Clinical trial results:
A Phase III Randomised, Double-blind, Multicentre Study to Compare the Efficacy, Safety, Pharmacokinetics, and Immunogenicity between SB12 (proposed eculizumab biosimilar) and Soliris® in Subjects with Paroxysmal Nocturnal Haemoglobinuria

Summary

EudraCT number	2018-002857-31
Trial protocol	RO
Global end of trial date	21 October 2021

Results information

Result version number	v1 (current)
This version publication date	20 April 2024
First version publication date	20 April 2024

Trial information

Trial identification

Sponsor protocol code	SB12-3003

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04058158
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Samsung Bioepis Co., Ltd.
Sponsor organisation address	76, Songdogyoyuk-ro, Yeonsu-gu, Incheon, Korea, Republic of, 21987
Public contact	Information Desk, Samsung Bioepis Co., Ltd., +82 032 728 0114, bioepisinfo@samsung.com
Scientific contact	Information Desk, Samsung Bioepis Co., Ltd., +82 032 728 0114, bioepisinfo@samsung.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	21 October 2021
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	21 October 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study is to demonstrate comparable clinical efficacy of SB12 and Soliris®, by evaluating the lactate dehydrogenase (LDH) in subjects with paroxysmal nocturnal haemoglobinuria (PNH).

Protection of trial subjects:

Subjects should be monitored and documented for at least one hour following completion of the infusion for signs or symptoms of an infusion reaction. If an adverse reaction occurs during the administration of IPs, the infusion may be slowed or stopped at the discretion of the Investigator. If the infusion is slowed, the total infusion time may not exceed 2 hours.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	07 August 2019
Long term follow-up planned	Yes
Long term follow-up rationale	Ethical reason
Long term follow-up duration	2 Years
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	India: 6
Country: Number of subjects enrolled	Korea, Republic of: 3
Country: Number of subjects enrolled	Mexico: 5
Country: Number of subjects enrolled	Malaysia: 8
Country: Number of subjects enrolled	Romania: 9
Country: Number of subjects enrolled	Thailand: 4
Country: Number of subjects enrolled	Taiwan: 6
Country: Number of subjects enrolled	Ukraine: 9
Worldwide total number of subjects	50
EEA total number of subjects	9

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37	0

wk	
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)	48
From 65 to 84 years	2
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This study was conducted at a total of 24 study centres in 8 countries: 4 centres in India, 1 centre in Republic of Korea, 5 centres in Malaysia, 1 centre in Mexico, 4 centres in Romania, 3 centres in Taiwan, 2 centres in Thailand, and 4 centres in Ukraine.

Pre-assignment

Screening details:

Subjects who meet the eligibility criteria were randomly assigned in a 1:1 ratio to treatment sequence I (SB12 to Soliris) or treatment sequence II (Soliris to SB12).

Period 1

Period 1 title	Period 1
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Soliris to SB12

Arm description:

Subjects randomly assigned to treatment with Soliris received 600 mg of eculizumab intravenous (IV) infusion every week for first 4 weeks (initial phase) and 900 mg for the fifth week, followed by 900 mg every 2 weeks thereafter. Subjects who were randomised to initially receive Soliris were switched to receive SB12 at Week 26.

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

Dosage and administration details:

Soliris was administered 600 mg every 7 days for the first 4 weeks and 900 mg for the fifth week, followed by 900 mg every 14 ± 2 days via 25-45 minutes IV infusion until Week 24.

Arm title	SB12 to Soliris

Arm description:

Subjects randomly assigned to treatment with SB12 received 600 mg of eculizumab intravenous (IV) infusion every week for first 4 weeks (initial phase) and 900 mg for the fifth week, followed by 900 mg every 2 weeks thereafter. Subjects who were randomised to initially receive SB12 were switched to receive Soliris at Week 26.

Arm type	Experimental
Investigational medicinal product name	SB12
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

SB12 was administered 600 mg every 7 days for the first 4 weeks and 900 mg for the fifth week, followed by 900 mg every 14 ± 2 days via 25-45 minutes IV infusion until Week 24.

Number of subjects in period 1	Soliris to SB12	SB12 to Soliris
Started	25	25
Completed	23	23
Not completed	2	2
Adverse event, serious fatal	1	-
Adverse event, non-fatal	1	1
Pregnancy	-	1

Period 2

Period 2 title	Period 2
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Soliris to SB12

Arm description:

Subjects randomly assigned to treatment with Soliris received 600 mg of eculizumab intravenous (IV) infusion every week for first 4 weeks (initial phase) and 900 mg for the fifth week, followed by 900 mg every 2 weeks thereafter. Subjects who were randomised to initially receive Soliris were switched to receive SB12 at Week 26.

Arm type	Experimental
Investigational medicinal product name	SB12
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

SB12 was administered 900 mg every 14 ± 2 days via 25-45 minutes IV infusion until Week 50.

Arm title	SB12 to Soliris

Arm description:

Subjects randomly assigned to treatment with SB12 received 600 mg of eculizumab intravenous (IV) infusion every week for first 4 weeks (initial phase) and 900 mg for the fifth week, followed by 900 mg every 2 weeks thereafter. Subjects who were randomised to initially receive SB12 were switched to receive Soliris at Week 26.

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

Dosage and administration details:

Soliris was administered 900 mg every 14 ± 2 days via 25-45 minutes IV infusion until Week 50.

Number of subjects in period 2	Soliris to SB12	SB12 to Soliris
Started	23	23
Completed	23	23

Baseline characteristics

Reporting groups	
Reporting group title	Soliris to SB12
Reporting group description:	
Subjects randomly assigned to treatment with Soliris received 600 mg of eculizumab intravenous (IV) infusion every week for first 4 weeks (initial phase) and 900 mg for the fifth week, followed by 900 mg every 2 weeks thereafter. Subjects who were randomised to initially receive Soliris were switched to receive SB12 at Week 26.	
Reporting group title	SB12 to Soliris
Reporting group description:	
Subjects randomly assigned to treatment with SB12 received 600 mg of eculizumab intravenous (IV) infusion every week for first 4 weeks (initial phase) and 900 mg for the fifth week, followed by 900 mg every 2 weeks thereafter. Subjects who were randomised to initially receive SB12 were switched to receive Soliris at Week 26.	

Reporting group values	Soliris to SB12	SB12 to Soliris	Total
Number of subjects	25	25	50
Age categorical Units: Subjects			
Adults (18-64 years)	24	24	48
From 65-84 years	1	1	2
Age continuous Units: years			
arithmetic mean	36.3	40.0	
standard deviation	± 13.67	± 13.44	-
Gender categorical Units: Subjects			
Female	14	8	22
Male	11	17	28

End points

End points reporting groups

Reporting group title	Soliris to SB12
Reporting group description:	
Subjects randomly assigned to treatment with Soliris received 600 mg of eculizumab intravenous (IV) infusion every week for first 4 weeks (initial phase) and 900 mg for the fifth week, followed by 900 mg every 2 weeks thereafter. Subjects who were randomised to initially receive Soliris were switched to receive SB12 at Week 26.	
Reporting group title	SB12 to Soliris
Reporting group description:	
Subjects randomly assigned to treatment with SB12 received 600 mg of eculizumab intravenous (IV) infusion every week for first 4 weeks (initial phase) and 900 mg for the fifth week, followed by 900 mg every 2 weeks thereafter. Subjects who were randomised to initially receive SB12 were switched to receive Soliris at Week 26.	
Reporting group title	Soliris to SB12
Reporting group description:	
Subjects randomly assigned to treatment with Soliris received 600 mg of eculizumab intravenous (IV) infusion every week for first 4 weeks (initial phase) and 900 mg for the fifth week, followed by 900 mg every 2 weeks thereafter. Subjects who were randomised to initially receive Soliris were switched to receive SB12 at Week 26.	
Reporting group title	SB12 to Soliris
Reporting group description:	
Subjects randomly assigned to treatment with SB12 received 600 mg of eculizumab intravenous (IV) infusion every week for first 4 weeks (initial phase) and 900 mg for the fifth week, followed by 900 mg every 2 weeks thereafter. Subjects who were randomised to initially receive SB12 were switched to receive Soliris at Week 26.	

Primary: LDH (U/L) at Week 26

End point title	LDH (U/L) at Week 26
End point description:	
End point type	Primary
End point timeframe:	
At Week 26	

End point values	Soliris to SB12	SB12 to Soliris		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	23	23		
Units: LDH (U/L)				
least squares mean (standard deviation)				
LDH (U/L) at Week 26	249.72 (± 103.67)	284.20 (± 456.73)		

Statistical analyses

Statistical analysis title	Equivalence test
Comparison groups	Soliris to SB12 v SB12 to Soliris
Number of subjects included in analysis	46
Analysis specification	Pre-specified
Analysis type	equivalence
Parameter estimate	Least squares mean difference
Point estimate	34.48
Confidence interval	
level	95 %
sides	2-sided
lower limit	-47.66
upper limit	116.62

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events (AEs) were collected from the time of signing the informed consent form until the end of study (EOS).

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	21.0

Reporting groups

Reporting group title	SB12

Reporting group description:

N for SB12 represents the total number of pooled subjects who had been treated with SB12 in either Periods 1 or 2.

Reporting group title	Soliris

Reporting group description:

N for Soliris represents the total number of pooled subjects who had been treated with Soliris in either Periods 1 or 2.

Serious adverse events	SB12	Soliris	
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 47 (6.38%)	2 / 47 (4.26%)	
number of deaths (all causes)	0	1	
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Hand fracture			
subjects affected / exposed	1 / 47 (2.13%)	0 / 47 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Haemolysis			
subjects affected / exposed	1 / 47 (2.13%)	0 / 47 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Infusion site hypersensitivity			

subjects affected / exposed	0 / 47 (0.00%)	1 / 47 (2.13%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Portal vein thrombosis			
subjects affected / exposed	0 / 47 (0.00%)	1 / 47 (2.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Infections and infestations			
Cellulitis			
subjects affected / exposed	0 / 47 (0.00%)	1 / 47 (2.13%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound infection bacterial			
subjects affected / exposed	1 / 47 (2.13%)	0 / 47 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	SB12	Soliris	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	18 / 47 (38.30%)	11 / 47 (23.40%)	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	3 / 47 (6.38%)	2 / 47 (4.26%)	
occurrences (all)	3	2	
Vascular disorders			
Hypertension			
subjects affected / exposed	3 / 47 (6.38%)	0 / 47 (0.00%)	
occurrences (all)	4	0	
Nervous system disorders			
Headache			
subjects affected / exposed	2 / 47 (4.26%)	3 / 47 (6.38%)	
occurrences (all)	4	5	
Gastrointestinal disorders			

Diarrhoea subjects affected / exposed occurrences (all)	4 / 47 (8.51%) 6	2 / 47 (4.26%) 2	
Renal and urinary disorders Haemoglobinuria subjects affected / exposed occurrences (all)	8 / 47 (17.02%) 15	2 / 47 (4.26%) 2	
Infections and infestations Corona virus infection subjects affected / exposed occurrences (all)	8 / 47 (17.02%) 8	3 / 47 (6.38%) 3	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
08 October 2018	This amendment considered clarifications on: •To extend the period from randomization to initiation of study drug taking account of IP shipment •To change platelet count criteria •To remove several hematology parameters
12 December 2018	This amendment considered clarifications on: •To add the additional information for SB12 provision (in case of serious hemolysis after completion of study treatment, up to 1 year) •To add exclusion criteria (to exclude the subjects with history of serious thrombotic events)
29 November 2019	This amendment considered clarifications on: •To implement the changes due to 2-year extension period (to all patients, up to 2 years) •To clarify dosing and treatment schedule •To add several hematology parameters
21 August 2020	This amendment considered clarifications on: •To update study design/process in order to minimize the risk of COVID-19 pandemic •To add clarification of dosing interval adjustment DSMB feedback
27 November 2020	This amendment considered clarifications on: •To update safety design/process in order to address a special circumstances of a shortage of the comparator

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported