Consistent responses with guselkumab treatment in Asian and non-Asian patients with psoriasis: An analysis from VOYAGE 1 and VOYAGE 2

Kristian REICH,1 Michael SONG,2 Shu LI,2 Jingzhi JIANG,2 Sang Woong YOUN,3 Tsen-Fang TSAI,4 Yong Beom CHOE,5 Yu-Huei HUANG,6 Kenneth B. GORDON7
1Center for Translational Research in Inflammatory Skin Diseases, Institute for Health Services Research in Dermatology and Nursing, University Medical Center Hamburg-Eppendorf, Skinflammation® Center, Hamburg, Germany, 2Janssen Research & Development, LLC, Spring House, Pennsylvania, USA, 3Seoul National University College of Medicine, Seoul National University Bundang Hospital, Seongnam, South Korea, 4National Taiwan University Hospital and National Taiwan University College of Medicine, Taipei, Taiwan, 5Konkuk University School of Medicine, Seoul, South Korea, 6Chang Gung Memorial Hospital and School of Medicine, Chang Gung University, Taoyuan City, Taiwan, 7Medical College of Wisconsin, Milwaukee, Wisconsin, USA

ABSTRACT

Guselkumab, an interleukin-23 blocker, was superior to placebo and adalimumab and well-tolerated in phase 3 psoriasis studies (VOYAGE 1 and VOYAGE 2). This analysis evaluated the consistency of response in the Asian subpopulation in VOYAGE 1 and VOYAGE 2. Study designs were identical through week 24; patients were randomized to guselkumab, placebo, or adalimumab. Investigator’s Global Assessment (IGA), Psoriasis Area and Severity Index (PASI), safety, and pharmacokinetic and immunogenicity data from VOYAGE 1 and VOYAGE 2 were pooled and compared by race (Asian, n = 199; non-Asian, n = 1630). At week 16, treatment differences between guselkumab and placebo were 78.2 (95% confidence interval [CI], 66.9–89.6) and 76.4 (95% CI, 72.7–80.2) percentage points for IGA 0/1 (score of 0 or 1) and 70.1 (95% CI, 60.0–80.1) and 68.5 (95% CI, 64.9–72.2) percentage points for PASI 90 (≥90% improvement) in the Asian and non-Asian populations, respectively. Treatment differences between guselkumab and adalimumab were 31.1 (95% CI, 17.7–44.6) and 21.0 (95% CI, 11.2–21.0) percentage points for IGA 0/1 and 24.9 (95% CI, 9.4–40.5) and 23.2 (95% CI, 17.7–28.6) percentage points for PASI 90 in the Asian and non-Asian populations, respectively. Similar results were observed at week 24. Safety was generally similar between populations and among treatment groups. Median serum guselkumab concentrations over time were comparable between the populations. Comparable responses between the Asian and non-Asian populations in this analysis suggest that the overall efficacy, safety, and the resulting benefit/risk analyses from VOYAGE 1 and VOYAGE 2 are applicable to Asian populations.

Key words: guselkumab, interleukin-23 monoclonal antibody, psoriasis, South Korea, Taiwan.

INTRODUCTION

Psoriasis, a chronic, immune-mediated, inflammatory skin disease, is a serious global problem, with the reported country prevalence ranging from 0.12–1.24%.1,2 The prevalence of psoriasis in East Asian countries is relatively low, although it has been reported to be increasing.2,3 In studies of the prevalence of psoriasis in China, Japan, South Korea, and Taiwan, estimates ranged from 0.12–2.14%.1,2,4 Differences in the expression of genes that play a role in the pathophysiology of psoriasis between Asian and Western populations have been reported,5–8 and it is therefore important to evaluate the safety and efficacy of new therapeutic agents specifically in the Asian population.

Historically, studies of psoriasis therapies in Asian patients have been limited; however, since the introduction of biologic agents, more studies in this population have been reported.9 Studies of anti-tumor necrosis factor (TNF) agents in Asian patients have been reported, but many of these studies are smaller and later in the development cycle of the agent than studies in populations of mixed race.10–12 Substantial numbers of Asian patients were included in the pivotal studies of agents targeting interleukin (IL)-12/23, IL-23, and IL-17, allowing for subanalyses of the Asian populations in these studies.13–16
Separate studies of these agents have also been conducted specifically in Asian countries.4,17–19

Guselkumab (TREMFYA®; Janssen Research & Development, LLC, Spring House, PA, USA) is a fully human immunoglobulin G1 lambda monoclonal antibody that inhibits IL-23-mediated intracellular and downstream signaling by binding to the IL-23 p19 protein subunit with high specificity and affinity.20,21 IL-23 is required for the survival and expansion of T-helper 17 cells22,23 and plays a central role in the pathogenesis of psoriasis.24,25 In phase 3 global clinical trials (VOYAGE 1 and VOYAGE 2), guselkumab therapy was well-tolerated and demonstrated superior clinical responses compared with placebo and adalimumab in patients with moderate to severe plaque psoriasis.26,27

Here, we compare the efficacy, safety, and pharmacokinetics of guselkumab in the Asian and non-Asian subpopulations of the VOYAGE 1 and VOYAGE 2 guselkumab psoriasis studies.

METHODS

Patients

VOYAGE 1 and VOYAGE 2 were conducted in 10 countries, including the USA, Canada, Poland, Czech Republic, Germany, Spain, Russia, Australia, South Korea, and Taiwan (VOYAGE 1 only). These studies had identical patient populations; both included patients aged 18 years or older who had moderate to severe plaque psoriasis (Investigator’s Global Assessment [IGA] score ≥3, Psoriasis Area and Severity Index [PASI] ≥12, and body surface area [BSA] involvement ≥10%) for at least 6 months and were candidates for systemic therapy or phototherapy (full inclusion and exclusion criteria are described elsewhere).26,27 The study protocols were reviewed by an institutional review board or independent ethics committee at participating sites, and both studies conformed to local standards. All patients provided written consent. This study was registered at ClinicalTrials.gov (NCT02207231, NCT02207244).

For this post-hoc analysis, Asian patients were defined as participants in centers located in Taiwan or South Korea. Non-Asian patients were defined as participants in centers located in the USA, Canada, Poland, Czech Republic, Germany, Spain, Russia, or Australia. If patients of Asian descent participated at a center located in a non-Asian country, they were considered non-Asian.

Study design

Detailed study design information is described elsewhere.26,27 Briefly, VOYAGE 1 and VOYAGE 2 were phase 3, randomized, double-blind, placebo- and active comparator-controlled studies with identical study designs through week 24. Each study included a placebo-controlled period (from week 0 through week 16), an active comparator-controlled period (from week 0 through week 28), and a placebo-crossover period (from week 16 through week 28). In both studies, patients were randomized to receive guselkumab 100 mg at weeks 0, 4, 12, and 20; placebo at weeks 0, 4, 12, and 12; followed by guselkumab 100 mg at weeks 16 and 20; or adalimumab (HUMIRA®; Abbott Laboratories, North Chicago, IL, USA) 80 mg at week 0, 40 mg at week 1, and then 40 mg every 2 weeks through week 23 (Fig. 1). In VOYAGE 1, patients in the adalimumab group received adalimumab every 2 weeks through week 28. In VOYAGE 2, patients in the adalimumab group received adalimumab every 2 weeks through week 23 and then did not receive any study drug until week 28.

Study procedures and evaluations

Because VOYAGE 1 and VOYAGE 2 had identical study populations and similar study designs up to week 28, data were pooled to provide a relatively large sample size of Asian patients and to improve the precision of the analyses by race. Although the timing of adalimumab administration between weeks 24 and 28 was different between the studies, guselkumab administration was the same for the placebo-crossover and guselkumab groups. Therefore, efficacy was evaluated through week 24, while safety, pharmacokinetics, and immunogenicity were evaluated through week 28. Pooled IGA (0, cleared; 1, minimal; 2, mild; 3, moderate; and 4, severe) and PASI data were analyzed at week 16 and week 24 and compared by race (Asian vs non-Asian). The co-primary efficacy end points at week 16 were IGA score of 0 or 1 (IGA 0/1) and PASI 90 response (≥90% improvement in PASI from baseline), PASI 75 response (≥75% improvement in PASI from baseline) and PASI 100 response (100% improvement in PASI from baseline) were secondary week-16 endpoints. Week-24 efficacy assessments included IGA 0, IGA 0/1, PASI 75, PASI 90, and PASI 100 responses. Dermatology Life Quality Index (DLQI) was also assessed at week 16 and week 24. Pooled data for adverse events, laboratory testing, and investigator-assessed injection-site reactions were analyzed through week 16 and week 28 by race (Asian and non-Asian).

Pooled data for serum guselkumab concentrations measured by a validated, specific and sensitive electrochemiluminescence immunoassay (ECLIA) method using the Meso Scale Discovery platform (MSD®, Gaithersburg, MD, USA) were analyzed through week 28 by race (Asian and non-Asian). The lowest quantifiable sample concentration of the assay was 0.01 µg/mL (lower limit of quantification multiplied by the minimum required dilution of 1:10).

Antibodies to guselkumab were detected using a highly sensitive and drug-tolerant ECLIA (sensitivity of 3.1 ng/mL in guselkumab-free serum and 15 ng/mL with serum guselkumab concentration of ≤3.125 µg/mL, exceeding mean trough serum guselkumab levels) and were analyzed through week 28 by race (Asian and non-Asian).28

Statistical methods

Baseline characteristics and efficacy analyses were based on all patients who were randomized at week 0 according to their assigned treatment. P-values comparing the proportion of patients achieving a clinical response between treatment groups were based on the Cochran–Mantel–Haenszel χ²-test stratified by study (VOYAGE 1 and VOYAGE 2). Treatment differences and confidence intervals (CI) were adjusted by study
RESULTS

Patient disposition and disease characteristics

A total of 1829 patients were included in this analysis; 199 randomized patients were classified as Asian (placebo, n = 45; guselkumab, n = 94; adalimumab, n = 60) and 1630 were classified as non-Asian (placebo, n = 377; guselkumab, n = 731; adalimumab, n = 522) (Fig. 2). Baseline patient demographics and disease characteristics are summarized in Table 1. The mean age and proportion of men were comparable between the Asian and non-Asian populations. Overall, Asian patients had lower bodyweight (Fig. S1) and body mass index (BMI) compared with non-Asian patients. Asian patients also had more severe psoriasis at baseline (higher percentage of BSA involvement, higher baseline PASI, higher proportion of patients with a baseline IGA score of 4 [severe], and higher baseline DLQI) and were more likely to have had prior treatment with phototherapy and/or non-biologic and biologic systemic therapies compared with non-Asian patients (Table 1).

Efficacy results

Treatment effects for IGA and PASI responses at weeks 16 and 24 were generally consistent between the Asian and non-Asian populations (Figs 3,4). The CI for the treatment differences for the Asian population were wide and generally encompassed those of the non-Asian population (Fig. 4). At week 16, the treatment differences between guselkumab and placebo treatments (proportion of guselkumab responders minus the proportion of placebo responders) were significant for IGA 0/1 and PASI 90 responses (all \( P < 0.001 \)) and were comparable between populations (Fig. 4). The treatment differences between guselkumab and adalimumab treatments (proportion of guselkumab responders minus the proportion of adalimumab responders) were also significant at week 16 for IGA 0/1 and PASI 90 responses (all \( P \leq 0.002 \)) and comparable between populations for the PASI 90 response (24.9 [95% CI, 95% CI]...
The treatment difference for IGA 0/1 was greater in the Asian population (31.1 [95% CI, 17.7–44.6] and 16.1 [95% CI, 11.2–21.0] percentage points in the Asian and non-Asian populations, respectively). Treatment differences for PASI 75 and PASI 100 responses at week 16 were similar to those observed for PASI 90 response at this timepoint.

At week 24, the treatment differences between guselkumab and adalimumab treatments maintained significance for IGA 0/1 and PASI 90 responses (all \( P \leq 0.004 \)) and were comparable between the Asian and non-Asian populations (IGA 0/1, 31.1 [95% CI, 17.7–44.6] and 16.1 [95% CI, 11.2–21.0] percentage points in the Asian and non-Asian populations, respectively; PASI 90, 22.8 [95% CI, 7.3–38.3] and 24.0 [95% CI, 18.7–29.2] percentage points in the Asian and non-Asian populations, respectively) (Figs 3b, 4). Similar treatment differences were observed for IGA 0 and PASI 100 responses at this timepoint.

The proportion of patients who achieved a PASI 100 response was greater in the non-Asian compared with the Asian population for both guselkumab and adalimumab at week 16 and week 24. At week 16, 14.9% of Asian patients treated with guselkumab and 3.3% treated with adalimumab achieved a PASI 100 response compared with 38.0% and 20.3% of non-Asian patients treated with guselkumab and adalimumab, respectively (Fig. 3a). Similarly, at week 24, 23.4% and 13.3% of Asian patients treated with guselkumab...
Table 1. Summary of patient demographics, characteristics, and disease characteristics at baseline in Asian and non-Asian patients in VOYAGE 1 and VOYAGE 2

|                      | Asian patients | Non-Asian patients |
|----------------------|----------------|-------------------|
|                      | Placebo        | Gusekumab        | Adalimumab       |
| Patients randomized, n | 45             | 94               | 60               |
| Age (years), mean ± SD  | 42.6 ± 11.75   | 41.2 ± 12.20     | 38.1 ± 10.14     |
| Men, n (%)             | 31 (68.9)      | 73 (77.7)        | 50 (83.3)        |
| Race, n (%)            |                |                  |                  |
| Asian†                 | 45 (100.0)     | 94 (100.0)       | 60 (100.0)       |
| White                  | 6 (13.3)       | 15 (16.0)        | 13 (21.7)        |
| Black or African American | 35 (77.8)  | 87 (92.6)        | 54 (90.0)        |
| American Indian or Alaska Native | 54 (11.7) | 13 (16.0) | 13 (21.7) |
| Native Hawaiian or other Pacific | 2 (0.3) | 2 (0.3) | 2 (0.3) |
| Islander               |                |                  |                  |
| Other                  | 5 (1.3)        | 2 (0.3)          | 2 (0.3)          |
| Multiple               | 2 (0.5)        | 2 (0.5)          | 1 (0.2)          |
| Height (cm), Mean ± SD  | 168.5 ± 7.92   | 169.2 ± 8.49     | 169.9 ± 8.71     |
| Weight (kg)            |                |                  |                  |
| Mean ± SD              | 74.3 ± 14.32   | 76.5 ± 17.43     | 80.5 ± 15.68     |
| >90 kg, n (%)          | 6 (13.3)       | 15 (16.0)        | 13 (21.7)        |
| >70 to <90 kg, n (%)   | 19 (42.2)      | 44 (46.8)        | 34 (56.7)        |
| ≤70 kg, n (%)          | 20 (44.4)      | 35 (37.2)        | 13 (21.7)        |
| BMI (kg/m²), mean ± SD | 26.1 ± 4.18    | 26.6 ± 5.19      | 27.8 ± 4.59      |
| Duration of psoriasis (years), mean ± SD | 12.6 ± 6.32 | 15.3 ± 9.84 | 12.1 ± 7.10 |
| BSA (%), mean ± SD     | 32.6 ± 17.54   | 32.8 ± 16.34     | 34.3 ± 21.19     |
| PASI (0–24), mean ± SD | 24.6 ± 9.20    | 24.7 ± 9.01      | 26.8 ± 12.61     |
| IGA score of 4 (severe), n (%) | 14 (31.1) | 26 (27.7) | 21 (35.0) |
| DLQI (0–30), mean ± SD | 18.8 ± 6.79    | 18.1 ± 6.66      | 18.6 ± 6.88      |
| Prior psoriasis treatments (ever used), n (%) |                |                  |                  |
| Phototherapy (PUVA or UV-B) | 36 (80.0) | 82 (87.2) | 49 (81.7) |
| Non-biologics† systems | 35 (77.8)      | 87 (92.6)        | 54 (90.0)        |
| Biologics‡            | 12 (26.7)      | 26 (27.7)        | 16 (26.7)        |
| Non-biologic systems or biologics | 37 (82.2) | 87 (92.6) | 55 (91.7) |

If patients of Asian descent participated at a center located in a non-Asian country, they were considered non-Asian. †Non-biologics include PUVA, methotrexate, cyclosporin, acitretin, apremilast, or tofacitinib. ‡Biologics include etanercept, infliximab, alefacept, efalizumab, ustekinumab, briakinumab, secukinumab, ixekizumab, or brodalumab.

and adalimumab, respectively, achieved a PASI 100 response compared with 46.9% and 27.0% of non-Asian patients, respectively (Fig. 3b).

Treatment effects for DLQI of 0 or 1 (DLQI 0/1) differed between the Asian and non-Asian populations at week 16 but were comparable at week 24 (Fig. 5). At week 16, the treatment difference between guselkumab and placebo treatments for the proportion of patients with DLQI 0/1 was 23.5 (95% CI, 15.0–32.1) percentage points in the Asian population and 53.4 (95% CI, 49.3–57.6) percentage points in the non-Asian population. The treatment difference between guselkumab and adalimumab treatments for DLQI 0/1 response at week 16 was 4.1 (95% CI, –0.9 to 17.6) percentage points in the Asian population and 17.0 (95% CI, 11.3–22.7) percentage points in the non-Asian population. At week 24, the treatment difference between guselkumab and adalimumab treatments for DLQI 0/1 response was 14.4 (95% CI, –0.1 to 28.9) percentage points in the Asian population and 19.9 (95% CI, 14.3–25.6) percentage points in the non-Asian population.

Safety results

Through week 16, the proportions of patients who reported experiencing one or more adverse events, adverse events leading to discontinuation, serious adverse events, infection, or infection requiring antibiotics were generally comparable between the Asian and non-Asian patient populations (Table 2). In the Asian population, a slightly higher proportion of guselkumab-treated patients experienced one or more adverse events compared with placebo- and adalimumab-treated patients (60.6%, 40.0%, and 50.0%, respectively). However, in the non-Asian population, the proportion of patients who reported one or more adverse events was comparable among treatment groups (47.7%, 47.5%, and 49.9%, respectively). Nasopharyngitis and upper respiratory tract infection were the most
Figure 3. (a,b) IGA and PASI responses in Asian and non-Asian patients in VOYAGE 1 and VOYAGE 2 at (a) week 16 and (b) week 24. P-values are based on Cochran–Mantel–Haenszel $\chi^2$-test stratified by study. IGA, Investigator’s Global Assessment; $n$, number of patients; PASI, Psoriasis Area and Severity Index. (a) In the Asian population ($n = 199$), placebo $n = 45$, guselkumab $n = 94$ and adalimumab $n = 60$. In the non-Asian population ($n = 1630$), placebo $n = 377$, guselkumab $n = 731$ and adalimumab $n = 522$. *$P < 0.001$ for guselkumab versus placebo and guselkumab versus adalimumab, †$P \leq 0.002$ for guselkumab versus placebo and guselkumab versus adalimumab, ‡$P = 0.005$ for guselkumab versus placebo and guselkumab versus adalimumab, §$P \leq 0.010$ for guselkumab versus adalimumab. (b) In the Asian population ($n = 154$), guselkumab $n = 94$ and adalimumab $n = 60$. In the non-Asian population ($n = 1253$), guselkumab $n = 731$ and adalimumab $n = 522$. *$P \leq 0.004$, †$P = 0.115$ for guselkumab versus adalimumab.
commonly reported adverse events in both populations. Overall, adverse events were generally not serious in nature and did not lead to discontinuation of study agent. Among patients treated with guselkumab, 1.1% in the Asian population and 2.1% in the non-Asian population experienced a serious adverse event, and 2.1% in the Asian population and 1.2% in the non-Asian population discontinued the study because of an adverse event.

Through week 28, the proportions of patients who reported experiencing one or more adverse events, adverse events leading to discontinuation, serious adverse events, infection, or infection requiring antibiotics were also generally comparable among treatment groups in both the Asian and non-Asian patient populations (Table 2). As was observed through week 16, the proportion of patients who experienced one or more adverse events through week 28 was slightly higher with guselkumab treatment compared with adalimumab treatment in the Asian population (72.3% vs 66.7%, respectively) but not in the non-Asian population (59.3% vs 64.1%, respectively). Nasopharyngitis and upper respiratory tract infection remained the most commonly reported adverse events in both populations.

Figure 4. Proportion differences and 95% CI in IGA and PASI responses at weeks 16 and 24 for guselkumab-treated versus placebo- or adalimumab-treated Asian and non-Asian patients in VOYAGE 1 and VOYAGE 2. P-values are based on Cochran-Mantel-Haenszel \( \chi^2 \)-test stratified by study. Treatment differences and CI are adjusted by study with Cochran-Mantel-Haenszel weight. CI, confidence interval; IGA, Investigator’s Global Assessment; PASI, Psoriasis Area and Severity Index.
Through week 28, fewer guselkumab-treated patients than adalimumab-treated patients in both populations experienced one or more injection-site reactions (3.2% vs 15.0%, respectively, in the Asian population and 2.7% vs 7.7%, respectively, in the non-Asian population) (Table 3). In both studies, the adalimumab formulation contained sodium citrate. Among patients treated with guselkumab, no injection-site treatment-emergent adverse events associated with a guselkumab injection occurred in more than 1.2% of patients in either population. Among patients treated with adalimumab, injection-site erythema, injection-site pruritus, injection-site pain, and injection-site swelling associated with adalimumab injections occurred in 3% or more of patients in the Asian or non-Asian populations. However, the number of injections associated with an injection-site reaction was low in both populations for both guselkumab (0.8% in both populations) and adalimumab (1.6% in the Asian population and 1.5% in the non-Asian population).

**Pharmacokinetics**

The pattern of median serum guselkumab concentration over time was comparable between the Asian and non-Asian populations (Fig. 6a). Steady state of serum guselkumab concentration was achieved by approximately week 20 in both the Asian and non-Asian populations. The median steady-state trough serum guselkumab concentration at week 20 in patients randomized to guselkumab was 0.89 µg/mL in the Asian population.
population and 1.10 µg/mL in the non-Asian population. The median steady-state serum trough guselkumab concentrations were slightly lower in Asian patients than in non-Asian patients; however, the distributions (i.e., interquartile ranges) of serum guselkumab concentrations overlapped substantially between Asian and non-Asian patients, demonstrating that serum guselkumab concentrations were generally similar between the populations (Fig. 6a). When evaluated by weight categories

Table 3. Injection-site reactions and injection-site TEAEs\(\dagger\) associated with guselkumab or adalimumab injections through week 28 in Asian and non-Asian patients in VOYAGE 1 and VOYAGE 2

|                | Asian Guselkumab injection | Asian Adalimumab injection | Non-Asian Guselkumab injection | Non-Asian Adalimumab injection |
|----------------|-----------------------------|-----------------------------|-------------------------------|-------------------------------|
| Patients randomized, n | 94                          | 60                          | 729                           | 521                           |
| ≥1 injection-site reactions\(\dagger\) | 3 (3.2)                     | 9 (15.0)                    | 20 (2.7)                      | 40 (7.7)                      |
| Injection-site erythema | 1 (1.1)                     | 4 (6.7)                     | 9 (1.2)                       | 25 (4.8)                      |
| Injection-site pruritus | 1 (1.1)                     | 3 (5.0)                     | 1 (0.1)                       | 9 (1.7)                       |
| Injection-site pain    | 1 (1.1)                     | 2 (3.3)                     | 2 (0.3)                       | 13 (2.5)                      |
| Injection-site swelling| 0                           | 2 (3.3)                     | 4 (0.5)                       | 6 (1.2)                       |

All values are n (%) unless otherwise noted. \(\dagger\)Reported as a TEAE by ≥3.3% of patients in any treatment group in either population. \(\dagger\)Determined by the investigator. n, number of patients; TEAE, treatment-emergent adverse event.

Figure 6. (a–d) Time course of median serum guselkumab concentration through week 28 (a) overall and in Asian and non-Asian patients in VOYAGE 1 and VOYAGE 2 who weighed (b) ≤70 kg, (c) >70 kg to <90 kg, and (d) >90 kg at baseline. Box-and-whisker plots show the minimum, 25th percentile, median, 75th percentile, and maximum. The number of patients includes those who were initially randomized to guselkumab at week 0 and does not include placebo-crossover patients. The number of patients (n) with an evaluable serum sample for each group at each time point is provided below the x-axis.
(≤70 kg, >70 to ≤90 kg, and >90 kg), serum guselkumab concentrations remained comparable between Asian and non-Asian patients in each weight category, with overlapping distributions (Fig. 6b–d).

**Immunogenicity**

Of the 819 guselkumab-treated patients with post-treatment serum samples evaluable for antibodies to guselkumab through week 28, 93 were Asian and 726 were non-Asian. The incidence rates of antibodies to guselkumab through week 28 were low in both the Asian and non-Asian subpopulations and generally comparable (5.4% and 4.1%, respectively).

**DISCUSSION**

The global, pivotal guselkumab psoriasis studies, VOYAGE 1 and VOYAGE 2, included 199 patients from South Korea and Taiwan, allowing for the comparison of guselkumab efficacy and safety in Asian versus non-Asian patients. This pooled analysis of data from VOYAGE 1 and VOYAGE 2 confirmed that guselkumab treatment effects were comparable between Asian and non-Asian patients despite differences in baseline demographics and disease characteristics, including lower bodyweight and BMI and more severe psoriasis at baseline in the Asian population.

Treatment differences were generally consistent between the Asian and non-Asian populations for all efficacy endpoints at weeks 16 and 24. The CI for the Asian population treatment effects were wide, as expected due to the smaller sample size, and generally encompassed the CI of the non-Asian population. In contrast, early studies of anti-TNF biologics in Asian populations produced variable efficacy results, possibly due to small sample size. More recent studies with agents targeting IL-12/23, IL-23, or IL-17 have demonstrated efficacy results in Asian patients that are generally comparable with those reported in non-Asian patients,

Although the proportion of guselkumab-treated patients who achieved a PASI 100 response was numerically higher in the non-Asian compared with the Asian population at week 16 and week 24, the proportions of guselkumab-treated patients who achieved PASI 75, PASI 90, IGA 0/1, and IGA 0 responses were similar between the Asian and non-Asian populations. The results reported here support the conclusion that the efficacy of guselkumab is consistent between Asian and non-Asian patients. The difference in PASI 100 response rates between Asian and non-Asian patients may be due to random variability and the small proportions of patients who achieved a PASI 100 response. The results of previous studies with brodalumab and ustekinumab suggest that the higher proportion of patients with prior use of systemic and biologic agents in the Asian population may also play a role.

The treatment effects for DLQI 0/1 response between guselkumab and placebo treatments and between guselkumab and adalimumab treatments were different between the Asian and non-Asian populations at week 16. In general, compared with the non-Asian population, a smaller proportion of the Asian population achieved a DLQI 0/1 response regardless of treatment. A similar trend was observed at week 24, although the treatment differences for DLQI 0/1 response between guselkumab and adalimumab treatments were comparable between populations. The reason for this observation is not clear, but it may be related to the fact that baseline DLQI in all treatment groups in the Asian population were higher than those in all treatment groups in the non-Asian population.

Guselkumab was well-tolerated in both populations, with a safety profile generally comparable with those of placebo and adalimumab in both Asian and non-Asian patients. The proportion of patients with one or more adverse events was slightly higher in the guselkumab group compared with the placebo and adalimumab groups through week 16 and week 28 in the Asian population, but not in the non-Asian population. This was largely due to nasopharyngitis and upper respiratory tract infection adverse events. Nonetheless, the proportions of patients with serious adverse events and adverse events leading to discontinuation were low among guselkumab-treated patients, consistent with those observed for placebo-treated patients through week 16 in both populations, and remained consistent and low through week 28.

Serum guselkumab concentrations were generally comparable between Asian and non-Asian patients despite the difference in baseline bodyweight between these populations. In the overall population and in weight category subgroups, median serum guselkumab concentrations were comparable between the Asian and non-Asian populations at each timepoint, with considerable overlap in distributions. The frequency of antibodies to guselkumab was also low and comparable between the Asian and non-Asian populations.

A limitation of this study is that it is a post-hoc analysis of a relatively small number of Asian patients. In addition, the data are derived from relatively short-term follow up, with efficacy data considered only available through 24 weeks due to the difference in study design between the studies after week 24.

In summary, the overall profile of guselkumab efficacy, safety, immunogenicity, and pharmacokinetics in patients with moderate to severe psoriasis evaluated in this pooled analysis of two global pivotal psoriasis studies was generally comparable between the Asian and non-Asian populations. Response to guselkumab was rapid and highly effective, including demonstrated superiority to adalimumab through week 24. Guselkumab was generally well-tolerated and no new safety concerns were identified within the Asian population. Therefore, guselkumab offers a highly effective, convenient, and well-tolerated option for the treatment of psoriasis in South Korea and Taiwan. These results provide practical information to prescribers, indicating that overall efficacy, safety, and the resulting benefit/risk analyses of guselkumab are applicable to Asian populations.

**ACKNOWLEDGMENTS:** The authors wish to thank Cynthia Guzzo, Kelly Global Services, Troy, MI, USA; Holly Capasso-Harris, Synchrogenix, a Certara Company, Wilmington, DE, USA; and Kristin Ruley Sharples, Janssen Scientific Affairs, Spring House, PA, USA, for their editorial assistance and writing support in the preparation of this manuscript. This work was supported by Janssen Research & Development, LLC, Spring House, PA, USA, including funding and guidance for the conduct of the research and the preparation of the article, including
CONFLICT OF INTEREST: K. R. has served as paid advisor and/or paid speaker for and/or participated in clinical trials (site received patient fees, received fees if acting as coordinating investigator) sponsored by AbbVie, Affibody, Amiraal, Amgen, Biogen-Idec, Boehinger Ingelheim Pharma, Celgene, Covagen, Forward Pharma, Fresenius Medical Care, GlaxoSmithKline, Janssen, Janssen-Cilag, Kyowa Kirin, Leo, Eli Lilly, Medac, Merck Sharp & Dohme, Miltényi, Novartis, Ocean Pharma, Pfizer, Samsung Bioepis, Sanofi, Takeda, UCB Pharma, Valeant, and Xenonport. M. S., S., L., and J. J. are employees of Janssen Research & Development, a wholly owned subsidiary of Johnson & Johnson, and owns stock in Johnson & Johnson. S. W. Y. has served as a paid advisor for Janssen Research & Development, LLC. T.-F. T. has conducted clinical trials or received honoraria for serving as an advisory board member for AbbVie, Boehinger Ingelheim, Celgene, Eli Lilly, Janssen-Cilag, Novartis International AG, and Pfizer. Y. B. C. has no conflict of interest to declare. Y.-H. H. has received honoraria for serving as an advisory board member for Novartis, Eli Lilly, and Janssen-Cilag Pharmaceutica, and received consultant fees from AbbVie and Pfizer. K. B. G. has received honoraria as a consultant for AbbVie, Almirall, Amgen, Boehinger Ingelheim, Bristol-Myers Squibb, Celgene, Dermira, Eli Lilly, Novartis, Pfizer, Sun, and UCB Pharma, and has received grants for research support from AbbVie, Bristol-Myers Squibb, Celgene, Eli Lilly, Janssen, and Novartis.

REFERENCES

1 World Health Organization. Global report on psoriasis[Cited 2018 July 05]. Available from URL: http://apps.who.int/iris/bitstream/10665/204417/1/9789241565189_eng.pdf, 2016.

2 Han JH, Lee JH, Han KD et al. Epidemiology and medication trends in patients with psoriasis: a nationwide population-based cohort study from Korea. Acta Derm Venereol 2018; 98: 396–400.

3 Wang TS, Hsieh CF, Tsai TF. Epidemiology of psoriatic disease and current treatment patterns from 2003 to 2013: a nationwide, population-based observational study in Taiwan. J Dermatol Sci 2016; 84: 340–345.

4 Tsai TF, Ho JC, Song M et al. Efficacy and safety of ustekinumab for the treatment of moderate-to-severe psoriasis: a Phase III, randomized, placebo-controlled trial in Taiwanese and Korean patients (PEARL). J Dermatol Sci 2011; 63: 54–63.

5 Kim TG, Lee HJ, Youn JI, Kim TY, Han H. The association of psoriasis with human leukocyte antigens in Korean population and the influence of age of onset and sex. J Invest Dermatol 2000; 114: 309–313.

6 Kim J, Oh CH, Jeon J et al. Molecular phenotyping small (Asian) versus large (Western) plaque psoriasis shows common activation of IL-17 pathway genes but different regulatory gene sets. J Invest Dermatol 2016; 136: 161–172.

7 Nakagawa H, Akazaki S, Ashahira A et al. Study of HLA class I, class II and complement genes (C2, C4A, C4B, and BF) in Japanese psoriatics and analysis of a newly found high-risk haplotype by pulsed field gel electrophoresis. Arch Dermatol Res 1991; 283: 281–284.

8 Tsai TF, Hu CY, Tsai WL et al. HLA-Cw6 specificity and polymorphic residues are associated with susceptibility among Chinese psoriatics in Taiwan. Arch Dermatol Res 2002; 294: 214–220.

9 Tsai YC, Tsai TF. A review of clinical trials of biologic agents and small molecules for psoriasis in Asian subjects. G Ital Dermatol Venereol 2016; 151: 412–431.

10 Na JI, Kim JH, Park KC, Youn SW. Low-dose etanercept therapy in moderate to severe psoriasis in Korean. J Dermatol 2008; 35: 484–490.

11 Ashahira A, Nakagawa H, Etho T, Ohtsuki M, Adilumabum M04-688 Study Group. Adilumabum in Japanese patients with moderate to severe chronic plaque psoriasis: efficacy and safety results from a Phase II/III randomized controlled study. J Dermatol 2010; 37: 299–310.

12 Cai L, Gu J, Zheng J et al. Efficacy and safety of adalimumab in Chinese patients with moderate-to-severe plaque psoriasis: results from a Phase 3, randomized, placebo-controlled, double-blind study. J Eur Acad Dermatol Venereol 2017; 31: 89–95.

13 Imakuku S, Torius-Itakura H, Nishikawa A, Zhao F, Cameron GS, Japanese UNCOVER-1 Study Group. Efficacy and safety of ixekizumab treatment in Japanese patients with moderate-to-severe plaque psoriasis: subgroup analysis of a placebo-controlled, Phase 3 study (UNCOVER-1). J Dermatol 2017; 44: 1285–1290.

14 Wu NL, Hsu CJ, Sun FJ, Tsai TF. Efficacy and safety of secukinumab in Taiwanese patients with moderate to severe plaque psoriasis: subanalysis from ERASURE Phase III study. J Dermatol 2017; 44: 1129–1137.

15 Ohtsuki M, Morita A, Abe M et al. Secukinumab efficacy and safety in Japanese patients with moderate-to-severe plaque psoriasis: subanalysis from ERASURE, a randomized, placebo-controlled, Phase 3 study. J Dermatol 2014; 41: 1039–1046.

16 Youn SW, Tsai TF, Cheng C et al. The MARCOPOLO study of ustekinumab utilization and efficacy in a real-world setting: treatment of patients with plaque psoriasis in Asia-Pacific countries. Ann Dermatol 2016; 28: 222–231.

17 Igarashi A, Kato T, Kato M, Song M, Nakagawa H, Japanese Ustekinumab Study Group. Efficacy and safety of ustekinumab in Japanese patients with moderate-to-severe plaque-type psoriasis: long-term results from a Phase 2/3 clinical trial. J Dermatol 2012; 39: 242–252.

18 Zhu X, Zheng M, Song M et al. Efficacy and safety of ustekinumab in Chinese patients with moderate to severe plaque-type psoriasis: results from a Phase 3 clinical trial (LOTUS), J Drugs Dermatol 2013; 12: 166–174.

19 Saeli H, Nakagawa H, Nakajo K et al. Efficacy and safety of ixekizumab treatment for Japanese patients with moderate to severe plaque psoriasis, erythrodermic psoriasis and generalized pustular psoriasis: results from a 52-week, open-label, Phase 3 study (UNCOVER-5). J Dermatol 2017; 44: 355–362.

20 Gordon KB, Duffin KC, Bissonnette R et al. A Phase 2 trial of guselkumab versus adalimumab for plaque psoriasis. N Engl J Med 2015; 373: 136–144.

21 Sofen H, Smith S, Matheson RT et al. Guselkumab (an IL-23-specific mAb) demonstrates clinical and molecular response in patients with moderate-to-severe psoriasis. J Allergy Clin Immunol 2014; 133: 1032–1040.

22 Wilson NJ, Boniface K, Chan JR et al. Development, cytokine profile and function of human interleukin 17-producing helper T cells. Nat Immunol 2007; 8: 950–957.

23 Teng MW, Bowman EP, McElwee JJ et al. IL-12 and IL-23 cytokines: from discovery to targeted therapies for immune-mediated inflammatory diseases. Nat Med 2015; 21: 719–729.

24 Kopp T, Riedl E, Bangert C et al. Clinical improvement in psoriasis with randomized withdrawal and retreatment: results from the Phase III, double-blind, placebo- and active comparator-controlled VOYAGE 1 trial. J Am Acad Dermatol 2017; 76: 403–417.

25 Reich K, Armstrong AW, Foley P et al. Efficacy and safety of guselkumab, an anti-interleukin-23 monoclonal antibody, compared with adalimumab for the continuous treatment of patients with moderate to severe psoriasis: results from the Phase III, double-blind, placebo- and active comparator-controlled VOYAGE 2 trial. J Am Acad Dermatol 2017; 76: 418–431.
K. Reich et al.

28 Lebwohl M, Langley RG, Zhu Y et al. Use of dose-exposure-response relationships in Phase 2 and Phase 3 guselkumab studies to optimize dose selection in psoriasis. J Eur Acad Dermatol Venereol 2019; https://doi.org/10.1111/jdv.15668

29 Tsai TF, Yeh TY. An update of the published reports on biologics use for psoriasis and the reimbursement status in Asia-Pacific region. Curr Rheumatol Rev 2012; 8: 227-234.

30 Papp KA, Gordon KB, Langley RG et al. Impact of previous biologic use on the efficacy and safety of brodalumab and ustekinumab in patients with moderate-to-severe plaque psoriasis: integrated analysis of the randomized controlled trials AMAGINE-2 and AMAGINE-3. Br J Dermatol 2018; 179: 320-328.

SUPPORTING INFORMATION

Additional Supporting Information may be found in the online version of this article:

Figure S1. Baseline bodyweight in Asian versus non-Asian patients in VOYAGE 1 and VOYAGE 2. Box-and-whisker plots show the minimum, 25th percentile, median, 75th percentile, and maximum. The number of patients randomized to each group is provided below the x-axis. n, number of patients.