Clinical trial results:
A Randomized, Double-Blind, Placebo-Controlled Clinical Trial to Evaluate the Safety, Tolerability, Pharmacokinetics, and Efficacy of a Single Infusion of Bezlotoxumab (MK-6072, Human Monoclonal Antibody to C. difficile Toxin B) in Children Aged 1 to <18 Years Receiving Antibacterial Drug Treatment for C. difficile Infection (MODIFY III)

Summary

EudraCT number	2017-000070-11
Trial protocol	CZ ES PT SE DE NO HU PL Outside EU/EEA GB
Global end of trial date	12 May 2022

Results information

Result version number	v2 (current)
This version publication date	28 June 2023
First version publication date	22 October 2022
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	6072-001

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03182907
WHO universal trial number (UTN)	-
Other trial identifiers	Merck Protocol Number: MK-6072-001

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)	EMEA-001645-PIP01-14
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	12 May 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	12 May 2022
Global end of trial reached?	Yes
Global end of trial date	12 May 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objectives of this study are to evaluate the pharmacokinetics (PK), safety, and tolerability of bezlotoxumab (MK-6072) in children aged 1 to <18 years of age with a confirmed diagnosis of Clostridium difficile (C. Difficile) infection (CDI) who are receiving antibacterial drug treatment.

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:

Antibacterial drug treatment (ABD) will be administered for 10-21 days including the duration of ABD prior to the screening visit, during the screening period, and after the infusion of study treatment, per institutional guidelines, at the investigator's discretion. ABD is defined as the receipt of oral metronidazole, oral vancomycin, intravenous (IV) metronidazole concurrent with oral vancomycin, oral fidaxomicin, or oral fidaxomicin concurrent with IV metronidazole.

Evidence for comparator: -

Actual start date of recruitment	27 March 2018
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	Brazil: 19
Country: Number of subjects enrolled	Colombia: 4
Country: Number of subjects enrolled	Czechia: 24
Country: Number of subjects enrolled	Germany: 8
Country: Number of subjects enrolled	Hungary: 14
Country: Number of subjects enrolled	Malaysia: 3
Country: Number of subjects enrolled	Mexico: 10
Country: Number of subjects enrolled	Norway: 2
Country: Number of subjects enrolled	Poland: 4
Country: Number of subjects enrolled	Portugal: 2
Country: Number of subjects enrolled	South Africa: 3
Country: Number of subjects enrolled	Spain: 19
Country: Number of subjects enrolled	Sweden: 1

Country: Number of subjects enrolled	United Kingdom: 3
Country: Number of subjects enrolled	United States: 32
Worldwide total number of subjects	148
EEA total number of subjects	74

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	6
Children (2-11 years)	80
Adolescents (12-17 years)	62
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

148 participants were randomized in the study of which 143 participants received study intervention and were used for safety analysis.

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Bezlotoxumab

Arm description:

Participants received 10 mg of bezlotoxumab per kg body weight via a single 60-minute (±10 minutes) intravenous (IV) infusion on Day 1. Additionally, participants received background ABD for 10-21 days per institutional guidelines, at the investigator's discretion.

Arm type	Experimental
Investigational medicinal product name	Bezlotoxumab
Investigational medicinal product code	
Other name	MK-6072
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

10 mg of bezlotoxumab per kg body weight via a 60-minute (±10 minutes) IV infusion on Day 1

Arm title	Placebo

Arm description:

Participants received placebo for bezlotoxumab consisting of either 0.9% sodium chloride or 5% dextrose via a single 60-minute (±10 minutes) IV infusion on Day 1. Additionally, participants received background ABD for 10-21 days per institutional guidelines, at the investigator's discretion.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

0.9% sodium chloride or 5% dextrose via a 60-minute (±10 minutes) IV infusion on Day 1

Number of subjects in period 1	Bezlotoxumab	Placebo
Started	111	37
Treated	107	36
Completed	103	35
Not completed	8	2
Death	3	-
Withdrawal by Parent/Guardian	-	2
Lost to follow-up	1	-
Protocol deviation	4	-

Baseline characteristics

Reporting groups	
Reporting group title	Bezlotoxumab
Reporting group description:	
Participants received 10 mg of bezlotoxumab per kg body weight via a single 60-minute (±10 minutes) intravenous (IV) infusion on Day 1. Additionally, participants received background ABD for 10-21 days per institutional guidelines, at the investigator's discretion.	
Reporting group title	Placebo
Reporting group description:	
Participants received placebo for bezlotoxumab consisting of either 0.9% sodium chloride or 5% dextrose via a single 60-minute (±10 minutes) IV infusion on Day 1. Additionally, participants received background ABD for 10-21 days per institutional guidelines, at the investigator's discretion.	

Reporting group values	Bezlotoxumab	Placebo	Total
Number of subjects	111	37	148
Age Categorical Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)			
From 65-84 years			
85 years and over			
Age Continuous Units: years			
arithmetic mean	9.2	9.3	
standard deviation	± 5.4	± 5.3	-
Gender Categorical Units: Participants			
Female	51	18	69
Male	60	19	79
Race Units: Subjects			
American Indian or Alaska Native	2	0	2
Asian	3	2	5
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	6	1	7
White	87	32	119
More than one race	9	1	10
Unknown or Not Reported	4	1	5
Ethnicity Units: Subjects			
Hispanic Or Latino	29	9	38
Not Hispanic Or Latino	72	27	99

Not Reported	10	1	11

End points

End points reporting groups

Reporting group title	Bezlotoxumab
Reporting group description:	
Participants received 10 mg of bezlotoxumab per kg body weight via a single 60-minute (±10 minutes) intravenous (IV) infusion on Day 1. Additionally, participants received background ABD for 10-21 days per institutional guidelines, at the investigator's discretion.	
Reporting group title	Placebo
Reporting group description:	
Participants received placebo for bezlotoxumab consisting of either 0.9% sodium chloride or 5% dextrose via a single 60-minute (±10 minutes) IV infusion on Day 1. Additionally, participants received background ABD for 10-21 days per institutional guidelines, at the investigator's discretion.	
Subject analysis set title	Bezlotoxumab: Cohort 1 (12 to <18 years age)
Subject analysis set type	Per protocol
Subject analysis set description:	
Participants aged 12 to <18 years of age received 10 mg of bezlotoxumab per kg body weight via a single 60-minute (±10 minutes) IV infusion on Day 1. Additionally, participants received background ABD for 10-21 days per institutional guidelines, at the investigator's discretion.	
Subject analysis set title	Bezlotoxumab: Cohort 2 (1 to <12 years of age)
Subject analysis set type	Per protocol
Subject analysis set description:	
Participants aged 1 to <12 years of age received 10 mg of bezlotoxumab per kg body weight via a single 60-minute (±10 minutes) IV infusion on Day 1. Additionally, participants received background ABD for 10-21 days per institutional guidelines, at the investigator's discretion.	

Primary: Percentage of Participants Who Experienced an Adverse Event (AE)

End point title	Percentage of Participants Who Experienced an Adverse Event (AE)
End point description:	
An AE was defined as any untoward medical occurrence associated with the use of a drug in a participant, whether or not considered drug related. An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding, for example), symptom, or disease temporally associated with the use of a medicinal product and does not imply any judgment about causality. The analysis population included all participants who received study intervention. Per protocol, percentage of participants with AEs in the bezlotoxumab and placebo groups were presented.	
End point type	Primary
End point timeframe:	
Up to approximately 12 weeks	

End point values	Bezlotoxumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	107	36		
Units: Percentage of participants				
number (not applicable)	88.8	94.4		

Statistical analyses

Statistical analysis title	Estimated difference in percentage
Comparison groups	Bezlotoxumab v Placebo
Number of subjects included in analysis	143
Analysis specification	Pre-specified
Analysis type	other[1]
Parameter estimate	Difference in percentage
Point estimate	-5.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-14.5
upper limit	7.7

Notes:

[1] - Miettinen & Nurminen method was used to generate the estimated difference in percentage and associated 95% confidence intervals (CIs) in bezlotoxumab versus placebo arms.

Primary: Area Under the Concentration-Time Curve of Bezlotoxumab From Time 0 to Infinity (AUC 0-inf)

End point title	Area Under the Concentration-Time Curve of Bezlotoxumab From Time 0 to Infinity (AUC 0-inf)[2]

End point description:

Blood samples were collected at specified intervals for the determination of AUC0-inf. AUC0-inf was defined as the area under the concentration-time curve of bezlotoxumab from time zero to infinity. The analysis population included all participants who received bezlotoxumab, had at least 4 postdose AUC0-inf samples and complied with the protocol. Per protocol, AUC0-inf of bezlotoxumab was determined for each age cohort.

End point type	Primary

End point timeframe:

Day 1 (2 hours postdose), Days 10, 29, 57, and 85

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: There was no between arm statistical analysis planned for this endpoint.

End point values	Bezlotoxumab: Cohort 1 (12 to <18 years age)	Bezlotoxumab: Cohort 2 (1 to <12 years of age)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	36	54		
Units: hr*ug/mL				
geometric mean (confidence interval 95%)	56100 (49400 to 63700)	43200 (38900 to 47900)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants Who Discontinued Study Due to an AE

End point title	Percentage of Participants Who Discontinued Study Due to an AE

End point description:

An AE was defined as any untoward medical occurrence associated with the use of a drug in a

participant, whether or not considered drug related. An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding, for example), symptom, or disease temporally associated with the use of a medicinal product and does not imply any judgment about causality. The analysis population included all participants who received study intervention. Per protocol, percentage of participants who discontinued study due to AEs in the bezlotoxumab and placebo groups were presented.

End point type	Primary

End point timeframe:

Up to approximately 12 weeks

End point values	Bezlotoxumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	107	36		
Units: Percentage of participants				
number (not applicable)	0	0		

Statistical analyses

Statistical analysis title	Estimated difference in percentage
Comparison groups	Bezlotoxumab v Placebo
Number of subjects included in analysis	143
Analysis specification	Pre-specified
Analysis type	other[3]
Parameter estimate	Difference in percentage
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.7
upper limit	3.5

Notes:

[3] - Miettinen & Nurminen method was used to generate the estimated difference in percentage and associated 95% CIs in bezlotoxumab versus placebo arms.

Secondary: Percentage of Participants Who Had a Clostridium Difficile Infection (CDI) Recurrence

End point title	Percentage of Participants Who Had a Clostridium Difficile Infection (CDI) Recurrence

End point description:

CDI recurrence was defined as diarrhea recurrence (new episode of diarrhea after initial clinical response [ICR] as defined by a change in normal bowel habits for ≥2 days with either watery diarrhea or at least 6 unformed bowel movements [UBMs] within 48-hours) associated with a positive stool test for C. difficile toxin, and for which the participant, in the investigator's opinion, requires and receives ABD treatment for CDI. The analysis population included all participants who received any amount of study intervention, had positive local stool for C. difficile toxin, were taking protocol-defined ABD treatment for CDI on the day of infusion, and achieved an ICR of baseline CDI. Per protocol, percentage of participants who had a CDI recurrence in the bezlotoxumab and placebo groups were reported.

End point type	Secondary

End point timeframe:

Up to approximately 12 Weeks

End point values	Bezlotoxumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	98	34		
Units: Percentage of participants				
number (not applicable)	11.2	14.7		

Statistical analyses

Statistical analysis title	Treatment difference
Comparison groups	Bezlotoxumab v Placebo
Number of subjects included in analysis	132
Analysis specification	Pre-specified
Analysis type	other[4]
P-value	= 0.5701
Method	Stratified Miettinen and Nurminen method
Parameter estimate	Adjusted difference
Point estimate	-3.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-20
upper limit	8

Notes:

[4] - Miettinen and Nurminen method stratified by age cohort (12 to <18 years of age, 1 to <12 years of age) with a Cochran-Mantel-Haenszel weight was used to generate the treatment difference, associated 95% CIs and a 2-sided p-value.

Secondary: Percentage of Participants Who Had a Sustained Clinical Response (SCR)

End point title	Percentage of Participants Who Had a Sustained Clinical Response (SCR)

End point description:

SCR was defined as the ICR of baseline CDI episode (improvement in number and character of bowel movements and doesn’t require further CDI therapy within 2 days after completion of up to 21 days of ABD treatment for CDI) and no CDI recurrence (diarrhea recurrence associated with a positive stool test for C. difficile toxin, and for which the participant, in investigator's opinion, requires and receives ABD for CDI). The analysis population included all participants who received any amount of study intervention, had positive local stool for C. difficile toxin, and were taking protocol-defined ABD treatment for CDI on the day of infusion. Per protocol, percentage of participants who had a SCR in bezlotoxumab and placebo groups were presented.

End point type	Secondary

End point timeframe:

Up to approximately 12 Weeks

End point values	Bezlotoxumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	104	35		
Units: Percentage of participants				
number (not applicable)	83.7	82.9		

Statistical analyses

Statistical analysis title	Treatment difference
Comparison groups	Bezlotoxumab v Placebo
Number of subjects included in analysis	139
Analysis specification	Pre-specified
Analysis type	other[5]
P-value	= 0.9165
Method	Stratified Miettinen and Nurminen method
Parameter estimate	Adjusted difference
Point estimate	0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-11.8
upper limit	17.6

Notes:

[5] - Miettinen and Nurminen method stratified by age cohort (12 to <18 years of age, 1 to <12 years of age) with a Cochran-Mantel-Haenszel weight was used to generate the treatment difference, associated 95% CIs and a 2-sided p-value.

Secondary: Percentage of High-Risk Participants Who Experienced a CDI Recurrence

End point title	Percentage of High-Risk Participants Who Experienced a CDI Recurrence

End point description:

CDI recurrence was defined as diarrhea recurrence (new diarrhea episode after ICR defined by change in normal bowel habits for ≥2 days with watery diarrhea or at least 6 UBMs within 48-hours) with positive stool test for C. difficile toxin for which participant, in investigator's opinion, requires and receives ABD for CDI. High-risk was meeting ≥1 criteria at/before randomization: a) was immunocompromised b) had ≥1 CDI episode prior to baseline episode c) had severe CDI baseline episode d) had C. difficile ribotype027 in stool at baseline CDI episode e) received ≥1 systemic ABD known to increase CDI risk. The analysis population included all participants who received study intervention, had positive local stool for C. difficile toxin, were taking ABD for CDI on infusion day, achieved ICR of baseline CDI, and were at high-risk of CDI recurrence. Per protocol, percentage of high-risk participants who experienced a CDI recurrence in the bezlotoxumab and placebo groups were presented.

End point type	Secondary

End point timeframe:

Up to approximately 12 Weeks

End point values	Bezlotoxumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	91	33		
Units: Percentage of participants				
number (not applicable)	12.1	15.2		

Statistical analyses

Statistical analysis title	Treatment Difference
Comparison groups	Bezlotoxumab v Placebo
Number of subjects included in analysis	124
Analysis specification	Pre-specified
Analysis type	other[6]
P-value	= 0.6542
Method	Unstratified Miettinen & Nurminen method
Parameter estimate	Adjusted Difference
Point estimate	-3.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-19.9
upper limit	9

Notes:

[6] - Unstratified Miettinen and Nurminen method was used to generate the treatment difference, associated 95% CIs and a 2-sided p-value.

Secondary: Percentage of High-Risk Participants Who Experienced a SCR

End point title	Percentage of High-Risk Participants Who Experienced a SCR

End point description:

SCR was ICR of baseline CDI episode (improvement in number and character of bowel movements and doesn’t require further CDI therapy within 2 days after completion of upto 21 days of ABD for CDI) and no CDI recurrence (diarrhea recurrence with positive stool test for C. difficile toxin, for which participant, in investigator's opinion, requires and receives ABD for CDI). High-risk was meeting ≥1 criteria: a) was immunocompromised b) had ≥1 episodes of CDI prior to baseline episode c) had severe CDI baseline episode d) had C. difficile ribotype027 in stool at baseline CDI episode e) received ≥1 systemic ABD known to increase CDI risk. The analysis population included all participants who received study intervention, had positive local stool for C. difficile toxin, were taking protocol-defined ABD for CDI on the day of infusion, and were at high risk of CDI recurrence. Per protocol, percentage of high-risk participants who had SCR in bezlotoxumab and placebo groups were presented.

End point type	Secondary

End point timeframe:

Up to approximately 12 Weeks

End point values	Bezlotoxumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	97	34		
Units: Percentage of participants				
number (not applicable)	82.5	82.4		

Statistical analyses

Statistical analysis title	Treatment difference
Comparison groups	Bezlotoxumab v Placebo
Number of subjects included in analysis	131
Analysis specification	Pre-specified
Analysis type	other[7]
P-value	= 0.9873
Method	Unstratified Miettinen & Nurminen method
Parameter estimate	Adjusted difference
Point estimate	0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-13
upper limit	17.4

Notes:

[7] - Unstratified Miettinen and Nurminen method was used to generate treatment difference, associated 95% CIs and a 2-sided p-value.

Secondary: Percentage of Participants Who Experienced One or More Infusion Related Reaction

End point title	Percentage of Participants Who Experienced One or More Infusion Related Reaction

End point description:

Infusion related reaction included events meeting any of the 3 criteria: 1) acute onset of an illness involving skin, mucosal tissue, or both and at least 1 of the following: respiratory compromise, reduced blood pressure (BP) or associated symptoms of end-organ dysfunction 2) two or more of the following after onset of study infusion: involving skin-mucosal tissue, respiratory compromise, reduced BP or associated symptoms, or persistent gastrointestinal symptoms 3) reduced BP after onset of infusion or >30% decrease in systolic BP from baseline. The analysis population included all participants who received study intervention. Per protocol, percentage of participants experiencing 1 or more infusion-related reactions within 24 hours following the start of study medication infusion were reported.

End point type	Secondary

End point timeframe:

Up to approximately 24 hours after infusion on Day 1

End point values	Bezlotoxumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	107	36		
Units: Percentage of participants				
number (not applicable)	0.93	2.78		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Who Had Positive Antibodies to Bezlotoxumab

End point title	Percentage of Participants Who Had Positive Antibodies to Bezlotoxumab

End point description:

Blood samples were collected to determine antibodies to bezlotoxumab. The analysis population included all participants who received any amount of bezlotoxumab, had a positive local stool for C. difficile toxin, were taking protocol-defined ABD drug treatment for CDI on the day of infusion, and achieved an ICR of baseline CDI. Per protocol, percentage of participants with treatment-emergent positive antibodies to bezlotoxumab following single infusion of bezlotoxumab were reported for each age cohort.

End point type	Secondary

End point timeframe:

Up to approximately 12 Weeks

End point values	Bezlotoxumab: Cohort 1 (12 to <18 years age)	Bezlotoxumab: Cohort 2 (1 to <12 years of age)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	44	62		
Units: Percentage of participants				
number (not applicable)	2.4	1.7		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to approximately 14 months

Adverse event reporting additional description:

All cause mortality was reported on all randomized participants and non-serious and serious AEs were reported on all participants who received study intervention.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	25.0

Reporting groups

Reporting group title	Placebo

Reporting group description:

Participants received placebo for bezlotoxumab consisting of either 0.9% sodium chloride or 5% dextrose via a single 60-minute (±10 minutes) IV infusion on Day 1. Additionally, participants received background ABD for 10-21 days per institutional guidelines, at the investigator's discretion.

Reporting group title	Bezlotoxumab

Reporting group description:

Participants received 10 mg of bezlotoxumab per kg body weight via a single 60-minute (±10 minutes) intravenous (IV) infusion on Day 1. Additionally, participants received background ABD for 10-21 days per institutional guidelines, at the investigator's discretion.

Serious adverse events	Placebo	Bezlotoxumab	
Total subjects affected by serious adverse events			
subjects affected / exposed	29 / 36 (80.56%)	57 / 107 (53.27%)	
number of deaths (all causes)	1	6	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Neuroblastoma			
subjects affected / exposed	1 / 36 (2.78%)	0 / 107 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Neoplasm progression			
subjects affected / exposed	1 / 36 (2.78%)	0 / 107 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Leukaemia			

subjects affected / exposed	0 / 36 (0.00%)	1 / 107 (0.93%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Acute myeloid leukaemia			
subjects affected / exposed	0 / 36 (0.00%)	1 / 107 (0.93%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Vascular disorders			
Venoocclusive disease			
subjects affected / exposed	1 / 36 (2.78%)	1 / 107 (0.93%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 36 (2.78%)	0 / 107 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mucosal inflammation			
subjects affected / exposed	0 / 36 (0.00%)	1 / 107 (0.93%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	3 / 36 (8.33%)	4 / 107 (3.74%)	
occurrences causally related to treatment / all	0 / 3	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	0 / 36 (0.00%)	1 / 107 (0.93%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Graft versus host disease			
subjects affected / exposed	0 / 36 (0.00%)	1 / 107 (0.93%)	
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			
Respiratory tract oedema			
subjects affected / exposed	0 / 36 (0.00%)	1 / 107 (0.93%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute respiratory distress syndrome			
subjects affected / exposed	0 / 36 (0.00%)	1 / 107 (0.93%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
C-reactive protein increased			
subjects affected / exposed	0 / 36 (0.00%)	1 / 107 (0.93%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
SARS-CoV-2 test positive			
subjects affected / exposed	0 / 36 (0.00%)	1 / 107 (0.93%)	
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			
Allergic transfusion reaction			
subjects affected / exposed	1 / 36 (2.78%)	0 / 107 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Loss of consciousness			
subjects affected / exposed	0 / 36 (0.00%)	1 / 107 (0.93%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Headache			
subjects affected / exposed	1 / 36 (2.78%)	0 / 107 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Seizure			

subjects affected / exposed	0 / 36 (0.00%)	1 / 107 (0.93%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nystagmus			
subjects affected / exposed	0 / 36 (0.00%)	1 / 107 (0.93%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neurotoxicity			
subjects affected / exposed	0 / 36 (0.00%)	1 / 107 (0.93%)	
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			
Bone marrow failure			
subjects affected / exposed	0 / 36 (0.00%)	1 / 107 (0.93%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Agranulocytosis			
subjects affected / exposed	0 / 36 (0.00%)	1 / 107 (0.93%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Leukocytosis			
subjects affected / exposed	0 / 36 (0.00%)	1 / 107 (0.93%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile neutropenia			
subjects affected / exposed	11 / 36 (30.56%)	22 / 107 (20.56%)	
occurrences causally related to treatment / all	0 / 17	0 / 30	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombocytopenia			
subjects affected / exposed	1 / 36 (2.78%)	3 / 107 (2.80%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenia			

subjects affected / exposed	0 / 36 (0.00%)	1 / 107 (0.93%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Intussusception			
subjects affected / exposed	0 / 36 (0.00%)	1 / 107 (0.93%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea			
subjects affected / exposed	0 / 36 (0.00%)	1 / 107 (0.93%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis			
subjects affected / exposed	1 / 36 (2.78%)	0 / 107 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stomatitis			
subjects affected / exposed	1 / 36 (2.78%)	1 / 107 (0.93%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	1 / 36 (2.78%)	0 / 107 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anal inflammation			
subjects affected / exposed	0 / 36 (0.00%)	1 / 107 (0.93%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain			
subjects affected / exposed	0 / 36 (0.00%)	3 / 107 (2.80%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			

Biliary-bronchial fistula			
subjects affected / exposed	0 / 36 (0.00%)	1 / 107 (0.93%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis			
subjects affected / exposed	1 / 36 (2.78%)	0 / 107 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	1 / 36 (2.78%)	0 / 107 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Myopathy			
subjects affected / exposed	0 / 36 (0.00%)	1 / 107 (0.93%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Acinetobacter sepsis			
subjects affected / exposed	0 / 36 (0.00%)	1 / 107 (0.93%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Adenovirus infection			
subjects affected / exposed	0 / 36 (0.00%)	1 / 107 (0.93%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenic infection			
subjects affected / exposed	0 / 36 (0.00%)	1 / 107 (0.93%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacterial sepsis			

subjects affected / exposed	0 / 36 (0.00%)	1 / 107 (0.93%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
COVID-19			
subjects affected / exposed	0 / 36 (0.00%)	2 / 107 (1.87%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Candida sepsis			
subjects affected / exposed	0 / 36 (0.00%)	2 / 107 (1.87%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clostridium difficile colitis			
subjects affected / exposed	2 / 36 (5.56%)	1 / 107 (0.93%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clostridium difficile infection			
subjects affected / exposed	1 / 36 (2.78%)	0 / 107 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronavirus infection			
subjects affected / exposed	1 / 36 (2.78%)	1 / 107 (0.93%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cytomegalovirus infection			
subjects affected / exposed	0 / 36 (0.00%)	1 / 107 (0.93%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enterobacter bacteraemia			
subjects affected / exposed	1 / 36 (2.78%)	1 / 107 (0.93%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Escherichia bacteraemia			

subjects affected / exposed	0 / 36 (0.00%)	1 / 107 (0.93%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fungal sepsis			
subjects affected / exposed	0 / 36 (0.00%)	1 / 107 (0.93%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	0 / 36 (0.00%)	1 / 107 (0.93%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Klebsiella bacteraemia			
subjects affected / exposed	0 / 36 (0.00%)	2 / 107 (1.87%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis sapovirus			
subjects affected / exposed	1 / 36 (2.78%)	0 / 107 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacteraemia			
subjects affected / exposed	0 / 36 (0.00%)	2 / 107 (1.87%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenic sepsis			
subjects affected / exposed	0 / 36 (0.00%)	1 / 107 (0.93%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nosocomial infection			
subjects affected / exposed	0 / 36 (0.00%)	1 / 107 (0.93%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Otitis media acute			

subjects affected / exposed	1 / 36 (2.78%)	0 / 107 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pharyngitis streptococcal			
subjects affected / exposed	1 / 36 (2.78%)	0 / 107 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pharyngotonsillitis			
subjects affected / exposed	0 / 36 (0.00%)	1 / 107 (0.93%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	0 / 36 (0.00%)	2 / 107 (1.87%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia aspiration			
subjects affected / exposed	0 / 36 (0.00%)	1 / 107 (0.93%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia fungal			
subjects affected / exposed	1 / 36 (2.78%)	0 / 107 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pseudomonal bacteraemia			
subjects affected / exposed	0 / 36 (0.00%)	1 / 107 (0.93%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pseudomonal sepsis			
subjects affected / exposed	0 / 36 (0.00%)	1 / 107 (0.93%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory syncytial virus infection			

subjects affected / exposed	1 / 36 (2.78%)	0 / 107 (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	1 / 36 (2.78%)	3 / 107 (2.80%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Septic shock			
subjects affected / exposed	0 / 36 (0.00%)	3 / 107 (2.80%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 1	
Serratia bacteraemia			
subjects affected / exposed	0 / 36 (0.00%)	1 / 107 (0.93%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Soft tissue infection			
subjects affected / exposed	0 / 36 (0.00%)	1 / 107 (0.93%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Staphylococcal bacteraemia			
subjects affected / exposed	1 / 36 (2.78%)	4 / 107 (3.74%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Staphylococcal sepsis			
subjects affected / exposed	1 / 36 (2.78%)	0 / 107 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Streptococcal bacteraemia			
subjects affected / exposed	0 / 36 (0.00%)	1 / 107 (0.93%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			

subjects affected / exposed	2 / 36 (5.56%)	3 / 107 (2.80%)	
occurrences causally related to treatment / all	0 / 2	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urosepsis			
subjects affected / exposed	0 / 36 (0.00%)	1 / 107 (0.93%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral infection			
subjects affected / exposed	1 / 36 (2.78%)	0 / 107 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vulval cellulitis			
subjects affected / exposed	1 / 36 (2.78%)	0 / 107 (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			
Hyponatraemia			
subjects affected / exposed	0 / 36 (0.00%)	1 / 107 (0.93%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypokalaemia			
subjects affected / exposed	0 / 36 (0.00%)	1 / 107 (0.93%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dehydration			
subjects affected / exposed	1 / 36 (2.78%)	0 / 107 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Placebo	Bezlotoxumab	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	28 / 36 (77.78%)	65 / 107 (60.75%)	
Investigations			
C-reactive protein increased			
subjects affected / exposed	2 / 36 (5.56%)	4 / 107 (3.74%)	
occurrences (all)	3	4	
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 36 (0.00%)	8 / 107 (7.48%)	
occurrences (all)	0	8	
Alanine aminotransferase increased			
subjects affected / exposed	0 / 36 (0.00%)	9 / 107 (8.41%)	
occurrences (all)	0	12	
Injury, poisoning and procedural complications			
Transfusion reaction			
subjects affected / exposed	2 / 36 (5.56%)	0 / 107 (0.00%)	
occurrences (all)	2	0	
Nervous system disorders			
Headache			
subjects affected / exposed	7 / 36 (19.44%)	15 / 107 (14.02%)	
occurrences (all)	8	22	
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	2 / 36 (5.56%)	7 / 107 (6.54%)	
occurrences (all)	2	7	
Leukopenia			
subjects affected / exposed	2 / 36 (5.56%)	4 / 107 (3.74%)	
occurrences (all)	2	4	
Febrile neutropenia			
subjects affected / exposed	2 / 36 (5.56%)	1 / 107 (0.93%)	
occurrences (all)	2	2	
Anaemia			
subjects affected / exposed	6 / 36 (16.67%)	8 / 107 (7.48%)	
occurrences (all)	10	8	
Thrombocytopenia			

subjects affected / exposed	3 / 36 (8.33%)	7 / 107 (6.54%)	
occurrences (all)	3	8	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	8 / 36 (22.22%)	15 / 107 (14.02%)	
occurrences (all)	12	22	
Gastrointestinal disorders			
Stomatitis			
subjects affected / exposed	2 / 36 (5.56%)	8 / 107 (7.48%)	
occurrences (all)	2	10	
Nausea			
subjects affected / exposed	4 / 36 (11.11%)	7 / 107 (6.54%)	
occurrences (all)	5	10	
Diarrhoea			
subjects affected / exposed	5 / 36 (13.89%)	8 / 107 (7.48%)	
occurrences (all)	14	9	
Constipation			
subjects affected / exposed	2 / 36 (5.56%)	7 / 107 (6.54%)	
occurrences (all)	2	11	
Abdominal pain			
subjects affected / exposed	6 / 36 (16.67%)	13 / 107 (12.15%)	
occurrences (all)	10	28	
Vomiting			
subjects affected / exposed	8 / 36 (22.22%)	14 / 107 (13.08%)	
occurrences (all)	12	16	
Respiratory, thoracic and mediastinal disorders			
Nasal congestion			
subjects affected / exposed	2 / 36 (5.56%)	0 / 107 (0.00%)	
occurrences (all)	2	0	
Dyspnoea			
subjects affected / exposed	2 / 36 (5.56%)	1 / 107 (0.93%)	
occurrences (all)	2	1	
Cough			
subjects affected / exposed	2 / 36 (5.56%)	3 / 107 (2.80%)	
occurrences (all)	2	4	
Skin and subcutaneous tissue disorders			

Alopecia			
subjects affected / exposed	2 / 36 (5.56%)	0 / 107 (0.00%)	
occurrences (all)	2	0	
Erythema			
subjects affected / exposed	2 / 36 (5.56%)	0 / 107 (0.00%)	
occurrences (all)	2	0	
Urticaria			
subjects affected / exposed	2 / 36 (5.56%)	1 / 107 (0.93%)	
occurrences (all)	2	1	
Vancomycin infusion reaction			
subjects affected / exposed	2 / 36 (5.56%)	1 / 107 (0.93%)	
occurrences (all)	2	1	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	3 / 36 (8.33%)	2 / 107 (1.87%)	
occurrences (all)	3	2	
Infections and infestations			
Bacteraemia			
subjects affected / exposed	2 / 36 (5.56%)	0 / 107 (0.00%)	
occurrences (all)	2	0	
Rhinitis			
subjects affected / exposed	2 / 36 (5.56%)	2 / 107 (1.87%)	
occurrences (all)	3	2	
Oral herpes			
subjects affected / exposed	2 / 36 (5.56%)	5 / 107 (4.67%)	
occurrences (all)	4	5	
Upper respiratory tract infection			
subjects affected / exposed	2 / 36 (5.56%)	1 / 107 (0.93%)	
occurrences (all)	2	1	
Metabolism and nutrition disorders			
Hypokalaemia			
subjects affected / exposed	6 / 36 (16.67%)	8 / 107 (7.48%)	
occurrences (all)	6	9	
Decreased appetite			
subjects affected / exposed	2 / 36 (5.56%)	1 / 107 (0.93%)	
occurrences (all)	2	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
18 March 2019	The major changes of amendment 1 were shortening the enrollment timeline by removing the pre-specified enrollment pause for pharmacokinetic evaluation and determining that dose modifications were not needed.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
22 February 2019	Amendment 1 submission to eliminate pre-specified enrollment pauses.	21 March 2019
09 March 2022	Proposal submission to European Union Pediatric Committee (EU PDCO) and the United States Food and Drug Administration (US FDA) to request concurrence with plan to conclude enrollment. The enrollment was not restarted.	-

Notes:

Limitations and caveats

None reported