A randomized, double-blind, phase III study assessing clinical similarity of SB17 (proposed ustekinumab biosimilar) to reference ustekinumab in subjects with moderate-to-severe plaque psoriasis

Steven R. Feldman, MD, PhD,[a] Joanna Narbutt, MD,[b] Giampiero Girolomoni, MD,[c] Jan Brzezicki, MD, PhD,[d] Nataliya Reznichenko, MD, PhD,[e] Maria Agnieszka Zegadło-Mylik, MD,[f] Grazyna Pulka, MD, PhD,[g] Magdalena Dmowska-Stecewicz, MD,[h] Elżbieta Kłujszo, MD,[i] Dmytro Rekalov, MD,[j] Lidia Rajzer, MD, PhD,[k] Jiyoon Lee, MS,[l] Minkyung Lee, MS,[l] and Young Hee Rho, MD, PhD, MPH[l]

Background: Ustekinumab (UST) is a safe and effective treatment for moderate-to-severe psoriasis.

Objectives: To compare efficacy, safety, pharmacokinetics (PK), and immunogenicity of the proposed UST biosimilar SB17 with reference UST in subjects with moderate-to-severe plaque psoriasis.

Methods: In this randomized double-blind study, subjects were randomized to receive 45 mg of SB17 or UST subcutaneously at week 0, 4, and every 12 weeks. The primary endpoint was the percent change from baseline in Psoriasis Area and Severity Index at week 12 with an equivalence margin of [−15%, 15%]. Other secondary efficacy, safety, PK, and immunogenicity endpoints were measured through week 28.

Results: Two hundred forty-nine subjects were randomized to SB17, 254 to UST. Adjusted difference of Psoriasis Area and Severity Index change from baseline at week 12 of −0.6% (95% confidence interval; −3.780, 2.579) was within the equivalence margin. Physician's Global Assessment and Dermatology Life Quality Index were also comparable. Overall treatment-emergent adverse events were comparable (SB17: 48.2%, UST: 48.8%). The overall incidence of antidrug antibodies up to Week 28 was 13.3% with SB17 and 39.4% with UST.

Limitations: Data were only through week 28.

Conclusion: SB17 was clinically biosimilar to UST up to week 28. (J Am Acad Dermatol 2024;91:440-7.)

From the Department of Dermatology, Wake Forest University School of Medicine, Winston Salem, North Carolina[a]; Dermoklinika Centrum Medyczne s.c. M. Kierstan, J. Narbutt, A. Lesiak, Łódź, Poland[b]; Division of Dermatology, Department of Medicine, University of Verona, Verona, Italy[c]; Centrum Kliniczno-Badawcze J.Brzezicki, B.Górnikiewicz-Brzezicka, Lekarze Spóka Partnerska, Elbląg, Poland[d]; Therapeutic Department, Military Hospital (Military Unit A3309) of Military Medical Clinical Center of Eastern Region, Zaporizhzhia, Ukraine[e]; ETG WARSZAWA, Warsaw, Poland[f]; Centrum Medyczne All-med BADANIA KLINICZNE, Kraków, Poland[g]; ETG Siedlce, Siedlce, Poland[h]; Prywatny Gabinet Dermatologiczny Elżbieta Kłujszo, Kielce, Poland[i]; Medical Center of LLC "Suchasna klinika", Zaporizhzhia, Ukraine[j]; L.Rajzer Specjalistyczny Gabinet Dermatologiczno-Kosmetyczny, Kraków, Poland[k]; and Samsung Bioepis, Co. Ltd, Incheon, South Korea.[l]

Funding sources: This study was funded by Samsung Bioepis, Co Ltd.

A portion of this manuscript has been previously presented at EADV 2023 (Abstract #1320), Berlin, Germany, October 11-14, 2023.

Patient consent: Consent for the publication of recognizable patient photographs or other identifiable material was obtained by the authors and included at the time of article submission to the journal stating that all patients gave consent with the understanding that this information may be publicly available.

IRB approval status: Ethics approval was received from each national central or local ethical committee or institutional review board.

Accepted for publication April 5, 2024.

Correspondence to: Steven R. Feldman, MD, PhD, Wake Forest University School of Medicine, 4618 Country Club Road, Winston-Salem, NC 27104. E-mail: sfeldman@wakehealth.edu.

Published online April 27, 2024.

0190-9622

© 2024 by the American Academy of Dermatology, Inc. Published by Elsevier Inc. This is an open access article under the CC BY license (http://creativecommons.org/licenses/by/4.0/).

https://doi.org/10.1016/j.jaad.2024.04.045

Key words: biologics; biosimilar; psoriasis; randomized clinical trial; ustekinumab.

CAPSULE SUMMARY

- SB17 is a proposed biosimilar of ustekinumab, a biologic used for inflammatory diseases including moderate-to-severe plaque psoriasis.
- In this phase 3 randomized clinical trial, SB17 was biosimilar to reference ustekinumab up to week 28 in terms of efficacy, safety, pharmacokinetics, and immunogenicity.

INTRODUCTION

With their efficacy and safety, biologics have had profound impact on the treatment of chronic inflammatory diseases such as psoriasis[1] and rheumatoid arthritis.[2] Biologics have a unique role in treatment of chronic inflammatory diseases, including psoriasis; however, high cost has been a barrier to treatment access. The large size and complexity of biologics precludes perfect duplication and development of generic versions. However, the development of biosimilars, which are highly similar to the innovator product and without clinically meaningful differences in performance, is intended to improve the quality of patient care by reducing barriers to access,[3] with realizations of cost-savings, in both the United States and Europe.[4-6]

The majority of biosimilars developed for psoriasis and other inflammatory diseases are tumor necrosis factor (TNF) inhibitors.[7-10] While TNF inhibitors are valuable treatments for psoriasis, newer, safer biologics for psoriasis have been developed. The first of these was interleukin 12/23 inhibitor reference ustekinumab (UST),[11,12] approved for psoriasis, psoriatic arthritis, and inflammatory bowel disease.[13,14] Advantages of UST over TNF inhibitors include less frequent dosing and perhaps a better safety profile.[15,16]

SB17 (Samsung Bioepis Co, Ltd) is a proposed biosimilar of reference UST (Stelara, Janssen Biotech, Inc). To be approved, biosimilars require a rigorous physicochemical and biological characterization to prove similarity on the molecular level (including in vivo and in vitro assays), followed by a phase I study for pharmacokinetic (PK) bioequivalence and a phase III study for clinical biosimilarity.[17,18] SB17 is physicochemically similar to UST and was pharmacokinetically bioequivalent in a phase I study.[19]

The objective of this study is to assess whether SB17 has similar clinical efficacy, safety, PK, and immunogenicity to UST up to week 28.

METHODS

Patients

Subjects were 18 years or older, with plaque psoriasis for at least 6 months and candidates for phototherapy or systemic therapy. Subjects had to have a Psoriasis Area and Severity Index (PASI) of ≥12, (static) Physician's Global Assessment (PGA) of ≥3 (moderate), and a body surface area involvement of ≥10% at screening and randomization. Subjects generally required a washout period of prior psoriasis treatment for 2 weeks (topical therapy), 4 weeks (oral systemic and phototherapy), or 6 months (for TNF inhibitors) before randomization; use of UST, interleukin 17 inhibitors, or other interleukin 23 inhibitors were exclusions. Subjects were also excluded if pregnant or positive for hepatitis B or C, human immunodeficiency virus, or latent or active tuberculosis. Subjects of childbearing potential were required to practice contraception until 15 weeks after the last dose of study drug. Since UST has 2 dosage forms (45 mg and 90 mg), and 90 mg is given to subjects >100 kg[13,14], the initial study population was limited to subjects <95 kg to achieve a uniform 45 mg-dosed population, in alignment with regulatory input, to help assure a homogenous patient population designed to have the best sensitivity to detect clinically meaningful differences.

Study design

This study was a phase III, randomized, double-blind, multicenter study conducted in 45 centers from 8 countries during Jul 2021 to Nov 2022 (NCT04967508; the scope of this report covers data collected approximately up to Aug 2022). The study was conducted according to the Declaration of Helsinki and Good Clinical Practice issued by the International Committee for Harmonisation. All subjects gave formal written informed consent before participating in the study. The protocol was amended later in the transition period due to the Ukraine-Russian war to address logistic issues such as central lab assessment.

Subjects were initially randomized (1:1, block size of 4) to receive either SB17 or UST at week 0, 4, and then every 12 weeks thereafter until week 40 (Supplementary Fig 1, available via Mendeley at https://data.mendeley.com/datasets/bh6p4rk5j9/1). Automated random assignment of subject numbers to randomization numbers linked to study

Abbreviations used:

ADA:	antidrug antibody
CI:	confidence interval
DLQI:	Dermatology Life Quality Index
FAS:	full analysis set
IP:	investigational product
PASI:	Psoriasis Area and Severity Index
PGA:	Physician's Global Assessment
PK:	pharmacokinetics
PPS:	per-protocol set
TEAE:	treatment-emergent adverse events
TNF:	tumor necrosis factor
UST:	ustekinumab

medication was generated by an Interactive Web Recognition System. The study was divided into a main period (up to week 28) and a transition period (up to week 52). This report presents the results for the main period. All subjects initially received 45 mg of SB17 or UST at week 0. If the subject weighed over 100 kg at later dosing visits, the subject received 90 mg of SB17 or UST in the form of two 45 mg doses.

During the study, biologics, topical, systemic therapy, or phototherapy for psoriasis were prohibited, except for emollients or moisturizers that did not contain prohibited medications (eg, corticosteroids, tar, salicylic acid, urea, etc.); class 6 or 7 (mild strength or least potent) topical corticosteroids on the face or groin region were permitted after week 12.

Assessments

Efficacy was measured by PASI, PGA, and Dermatologic Life Quality Index (DLQI).[20] The primary endpoint of the study was the difference of percent change from baseline of PASI between SB17 and UST at week 12. Secondary efficacy endpoints included PASI50, PASI75, PASI90, and PASI100 response, PGA 0 or 1 response, and DLQI change from baseline.

Safety endpoints were the incidence of treatment-emergent adverse events (TEAEs), serious adverse events, and adverse events of special interest (systemic hypersensitivity, injection site reactions, infections, and pulmonary events [ie, noninfectious pneumonia/pulmonary hypersensitivity]), which were collected continuously during the study. In addition, laboratory assessments were done at selected visits. Adverse events were reported and coded according to Medical dictionary for regulatory activities 23.1.

Pharmacokinetic endpoints were serum ustekinumab concentrations measured up to week 28. Immunogenicity was assessed by the development of serum antidrug antibodies (ADAs) and neutralizing antibodies among subjects who were positive for ADA. Positive ADA was determined as either being treatment-induced, or if positive at baseline, treatment-boosted ADA (an increase of titer after baseline).

Sample size and statistical analysis

Based on the equivalence margin [−15%, 15%], with the assumptions of common standard deviation of 31.33, 10% loss from the primary analysis, and approximately 100 remainders per treatment group after transition, a sample size of 464 subjects (232 per treatment group) was required to provide >90% power at a 5% significance level for the primary end point. Efficacy results were analyzed based on the full analysis set (FAS) and the per-protocol set (PPS).

Efficacy results were analyzed based on the full analysis set (FAS) and the per-protocol set (PPS). The FAS consisted of all subjects who were randomized, and was analyzed according to the treatment group they were assigned to at randomization, according to the intention-to-treat principle. However, subjects who did not have any efficacy assessment result after randomization or did not receive investigation product (IP; SB17 or UST) during the study period were excluded from the FAS. For analysis of the primary endpoint, missing values at week 12 from the FAS were imputed through multiple imputation. The PPS consisted of all FAS subjects with weight ≤100 kg and received 45 mg IP at week 0 and week 4 and have PASI assessment result at baseline and week 12 without any major protocol deviations that have impact on primary efficacy assessment. The primary endpoint was analyzed using an analysis of covariance model with the baseline value of PASI as a covariate and pooled centers (country) and treatment groups as factors, with a prespecified equivalence margin of [−15%, 15%] when using the 95% confidence interval (CI) of the difference for the PPS. Another equivalence margin of [−10%, 10%] when using the 90% CI of the difference for the FAS was also used as a sensitivity analysis. The equivalence margin was discussed and agreed with regulatory agencies. All other secondary endpoints were presented descriptively.

Safety and immunogenicity were analyzed based on the safety set 1 which consisted of all subjects who received at least 1 IP during the study period. Pharmacokinetic analysis was done based on the pharmacokinetic analysis set which consisted of all subjects in the safety set 1 who have at least 1 serum ustekinumab concentration data. Analyses were performed using SAS version 9.4 (SAS Institute).

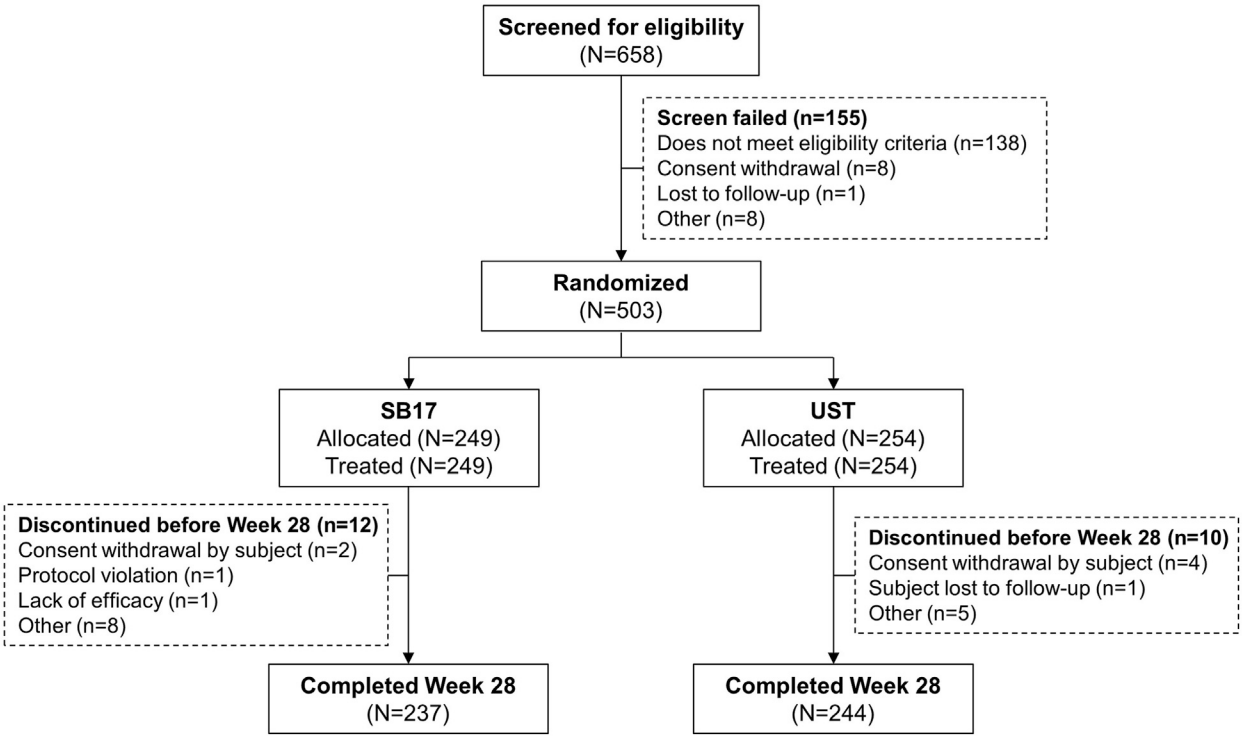

Fig 1. Subject disposition of the enrolled study population. Subjects with moderate-to-severe psoriasis were randomized to reference ustekinumab or the proposed biosimilar ustekinumab SB17. Discontinuations due to "other" were due to the Ukraine-Russian war. *UST*, Reference ustekinumab.

RESULTS

Patients

At baseline, 249 subjects were randomized to SB17 and 254 subjects to UST, a total of 503 subjects (Fig 1). Most (>95%) of the subjects completed week 28 with a balanced drop-out pattern. During the study period, the Ukraine-Russian war started on Feb 2022, and some subjects in Ukraine were affected by the war, generally from week 16, resulting in premature discontinuations. However, the proportion was relatively small compared with the total Ukrainian population (n = 146) and was comparable between treatment groups.

Subject demographics and disease characteristics of the randomized population were well balanced among SB17 and UST treatment groups (Table I). The population was a predominantly middle-aged Caucasian population with a slightly higher male proportion with balanced disease characteristics.

Efficacy

The time-response curve of the primary efficacy outcome in terms of percent change of PASI from baseline during the main period was nearly identical between SB17 and UST up to week 28 (Fig 2). At week 12, the adjusted least squares mean difference for percent change of PASI from baseline for the PPS was −0.6 (95% CI [−3.780, 2.579]), which was contained within the prespecified equivalence margin [−15%, 15%] (Fig 3). Such equivalent results were similarly replicated when using a 90% CI with the FAS; the adjusted least squares mean difference was −0.7 (90% CI [−3.343, 1.933]), which was also contained within the prespecified equivalence margin of [−10%, 10%], supporting similar efficacy of SB17 and UST.

The secondary efficacy endpoints PASI50, PASI75, PASI90, PASI100, PGA 0 or 1 response, and DLQI at week 12 and 28 were also comparable between SB17 and UST (Supplementary Table I, available via Mendeley at https://data.mendeley.com/datasets/bh6p4rk5j9/1). Only 4 (1.6%) subjects from SB17 and 3 (1.2%) from UST respectively received 90 mg of the IP during the main period, and all were after the primary endpoint timepoint week 12.

Safety

In general, the safety profile was comparable between SB17 and UST (Table II). The overall cumulative incidence of TEAEs during the main

Table I. Subject demographics and baseline disease characteristics of the randomized study population

	SB17 *N* = 249	UST *N* = 254
Age (years)	44.0 (13.21)	44.3 (12.42)
Gender (male)	150 (60.2%)	162 (63.8%)
Race	White: 247 (99.2%) Asian: 2 (0.8%)	White: 250 (98.4%) Asian: 4 (1.6%)
BMI (kg/m^2)	27.2 (3.94)	26.8 (3.66)
Subjects with psoriatic arthritis	64 (25.7%)	54 (21.3%)
Duration of psoriasis (years)	15.0 (11.38)	16.1 (11.88)
Total psoriasis BSA involvement (%)	27.3 (13.49)	26.7 (13.77)
PASI score	22.5 (7.82)	22.1 (7.69)
PGA of 4 or 5 (marked or severe)	92 (36.9%)	94 (37.0%)
DLQI score	13.4 (7.24)	13.2 (6.96)
Prior topical treatment	232 (93.2%)	234 (92.1%)
Prior conventional systemic treatment	117 (47.0%)	133 (52.4%)
Prior biologic treatment	17 (6.8%)	19 (7.5%)
Prior phototherapy	114 (45.8%)	128 (50.4%)

Data are presented as either mean (SD) or *n* (%).
BMI, Body mass index; *BSA*, body surface area; *DLQI*, Dermatology Life Quality Index; *PASI*, Psoriasis Area and Severity Index; *PGA*, Physician's Global Assessment; *UST*, Reference ustekinumab.

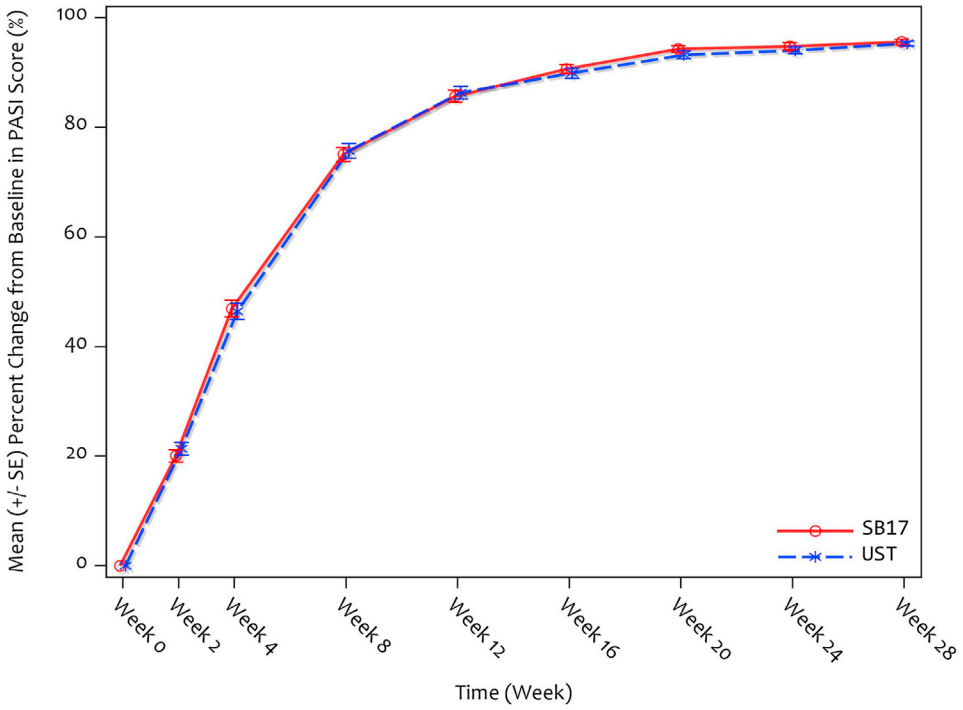

Fig 2. Percent change of PASI from baseline during the main period (full analysis set). *PASI*, Psoriasis Area and Severity Index; *UST*, Reference ustekinumab.

period were 48.2% for SB17 and 48.8% for UST. Most were mild to moderate and considered not related to the IP. The most commonly reported TEAEs were nasopharyngitis, COVID-19, and upper respiratory tract infection. Serious TEAEs occurred in 6 subjects (2.4%) in SB17 and 3 subjects (1.2%) in UST (Supplementary Table II, available via Mendeley at https://data.mendeley.com/datasets/bh6p4rk5j9/1). About half of the serious events from the SB17 treatment group were due to injury and there was 1

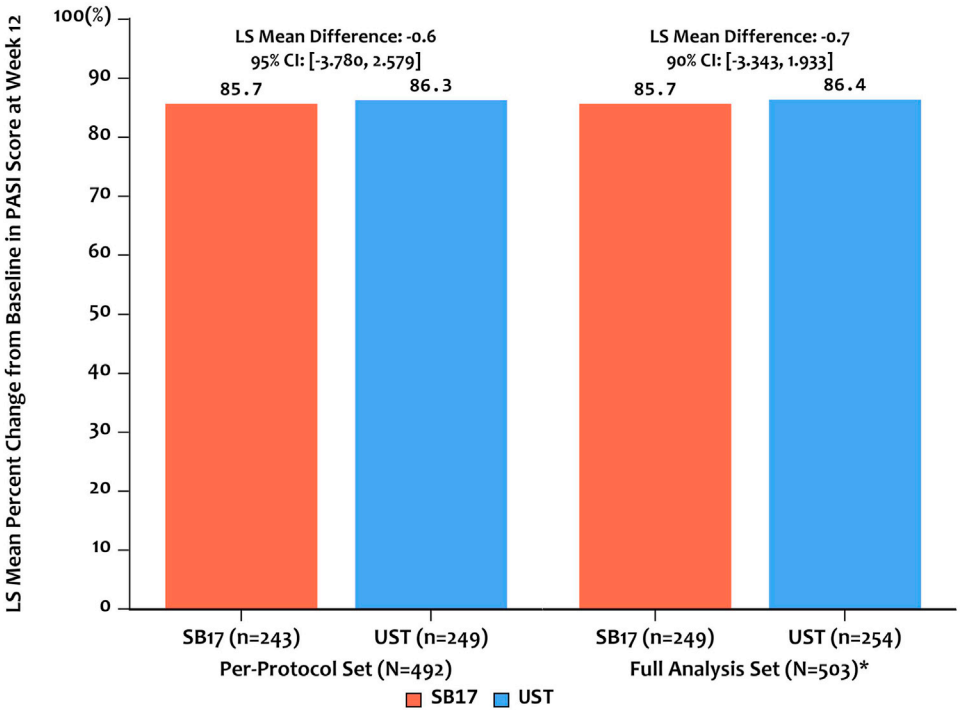

Fig 3. Primary analysis of percent change of PASI from baseline at week 12. *: Change from baseline in PASI scores have been imputed by multiple imputation method under the assumption of missing at random. *LS*, Least squares; *PASI*, Psoriasis Area and Severity Index; *UST*, Reference ustekinumab.

case of cardiovascular event (acute myocardial infarction), however none of the serious events were considered related to the IP by the investigator. There was no case of death. There was 1 subject reporting a TEAE that led to IP discontinuation (hepatic steatosis) in the UST treatment group. The majority of TEAEs of special interest were infections (SB17: 28.1%, UST: 29.5%); there were 2 subjects each reporting systemic hypersensitivity and injection site reactions from the UST group; however, no serious hypersensitivity such as anaphylaxis occurred. The incidence of TEAEs related to COVID-19 or the Ukraine-Russian war was comparable between SB17 and UST.

PK and immunogenicity

The PK profile was generally comparable between SB17 and UST (Supplementary Fig 2, available via Mendeley at https://data.mendeley.com/datasets/bh6p4rk5j9/1). The incidence of overall ADA for SB17 up to week 28 was lower than UST: 13.3% for SB17 and 39.4% for UST. The incidence of neutralizing antibodies up to week 28 was 13.7% for SB17 and 35.4% for UST. When the primary efficacy outcome was subgrouped by overall ADA status, the response patterns were comparable within ADA-positive and ADA-negative subgroups (Supplementary Fig 3, available via Mendeley at https://data.mendeley.com/datasets/bh6p4rk5j9/1).

DISCUSSION

Biologics revolutionized the management of chronic inflammatory disease. The development of generic biologics is precluded, as biologics are too complex to be perfectly duplicated. The inability for anyone to perfectly duplicate a biologic also means there is variation in the innovator product from batch to batch.[21] Despite that variation, with similar PK and target binding, different batches of innovator biologics generally perform consistently. Biosimilars are required to have similar structure, PK, and target binding to the reference product; they ought to perform similarly clinically as would another batch of the innovator product. A clinical trial provides further evidence confirming that biosimilars have similar efficacy and safety to the innovator product. In this phase 3, randomized, double-blind study, SB17 had similar efficacy and comparable safety and PK to the originator UST.

Efficacy of SB17 and UST was similar in the primary endpoint as well as in multiple other secondary efficacy endpoints. The observed response

Table II. Summary of safety profile for the main period (safety set 1)

	SB17 *N* = 249 *n* (%)	UST *N* = 254 *n* (%)
Overall incidence of TEAE	120 (48.2)	124 (48.8)
Serious TEAE	6 (2.4)	3 (1.2)
TEAE leading to discontinuation of IP	0 (0.0)	1 (0.4)
Treatment-related TEAE	11 (4.4)	12 (4.7)
TEAE of special interest	70 (28.1)	76 (29.9)
Systemic hypersensitivity*	0 (0.0)	2 (0.8)
Infections	70 (28.1)	75 (29.5)
Injection site reaction	0 (0.0)	2 (0.8)
Pulmonary events	0 (0.0)	0 (0.0)
Deaths	0 (0.0)	0 (0.0)
COVID-19 related TEAEs†	21 (8.4)	24 (9.4)
TEAEs related to war in Ukraine‡	2 (0.8)	0 (0.0)
TEAEs of >5% incidence§	46 (18.5)	54 (21.3)
Nasopharyngitis	22 (8.8)	21 (8.3)
COVID-19	16 (6.4)	23 (9.1)
Upper respiratory tract infection	10 (4.0)	13 (5.1)

IP, Investigational product; *TEAE*, treatment-emergent adverse event; *UST*, Reference ustekinumab.

*Two events of abdominal pain in 1 subject and 1 event of dermatitis allergic in 1 subject each.

†Includes all TEAEs considered related to COVID-19.

‡Two events of anxiety and insomnia each by 2 subjects, due to the war.

§Includes preferred terms occurring >5% in either treatment groups.

rate for both groups was somewhat higher than the originator studies; the percent change from baseline in PASI at week 12 was around 75% to 77% in PHOENIX I and II[11,12] and around 85% in our study. This may be due to the lower mean body weight in our study (as the efficacy of the 45 mg UST dose tends to correlate with body weight[14]) or to the lack of a placebo group. Biosimilar studies, which do not have a placebo group, often report a higher response rate than placebo-controlled studies.[7-9]

The safety profiles of SB17 and UST were comparable and generally reflective of what has been reported for UST; most of them were mild to moderate, with few serious events. The COVID-19 pandemic has affected all aspects of life including our study; however, the occurrence of COVID-19 among subjects did not seem to affect the study results.

A generally lower immunogenicity profile was observed in SB17 compared to UST; however, efficacy was comparable between treatment groups within each ADA subgroup. The relative difference of ADA incidence may be due to differences in cell lines that produce the monoclonal antibodies; UST used the Sp2/0 cell line while SB17 used a Chinese hamster ovary cell line. Similar differences in immunogenicity have occurred with other UST biosimilars.[22-24] Lower immunogenicity does not preclude biosimilarity if the ADA-negative subgroups of the biosimilar and the originator have similar efficacy,[17] which was observed in our study.

This study was designed to maximize the ability to detect differences between UST and the proposed biosimilar SB17, which is a strength of this study. Our study aimed a homogenous population (in terms of weight and dose) to reduce variability that might obscure small differences in efficacy and safety.[17] Since less than 2% of the study population received 90 mg of the IP during the main period any bias due to heterogenous dosing schemes is considered to be minimized. Another strength is using mean change in severity as the primary outcome; a percent of subjects who achieve success outcome (ie, response rate) would be expected to be less sensitive for detecting differences in efficacy between the 2 study groups. Limitations of this study would be the study population being predominantly Caucasian, having less data for other races. The Ukraine-Russian war resulted in study conduct disruption in some sites; however, only a small proportion of subjects discontinued in a comparable pattern and most sites managed to continue the study. This study does not directly address the impact of mandatory nonmedical switching (which might be associated with 'nocebo' effects[25]) in long-term originator UST users; this will require further real-world studies.

CONCLUSIONS

SB17, a UST biosimilar, has similar efficacy and comparable safety and PK to reference UST and lower immunogenicity up to week 28 in subjects with moderate-to-severe psoriasis.

The authors thank the patients who were involved in this study, the study personnel (both from the sponsor and IQVIA) who made this work possible, and the study investigators of this study.

Conflicts of interest

Dr Feldman has received research, speaking, and/or consulting support from Eli Lilly and Company, GlaxoSmithKline/Stiefel, AbbVie, Janssen, Alovtech, vTv Therapeutics, Bristol-Myers Squibb, Samsung Bioepis, Pfizer, Boehringer Ingelheim, Amgen, Dermavant, Arcutis, Novartis, Novan, UCB, Helsinn, Sun Pharma, Almirall, Galderma, Leo Pharma, Mylan, Celgene, Ortho Dermatology, Menlo, Merck & Co, Qurient, Forte, Arena, Biocon, Accordant, Argenx, Sanofi, Regeneron, the National Biological Corporation, Caremark, Teladoc,

BMS, Ono, Micreos, Eurofins, Informa, UpToDate, and the National Psoriasis Foundation. Dr Feldman is founder and part owner of Causa Research and holds stock in Sensal Health. Dr Narbutt is an investigator and/or lecturer for Novartis, Eli Lilly, Almirall, AbbVie, Celltrion, Pfizer, Leo Pharma, Janssen, and UCB and participated in SB17-3001 study as an investigator and received investigational grant from Samsung Bioepis. Dr Girolomoni has received personal fees from AbbVie, Abiogen, Almirall, Amgen, Biogen, Boehringer-Ingelheim, Bristol-Myers Squibb, Eli-Lilly, Leo Pharma, Merck Serono, Novartis, Pfizer, Samsung Bioepis, and Sanofi. Drs Brzezicki, Reznichenko, Zegadlo-Myłik, Pulka, Dmowska-Stecewicz, Klujszo, Rekalov, and Rajzer participated in SB17-3001 study as an investigator and received investigator grants from Samsung Bioepis. Authors J. Lee, M. Lee, and Dr Rho are employees of Samsung Bioepis Co, Ltd and owns stocks of Samsung Biologics.

REFERENCES

1. Menter A, Strober BE, Kaplan DH, et al. Joint AAD-NPF guidelines of care for the management and treatment of psoriasis with biologics. *J Am Acad Dermatol*. 2019;80(4):1029-1072.
2. Smolen JS, Landewé RBM, Bijlsma JWJ, et al. EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2022 update. *Ann Rheum Dis*. 2023;82(1):3-18.
3. Cohen AD, Vender R, Naldi L, et al. Biosimilars for the treatment of patients with psoriasis: a consensus statement from the biosimilar working group of the International psoriasis Council. *JAAD Int*. 2020;1(2):224-230.
4. Mulcahy AW, Hlavka JP, Case SR. Biosimilar cost savings in the United States: initial experience and future potential. *Rand Health Q*. 2018;7(4):3.
5. Association for Accessible Medicines. Report: 2023 U.S. Generic and Biosimilar Medicines Savings Report. AAM; 2023.
6. Kvien TK, Patel K, Strand V. The cost savings of biosimilars can help increase patient access and lift the financial burden of health care systems. *Semin Arthritis Rheum*. 2022;52:151939.
7. Griffiths CEM, Thaçi D, Gerdes S, et al. The EGALITY study: a confirmatory, randomized, double-blind study comparing the efficacy, safety and immunogenicity of GP2015, a proposed etanercept biosimilar, vs. the originator product in patients with moderate-to-severe chronic plaque-type psoriasis. *Br J Dermatol*. 2017;176(4):928-938.
8. Hercogová J, Papp KA, Chyrok V, Ullmann M, Vlachos P, Edwards CJ. AURIEL-PsO: a randomized, double-blind phase III equivalence trial to demonstrate the clinical similarity of the proposed biosimilar MSB11022 to reference adalimumab in patients with moderate-to-severe chronic plaque-type psoriasis. *Br J Dermatol*. 2020;182(2):316-326.
9. Papp K, Bachelez H, Costanzo A, et al. Clinical similarity of biosimilar ABP 501 to adalimumab in the treatment of patients with moderate to severe plaque psoriasis: a randomized, double-blind, multicenter, phase III study. *J Am Acad Dermatol*. 2017;76(6):1093-1102.
10. Menter A, Arenberger P, Balser S, et al. Similar efficacy, safety, and immunogenicity of the biosimilar BI 695501 and adalimumab reference product in patients with moderate-to-severe chronic plaque psoriasis: results from the randomized Phase III VOLTAIRE-PSO study. *Expert Opin Biol Ther*. 2021;21(1):87-96.
11. Leonardi CL, Kimball AB, Papp KA, et al. Efficacy and safety of ustekinumab, a human interleukin-12/23 monoclonal antibody, in patients with psoriasis: 76-week results from a randomised, double-blind, placebo-controlled trial (PHOENIX 1). *Lancet*. 2008;371(9625):1665-1674.
12. Papp KA, Langley RG, Lebwohl M, et al. Efficacy and safety of ustekinumab, a human interleukin-12/23 monoclonal antibody, in patients with psoriasis: 52-week results from a randomised, double-blind, placebo-controlled trial (PHOENIX 2). *Lancet*. 2008;371(9625):1675-1684.
13. EMA. Stelara®: EPAR—Product Information; Annex I, Summary of Product Characteristics. EMA; 2023.
14. FDA. Stelara®: Prescribing Information. FDA; 2023.
15. Kalb RE, Fiorentino DF, Lebwohl MG, et al. Risk of serious infection with biologic and systemic treatment of psoriasis: results from the psoriasis longitudinal assessment and registry (PSOLAR). *JAMA Dermatol*. 2015;151(9):961-969.
16. Singh S, Kim J, Luo J, et al. Comparative safety and effectiveness of biologic therapy for Crohn's disease: a CA-IBD cohort study. *Clin Gastroenterol Hepatol*. 2023;21(9):2359-2369.e5.
17. EMA. Guideline on Similar Biological Medicinal Products Containing Monoclonal Antibodies—Nonclinical and Clinical Issues. EMA; 2012.
18. FDA. Scientific Considerations in Demonstrating Biosimilarity to a Reference Product. FDA; 2015.
19. Jeong H, Kang T, Lee J, Im S. Comparison of SB17 and reference ustekinumab in healthy adults: a randomized, double-blind, single-dose, phase I Study. *Int J Clin Pharmacol Ther*. 2024;62:231-240.
20. Finlay AY, Khan GK. Dermatology Life Quality Index (DLQI)—a simple practical measure for routine clinical use. *Clin Exp Dermatol*. 1994;19(3):210-216.
21. FDA. Overview for Health Care Professionals. FDA; 2022.
22. Chow V, Mytych DT, Das S, Franklin J. Pharmacokinetic similarity of ABP 654, an ustekinumab biosimilar candidate: results from a randomized, double-blind study in healthy subjects. *Clin Pharmacol Drug Dev*. 2023;12(9):863-873.
23. Feldman SR, Reznichenko N, Berti F, et al. Randomized, double-blind, multicenter study to evaluate efficacy, safety, tolerability, and immunogenicity between AVT04 and the reference product ustekinumab in patients with moderate-to-severe chronic plaque psoriasis. *Expert Opin Biol Ther*. 2023;23(8):759-771.
24. Papp KA, Lebwohl MG, Thaçi D, et al. Efficacy and safety of candidate biosimilar CT-P43 versus originator ustekinumab in moderate to severe plaque psoriasis: 28-week results of a randomised, active-controlled, double-blind, phase III study. *BioDrugs*. 2024;38:121-131.
25. D'Aguanno K, Muntyanu A, Ouchene L, Litvinov IV, Netchiporouk E. In preparation for biosimilar "switch" policy: how to mitigate the nocebo effect. *J Cutan Med Surg*. 2022;26(2):203-205.