



## 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	v2 (current)
This version publication date	24 May 2025
First version publication date	29 September 2024
Version creation reason	<ul style="list-style-type: none"><li>• Correction of full data set</li><li>• Need to align with CT.gov draft post NIH comments.</li></ul>

#### 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	Part 1 (Up to 24 weeks)
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/BCX9930
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Arm description:

Participants were randomized to receive BCX9930 during Part 1 and continued to receive the same during Part 2. Per protocol amendment, participants who previously received 500 mg twice daily (BID) orally and remained on study treatment were dose adjusted to 400 mg BID. For all newly enrolled participants, at the initiation of BCX9930 dosing, participants were administered a dose of 200 mg BID for the first 14 days of treatment before increasing to 400 mg BID. The maximum treatment duration on BCX9930 in Part 1 was 24 weeks. The overall maximum treatment duration on BCX9930 was 377 days.

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-Inhibitor (C5-INH)/BCX9930
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Arm description:

Participants randomized to this group continued the existing C5-INH therapy during Part 1. After the sponsor decided to halt enrolment in the study permanently and terminate the study, participants entered Part 2 where they switched to open-label BCX9930 monotherapy prior to Week 24, if earlier. The maximum treatment duration on C5-INH in Part 1 was 24 weeks. The maximum treatment duration on BCX9930 was 197 days.

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

Dosage and administration details:

Administered by intravenous infusion per current dose regimen.

Investigational medicinal product name	Ravulizumab
Investigational medicinal product code	
Other name	Ultomiris, ALXN1210, ravulizumab-cwvz
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous drip use

Dosage and administration details:

Administered by intravenous infusion per current dose regimen

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.

Number of subjects in period 1	BCX9930/BCX9930	C5-Inhibitor (C5-INH)/BCX9930
Started	8	4
Completed	7	3
Not completed	1	1
Consent withdrawn by subject	-	1
Adverse event, non-fatal	1	-

## Period 2

Period 2 title	Part 2 (Up to 52 weeks)
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

## Arms

Are arms mutually exclusive?	Yes
Arm title	BCX9930/BCX9930

Arm description:

Participants were randomized to receive BCX9930 during Part 1 and continued to receive the same during Part 2. Per protocol amendment, participants who previously received 500 mg twice daily (BID) orally and remained on study treatment were dose adjusted to 400 mg BID. For all newly enrolled participants, at the initiation of BCX9930 dosing, participants were administered a dose of 200 mg BID for the first 14 days of treatment before increasing to 400 mg BID. The maximum treatment duration on BCX9930 in Part 1 was 24 weeks. The overall maximum treatment duration on BCX9930 was 377 days.

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-Inhibitor (C5-INH)/BCX9930
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Arm description:

Participants randomized to this group continued the existing C5-INH therapy during Part 1. After the sponsor decided to halt enrolment in the study permanently and terminate the study, participants

entered Part 2 where they switched to open-label BCX9930 monotherapy prior to Week 24, if earlier. The maximum treatment duration on C5-INH in Part 1 was 24 weeks. The maximum treatment duration on BCX9930 was 197 days.

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

Dosage and administration details:

Administered by intravenous infusion per current dose regimen.

Investigational medicinal product name	Ravulizumab
Investigational medicinal product code	
Other name	Ultomiris, ALXN1210, ravulizumab-cwvz
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous drip use

Dosage and administration details:

Administered by intravenous infusion per current dose regimen

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 2</b>	<b>BCX9930/BCX9930</b>	<b>C5-Inhibitor (C5-INH)/BCX9930</b>
Started	7	3
Completed	3	2
Not completed	4	1
Adverse event, non-fatal	1	-
Miscellaneous	3	1

## Baseline characteristics

### Reporting groups

Reporting group title	BCX9930/BCX9930
Reporting group description:	
Participants were randomized to receive BCX9930 during Part 1 and continued to receive the same during Part 2. Per protocol amendment, participants who previously received 500 mg twice daily (BID) orally and remained on study treatment were dose adjusted to 400 mg BID. For all newly enrolled participants, at the initiation of BCX9930 dosing, participants were administered a dose of 200 mg BID for the first 14 days of treatment before increasing to 400 mg BID. The maximum treatment duration on BCX9930 in Part 1 was 24 weeks. The overall maximum treatment duration on BCX9930 was 377 days.	
Reporting group title	C5-Inhibitor (C5-INH)/BCX9930
Reporting group description:	
Participants randomized to this group continued the existing C5-INH therapy during Part 1. After the sponsor decided to halt enrolment in the study permanently and terminate the study, participants entered Part 2 where they switched to open-label BCX9930 monotherapy prior to Week 24, if earlier. The maximum treatment duration on C5-INH in Part 1 was 24 weeks. The maximum treatment duration on BCX9930 was 197 days.	

Reporting group values	BCX9930/BCX9930	C5-Inhibitor (C5-INH)/BCX9930	Total
Number of subjects	8	4	12
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	58.8	48.5	
standard deviation	± 17.66	± 14.25	-
Gender categorical Units: Subjects			
Female	4	3	7
Male	4	1	5
Ethnicity Units: Subjects			
Not Hispanic or Latino	5	2	7
Unknown or Not Reported	3	2	5
Race Units: Subjects			
Asian	0	1	1
Black or African American	2	0	2
White	5	2	7
Unknown or Not Reported	1	1	2

## End points

### End points reporting groups

Reporting group title	BCX9930/BCX9930
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Reporting group description:

Participants were randomized to receive BCX9930 during Part 1 and continued to receive the same during Part 2. Per protocol amendment, participants who previously received 500 mg twice daily (BID) orally and remained on study treatment were dose adjusted to 400 mg BID. For all newly enrolled participants, at the initiation of BCX9930 dosing, participants were administered a dose of 200 mg BID for the first 14 days of treatment before increasing to 400 mg BID. The maximum treatment duration on BCX9930 in Part 1 was 24 weeks. The overall maximum treatment duration on BCX9930 was 377 days.

Reporting group title	C5-Inhibitor (C5-INH)/BCX9930
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Reporting group description:

Participants randomized to this group continued the existing C5-INH therapy during Part 1. After the sponsor decided to halt enrolment in the study permanently and terminate the study, participants entered Part 2 where they switched to open-label BCX9930 monotherapy prior to Week 24, if earlier. The maximum treatment duration on C5-INH in Part 1 was 24 weeks. The maximum treatment duration on BCX9930 was 197 days.

Reporting group title	BCX9930/BCX9930
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Reporting group description:

Participants were randomized to receive BCX9930 during Part 1 and continued to receive the same during Part 2. Per protocol amendment, participants who previously received 500 mg twice daily (BID) orally and remained on study treatment were dose adjusted to 400 mg BID. For all newly enrolled participants, at the initiation of BCX9930 dosing, participants were administered a dose of 200 mg BID for the first 14 days of treatment before increasing to 400 mg BID. The maximum treatment duration on BCX9930 in Part 1 was 24 weeks. The overall maximum treatment duration on BCX9930 was 377 days.

Reporting group title	C5-Inhibitor (C5-INH)/BCX9930
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Reporting group description:

Participants randomized to this group continued the existing C5-INH therapy during Part 1. After the sponsor decided to halt enrolment in the study permanently and terminate the study, participants entered Part 2 where they switched to open-label BCX9930 monotherapy prior to Week 24, if earlier. The maximum treatment duration on C5-INH in Part 1 was 24 weeks. The maximum treatment duration on BCX9930 was 197 days.

Subject analysis set title	BCX9930
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Subject analysis set type	Sub-group analysis
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Subject analysis set description:

Participants were randomized to receive BCX9930 during Part 1. Per protocol amendment, participants who previously received 500 mg BID and remained on study treatment were dose adjusted to 400 mg BID. For all newly enrolled participants, at the initiation of BCX9930 dosing, participants were administered a dose of 200 mg BID for the first 14 days of treatment before increasing to 400 mg BID. The maximum treatment duration on BCX9930 in Part 1 was 24 weeks.

Subject analysis set title	C5-INH
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Subject analysis set type	Sub-group analysis
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Subject analysis set description:

Participants randomized to this group continued the existing C5-INH therapy during Part 1. The maximum treatment duration on C5-INH in Part 1 was 24 weeks.

### Primary: Part 1: Change From Baseline in Hemoglobin at Week 24

End point title	Part 1: Change From Baseline in Hemoglobin at Week 24 <sup>[1]</sup>
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End point description:

Participants in the All Subjects as Treated (ASaT) population in Part 1 with available data were analyzed.

End point type	Primary
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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.

End point values	BCX9930	C5-INH		
Subject group type	Subject analysis set	Subject analysis set		
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: Part 1: Number of Participants Who Were Transfusion-free

End point title	Part 1: Number of Participants Who Were Transfusion-free
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End point description:

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  $\leq 9$  g/dL with symptoms assessed by the investigator as warranting transfusion or a Hb value  $\leq 7$  g/dL regardless of symptoms were not considered transfusion free.

Participants in the ASaT population in Part 1 were analyzed.

End point type	Secondary
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End point timeframe:

From Week 4 to Week 24

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

## Statistical analyses

No statistical analyses for this end point

### Secondary: Part 1: Number of Units of pRBCs Transfused

End point title	Part 1: Number of Units of pRBCs Transfused
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End point description:

Participants in the ASaT population in Part 1 were analyzed.

End point type	Secondary
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End point timeframe:

From Week 4 to Week 24

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

## Statistical analyses

No statistical analyses for this end point

### Secondary: Part 1: Change From Baseline in Functional Assessment of Chronic Illness Therapy (FACIT)-Fatigue Scale Score

End point title	Part 1: Change From Baseline in Functional Assessment of Chronic Illness Therapy (FACIT)-Fatigue Scale Score
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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 in Part 1 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

End point values	BCX9930	C5-INH		
Subject group type	Subject analysis set	Subject analysis set		
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

**Secondary: Part 1: Percent Change From Baseline in Lactate Dehydrogenase**

End point title	Part 1: Percent Change From Baseline in Lactate Dehydrogenase
End point description: Participants in the ASaT population in Part 1 with available data were analyzed.	
End point type	Secondary
End point timeframe: Baseline, Week 24	

End point values	BCX9930	C5-INH		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	7	2		
Units: percent change				
arithmetic mean (standard deviation)	24.3 (± 53.07)	-21.0 (± 4.03)		

**Statistical analyses**

No statistical analyses for this end point

**Secondary: Part 1: Percentage (%) Reduction in the Rate of pRBC Units Transfused**

End point title	Part 1: Percentage (%) Reduction in the Rate of pRBC Units Transfused
End point description: The rate of pRBC units transfused from Week 4 to Week 24 was calculated and compared to the rate of pRBC units transfused prestudy during the 12 months prior to screening. The percent reduction in rate of pRBC units transfused was the percent difference in rate relative to the prestudy rate, calculated as: (current rate - prestudy rate)/prestudy rate * 100%. Total rate among all participants was evaluated here. Rate of pRBC units transfusion was defined as the percentage of participants who received pRBC transfusions. Participants in the ASaT population in Part 1 were analyzed. 99999= Not evaluable. No participants received pRBC transfusion at pre-study in the "C5-INH" arm, and therefore the percentage reduction, based on the formula provided, was not calculable.	
End point type	Secondary
End point timeframe: Prestudy (12 months prior to screening) and from Week 4 to Week 24	

End point values	BCX9930	C5-INH		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	8	4		
Units: percent reduction	100	99999		

**Statistical analyses**

No statistical analyses for this end point

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**Secondary: Part 1: Number of Participants With Hemoglobin  $\geq$  12 Grams Per Deciliter (g/dL)**

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End point title	Part 1: Number of Participants With Hemoglobin $\geq$ 12 Grams Per Deciliter (g/dL)
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End point description:

Participants in the ASaT population in Part 1 with available data were analyzed.

End point type	Secondary
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End point timeframe:

Week 24

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End point values	BCX9930	C5-INH		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	6	4		
Units: participants	6	0		

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**Statistical analyses**

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No statistical analyses for this end point

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**Secondary: Part 1: Number of Participants Who Achieved Hemoglobin Stabilization**

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End point title	Part 1: Number of Participants Who Achieved Hemoglobin Stabilization
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End point description:

Hemoglobin stabilization was defined as the participants who avoided 2 g/dL or greater decrease in hemoglobin in the absence of transfusion from Week 4 to Week 24. Participants in the ASaT population in Part 1 with available data were analyzed.

End point type	Secondary
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End point timeframe:

From Week 4 to Week 24

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End point values	BCX9930	C5-INH		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	5	4		
Units: participants	5	4		

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**Statistical analyses**

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No statistical analyses for this end point

**Secondary: Part 1: Change From Baseline in Complement Component 3 (C3)-Opsonized Red Blood Cells (RBCs)**

End point title	Part 1: Change From Baseline in Complement Component 3 (C3)-Opsonized Red Blood Cells (RBCs)
End point description: Red blood cells opsonized by C3 were to be assessed by flow cytometry. No data was collected for this endpoint.	
End point type	Secondary
End point timeframe: Baseline, Week 24	

End point values	BCX9930	C5-INH		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	0 <sup>[2]</sup>	0 <sup>[3]</sup>		
Units: percentage of opsonized RBCs				
arithmetic mean (standard deviation)	()	()		

Notes:

[2] - No data was collected for this endpoint.

[3] - No data was collected for this endpoint.

**Statistical analyses**

No statistical analyses for this end point

**Secondary: Part 1: Change From Baseline in Total Paroxysmal Nocturnal Hemoglobinuria (PNH) RBC Clone Size**

End point title	Part 1: Change From Baseline in Total Paroxysmal Nocturnal Hemoglobinuria (PNH) RBC Clone Size
End point description: The total PNH RBC clone size refers to the percentage of PNH affected (ie, Type 2 and 3) RBC cells within the total RBC population. Participants in the ASaT population in Part 1 with available data were analyzed.	
End point type	Secondary
End point timeframe: Baseline, Week 24	

End point values	BCX9930	C5-INH		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	6	3		
Units: % of PNH-RBC within total RBC population				
arithmetic mean (standard deviation)				
Baseline (n=6,3)	80.51 (± 16.94)	83.40 (± 14.34)		
Change at Week 24 (n=3,2)	23.18 (± 11.81)	-6.34 (± 8.986)		

## Statistical analyses

No statistical analyses for this end point

### Secondary: Part 1: Change From Baseline in Ratio of Total PNH RBC Clone Size to PNH White Blood Cell (WBC) Clone Size

End point title	Part 1: Change From Baseline in Ratio of Total PNH RBC Clone Size to PNH White Blood Cell (WBC) Clone Size
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End point description:

The total PNH RBC clone size refers to the percentage of PNH affected (ie, Type 2 and 3) RBCs within the total RBC population. The PNH WBC clone size refers to the percentage of PNH-affected WBCs within the total WBC population. The ratio of total PNH RBC clone size to PNH WBC clone size = ratio of percent total PNH RBCs / percent PNH WBCs. Participants in the ASaT population in Part 1 with available data were analyzed.

End point type	Secondary
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End point timeframe:

Baseline, Week 24

End point values	BCX9930	C5-INH		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	4	2		
Units: ratio				
arithmetic mean (standard deviation)				
Baseline (n=4,2)	0.8128 (± 0.16528)	0.9059 (± 0.12113)		
Change at Week 24 (n=3,2)	0.2336 (± 0.11595)	-0.0668 (± 0.09462)		

## Statistical analyses

No statistical analyses for this end point

### Secondary: Part 1: Change From Baseline in Absolute Reticulocyte Count (ARC)

End point title	Part 1: Change From Baseline in Absolute Reticulocyte Count (ARC)
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End point description:

Participants in the ASaT population in Part 1 with available data were analyzed.

End point type	Secondary
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End point timeframe:

Baseline, Week 24

End point values	BCX9930	C5-INH		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	7	4		
Units: 10 <sup>6</sup> cells/microliter (µL)				
arithmetic mean (standard deviation)				
Baseline (n=7,4)	0.2933 (± 0.10453)	0.3129 (± 0.16201)		
Change at Week 24 (n=6,4)	-0.2142 (± 0.05384)	-0.0462 (± 0.01823)		

### Statistical analyses

No statistical analyses for this end point

### Secondary: Part 1: Number of Participants With ARC in the Normal Range

End point title	Part 1: Number of Participants With ARC in the Normal Range
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End point description:

Number of participants with ARC in the normal range (0.03 - 0.12 10<sup>6</sup> cells/uL) were reported. Participants in the ASaT population in Part 1 with available data were analyzed.

End point type	Secondary
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End point timeframe:

Week 24

End point values	BCX9930	C5-INH		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	6	4		
Units: participants	4	1		

### Statistical analyses

No statistical analyses for this end point

### Secondary: Part 1: Change From Baseline in Haptoglobin

End point title	Part 1: Change From Baseline in Haptoglobin
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End point description:

Participants in the ASaT population in Part 1 with available data were analyzed.

End point type	Secondary
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End point timeframe:

Baseline, Week 24

End point values	BCX9930	C5-INH		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	7	4		
Units: grams per liter (g/L)				
arithmetic mean (standard deviation)				
Baseline	0.126 (± 0.0732)	0.105 (± 0.0268)		
Change at Week 24	-0.024 (± 0.0409)	-0.015 (± 0.0268)		

### Statistical analyses

No statistical analyses for this end point

### Secondary: Part 1: Number of Participants With Haptoglobin ≥ Lower Limit of Normal (LLN) Reference Range

End point title	Part 1: Number of Participants With Haptoglobin ≥ Lower Limit of Normal (LLN) Reference Range
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End point description:

Number of Participants With Haptoglobin ≥ LLN Reference Range (≥0.3 g/L) were reported. Participants in the ASaT population in Part 1 with available data were analyzed.

End point type	Secondary
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End point timeframe:

Week 24

End point values	BCX9930	C5-INH		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	7	4		
Units: participants	0	0		

### Statistical analyses

No statistical analyses for this end point

### Secondary: Part 1: Change From Baseline in Total Bilirubin

End point title	Part 1: Change From Baseline in Total Bilirubin
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End point description:

Participants in the ASaT population in Part 1 with available data were analyzed.

End point type	Secondary
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End point timeframe:

Baseline, Week 24



End point values	BCX9930	C5-INH		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	7	4		
Units: milligram per deciliter (mg/dL)				
arithmetic mean (standard deviation)				
Baseline	3.44 (± 3.679)	1.10 (± 0.424)		
Change at Week 24	-2.66 (± 3.672)	-0.02 (± 0.250)		

### 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/BCX9930
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Reporting group description:

Participants were randomized to receive BCX9930 during Part 1 and continued to receive the same during Part 2. Per protocol amendment, participants who previously received 500 mg BID and remained on study treatment were dose adjusted to 400 mg BID. For all newly enrolled participants, at the initiation of BCX9930 dosing, participants were administered a dose of 200 mg BID for the first 14 days of treatment before increasing to 400 mg BID. The maximum treatment duration on BCX9930 in Part 1 was 24 weeks. The overall maximum treatment duration on BCX9930 was 377 days.

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 date when sponsor decided to halt enrolment in the study permanently and terminate the study. Initially participants were to receive BCX9930 500 mg BID orally. Per protocol amendment, participants who previously received 500 mg BID and remained on study treatment were dose adjusted to 400 mg BID. For all newly enrolled participants, at the initiation of BCX9930 dosing, participants were administered a dose of 200 mg BID for the first 14 days of treatment before increasing to 400 mg BID. The maximum treatment duration on BCX9930 was 197 days.

Reporting group title	C5-INH
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Reporting group description:

Participants randomized to this group continued the existing C5-INH therapy during Part 1. The maximum treatment duration on C5-INH was 24 weeks.

Serious adverse events	BCX9930/BCX9930	BCX9930 After C5-INH	C5-INH
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 8 (25.00%)	1 / 3 (33.33%)	0 / 4 (0.00%)
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 / 3 (0.00%)	0 / 4 (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%)	1 / 3 (33.33%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
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 / 3 (0.00%)	0 / 4 (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/BCX9930	BCX9930 After C5-INH	C5-INH
Total subjects affected by non-serious adverse events			
subjects affected / exposed	7 / 8 (87.50%)	3 / 3 (100.00%)	3 / 4 (75.00%)
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 8 (12.50%)	0 / 3 (0.00%)	3 / 4 (75.00%)
occurrences (all)	1	0	4
Chest pain			
subjects affected / exposed	1 / 8 (12.50%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Face oedema			
subjects affected / exposed	0 / 8 (0.00%)	0 / 3 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Fatigue			
subjects affected / exposed	3 / 8 (37.50%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	5	0	0
Pain			
subjects affected / exposed	1 / 8 (12.50%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Pyrexia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 3 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Reproductive system and breast disorders			

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

Headache			
subjects affected / exposed	4 / 8 (50.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	4	0	0
Lethargy			
subjects affected / exposed	1 / 8 (12.50%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Loss of consciousness			
subjects affected / exposed	1 / 8 (12.50%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Nervous system disorder			
subjects affected / exposed	0 / 8 (0.00%)	0 / 3 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Sciatica			
subjects affected / exposed	0 / 8 (0.00%)	1 / 3 (33.33%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 3 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Haemolysis			
subjects affected / exposed	1 / 8 (12.50%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	1 / 8 (12.50%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Eye disorders			
Vision blurred			
subjects affected / exposed	1 / 8 (12.50%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 8 (12.50%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Abdominal pain upper			
subjects affected / exposed	1 / 8 (12.50%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0

Diarrhoea			
subjects affected / exposed	2 / 8 (25.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	4	0	0
Dysphagia			
subjects affected / exposed	3 / 8 (37.50%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	3	0	0
Inguinal hernia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 3 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Nausea			
subjects affected / exposed	3 / 8 (37.50%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	3	0	0
Vomiting			
subjects affected / exposed	0 / 8 (0.00%)	0 / 3 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Hepatobiliary disorders			
Hepatic cytolysis			
subjects affected / exposed	0 / 8 (0.00%)	1 / 3 (33.33%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Jaundice			
subjects affected / exposed	1 / 8 (12.50%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	3 / 8 (37.50%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	6	0	0
Rash erythematous			
subjects affected / exposed	0 / 8 (0.00%)	1 / 3 (33.33%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Rash macular			
subjects affected / exposed	1 / 8 (12.50%)	1 / 3 (33.33%)	0 / 4 (0.00%)
occurrences (all)	1	1	0
Rash maculo-papular			
subjects affected / exposed	1 / 8 (12.50%)	1 / 3 (33.33%)	0 / 4 (0.00%)
occurrences (all)	1	1	0
Renal and urinary disorders			

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

subjects affected / exposed	0 / 8 (0.00%)	0 / 3 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Localised infection			
subjects affected / exposed	0 / 8 (0.00%)	1 / 3 (33.33%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Nasopharyngitis			
subjects affected / exposed	2 / 8 (25.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	3	0	0
Respiratory tract infection			
subjects affected / exposed	1 / 8 (12.50%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Subcutaneous abscess			
subjects affected / exposed	1 / 8 (12.50%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Upper respiratory tract infection			
subjects affected / exposed	1 / 8 (12.50%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Urinary tract infection			
subjects affected / exposed	1 / 8 (12.50%)	1 / 3 (33.33%)	0 / 4 (0.00%)
occurrences (all)	1	1	0
Viral infection			
subjects affected / exposed	1 / 8 (12.50%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Metabolism and nutrition disorders			
Hypokalaemia			
subjects affected / exposed	1 / 8 (12.50%)	0 / 3 (0.00%)	0 / 4 (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 terminate the development program including this study.

Notes: