



Clinical trial results:

A Double-blind, Randomized, Placebo-controlled, Single Ascending Dose Study to Evaluate the Safety, Tolerability, and Pharmacokinetics of MK-1654 in Pre-Term and Full-Term Infants

Summary

EudraCT number	2017-005062-21
Trial protocol	ES Outside EU/EEA
Global end of trial date	14 September 2022

Results information

Result version number	v1
This version publication date	05 August 2023
First version publication date	05 August 2023

Trial information

Trial identification

Sponsor protocol code	1654-002
-----------------------	----------

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03524118
WHO universal trial number (UTN)	-
Other trial identifiers	EudraCT: 2017-005062-21

Notes:

Sponsors

Sponsor organisation name	Merck Sharp & Dohme LLC
Sponsor organisation address	126 East Lincoln Avenue, P.O. Box 2000, Rahway, NJ, United States, 07065
Public contact	Clinical Trials Disclosure, Merck Sharp & Dohme LLC, ClinicalTrialsDisclosure@merck.com
Scientific contact	Clinical Trials Disclosure, Merck Sharp & Dohme LLC, ClinicalTrialsDisclosure@merck.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMA-002755-PIP01-19
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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	14 September 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	14 September 2022
Global end of trial reached?	Yes
Global end of trial date	14 September 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The purpose of this study is to evaluate the safety, tolerability, pharmacokinetics, and incidence of anti-drug antibodies (ADAs) of single ascending doses of clesrovimab in healthy pre-term (born at 29 to 35 weeks gestational age) and full-term (born at >35 weeks gestational age) infants. Participants will be randomized into 1 of 4 dose escalation panels (Panels A to D); an additional panel (Panel E) of full-term infants will receive the same dose as Panel D. Key safety and tolerability variables will be reviewed after each dose panel prior to administering the next-highest dose. Participants in Dose Panels A, B, C, D1, and E1 will be followed for up to 365 days. After protocol Amendment 4 (AM4), participants in Dose Panels D2 and E2 will be followed for up to 545 days.

Protection of trial subjects:

This study was conducted in conformance with Good Clinical Practice standards and applicable country and/or local statutes and regulations regarding ethical committee review, informed consent, and the protection of human subjects participating in biomedical research.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	20 September 2018
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Chile: 22
Country: Number of subjects enrolled	Colombia: 36
Country: Number of subjects enrolled	South Africa: 49
Country: Number of subjects enrolled	Korea, Republic of: 5
Country: Number of subjects enrolled	Spain: 3
Country: Number of subjects enrolled	United States: 68
Worldwide total number of subjects	183
EEA total number of subjects	3

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0

Newborns (0-27 days)	10
Infants and toddlers (28 days-23 months)	173
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:

183 participants were randomized and 181 were dosed and included in the All Participants as Treated (APaT) population. Two participants who were randomized to the MK-1654 20 mg dose group actually received MK-1654 50 mg and were included in the MK-1654 50 mg group for all safety analyses.

Pre-assignment

Screening details:

Participants enrolled in panels D and E prior to protocol amendment 04 who chose not to participate in the modified schedule followed the D1 and E1 schedule of activities. Participants enrolled in panels D and E prior to protocol amendment 04 who chose to participate in the modified schedule followed the D2 and E2 schedule of activities.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Panel A: Preterm Clesrovimab 20mg

Arm description:

Pre-term infants received clesrovimab 20mg via intramuscular (IM) injection and were followed for up to 365 days.

Arm type	Experimental
Investigational medicinal product name	Clesrovimab
Investigational medicinal product code	
Other name	MK-1654
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Pre-term infants were administered clesrovimab 20mg via intramuscular (IM) injection and were followed for up to 365 days.

Arm title	Panel B: Pre-term Clesrovimab 50mg
------------------	------------------------------------

Arm description:

Pre-term infants received clesrovimab 50mg via IM injection and were followed for up to 365 days.

Arm type	Experimental
Investigational medicinal product name	Clesrovimab
Investigational medicinal product code	
Other name	MK-1654
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Pre-term infants received clesrovimab 50mg via IM injection and were followed for up to 365 days.

Arm title	Panel C: Pre-term Clesrovimab 75mg
------------------	------------------------------------

Arm description:

Pre-term infants received clesrovimab 75mg via IM injection and were followed for up to 365 days.

Arm type	Experimental
----------	--------------

Investigational medicinal product name	Clesrovimab
Investigational medicinal product code	
Other name	MK-1654
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Pre-term infants received clesrovimab 75mg via IM injection and were followed for up to 365 days.

Arm title	Panel D1 and D2: Pre-term Clesrovimab 100mg
------------------	---

Arm description:

Pre-term infants in Panel D1 and D2 received clesrovimab 100mg via IM injection and were followed for up to 365 and 545 days respectively.

Arm type	Experimental
Investigational medicinal product name	Clesrovimab
Investigational medicinal product code	
Other name	MK-1654
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Pre-term infants in Panel D1 and D2 received clesrovimab 100mg via IM injection and were followed for up to 365 and 545 days respectively.

Arm title	Panel E1 and E2: Full-term Clesrovimab 100mg
------------------	--

Arm description:

Full-term infants in Panel E1 and E2 received clesrovimab 100mg via IM injection and were followed for up to 365 and 545 days respectively.

Arm type	Experimental
Investigational medicinal product name	Clesrovimab
Investigational medicinal product code	
Other name	MK-1654
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Full-term infants in Panel E1 and E2 received clesrovimab 100mg via IM injection and were followed for up to 365 and 545 days respectively.

Arm title	Placebo
------------------	---------

Arm description:

Pre-term and Full-term infants received placebo via IM injection.

Arm type	Placebo
Investigational medicinal product name	Normal Saline
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Pre-term and Full-term infants received 0.90% w/v sodium chloride via IM injection.

Number of subjects in period 1	Panel A: Preterm Clesrovimab 20mg	Panel B: Pre-term Clesrovimab 50mg	Panel C: Pre-term Clesrovimab 75mg
Started	8	31	41
Completed	8	29	40
Not completed	0	2	1
Physician decision	-	-	-
Unknown	-	1	-
Withdrawal by Parent/Guardian	-	1	-
Lost to follow-up	-	-	-
Protocol deviation	-	-	1

Number of subjects in period 1	Panel D1 and D2: Pre-term Clesrovimab 100mg	Panel E1 and E2: Full-term Clesrovimab 100mg	Placebo
Started	32	33	38
Completed	31	26	37
Not completed	1	7	1
Physician decision	-	1	-
Unknown	-	1	1
Withdrawal by Parent/Guardian	1	3	-
Lost to follow-up	-	1	-
Protocol deviation	-	1	-

Baseline characteristics

Reporting groups

Reporting group title	Panel A: Preterm Clesrovimab 20mg
Reporting group description: Pre-term infants received clesrovimab 20mg via intramuscular (IM) injection and were followed for up to 365 days.	
Reporting group title	Panel B: Pre-term Clesrovimab 50mg
Reporting group description: Pre-term infants received clesrovimab 50mg via IM injection and were followed for up to 365 days.	
Reporting group title	Panel C: Pre-term Clesrovimab 75mg
Reporting group description: Pre-term infants received clesrovimab 75mg via IM injection and were followed for up to 365 days.	
Reporting group title	Panel D1 and D2: Pre-term Clesrovimab 100mg
Reporting group description: Pre-term infants in Panel D1 and D2 received clesrovimab 100mg via IM injection and were followed for up to 365 and 545 days respectively.	
Reporting group title	Panel E1 and E2: Full-term Clesrovimab 100mg
Reporting group description: Full-term infants in Panel E1 and E2 received clesrovimab 100mg via IM injection and were followed for up to 365 and 545 days respectively.	
Reporting group title	Placebo
Reporting group description: Pre-term and Full-term infants received placebo via IM injection.	

Reporting group values	Panel A: Preterm Clesrovimab 20mg	Panel B: Pre-term Clesrovimab 50mg	Panel C: Pre-term Clesrovimab 75mg
Number of subjects	8	31	41
Age Categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	2	3
Infants and toddlers (28 days-23 months)	8	29	38
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: days			
median	68.0	109.0	94.0
full range (min-max)	31 to 257	23 to 255	24 to 245
Gender Categorical Units: Subjects			
Female	6	15	20
Male	2	16	21

Race (NIH/OMB)			
Units: Subjects			
American Indian Or Alaska Native	0	0	1
Asian	0	1	0
Black Or African American	4	8	9
Multiple	0	1	17
White	4	20	14
Missing	0	1	0
Ethnicity (NIH/OMB)			
Units: Subjects			
Hispanic or Latino	1	12	25
Non Hispanic or Latino	7	19	16

Reporting group values	Panel D1 and D2: Pre-term Clesrovimab 100mg	Panel E1 and E2: Full-term Clesrovimab 100mg	Placebo
Number of subjects	32	33	38
Age Categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	3	0	2
Infants and toddlers (28 days-23 months)	29	33	36
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: days			
median	139.5	164.0	128.0
full range (min-max)	14 to 239	46 to 250	26 to 275
Gender Categorical			
Units: Subjects			
Female	17	13	19
Male	15	20	19
Race (NIH/OMB)			
Units: Subjects			
American Indian Or Alaska Native	1	1	2
Asian	5	0	0
Black Or African American	14	14	11
Multiple	2	7	9
White	8	11	14
Missing	2	0	2
Ethnicity (NIH/OMB)			
Units: Subjects			
Hispanic or Latino	9	14	18
Non Hispanic or Latino	23	19	20

Reporting group values	Total		
Number of subjects	183		

Age Categorical			
Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	0		
Newborns (0-27 days)	10		
Infants and toddlers (28 days-23 months)	173		
Children (2-11 years)	0		
Adolescents (12-17 years)	0		
Adults (18-64 years)	0		
From 65-84 years	0		
85 years and over	0		
Age Continuous			
Units: days			
median			
full range (min-max)	-		
Gender Categorical			
Units: Subjects			
Female	90		
Male	93		
Race (NIH/OMB)			
Units: Subjects			
American Indian Or Alaska Native	5		
Asian	6		
Black Or African American	60		
Multiple	36		
White	71		
Missing	5		
Ethnicity (NIH/OMB)			
Units: Subjects			
Hispanic or Latino	79		
Non Hispanic or Latino	104		

End points

End points reporting groups

Reporting group title	Panel A: Preterm Clesrovimab 20mg
Reporting group description: Pre-term infants received clesrovimab 20mg via intramuscular (IM) injection and were followed for up to 365 days.	
Reporting group title	Panel B: Pre-term Clesrovimab 50mg
Reporting group description: Pre-term infants received clesrovimab 50mg via IM injection and were followed for up to 365 days.	
Reporting group title	Panel C: Pre-term Clesrovimab 75mg
Reporting group description: Pre-term infants received clesrovimab 75mg via IM injection and were followed for up to 365 days.	
Reporting group title	Panel D1 and D2: Pre-term Clesrovimab 100mg
Reporting group description: Pre-term infants in Panel D1 and D2 received clesrovimab 100mg via IM injection and were followed for up to 365 and 545 days respectively.	
Reporting group title	Panel E1 and E2: Full-term Clesrovimab 100mg
Reporting group description: Full-term infants in Panel E1 and E2 received clesrovimab 100mg via IM injection and were followed for up to 365 and 545 days respectively.	
Reporting group title	Placebo
Reporting group description: Pre-term and Full-term infants received placebo via IM injection.	
Subject analysis set title	Panel A: Pre-term Clesrovimab 20mg Single Dose IM Injection
Subject analysis set type	Safety analysis
Subject analysis set description: Pre-term infants received clesrovimab 20mg via intramuscular (IM) injection and were followed for up to 365 days.	
Subject analysis set title	Panel B: Pre-term Clesrovimab 50mg Single Dose IM Injection
Subject analysis set type	Safety analysis
Subject analysis set description: Pre-term infants received clesrovimab 50mg via IM injection and were followed for up to 365 days.	
Subject analysis set title	Panel C: Pre-term Clesrovimab 75mg Single Dose IM Injection
Subject analysis set type	Safety analysis
Subject analysis set description: Pre-term infants received clesrovimab 75mg via IM injection and were followed for up to 365 days.	
Subject analysis set title	Panel D1 & D2: Pre-term Clesrovimab 100mg Single Dose IM Inj
Subject analysis set type	Safety analysis
Subject analysis set description: Pre-term infants in Panel D1 and D2 received clesrovimab 100mg via IM injection and were followed for up to 365 and 545 days respectively.	
Subject analysis set title	Panel E1 & E2: Full-term Clesrovimab 100mg Single Dose IM Inj
Subject analysis set type	Safety analysis
Subject analysis set description: Full-term infants in Panel E1 and E2 received clesrovimab 100mg via IM injection and were followed for up to 365 and 545 days respectively.	
Subject analysis set title	Placebo: Pre & Full-term Placebo 0.2, 0.5 Single Dose IM Inj
Subject analysis set type	Safety analysis
Subject analysis set description: Pre-term and Full-term infants received placebo via IM injection.	

Primary: Percentage of Participants Who Experienced At Least One Solicited Injection Site Adverse Event (AE)

End point title	Percentage of Participants Who Experienced At Least One Solicited Injection Site Adverse Event (AE) ^[1]
-----------------	--

End point description:

An AE is any untoward medical occurrence in a clinical study participant, temporally associated with the use of study intervention, whether or not considered related to the study intervention. Solicited injection site AEs were monitored from Day 1 to Day 5.

End point type	Primary
----------------	---------

End point timeframe:

Up to Day 5

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 between-group statistical analyses were performed for this endpoint."

End point values	Panel A: Pre-term Clesrovimab 20mg Single Dose IM Injection	Panel B: Pre-term Clesrovimab 50mg Single Dose IM Injection	Panel C: Pre-term Clesrovimab 75mg Single Dose IM Injection	Panel D1 & D2: Pre-term Clesrovimab 100mg Single Dose IM Inj
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	6	33	40	32
Units: Participants				
with solicited injection site adverse events	3	3	3	2
without solicited injection site adverse events	3	30	37	30

End point values	Panel E1 & E2: Full-term Clesrovimab 100mg Single Dose IM Inj	Placebo: Pre & Full-term Placebo 0.2, 0.5 Single Dose IM Inj		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	32	38		
Units: Participants				
with solicited injection site adverse events	2	2		
without solicited injection site adverse events	30	36		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants Who Experienced At Least One Solicited Systemic Adverse Event (AE)

End point title	Percentage of Participants Who Experienced At Least One Solicited Systemic Adverse Event (AE) ^[2]
-----------------	--

End point description:

An AE is any untoward medical occurrence in a clinical study participant, temporally associated with the use of study intervention, whether or not considered related to the study intervention. Solicited systemic AEs were monitored from Day 1 to Day 5.

End point type	Primary
----------------	---------

End point timeframe:

Up to Day 5

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: No between-group statistical analyses were performed for this endpoint."

End point values	Panel A: Pre-term Clesrovimab 20mg Single Dose IM Injection	Panel B: Pre-term Clesrovimab 50mg Single Dose IM Injection	Panel C: Pre-term Clesrovimab 75mg Single Dose IM Injection	Panel D1 & D2: Pre-term Clesrovimab 100mg Single Dose IM Inj
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	6	33	40	32
Units: Participants				
with solicited systemic adverse events	2	8	9	2
without solicited systemic adverse events	4	25	31	30

End point values	Panel E1 & E2: Full-term Clesrovimab 100mg Single Dose IM Inj	Placebo: Pre & Full-term Placebo 0.2, 0.5 Single Dose IM Inj		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	32	38		
Units: Participants				
with solicited systemic adverse events	3	9		
without solicited systemic adverse events	29	29		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants Who Experienced At Least One Serious Adverse Event (SAE)

End point title	Percentage of Participants Who Experienced At Least One Serious Adverse Event (SAE) ^[3]
-----------------	--

End point description:

An SAE is any untoward medical occurrence that, at any dose, results in death; is life-threatening; requires inpatient hospitalization or prolongation of existing hospitalization; results in persistent or significant injury/incapacity; is a congenital anomaly/birth defect; or is an other important medical event.

End point type	Primary
----------------	---------

End point timeframe:

Up to Day 545

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: No between-group statistical analyses were performed for this endpoint.

End point values	Panel A: Pre-term Clesrovimab 20mg Single Dose IM Injection	Panel B: Pre-term Clesrovimab 50mg Single Dose IM Injection	Panel C: Pre-term Clesrovimab 75mg Single Dose IM Injection	Panel D1 & D2: Pre-term Clesrovimab 100mg Single Dose IM Inj
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	6	33	40	32
Units: Participants				
with serious adverse events (SAE)	1	4	1	3
without SAE	5	29	39	29

End point values	Panel E1 & E2: Full-term Clesrovimab 100mg Single Dose IM Inj	Placebo: Pre & Full-term Placebo 0.2, 0.5 Single Dose IM Inj		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	32	38		
Units: Participants				
with serious adverse events (SAE)	6	6		
without SAE	26	32		

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Serum-Concentration Time Curve From Zero to Infinity (AUC0-∞)

End point title	Area Under the Serum-Concentration Time Curve From Zero to Infinity (AUC0-∞)
-----------------	--

End point description:

AUC0-∞ is a measure of the extrapolated mean concentration in serum from dosing to infinity.

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

End point timeframe:

At designated time points (up to 1 year post-dose)

End point values	Panel A: Pre-term Clesrovimab 20mg Single Dose IM Injection	Panel B: Pre-term Clesrovimab 50mg Single Dose IM Injection	Panel C: Pre-term Clesrovimab 75mg Single Dose IM Injection	Panel D1 & D2: Pre-term Clesrovimab 100mg Single Dose IM Inj
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	5	33	40	32
Units: day*µg/mL				
geometric mean (geometric coefficient of variation)	1560 (± 43.5)	3520 (± 22.8)	5510 (± 22.4)	6790 (± 25.4)

End point values	Panel E1 & E2: Full-term Clesrovimab 100mg Single Dose IM Inj			
Subject group type	Subject analysis set			
Number of subjects analysed	31			
Units: day*µg/mL				
geometric mean (geometric coefficient of variation)	5690 (± 15.9)			

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Maximum Serum Concentration (Tmax) of Clesrovimab

End point title	Time to Maximum Serum Concentration (Tmax) of Clesrovimab
End point description:	Tmax is the amount of time required to reach Cmax.
End point type	Secondary
End point timeframe:	At designated time points (up to 1 year post-dose)

End point values	Panel A: Pre-term Clesrovimab 20mg Single Dose IM Injection	Panel B: Pre-term Clesrovimab 50mg Single Dose IM Injection	Panel C: Pre-term Clesrovimab 75mg Single Dose IM Injection	Panel D1 & D2: Pre-term Clesrovimab 100mg Single Dose IM Inj
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	5	33	40	32
Units: day				
median (full range (min-max))	4.0 (3.80 to 4.60)	4.20 (3.70 to 5.30)	4.20 (3.00 to 5.80)	4.10 (3.70 to 6.00)

End point values	Panel E1 & E2: Full-term Clesrovimab 100mg Single Dose IM Inj			
Subject group type	Subject analysis set			
Number of subjects analysed	31			
Units: day				
median (full range (min-max))	4.10 (3.70 to 4.90)			

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum Serum Concentration (Cmax) of Clesrovimab

End point title	Maximum Serum Concentration (Cmax) of Clesrovimab
End point description: Cmax is the highest observed serum drug concentration.	
End point type	Secondary
End point timeframe: At designated time points (up to 1 year post-dose)	

End point values	Panel A: Pre-term Clesrovimab 20mg Single Dose IM Injection	Panel B: Pre-term Clesrovimab 50mg Single Dose IM Injection	Panel C: Pre-term Clesrovimab 75mg Single Dose IM Injection	Panel D1 & D2: Pre-term Clesrovimab 100mg Single Dose IM Inj
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	5	33	40	32
Units: µg/mL				
geometric mean (geometric coefficient of variation)	26.3 (± 19.3)	61.7 (± 21.8)	94.5 (± 20.5)	117 (± 23.5)

End point values	Panel E1 & E2: Full-term Clesrovimab 100mg Single Dose IM Inj			
Subject group type	Subject analysis set			
Number of subjects analysed	31			
Units: µg/mL				
geometric mean (geometric coefficient of variation)	99.9 (± 13.7)			

Statistical analyses

No statistical analyses for this end point

Secondary: Apparent Terminal Half-life (t_{1/2}) of Clesrovimab

End point title	Apparent Terminal Half-life (t _{1/2}) of Clesrovimab
End point description: t _{1/2} is the time required for 50% of drug to be cleared from serum.	
End point type	Secondary
End point timeframe: At designated time points (up to 1 year post-dose)	

End point values	Panel A: Pre-term Clesrovimab 20mg Single Dose IM Injection	Panel B: Pre-term Clesrovimab 50mg Single Dose IM Injection	Panel C: Pre-term Clesrovimab 75mg Single Dose IM Injection	Panel D1 & D2: Pre-term Clesrovimab 100mg Single Dose IM Inj
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	5	33	40	32
Units: day				
geometric mean (geometric coefficient of variation)	48.8 (± 34.6)	44.6 (± 10.9)	46.1 (± 15.1)	45.2 (± 13.7)

End point values	Panel E1 & E2: Full-term Clesrovimab 100mg Single Dose IM Inj			
Subject group type	Subject analysis set			
Number of subjects analysed	31			
Units: day				
geometric mean (geometric coefficient of variation)	43.0 (± 9.72)			

Statistical analyses

No statistical analyses for this end point

Secondary: Serum Concentration of Clesrovimab on Day 7 (C7days)

End point title	Serum Concentration of Clesrovimab on Day 7 (C7days)
End point description: Serum concentration of clesrovimab was measured on Day 7.	
End point type	Secondary
End point timeframe: Day 7	

End point values	Panel A: Pre-term Clesrovimab 20mg Single Dose IM Injection	Panel B: Pre-term Clesrovimab 50mg Single Dose IM Injection	Panel C: Pre-term Clesrovimab 75mg Single Dose IM Injection	Panel D1 & D2: Pre-term Clesrovimab 100mg Single Dose IM Inj
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	5	33	40	32
Units: µg/mL				
geometric mean (geometric coefficient of variation)	24.4 (± 20.4)	57.8 (± 21.6)	88.1 (± 20.4)	109 (± 23.0)

End point values	Panel E1 & E2: Full-term Clesrovimab 100mg Single Dose IM Inj			
Subject group type	Subject analysis set			
Number of subjects analysed	31			
Units: µg/mL				
geometric mean (geometric coefficient of variation)	92.8 (± 13.3)			

Statistical analyses

No statistical analyses for this end point

Secondary: Serum Concentration of Clesrovimab on Day 14 (C14days)

End point title	Serum Concentration of Clesrovimab on Day 14 (C14days)
End point description: Serum concentration of clesrovimab was measured on Day 14.	
End point type	Secondary
End point timeframe: Day 14	

End point values	Panel A: Pre-term Clesrovimab 20mg Single Dose IM Injection	Panel B: Pre-term Clesrovimab 50mg Single Dose IM Injection	Panel C: Pre-term Clesrovimab 75mg Single Dose IM Injection	Panel D1 & D2: Pre-term Clesrovimab 100mg Single Dose IM Inj
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	5	33	40	32
Units: µg/mL				
geometric mean (geometric coefficient of variation)	19.4 (± 22.1)	46.8 (± 20.6)	71.1 (± 19.7)	88.6 (± 21.8)

End point values	Panel E1 & E2: Full-term Clesrovimab 100mg Single Dose IM Inj			
Subject group type	Subject analysis set			
Number of subjects analysed	31			
Units: µg/mL				
geometric mean (geometric coefficient of variation)	75.4 (± 12.9)			

Statistical analyses

No statistical analyses for this end point

Secondary: Serum Concentration of Clesrovimab on Day 90 (C90days)

End point title	Serum Concentration of Clesrovimab on Day 90 (C90days)
End point description:	Serum concentration of clesrovimab was measured on Day 90.
End point type	Secondary
End point timeframe:	Day 90

End point values	Panel A: Pre-term Clesrovimab 20mg Single Dose IM Injection	Panel B: Pre-term Clesrovimab 50mg Single Dose IM Injection	Panel C: Pre-term Clesrovimab 75mg Single Dose IM Injection	Panel D1 & D2: Pre-term Clesrovimab 100mg Single Dose IM Inj
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	5	33	40	32
Units: µg/mL				
geometric mean (geometric coefficient of variation)	5.60 (± 49.5)	13.0 (± 25.4)	20.4 (± 25.8)	25.2 (± 28.6)

End point values	Panel E1 & E2: Full-term Clesrovimab 100mg Single Dose IM Inj			
Subject group type	Subject analysis set			
Number of subjects analysed	31			
Units: µg/mL				
geometric mean (geometric coefficient of variation)	21.1 (± 18.8)			

Statistical analyses

No statistical analyses for this end point

Secondary: Serum Concentration of Clesrovimab on Day 150 (C150days)

End point title	Serum Concentration of Clesrovimab on Day 150 (C150days)
End point description:	Serum concentration of clesrovimab was measured on Day 150.
End point type	Secondary
End point timeframe:	Day 150

End point values	Panel A: Pre-term Clesrovimab 20mg Single Dose IM Injection	Panel B: Pre-term Clesrovimab 50mg Single Dose IM Injection	Panel C: Pre-term Clesrovimab 75mg Single Dose IM Injection	Panel D1 & D2: Pre-term Clesrovimab 100mg Single Dose IM Inj
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	5	33	40	32
Units: µg/mL				
geometric mean (geometric coefficient of variation)	2.24 (± 80.6)	4.98 (± 34.2)	8.05 (± 37.7)	9.70 (± 40.2)

End point values	Panel E1 & E2: Full-term Clesrovimab 100mg Single Dose IM Inj			
Subject group type	Subject analysis set			
Number of subjects analysed	31			
Units: µg/mL				
geometric mean (geometric coefficient of variation)	7.96 (± 26.7)			

Statistical analyses

No statistical analyses for this end point

Secondary: Serum Concentration of Clesrovimab on Day 365 (C365days)

End point title	Serum Concentration of Clesrovimab on Day 365 (C365days)
-----------------	--

End point description:

Serum concentration of clesrovimab was measured on Day 365.

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

End point timeframe:

Day 365

End point values	Panel A: Pre-term Clesrovimab 20mg Single Dose IM Injection	Panel B: Pre-term Clesrovimab 50mg Single Dose IM Injection	Panel C: Pre-term Clesrovimab 75mg Single Dose IM Injection	Panel D1 & D2: Pre-term Clesrovimab 100mg Single Dose IM Inj
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	5	33	40	32
Units: µg/mL				
geometric mean (geometric coefficient of variation)	0.0953 (± 362)	0.177 (± 79.4)	0.313 (± 107)	0.355 (± 104)

End point values	Panel E1 & E2: Full-term Clesrovimab 100mg Single Dose IM Inj			
Subject group type	Subject analysis set			
Number of subjects analysed	31			
Units: µg/mL				
geometric mean (geometric coefficient of variation)	0.248 (± 63.1)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with positive titer of Anti-Drug Antibodies

(ADAs) for Clesrovimab: Panels A, B, C, D1, D2, E1, and E2

End point title	Number of participants with positive titer of Anti-Drug Antibodies (ADAs) for Clesrovimab: Panels A, B, C, D1, D2, E1, and E2
End point description: Titer of ADAs to Clesrovimab was measured at several time points. ADA status of participants was reported.	
End point type	Secondary
End point timeframe: Days 14, 90, 150, 365 and 545.	

End point values	Panel A: Pre-term Clesrovimab 20mg Single Dose IM Injection	Panel B: Pre-term Clesrovimab 50mg Single Dose IM Injection	Panel C: Pre-term Clesrovimab 75mg Single Dose IM Injection	Panel D1 & D2: Pre-term Clesrovimab 100mg Single Dose IM Inj
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	6	33	40	32
Units: Participants				
Unevaluable participants	0	1	1	0
Evaluable participants	6	32	39	32
ADA Negative status	4	23	35	15
Inconclusive ADA status	0	0	0	0
Non-treatment emergent positive	0	0	0	1
ADA Positive response to MK-1654	2	9	4	16
Maximum Postdose Titer of 20 to < 189 of ADA	0	6	2	4
Maximum Postdose Titer of 189 to < 1077.5 of ADA	0	1	1	3
Maximum Postdose Titer of 1077.5 to < 9285 of ADA	0	0	1	4
Maximum Postdose Titer of 9285 to 160000 of ADA	2	2	0	4

End point values	Panel E1 & E2: Full-term Clesrovimab 100mg Single Dose IM Inj			
Subject group type	Subject analysis set			
Number of subjects analysed	32			
Units: Participants				
Unevaluable participants	2			
Evaluable participants	30			
ADA Negative status	9			
Inconclusive ADA status	0			
Non-treatment emergent positive	1			
ADA Positive response to MK-1654	20			
Maximum Postdose Titer of 20 to < 189 of ADA	2			

Maximum Postdose Titer of 189 to < 1077.5 of ADA	7			
Maximum Postdose Titer of 1077.5 to < 9285 of ADA	7			
Maximum Postdose Titer of 9285 to 160000 of ADA	4			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Through database cutoff date of 14-Sep-2022 (Up to approximately 48 months).

Adverse event reporting additional description:

Although, 183 participants were randomized and 181 were dosed, and included in the All Participants as Treated (APaT) population, two participants who were randomized to the MK-1654 20 mg dose group actually received MK-1654 50 mg and were included in the MK-1654 50 mg group for all safety analyses.

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

Dictionary used

Dictionary name	MedDRA
-----------------	--------

Dictionary version	25.0
--------------------	------

Reporting groups

Reporting group title	MK-1654 20 mg in Pre-term Infants
-----------------------	-----------------------------------

Reporting group description: -

Reporting group title	MK-1654 50 mg in Pre-term Infants
-----------------------	-----------------------------------

Reporting group description: -

Reporting group title	Placebo
-----------------------	---------

Reporting group description: -

Reporting group title	MK-1654 100 mg Pre-Term Infants
-----------------------	---------------------------------

Reporting group description: -

Reporting group title	MK-1654 100 mg Full-Term Infants
-----------------------	----------------------------------

Reporting group description: -

Reporting group title	MK-1654 75 mg in Pre-term Infants
-----------------------	-----------------------------------

Reporting group description: -

Serious adverse events	MK-1654 20 mg in Pre-term Infants	MK-1654 50 mg in Pre-term Infants	Placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 6 (16.67%)	4 / 33 (12.12%)	6 / 38 (15.79%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Wound dehiscence			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Toxicity to various agents			
subjects affected / exposed	0 / 6 (0.00%)	1 / 33 (3.03%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Gastrointestinal disorders			
Gastroesophageal reflux disease			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	1 / 38 (2.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Biliary cyst			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Irregular breathing			
subjects affected / exposed	0 / 6 (0.00%)	1 / 33 (3.03%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Pneumonia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 33 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 33 (3.03%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Croup infectious			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19			

subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchiolitis			
subjects affected / exposed	1 / 6 (16.67%)	0 / 33 (0.00%)	2 / 38 (5.26%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rhinovirus infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory syncytial virus infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory syncytial virus bronchiolitis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 33 (3.03%)	3 / 38 (7.89%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 6 (0.00%)	1 / 33 (3.03%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	MK-1654 100 mg Pre-Term Infants	MK-1654 100 mg Full-Term Infants	MK-1654 75 mg in Pre-term Infants
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 32 (9.38%)	6 / 32 (18.75%)	1 / 40 (2.50%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Wound dehiscence			

subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	1 / 40 (2.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Toxicity to various agents			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Gastroesophageal reflux disease			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Biliary cyst			
subjects affected / exposed	0 / 32 (0.00%)	1 / 32 (3.13%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Irregular breathing			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Pneumonia			
subjects affected / exposed	0 / 32 (0.00%)	2 / 32 (6.25%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	0 / 32 (0.00%)	1 / 32 (3.13%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Croup infectious			

subjects affected / exposed	0 / 32 (0.00%)	1 / 32 (3.13%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	1 / 32 (3.13%)	0 / 32 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19			
subjects affected / exposed	1 / 32 (3.13%)	0 / 32 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchiolitis			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rhinovirus infection			
subjects affected / exposed	0 / 32 (0.00%)	1 / 32 (3.13%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory syncytial virus infection			
subjects affected / exposed	1 / 32 (3.13%)	1 / 32 (3.13%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory syncytial virus bronchiolitis			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	MK-1654 20 mg in Pre-term Infants	MK-1654 50 mg in Pre-term Infants	Placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 6 (100.00%)	29 / 33 (87.88%)	33 / 38 (86.84%)
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	1 / 6 (16.67%)	0 / 33 (0.00%)	0 / 38 (0.00%)
occurrences (all)	1	0	0
Accidental overdose			
subjects affected / exposed	0 / 6 (0.00%)	2 / 33 (6.06%)	0 / 38 (0.00%)
occurrences (all)	0	2	0
Nervous system disorders			
Somnolence			
subjects affected / exposed	1 / 6 (16.67%)	2 / 33 (6.06%)	4 / 38 (10.53%)
occurrences (all)	1	2	4
General disorders and administration site conditions			
Injection site pain			
subjects affected / exposed	2 / 6 (33.33%)	0 / 33 (0.00%)	1 / 38 (2.63%)
occurrences (all)	2	0	2
Injection site erythema			
subjects affected / exposed	1 / 6 (16.67%)	2 / 33 (6.06%)	1 / 38 (2.63%)
occurrences (all)	1	2	1
Pyrexia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 33 (3.03%)	1 / 38 (2.63%)
occurrences (all)	0	1	1
Injection site swelling			
subjects affected / exposed	2 / 6 (33.33%)	1 / 33 (3.03%)	1 / 38 (2.63%)
occurrences (all)	2	1	1
Gastrointestinal disorders			
Teething			
subjects affected / exposed	0 / 6 (0.00%)	1 / 33 (3.03%)	0 / 38 (0.00%)
occurrences (all)	0	2	0
Flatulence			

subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 33 (0.00%) 0	0 / 38 (0.00%) 0
Diarrhoea subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	5 / 33 (15.15%) 5	5 / 38 (13.16%) 5
Constipation subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	0 / 33 (0.00%) 0	0 / 38 (0.00%) 0
Respiratory, thoracic and mediastinal disorders Rhinoorrhoea subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	2 / 33 (6.06%) 2	1 / 38 (2.63%) 1
Cough subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	3 / 33 (9.09%) 3	2 / 38 (5.26%) 2
Nasal congestion subjects affected / exposed occurrences (all)	2 / 6 (33.33%) 2	5 / 33 (15.15%) 6	5 / 38 (13.16%) 5
Skin and subcutaneous tissue disorders Pruritus subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	0 / 33 (0.00%) 0	0 / 38 (0.00%) 0
Miliaria subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 33 (0.00%) 0	1 / 38 (2.63%) 1
Dermatitis diaper subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	2 / 33 (6.06%) 2	1 / 38 (2.63%) 1
Rash papular subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 33 (3.03%) 1	0 / 38 (0.00%) 0
Rash maculo-papular subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 33 (0.00%) 0	2 / 38 (5.26%) 2
Rash			

subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 33 (3.03%) 1	0 / 38 (0.00%) 0
Psychiatric disorders Irritability subjects affected / exposed occurrences (all)	2 / 6 (33.33%) 2	7 / 33 (21.21%) 7	9 / 38 (23.68%) 10
Infections and infestations Croup infectious subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 33 (0.00%) 0	2 / 38 (5.26%) 2
Ear infection subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 33 (0.00%) 0	0 / 38 (0.00%) 0
Gastroenteritis subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 33 (3.03%) 1	0 / 38 (0.00%) 0
Lower respiratory tract infection subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 33 (3.03%) 1	1 / 38 (2.63%) 1
Conjunctivitis subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 33 (0.00%) 0	0 / 38 (0.00%) 0
COVID-19 subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 33 (0.00%) 0	3 / 38 (7.89%) 3
Bronchitis subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	3 / 33 (9.09%) 7	1 / 38 (2.63%) 1
Nasopharyngitis subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	2 / 33 (6.06%) 7	7 / 38 (18.42%) 19
Bronchiolitis subjects affected / exposed occurrences (all)	2 / 6 (33.33%) 3	2 / 33 (6.06%) 3	5 / 38 (13.16%) 9
Otitis media			

subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	3 / 38 (7.89%)
occurrences (all)	0	0	3
Otitis media acute			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	2 / 38 (5.26%)
occurrences (all)	0	0	2
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 6 (0.00%)	2 / 33 (6.06%)	5 / 38 (13.16%)
occurrences (all)	0	2	7
Viral pharyngitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	1 / 38 (2.63%)
occurrences (all)	0	0	1
Upper respiratory tract infection			
subjects affected / exposed	2 / 6 (33.33%)	17 / 33 (51.52%)	12 / 38 (31.58%)
occurrences (all)	2	22	22
Respiratory tract infection			
subjects affected / exposed	0 / 6 (0.00%)	1 / 33 (3.03%)	0 / 38 (0.00%)
occurrences (all)	0	1	0
Rhinitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	2 / 38 (5.26%)
occurrences (all)	0	0	2
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 6 (16.67%)	1 / 33 (3.03%)	1 / 38 (2.63%)
occurrences (all)	1	1	1

Non-serious adverse events	MK-1654 100 mg Pre-Term Infants	MK-1654 100 mg Full-Term Infants	MK-1654 75 mg in Pre-term Infants
Total subjects affected by non-serious adverse events			
subjects affected / exposed	26 / 32 (81.25%)	29 / 32 (90.63%)	29 / 40 (72.50%)
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	0 / 40 (0.00%)
occurrences (all)	0	0	0
Accidental overdose			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	0 / 40 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			

Somnolence subjects affected / exposed occurrences (all)	1 / 32 (3.13%) 1	1 / 32 (3.13%) 1	5 / 40 (12.50%) 5
General disorders and administration site conditions			
Injection site pain subjects affected / exposed occurrences (all)	2 / 32 (6.25%) 2	0 / 32 (0.00%) 0	2 / 40 (5.00%) 3
Injection site erythema subjects affected / exposed occurrences (all)	1 / 32 (3.13%) 1	1 / 32 (3.13%) 1	1 / 40 (2.50%) 1
Pyrexia subjects affected / exposed occurrences (all)	2 / 32 (6.25%) 2	1 / 32 (3.13%) 2	0 / 40 (0.00%) 0
Injection site swelling subjects affected / exposed occurrences (all)	0 / 32 (0.00%) 0	1 / 32 (3.13%) 2	0 / 40 (0.00%) 0
Gastrointestinal disorders			
Teething subjects affected / exposed occurrences (all)	0 / 32 (0.00%) 0	3 / 32 (9.38%) 3	0 / 40 (0.00%) 0
Flatulence subjects affected / exposed occurrences (all)	0 / 32 (0.00%) 0	0 / 32 (0.00%) 0	3 / 40 (7.50%) 3
Diarrhoea subjects affected / exposed occurrences (all)	2 / 32 (6.25%) 2	4 / 32 (12.50%) 4	2 / 40 (5.00%) 2
Constipation subjects affected / exposed occurrences (all)	0 / 32 (0.00%) 0	2 / 32 (6.25%) 2	0 / 40 (0.00%) 0
Respiratory, thoracic and mediastinal disorders			
Rhinorrhoea subjects affected / exposed occurrences (all)	4 / 32 (12.50%) 6	3 / 32 (9.38%) 11	1 / 40 (2.50%) 1
Cough subjects affected / exposed occurrences (all)	2 / 32 (6.25%) 3	3 / 32 (9.38%) 8	1 / 40 (2.50%) 1

Nasal congestion subjects affected / exposed occurrences (all)	6 / 32 (18.75%) 6	8 / 32 (25.00%) 11	2 / 40 (5.00%) 2
Skin and subcutaneous tissue disorders			
Pruritus subjects affected / exposed occurrences (all)	0 / 32 (0.00%) 0	0 / 32 (0.00%) 0	0 / 40 (0.00%) 0
Miliaria subjects affected / exposed occurrences (all)	2 / 32 (6.25%) 2	1 / 32 (3.13%) 1	0 / 40 (0.00%) 0
Dermatitis diaper subjects affected / exposed occurrences (all)	2 / 32 (6.25%) 2	1 / 32 (3.13%) 1	0 / 40 (0.00%) 0
Rash papular subjects affected / exposed occurrences (all)	0 / 32 (0.00%) 0	4 / 32 (12.50%) 4	0 / 40 (0.00%) 0
Rash maculo-papular subjects affected / exposed occurrences (all)	0 / 32 (0.00%) 0	0 / 32 (0.00%) 0	0 / 40 (0.00%) 0
Rash subjects affected / exposed occurrences (all)	2 / 32 (6.25%) 2	0 / 32 (0.00%) 0	1 / 40 (2.50%) 1
Psychiatric disorders			
Irritability subjects affected / exposed occurrences (all)	2 / 32 (6.25%) 2	2 / 32 (6.25%) 2	5 / 40 (12.50%) 6
Infections and infestations			
Croup infectious subjects affected / exposed occurrences (all)	0 / 32 (0.00%) 0	3 / 32 (9.38%) 5	1 / 40 (2.50%) 1
Ear infection subjects affected / exposed occurrences (all)	2 / 32 (6.25%) 2	1 / 32 (3.13%) 1	0 / 40 (0.00%) 0
Gastroenteritis subjects affected / exposed occurrences (all)	1 / 32 (3.13%) 1	6 / 32 (18.75%) 8	0 / 40 (0.00%) 0
Lower respiratory tract infection			

subjects affected / exposed	2 / 32 (6.25%)	2 / 32 (6.25%)	0 / 40 (0.00%)
occurrences (all)	2	2	0
Conjunctivitis			
subjects affected / exposed	1 / 32 (3.13%)	2 / 32 (6.25%)	0 / 40 (0.00%)
occurrences (all)	1	2	0
COVID-19			
subjects affected / exposed	0 / 32 (0.00%)	2 / 32 (6.25%)	2 / 40 (5.00%)
occurrences (all)	0	2	2
Bronchitis			
subjects affected / exposed	1 / 32 (3.13%)	1 / 32 (3.13%)	3 / 40 (7.50%)
occurrences (all)	1	1	4
Nasopharyngitis			
subjects affected / exposed	10 / 32 (31.25%)	10 / 32 (31.25%)	11 / 40 (27.50%)
occurrences (all)	20	22	19
Bronchiolitis			
subjects affected / exposed	7 / 32 (21.88%)	5 / 32 (15.63%)	4 / 40 (10.00%)
occurrences (all)	8	6	6
Otitis media			
subjects affected / exposed	1 / 32 (3.13%)	1 / 32 (3.13%)	0 / 40 (0.00%)
occurrences (all)	1	5	0
Otitis media acute			
subjects affected / exposed	0 / 32 (0.00%)	1 / 32 (3.13%)	0 / 40 (0.00%)
occurrences (all)	0	1	0
Viral upper respiratory tract infection			
subjects affected / exposed	1 / 32 (3.13%)	1 / 32 (3.13%)	0 / 40 (0.00%)
occurrences (all)	1	1	0
Viral pharyngitis			
subjects affected / exposed	0 / 32 (0.00%)	2 / 32 (6.25%)	0 / 40 (0.00%)
occurrences (all)	0	2	0
Upper respiratory tract infection			
subjects affected / exposed	12 / 32 (37.50%)	18 / 32 (56.25%)	7 / 40 (17.50%)
occurrences (all)	19	52	8
Respiratory tract infection			
subjects affected / exposed	1 / 32 (3.13%)	2 / 32 (6.25%)	0 / 40 (0.00%)
occurrences (all)	1	2	0
Rhinitis			

subjects affected / exposed occurrences (all)	0 / 32 (0.00%) 0	0 / 32 (0.00%) 0	1 / 40 (2.50%) 1
Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all)	0 / 32 (0.00%) 0	0 / 32 (0.00%) 0	0 / 40 (0.00%) 0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
04 September 2018	The primary reason for amendment 1 was to extend the scope and duration of post-dose safety monitoring to support the safety evaluation of MK-1654.
07 February 2019	The primary reason for amendment 2 was to ensure that all instances of hives or welts are evaluated to ensure consistent follow-up of potential allergic reactions.
28 February 2020	The primary reason for amendment 3 was to remove the restrictions for the administration of rotavirus vaccine.
05 October 2020	The primary reason for amendment 4 was to modify the blood collection schedule for Panels D and E adding Day 545 postdose blood draw for ADA and SNA collection for participants enrolled in Panels D and E prior to Amendment 04 who chose to participate in the modified blood collection schedule and Panel D and E participants enrolled under Amendment 04. The SAE follow-up period for these participants was extended to Day 545 accordingly; to discontinue the collection of microsample blood for ADA for all Panels; to discontinue the collection of microsample blood for PK for Panels D and E; document 100 mg as the selected dose for Panels D and E; to allow the oral polio vaccine to be administered concomitantly with MK- 1654

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
01 April 2019	An out of specification (OOS) pause on enrollment and dosing was initiated by MSD as a precautionary measure on 1-APR-2019 due to small number of visible particles per vial on stability testing on the original MK-1654 lot used for P002 supply. Further investigations revealed the visible particles were MK-1654 aggregates. The original lot was replaced with a new one, meeting all criteria, resuming dosing in the study on 31-Aug-2019 with agreement from FDA.	31 August 2019

Notes:

Limitations and caveats

None reported