Clinical trial results:
A Randomized, Double-Blind, Multicenter, Placebo-Controlled, Parallel-Group Study to Evaluate the Efficacy, Safety, and Tolerability of Oral BCX9930 Monotherapy for the Treatment of Paroxysmal Nocturnal Hemoglobinuria

Summary

EudraCT number	2020-004403-14
Trial protocol	ES LT CZ IT
Global end of trial date	18 September 2023

Results information

Result version number	v2 (current)
This version publication date	23 August 2025
First version publication date	29 September 2024
Version creation reason	• Correction of full data set Post NIH comments, need to align the draft with the already posted CT.gov draft.

Trial information

Trial identification

Sponsor protocol code	BCX9930-203

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05116787
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	18 September 2023
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	18 September 2023
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy of oral BCX9930 monotherapy administered for 12 weeks, as compared to placebo, in participants with paroxysmal nocturnal hemoglobinuria (PNH).

Protection of trial subjects:

This trial was conducted in compliance with International Conference on Harmonisation (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	26 October 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	Malaysia: 3
Country: Number of subjects enrolled	South Africa: 8
Country: Number of subjects enrolled	Korea, Republic of: 1
Worldwide total number of subjects	12
EEA total number of subjects	0

Notes:

Subjects enrolled per age group

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

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted in Malaysia, South Africa, and Korea.

Pre-assignment

Screening details:

A total 12 participants were randomized and treated.

Period 1

Period 1 title	Part 1:DB Phase (up to 12 Weeks)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	No
Arm title	BCX9930/BCX9930

Arm description:

Participants received BCX9930 monotherapy in double blind (DB) manner (Part 1) for 12 weeks, then in an open-label manner for the remainder of the study (Part 2). After the sponsor decided to halt enrolment in the study permanently and terminate the study, participants on blinded study treatment were switched to open-label BCX9930 prior to Week 12. Initially participants were to receive BCX9930 500 mg twice daily (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 in Part 1 was 12 weeks. The overall maximum duration on BCX9930 was 378 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	Placebo/BCX9930

Arm description:

Participants received BCX9930 matching placebo in double blind manner for 12 weeks (Part 1). After the sponsor decided to halt enrolment in the study permanently and terminate the study, participants switched to open-label BCX9930 monotherapy (Part 2) prior to Week 12, if earlier. The maximum duration on Placebo in Part 1 was 12 weeks. The maximum treatment duration on BCX9930 was 281 days.

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

Dosage and administration details:

Administered orally twice daily.

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	Placebo/BCX9930
Started	10	2
Completed	8	1
Not completed	2	1
Consent withdrawn by subject	-	1
Adverse event, non-fatal	1	-
Pregnancy	1	-

Period 2

Period 2 title	Part 2:Open Label Phase (Up to 52 weeks)
Is this the baseline period?	No
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	No
Arm title	BCX9930/BCX9930

Arm description:

Participants received BCX9930 monotherapy in double blind (DB) manner (Part 1) for 12 weeks, then in an open-label manner for the remainder of the study (Part 2). After the sponsor decided to halt enrolment in the study permanently and terminate the study, participants on blinded study treatment were switched to open-label BCX9930 prior to Week 12. Initially participants were to receive BCX9930 500 mg twice daily (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 in Part 1 was 12 weeks. The overall maximum duration on BCX9930 was 378 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	Placebo/BCX9930

Arm description:

Participants received BCX9930 matching placebo in double blind manner for 12 weeks (Part 1). After the sponsor decided to halt enrolment in the study permanently and terminate the study, participants switched to open-label BCX9930 monotherapy (Part 2) prior to Week 12, if earlier. The maximum duration on Placebo in Part 1 was 12 weeks. The maximum treatment duration on BCX9930 was 281 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.

Number of subjects in period 2	BCX9930/BCX9930	Placebo/BCX9930
Started	8	1
Completed	4	1
Not completed	4	0
Miscellaneous	4	-

Baseline characteristics

Reporting groups

Reporting group title	BCX9930/BCX9930

Reporting group description:

Participants received BCX9930 monotherapy in double blind (DB) manner (Part 1) for 12 weeks, then in an open-label manner for the remainder of the study (Part 2). After the sponsor decided to halt enrolment in the study permanently and terminate the study, participants on blinded study treatment were switched to open-label BCX9930 prior to Week 12. Initially participants were to receive BCX9930 500 mg twice daily (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 in Part 1 was 12 weeks. The overall maximum duration on BCX9930 was 378 days.

Reporting group title	Placebo/BCX9930

Reporting group description:

Participants received BCX9930 matching placebo in double blind manner for 12 weeks (Part 1). After the sponsor decided to halt enrolment in the study permanently and terminate the study, participants switched to open-label BCX9930 monotherapy (Part 2) prior to Week 12, if earlier. The maximum duration on Placebo in Part 1 was 12 weeks. The maximum treatment duration on BCX9930 was 281 days.

Reporting group values	BCX9930/BCX9930	Placebo/BCX9930	Total
Number of subjects	10	2	12
Age categorical Units: Subjects			
Adults (18-64 years)	10	2	12
Age continuous Units: years			
arithmetic mean	37.8	37.0	
standard deviation	± 12.70	± 9.90	-
Gender categorical Units: Subjects			
Female	6	2	8
Male	4	0	4
Ethnicity Units: Subjects			
Hispanic or Latino	0	0	0
Not Hispanic or Latino	10	2	12
Race Units: Subjects			
Asian	3	2	5
Black or African American	7	0	7

End points

End points reporting groups

Reporting group title	BCX9930/BCX9930

Reporting group description:

Participants received BCX9930 monotherapy in double blind (DB) manner (Part 1) for 12 weeks, then in an open-label manner for the remainder of the study (Part 2). After the sponsor decided to halt enrolment in the study permanently and terminate the study, participants on blinded study treatment were switched to open-label BCX9930 prior to Week 12. Initially participants were to receive BCX9930 500 mg twice daily (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 in Part 1 was 12 weeks. The overall maximum duration on BCX9930 was 378 days.

Reporting group title	Placebo/BCX9930

Reporting group description:

Participants received BCX9930 matching placebo in double blind manner for 12 weeks (Part 1). After the sponsor decided to halt enrolment in the study permanently and terminate the study, participants switched to open-label BCX9930 monotherapy (Part 2) prior to Week 12, if earlier. The maximum duration on Placebo in Part 1 was 12 weeks. The maximum treatment duration on BCX9930 was 281 days.

Reporting group title	BCX9930/BCX9930

Reporting group description:

Participants received BCX9930 monotherapy in double blind (DB) manner (Part 1) for 12 weeks, then in an open-label manner for the remainder of the study (Part 2). After the sponsor decided to halt enrolment in the study permanently and terminate the study, participants on blinded study treatment were switched to open-label BCX9930 prior to Week 12. Initially participants were to receive BCX9930 500 mg twice daily (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 in Part 1 was 12 weeks. The overall maximum duration on BCX9930 was 378 days.

Reporting group title	Placebo/BCX9930

Reporting group description:

Participants received BCX9930 matching placebo in double blind manner for 12 weeks (Part 1). After the sponsor decided to halt enrolment in the study permanently and terminate the study, participants switched to open-label BCX9930 monotherapy (Part 2) prior to Week 12, if earlier. The maximum duration on Placebo in Part 1 was 12 weeks. The maximum treatment duration on BCX9930 was 281 days.

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

Subject analysis set description:

Participants received BCX9930 monotherapy in double blind manner (Part 1) for 12 weeks. 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.

Subject analysis set title	Placebo
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received BCX9930 matching placebo in double blind manner for 12 weeks (Part 1).

Primary: Part 1: Change From Baseline in Hemoglobin at Week 12

End point title	Part 1: Change From Baseline in Hemoglobin at Week 12[1]

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) in Part 1 were analyzed.

End point type	Primary

End point timeframe:

Baseline, Week 12

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, only descriptive analyses was performed.

End point values	BCX9930	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	10	2		
Units: grams per deciliter (g/dL)				
arithmetic mean (standard deviation)				
Baseline	8.49 (± 1.556)	9.48 (± 1.721)		
Change at Week 12	2.23 (± 2.146)	-1.23 (± 0.330)		

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

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 12, or (2) did not receive a transfusion during the period of interest despite recording a Hemoglobin (Hb) value ≤ 9 g/dL with symptoms assessed by the investigator as warranting transfusion or a Hb value ≤ 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

End point timeframe:

From Week 4 to Week 12

End point values	BCX9930	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	10	2		
Units: participants	8	1		

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

End point description:

Participants in the ASaT population in Part 1 were analyzed.

End point type	Secondary

End point timeframe:

From Week 4 to Week 12

End point values	BCX9930	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	10	2		
Units: units of pRBCs	1	0		

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 were analyzed.

End point type	Secondary

End point timeframe:

Baseline, Week 12

End point values	BCX9930	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	10	2		
Units: percent change				
arithmetic mean (standard deviation)				
Part 1: Percent Change From Baseline	-69.8 (± 26.00)	9.1 (± 45.47)		

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

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.

End point type	Secondary

End point timeframe:

Baseline, Week 12

End point values	BCX9930	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	9	2		
Units: scores on a scale				
arithmetic mean (standard deviation)				
Baseline (n=9, n=2)	34.3 (± 13.47)	13.0 (± 8.49)		
Change at Week 12 (n=8, n=2)	-2.3 (± 13.48)	-2.0 (± 0.00)		

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 12 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.

End point type	Secondary

End point timeframe:

Prestudy (12 months prior to screening) and from Week 4 to Week 12

End point values	BCX9930	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	10	2		
Units: percent reduction				
number (not applicable)	89	100		

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1: Number of Participants With Hemoglobin ≥ 12 g/dL

End point title	Part 1: Number of Participants With Hemoglobin ≥ 12 g/dL

End point description:

Participants in the ASaT population in Part 1 were analyzed.

End point type	Secondary

End point timeframe:

At Week 12

End point values	BCX9930	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	10	2		
Units: participants	2	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1: Number of Participants Achieving Hemoglobin Stabilization

End point title	Part 1: Number of Participants Achieving Hemoglobin Stabilization

End point description:

Hemoglobin (Hb) 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 12. Participants in the ASaT population in Part 1 with available data were analyzed.

End point type	Secondary

End point timeframe:

From Week 4 to Week 12

End point values	BCX9930	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	8	2		
Units: participants	8	2		

Statistical analyses

No statistical analyses for this end point

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

End point title	Part 1: Change From Baseline in Total Paroxysmal Nocturnal Hemoglobinuria (PNH) Red Blood Cell (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 Part 1 were analyzed.

End point type	Secondary

End point timeframe:

Baseline, Week 12

End point values	BCX9930	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	10	2		
Units: % of PNH-RBC within total RBC population				
arithmetic mean (standard deviation)				
Baseline	50.16 (± 30.386)	33.72 (± 3.765)		
Change at Week 12	30.76 (± 25.925)	-2.15 (± 0.032)		

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

End point description:

The total PNH RBC clone size refers to the percentage of PNH-affected (i.e, 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. The value 99999 denotes not applicable (NA).

End point type	Secondary

End point timeframe:

Baseline, Week 12

End point values	BCX9930	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	7	1		
Units: ratio				
arithmetic mean (standard deviation)				

Baseline	0.6425 (± 0.28016)	0.6860 (± 99999)		
Change at Week 12	0.2905 (± 0.26628)	-0.3052 (± 99999)		

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)

End point description:

Participants in the ASaT population in Part 1 with available data were analyzed. The value 99999 represents NA.

End point type	Secondary

End point timeframe:

Baseline, Week 12

End point values	BCX9930	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	10	2		
Units: 10^9 cells/ microliter (µL)				
arithmetic mean (standard deviation)				
Baseline (n=10,n=2)	200.01 (± 81.094)	261.47 (± 13.529)		
Change at Week 12 (n=9, n=1)	-111.01 (± 80.799)	-21.43 (± 99999)		

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

End point description:

Number of participants with ARC in the normal range (50 - 100 x 10^9 cells/L) were reported. Participants in the ASaT population in Part 1 with available data were analyzed.

End point type	Secondary

End point timeframe:

Week 12

End point values	BCX9930	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	9	1		
Units: participants	5	0		

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

End point description:

Participants in the ASaT population in Part 1 were analyzed.

End point type	Secondary

End point timeframe:

Baseline, Week 12

End point values	BCX9930	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	10	2		
Units: grams per liter (g/L)				
arithmetic mean (standard deviation)				
Baseline	0.182 (± 0.0711)	0.195 (± 0.1485)		
Change at Week 12	0.493 (± 0.6948)	0.000 (± 0.0000)		

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

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 were analyzed.

End point type	Secondary

End point timeframe:

Week 12

End point values	BCX9930	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	10	2		
Units: participants	5	1		

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

End point description:

Participants in the ASaT population in Part 1 were analyzed.

End point type	Secondary

End point timeframe:

Baseline, Week 12

End point values	BCX9930	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	10	2		
Units: milligram per deciliter (mg/dL)				
arithmetic mean (standard deviation)				
Baseline	1.66 (± 1.944)	3.45 (± 2.475)		
Change at Week 12	-0.97 (± 1.706)	0.80 (± 0.283)		

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1: Change From Baseline in Aspartate Aminotransferase (AST)

End point title	Part 1: Change From Baseline in Aspartate Aminotransferase (AST)

End point description:

Participants in the ASaT population in Part 1 were analyzed.

End point type	Secondary

End point timeframe:

Baseline, Week 12

End point values	BCX9930	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	10	2		
Units: Units per liter (U/L)				
arithmetic mean (standard deviation)				
Baseline	107.43 (± 71.295)	83.60 (± 6.505)		
Change at Week 12	-68.83 (± 58.333)	13.00 (± 36.487)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From Day 1 up to 408 days

Adverse event reporting additional description:

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

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24

Reporting groups

Reporting group title	BCX9930/BCX9930

Reporting group description:

Participants received BCX9930 monotherapy in double blind manner (Part 1) for 12 weeks, then in an open label manner for the remainder of the study (Part 2). After the sponsor decided to halt enrolment in the study permanently and terminate the study, participants on blinded study treatment were switched to open label BCX9930 prior to Week 12. 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 was 378 days.

Reporting group title	Placebo

Reporting group description:

Participants received BCX9930 matching placebo in double blind manner for 12 weeks (Part 1).

Reporting group title	BCX9930 After Placebo

Reporting group description:

Participants who were initially randomized to placebo group received BCX9930 monotherapy in open label manner, if they had completed Week 12 on placebo, or earlier after the 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 was 281 days.

Serious adverse events	BCX9930/BCX9930	Placebo	BCX9930 After Placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 10 (50.00%)	1 / 2 (50.00%)	1 / 1 (100.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Blood and lymphatic system disorders			
Breakthrough haemolysis			
subjects affected / exposed	1 / 10 (10.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			

Budd-Chiari syndrome			
subjects affected / exposed	0 / 10 (0.00%)	1 / 2 (50.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Renal failure			
subjects affected / exposed	1 / 10 (10.00%)	0 / 2 (0.00%)	0 / 1 (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
Musculoskeletal and connective tissue disorders			
Intervertebral disc protrusion			
subjects affected / exposed	1 / 10 (10.00%)	0 / 2 (0.00%)	0 / 1 (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
Infections and infestations			
Enterovirus infection			
subjects affected / exposed	0 / 10 (0.00%)	0 / 2 (0.00%)	1 / 1 (100.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza			
subjects affected / exposed	1 / 10 (10.00%)	0 / 2 (0.00%)	0 / 1 (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
Pneumonia fungal			
subjects affected / exposed	1 / 10 (10.00%)	0 / 2 (0.00%)	0 / 1 (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
Tuberculosis			
subjects affected / exposed	1 / 10 (10.00%)	0 / 2 (0.00%)	0 / 1 (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
Urinary tract infection			

subjects affected / exposed	1 / 10 (10.00%)	0 / 2 (0.00%)	0 / 1 (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

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

Non-serious adverse events	BCX9930/BCX9930	Placebo	BCX9930 After Placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	10 / 10 (100.00%)	2 / 2 (100.00%)	1 / 1 (100.00%)
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	1 / 10 (10.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Fatigue			
subjects affected / exposed	3 / 10 (30.00%)	1 / 2 (50.00%)	0 / 1 (0.00%)
occurrences (all)	4	1	0
Influenza like illness			
subjects affected / exposed	1 / 10 (10.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Malaise			
subjects affected / exposed	1 / 10 (10.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Peripheral swelling			
subjects affected / exposed	0 / 10 (0.00%)	1 / 2 (50.00%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Swelling face			
subjects affected / exposed	1 / 10 (10.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Vaccination site pruritus			
subjects affected / exposed	1 / 10 (10.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	1 / 10 (10.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0

Reproductive system and breast disorders			
Breast pain			
subjects affected / exposed[1]	1 / 6 (16.67%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Dysmenorrhoea			
subjects affected / exposed[2]	1 / 6 (16.67%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	2	0	0
Heavy menstrual bleeding			
subjects affected / exposed[3]	1 / 6 (16.67%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	2	0	0
Menometrorrhagia			
subjects affected / exposed[4]	0 / 6 (0.00%)	0 / 2 (0.00%)	1 / 1 (100.00%)
occurrences (all)	0	0	1
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	2 / 10 (20.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	2	0	0
Epistaxis			
subjects affected / exposed	1 / 10 (10.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	2	0	0
Oropharyngeal pain			
subjects affected / exposed	0 / 10 (0.00%)	0 / 2 (0.00%)	1 / 1 (100.00%)
occurrences (all)	0	0	1
Rhinitis allergic			
subjects affected / exposed	0 / 10 (0.00%)	0 / 2 (0.00%)	1 / 1 (100.00%)
occurrences (all)	0	0	1
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 10 (0.00%)	0 / 2 (0.00%)	1 / 1 (100.00%)
occurrences (all)	0	0	1
Depression			
subjects affected / exposed	1 / 10 (10.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	2	0	0
Insomnia			
subjects affected / exposed	1 / 10 (10.00%)	0 / 2 (0.00%)	1 / 1 (100.00%)
occurrences (all)	1	0	1

Investigations			
Blood uric acid increased			
subjects affected / exposed	1 / 10 (10.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Serum ferritin decreased			
subjects affected / exposed	1 / 10 (10.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Weight increased			
subjects affected / exposed	0 / 10 (0.00%)	0 / 2 (0.00%)	1 / 1 (100.00%)
occurrences (all)	0	0	1
Injury, poisoning and procedural complications			
Subcutaneous haematoma			
subjects affected / exposed	0 / 10 (0.00%)	0 / 2 (0.00%)	1 / 1 (100.00%)
occurrences (all)	0	0	1
Cardiac disorders			
Tachycardia			
subjects affected / exposed	1 / 10 (10.00%)	0 / 2 (0.00%)	1 / 1 (100.00%)
occurrences (all)	1	0	1
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 10 (10.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Headache			
subjects affected / exposed	4 / 10 (40.00%)	0 / 2 (0.00%)	1 / 1 (100.00%)
occurrences (all)	6	0	1
Blood and lymphatic system disorders			
Breakthrough haemolysis			
subjects affected / exposed	2 / 10 (20.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	2	0	0
Haemolysis			
subjects affected / exposed	2 / 10 (20.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	2	0	0
Neutropenia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 2 (0.00%)	1 / 1 (100.00%)
occurrences (all)	0	0	2
Gastrointestinal disorders			

Abdominal pain			
subjects affected / exposed	3 / 10 (30.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	4	0	0
Abdominal tenderness			
subjects affected / exposed	1 / 10 (10.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Constipation			
subjects affected / exposed	1 / 10 (10.00%)	1 / 2 (50.00%)	0 / 1 (0.00%)
occurrences (all)	1	1	0
Diarrhoea			
subjects affected / exposed	3 / 10 (30.00%)	0 / 2 (0.00%)	1 / 1 (100.00%)
occurrences (all)	3	0	2
Dyspepsia			
subjects affected / exposed	1 / 10 (10.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	2	0	0
Dysphagia			
subjects affected / exposed	2 / 10 (20.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	2	0	0
Gastric varices			
subjects affected / exposed	1 / 10 (10.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 10 (10.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Nausea			
subjects affected / exposed	1 / 10 (10.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Varices oesophageal			
subjects affected / exposed	1 / 10 (10.00%)	1 / 2 (50.00%)	0 / 1 (0.00%)
occurrences (all)	1	1	0
Vomiting			
subjects affected / exposed	2 / 10 (20.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	2	0	0
Hepatobiliary disorders			
Jaundice			

subjects affected / exposed	1 / 10 (10.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 2 (0.00%)	1 / 1 (100.00%)
occurrences (all)	0	0	1
Hyperhidrosis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 2 (0.00%)	1 / 1 (100.00%)
occurrences (all)	0	0	1
Pruritus			
subjects affected / exposed	6 / 10 (60.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	8	0	0
Rash			
subjects affected / exposed	1 / 10 (10.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Rash maculo-papular			
subjects affected / exposed	3 / 10 (30.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	5	0	0
Rash papular			
subjects affected / exposed	1 / 10 (10.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Skin ulcer			
subjects affected / exposed	1 / 10 (10.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 10 (10.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Haematuria			
subjects affected / exposed	1 / 10 (10.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Haemoglobinuria			
subjects affected / exposed	1 / 10 (10.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Nephropathy			

subjects affected / exposed	1 / 10 (10.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	3 / 10 (30.00%)	0 / 2 (0.00%)	1 / 1 (100.00%)
occurrences (all)	4	0	1
Arthritis reactive			
subjects affected / exposed	1 / 10 (10.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Flank pain			
subjects affected / exposed	1 / 10 (10.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Joint stiffness			
subjects affected / exposed	1 / 10 (10.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal stiffness			
subjects affected / exposed	0 / 10 (0.00%)	0 / 2 (0.00%)	1 / 1 (100.00%)
occurrences (all)	0	0	1
Periarthritis			
subjects affected / exposed	1 / 10 (10.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Infections and infestations			
COVID-19			
subjects affected / exposed	2 / 10 (20.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	2	0	0
Conjunctivitis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 2 (0.00%)	1 / 1 (100.00%)
occurrences (all)	0	0	1
Influenza			
subjects affected / exposed	1 / 10 (10.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Pneumonia			
subjects affected / exposed	1 / 10 (10.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Pulmonary tuberculosis			

subjects affected / exposed	1 / 10 (10.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Tonsillitis			
subjects affected / exposed	1 / 10 (10.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Upper respiratory tract infection			
subjects affected / exposed	4 / 10 (40.00%)	0 / 2 (0.00%)	1 / 1 (100.00%)
occurrences (all)	5	0	1
Urinary tract infection			
subjects affected / exposed	1 / 10 (10.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 10 (10.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0

Notes:

[1] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: This is a gender specific event occurring only in female participants therefore, the numbers vary.
[2] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: This is a gender specific event occurring only in female participants therefore, the numbers vary.
[3] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: This is a gender specific event occurring only in female participants therefore, the numbers vary.
[4] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: This is a gender specific event occurring only in female participants therefore, the numbers vary.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
27 May 2021	- The primary efficacy endpoint for Part 1 was updated from percent change in lactate dehydrogenase at Week 12 to change from baseline in Hb at Week 12. - The secondary efficacy endpoints for Part 1 were revised to emphasize key secondary endpoints that will demonstrate clinical benefit in support of the new primary endpoint. - The sample size calculation and power statement were updated to reflect the change in the primary endpoint. - The remaining endpoints were categorized as other secondary efficacy endpoints, other health-related quality of life endpoints, or exploratory endpoints. - The secondary endpoints for Part 2 were revised to reflect the changes made to the Part 1 endpoints. - New secondary endpoints were described for both parts and others were removed. - The statistical methods described were revised extensively to reflect the changes made to the endpoints. - 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. - The benefit-risk was updated in accordance with the currently available clinical and nonclinical data. - Section (Prohibited and Restricted Medications) was extensively revised. Prohibited medications were redefined.
29 June 2022	- The recommended dose of BCX9930 was reduced from 500 mg BID to 400 mg BID for all participants. - For newly randomized participants, treatment with BCX9930 was to begin at 200 mg BID for the first 14 days before escalation to 400 mg BID. - Additional safety assessments were added for all participants through the first 12 weeks of BCX9930 dosing. - Guidance was provided for the management of participants with treatment-emergent increases in serum creatinine. - Inclusion Criterion 5(f) was modified. - Recommendations were provided for dose tapering following discontinuation of BCX9930.
01 August 2022	- A study stopping rule was added.

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: