Clinical trial results:
Placebo-Controlled Proof of Concept Study to Investigate ANB020 Activity in Adult Patients with Severe Eosinophilic Asthma

Summary

EudraCT number	2017-000647-40
Trial protocol	GB
Global end of trial date	30 October 2018

Results information

Result version number	v1 (current)
This version publication date	16 April 2021
First version publication date	16 April 2021

Trial information

Trial identification

Sponsor protocol code	ANB020-004

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03469934
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	AnaptysBio, Inc
Sponsor organisation address	10421 Pacific Center Court, Suite 200, San Diego, United States, CA 92121
Public contact	AnaptysBio Clinical Trials Information, AnaptysBio, Inc, +1 8583626387, clinicaltrialinfo@anaptysbio.com
Scientific contact	AnaptysBio Clinical Trials Information, AnaptysBio, Inc, +1 8583626387, clinicaltrialinfo@anaptysbio.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	30 October 2018
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	30 October 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objectives of the study were:
- To measure the reduction of eosinophils (blood eosinophil count) from Baseline (Day 1 pre-dose) to Day 22 in adult severe eosinophilic asthma patients administered with etokimab;
- To assess the safety and tolerability of a single, intravenous (IV) dose of etokimab compared to placebo in adult patients with severe eosinophilic asthma.

Protection of trial subjects:

This study was conducted in accordance with the protocol and with the following:
- Consensus ethical principles derived from international guidelines including the Declaration of Helsinki and Council for International Organizations of Medical Sciences International Ethical Guidelines;
- Applicable International Conference on Harmonisation Good Clinical Practice Guidelines;
- Applicable laws and regulations.

Background therapy:

Patients with eosinophilic asthma with exacerbations requiring rescue medication were expected to be on bronchodilators and were required to be on high-dose inhaled corticosteroids and long-acting beta-2 agonists.

Evidence for comparator: -

Actual start date of recruitment	14 November 2017
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	United Kingdom: 9
Country: Number of subjects enrolled	United States: 16
Worldwide total number of subjects	25
EEA total number of subjects	0

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)	0

Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	25
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This study was conducted in adults with severe eosinophilic asthma. Patients were randomized on Day 1 to receive a single IV dose of either etokimab or placebo in a 1:1 ratio.

Pre-assignment

Screening details:

This study consisted of a screening period (7 to 14 days), treatment period, and follow-up period (total of 127 days). The total duration of the study was approximately 141 days.

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	Etokimab

Arm description:

Etokimab 300 milligrams (mg)/100 milliliters (mL) was administered by IV infusion once on Day 1.

Arm type	Experimental
Investigational medicinal product name	Etokimab
Investigational medicinal product code	ANB020
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

A single dose of 300 mg etokimab was administered on Day 1 over 1 hour by IV infusion in polyvinyl chloride or polyolefin bags following dilution to a total volume of 100 mL with 0.9% sodium chloride (NaCl).

Arm title	Placebo

Arm description:

Placebo was administered by IV infusion once on Day 1.

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

Dosage and administration details:

A single dose of 100 mL of placebo (0.9% NaCl) was administered on Day 1 over 1 hour by IV infusion.

Number of subjects in period 1	Etokimab	Placebo
Started	12	13
Completed	12	12
Not completed	0	1
Consent withdrawn by subject	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Etokimab
Reporting group description:	
Etokimab 300 milligrams (mg)/100 milliliters (mL) was administered by IV infusion once on Day 1.	
Reporting group title	Placebo
Reporting group description:	
Placebo was administered by IV infusion once on Day 1.	

Reporting group values	Etokimab	Placebo	Total
Number of subjects	12	13	25
Age categorical Units: Subjects			
In utero			0
Preterm newborn infants (gestational age < 37 wks)			0
Newborns (0-27 days)			0
Infants and toddlers (28 days-23 months)			0
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: years			
arithmetic mean	40.6	36.3	
standard deviation	± 14.72	± 14.70	-
Gender categorical Units: Subjects			
Female	3	4	7
Male	9	9	18
Race Units: Subjects			
Black or African American	0	2	2
White	12	11	23
Ethnicity Units: Subjects			
Not Hispanic or Latino	12	12	24
Not reported	0	1	1
Height Units: centimeters			
arithmetic mean	175.7	173.9	
standard deviation	± 7.73	± 11.26	-
Weight Units: kilograms			
arithmetic mean	95.0	79.6	
standard deviation	± 18.04	± 19.30	-

Body Mass Index			
Units: kilogram/meter squared			
arithmetic mean	30.7	26.4	
standard deviation	± 4.94	± 6.00	-

End points

End points reporting groups

Reporting group title	Etokimab
Reporting group description:	
Etokimab 300 milligrams (mg)/100 milliliters (mL) was administered by IV infusion once on Day 1.	
Reporting group title	Placebo
Reporting group description:	
Placebo was administered by IV infusion once on Day 1.	

Primary: Change in Peripheral Eosinophil Count from Baseline to Day 22

End point title	Change in Peripheral Eosinophil Count from Baseline to Day 22
End point description:	
Blood samples to determine the eosinophil count were obtained as part of the standard hematology safety laboratory panel. The Pharmacodynamic (PD) Analysis Set included all patients who received etokimab or placebo and provided at least 1 evaluable post-dose PD measurement without any events or protocol deviation deemed to affect PD assessment.	
End point type	Primary
End point timeframe:	
Baseline (Day 1) and Day 22	

End point values	Etokimab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	13		
Units: 10^9/liter (L)				
least squares mean (confidence interval 95%)	-0.199 (-0.351 to -0.046)	-0.141 (-0.280 to -0.002)		

Statistical analyses

Statistical analysis title	Etokimab versus (vs) Placebo
Statistical analysis description:	
Results based on a linear mixed model with fixed effects for treatment, timepoint, treatment × timepoint, and baseline value and a repeated timepoint effect within a patient under an unstructured covariance matrix.	
Comparison groups	Etokimab v Placebo
Number of subjects included in analysis	24
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.5703
Method	Mixed models analysis
Parameter estimate	Least-squares (LS) mean difference
Point estimate	-0.058

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.265
upper limit	0.15

Primary: Number of Patients who Experienced an Adverse Event (AE)

End point title	Number of Patients who Experienced an Adverse Event (AE)[1]

End point description:

An AE is any untoward medical occurrence in a patient or clinical investigation patient administered a pharmaceutical product and which does not necessarily have a causal relationship with this treatment. A treatment-emergent AE (TEAE) is an AE that started or worsened in severity on or after the date and time of the study drug infusion. A serious adverse event (SAE), experience or reaction, is any untoward medical occurrence (whether considered to be related to the study drug or not) that at any dose:
- Results in death;
- Is life-threatening;
- Requires inpatient hospitalization or prolongation of existing hospitalization;
- Results in persistent or significant disability/incapacity;
- Is a congenital anomaly/birth defect;
- Other medically important event.

The Safety Analysis Set included all patients who received etokimab or placebo.

End point type	Primary

End point timeframe:

Day 1 to Day 127

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 additional statistical analysis was pre-specified for this endpoint.

End point values	Etokimab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	13		
Units: patients				
Any non-TEAEs	1	0		
Any TEAEs	6	5		
Any SAEs	0	0		
Any TEAEs leading to withdrawal from the study	0	0		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Patients with Clinically Meaningful Findings in Physical Examination Assessments

End point title	Number of Patients with Clinically Meaningful Findings in Physical Examination Assessments[2]

End point description:

The physical examination included evaluation of general appearance, head, eyes, ears, nose, and throat, and the pulmonary, cardiovascular, gastrointestinal, renal/genitourological, endocrine (including thyroid), musculoskeletal/spinal, lymphatic, and dermatologic systems. The Safety Analysis Set included

all patients who received etokimab or placebo.

End point type	Primary

End point timeframe:

Day 1 to Day 127

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 additional statistical analysis was pre-specified for this endpoint.

End point values	Etokimab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	13		
Units: patients	0	0		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Patients with Clinically Meaningful Findings in Vital Signs Measurements

End point title	Number of Patients with Clinically Meaningful Findings in Vital Signs Measurements[3]

End point description:

Vital signs included pulse rate, respiratory rate, body temperature, systolic blood pressure (BP), and diastolic BP. The Safety Analysis Set included all patients who received etokimab or placebo.

End point type	Primary

End point timeframe:

Day 1 to Day 127

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 additional statistical analysis was pre-specified for this endpoint.

End point values	Etokimab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	13		
Units: patients	0	0		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Patients with Clinically Meaningful Findings in Clinical Safety Laboratory Evaluations

End point title	Number of Patients with Clinically Meaningful Findings in Clinical Safety Laboratory Evaluations[4]

End point description:

Hematology, clinical chemistry, virology, urinalysis, and drugs of abuse testing was performed. The

clinical laboratory test results were reviewed for potential clinical significance, based on Investigator's discretion throughout the study. The Investigator evaluated any change in laboratory values. If the Investigator determined a laboratory abnormality to be clinically significant, it was considered a laboratory AE; however, if the abnormal laboratory value was consistent with a current diagnosis, it was documented accordingly. The Safety Analysis Set included all patients who received etokimab or placebo.

End point type	Primary

End point timeframe:

Day 1 to Day 127

Notes:

[4] - 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 additional statistical analysis was pre-specified for this endpoint.

End point values	Etokimab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	13		
Units: patients	0	0		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Patients with Clinically Meaningful Findings in Electrocardiogram (ECG) Assessments

End point title	Number of Patients with Clinically Meaningful Findings in Electrocardiogram (ECG) Assessments[5]

End point description:

A standard 12-lead ECG was performed by a qualified physician or nurse. The following parameters were documented: heart rate, PR interval, QRS interval, QT interval, and QTc interval. The Safety Analysis Set included all patients who received etokimab or placebo.

End point type	Primary

End point timeframe:

Day 1 to Day 127

Notes:

[5] - 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 additional statistical analysis was pre-specified for this endpoint.

End point values	Etokimab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	13		
Units: patients	0	0		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Asthma Exacerbations

End point title	Number of Asthma Exacerbations[6]

End point description:

The definition of asthma exacerbation for this endpoint included:
- Use of systemic corticosteroids (or a temporary increase in a stable oral corticosteroid background dose) for at least 3 days; a single depo-injectable dose of corticosteroids was considered equivalent to a 3-day course of systemic corticosteroids; or
- An emergency room/urgent care visit (defined as evaluation and treatment for <24 hours in an emergency department or urgent care center) due to asthma that required systemic corticosteroids (as per above); or
- An inpatient hospitalization (defined as admission to an inpatient facility and/or evaluation and treatment in a healthcare facility for ≥24 hours due to asthma).
The Full Analysis Set included all patients who received etokimab or placebo and had at least 1 post-baseline blood eosinophils count assessment (Day 2).

End point type	Primary

End point timeframe:

Day 1 to Day 127

Notes:

[6] - 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 additional statistical analysis was pre-specified for this endpoint.

End point values	Etokimab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	13		
Units: exacerbations	1	1		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Patients with Anti-drug Antibodies (ADA)

End point title	Number of Patients with Anti-drug Antibodies (ADA)[7]

End point description:

Number of patients with positive ADA assay result is reported. The Safety Analysis Set included all patients who received etokimab or placebo.

End point type	Primary

End point timeframe:

Day 1 pre-dose and Days 8, 36, 85, 106 and 127

Notes:

[7] - 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 additional statistical analysis was pre-specified for this endpoint.

End point values	Etokimab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	13		
Units: patients				
Day 1 (n = 12, 13)	1	1		
Day 8 (n = 12, 13)	0	2		
Day 36 (n = 12, 13)	0	2		
Day 85 (n = 12, 13)	1	1		
Day 106 (n = 12, 12)	1	1		

Day 127 (n = 12, 12)	2	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Peripheral Eosinophil Count from Baseline to Day 127

End point title	Change in Peripheral Eosinophil Count from Baseline to Day 127

End point description:

Blood samples to determine the eosinophil count were obtained as part of the standard hematology safety laboratory panel. The PD Analysis Set included all patients who received etokimab or placebo and provided at least 1 evaluable post-dose PD measurement without any events or protocol deviation deemed to affect PD assessment.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and Day 127

End point values	Etokimab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	13		
Units: 10^9/L				
least squares mean (confidence interval 95%)	-0.194 (-0.330 to -0.058)	-0.144 (-0.275 to -0.014)		

Statistical analyses

Statistical analysis title	Etokimab vs Placebo

Statistical analysis description:

Results based on a linear mixed model with fixed effects for treatment, timepoint, treatment × timepoint, and baseline value and a repeated timepoint effect within a patient under an unstructured covariance matrix.

Comparison groups	Etokimab v Placebo
Number of subjects included in analysis	25
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.5901
Method	Mixed models analysis
Parameter estimate	LS mean difference
Point estimate	-0.05

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.239
upper limit	0.139

Secondary: Change in Forced Expiratory Volume in 1 Second from Baseline to Day 127

End point title	Change in Forced Expiratory Volume in 1 Second from Baseline to Day 127

End point description:

Spirometry was performed according to the American Thoracic Society/European Respiratory Society guidelines (ATS/ERS). Pre-bronchodilator spirometry was performed after appropriate bronchodilator withholding period in the morning. Forced expiratory maneuvers were performed with the patient seated in an upright position if possible. Three acceptable maneuvers were obtained for each test. The Full Analysis Set included all patients who received etokimab or placebo and had at least 1 post-baseline blood eosinophils count assessment (Day 2).

End point type	Secondary

End point timeframe:

Baseline (Day 1) and Day 127

End point values	Etokimab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	12		
Units: liters				
least squares mean (standard error)	0.27 (± 0.116)	0.18 (± 0.116)		

Statistical analyses

Statistical analysis title	Etokimab vs Placebo

Statistical analysis description:

P-value was obtained using analysis of covariance (ANCOVA) model with treatment as fixed effect and baseline result as covariate.

Comparison groups	Etokimab v Placebo
Number of subjects included in analysis	24
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.596
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	0.09
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.25
upper limit	0.43

Variability estimate	Standard error of the mean
Dispersion value	0.164

Secondary: Change in Fractional Exhaled Nitric Oxide (FeNO) from Baseline to Day 127

End point title	Change in Fractional Exhaled Nitric Oxide (FeNO) from Baseline to Day 127

End point description:

Measurement of FeNO was performed in accordance with the guidelines published by ATS/ERS. The FeNO test was performed before the spirometry testing. The Full Analysis Set included all patients who received etokimab or placebo and had at least 1 post-baseline blood eosinophils count assessment (Day 2).

End point type	Secondary

End point timeframe:

Baseline (Day 1) and Day 127

End point values	Etokimab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	12		
Units: parts per billion				
least squares mean (standard error)	2.10 (± 6.580)	-0.43 (± 6.580)		

Statistical analyses

Statistical analysis title	Etokimab vs Placebo

Statistical analysis description:

P-value is obtained using ANCOVA model with treatment as fixed effect and baseline result as covariate.

Comparison groups	Etokimab v Placebo
Number of subjects included in analysis	24
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.7993
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	2.53
Confidence interval	
level	95 %
sides	2-sided
lower limit	-17.9
upper limit	22.96
Variability estimate	Standard error of the mean
Dispersion value	9.823

Secondary: Whole Blood Ex-vivo Induced Interferon-Gamma (IFN-γ) Levels (United Kingdom [UK] Sites Only)

End point title	Whole Blood Ex-vivo Induced Interferon-Gamma (IFN-γ) Levels (United Kingdom [UK] Sites Only)

End point description:

Blood samples for ex-vivo induced IFN-γ assessment were collected in a sodium heparin tube and the measurement of ex-vivo induced IFN-γ was performed using validated assay methods. The PD Analysis Set included all patients who received etokimab or placebo and provided at least 1 evaluable post-dose PD measurement without any events or protocol deviation deemed to affect PD assessment. Only patients randomized within the UK were included. 9999 = below the lower limit of quantification; 99999 = not determined; 999999 = no patients were analyzed at that specific timepoint.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and Days 8, 36, 85, 106 and 127

End point values	Etokimab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	5		
Units: nanograms/L				
arithmetic mean (standard deviation)				
Day 1 (n = 4, 4)	702.215 (± 581.947)	2490.575 (± 3577.893)		
Day 8 (n = 3, 2)	9999 (± 99999)	99999 (± 99999)		
Day 36 (n = 2, 3)	99999 (± 99999)	8208.247 (± 4012.238)		
Day 85 (n = 2, 1)	99999 (± 99999)	99999 (± 99999)		
Day 106 (n = 2, 0)	99999 (± 99999)	999999 (± 999999)		
Day 127 (n = 4, 5)	1103.323 (± 1086.280)	7308.442 (± 8458.639)		

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum Observed Concentration (Cmax) of Etokimab

End point title	Maximum Observed Concentration (Cmax) of Etokimab[8]

End point description:

Cmax was derived using non-compartmental methods. The PK Analysis Set included all patients who received etokimab and had at least 1 post-dose serum concentration data available for etokimab without any events or protocol deviation deemed to affect PK assessments.

End point type	Secondary

End point timeframe:

Day 1 pre-dose, 0.5 hours post-start of infusion, end of infusion (EOI), EOI + 3 hours, EOI + 6 hours, and Days 2, 8, 22, 36 and 64

Notes:

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: PK assessment was pre-specified for the etokimab arm only.

End point values	Etokimab			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: micrograms (µg)/mL				
geometric mean (geometric coefficient of variation)	77.71 (± 24.1)			

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Maximum Observed Concentration (Tmax) of Etokimab

End point title	Time to Maximum Observed Concentration (Tmax) of

End point description:

Tmax was derived using non-compartmental methods. The PK Analysis Set included all patients who received etokimab and had at least 1 post-dose serum concentration data available for etokimab without any events or protocol deviation deemed to affect PK assessments.

End point type	Secondary

End point timeframe:

Day 1 pre-dose, 0.5 hours post-start of infusion, EOI, EOI + 3 hours, EOI + 6 hours, and Days 2, 8, 22, 36 and 64

Notes:

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: PK assessment was pre-specified for the etokimab arm only.

End point values	Etokimab			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: hours				
median (full range (min-max))	1.020 (0.53 to 4.08)			

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Concentration-time Curve in Serum from Time Zero (pre-dose) Extrapolated to Infinite Time (AUC[0-inf]) of Etokimab

End point title	Area Under the Concentration-time Curve in Serum from Time Zero (pre-dose) Extrapolated to Infinite Time (AUC[0-inf]) of

	Etokimab[10]

End point description:

AUC(0-inf) was derived using non-compartmental methods. The PK Analysis Set included all patients who received etokimab and had at least 1 post-dose serum concentration data available for etokimab without any events or protocol deviation deemed to affect PK assessments.

End point type	Secondary

End point timeframe:

Day 1 pre-dose, 0.5 hours post-start of infusion, EOI, EOI + 3 hours, EOI + 6 hours, and Days 2, 8, 22, 36 and 64

Notes:

[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: PK assessment was pre-specified for the etokimab arm only.

End point values	Etokimab			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: hours (h)*µg/mL				
geometric mean (geometric coefficient of variation)	13750 (± 32.3)			

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Serum Concentration-time Curve from Time Zero to the Time of the Last Quantifiable Concentration (AUC[0-last]) of Etokimab

End point title	Area Under the Serum Concentration-time Curve from Time Zero to the Time of the Last Quantifiable Concentration (AUC[0-last]) of Etokimab[11]

End point description:

AUC0-last was derived using non-compartmental methods. The PK Analysis Set included all patients who received etokimab and had at least 1 post-dose serum concentration data available for etokimab without any events or protocol deviation deemed to affect PK assessments.

End point type	Secondary

End point timeframe:

Day 1 pre-dose, 0.5 hours post-start of infusion, EOI, EOI + 3 hours, EOI + 6 hours, and Days 2, 8, 22, 36 and 64

Notes:

[11] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: PK assessment was pre-specified for the etokimab arm only.

End point values	Etokimab			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: h*µg/mL				
geometric mean (geometric coefficient of variation)	13050 (± 30.4)			

Statistical analyses

No statistical analyses for this end point

Secondary: Apparent Total Body Clearance (CL) of Etokimab

End point title	Apparent Total Body Clearance (CL) of Etokimab[12]

End point description:

CL was derived using non-compartmental methods. The PK Analysis Set included all patients who received etokimab and had at least 1 post-dose serum concentration data available for etokimab without any events or protocol deviation deemed to affect PK assessments.

End point type	Secondary

End point timeframe:

Day 1 pre-dose, 0.5 hours post-start of infusion, EOI, EOI + 3 hours, EOI + 6 hours, and Days 2, 8, 22, 36 and 64

Notes:

[12] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: PK assessment was pre-specified for the etokimab arm only.

End point values	Etokimab			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: L/h				
geometric mean (geometric coefficient of variation)	0.02180 (± 32.4)			

Statistical analyses

No statistical analyses for this end point

Secondary: Apparent Terminal Rate Constant (λz) of Etokimab

End point title	Apparent Terminal Rate Constant (λz) of Etokimab[13]

End point description:

λz was derived using non-compartmental methods. The PK Analysis Set included all patients who received etokimab and had at least 1 post-dose serum concentration data available for etokimab without any events or protocol deviation deemed to affect PK assessments.

End point type	Secondary

End point timeframe:

Day 1 pre-dose, 0.5 hours post-start of infusion, EOI, EOI + 3 hours, EOI + 6 hours, and Days 2, 8, 22, 36 and 64

Notes:

[13] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: PK assessment was pre-specified for the etokimab arm only.

End point values	Etokimab			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: 1/h				
geometric mean (geometric coefficient of variation)	0.002096 (± 29.2)			

Statistical analyses

No statistical analyses for this end point

Secondary: Apparent Terminal Half-life (t1/2) of Etokimab

End point title	Apparent Terminal Half-life (t1/2) of Etokimab[14]

End point description:

t1/2 was derived using non-compartmental methods. The PK Analysis Set included all patients who received etokimab and had at least 1 post-dose serum concentration data available for etokimab without any events or protocol deviation deemed to affect PK assessments.

End point type	Secondary

End point timeframe:

Day 1 pre-dose, 0.5 hours post-start of infusion, EOI, EOI + 3 hours, EOI + 6 hours, and Days 2, 8, 22, 36 and 64

Notes:

[14] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: PK assessment was pre-specified for the etokimab arm only.

End point values	Etokimab			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: hours				
geometric mean (geometric coefficient of variation)	330.5 (± 29.2)			

Statistical analyses

No statistical analyses for this end point

Secondary: Volume of Distribution During Terminal Phase (Vz) of Etokimab

End point title	Volume of Distribution During Terminal Phase (Vz) of

End point description:

Vz was derived using non-compartmental methods. The PK Analysis Set included all patients who received etokimab and had at least 1 post-dose serum concentration data available for etokimab without any events or protocol deviation deemed to affect PK assessments.

End point type	Secondary

End point timeframe:

Day 1 pre-dose, 0.5 hours post-start of infusion, EOI, EOI + 3 hours, EOI + 6 hours, and Days 2, 8, 22, 36 and 64

Notes:

[15] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: PK assessment was pre-specified for the etokimab arm only.

End point values	Etokimab			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: liters				
geometric mean (geometric coefficient of variation)	10.40 (± 19.2)			

Statistical analyses

No statistical analyses for this end point

Secondary: Volume of Distribution at Steady State Following IV Dosing (Vss) of Etokimab

End point title	Volume of Distribution at Steady State Following IV Dosing (Vss) of Etokimab[16]

End point description:

Vss was derived using non-compartmental methods. The PK Analysis Set included all patients who received etokimab and had at least 1 post-dose serum concentration data available for etokimab without any events or protocol deviation deemed to affect PK assessments.

End point type	Secondary

End point timeframe:

Day 1 pre-dose, 0.5 hours post-start of infusion, EOI, EOI + 3 hours, EOI + 6 hours, and Days 2, 8, 22, 36 and 64

Notes:

[16] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: PK assessment was pre-specified for the etokimab arm only.

End point values	Etokimab			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: liters				
geometric mean (geometric coefficient of variation)	8.382 (± 16.6)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: Day 1 to Day 127	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	20
Reporting groups	
Reporting group title	Etokimab
Reporting group description: Etokimab 300 mg/100 mL was administered by IV infusion once on Day 1.	
Reporting group title	Placebo
Reporting group description: Placebo was administered by IV infusion once on Day 1.	

Serious adverse events	Etokimab	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 12 (0.00%)	0 / 13 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Etokimab	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 12 (50.00%)	5 / 13 (38.46%)	
Injury, poisoning and procedural complications			
Arthropod bite			
subjects affected / exposed	0 / 12 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Contusion			
subjects affected / exposed	1 / 12 (8.33%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Face injury			

subjects affected / exposed	0 / 12 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Soft tissue injury			
subjects affected / exposed	0 / 12 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 12 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	1 / 12 (8.33%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	0 / 12 (0.00%)	2 / 13 (15.38%)	
occurrences (all)	0	2	
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	1 / 12 (8.33%)	2 / 13 (15.38%)	
occurrences (all)	1	2	
Cough			
subjects affected / exposed	0 / 12 (0.00%)	2 / 13 (15.38%)	
occurrences (all)	0	2	
Psychiatric disorders			
Panic attack			
subjects affected / exposed	1 / 12 (8.33%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 12 (8.33%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Infections and infestations			
Pharyngitis streptococcal			
subjects affected / exposed	2 / 12 (16.67%)	0 / 13 (0.00%)	
occurrences (all)	2	0	
Pharyngitis			

subjects affected / exposed	1 / 12 (8.33%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Sinusitis			
subjects affected / exposed	1 / 12 (8.33%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Upper respiratory tract infection			
subjects affected / exposed	1 / 12 (8.33%)	0 / 13 (0.00%)	
occurrences (all)	1	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
08 May 2017	Changes encompassed by this amendment included administrative changes and updates to the inclusion criteria, patient restrictions, and blinding.
04 January 2018	Changes encompassed by this amendment included administrative changes, and updates to the synopsis, background information, discussion of study design, summary of study design, inclusion criteria, exclusion criteria, patient restrictions, patient withdrawal, excluded medications, spirometry, timing of procedures, appendix VI - IFN-y collection timepoints, and schedule of events.
16 February 2018	Changes encompassed by this amendment included updates to the inclusion criteria, method of assigning patients to treatment group, and unblinding.
30 October 2018	Amendment dated 31-Oct-2018. This amendment combined the United States and UK ANB020-004 protocols and updated the clinical study background to incorporate the most recent updates to the Investigator Brochure. No changes were made to study procedures in this amendment. Changes encompassed by this amendment included administrative changes, clinical updates, and country specific assessments combined into 1 global protocol.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported