Five-year follow-up of the Phase 3 study comparing SB3 (trastuzumab biosimilar) and reference trastuzumab in patients with HER2 positive early or locally advanced breast cancer

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Introduction

- SB3 was approved as a biosimilar of the reference trastuzumab (TRZ) based on its similarity demonstrated by the quality, non-clinical, Phase 1, and Phase 3 clinical comparative studies.[1,2,3]
- SB3 is globally available in regions including the United States, Australia, Europe, and the Republic of Korea. SB3 is the first trastuzumab biosimilar to obtain World Health Organization's prequalification certification enabling wider biosimilar access worldwide.[4]
- A follow-up study (SB3-G31-BC-E) was conducted to assess cardiac safety and survival outcome in a subset of patients from the Phase 3 study (SB3-G31-BC).
- Here, we report the five-year follow-up results of the Phase 3 study comparing SB3 and TRZ in patients with HER2-positive early or locally advanced breast cancer.

Objective

- Primary objectives
  - To observe the incidence of symptomatic congestive heart failure (CHF), and asymptomatic significant left ventricular ejection fraction (LVEF) decrease
- Secondary objectives
  - To observe the incidence of cardiac death and other significant cardiac conditions
  - To observe event-free survival (EFS) and overall survival (OS)

Methods

Study design

- Following regulatory recommendations, patients from prespecified countries who completed the SB3-G31-BC study and provided informed consent were enrolled in the treatment-free follow-up study which was planned for additional 5 years.

Endpoints and statistical assessment

- Safety endpoints
  - CHF is defined as NYHA II, III, and IV confirmed by a cardiologist, accompanied by a significant LVEF decrease.
  - Significant LVEF decrease is defined as an absolute decline of at least 10% points from baseline LVEF (LVEF at screening of SB3-G31-BC study) and resulting LVEF less than 50%.
- Efficacy endpoints
  - EFS, defined as the time from the date of randomization to the date where an event (disease recurrence, progression, or death) occurred
  - OS, defined as the time from the date of randomization to the date of death
- Statistical assessment
  - EFS and OS were estimated by treatment groups and subgroups using the Kaplan-Meier method; hazard ratio with 95% CI from stratified Cox regression model.

Results

Patient disposition

- Among 875 patients randomized in the main study, a total of 367 patients (SB3, N=186; TRZ, N=181) were enrolled in the extension study.
- Median follow-up duration from randomization for the Phase 3 study was 68 months.

Baseline characteristics

- There were no marked differences in demographic and disease characteristics among the treatment groups in the extension study.

Cardiac safety

- During the follow-up period after adjuvant therapy, incidence of asymptomatic significant LVEF decrease rarely occurred and was comparable between SB3 and TRZ (SB3, n=1; TRZ, n=2).
- All incidences were reported within 2 years from 1st administration of the investigational products. All of the patients who experienced asymptomatic significant LVEF decrease eventually recovered with LVEF above 50%.
- No symptomatic CHF, or cardiac death occurred in either group during the follow-up period.
- One event of cardiac condition termed as "associated with palliative chemotherapy cardiofibrosis" was reported in the TRZ arm.

Efficacy

- No difference was observed between SB3 and TRZ in terms of EFS and OS at 68 months of follow-up (Figure 1).
  - 32 events (17.2%) and 38 events (21.0%) were reported in SB3 arm and TRZ arm, respectively (Hazard ratio [95% CI] (SB3/TRZ) 0.78 [0.48, 1.25], p=0.30).
  - Five-year EFS rates were 82.8% for SB3 and 79.7% for TRZ.
  - 14 deaths (7.5%) and 23 deaths (12.7%) were reported in SB3 arm and TRZ arm, respectively (Hazard ratio [95% CI] (SB3/TRZ) 0.62 [0.32, 1.22], p=0.17).
  - Five-year OS rates were 93.1% for SB3 and 86.7% for TRZ.

SUMMARY

SB3 is a globally approved trastuzumab biosimilar based on the totality of evidence demonstrated through analytical, non-clinical, and clinical assessments.

Similarity of SB3 to reference trastuzumab was further supported by comparable cardiac safety profile and long-term efficacy at more than 5 years of follow-up.

- **SB3 and reference trastuzumab had comparable cardiac safety profiles during the follow-up period.**
- **SB3 and reference trastuzumab had comparable long-term efficacy in terms of event-free survival and overall survival.**

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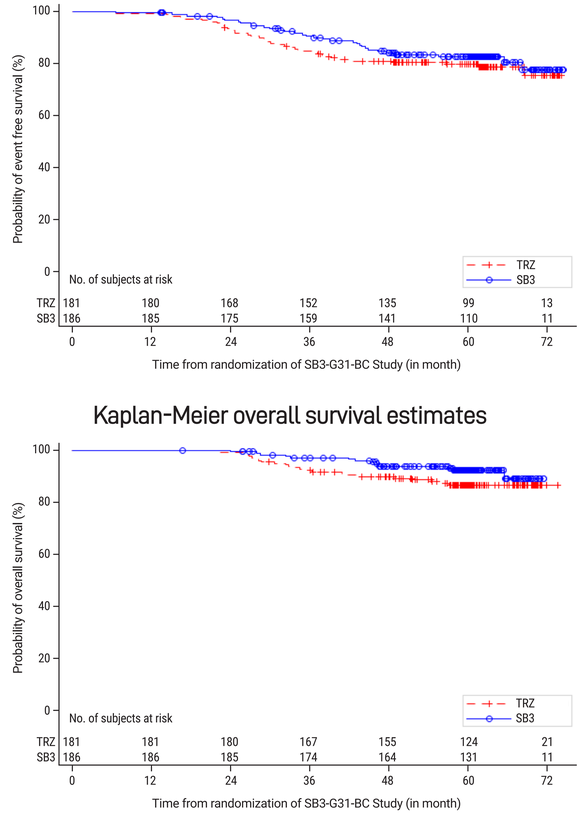
For any questions, please contact med.info@samsung.com

Figure 1 Kaplan-Meier Plot of EFS and OS comparing SB3 and TRZ



Conclusion

This five-year analysis of the subpopulation from the Phase 3 study further supports similarity of SB3 and TRZ with comparable cardiac safety profile, and long-term efficacy.

References

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