



Clinical trial results:

A Phase 2, Open-Label Study to Evaluate the Long-term Safety of Oral BCX9930 in Subjects with Paroxysmal Nocturnal Hemoglobinuria (PNH)

Summary

EudraCT number	2020-000501-93
Trial protocol	GB AT DK IT
Global end of trial date	04 October 2023

Results information

Result version number	v1
This version publication date	19 October 2024
First version publication date	19 October 2024

Trial information

Trial identification

Sponsor protocol code	BCX9930-201
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04702568
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	BioCryst Pharmaceuticals Inc.
Sponsor organisation address	4505 Emperor Blvd., Suite 200, Durham, United States, NC 27703
Public contact	BioCryst Pharmaceuticals Inc, Study Director, +001 919859 1302, clinicaltrials@biocryst.com
Scientific contact	BioCryst Pharmaceuticals Inc, Study Director, +001 919859 1302, clinicaltrials@biocryst.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	04 October 2023
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	04 October 2023
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To assess long-term safety and tolerability data in eligible participants with paroxysmal nocturnal hemoglobinuria (PNH) who previously received BCX9930 in a BioCryst-sponsored study and derived benefit from BCX9930 treatment.

Protection of trial subjects:

This trial was conducted in compliance with International Conference on Harmonization (ICH) Good Clinical Practice (GCP) guidelines for conducting, recording, and reporting trials, and in accordance with the Declaration of Helsinki.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	18 December 2020
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 5
Country: Number of subjects enrolled	Austria: 2
Country: Number of subjects enrolled	South Africa: 12
Worldwide total number of subjects	19
EEA total number of subjects	2

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)	18
From 65 to 84 years	1

85 years and over	0
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Subject disposition

Recruitment

Recruitment details:

Participants who had participated in previous BCX9930 trials (BCX9930-101 [NCT04330534], BCX9930-202 [NCT05116774], or BCX9930-203 [NCT05116787]) for Paroxysmal Nocturnal Hemoglobinuria (PNH) and showed a benefit of treatment as determined by the investigator were enrolled in this long-term safety trial.

Pre-assignment

Screening details:

A total of 19 participants were treated.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Complement Component 5 (C5) Inhibitor (C5-INH) Naïve Group

Arm description:

This group included participants who, prior to enrolling in their previous BCX9930 study, were either naïve to eculizumab or ravulizumab treatment, or naïve to treatment with any complement inhibitor therapy (or had received no treatment in the prior 12 months), and with anemia due to ongoing intravascular hemolysis. Participants were to commence treatment at the same BCX9930 dose level and regimen last administered to that individual in the prior study. Per last protocol amendment, all participants received BCX9930 400 milligrams (mg) orally twice daily (BID). Treatment duration was up to 144 weeks.

Arm type	Experimental
Investigational medicinal product name	BCX9930
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Administered orally twice daily.

Arm title	C5 INH Inadequate Response Group
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Arm description:

This group included participants who, prior to enrolling in their previous BCX9930 study, were receiving stable treatment with eculizumab or ravulizumab and had an inadequate response to that therapy (ie, residual anemia and/or ongoing need for transfusion). Depending on the prior study, participants may have continued the C5 inhibitor, with BCX9930 provided as an add-on therapy. Participants were to commence treatment at the same BCX9930 dose level and regimen last administered to that individual in the prior study. Per last protocol amendment, all participants received BCX9930 400 mg orally BID. Treatment duration was up to 144 weeks.

Arm type	Experimental
Investigational medicinal product name	BCX9930
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Other use

Dosage and administration details:

Administered orally twice daily.

Number of subjects in period 1	Complement Component 5 (C5) Inhibitor (C5-INH) Naïve Group	C5 INH Inadequate Response Group
Started	12	7
Completed	0	0
Not completed	12	7
Pregnancy	1	-
Transitioned to the BCX9930-205 roll-over study	10	4
Withdrawal by Subject	-	2
Withdrawn due to Investigator decision	-	1
Bone marrow transplant	1	-

Baseline characteristics

Reporting groups

Reporting group title	Complement Component 5 (C5) Inhibitor (C5-INH) Naïve Group
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Reporting group description:

This group included participants who, prior to enrolling in their previous BCX9930 study, were either naïve to eculizumab or ravulizumab treatment, or naïve to treatment with any complement inhibitor therapy (or had received no treatment in the prior 12 months), and with anemia due to ongoing intravascular hemolysis. Participants were to commence treatment at the same BCX9930 dose level and regimen last administered to that individual in the prior study. Per last protocol amendment, all participants received BCX9930 400 milligrams (mg) orally twice daily (BID). Treatment duration was up to 144 weeks.

Reporting group title	C5 INH Inadequate Response Group
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Reporting group description:

This group included participants who, prior to enrolling in their previous BCX9930 study, were receiving stable treatment with eculizumab or ravulizumab and had an inadequate response to that therapy (ie, residual anemia and/or ongoing need for transfusion). Depending on the prior study, participants may have continued the C5 inhibitor, with BCX9930 provided as an add-on therapy. Participants were to commence treatment at the same BCX9930 dose level and regimen last administered to that individual in the prior study. Per last protocol amendment, all participants received BCX9930 400 mg orally BID. Treatment duration was up to 144 weeks.

Reporting group values	Complement Component 5 (C5) Inhibitor (C5-INH) Naïve Group	C5 INH Inadequate Response Group	Total
Number of subjects	12	7	19
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	12	6	18
From 65-84 years	0	1	1
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	29.3	44.6	
standard deviation	± 7.82	± 18.59	-
Gender categorical Units: Subjects			
Female	3	5	8
Male	9	2	11
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	0	0	0
Not Hispanic or Latino	12	7	19
Unknown or Not Reported	0	0	0

Race (NIH/OMB)			
Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	1	1	2
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	7	2	9
White	3	4	7
More than one race	0	0	0
Unknown or Not Reported	1	0	1

End points

End points reporting groups

Reporting group title	Complement Component 5 (C5) Inhibitor (C5-INH) Naïve Group
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Reporting group description:

This group included participants who, prior to enrolling in their previous BCX9930 study, were either naïve to eculizumab or ravulizumab treatment, or naïve to treatment with any complement inhibitor therapy (or had received no treatment in the prior 12 months), and with anemia due to ongoing intravascular hemolysis. Participants were to commence treatment at the same BCX9930 dose level and regimen last administered to that individual in the prior study. Per last protocol amendment, all participants received BCX9930 400 milligrams (mg) orally twice daily (BID). Treatment duration was up to 144 weeks.

Reporting group title	C5 INH Inadequate Response Group
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Reporting group description:

This group included participants who, prior to enrolling in their previous BCX9930 study, were receiving stable treatment with eculizumab or ravulizumab and had an inadequate response to that therapy (ie, residual anemia and/or ongoing need for transfusion). Depending on the prior study, participants may have continued the C5 inhibitor, with BCX9930 provided as an add-on therapy. Participants were to commence treatment at the same BCX9930 dose level and regimen last administered to that individual in the prior study. Per last protocol amendment, all participants received BCX9930 400 mg orally BID. Treatment duration was up to 144 weeks.

Primary: Number of Participants With Treatment Emergent Adverse Events (TEAEs)

End point title	Number of Participants With Treatment Emergent Adverse Events (TEAEs) ^[1]
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End point description:

An AE was defined as any untoward medical occurrence associated with the use of an intervention in humans, whether or not considered intervention-related in a participant or clinical investigation participant who administered a pharmaceutical product regardless of its causal relationship to the study treatment. An AE was considered treatment emergent if its start date and time was on or after the date and time of first on-study dose of study drug. The safety population included all participants who received at least 1 capsule or tablet of study drug.

End point type	Primary
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End point timeframe:

From first dose of study drug up to 3 weeks after last dose (Week 147)

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: There was no formal hypothesis testing and only descriptive analyses was performed.

End point values	Complement Component 5 (C5) Inhibitor (C5-INH) Naïve Group	C5 INH Inadequate Response Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	7		
Units: participants				
number (not applicable)	12	7		

Statistical analyses

Secondary: Number of Participants with Clinical PNH Symptom Based on Severity: Fatigue

End point title	Number of Participants with Clinical PNH Symptom Based on Severity: Fatigue
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End point description:

Data was reported for number of participants with clinical PNH symptom of fatigue. The severity of clinical PNH symptom of fatigue was graded as none, mild, moderate and severe based solely on investigator's discretion. mITT population included all participants who received at least 1 capsule or tablet of study drug and had post baseline assessment of PNH symptoms and/or laboratory data. Participants with available data at each visit were included.

End point type	Secondary
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End point timeframe:

Baseline, Weeks 24, 48, 72, 96, and 120

End point values	Complement Component 5 (C5) Inhibitor (C5-INH) Naïve Group	C5 INH Inadequate Response Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	7		
Units: participants				
number (not applicable)				
Baseline-none (n=12,7)	8	6		
Baseline-mild (n=12,7)	3	2		
Baseline-moderate (n=12,7)	0	1		
Baseline-severe (n=12,7)	1	0		
Week 24-none (n=12,7)	10	3		
Week 24-mild (n=12,7)	2	3		
Week 24-moderate (n=12,7)	0	1		
Week 24-severe (n=12,7)	0	0		
Week 48-none (n=8,3)	6	2		
Week 48-mild (n=8,3)	2	0		
Week 48-moderate (n=8,3)	0	1		
Week 48-severe (n=8,3)	0	0		
Week 72-none (n=8,3)	7	1		
Week 72-mild (n=8,3)	1	2		
Week 72-moderate (n=8,3)	0	0		
Week 72-severe (n=8,3)	0	0		
Week 96-none (n=8,3)	6	2		
Week 96-mild (n=8,3)	2	0		
Week 96-moderate (n=8,3)	0	0		
Week 96-severe (n=8,3)	0	1		
Week 120-none (n=8,3)	8	2		
Week 120-mild (n=8,3)	0	0		
Week 120-moderate (n=8,3)	0	1		
Week 120-severe (n=8,3)	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Clinical PNH Symptom Based on Severity: Dyspnea

End point title	Number of Participants with Clinical PNH Symptom Based on Severity: Dyspnea
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End point description:

Data was reported for number of participants with clinical PNH symptom of dyspnea. The severity of clinical PNH symptom of dyspnea was graded as none, mild, moderate and severe based solely on investigator's discretion. Participants in the mITT population with available data were analyzed.

End point type	Secondary
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End point timeframe:

Baseline, Weeks 24, 48, 72, 96, and 120

End point values	Complement Component 5 (C5) Inhibitor (C5-INH) Naïve Group	C5 INH Inadequate Response Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	7		
Units: participants				
number (not applicable)				
Baseline-none (n=12,7)	11	7		
Baseline-mild (n=12,7)	1	0		
Baseline-moderate (n=12,7)	0	0		
Baseline-severe (n=12,7)	0	0		
Week 24-none (n=12,7)	11	7		
Week 24-mild (n=12,7)	1	0		
Week 24-moderate (n=12,7)	0	0		
Week 24-severe (n=12,7)	0	0		
Week 48-none (n=8,3)	6	2		
Week 48-mild (n=8,3)	2	1		
Week 48-moderate (n=8,3)	0	0		
Week 48-severe (n=8,3)	0	0		
Week 72-none (n=8,3)	7	2		
Week 72-mild (n=8,3)	1	1		
Week 72-moderate (n=8,3)	0	0		
Week 72-severe (n=8,3)	0	0		
Week 96-none (n=8,3)	7	2		
Week 96-mild (n=8,3)	0	0		
Week 96-moderate (n=8,3)	1	1		

Week 96-severe (n=8,3)	0	0		
Week 120-none (n=8,3)	8	2		
Week 120-mild (n=8,3)	0	1		
Week 120-moderate (n=8,3)	0	0		
Week 120-severe (n=8,3)	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Clinical PNH Symptom Based on Severity: Chest Pain/Discomfort

End point title	Number of Participants with Clinical PNH Symptom Based on Severity: Chest Pain/Discomfort
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End point description:

Data was reported for number of participants with clinical PNH symptom of chest pain/discomfort. The severity of clinical PNH symptom of chest pain/discomfort was graded as none, mild, moderate and severe based solely on investigator's discretion. Participants in the mITT population with available data were analyzed.

End point type	Secondary
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End point timeframe:

Baseline, Weeks 24, 48, 72, 96, and 12

End point values	Complement Component 5 (C5) Inhibitor (C5-INH) Naïve Group	C5 INH Inadequate Response Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	7		
Units: participants				
number (not applicable)				
Baseline-none (n=12,7)	12	7		
Baseline-mild (n=12,7)	0	0		
Baseline-moderate (n=12,7)	0	0		
Baseline-severe (n=12,7)	0	0		
Week 24-none (n=12,7)	12	7		
Week 24-mild (n=12,7)	0	0		
Week 24-moderate (n=12,7)	0	0		
Week 24-severe (n=12,7)	0	0		
Week 48-none (n=8,3)	7	2		
Week 48-mild (n=8,3)	1	1		
Week 48-moderate (n=8,3)	0	0		
Week 48-severe (n=8,3)	0	0		
Week 72-none (n=8,3)	7	2		
Week 72-mild (n=8,3)	1	0		
Week 72-moderate (n=8,3)	0	1		
Week 72-severe (n=8,3)	0	0		
Week 96-none (n=8,3)	7	3		

Week 96-mild (n=8,3)	1	0		
Week 96-moderate (n=8,3)	0	0		
Week 96-severe (n=8,3)	0	0		
Week 120-none (n=8,3)	8	3		
Week 120-mild (n=8,3)	0	0		
Week 120-moderate (n=8,3)	0	0		
Week 120-severe (n=8,3)	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Clinical PNH Symptom Based on Severity: Difficulty Swallowing

End point title	Number of Participants with Clinical PNH Symptom Based on Severity: Difficulty Swallowing
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End point description:

Data was reported for number of participants with clinical PNH symptom of difficulty swallowing. The severity of clinical PNH symptom of difficulty swallowing was graded as none, mild, moderate and severe based solely on investigator's discretion. Participants in the mITT population with available data were analyzed.

End point type	Secondary
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End point timeframe:

Baseline, Weeks 24, 48, 72, 96, and 120

End point values	Complement Component 5 (C5) Inhibitor (C5-INH) Naïve Group	C5 INH Inadequate Response Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	7		
Units: participants				
number (not applicable)				
Baseline-none (n=12,7)	11	6		
Baseline-mild (n=12,7)	1	1		
Baseline-moderate (n=12,7)	0	0		
Baseline-severe (n=12,7)	0	0		
Week 24-none (n=12,7)	12	7		
Week 24-mild (n=12,7)	0	0		
Week 24-moderate (n=12,7)	0	0		
Week 24-severe (n=12,7)	0	0		
Week 48-none (n=8,3)	6	2		
Week 48-mild (n=8,3)	2	1		
Week 48-moderate (n=8,3)	0	0		
Week 48-severe (n=8,3)	0	0		
Week 72-none (n=8,3)	7	2		
Week 72-mild (n=8,3)	1	1		
Week 72-moderate (n=8,3)	0	0		

Week 72-severe (n=8,3)	0	0		
Week 96-none (n=8,3)	7	2		
Week 96-mild (n=8,3)	1	1		
Week 96-moderate (n=8,3)	0	0		
Week 96-severe (n=8,3)	0	0		
Week 120-none (n=8,3)	8	3		
Week 120-mild (n=8,3)	0	0		
Week 120-moderate (n=8,3)	0	0		
Week 120-severe (n=8,3)	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Clinical PNH Symptom Based on Severity: Abdominal Pain

End point title	Number of Participants with Clinical PNH Symptom Based on Severity: Abdominal Pain
End point description:	
Data was reported for number of participants with clinical PNH symptom of abdominal pain. The severity of clinical PNH symptom of abdominal pain was graded as none, mild, moderate and severe based solely on investigator's discretion. Participants in the mITT population with available data were analyzed.	
End point type	Secondary
End point timeframe:	
Baseline, Weeks 24, 48, 72, 96, and 120	

End point values	Complement Component 5 (C5) Inhibitor (C5-INH) Naïve Group	C5 INH Inadequate Response Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	7		
Units: participants				
number (not applicable)				
Baseline-none (n=12,7)	10	7		
Baseline-mild (n=12,7)	1	0		
Baseline-moderate (n=12,7)	1	0		
Baseline-severe (n=12,7)	0	0		
Week 24-none (n=12,7)	9	6		
Week 24-mild (n=12,7)	2	0		
Week 24-moderate (n=12,7)	1	1		
Week 24-severe (n=12,7)	0	0		
Week 48-none (n=8,3)	6	2		
Week 48-mild (n=8,3)	1	1		
Week 48-moderate (n=8,3)	0	0		
Week 48-severe (n=8,3)	1	0		
Week 72-none (n=8,3)	7	2		
Week 72-mild (n=8,3)	1	1		

Week 72-moderate (n=8,3)	0	0		
Week 72-severe (n=8,3)	0	0		
Week 96-none (n=8,3)	7	2		
Week 96-mild (n=8,3)	1	1		
Week 96-moderate (n=8,3)	0	0		
Week 96-severe (n=8,3)	0	0		
Week 120-none (n=8,3)	8	3		
Week 120-mild (n=8,3)	0	0		
Week 120-moderate (n=8,3)	0	0		
Week 120-severe (n=8,3)	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Clinical PNH Symptom Based on Severity: Headache

End point title	Number of Participants With Clinical PNH Symptom Based on Severity: Headache
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End point description:

Data was reported for number of participants with clinical PNH symptom of headache. The severity of clinical PNH symptom of headache was graded as none, mild, moderate and severe based solely on investigator's discretion. Participants in the mITT population with available data were analyzed.

End point type	Secondary
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End point timeframe:

Baseline, Weeks 24, 48, 72, 96, and 120

End point values	Complement Component 5 (C5) Inhibitor (C5-INH) Naïve Group	C5 INH Inadequate Response Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	7		
Units: participants				
number (not applicable)				
Baseline-none (n=12,7)	10	7		
Baseline-mild (n=12,7)	2	0		
Baseline-moderate (n=12,7)	0	0		
Baseline-severe (n=12,7)	0	0		
Week 24-none (n=12,7)	11	6		
Week 24-mild (n=12,7)	1	1		
Week 24-moderate (n=12,7)	0	0		
Week 24-severe (n=12,7)	0	0		
Week 48-none (n=8,3)	7	2		
Week 48-mild (n=8,3)	0	0		
Week 48-moderate (n=8,3)	1	1		
Week 48-severe (n=8,3)	0	0		
Week 72-none (n=8,3)	8	3		

Week 72-mild (n=8,3)	0	0		
Week 72-moderate (n=8,3)	0	0		
Week 72-severe (n=8,3)	0	0		
Week 96-none (n=8,3)	7	3		
Week 96-mild (n=8,3)	1	0		
Week 96-moderate (n=8,3)	0	0		
Week 96-severe (n=8,3)	0	0		
Week 120-none (n=8,3)	8	2		
Week 120-mild (n=8,3)	0	1		
Week 120-moderate (n=8,3)	0	0		
Week 120-severe (n=8,3)	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Clinical PNH Symptom Based on Severity: Erectile Dysfunction

End point title	Number of Participants with Clinical PNH Symptom Based on Severity: Erectile Dysfunction
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End point description:

Data was reported for number of participants with clinical PNH symptom of erectile dysfunction. The severity of clinical PNH symptom of erectile dysfunction was graded as none, mild, moderate and severe based solely on investigator's discretion. Participants in the mITT population with available data were analyzed.

End point type	Secondary
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End point timeframe:

Baseline, Weeks 24, 48, 72, 96, and 120

End point values	Complement Component 5 (C5) Inhibitor (C5-INH) Naïve Group	C5 INH Inadequate Response Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	7		
Units: participants				
number (not applicable)				
Baseline-none (n=9,2)	9	2		
Baseline-mild (n=9,2)	0	0		
Baseline-moderate (n=9,2)	0	0		
Baseline-severe (n=9,2)	0	0		
Week 24-none (n=9,2)	9	2		
Week 24-mild (n=9,2)	0	0		
Week 24-moderate (n=9,2)	0	0		
Week 24-severe (n=9,2)	0	0		
Week 48-none (n=8,1)	7	1		
Week 48-mild (n=8,1)	1	0		
Week 48-moderate (n=8,1)	0	0		

Week 48- severe (n=8,1)	0	0		
Week 72-none (n=8,1)	7	1		
Week 72-mild (n=8,1)	1	0		
Week 72-moderate (n=8,1)	0	0		
Week 72-severe (n=8,1)	0	0		
Week 96-none (n=8,2)	7	2		
Week 96-mild (n=8,2)	1	0		
Week 96-moderate (n=8,2)	0	0		
Week 96-severe (n=8,2)	0	0		
Week 120-none (n=8,1)	7	1		
Week 120-mild (n=8,1)	1	0		
Week 120-moderate (n=8,1)	0	0		
Week 120-severe (n=8,1)	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Clinical PNH Symptom Based on Severity: Hemoglobinuria

End point title	Number of Participants with Clinical PNH Symptom Based on Severity: Hemoglobinuria
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End point description:

Data was reported for number of participants with clinical PNH symptom of hemoglobinuria. The severity of clinical PNH symptom of hemoglobinuria was graded as none, mild, moderate and severe based solely on investigator's discretion. Participants in the mITT population with available data were analyzed.

End point type	Secondary
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End point timeframe:

Baseline, Weeks 24, 48, 72, 96, and 120

End point values	Complement Component 5 (C5) Inhibitor (C5-INH) Naïve Group	C5 INH Inadequate Response Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	7		
Units: participants				
number (not applicable)				
Baseline-none (n=12,7)	10	7		
Baseline-mild (n=12,7)	0	0		
Baseline-moderate (n=12,7)	0	0		
Baseline-severe (n=12,7)	0	0		
Baseline-missing severity (n=12,6)	2	0		
Week 24-none (n=12,7)	11	5		
Week 24-mild (n=12,7)	0	0		
Week 24-moderate (n=12,7)	0	0		
Week 24-severe (n=12,7)	0	0		
Week 24-missing severity (n=12,7)	1	2		

Week 48-none (n=8,3)	6	3		
Week 48-mild (n=8,3)	0	0		
Week 48-moderate (n=8,3)	1	0		
Week 48- severe (n=8,3)	0	0		
Week 48-missing severity (n=8,3)	1	0		
Week 72-none (n=8,3)	7	2		
Week 72-mild (n=8,3)	0	1		
Week 72-moderate (n=8,3)	0	0		
Week 72-severe (n=8,3)	0	0		
Week 72-missing severity (n=8,3)	1	0		
Week 96-none (n=8,3)	6	3		
Week 96-mild (n=8,3)	0	0		
Week 96-moderate (n=8,3)	0	0		
Week 96-severe (n=8,3)	0	0		
Week 96-missing severity (n=8,3)	2	0		
Week 120-none (n=8,3)	7	3		
Week 120-mild (n=8,3)	0	0		
Week 120-moderate (n=8,3)	0	0		
Week 120-severe (n=8,3)	0	0		
Week 120-missing severity (n=8,3)	1	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Clinical PNH Symptom Based on Severity: Jaundice

End point title	Number of Participants with Clinical PNH Symptom Based on Severity: Jaundice
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End point description:

Data was reported for number of participants with clinical PNH symptom of jaundice. The severity of clinical PNH symptom of jaundice was graded as none, mild, moderate and severe based solely on investigator's discretion. Participants in the population with available data were analyzed.

End point type	Secondary
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End point timeframe:

Baseline, Weeks 24, 48, 72, 96, and 120

End point values	Complement Component 5 (C5) Inhibitor (C5-INH) Naïve Group	C5 INH Inadequate Response Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	7		
Units: participants				
number (not applicable)				
Baseline-none (n=12,7)	11	7		
Baseline-mild (n=12,7)	0	0		
Baseline-moderate (n=12,7)	0	0		

Baseline-severe (n=12,7)	0	0		
Baseline-missing severity (n=12,7)	1	0		
Week 24-none (n=12,7)	12	7		
Week 24-mild (n=12,7)	0	0		
Week 24-moderate (n=12,7)	0	0		
Week 24-severe (n=12,7)	0	0		
Week 48-none (n=8,3)	8	3		
Week 48-mild (n=8,3)	0	0		
Week 48-moderate (n=8,3)	0	0		
Week 48- severe (n=8,3)	0	0		
Week 72-none (n=8,3)	8	3		
Week 72-mild (n=8,3)	0	0		
Week 72-moderate (n=8,3)	0	0		
Week 72-severe (n=8,3)	0	0		
Week 96-none (n=8,3)	8	3		
Week 96-mild (n=8,3)	0	0		
Week 96-moderate (n=8,3)	0	0		
Week 96-severe (n=8,3)	0	0		
Week 120-none (n=8,3)	8	3		
Week 120-mild (n=8,3)	0	0		
Week 120-moderate (n=8,3)	0	0		
Week 120-severe (n=8,3)	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Lactate Dehydrogenase (LDH)

End point title	Change From Baseline in Lactate Dehydrogenase (LDH)
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End point description:

Participants in the mITT population with available data were analyzed. Here "99999" represents that mean and standard deviation (SD) was not estimable as there were less than 2 participants at the given timepoint.

End point type	Secondary
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End point timeframe:

Baseline, Weeks, 24, 48, 72, 96, 120, and 144

End point values	Complement Component 5 (C5) Inhibitor (C5-INH) Naïve Group	C5 INH Inadequate Response Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	6		
Units: Units per liter (U/L)				
arithmetic mean (standard deviation)				
Baseline (n=12,6)	475.6 (± 210.98)	248.3 (± 125.71)		

Change at Week 24 (n=11,5)	-46.7 (± 154.55)	38.6 (± 45.51)		
Change at Week 48 (n=8,2)	-62.5 (± 80.97)	38.5 (± 65.76)		
Change at Week 72 (n=8,2)	-6.1 (± 238.41)	163.5 (± 118.09)		
Change at Week 96 (n=8,2)	237.4 (± 347.65)	-4.0 (± 134.35)		
Change at Week 120 (n=8,2)	195.4 (± 355.03)	31.0 (± 125.87)		
Change at Week 144 (n=1,0)	-59.0 (± 99999)	99999 (± 99999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Hemoglobin

End point title	Change From Baseline in Hemoglobin
End point description:	
Participants in the mITT population with available data were analyzed. Here "99999" represents that mean and SD was not estimable as there were less than 2 participants at the given timepoint.	
End point type	Secondary
End point timeframe:	
Baseline, Weeks 24, 48, 72, 96, 120, and 144	

End point values	Complement Component 5 (C5) Inhibitor (C5-INH) Naïve Group	C5 INH Inadequate Response Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	7		
Units: grams per deciliter (g/dl)				
arithmetic mean (standard deviation)				
Baseline (n=12,7)	11.88 (± 1.688)	11.53 (± 1.803)		
Change at Week 24 (n=11,6)	0.75 (± 1.159)	-1.32 (± 2.578)		
Change at Week 48 (n=8,2)	-0.61 (± 1.974)	-0.95 (± 2.333)		
Change at Week 72 (n=8,3)	-0.64 (± 2.327)	-0.93 (± 1.484)		
Change at Week 96 (n=8,2)	-0.33 (± 1.914)	-0.70 (± 2.687)		
Change at Week 120 (n=8,3)	0.38 (± 1.555)	-0.47 (± 2.098)		
Change at Week 144 (n=1,0)	-2.70 (± 99999)	99999 (± 99999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Haptoglobin

End point title	Change From Baseline in Haptoglobin
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End point description:

Participants in the mITT population with available data were analyzed. Here "99999" represents that mean and SD was not estimable as there were less than 2 participants at the given timepoint.

End point type	Secondary
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End point timeframe:

Baseline, Weeks 24, 48, 72, 96, and 120

End point values	Complement Component 5 (C5) Inhibitor (C5-INH) Naïve Group	C5 INH Inadequate Response Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	5		
Units: grams per liter (g/L)				
arithmetic mean (standard deviation)				
Baseline (n=12,5)	0.325 (± 0.2832)	0.216 (± 0.1350)		
Change at Week 24 (n=11,5)	0.000 (± 0.0447)	-0.082 (± 0.0844)		
Change at Week 48 (n=8,0)	0.213 (± 0.1126)	99999 (± 99999)		
Change at Week 72 (n=8,2)	0.025 (± 0.1165)	-0.210 (± 0.1414)		
Change at Week 96 (n=8,2)	-0.013 (± 0.0354)	0.195 (± 0.4313)		
Change at Week 120 (n=8,1)	-0.013 (± 0.0354)	-0.100 (± 99999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Reticulocytes

End point title	Change From Baseline in Reticulocytes
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End point description:

Participants in the mITT population with available data were analyzed

End point type	Secondary
End point timeframe:	
Baseline, Weeks 24, 48, 72, 96, and 120	

End point values	Complement Component 5 (C5) Inhibitor (C5-INH) Naïve Group	C5 INH Inadequate Response Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	7		
Units: 10 ⁶ cells per microliter (µL)				
arithmetic mean (standard deviation)				
Baseline (n=12,7)	0.1066 (± 0.02363)	0.0889 (± 0.03939)		
Change at Week 24 (n=11,6)	0.0164 (± 0.02339)	0.0913 (± 0.09144)		
Change at Week 48 (n=8,2)	0.0048 (± 0.03518)	0.0507 (± 0.03161)		
Change at Week 72 (n=8,3)	0.0044 (± 0.03643)	0.0463 (± 0.03008)		
Change at Week 96 (n=8,2)	0.0409 (± 0.03805)	0.0607 (± 0.03585)		
Change at Week 120 (n=8,3)	0.0173 (± 0.03303)	0.0653 (± 0.02380)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Blood Transfusions or Thromboses

End point title	Number of Participants With Blood Transfusions or Thromboses
End point description:	
Data was reported for number of participants for whom blood transfusion was required or who experienced the thrombosis events. Participants in the mITT population with available data were analyzed.	
End point type	Secondary
End point timeframe:	
From first dose of study drug up to 3 weeks after last dose (Week 147)	

End point values	Complement Component 5 (C5) Inhibitor (C5-INH) Naïve Group	C5 INH Inadequate Response Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	7		
Units: participants				

number (not applicable)				
Blood transfusions	3	4		
Thromboses	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Blood Transfusions

End point title	Number of Blood Transfusions
End point description: Number of blood transfusions were reported. Participants from mITT population who required blood transfusions were evaluated.	
End point type	Secondary
End point timeframe: From first dose of study drug up to 3 weeks after last dose (Week 147)	

End point values	Complement Component 5 (C5) Inhibitor (C5-INH) Naïve Group	C5 INH Inadequate Response Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	4		
Units: Number of blood transfusions				
number (not applicable)				
Number of Blood Transfusion	13	25		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Functional Assessment of Chronic Illness Therapy (FACIT) - Fatigue Scale Total Score

End point title	Change From Baseline in Functional Assessment of Chronic Illness Therapy (FACIT) - Fatigue Scale Total Score
End point description: The FACIT-Fatigue scale questionnaire was used to determine the level of fatigue experienced by participants. This questionnaire was a 13-item measure that assessed self-reported fatigue and its impact upon daily activities and function. Item scores ranged from 0 ("not at all") to 4 ("very much"), and the total score ranged from 0 to 52, with higher scores indicating greater quality of life. Participants in the mITT population with available data were analyzed.	
End point type	Secondary
End point timeframe: Baseline, Weeks 24, 48, 72, and 96	

End point values	Complement Component 5 (C5) Inhibitor (C5-INH) Naïve Group	C5 INH Inadequate Response Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	7		
Units: Scores on a scale				
arithmetic mean (standard deviation)				
Baseline (n=11,7)	43.82 (± 9.400)	40.14 (± 13.533)		
Change at Week 24 (n=11,7)	0.09 (± 4.110)	-3.36 (± 8.066)		
Change at Week 48 (n=8,3)	-0.63 (± 2.387)	2.33 (± 3.215)		
Change at Week 72 (n=8,3)	-0.38 (± 2.875)	-4.64 (± 12.016)		
Change at Week 96 (n=8,3)	-1.13 (± 4.357)	-18.00 (± 27.185)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From first dose of study drug up to 3 weeks after last dose (Week 147)

Adverse event reporting additional description:

The safety analysis population included all participants who received at least 1 capsule or tablet of study drug.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	24
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Reporting groups

Reporting group title	C5-INH Naïve Group
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Reporting group description:

This group included participants who, prior to enrolling in their previous BCX9930 study, were either naïve to eculizumab or ravulizumab treatment, or naïve to treatment with any complement inhibitor therapy (or had received no treatment in the prior 12 months), and with anemia due to ongoing intravascular hemolysis. Participants were to commence treatment at the same BCX9930 dose level and regimen last administered to that individual in the prior study. Per last protocol amendment, all participants received BCX9930 400 mg orally BID. Treatment duration was up to 144 weeks.

Reporting group title	C5-INH Inadequate Response Group
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Reporting group description:

This group included participants who, prior to enrolling in their previous BCX9930 study, were receiving stable treatment with eculizumab or ravulizumab and had an inadequate response to that therapy (ie, residual anemia and/or ongoing need for transfusion). Depending on the prior study, participants may have continued the C5 inhibitor, with BCX9930 provided as an add-on therapy. Participants were to commence treatment at the same BCX9930 dose level and regimen last administered to that individual in the prior study. Per last protocol amendment, all participants were to receive BCX9930 400 mg orally BID. Treatment duration was up to 144 weeks.

Serious adverse events	C5-INH Naïve Group	C5-INH Inadequate Response Group	
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 12 (50.00%)	3 / 7 (42.86%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Epstein-Barr virus associated lymphoma			
subjects affected / exposed	0 / 12 (0.00%)	1 / 7 (14.29%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Breakthrough haemolysis			

subjects affected / exposed	3 / 12 (25.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 5	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile neutropenia			
subjects affected / exposed	1 / 12 (8.33%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemolysis			
subjects affected / exposed	1 / 12 (8.33%)	1 / 7 (14.29%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 12 (0.00%)	1 / 7 (14.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Crohn's disease			
subjects affected / exposed	0 / 12 (0.00%)	1 / 7 (14.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastritis			
subjects affected / exposed	1 / 12 (8.33%)	0 / 7 (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			
Acute kidney injury			
subjects affected / exposed	1 / 12 (8.33%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Boutonneuse fever			

subjects affected / exposed	1 / 12 (8.33%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis			
subjects affected / exposed	0 / 12 (0.00%)	1 / 7 (14.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	0 / 12 (0.00%)	1 / 7 (14.29%)	
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	1 / 12 (8.33%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	C5-INH Naïve Group	C5-INH Inadequate Response Group	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	12 / 12 (100.00%)	7 / 7 (100.00%)	
Vascular disorders			
Hypertension			
subjects affected / exposed	2 / 12 (16.67%)	0 / 7 (0.00%)	
occurrences (all)	2	0	
Vasculitis			
subjects affected / exposed	1 / 12 (8.33%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			
Axillary pain			
subjects affected / exposed	0 / 12 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Chest discomfort			

subjects affected / exposed	0 / 12 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Chest pain			
subjects affected / exposed	0 / 12 (0.00%)	2 / 7 (28.57%)	
occurrences (all)	0	2	
Condition aggravated			
subjects affected / exposed	0 / 12 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	2	
Fatigue			
subjects affected / exposed	0 / 12 (0.00%)	3 / 7 (42.86%)	
occurrences (all)	0	8	
Feeling abnormal			
subjects affected / exposed	0 / 12 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	3	
Influenza like illness			
subjects affected / exposed	1 / 12 (8.33%)	2 / 7 (28.57%)	
occurrences (all)	1	3	
Oedema			
subjects affected / exposed	0 / 12 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	2	
Pain			
subjects affected / exposed	0 / 12 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	3	
Pyrexia			
subjects affected / exposed	1 / 12 (8.33%)	2 / 7 (28.57%)	
occurrences (all)	1	2	
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	0 / 12 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Reproductive system and breast disorders			
Erectile dysfunction			
subjects affected / exposed	1 / 12 (8.33%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Heavy menstrual bleeding			

subjects affected / exposed	1 / 12 (8.33%)	2 / 7 (28.57%)	
occurrences (all)	1	2	
Pelvic pain			
subjects affected / exposed	0 / 12 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 12 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Dyspnoea			
subjects affected / exposed	1 / 12 (8.33%)	3 / 7 (42.86%)	
occurrences (all)	1	8	
Epistaxis			
subjects affected / exposed	0 / 12 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Oropharyngeal pain			
subjects affected / exposed	0 / 12 (0.00%)	3 / 7 (42.86%)	
occurrences (all)	0	4	
Painful respiration			
subjects affected / exposed	0 / 12 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	2	
Productive cough			
subjects affected / exposed	1 / 12 (8.33%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Sinus disorder			
subjects affected / exposed	0 / 12 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Sinus pain			
subjects affected / exposed	0 / 12 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Psychiatric disorders			
Anxiety			
subjects affected / exposed	2 / 12 (16.67%)	0 / 7 (0.00%)	
occurrences (all)	2	0	
Depression			

subjects affected / exposed occurrences (all)	2 / 12 (16.67%) 3	1 / 7 (14.29%) 1	
Insomnia subjects affected / exposed occurrences (all)	2 / 12 (16.67%) 2	0 / 7 (0.00%) 0	
Stress subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 7 (0.00%) 0	
Investigations Alanine aminotransferase increased subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 7 (0.00%) 0	
Aspartate aminotransferase increased subjects affected / exposed occurrences (all)	4 / 12 (33.33%) 4	0 / 7 (0.00%) 0	
Blood alkaline phosphatase increased subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 7 (0.00%) 0	
Blood bilirubin increased subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 7 (0.00%) 0	
Blood creatinine increased subjects affected / exposed occurrences (all)	5 / 12 (41.67%) 7	0 / 7 (0.00%) 0	
Blood iron decreased subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 7 (0.00%) 0	
Blood uric acid increased subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 7 (0.00%) 0	
C-reactive protein increased subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 7 (0.00%) 0	
Creatinine urine increased			

subjects affected / exposed	1 / 12 (8.33%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Fibrin D dimer increased			
subjects affected / exposed	1 / 12 (8.33%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Glomerular filtration rate decreased			
subjects affected / exposed	1 / 12 (8.33%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Haemoglobin decreased			
subjects affected / exposed	1 / 12 (8.33%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Neutrophil count increased			
subjects affected / exposed	1 / 12 (8.33%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
SARS-CoV-2 test positive			
subjects affected / exposed	1 / 12 (8.33%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Urine albumin/creatinine ratio increased			
subjects affected / exposed	3 / 12 (25.00%)	0 / 7 (0.00%)	
occurrences (all)	6	0	
Weight increased			
subjects affected / exposed	1 / 12 (8.33%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Injury, poisoning and procedural complications			
Arthropod bite			
subjects affected / exposed	0 / 12 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Contusion			
subjects affected / exposed	0 / 12 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Joint injury			
subjects affected / exposed	1 / 12 (8.33%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Ligament sprain			

subjects affected / exposed	0 / 12 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Maternal exposure via partner during pregnancy			
subjects affected / exposed	1 / 12 (8.33%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Cardiac disorders			
Palpitations			
subjects affected / exposed	0 / 12 (0.00%)	2 / 7 (28.57%)	
occurrences (all)	0	3	
Nervous system disorders			
Ageusia			
subjects affected / exposed	0 / 12 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Headache			
subjects affected / exposed	4 / 12 (33.33%)	4 / 7 (57.14%)	
occurrences (all)	6	12	
Neuralgia			
subjects affected / exposed	0 / 12 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Restless legs syndrome			
subjects affected / exposed	1 / 12 (8.33%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 12 (8.33%)	1 / 7 (14.29%)	
occurrences (all)	1	1	
Breakthrough haemolysis			
subjects affected / exposed	4 / 12 (33.33%)	4 / 7 (57.14%)	
occurrences (all)	5	4	
Haemolysis			
subjects affected / exposed	0 / 12 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Lymphadenopathy			
subjects affected / exposed	0 / 12 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Lymphopenia			

subjects affected / exposed	1 / 12 (8.33%)	0 / 7 (0.00%)	
occurrences (all)	10	0	
Neutropenia			
subjects affected / exposed	2 / 12 (16.67%)	0 / 7 (0.00%)	
occurrences (all)	5	0	
Splenomegaly			
subjects affected / exposed	0 / 12 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Thrombocytopenia			
subjects affected / exposed	2 / 12 (16.67%)	0 / 7 (0.00%)	
occurrences (all)	4	0	
Ear and labyrinth disorders			
Ear haemorrhage			
subjects affected / exposed	0 / 12 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Tympanic membrane disorder			
subjects affected / exposed	1 / 12 (8.33%)	0 / 7 (0.00%)	
occurrences (all)	1	1	
Vertigo			
subjects affected / exposed	0 / 12 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	1 / 12 (8.33%)	1 / 7 (14.29%)	
occurrences (all)	1	4	
Abdominal pain			
subjects affected / exposed	2 / 12 (16.67%)	2 / 7 (28.57%)	
occurrences (all)	4	9	
Abdominal pain lower			
subjects affected / exposed	0 / 12 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	4	
Ascites			
subjects affected / exposed	0 / 12 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Colitis			

subjects affected / exposed	1 / 12 (8.33%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Constipation			
subjects affected / exposed	0 / 12 (0.00%)	2 / 7 (28.57%)	
occurrences (all)	0	3	
Diarrhoea			
subjects affected / exposed	3 / 12 (25.00%)	1 / 7 (14.29%)	
occurrences (all)	4	2	
Dyspepsia			
subjects affected / exposed	1 / 12 (8.33%)	1 / 7 (14.29%)	
occurrences (all)	1	1	
Dysphagia			
subjects affected / exposed	0 / 12 (0.00%)	2 / 7 (28.57%)	
occurrences (all)	0	4	
Gastritis			
subjects affected / exposed	1 / 12 (8.33%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Nausea			
subjects affected / exposed	4 / 12 (33.33%)	1 / 7 (14.29%)	
occurrences (all)	7	3	
Toothache			
subjects affected / exposed	2 / 12 (16.67%)	1 / 7 (14.29%)	
occurrences (all)	2	1	
Vomiting			
subjects affected / exposed	2 / 12 (16.67%)	1 / 7 (14.29%)	
occurrences (all)	3	1	
Hepatobiliary disorders			
Jaundice			
subjects affected / exposed	1 / 12 (8.33%)	1 / 7 (14.29%)	
occurrences (all)	1	1	
Skin and subcutaneous tissue disorders			
Dermatitis			
subjects affected / exposed	1 / 12 (8.33%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Dermatitis allergic			

subjects affected / exposed	1 / 12 (8.33%)	0 / 7 (0.00%)	
occurrences (all)	5	0	
Erythema			
subjects affected / exposed	1 / 12 (8.33%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Photosensitivity reaction			
subjects affected / exposed	0 / 12 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Pityriasis rosea			
subjects affected / exposed	1 / 12 (8.33%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Rash			
subjects affected / exposed	0 / 12 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	8	
Skin reaction			
subjects affected / exposed	1 / 12 (8.33%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 12 (8.33%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Chromaturia			
subjects affected / exposed	0 / 12 (0.00%)	2 / 7 (28.57%)	
occurrences (all)	0	3	
Dysuria			
subjects affected / exposed	1 / 12 (8.33%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Haemoglobinuria			
subjects affected / exposed	1 / 12 (8.33%)	4 / 7 (57.14%)	
occurrences (all)	2	5	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 12 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Back pain			

subjects affected / exposed occurrences (all)	3 / 12 (25.00%) 4	3 / 7 (42.86%) 4	
Joint swelling subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	1 / 7 (14.29%) 1	
Muscle spasms subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 7 (0.00%) 0	
Myalgia subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	2 / 7 (28.57%) 2	
Infections and infestations			
Bacterial vaginosis subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	1 / 7 (14.29%) 1	
Bronchitis subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 7 (0.00%) 0	
COVID-19 subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	1 / 7 (14.29%) 1	
Folliculitis subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 7 (0.00%) 0	
Fungal infection subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	1 / 7 (14.29%) 1	
Gastroenteritis viral subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	2 / 7 (28.57%) 2	
Genital herpes subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	1 / 7 (14.29%) 2	
Helicobacter gastritis subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 7 (0.00%) 0	

Hordeolum		
subjects affected / exposed	1 / 12 (8.33%)	0 / 7 (0.00%)
occurrences (all)	1	0
Infection		
subjects affected / exposed	0 / 12 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	1
Influenza		
subjects affected / exposed	1 / 12 (8.33%)	2 / 7 (28.57%)
occurrences (all)	1	3
Nasopharyngitis		
subjects affected / exposed	2 / 12 (16.67%)	3 / 7 (42.86%)
occurrences (all)	2	6
Pharyngitis		
subjects affected / exposed	1 / 12 (8.33%)	0 / 7 (0.00%)
occurrences (all)	1	0
Post procedural infection		
subjects affected / exposed	1 / 12 (8.33%)	0 / 7 (0.00%)
occurrences (all)	1	0
Rhinovirus infection		
subjects affected / exposed	0 / 12 (0.00%)	2 / 7 (28.57%)
occurrences (all)	0	2
Soft tissue infection		
subjects affected / exposed	1 / 12 (8.33%)	0 / 7 (0.00%)
occurrences (all)	2	0
Tonsillitis		
subjects affected / exposed	2 / 12 (16.67%)	0 / 7 (0.00%)
occurrences (all)	2	0
Tooth abscess		
subjects affected / exposed	1 / 12 (8.33%)	0 / 7 (0.00%)
occurrences (all)	1	0
Upper respiratory tract infection		
subjects affected / exposed	3 / 12 (25.00%)	1 / 7 (14.29%)
occurrences (all)	4	1
Urinary tract infection		
subjects affected / exposed	3 / 12 (25.00%)	1 / 7 (14.29%)
occurrences (all)	3	1

Viral infection subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	1 / 7 (14.29%) 1	
Vulvovaginal candidiasis subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	1 / 7 (14.29%) 1	
Metabolism and nutrition disorders			
Decreased appetite subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	1 / 7 (14.29%) 2	
Dehydration subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 7 (0.00%) 0	
Folate deficiency subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	1 / 7 (14.29%) 3	
Hypomagnesaemia subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 7 (0.00%) 0	
Hyponatraemia subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 7 (0.00%) 0	
Vitamin B12 deficiency subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	1 / 7 (14.29%) 1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
18 August 2020	Added an exclusion criterion for participants with elevated serum bilirubin. - Revised text for exclusion criteria for liver enzymes aspartate aminotransferase (AST) and alanine transaminase (ALT) for consistency with the new serum bilirubin exclusion criterion. - Added the requirement for participant discontinuation in the event of meningococcal infection or any serious infection that occurred after treatment was initiated. - Clarified that if the trial was to be halted due to safety concerns or based on a data monitoring committee (DMC) decision, restarting the trial would only occur following the appropriate authorization via a substantial amendment.
12 November 2020	Updated the visit schedule to every 4 week visits throughout the study for regular safety laboratory tests. Following findings of possible clinical chemistry changes in nonclinical toxicology studies, 4 week visits were continued after Week 24 as a precaution, - Updated text to include new nonclinical data. - Updated text to include new clinical data. - Clarification for tapering off or discontinuation of eculizumab or ravulizumab in former BCX9930 101 study participants who had added BCX9930 to their existing therapy with eculizumab or ravulizumab. - Updated information on prohibited medications. - Introduced additional text in case a new tablet formulation in development replaced the original hard gelatin capsule formulation. The introduction of the new tablet formulation was pending the results from a relative bioavailability study of the tablet and capsule formulations.
24 June 2021	Transitioned all participants from hard gelatin capsules to tablets. - Following assessment of the BCX9930-101 and BCX9930-201 study data, combined with pharmacokinetic (PK) modelling activities, it was concluded that 500 mg BID administered using the new tablet formulation was the most appropriate dose. This was the dose that was taken into the registration studies, BCX9930-202 and BCX9930-203. Therefore, all participants in this study were to take 500 mg BID with no dose modifications permitted. - Increased study treatment period from 48 weeks to 96 weeks to allow continued access following the assessment of chronic toxicology studies. - Updated the risk-benefit in accordance with the current available clinical and nonclinical data. - Updated the participant withdrawal criteria to provide adequate participant protection against treatment related injury following a review of the nonclinical data, and current available clinical data. - Updated dosing compliance language following availability of PK modelling data and transition to tablets. - Added laboratory parameters to strengthen ability to detect treatment emergent adverse changes.
01 July 2022	Participants enrolled into this study were to reach Week 96 in October and November 2022. Therefore, this amendment was submitted to extend the duration of treatment for an additional 48 weeks; i.e., up to Week 144. Additional measures for safety monitoring were included to mirror safety monitoring assessments in registration studies, BCX9930-202 and BCX9930-203.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

The sponsor decided to prematurely terminate the study due to changes in the competitive landscape. Per change in planned analysis, data were analyzed and reported for safety and selected efficacy parameters

Notes: