	1 / 52 (1.92%)	0 / 48 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Epilepsy			
subjects affected / exposed	0 / 52 (0.00%)	1 / 48 (2.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intracranial pressure increased			
subjects affected / exposed	1 / 52 (1.92%)	0 / 48 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Seizure			
subjects affected / exposed	1 / 52 (1.92%)	0 / 48 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Thrombocytopenia			
subjects affected / exposed	2 / 52 (3.85%)	0 / 48 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemolytic anaemia			
subjects affected / exposed	0 / 52 (0.00%)	1 / 48 (2.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anaemia			
subjects affected / exposed	1 / 52 (1.92%)	0 / 48 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Febrile neutropenia			
subjects affected / exposed	2 / 52 (3.85%)	0 / 48 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Volvulus			
subjects affected / exposed	1 / 52 (1.92%)	0 / 48 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal obstruction			
subjects affected / exposed	0 / 52 (0.00%)	1 / 48 (2.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Hepatic cytolysis			
subjects affected / exposed	1 / 52 (1.92%)	0 / 48 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Nephrotic syndrome			
subjects affected / exposed	2 / 52 (3.85%)	0 / 48 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
Adrenal insufficiency			
subjects affected / exposed	0 / 52 (0.00%)	1 / 48 (2.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Bacterial infection			
subjects affected / exposed	0 / 52 (0.00%)	1 / 48 (2.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			

subjects affected / exposed	0 / 52 (0.00%)	1 / 48 (2.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacteraemia			
subjects affected / exposed	2 / 52 (3.85%)	0 / 48 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID-19			
subjects affected / exposed	3 / 52 (5.77%)	1 / 48 (2.08%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis Escherichia coli			
subjects affected / exposed	1 / 52 (1.92%)	0 / 48 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	1 / 52 (1.92%)	1 / 48 (2.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Escherichia pyelonephritis			
subjects affected / exposed	1 / 52 (1.92%)	0 / 48 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enterobacter sepsis			
subjects affected / exposed	0 / 52 (0.00%)	1 / 48 (2.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device related sepsis			
subjects affected / exposed	1 / 52 (1.92%)	0 / 48 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Candida sepsis			

subjects affected / exposed	0 / 52 (0.00%)	2 / 48 (4.17%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal viral infection			
subjects affected / exposed	0 / 52 (0.00%)	1 / 48 (2.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia viral			
subjects affected / exposed	1 / 52 (1.92%)	0 / 48 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	4 / 52 (7.69%)	1 / 48 (2.08%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oral herpes			
subjects affected / exposed	1 / 52 (1.92%)	0 / 48 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower respiratory tract infection viral			
subjects affected / exposed	1 / 52 (1.92%)	0 / 48 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower respiratory tract infection			
subjects affected / exposed	3 / 52 (5.77%)	1 / 48 (2.08%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Klebsiella sepsis			
subjects affected / exposed	2 / 52 (3.85%)	0 / 48 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Klebsiella bacteraemia			

subjects affected / exposed	1 / 52 (1.92%)	0 / 48 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Giardiasis			
subjects affected / exposed	1 / 52 (1.92%)	0 / 48 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postoperative wound infection			
subjects affected / exposed	1 / 52 (1.92%)	0 / 48 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory syncytial virus infection			
subjects affected / exposed	0 / 52 (0.00%)	1 / 48 (2.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral upper respiratory tract infection			
subjects affected / exposed	1 / 52 (1.92%)	0 / 48 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral diarrhoea			
subjects affected / exposed	0 / 52 (0.00%)	2 / 48 (4.17%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection bacterial			
subjects affected / exposed	0 / 52 (0.00%)	1 / 48 (2.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urethritis			
subjects affected / exposed	1 / 52 (1.92%)	0 / 48 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper respiratory tract infection			

subjects affected / exposed	0 / 52 (0.00%)	1 / 48 (2.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Staphylococcal bacteraemia			
subjects affected / exposed	1 / 52 (1.92%)	0 / 48 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rhinovirus infection			
subjects affected / exposed	0 / 52 (0.00%)	2 / 48 (4.17%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	0 / 52 (0.00%)	1 / 48 (2.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Septic shock			
subjects affected / exposed	0 / 52 (0.00%)	1 / 48 (2.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Serratia sepsis			
subjects affected / exposed	1 / 52 (1.92%)	0 / 48 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Malnutrition			
subjects affected / exposed	1 / 52 (1.92%)	0 / 48 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyponatraemia			
subjects affected / exposed	0 / 52 (0.00%)	1 / 48 (2.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Feeding intolerance			

subjects affected / exposed	1 / 52 (1.92%)	0 / 48 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dehydration			
subjects affected / exposed	0 / 52 (0.00%)	1 / 48 (2.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Nirsevimab 200mg	Nirsevimab 50mg/100mg	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	45 / 52 (86.54%)	36 / 48 (75.00%)	
Blood and lymphatic system disorders			
Febrile neutropenia			
subjects affected / exposed	2 / 52 (3.85%)	3 / 48 (6.25%)	
occurrences (all)	4	4	
Anaemia			
subjects affected / exposed	3 / 52 (5.77%)	3 / 48 (6.25%)	
occurrences (all)	3	3	
Neutropenia			
subjects affected / exposed	3 / 52 (5.77%)	1 / 48 (2.08%)	
occurrences (all)	3	1	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	13 / 52 (25.00%)	13 / 48 (27.08%)	
occurrences (all)	27	25	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	10 / 52 (19.23%)	8 / 48 (16.67%)	
occurrences (all)	15	11	
Vomiting			
subjects affected / exposed	13 / 52 (25.00%)	8 / 48 (16.67%)	
occurrences (all)	16	13	
Constipation			

subjects affected / exposed	2 / 52 (3.85%)	4 / 48 (8.33%)	
occurrences (all)	3	5	
Abdominal pain			
subjects affected / exposed	3 / 52 (5.77%)	1 / 48 (2.08%)	
occurrences (all)	3	1	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	4 / 52 (7.69%)	6 / 48 (12.50%)	
occurrences (all)	5	6	
Rhinorrhoea			
subjects affected / exposed	7 / 52 (13.46%)	6 / 48 (12.50%)	
occurrences (all)	9	11	
Nasal congestion			
subjects affected / exposed	3 / 52 (5.77%)	1 / 48 (2.08%)	
occurrences (all)	3	1	
Skin and subcutaneous tissue disorders			
Dermatitis diaper			
subjects affected / exposed	8 / 52 (15.38%)	5 / 48 (10.42%)	
occurrences (all)	8	6	
Dry skin			
subjects affected / exposed	1 / 52 (1.92%)	4 / 48 (8.33%)	
occurrences (all)	1	4	
Eczema infantile			
subjects affected / exposed	0 / 52 (0.00%)	4 / 48 (8.33%)	
occurrences (all)	0	4	
Rash			
subjects affected / exposed	1 / 52 (1.92%)	4 / 48 (8.33%)	
occurrences (all)	1	6	
Urticaria			
subjects affected / exposed	0 / 52 (0.00%)	3 / 48 (6.25%)	
occurrences (all)	0	3	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	6 / 52 (11.54%)	6 / 48 (12.50%)	
occurrences (all)	9	13	
Lower respiratory tract infection			

subjects affected / exposed	3 / 52 (5.77%)	3 / 48 (6.25%)	
occurrences (all)	3	3	
Hand-foot-and-mouth disease			
subjects affected / exposed	3 / 52 (5.77%)	2 / 48 (4.17%)	
occurrences (all)	3	2	
Gastrointestinal viral infection			
subjects affected / exposed	4 / 52 (7.69%)	0 / 48 (0.00%)	
occurrences (all)	9	0	
Gastroenteritis viral			
subjects affected / exposed	4 / 52 (7.69%)	3 / 48 (6.25%)	
occurrences (all)	4	5	
COVID-19			
subjects affected / exposed	12 / 52 (23.08%)	4 / 48 (8.33%)	
occurrences (all)	12	4	
Conjunctivitis			
subjects affected / exposed	2 / 52 (3.85%)	4 / 48 (8.33%)	
occurrences (all)	3	5	
Ear infection			
subjects affected / exposed	3 / 52 (5.77%)	0 / 48 (0.00%)	
occurrences (all)	5	0	
Gastroenteritis			
subjects affected / exposed	6 / 52 (11.54%)	1 / 48 (2.08%)	
occurrences (all)	7	2	
Otitis media			
subjects affected / exposed	6 / 52 (11.54%)	5 / 48 (10.42%)	
occurrences (all)	7	7	
Viral upper respiratory tract infection			
subjects affected / exposed	3 / 52 (5.77%)	4 / 48 (8.33%)	
occurrences (all)	3	7	
Upper respiratory tract infection			
subjects affected / exposed	18 / 52 (34.62%)	18 / 48 (37.50%)	
occurrences (all)	33	49	
Rhinitis			
subjects affected / exposed	5 / 52 (9.62%)	2 / 48 (4.17%)	
occurrences (all)	5	2	
Otitis media acute			

subjects affected / exposed occurrences (all)	4 / 52 (7.69%) 5	2 / 48 (4.17%) 9	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
24 April 2020	New section and appendix required per protocol template for studies that include laboratory assessments.
17 December 2020	Clarified inclusion criteria and target population. Added 'clinical laboratory tests' and 'ethical conduct' sections and added Ethics and Regulatory Review at the end of section 7.3. Removed 'placebo' from 'Dose Preparation Steps and Treatment Administration' section as it is not applicable to the study, updated arm description. Removed ‘as needed’ from the visit number description for LRTI and Skin Reactions. Clarified LRTI, added sample storage and destruction details. Clarified that analyses were to be performed using an updated version of the RSV neutralizing antibodies assay previously described. Updates made to clarify Palivizumab use during the study.
23 June 2021	Pharmacokinetic endpoints revised to include only concentration of nirsevimab. Duration of use for prescription and over-the-counter medications deleted from the description of exploratory objective related to healthcare resource utilization. Additional countries added to study description. Revision of sample size. Addition of interim analysis. Text added that data were to be summarized for the overall study population, as well as for Japan only. Clinical chemistry and hematology removed from visit schedule. Study Visit 3 replaced with telephone call, consecutive visits renumbered appropriately. Estimated volume of blood to be collected was revised. IDMC added, description of hypersensitivity and thrombocytopenia revised to be more specific. Description of Japan-specific regulations removed.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported