Clinical trial results:
A Phase 2b Randomized, Double-blind, Placebo-controlled Study to Evaluate the Safety and Efficacy of MEDI8897, a Monoclonal Antibody with an Extended Half-life Against Respiratory Syncytial Virus, in Healthy Preterm Infants

Summary

EudraCT number	2016-001677-33
Trial protocol	GB ES CZ HU BG PL FR BE SE EE LV FI LT IT
Global end of trial date	06 December 2018

Results information

Result version number	v3 (current)
This version publication date	12 October 2019
First version publication date	21 June 2019
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	D5290C00003

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02878330
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	MedImmune, LLC
Sponsor organisation address	One MedImmune Way, Gaithersburg, Maryland, United States, 20878
Public contact	M. Pamela Griffin, MedImmune, LLC, +1 301-398-4059, information.center@astrazeneca.com
Scientific contact	M. Pamela Griffin, MedImmune, LLC, +1 301-398-4059, information.center@astrazeneca.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-001784-PIP01-15
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	14 February 2019
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	06 December 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study was to assess the efficacy of MEDI8897 for the reduction of medically attended lower respiratory tract infection (LRTI) due to reverse transcriptase-polymerase chain reaction (RT-PCR)-confirmed respiratory syncytial virus (RSV), compared to placebo.

Protection of trial subjects:

The conduct of this clinical study met all local and regulatory requirements. The study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and are consistent with International Conference on Harmonization guideline: Good Clinical Practice, and applicable regulatory requirements. Participants signed an informed consent form and could withdraw from the study at any time without any disadvantage and without having to provide a reason for this decision. Only investigators qualified by training and experience were selected as appropriate experts to investigate the study drug.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	03 November 2016
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Belgium: 2
Country: Number of subjects enrolled	Bulgaria: 141
Country: Number of subjects enrolled	Canada: 3
Country: Number of subjects enrolled	Czech Republic: 24
Country: Number of subjects enrolled	Estonia: 19
Country: Number of subjects enrolled	Finland: 7
Country: Number of subjects enrolled	France: 38
Country: Number of subjects enrolled	Hungary: 120
Country: Number of subjects enrolled	Italy: 72
Country: Number of subjects enrolled	Latvia: 12
Country: Number of subjects enrolled	Lithuania: 5
Country: Number of subjects enrolled	Poland: 38
Country: Number of subjects enrolled	Spain: 128
Country: Number of subjects enrolled	Sweden: 17
Country: Number of subjects enrolled	Turkey: 60
Country: Number of subjects enrolled	United Kingdom: 15
Country: Number of subjects enrolled	United States: 287

Country: Number of subjects enrolled	Argentina: 7
Country: Number of subjects enrolled	Australia: 13
Country: Number of subjects enrolled	Brazil: 26
Country: Number of subjects enrolled	Chile: 156
Country: Number of subjects enrolled	New Zealand: 13
Country: Number of subjects enrolled	South Africa: 250
Worldwide total number of subjects	1453
EEA total number of subjects	638

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	221
Infants and toddlers (28 days-23 months)	1232
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 from 03-Nov-2016 to 06-Dec-2018.

Pre-assignment

Screening details:

A total of 1540 participants were screened, out of which 1453 participants were randomized in the study.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Participants received a single intramuscular (IM) dose of placebo matched to MEDI8897 on Day 1 of the study.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Sterile concentrate
Routes of administration	Intramuscular use

Dosage and administration details:

Intramuscular (IM) dose of placebo matched to MEDI8897 on Day 1 of the study.

Arm title	MEDI8897 50 mg

Arm description:

Participants received a single IM dose of MEDI8897 50 milligrams (mg) on Day 1 of the study.

Arm type	Experimental
Investigational medicinal product name	MEDI8897 50 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Sterile concentrate
Routes of administration	Intramuscular use

Dosage and administration details:

Intramuscular (IM) dose of 50 milligrams (mg) MEDI8897 on Day 1 of the study.

Number of subjects in period 1	Placebo	MEDI8897 50 mg
Started	484	969
Completed	455	913
Not completed	29	56
Consent withdrawn by subject	11	21
Death	3	2
Not specified	4	7
Lost to follow-up	11	26

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Participants received a single intramuscular (IM) dose of placebo matched to MEDI8897 on Day 1 of the study.	
Reporting group title	MEDI8897 50 mg
Reporting group description:	
Participants received a single IM dose of MEDI8897 50 milligrams (mg) on Day 1 of the study.	

Reporting group values	Placebo	MEDI8897 50 mg	Total
Number of subjects	484	969	1453
Age Categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	83	138	221
Infants and toddlers (28 days-23 months)	401	831	1232
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	3.28	3.29	
standard deviation	± 2.31	± 2.22	-
Gender Categorical			
Units: Subjects			
Female	224	468	692
Male	260	501	761
Ethnicity (NIH/OMB)			
Units: Subjects			
Hispanic or Latino	91	225	316
Not Hispanic or Latino	393	743	1136
Unknown or Not Reported	0	1	1
Race (NIH/OMB)			
Units: Subjects			
American Indian or Alaska Native	1	0	1
Asian	10	5	15
Native Hawaiian or Other Pacific Islander	3	8	11
Black or African American	67	189	256
White	355	693	1048
More than one race	5	12	17
Other	43	61	104
Unknown or Not Reported	0	1	1

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Participants received a single intramuscular (IM) dose of placebo matched to MEDI8897 on Day 1 of the study.	
Reporting group title	MEDI8897 50 mg
Reporting group description:	
Participants received a single IM dose of MEDI8897 50 milligrams (mg) on Day 1 of the study.	

Primary: Number of Participants With Medically Attended Respiratory Syncytial Virus (RSV) Confirmed Lower Respiratory Tract Infection (LRTI)

End point title	Number of Participants With Medically Attended Respiratory Syncytial Virus (RSV) Confirmed Lower Respiratory Tract Infection (LRTI)
End point description:	
Medically attended RSV LRTI is determined based on objective clinical LRTI criteria and RSV test results which are analysed from respiratory secretions using RSV real time reverse transcriptase-polymerase chain reaction (RT-PCR) assay for detection of RSV A or RSV B subtypes. The criteria for LRTI is documented physical exam findings of rhonchi, rales, crackles, or wheeze and any of following: increased respiratory rate at rest (for age < 2 months: >= 60 breaths/min; 2–6 months: >= 50 breaths/min; and for > 6 months – 2 years, >= 40 breaths/min), or hypoxemia (in room air - oxygen saturation < 95% at altitudes <= 1800 meters or < 92% at altitudes > 1800 meters), or clinical signs of severe respiratory disease or dehydration secondary to inadequate oral intake due to respiratory distress. The intent-to-treat (ITT) population was analysed for this end point, which included all participants who were randomised in the study and analysed according to their randomised treatment group.	
End point type	Primary
End point timeframe:	
From Day 1 through Day 151	

End point values	Placebo	MEDI8897 50 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	484	969		
Units: Participants	46	25		

Statistical analyses

Statistical analysis title	Statistical Analysis
Comparison groups	Placebo v MEDI8897 50 mg

Number of subjects included in analysis	1453
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Poisson regression
Parameter estimate	Relative Risk Reduction
Point estimate	70.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	52.3
upper limit	81.2

Secondary: Number of Participants Hopitalized Due to Respiratory Syncytial Virus (RSV) Confirmed Lower Respiartory Tract Infection (LRTI)

End point title	Number of Participants Hopitalized Due to Respiratory Syncytial Virus (RSV) Confirmed Lower Respiartory Tract Infection (LRTI)

End point description:

A RSV hospitalization is defined as either 1) a respiratory hospitalization with a positive RSV test within 2 days of hospitalization (primary) or 2) new onset of respiratory symptoms in an already hospitalized child, with an objective measure of worsening respiratory status and positive RSV test (nosocomial). The ITT population was analysed for this end point, which included all participants who were randomised in the study and analysed according to their randomised treatment group.

End point type	Secondary

End point timeframe:

From Day 1 through Day 151

End point values	Placebo	MEDI8897 50 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	484	969		
Units: Participants	20	8		

Statistical analyses

Statistical analysis title	Statistical Analysis
Comparison groups	Placebo v MEDI8897 50 mg
Number of subjects included in analysis	1453
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0002
Method	Poisson regression
Parameter estimate	Relative Risk Reduction
Point estimate	78.4

Confidence interval	
level	95 %
sides	2-sided
lower limit	51.9
upper limit	90.3

Secondary: Number of Participants With Treatment Emergent Adverse Events (TEAEs) and Treatment Emergent Serious Adverse Events (TESAEs)

End point title	Number of Participants With Treatment Emergent Adverse Events (TEAEs) and Treatment Emergent Serious Adverse Events (TESAEs)

End point description:

An adverse event (AE) is any untoward medical occurrence in a participant who received study drug without regard to possibility of causal relationship. An serious adverse event (SAE) is an AE resulting in any of the following outcomes or deemed significant for any other reason: death; initial or prolonged inpatient hospitalization; life threatening experience (immediate risk of dying); persistent or significant disability/incapacity; congenital anomaly. TEAEs are defined as events present at baseline that worsened in intensity after administration of study drug or events absent at baseline that emerged after administration of study drug. As-treated population was analysed for this end point, which included all randomised participants who received any study drug and analysed according to the study drug they actually received.

End point type	Secondary

End point timeframe:

From Day 1 through Day 361

End point values	Placebo	MEDI8897 50 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	479	968		
Units: Participants				
TEAEs	416	834		
TESAEs	81	108		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Adverse Events of Special Interest (AESIs) and New Onset Chronic Diseases (NOCDs)

End point title	Number of Participants With Adverse Events of Special Interest (AESIs) and New Onset Chronic Diseases (NOCDs)

End point description:

An AESI was one of scientific and medical interest specific to understanding of study drug and may have required close monitoring and rapid communication by investigator to the sponsor. An AESI may be serious or non-serious. A NOCD is a newly diagnosed medical condition that is of a chronic, ongoing nature. It is observed after receiving study drug and is assessed by investigator as medically significant. As-treated population was analysed for this end point, which included all randomised participants who received any study drug and analysed according to the study drug they actually received.

End point type	Secondary

End point timeframe:

From Day 1 through Day 361

End point values	Placebo	MEDI8897 50 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	479	968		
Units: Participants				
AESIs	3	5		
NOCDs	4	4		

Statistical analyses

No statistical analyses for this end point

Secondary: Serum Concentration of MEDI8897

End point title	Serum Concentration of MEDI8897[1]

End point description:

As-treated population was analysed for this end point, which included all randomised participants who received any study drug and analysed according to the study drug they actually received. Here 'n' denotes number of participants analysed for specified time point.

End point type	Secondary

End point timeframe:

Days 91, 151, and 361

Notes:

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Serum concentration of MEDI8897 is only applicable to the MEDI8897 arm group and not to the Placebo arm group.

End point values	MEDI8897 50 mg			
Subject group type	Reporting group			
Number of subjects analysed	968			
Units: mcg/mL				
arithmetic mean (standard deviation)				
Day 91 (n= 883)	35.9 (± 10.9)			
Day 151 (n= 849)	18.9 (± 7.4)			
Day 361 (n= 771)	2.1 (± 1.1)			

Statistical analyses

No statistical analyses for this end point

Secondary: Elimination half-life (t1/2) of MEDI8897

End point title	Elimination half-life (t1/2) of MEDI8897[2]

End point description:

Terminal elimination half-life (t½) is the time required for half of the drug to be eliminated from the serum. As-treated population was analysed for this end point, which included all randomised participants who received any study drug and analysed according to the study drug they actually received. Participants with sufficient additional pharmacokinetics (PK) samples from unscheduled visits were analysed for this end point.

End point type	Secondary

End point timeframe:

Day 91 through Day 361

Notes:

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Elimination half-life is only applicable to the MEDI8897 arm group and not to the Placebo arm group.

End point values	MEDI8897 50 mg			
Subject group type	Reporting group			
Number of subjects analysed	48			
Units: Days				
arithmetic mean (standard deviation)	59.3 (± 9.6)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Positive Anti-drug Antibodies to MEDI8897

End point title	Number of Participants With Positive Anti-drug Antibodies to MEDI8897

End point description:

The number of participants with positive serum antibodies to MEDI8897 are reported. As-treated population was analysed for this end point, which included all randomised participants who received any study drug and analysed according to the study drug they actually received. Here 'n' denotes number of participants analysed for specified time point.

End point type	Secondary

End point timeframe:

Days 91, 151, and 361

End point values	Placebo	MEDI8897 50 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	479	968		
Units: Participants				
Day 91 (n= 455, 890)	4	11		
Day 151 (n= 445, 867)	6	17		
Day 361 (n= 418, 847)	8	30		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From Day 1 through Day 361

Adverse event reporting additional description:

As-treated population was analysed for this end point, which included all randomised participants who received any study drug and analysed according to the study drug they actually received.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	21.0

Reporting groups

Reporting group title	MEDI8897 50 mg

Reporting group description:

Participants received a single IM dose of MEDI8897 50 mg on Day 1 of the study.

Reporting group title	PLACEBO

Reporting group description:

Participants received a single IM dose of placebo matched to MEDI8897 on Day 1 of the study.

Serious adverse events	MEDI8897 50 mg	PLACEBO	
Total subjects affected by serious adverse events			
subjects affected / exposed	108 / 968 (11.16%)	81 / 479 (16.91%)	
number of deaths (all causes)	2	3	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Eyelid haemangioma			
subjects affected / exposed	1 / 968 (0.10%)	0 / 479 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Death			
subjects affected / exposed	1 / 968 (0.10%)	0 / 479 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pyrexia			
subjects affected / exposed	3 / 968 (0.31%)	1 / 479 (0.21%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	1 / 968 (0.10%)	0 / 479 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Penile adhesion			
subjects affected / exposed	0 / 968 (0.00%)	1 / 479 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Apnoea			
subjects affected / exposed	1 / 968 (0.10%)	1 / 479 (0.21%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Asthma			
subjects affected / exposed	1 / 968 (0.10%)	0 / 479 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Laryngeal stenosis			
subjects affected / exposed	0 / 968 (0.00%)	1 / 479 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia aspiration			
subjects affected / exposed	2 / 968 (0.21%)	0 / 479 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary vein stenosis			
subjects affected / exposed	1 / 968 (0.10%)	0 / 479 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Psychiatric disorders			
Irritability			

subjects affected / exposed	0 / 968 (0.00%)	1 / 479 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Exposure to toxic agent			
subjects affected / exposed	1 / 968 (0.10%)	0 / 479 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fall			
subjects affected / exposed	1 / 968 (0.10%)	0 / 479 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Palate injury			
subjects affected / exposed	0 / 968 (0.00%)	1 / 479 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thermal burn			
subjects affected / exposed	2 / 968 (0.21%)	0 / 479 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Congenital, familial and genetic disorders			
Muscular dystrophy			
subjects affected / exposed	1 / 968 (0.10%)	0 / 479 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Cardiac arrest			
subjects affected / exposed	1 / 968 (0.10%)	0 / 479 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure			

subjects affected / exposed	1 / 968 (0.10%)	0 / 479 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure congestive			
subjects affected / exposed	1 / 968 (0.10%)	0 / 479 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocarditis			
subjects affected / exposed	0 / 968 (0.00%)	1 / 479 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pericardial effusion			
subjects affected / exposed	0 / 968 (0.00%)	1 / 479 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	0 / 968 (0.00%)	1 / 479 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile convulsion			
subjects affected / exposed	1 / 968 (0.10%)	0 / 479 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypotonia			
subjects affected / exposed	0 / 968 (0.00%)	1 / 479 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infantile spasms			
subjects affected / exposed	0 / 968 (0.00%)	1 / 479 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intraventricular haemorrhage			

subjects affected / exposed	0 / 968 (0.00%)	1 / 479 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Seizure			
subjects affected / exposed	0 / 968 (0.00%)	1 / 479 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia neonatal			
subjects affected / exposed	0 / 968 (0.00%)	1 / 479 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
Deafness bilateral			
subjects affected / exposed	1 / 968 (0.10%)	0 / 479 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 968 (0.10%)	0 / 479 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	2 / 968 (0.21%)	1 / 479 (0.21%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dysphagia			
subjects affected / exposed	1 / 968 (0.10%)	0 / 479 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enteritis			
subjects affected / exposed	1 / 968 (0.10%)	1 / 479 (0.21%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 968 (0.10%)	0 / 479 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Incarcerated umbilical hernia			
subjects affected / exposed	1 / 968 (0.10%)	0 / 479 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inguinal hernia			
subjects affected / exposed	1 / 968 (0.10%)	6 / 479 (1.25%)	
occurrences causally related to treatment / all	0 / 1	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malabsorption			
subjects affected / exposed	1 / 968 (0.10%)	0 / 479 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	2 / 968 (0.21%)	0 / 479 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Jaundice			
subjects affected / exposed	1 / 968 (0.10%)	0 / 479 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Dermatitis allergic			
subjects affected / exposed	0 / 968 (0.00%)	1 / 479 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Nephrolithiasis			

subjects affected / exposed	2 / 968 (0.21%)	0 / 479 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Abscess limb			
subjects affected / exposed	1 / 968 (0.10%)	0 / 479 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Adenovirus infection			
subjects affected / exposed	0 / 968 (0.00%)	1 / 479 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anal abscess			
subjects affected / exposed	1 / 968 (0.10%)	0 / 479 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchiolitis			
subjects affected / exposed	20 / 968 (2.07%)	21 / 479 (4.38%)	
occurrences causally related to treatment / all	0 / 22	0 / 26	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			
subjects affected / exposed	14 / 968 (1.45%)	11 / 479 (2.30%)	
occurrences causally related to treatment / all	0 / 16	0 / 11	
deaths causally related to treatment / all	0 / 0	0 / 0	
Croup infectious			
subjects affected / exposed	2 / 968 (0.21%)	0 / 479 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cytomegalovirus infection			
subjects affected / exposed	0 / 968 (0.00%)	1 / 479 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			

subjects affected / exposed	9 / 968 (0.93%)	4 / 479 (0.84%)	
occurrences causally related to treatment / all	0 / 9	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis Escherichia coli			
subjects affected / exposed	0 / 968 (0.00%)	1 / 479 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis adenovirus			
subjects affected / exposed	1 / 968 (0.10%)	0 / 479 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis rotavirus			
subjects affected / exposed	0 / 968 (0.00%)	2 / 479 (0.42%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis salmonella			
subjects affected / exposed	1 / 968 (0.10%)	1 / 479 (0.21%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis viral			
subjects affected / exposed	1 / 968 (0.10%)	1 / 479 (0.21%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza			
subjects affected / exposed	0 / 968 (0.00%)	1 / 479 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Laryngitis			
subjects affected / exposed	1 / 968 (0.10%)	0 / 479 (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	14 / 968 (1.45%)	13 / 479 (2.71%)	
occurrences causally related to treatment / all	0 / 14	0 / 18	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower respiratory tract infection viral			
subjects affected / exposed	5 / 968 (0.52%)	3 / 479 (0.63%)	
occurrences causally related to treatment / all	0 / 5	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningitis			
subjects affected / exposed	0 / 968 (0.00%)	1 / 479 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningitis bacterial			
subjects affected / exposed	0 / 968 (0.00%)	1 / 479 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Otitis media			
subjects affected / exposed	2 / 968 (0.21%)	0 / 479 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritonsillar abscess			
subjects affected / exposed	0 / 968 (0.00%)	1 / 479 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pharyngitis			
subjects affected / exposed	1 / 968 (0.10%)	0 / 479 (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	13 / 968 (1.34%)	10 / 479 (2.09%)	
occurrences causally related to treatment / all	0 / 13	0 / 12	
deaths causally related to treatment / all	0 / 0	0 / 2	
Pneumonia bacterial			

subjects affected / exposed	0 / 968 (0.00%)	1 / 479 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia parainfluenzae viral			
subjects affected / exposed	0 / 968 (0.00%)	1 / 479 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia respiratory syncytial viral			
subjects affected / exposed	2 / 968 (0.21%)	2 / 479 (0.42%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia viral			
subjects affected / exposed	7 / 968 (0.72%)	2 / 479 (0.42%)	
occurrences causally related to treatment / all	0 / 8	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pseudomonal bacteraemia			
subjects affected / exposed	0 / 968 (0.00%)	1 / 479 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory syncytial virus bronchiolitis			
subjects affected / exposed	1 / 968 (0.10%)	2 / 479 (0.42%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Salmonellosis			
subjects affected / exposed	1 / 968 (0.10%)	0 / 479 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	2 / 968 (0.21%)	1 / 479 (0.21%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis neonatal			

subjects affected / exposed	1 / 968 (0.10%)	0 / 479 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Staphylococcal scalded skin syndrome			
subjects affected / exposed	0 / 968 (0.00%)	1 / 479 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tonsillitis			
subjects affected / exposed	1 / 968 (0.10%)	0 / 479 (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	3 / 968 (0.31%)	3 / 479 (0.63%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	0 / 968 (0.00%)	4 / 479 (0.84%)	
occurrences causally related to treatment / all	0 / 0	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral upper respiratory tract infection			
subjects affected / exposed	1 / 968 (0.10%)	0 / 479 (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			
Dehydration			
subjects affected / exposed	2 / 968 (0.21%)	1 / 479 (0.21%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoglycaemia			
subjects affected / exposed	1 / 968 (0.10%)	0 / 479 (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: 1 %

Non-serious adverse events	MEDI8897 50 mg	PLACEBO	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	804 / 968 (83.06%)	402 / 479 (83.92%)	
Injury, poisoning and procedural complications			
Arthropod bite			
subjects affected / exposed	14 / 968 (1.45%)	6 / 479 (1.25%)	
occurrences (all)	14	6	
Vaccination complication			
subjects affected / exposed	23 / 968 (2.38%)	15 / 479 (3.13%)	
occurrences (all)	28	19	
Congenital, familial and genetic disorders			
Plagiocephaly			
subjects affected / exposed	15 / 968 (1.55%)	3 / 479 (0.63%)	
occurrences (all)	15	3	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	29 / 968 (3.00%)	17 / 479 (3.55%)	
occurrences (all)	29	17	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	109 / 968 (11.26%)	63 / 479 (13.15%)	
occurrences (all)	133	75	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	5 / 968 (0.52%)	10 / 479 (2.09%)	
occurrences (all)	5	10	
Constipation			
subjects affected / exposed	34 / 968 (3.51%)	21 / 479 (4.38%)	
occurrences (all)	36	24	
Diarrhoea			
subjects affected / exposed	98 / 968 (10.12%)	49 / 479 (10.23%)	
occurrences (all)	113	55	
Gastrooesophageal reflux disease			

subjects affected / exposed	37 / 968 (3.82%)	22 / 479 (4.59%)	
occurrences (all)	38	22	
Teething			
subjects affected / exposed	62 / 968 (6.40%)	32 / 479 (6.68%)	
occurrences (all)	72	35	
Umbilical hernia			
subjects affected / exposed	11 / 968 (1.14%)	3 / 479 (0.63%)	
occurrences (all)	11	3	
Vomiting			
subjects affected / exposed	40 / 968 (4.13%)	15 / 479 (3.13%)	
occurrences (all)	46	17	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	37 / 968 (3.82%)	15 / 479 (3.13%)	
occurrences (all)	45	17	
Nasal congestion			
subjects affected / exposed	71 / 968 (7.33%)	24 / 479 (5.01%)	
occurrences (all)	83	27	
Nasal obstruction			
subjects affected / exposed	23 / 968 (2.38%)	17 / 479 (3.55%)	
occurrences (all)	23	17	
Rhinorrhoea			
subjects affected / exposed	63 / 968 (6.51%)	29 / 479 (6.05%)	
occurrences (all)	75	34	
Skin and subcutaneous tissue disorders			
Dermatitis			
subjects affected / exposed	20 / 968 (2.07%)	15 / 479 (3.13%)	
occurrences (all)	26	15	
Dermatitis atopic			
subjects affected / exposed	30 / 968 (3.10%)	8 / 479 (1.67%)	
occurrences (all)	34	9	
Dermatitis diaper			
subjects affected / exposed	76 / 968 (7.85%)	36 / 479 (7.52%)	
occurrences (all)	94	44	
Eczema			

subjects affected / exposed	34 / 968 (3.51%)	15 / 479 (3.13%)	
occurrences (all)	34	15	
Rash			
subjects affected / exposed	43 / 968 (4.44%)	17 / 479 (3.55%)	
occurrences (all)	49	18	
Seborrhoeic dermatitis			
subjects affected / exposed	17 / 968 (1.76%)	7 / 479 (1.46%)	
occurrences (all)	17	8	
Psychiatric disorders			
Irritability			
subjects affected / exposed	11 / 968 (1.14%)	7 / 479 (1.46%)	
occurrences (all)	20	14	
Infections and infestations			
Acarodermatitis			
subjects affected / exposed	13 / 968 (1.34%)	8 / 479 (1.67%)	
occurrences (all)	15	8	
Bronchiolitis			
subjects affected / exposed	83 / 968 (8.57%)	42 / 479 (8.77%)	
occurrences (all)	104	60	
Bronchitis			
subjects affected / exposed	91 / 968 (9.40%)	49 / 479 (10.23%)	
occurrences (all)	150	77	
Candida nappy rash			
subjects affected / exposed	12 / 968 (1.24%)	6 / 479 (1.25%)	
occurrences (all)	14	6	
Conjunctivitis			
subjects affected / exposed	86 / 968 (8.88%)	39 / 479 (8.14%)	
occurrences (all)	94	44	
Croup infectious			
subjects affected / exposed	12 / 968 (1.24%)	6 / 479 (1.25%)	
occurrences (all)	13	7	
Ear infection			
subjects affected / exposed	23 / 968 (2.38%)	13 / 479 (2.71%)	
occurrences (all)	34	21	
Exanthema subitum			

subjects affected / exposed	21 / 968 (2.17%)	11 / 479 (2.30%)	
occurrences (all)	22	11	
Fungal skin infection			
subjects affected / exposed	5 / 968 (0.52%)	8 / 479 (1.67%)	
occurrences (all)	5	8	
Gastroenteritis			
subjects affected / exposed	115 / 968 (11.88%)	44 / 479 (9.19%)	
occurrences (all)	138	49	
Gastroenteritis viral			
subjects affected / exposed	13 / 968 (1.34%)	5 / 479 (1.04%)	
occurrences (all)	15	5	
Hand-foot-and-mouth disease			
subjects affected / exposed	36 / 968 (3.72%)	14 / 479 (2.92%)	
occurrences (all)	36	14	
Impetigo			
subjects affected / exposed	12 / 968 (1.24%)	6 / 479 (1.25%)	
occurrences (all)	12	6	
Laryngitis			
subjects affected / exposed	24 / 968 (2.48%)	10 / 479 (2.09%)	
occurrences (all)	31	10	
Lower respiratory tract infection			
subjects affected / exposed	75 / 968 (7.75%)	46 / 479 (9.60%)	
occurrences (all)	103	65	
Lower respiratory tract infection viral			
subjects affected / exposed	9 / 968 (0.93%)	6 / 479 (1.25%)	
occurrences (all)	9	8	
Nasopharyngitis			
subjects affected / exposed	164 / 968 (16.94%)	94 / 479 (19.62%)	
occurrences (all)	264	158	
Oral candidiasis			
subjects affected / exposed	36 / 968 (3.72%)	26 / 479 (5.43%)	
occurrences (all)	39	26	
Otitis media			
subjects affected / exposed	63 / 968 (6.51%)	42 / 479 (8.77%)	
occurrences (all)	87	63	
Otitis media acute			

subjects affected / exposed	51 / 968 (5.27%)	24 / 479 (5.01%)	
occurrences (all)	82	33	
Pharyngitis			
subjects affected / exposed	57 / 968 (5.89%)	27 / 479 (5.64%)	
occurrences (all)	68	32	
Rhinitis			
subjects affected / exposed	111 / 968 (11.47%)	50 / 479 (10.44%)	
occurrences (all)	145	61	
Tonsillitis			
subjects affected / exposed	16 / 968 (1.65%)	5 / 479 (1.04%)	
occurrences (all)	16	6	
Upper respiratory tract infection			
subjects affected / exposed	392 / 968 (40.50%)	169 / 479 (35.28%)	
occurrences (all)	734	337	
Urinary tract infection			
subjects affected / exposed	12 / 968 (1.24%)	7 / 479 (1.46%)	
occurrences (all)	12	7	
Varicella			
subjects affected / exposed	19 / 968 (1.96%)	11 / 479 (2.30%)	
occurrences (all)	19	11	
Viral rash			
subjects affected / exposed	32 / 968 (3.31%)	15 / 479 (3.13%)	
occurrences (all)	34	16	
Viral upper respiratory tract infection			
subjects affected / exposed	48 / 968 (4.96%)	34 / 479 (7.10%)	
occurrences (all)	75	57	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
25 January 2018	The interim analysis was removed from the study. The two-sided significance level of α was changed from α equal to (=) 0.049 to α = 0.05. The p value required to achieve statistical significance of less than (<) 0.049 has returned to (less than or equal to) <= 0.05. A decision was made to conduct a primary analysis rather than an interim analysis and a text was added to explain that the primary analysis would now include all efficacy data from all randomized participants through Day 151 and all available safety data up to and beyond Day 151 at the time of the final data cut-off date.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported