Clinical trial results:
A Long-term Follow-up Study for Cardiac Safety in the Patients with HER2 Positive Early or Locally Advanced Breast Cancer Who Have Completed the SB3-G31-BC

Summary

EudraCT number	2015-005663-17
Trial protocol	CZ FR BG RO PL
Global end of trial date	21 January 2021

Results information

Result version number	v1 (current)
This version publication date	06 April 2022
First version publication date	06 April 2022

Trial information

Trial identification

Sponsor protocol code	SB3-G31-BC-E

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02771795
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,
Public contact	Quintiles Contact Centre, Quintiles Limited, 001 8622613634,
Scientific contact	Quintiles Contact Centre, Quintiles Limited, 001 8622613634,

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 January 2021
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	21 January 2021
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The primary objective is to observe the incidence of symptomatic congestive heart failure (CHF) NYHA class II,III and IV and asymptomatic LVEF decrease in patients who participated in the SB3-G31-BC Study and treated with SB3 (proposed trastuzumab biosimilar) or Herceptin® as neoadjuvant and adjuvant treatment.

Protection of trial subjects:

The study and clinical study protocols were reviewed and approved by Independent Ethics Committee (IEC) or Institutional Review Board (IRB) for each study centre.
This study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki (2013) and that are consistent with the latest International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use Good Clinical Practice (ICH E6 [R2] GCP) and applicable local regulatory requirements and laws.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	28 April 2016
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	India: 9
Country: Number of subjects enrolled	Korea, Republic of: 64
Country: Number of subjects enrolled	Malaysia: 19
Country: Number of subjects enrolled	Philippines: 5
Country: Number of subjects enrolled	Russian Federation: 177
Country: Number of subjects enrolled	Ukraine: 104
Country: Number of subjects enrolled	Viet Nam: 9
Country: Number of subjects enrolled	Poland: 92
Country: Number of subjects enrolled	Romania: 28
Country: Number of subjects enrolled	Bulgaria: 3
Country: Number of subjects enrolled	Czechia: 12
Country: Number of subjects enrolled	France: 16
Worldwide total number of subjects	538
EEA total number of subjects	151

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)	528
From 65 to 84 years	10
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Subjects who had received SB3 or Herceptin® according to the SB3-G31-BC study provided informed consent to participate in this study.

Period 1

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

Blinding implementation details:

There was no investigational product or a treatment administered to the subjects

Arms

Are arms mutually exclusive?	Yes
Arm title	SB3 (proposed trastuzumab biosimilar)

Arm description:

SB3 was administered in SB3-G31-BC study (2013-004172-35). No additional IP was administered for this study since it was an observational study.

Arm type	Experimental
Investigational medicinal product name	SB3
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

SB3 was administered intravenously at a loading dose of 8 mg/kg and at a maintenance dose of 6 mg/kg for the subsequent cycles in SB3-G31-BC study.

Arm title	Herceptin

Arm description:

Herceptin was administered in SB3-G31-BC study (2013-004172-35). No additional IP was administered for this study since it was an observational study.

Arm type	Active comparator
Investigational medicinal product name	Herceptin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Herceptin was administered intravenously at a loading dose of 8 mg/kg and at a maintenance dose of 6 mg/kg for the subsequent cycles in SB3-G31-BC study.

Number of subjects in period 1	SB3 (proposed trastuzumab biosimilar)	Herceptin
Started	267	271
Completed	45	56
Not completed	222	215
Termination by premature discontinuation of study	185	168
Early termination during the study period	37	47

Baseline characteristics

Reporting groups

Reporting group title	overall trial

Reporting group description: -

Reporting group values	overall trial	Total	
Number of subjects	538	538	
Age categorical Units: Subjects			
Less than 60 years	445	445	
60 years and over	92	92	
Missing	1	1	
Gender categorical Units: Subjects			
Female	538	538	
Male	0	0	

Subject analysis sets

Subject analysis set title	Survival Follow-up Set
Subject analysis set type	Safety analysis

Subject analysis set description:

This set consisted of all subjects who enrolled for this study. This set included Cardiac Safety and Survival Cohort and Survival Only Cohort.

Reporting group values	Survival Follow-up Set		
Number of subjects	538		
Age categorical Units: Subjects			
Less than 60 years	445		
60 years and over	92		
Missing	1		
Gender categorical Units: Subjects			
Female	538		
Male	0		

End points

End points reporting groups

Reporting group title	SB3 (proposed trastuzumab biosimilar)
Reporting group description:	
SB3 was administered in SB3-G31-BC study (2013-004172-35). No additional IP was administered for this study since it was an observational study.	
Reporting group title	Herceptin
Reporting group description:	
Herceptin was administered in SB3-G31-BC study (2013-004172-35). No additional IP was administered for this study since it was an observational study.	
Subject analysis set title	Survival Follow-up Set
Subject analysis set type	Safety analysis
Subject analysis set description:	
This set consisted of all subjects who enrolled for this study. This set included Cardiac Safety and Survival Cohort and Survival Only Cohort.	

Primary: The incidence of CHF and asymptomatic significant LVEF decrease

End point title	The incidence of CHF and asymptomatic significant LVEF decrease[1]
End point description:	
End point type	Primary
End point timeframe:	
during overall study period	

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: This is primarily designed to observe the incidence of symptomatic CHF, asymptomatic significant LVEF decrease, and other cardiac events in breast cancer patients treated with SB3 or Herceptin® according to the protocol SB3-G31-BC. There is no pre-defined hypothesis testing, therefore all analyses will be performed for the observational or exploratory purpose.

End point values	SB3 (proposed trastuzumab biosimilar)	Herceptin	Survival Follow-up Set	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	186[2]	181[3]	367[4]	
Units: no.	1	2	3	

Notes:

[2] - Long-term follow-up set

[3] - Long-term follow-up set

[4] - Long-term follow-up set

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

Since SB3-G31-BC-E study was to assess the long-term cardiac safety for SB3 or Herceptin®, which was mainly about post-dose cardiac toxicities captured through cardiac assessments, non-serious AEs were not intended to be collected through this study.

Assessment type	Systematic

Dictionary used

Dictionary name	N/A
Dictionary version	N/A

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

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.

Justification: Since SB3-G31-BC-E study was to assess the long-term cardiac safety for SB3 or Herceptin®, which was mainly about post-dose cardiac toxicities captured through cardiac assessments and not by AE reporting, other non-serious AEs were not intended to be collected through this study. However, for any type of serious AE (SAE; cardiac or non-cardiac) that could be determined by the Investigator to be related to the IP then that SAE was reported through a separate paper SAE report form to the Sponsor.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
26 November 2018	clarification on study design and eligibility criteria

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported