# 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 | v2 (current) |
| This version publication date | 10 November 2023 |
| First version publication date | 11 August 2023 |
| Version creation reason | |

## 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 enrollment.

### 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

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | Nirsevimab 50 mg/100 mg |

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.

| | |
|---|---|
| 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 IM injection in the anterolateral aspect of the thigh. Participants with body weight (BW) <5 kg received 50 mg and with BW >=5 kg received 100 mg. The maximum volume administered with each injection was 1.0 milliliter (mL).

| | |
|---|---|
| **Arm title** | Nirsevimab 200 mg |

Arm description:

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 IM injection in the anterolateral aspect of the thigh. Participants in their second year received 200 mg dose injection (administered as 2 injections) in each thigh. The maximum volume administered with each injection was 1.0 mL.

| **Number of subjects in period 1** | Nirsevimab 50 mg/100 mg | Nirsevimab 200 mg |
|---|---|---|
| Started | 48 | 52 |
| Completed | 45 | 49 |
| Not completed | 3 | 3 |
| Death | 2 | 1 |
| Unspecified | - | 1 |
| Lost to follow-up | 1 | - |
| Withdrawal by parent/guardian | - | 1 |

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | Nirsevimab 50 mg/100 mg |
| 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. | |
| Reporting group title | Nirsevimab 200 mg |
| Reporting group description: | |
| 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 50 mg/100 mg | Nirsevimab 200 mg | Total |
|---|---|---|---|
| Number of subjects | 48 | 52 | 100 |
| Age Categorical<br>Units: Subjects | | | |
| Age Continuous<br>Units: months | | | |
| arithmetic mean | 7.64 | 17.90 | |
| standard deviation | ± 3.270 | ± 3.748 | - |
| Gender Categorical<br>Units: Subjects | | | |
| Female | 18 | 17 | 35 |
| Male | 30 | 35 | 65 |
| Race<br>Units: Subjects | | | |
| Asian | 16 | 12 | 28 |
| American Indian or Alaskan Native | 1 | 0 | 1 |
| Black or African American | 9 | 11 | 20 |
| Native Hawaiian or Other Pacific Islander | 0 | 0 | 0 |
| White | 20 | 25 | 45 |
| Other | 2 | 2 | 4 |
| Multiple categories checked | 0 | 2 | 2 |
| Ethnicity<br>Units: Subjects | | | |
| Not Hispanic or Latino | 44 | 49 | 93 |
| Hispanic or Latino | 4 | 3 | 7 |

## End points

### End points reporting groups

| Reporting group title | Nirsevimab 50 mg/100 mg |
|---|---|

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.

| Reporting group title | Nirsevimab 200 mg |
|---|---|

Reporting group 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 50 mg/100 mg | Nirsevimab 200 mg | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 48 | 52 | | |
| Units: participants | | | | |
| number (not applicable) | | | | |
| Any TEAE | 36 | 45 | | |
| TESAE | 12 | 20 | | |
| AESI based on investigator assessment | 3 | 2 | | |
| AESI based on selected MedDRA PT codes | 16 | 13 | | |
| NOCD | 0 | 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). n=Only those participants with data available are included in the analysis.

| 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 | Reporting group | Reporting group | | |
| 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) | 206.76 (± 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. 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 50 mg/100 mg | Nirsevimab 200 mg | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 48 | 52 | | |
| Units: participants | | | | |
| number (not applicable) | | | | |
| Day 1 | 0 | 0 | | |
| Day 31 | 0 | 1 | | |
| Day 151 | 1 | 0 | | |
| Day 361 | 2 | 7 | | |

### 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. The As-treated population: All participants who were enrolled and received any dose of nirsevimab.

| End point type | Secondary |
|---|---|

End point timeframe:

Through 150 days post dose

| End point values | Nirsevimab 50 mg/100 mg | Nirsevimab 200 mg | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 48 | 52 | | |
| Units: participants | | | | |
| number (not applicable) | | | | |
| MA RSV LRTI | 0 | 0 | | |
| MA RSV LRTI with hospitalization | 0 | 0 | | |

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

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

Adverse event reporting additional description:

As treated population consisted of all participants who were enrolled and received any dose of nirsevimab.

| | |
|---|---|
| Assessment type | Systematic |

### Dictionary used

| | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 25.0 |

### Reporting groups

| | |
|---|---|
| Reporting group title | Nirsevimab 200 mg |

Reporting group description:

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

| | |
|---|---|
| Reporting group title | Nirsevimab 50 mg /100 mg |

Reporting group 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.

| Serious adverse events | Nirsevimab 200 mg | Nirsevimab 50 mg /100 mg | |
|---|---|---|---|
| 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 | | | |
| 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 | |
| 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 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| 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 | |
| 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 | |
| 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 | | | |
| 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 | |
| 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 | |

| | | | |
|---|---|---|---|
| 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 | |
| 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 | |
| Gastrointestinal disorders | | | |
| 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 | |
| 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 | |
| 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 | | | |
| 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 | |
| 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 | |
| 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 | |
| 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 | |
| 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 | |
| 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 | |
| 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 | |
| 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 | |
| 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 | |
| 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 | |
| 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 | |
| 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 | |
| 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 | |
| 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 | |
| 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 | |
| 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 | |
| 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 | |
| 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 | |
| Metabolism and nutrition disorders | | | |
| 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 | |
| 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 | |
| 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 | |
| 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 | |

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

| **Non-serious adverse events** | Nirsevimab 200 mg | Nirsevimab 50 mg /100 mg | |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 45 / 52 (86.54%) | 36 / 48 (75.00%) | |
| Blood and lymphatic system disorders | | | |
| Neutropenia | | | |
| subjects affected / exposed | 3 / 52 (5.77%) | 1 / 48 (2.08%) | |
| occurrences (all) | 3 | 1 | |
| 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 | |
| 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 | |

| | | | |
|---|---|---|---|
| Abdominal pain | | | |
| subjects affected / exposed | 3 / 52 (5.77%) | 1 / 48 (2.08%) | |
| occurrences (all) | 3 | 1 | |
| 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 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| 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 | |
| Cough | | | |
| subjects affected / exposed | 4 / 52 (7.69%) | 6 / 48 (12.50%) | |
| occurrences (all) | 5 | 6 | |
| 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 | | | |

| | | | |
|---|---|---|---|
| COVID-19 | | | |
| subjects affected / exposed | 12 / 52 (23.08%) | 4 / 48 (8.33%) | |
| occurrences (all) | 12 | 4 | |
| Ear infection | | | |
| subjects affected / exposed | 3 / 52 (5.77%) | 0 / 48 (0.00%) | |
| occurrences (all) | 5 | 0 | |
| Conjunctivitis | | | |
| subjects affected / exposed | 2 / 52 (3.85%) | 4 / 48 (8.33%) | |
| occurrences (all) | 3 | 5 | |
| Rhinitis | | | |
| subjects affected / exposed | 5 / 52 (9.62%) | 2 / 48 (4.17%) | |
| occurrences (all) | 5 | 2 | |
| Otitis media acute | | | |
| subjects affected / exposed | 4 / 52 (7.69%) | 2 / 48 (4.17%) | |
| occurrences (all) | 5 | 9 | |
| Otitis media | | | |
| subjects affected / exposed | 6 / 52 (11.54%) | 5 / 48 (10.42%) | |
| occurrences (all) | 7 | 7 | |
| 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 | |
| Gastroenteritis | | | |
| subjects affected / exposed | 6 / 52 (11.54%) | 1 / 48 (2.08%) | |
| occurrences (all) | 7 | 2 | |

| | | | |
|---|---|---|---|
| Upper respiratory tract infection<br>subjects affected / exposed<br>occurrences (all) | 18 / 52 (34.62%)<br>33 | 18 / 48 (37.50%)<br>49 | |
| Viral upper respiratory tract infection<br>subjects affected / exposed<br>occurrences (all) | 3 / 52 (5.77%)<br>3 | 4 / 48 (8.33%)<br>7 | |

## 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