



## Clinical trial results:

### A Randomized, Open-Label, Multicenter, Parallel-Group Study to Evaluate the Efficacy, Safety, and Tolerability of Oral BCX9930 Monotherapy for the Treatment of Paroxysmal Nocturnal Hemoglobinuria in Subjects with Inadequate Response to C5 Inhibitor Therapy

#### Summary

EudraCT number	2020-004438-39
Trial protocol	FR HU ES SK NL IT
Global end of trial date	14 September 2023

#### Results information

Result version number	v1
This version publication date	29 September 2024
First version publication date	29 September 2024

#### Trial information

##### Trial identification

Sponsor protocol code	BCX9930-202
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##### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05116774
WHO universal trial number (UTN)	-

Notes:

#### Sponsors

Sponsor organisation name	BioCryst Pharmaceuticals Inc.
Sponsor organisation address	4505 Emperor Boulevard Nottingham Hall, Suite 200, Durham, North Carolina, United States, 27703
Public contact	Study Director, BioCryst Pharmaceuticals Inc., +001 919859 1302, clinicaltrials@biocryst.com
Scientific contact	Study Director, BioCryst Pharmaceuticals Inc., +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	14 September 2023
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	14 September 2023
Was the trial ended prematurely?	Yes

Notes:

## General information about the trial

Main objective of the trial:

To determine the efficacy of oral BCX9930 monotherapy administered for 24 weeks, compared to continued complement component 5 (C5) inhibitor therapy, in participants with paroxysmal nocturnal hemoglobinuria (PNH) with an inadequate response to C5 inhibitor therapy.

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	06 December 2021
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	Spain: 2
Country: Number of subjects enrolled	France: 4
Country: Number of subjects enrolled	Hungary: 1
Country: Number of subjects enrolled	United Kingdom: 5
Worldwide total number of subjects	12
EEA total number of subjects	7

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)	7

From 65 to 84 years	5
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details:

The study was conducted in France, Hungary, Italy, Spain, and the United Kingdom (UK).

### Pre-assignment

Screening details:

A total 12 participants were randomized and treated.

### Period 1

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

### Arms

Are arms mutually exclusive?	No
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<b>Arm title</b>	BCX9930
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Arm description:

Participants received BCX9930 monotherapy throughout the study.

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.

<b>Arm title</b>	C5-INH
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Arm description:

Participants continued existing C5 INH therapy (eculizumab and ravulizumab) for 24 weeks. After the sponsor decided to halt enrolment in the study permanently and terminate the study, participants switched to open-label BCX9930 monotherapy prior to Week 24, if earlier. The maximum treatment duration was 24 weeks.

Arm type	Active comparator
Investigational medicinal product name	C5-INH
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Administered by intravenous infusion per current dose regimen.

<b>Arm title</b>	BCX9930 After C5-INH
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Arm description:

Participants who were initially randomized to continue C5-INH therapy received BCX9930 monotherapy after they had completed 24 weeks on C5-INH, or earlier after the sponsor decided to halt enrolment in the study permanently and terminate the study.

Arm type	Experimental
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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.

<b>Number of subjects in period 1</b>	BCX9930	C5-INH	BCX9930 After C5-INH
Started	8	4	3
Completed	3	2	2
Not completed	5	2	1
Consent withdrawn by subject	-	1	-
Adverse event, non-fatal	2	-	-
Miscellaneous	3	1	1

## Baseline characteristics

### Reporting groups

Reporting group title	BCX9930
Reporting group description: Participants received BCX9930 monotherapy throughout the study.	
Reporting group title	C5-INH
Reporting group description: Participants continued existing C5 INH therapy (eculizumab and ravulizumab) for 24 weeks. After the sponsor decided to halt enrolment in the study permanently and terminate the study, participants switched to open-label BCX9930 monotherapy prior to Week 24, if earlier. The maximum treatment duration was 24 weeks.	
Reporting group title	BCX9930 After C5-INH
Reporting group description: Participants who were initially randomized to continue C5-INH therapy received BCX9930 monotherapy after they had completed 24 weeks on C5-INH, or earlier after the sponsor decided to halt enrolment in the study permanently and terminate the study.	

Reporting group values	BCX9930	C5-INH	BCX9930 After C5-INH
Number of subjects	8	4	3
Age categorical Units: Subjects			

Age continuous Units: years arithmetic mean standard deviation	58.8 ± 17.66	48.5 ± 14.25	49.7 ± 17.21
Gender categorical Units: Subjects			
Female	4	3	2
Male	4	1	1
Ethnicity Units: Subjects			
Not Hispanic or Latino	5	2	2
Unknown or Not Reported	3	2	1
Race Units: Subjects			
Asian	0	1	1
Black or African American	2	0	0
White	5	2	2
Unknown or Not Reported	1	1	0

Reporting group values	Total		
Number of subjects	12		
Age categorical Units: Subjects			

Age continuous Units: years arithmetic mean standard deviation	-		
Gender categorical Units: Subjects			
Female	7		
Male	5		
Ethnicity Units: Subjects			
Not Hispanic or Latino	7		
Unknown or Not Reported	5		
Race Units: Subjects			
Asian	1		
Black or African American	2		
White	7		
Unknown or Not Reported	2		

## End points

### End points reporting groups

Reporting group title	BCX9930
Reporting group description: Participants received BCX9930 monotherapy throughout the study.	
Reporting group title	C5-INH
Reporting group description: Participants continued existing C5 INH therapy (eculizumab and ravulizumab) for 24 weeks. After the sponsor decided to halt enrolment in the study permanently and terminate the study, participants switched to open-label BCX9930 monotherapy prior to Week 24, if earlier. The maximum treatment duration was 24 weeks.	
Reporting group title	BCX9930 After C5-INH
Reporting group description: Participants who were initially randomized to continue C5-INH therapy received BCX9930 monotherapy after they had completed 24 weeks on C5-INH, or earlier after the sponsor decided to halt enrolment in the study permanently and terminate the study.	

### Primary: Change From Baseline in Hemoglobin at Week 24

End point title	Change From Baseline in Hemoglobin at Week 24 <sup>[1][2]</sup>
End point description: Participants in the All Subjects as Treated (ASaT) population (all participants who received at least 1 dose of study drug and had a post baseline laboratory assessment) with available data were analyzed.	
End point type	Primary
End point timeframe: Baseline, Week 24	

#### 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.

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: No participant who switched from C5-INH to BCX9930 had data available at Week 24. Therefore, BCX9930 after C5-INH group was not applicable for this endpoint.

End point values	BCX9930	C5-INH		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8	4		
Units: grams per deciliter (g/dL)				
arithmetic mean (standard deviation)				
Baseline (n=8, n=4)	9.12 (± 1.096)	9.13 (± 0.847)		
Change at Week 24 (n=6, n=2)	3.48 (± 0.674)	0.72 (± 0.884)		

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of Participants Who Were Transfusion-free



End point title	Number of Participants Who Were Transfusion-free
End point description:	
<p>The number of participants who did not receive any transfusions (packed red blood cells [pRBCs] or whole blood) during the period of interest were reported. Participants who were transfusion free were defined for each treatment group as the number of participants who did not receive any transfusions (pRBCs or whole blood) during the period of interest from the start to the end, inclusive, divided by the total number of participants in that treatment group at the start of the period of interest. Participants who (1) discontinued treatment prior to Week 24, or (2) did not receive a transfusion during the period of interest despite recording a hemoglobin (Hb) value <math>\leq 9</math> g/dL with symptoms assessed by the investigator as warranting transfusion or a Hb value <math>\leq 7</math> g/dL regardless of symptoms were not considered transfusion free.</p> <p>Participants in the ASaT population were analyzed.</p>	
End point type	Secondary
End point timeframe:	
From Week 4 to Week 24	

End point values	BCX9930	C5-INH	BCX9930 After C5-INH	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	8	4	3	
Units: participants	7	4	3	

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of Units of pRBCs Transfused

End point title	Number of Units of pRBCs Transfused
End point description:	
Participants in the ASaT population were analyzed.	
End point type	Secondary
End point timeframe:	
From Week 4 to Week 24	

End point values	BCX9930	C5-INH	BCX9930 After C5-INH	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	8	4	3	
Units: units of pRBCs	0	0	0	

### Statistical analyses

No statistical analyses for this end point

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

End point title	Change From Baseline in Functional Assessment of Chronic Illness Therapy (FACIT)-Fatigue Scale Score <sup>[3]</sup>
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### 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 ASaT population with available data were analyzed.

'99999' signifies standard deviation could not be calculated due to single participant.

End point type	Secondary
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### End point timeframe:

Baseline and Week 24

### Notes:

[3] - 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: No participant who switched from C5-INH to BCX9930 had data available at Week 24.

Therefore, BCX9930 after C5-INH group was not applicable for this endpoint.

End point values	BCX9930	C5-INH		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	2		
Units: Scores on a scale				
arithmetic mean (standard deviation)				
Baseline (n=6, n=2)	36.3 (± 9.69)	40.0 (± 8.49)		
Change at Week 24 (n=3, n=1)	-0.3 (± 12.86)	1.0 (± 99999)		

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Baseline up to Day 407

Adverse event reporting additional description:

The safety population included all participants who received at least 1 dose of study drug, whether C5 inhibitor or BCX9930.

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	BCX9930
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Reporting group description:

Participants received BCX9930 monotherapy throughout the study.

Reporting group title	C5-INH
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Reporting group description:

Participants continued existing C5 INH therapy (eculizumab and ravulizumab) for 24 weeks. After the sponsor decided to halt enrolment in the study permanently and terminate the study, participants switched to open-label BCX9930 monotherapy prior to Week 24, if earlier. The maximum treatment duration was 24 weeks.

Reporting group title	BCX9930 After C5-INH
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Reporting group description:

Participants who were initially randomized to continue C5-INH therapy received BCX9930 monotherapy after they had completed 24 weeks on C5-INH, or earlier after the sponsor decided to halt enrolment in the study permanently and terminate the study.

Serious adverse events	BCX9930	C5-INH	BCX9930 After C5-INH
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 8 (25.00%)	0 / 4 (0.00%)	1 / 3 (33.33%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Investigations			
Blood creatinine increased			
subjects affected / exposed	1 / 8 (12.50%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Rash erythematous			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 8 (12.50%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	BCX9930	C5-INH	BCX9930 After C5-INH
Total subjects affected by non-serious adverse events			
subjects affected / exposed	7 / 8 (87.50%)	3 / 4 (75.00%)	3 / 3 (100.00%)
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 8 (12.50%)	3 / 4 (75.00%)	0 / 3 (0.00%)
occurrences (all)	1	4	0
Chest pain			
subjects affected / exposed	1 / 8 (12.50%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Face oedema			
subjects affected / exposed	0 / 8 (0.00%)	1 / 4 (25.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Fatigue			
subjects affected / exposed	3 / 8 (37.50%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	5	0	0
Pain			
subjects affected / exposed	1 / 8 (12.50%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Pyrexia			
subjects affected / exposed	0 / 8 (0.00%)	1 / 4 (25.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Reproductive system and breast disorders			
Erectile dysfunction			
subjects affected / exposed	1 / 8 (12.50%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Scrotal oedema			

subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	1 / 4 (25.00%) 1	0 / 3 (0.00%) 0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 8 (12.50%)	0 / 4 (0.00%)	1 / 3 (33.33%)
occurrences (all)	1	0	1
Dyspnoea exertional			
subjects affected / exposed	0 / 8 (0.00%)	2 / 4 (50.00%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Rhinorrhoea			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Investigations			
Blood lactate dehydrogenase increased			
subjects affected / exposed	1 / 8 (12.50%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Prothrombin time prolonged			
subjects affected / exposed	1 / 8 (12.50%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	1 / 8 (12.50%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Cardiac disorders			
Palpitations			
subjects affected / exposed	1 / 8 (12.50%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Tachycardia			
subjects affected / exposed	1 / 8 (12.50%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	4 / 8 (50.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	4	0	0
Lethargy			

subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1	0 / 4 (0.00%) 0	0 / 3 (0.00%) 0
Loss of consciousness subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1	0 / 4 (0.00%) 0	0 / 3 (0.00%) 0
Nervous system disorder subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	1 / 4 (25.00%) 1	0 / 3 (0.00%) 0
Sciatica subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 4 (0.00%) 0	1 / 3 (33.33%) 1
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	1 / 4 (25.00%) 1	0 / 3 (0.00%) 0
Haemolysis subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1	0 / 4 (0.00%) 0	0 / 3 (0.00%) 0
Ear and labyrinth disorders Vertigo subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1	0 / 4 (0.00%) 0	0 / 3 (0.00%) 0
Eye disorders Vision blurred subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1	0 / 4 (0.00%) 0	0 / 3 (0.00%) 0
Gastrointestinal disorders Abdominal pain subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1	0 / 4 (0.00%) 0	0 / 3 (0.00%) 0
Abdominal pain upper subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1	0 / 4 (0.00%) 0	0 / 3 (0.00%) 0
Diarrhoea subjects affected / exposed occurrences (all)	2 / 8 (25.00%) 4	0 / 4 (0.00%) 0	0 / 3 (0.00%) 0
Dysphagia			

subjects affected / exposed occurrences (all)	3 / 8 (37.50%) 3	0 / 4 (0.00%) 0	0 / 3 (0.00%) 0
Inguinal hernia subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	1 / 4 (25.00%) 1	0 / 3 (0.00%) 0
Nausea subjects affected / exposed occurrences (all)	3 / 8 (37.50%) 3	0 / 4 (0.00%) 0	0 / 3 (0.00%) 0
Vomiting subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	1 / 4 (25.00%) 1	0 / 3 (0.00%) 0
Hepatobiliary disorders Hepatic cytolysis subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 4 (0.00%) 0	1 / 3 (33.33%) 1
Jaundice subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1	0 / 4 (0.00%) 0	0 / 3 (0.00%) 0
Skin and subcutaneous tissue disorders Rash subjects affected / exposed occurrences (all)	3 / 8 (37.50%) 6	0 / 4 (0.00%) 0	0 / 3 (0.00%) 0
Rash erythematous subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 4 (0.00%) 0	1 / 3 (33.33%) 1
Rash macular subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1	0 / 4 (0.00%) 0	1 / 3 (33.33%) 1
Rash maculo-papular subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1	0 / 4 (0.00%) 0	1 / 3 (33.33%) 1
Renal and urinary disorders Acute kidney injury subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1	0 / 4 (0.00%) 0	0 / 3 (0.00%) 0
Chromaturia			

subjects affected / exposed	1 / 8 (12.50%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	3	0	0
Haemoglobinuria			
subjects affected / exposed	1 / 8 (12.50%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Urinary incontinence			
subjects affected / exposed	1 / 8 (12.50%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	2 / 8 (25.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Axillary mass			
subjects affected / exposed	1 / 8 (12.50%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Back pain			
subjects affected / exposed	2 / 8 (25.00%)	2 / 4 (50.00%)	0 / 3 (0.00%)
occurrences (all)	3	2	0
Bone pain			
subjects affected / exposed	1 / 8 (12.50%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Myalgia			
subjects affected / exposed	1 / 8 (12.50%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 8 (0.00%)	1 / 4 (25.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
COVID-19			
subjects affected / exposed	1 / 8 (12.50%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Influenza			
subjects affected / exposed	0 / 8 (0.00%)	1 / 4 (25.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Localised infection			



subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Nasopharyngitis			
subjects affected / exposed	2 / 8 (25.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	3	0	0
Respiratory tract infection			
subjects affected / exposed	1 / 8 (12.50%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Subcutaneous abscess			
subjects affected / exposed	1 / 8 (12.50%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Upper respiratory tract infection			
subjects affected / exposed	1 / 8 (12.50%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Urinary tract infection			
subjects affected / exposed	1 / 8 (12.50%)	0 / 4 (0.00%)	1 / 3 (33.33%)
occurrences (all)	1	0	1
Viral infection			
subjects affected / exposed	1 / 8 (12.50%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Metabolism and nutrition disorders			
Hypokalaemia			
subjects affected / exposed	1 / 8 (12.50%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
27 May 2021	<ul style="list-style-type: none"><li>- The secondary efficacy endpoints for Part 1 were revised to emphasize key secondary endpoints that would demonstrate clinical benefit in support of the primary endpoint of change from baseline in hemoglobin (Hb).</li><li>- The randomization stratum based on receipt of any blood transfusion in the 6 months prior to baseline was redefined to refer to receipt of pRBC transfusion.</li><li>- The sample size calculation was reworked using an assumed treatment difference of 2 g/dL CFB in Hb (previously 1.5 g/dL) for participants randomly assigned to BCX9930 compared to participants randomly assigned to continue C5 INH therapy. This change allowed for the overall sample size to be reduced from 135 to 81 participants (with 54 participants in the BCX9930 group and 27 participants in the continued C5 INH therapy group).</li><li>- The benefit-risk text was updated in accordance with the currently available clinical and non-clinical data.</li><li>- Section (Prohibited and Restricted Medications) was extensively revised to take into account the preliminary results from a recently completed drug-drug interaction study, BCX9930 102.</li><li>- The requirement for the screening Hb value to be from a blood sample collected prior to pRBC transfusion or at least 14 days after transfusion was removed.</li></ul>
29 June 2022	<ul style="list-style-type: none"><li>- Recommended dose of BCX9930 was reduced from 500 mg BID to 400 mg BID for all participants.</li><li>- For newly randomly assigned participants, treatment with BCX9930 was to begin at 200 mg BID for the first 14 days before escalation to 400 mg BID.</li><li>- Additional safety assessments were added for all participants through the first 12 weeks of BCX9930 dosing.</li><li>- Revised guidance was provided for the management of participants with treatment-emergent increases in serum creatinine, including the discontinuation of any participant with a confirmed increase in serum creatinine.</li><li>- An independent Nephrology Risk Mitigation Working Group was established.</li><li>- Inclusion criterion 5(f) was modified.</li><li>- Recommendations were provided for dose tapering following discontinuation of BCX9930.</li></ul>
01 August 2022	<ul style="list-style-type: none"><li>- A study stopping rule was added.</li></ul>

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. As the study was terminated early and data was limited, per planned analysis only key efficacy endpoints and safety were analyzed and reported.

Notes: