Secukinumab shows significant efficacy in palmoplantar psoriasis: Results from GESTURE, a randomized controlled trial

Alice Gottlieb, MD, PhD,[a] John Sullivan, MD,[b] Martijn van Doorn, MD,[c] Alexey Kubanov, MD,[d] Ruquan You, MSc,[e] Anne Parneix, MD,[f] Sophie Hugot, MSc,[g] and Marina Milutinovic, MD[g]
Valhalla, New York; Darlinghurst, Australia; Rotterdam, The Netherlands; Moscow, Russia; Shanghai, China; East Hanover, New Jersey; and Basel, Switzerland

Background: Plaque psoriasis affecting palms and soles is disabling and often resistant to treatment.

Objective: Evaluate the efficacy and safety of secukinumab, an anti-interleukin 17A antibody, in subjects with palmoplantar psoriasis.

Methods: In this double-blinded, randomized controlled trial, 205 subjects were randomized 1:1:1 to secukinumab 300 mg, 150 mg, or placebo. The primary endpoint was Palmoplantar Investigator's Global Assessment (ppIGA) 0 (clear) or 1 (almost clear/minimal) response at week 16.

Results: At week 16, the percentage of subjects who achieved clear or almost clear palms and soles (or ppIGA 0/1) with secukinumab 300 mg (33.3%) and 150 mg (22.1%) was superior to the percentage achieved with placebo (1.5%, $P < .001$). Palmoplantar Psoriasis Area and Severity Index (ppPASI) was significantly reduced with secukinumab 300 mg (−54.5%) and 150 mg (−35.3%) compared with placebo (−4.0%, $P < .001$). Dermatology Life Quality Index (DLQI) 0/1 responses from subjects in the secukinumab groups were also significantly higher compared with placebo at week 16 ($P < .01$) and pain and function of palms and soles was markedly improved with secukinumab as measured by the palmoplantar Quality-of-Life Instrument. Secukinumab 300 mg consistently showed the best outcomes. The safety profile was favorable and similar to previous studies.

Limitations: Lack of active comparator.

Conclusion: In GESTURE, the largest randomized controlled trial in palmoplantar psoriasis, secukinumab demonstrated the greatest efficacy to date for treating difficult-to-treat psoriasis. (J Am Acad Dermatol 2017;76:70-80.)

Key words: palmoplantar psoriasis; clear or almost clear skin; clinical trial; secukinumab; superiority; quality of life.

From Department of Dermatology, New York Medical College, Valhalla[a]; Holdsworth House Medical Practice, Darlinghurst[b]; Erasmus MC, Rotterdam[c]; State Scientific Center of Dermatology, Venereology and Cosmetology, Moscow[d]; Beijing Novartis Pharma Co. Ltd, Shanghai[e]; Novartis Pharmaceuticals Corporation, East Hanover[f]; and Novartis Pharma AG, Basel.[g]

Supported by Novartis Pharma AG, Basel, Switzerland.

Disclosure: Dr Gottlieb has served as a consultant and advisory board member for Amgen Inc, Astellas, Akros, Centocor Inc (Janssen), Celgene Corp, Bristol Myers Squibb Co, Beiersdorf Inc, Abbott Labs (AbbVie), TEVA, Actelion, UCB, Novo Nordisk, Novartis, Dermipsor Ltd, Incyte, Pfizer, Canfite, Lilly, Coronado, Vertex, Karyopharm, CSL Behring Biotherapies for Life, Glaxo Smith Kline, Xenoport, Catabasis, Meiji Seika Pharma Co Ltd, Takeda, Mitsubishi and Tanabe Pharma Development America Inc, and Genentech and has received research and educational grants from Centocor Inc (Janssen), Amgen Inc, Abbott Labs (AbbVie), Novartis, Celgene, Pfizer, Lilly, Coronado, Levia, Merck, Xenoport, and Dermira. Dr Sullivan has participated in advisory boards for Novartis Australia. Dr van Doorn has participated in advisory boards for Janssen, Pfizer, MSD, and Leopharma and received a research grant from Janssen and Pfizer. Mr You, Dr Parneix, Ms Hugot, and Dr Milutinovic are employees of and/or own stock in Novartis. Dr Kubanov has no conflict of interest to declare.

Previously presented in the form of an oral presentation at the 23rd World Congress of Dermatology (Vancouver, BC, Canada, June 2015).

Accepted for publication July 28, 2016.

Reprints not available from the authors.

Correspondence to: Alice Gottlieb, MD, PhD, New York Medical College, 40 Sunshine Cottage Rd, Valhalla, NY 10595. E-mail: alice.gottlieb@gmail.com.

Published online October 1, 2016.

0190-9622

http://dx.doi.org/10.1016/j.jaad.2016.07.058

Palmoplantar psoriasis, plaque psoriasis on the palms and soles, is present in up to 40% of plaque psoriasis patients and is known to be difficult to treat.[1] Palms and soles are crucial for function and, as a consequence, palmoplantar psoriasis leads to a disproportionately greater impairment of health-related quality of life (HRQoL) compared with plaque psoriasis on other parts of the body.[2] Patients suffer from a significant amount of pain in the palms and soles, have impaired dexterity of the hands, difficulty walking, and an inability to work.[2-4] Many patients with palmoplantar psoriasis do not have extensive psoriasis on other body parts, therefore the total body surface area (BSA) affected by psoriasis is often lower than 10%, excluding them from most psoriasis clinical trials. Because of its profound impact on quality of life, even greater than in moderate-to-severe psoriasis,[5] and regardless of there often being a low BSA affected, the National Psoriasis Foundation considers palmoplantar psoriasis to be a severe form of psoriasis.[6]

CAPSULE SUMMARY

- Palmoplantar psoriasis is difficult-to-treat and significantly impacts quality of life.
- At 16 weeks, one-third of subjects treated with secukinumab 300 mg showed clear or almost clear palms and soles with a significant improvement in quality of life.
- Secukinumab represents a new therapeutic option for the treatment of palmoplantar psoriasis.

Palmoplantar psoriasis is known as recalcitrant due to it being difficult to treat. Biologics have shown better efficacy than other treatment options[7-9]; however, the efficacy achieved with biologics in treating palmoplantar psoriasis is markedly lower than that achieved by these agents in psoriasis on other parts of the body.

Palmoplantar psoriasis has rarely been studied in clinical trials, which may explain why there is no clear treatment algorithm[10] and has been recognized as one of the top priorities in psoriasis research by the International Psoriasis Council.[11] The data that does exist often comes from research with heterogeneous patient populations or small sample sizes and/or from a subgroup/post-hoc analysis from trials in which palmoplantar psoriasis was not the main focus of research.[12-15] Therefore, a high unmet need for an effective treatment, confirmed by large randomized placebo-controlled studies specifically designed for palmoplantar psoriasis patients, remains.

Interleukin (IL)-17A is a cytokine that plays a key role in immune-mediated disorders including psoriasis.[16,17] Secukinumab is a fully human IgG1κ monoclonal antibody that selectively binds and neutralizes IL-17A.[18,19] Results from phase 3 clinical trials have demonstrated high efficacy of secukinumab in moderate-to-severe psoriasis, starting at early time points, with a sustained effect and a favorable safety profile.[18-22] Secukinumab has also shown superiority to etanercept[20] and ustekinumab[23] in head-to-head trials. Post-hoc analysis of a relatively small subgroup of palmoplantar psoriasis subjects from a secukinumab phase 2 study in moderate-to-severe psoriasis showed promising initial results.[24]

The present phase 3b study, GESTURE, was designed to evaluate the efficacy and safety of secukinumab specifically in subjects with palmoplantar psoriasis. Here we report results up to week 16, the time point of the primary objective assessment.

MATERIALS AND METHODS

Study design

GESTURE was a randomized, double-blind, placebo-controlled, multicenter, phase 3b trial conducted across 15 countries (Clinicaltrials.gov NCT01806597). The first subject's first visit was on June 19, 2013, and the last subject's last 16-week visit occurred on July 2, 2014. The study was conducted in accordance with principles of the Declaration of Helsinki.

Eligible subjects were randomized 1:1:1, via an interactive response technology system, to secukinumab 300 mg, secukinumab 150 mg, or placebo delivered subcutaneously. Randomization was stratified at baseline by body weight (<90 kg or ≥90 kg). An overview of the study design is presented in Fig 1.

The primary endpoint was Palmoplantar Investigator's Global Assessment (ppIGA) 0 (clear) or 1 (almost clear/minimal) response at week 16. Investigators, subjects, and the sponsor study team remained blinded to treatment assignment until the end of study.

Subjects

Eligible subjects were ≥18 years old with moderate-to-severe palmoplantar psoriasis (ppIGA score of ≥3 [on a 5-point scale]) and at least one additional plaque outside of the palms and soles to confirm the diagnosis of plaque psoriasis.

Subjects must have had disease previously inadequately controlled by topicals, phototherapy, and/or systemic therapy. Subjects with forms of psoriasis other than plaque (such as palmoplantar

Abbreviations used:

AE:	adverse event
BSA:	body surface area
DLQI:	Dermatology Life Quality Index
EQ-5D:	Euro Quality-of-Life 5-Dimension Health Status Questionnaire
HRQoL:	health-related quality of life
IGA:	Investigator's Global Assessment
IgG:	immunoglobulin G
IL:	interleukin
PASI:	Psoriasis Area and Severity Index
ppIGA:	Palmoplantar Investigator's Global Assessment
ppPASI:	Palmoplantar Psoriasis Area and Severity Index
ppPGA:	Palmoplantar Physician Global Assessment
ppQLI:	Palmoplantar Quality-of-Life Instrument
QoL:	quality of life
SAE:	serious adverse event
SGA:	Subject Global Assessment

pustulosis) were excluded. Previous exposure to secukinumab or other drugs directly targeting IL-17A or the IL-17 receptor were prohibited. During the study, no concomitant use of any other psoriasis treatments was allowed, including topical therapies such as corticosteroids.

Assessments

The primary objective was to demonstrate the superiority of secukinumab 300 and/or 150 mg versus placebo based on a ppIGA of 0 or 1 response and a reduction of at least 2 points on the ppIGA scale from baseline to week 16. The ppIGA scale was based on the IGA modified version 2011,[25] specifically applied to the palms and soles. Secondary objectives included the evaluation of ppIGA and Palmoplantar Psoriasis Area and Severity Index (ppPASI) over time from baseline to week 16 comparing treatment groups with placebo. The ppPASI was based on the PASI[26,27] but applied only to the palms and soles: each palm contributed 20% and each sole contributed 30% to the total palmoplantar surface area. Subject-reported outcomes included the Dermatology Life Quality Index (DLQI),[28] Palmoplantar Quality-of-Life Instrument (ppQLI),[29] Subject Global Assessment (SGA) of disease activity, and EuroQoL 5-Dimension Health Status Questionnaire (EQ-5D).[30,31] The ppQLI assesses relevant dimensions affected by palmoplantar psoriasis: pain/discomfort, functionality, and social/activity limitations, and the SGA assesses subjects' well-being, considering all the ways palmoplantar psoriasis affected them, from very poor (0 mm) to very good (100 mm). Safety and tolerability were evaluated by adverse events (AE), laboratory and vital sign assessments, and physical examinations.

Statistical analyses

The ppIGA response was compared between secukinumab and placebo using Cochran-Mantel-Haenszel test stratified by body weight. Nonresponder imputation was used to impute missing ppIGA data, in which a subject was considered to be a ppIGA nonresponder regardless of the reason for missing data. An additional sensitivity analysis was carried out by using multiple imputation to predict the most likely value for the missing ppIGA data, based on known characteristics of a particular subject and all other subjects in the study.

RESULTS

Subjects

The distribution of the subjects across the sites/countries was balanced. Of the 277 subjects screened, 205 were randomized to one of the three study groups (Fig 2). Approximately 92% of subjects completed the 16-week treatment period.

The baseline characteristics were similar between treatment groups (Table I). All subjects had moderate to severe palmoplantar psoriasis with the majority (72.2%) having a BSA <10%. More than half of subjects (58.5%) were previously exposed to nonbiologic systemic therapies; 10.7% were exposed to biologics with the majority failing previous biologic therapy (7.8%).

Efficacy

Both secukinumab doses were superior to placebo at week 16 with respect to a ppIGA 0/1 response. Overall, 33.3% of subjects on secukinumab 300 mg, 22.1% on secukinumab 150 mg, and 1.5% on placebo ($P < .0001$ and $P = .0002$, respectively vs placebo) achieved this endpoint (Fig 3). Both secukinumab doses exhibited consistently higher percentages of ppIGA 0/1 responders compared to placebo over time to week 16, starting as early as week 2 for secukinumab 300 mg (Fig 3). Across all measures secukinumab 300 mg showed the greatest efficacy. Similar results were observed with multiple imputation data at week 16, with 39.3% of subjects on secukinumab 300 mg, 23.1% on secukinumab 150 mg, and 1.5% on placebo achieving a ppIGA 0/1 response ($P < .0001$ and $P = .0002$, respectively vs placebo) (data not shown). In subjects receiving secukinumab 300 mg that had previously failed biologics, ppIGA 0/1 response rate remained similar to the overall population (33.3%).

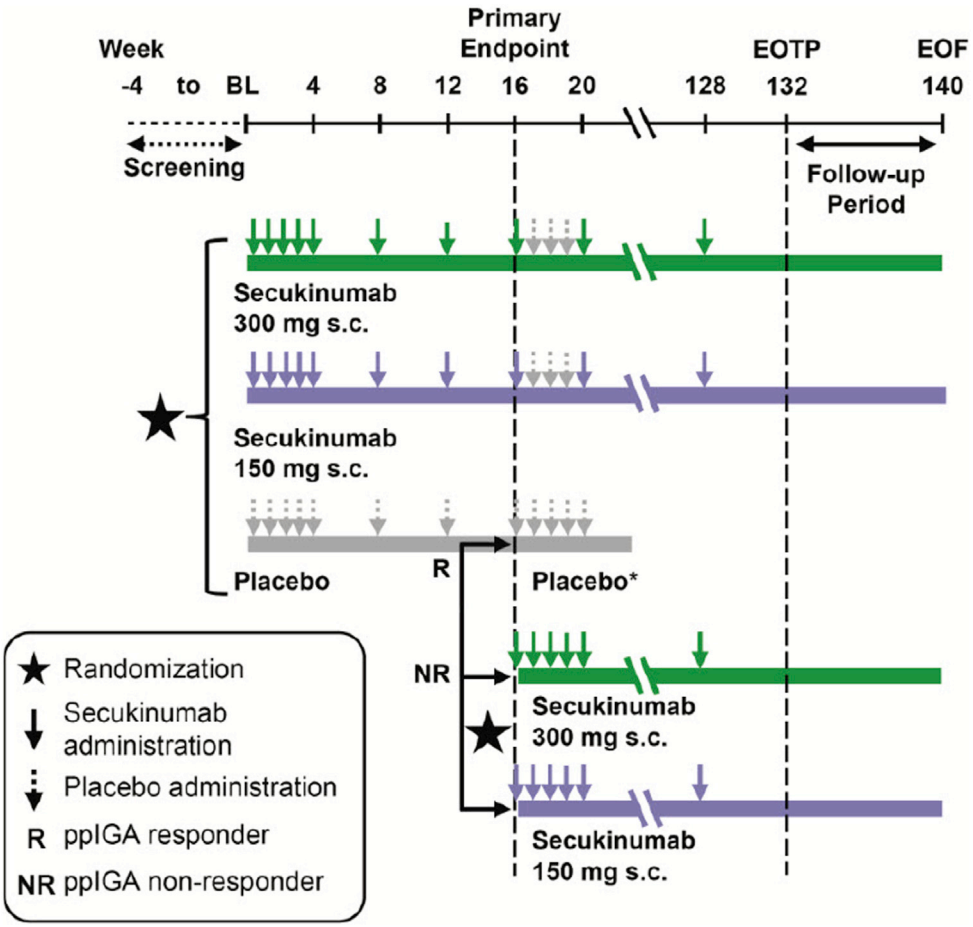

Fig 1. Study design. Subjects received secukinumab 300 mg, secukinumab 150 mg, or placebo every week from baseline to week 3 and then every 4 weeks from week 4 to 16. *Subjects in the placebo arm who were not ppIGA 0 or 1 responders at week 16 were re-randomized (1:1) to secukinumab 300 mg or 150 mg. ppIGA responders are subjects who achieved a ppIGA 0 or 1 score and at least a 2-point reduction on the ppIGA scale from baseline; ppIGA nonresponders are subjects who did not achieve a ppIGA 0 or 1 score and at least a 2-point reduction on the ppIGA scale from baseline. *BL*, Baseline; *EOTP*, end of treatment period; *EOF*, end of follow-up period; *ppIGA*, Palmoplantar Investigator's Global Assessment; *sc*, subcutaneous.

The reduction in ppPASI from baseline to week 16 was consistently greater with secukinumab compared with placebo. At week 16, ppPASI reduction from baseline was significant, with secukinumab 300 mg (−54.5%) and 150 mg (−35.3%) compared with placebo (−4.0%; $P < .0001$ and $P = .0006$, respectively) (Fig 4).

Fig 5 shows photographs of the palms and soles from subjects at baseline, week 4, and 16.

Subject-reported outcomes

At baseline, skin problems had a very large effect on subjects' lives (median DLQI 13-14). At week 16, the percentage of subjects achieving a DLQI score of 0/1, indicating no impact of skin problems on their lives, was significantly higher with secukinumab 300 mg (26.6%) and 150 mg (16.9%) compared with placebo (1.5%, $P < .0001$ and $P < .005$, respectively) (Fig 6).

ppQLI captured more HRQoL information because it is specific to aspects relevant for palmoplantar psoriasis. It showed that the percentage of subjects experiencing no difficulty due to involvement of both palms and soles increased from 0% at baseline to 12.5% and 10.8% at week 16 for secukinumab 300 mg and 150 mg, respectively, and did not change for placebo (Fig 7, *A*). Subjects reporting no difficulty due to palm (Fig 7, *B*) or sole (Fig 7, *C*) involvement at week 16 are presented separately. At baseline, HRQoL was overall more impaired due to psoriasis on the palms than on the soles. As a result of psoriasis of the palms, 50%-60% of subjects at baseline reported moderate-to-extreme hand pain, work limitation,

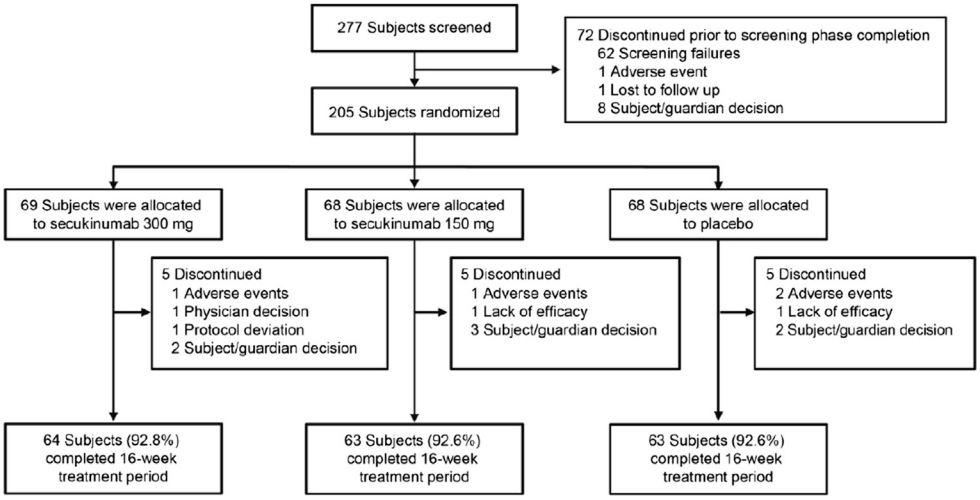

Fig 2. GESTURE subject disposition.

Table I. Patient demographic and baseline disease characteristics

Characteristic	Secukinumab 300 mg (n = 69)	Secukinumab 150 mg (n = 68)	Placebo (n = 68)
Age, years, mean ± SD	48.8 ± 14.2	52.4 ± 12.6	50.9 ± 13.0
Male sex, n (%)	38 (55.1)	40 (58.8)	34 (50.0)
Caucasian, n (%)	67 (97.1)	63 (92.6)	65 (95.6)
Weight, kg mean ± SD	84.8 ± 18.3	84.1 ± 18.4	84.4 ± 20.0
BMI, kg/m^2 mean ± SD	29.2 ± 5.8	28.8 ± 5.7	28.8 ± 5.7
Current smokers, n (%)	26 (37.7)	26 (38.2)	18 (26.5)
Time since palmoplantar psoriasis diagnosis, years	7.9 ± 8.2	7.5 ± 8.8	11.8 ± 10.4
ppIGA score, n (%)			
3 (moderate)	50 (72.5)	39 (57.4)	46 (67.6)
4 (severe)	19 (27.5)	29 (42.6)	22 (32.4)
ppPASI score, mean ± SD	23.9 ± 13.2	24.1 ± 15.8	24.1 ± 14.4
PASI score, mean ± SD	8.0 ± 9.6	8.7 ± 10.4	7.7 ± 7.3
BSA score, mean ± SD; Min-Max	9.7± (15.2; 0.3-66.0)	10.5 ± (15.3; 0.1-81.0)	9.5 ± (12.1; 0.3-68.0)
BSA <10%, n (%)	54 (78.3)	47 (69.1)	47 (69.1)
Previous exposure to nonbiologic systemic therapy, n (%)	42 (60.9)	36 (52.9)	42 (61.8)
Previous failure of nonbiologic systemic therapy, n (%)	38 (55.1)	35 (51.4)	35 (51.4)
Previous exposure to biologic therapies, n (%)	5 (7.2)	9 (13.2)	8 (11.8)
Previous failure of biologic therapies, n (%)	3 (4.3)	6 (8.8)	7 (10.3)
1 biologic	0 (0)	1 (1.5)	3 (4.4)
≥2 biologics	3 (4.3)	5 (7.3)	4 (5.9)
Previous exposure to anti-psoriatic topicals, n (%)	31 (44.9)	36 (52.9)	24 (35.3)
DLQI, median	14	13	13

Values represent mean ± SD unless otherwise stated.
BMI, Body mass index; *BSA*, body surface area; *DLQI*, Dermatology Life Quality Index; *Max*, maximum value; *Min*, minimum value; *ppIGA*, Palmoplantar Investigator's Global Assessment; *ppPASI*, Palmoplantar Psoriasis Area and Severity Index; *SD*, standard deviation.

and social limitation, as well as feeling embarrassed and less confident. Due to psoriasis of the soles, almost 50% of subjects reported moderate-to-extreme pain/inability to walk and work. At week 16, these percentages were halved with secukinumab 300 mg. With the SGA, subjects reported a median improvement in HRQoL after treatment for palmoplantar psoriasis: 55.4%, 29.6%, and 14.0% for secukinumab 300 mg, 150 mg, and placebo, respectively, at week 16 (Fig 7, *D*).

EQ-5D also revealed significant health impairment of subjects at baseline, with improvements being observed with both doses of secukinumab at week 16 (Fig 8).

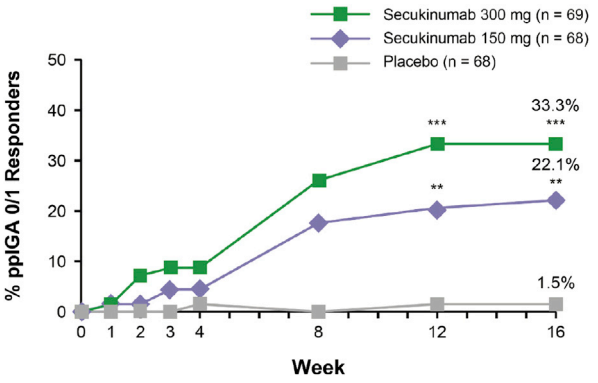

Fig 3. ppIGA 0/1 responders over time. The percentage of subjects with moderate-to-severe palmoplantar psoriasis who achieved a ppIGA 0/1 and a reduction of at least 2 points from baseline on the ppIGA scale over 16 weeks of treatment by nonresponder imputation. $^{**}P < .001$ vs placebo; $^{***}P < .0001$ vs placebo. *ppIGA*, Palmoplantar Investigator's Global Assessment.

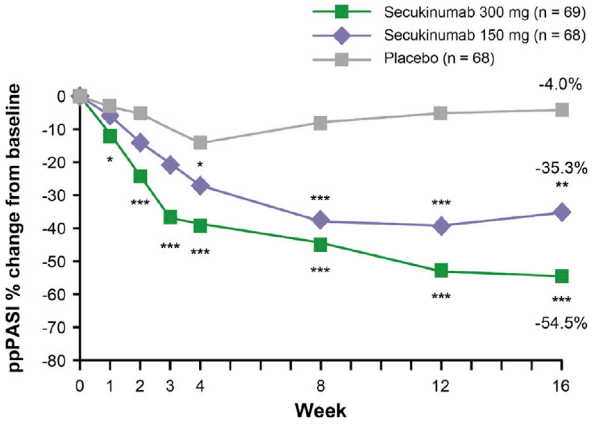

Fig 4. Percentage change in ppPASI over time. The mean percentage change from baseline of ppPASI in subjects with moderate-to-severe palmoplantar psoriasis over 16 weeks by multiple imputation. $^{*}P < .05$ vs placebo, $^{**}P < .001$ vs placebo, $^{***}P < .0001$ vs placebo. *ppPASI*, Palmoplantar Psoriasis Area and Severity Index.

Safety

All groups had a similar duration of exposure to the study treatments (Table II). The proportion of subjects experiencing at least one AE was slightly higher with secukinumab 300 mg and 150 mg (58.0% and 64.7%, respectively) than with placebo (50.0%). The most common AEs across all groups were headache, nasopharyngitis, and upper respiratory tract infection. The incidence of serious AEs (SAEs) was slightly higher with secukinumab 150 mg compared with secukinumab 300 mg and placebo (5.9%, 2.9%, and 2.9%, respectively). All SAEs were nonfatal and single events. No major cardiac events or opportunistic infections were reported. Rare AEs are not reported according to treatment here to maintain blinding until the end of the study. Three cases of nonserious superficial *Candida* infection were observed; all were mild to moderate, easily manageable, treated with appropriate medication, and did not lead to study treatment discontinuation.

DISCUSSION

The study met its primary objective. Both doses of secukinumab were superior to placebo in ppIGA 0/1 response, with secukinumab 300 mg consistently showing the highest efficacy. The one-third of subjects who received secukinumab 300 mg achieved clear or almost clear palms and soles (or ppIGA 0/1) at week 16 with clear differentiation from placebo as early as week 2. At week 16, palmoplantar disease improved on average by 55%, based on ppPASI. Prior failure with biologic therapies had no impact on secukinumabs efficacy, although the study was not statistically powered to compare biologic failure and non-failure cohorts. The improvement and dose response seen clinically with secukinumab also translated into improvements in HRQoL. Over one quarter of subjects taking secukinumab 300 mg reported that skin problems had no effect on their lives at week 16 (DLQI 0/1). HRQoL, as impacted by palmoplantar psoriasis, improved overall by 55% (as measured by SGA), and an absence of any difficulty due to palms and soles at week 16 was reported by 12.5% of subjects on secukinumab 300 mg (by ppQLI). The number of subjects with moderate-to-extreme pain and work limitations due to palmoplantar psoriasis was halved in the same period.

To date, GESTURE is the only large, randomized, double-blind, placebo-controlled study to report results on efficacy and safety in subjects with palmoplantar psoriasis. This study was specifically designed for palmoplantar psoriasis; subjects who did not have extensive plaque psoriasis on areas other than the palms and soles were also included (nearly 3 out of 4 subjects had a BSA <10%). Subjects were, however, required to have at least one additional plaque on a body part other than the palms and soles to confirm the psoriasis diagnosis. We included subjects regardless of previous biologic therapy or failure to better represent a population seen in everyday clinical practice. This study is also the first, to our knowledge, to examine in detail the impact of palmoplantar psoriasis on HRQoL at baseline in the absence of confounding therapies. Unlike prior published research,[2,5] we observed profound HRQoL impairment in palmoplantar psoriasis at baseline, even with the generic tool EQ-5D.

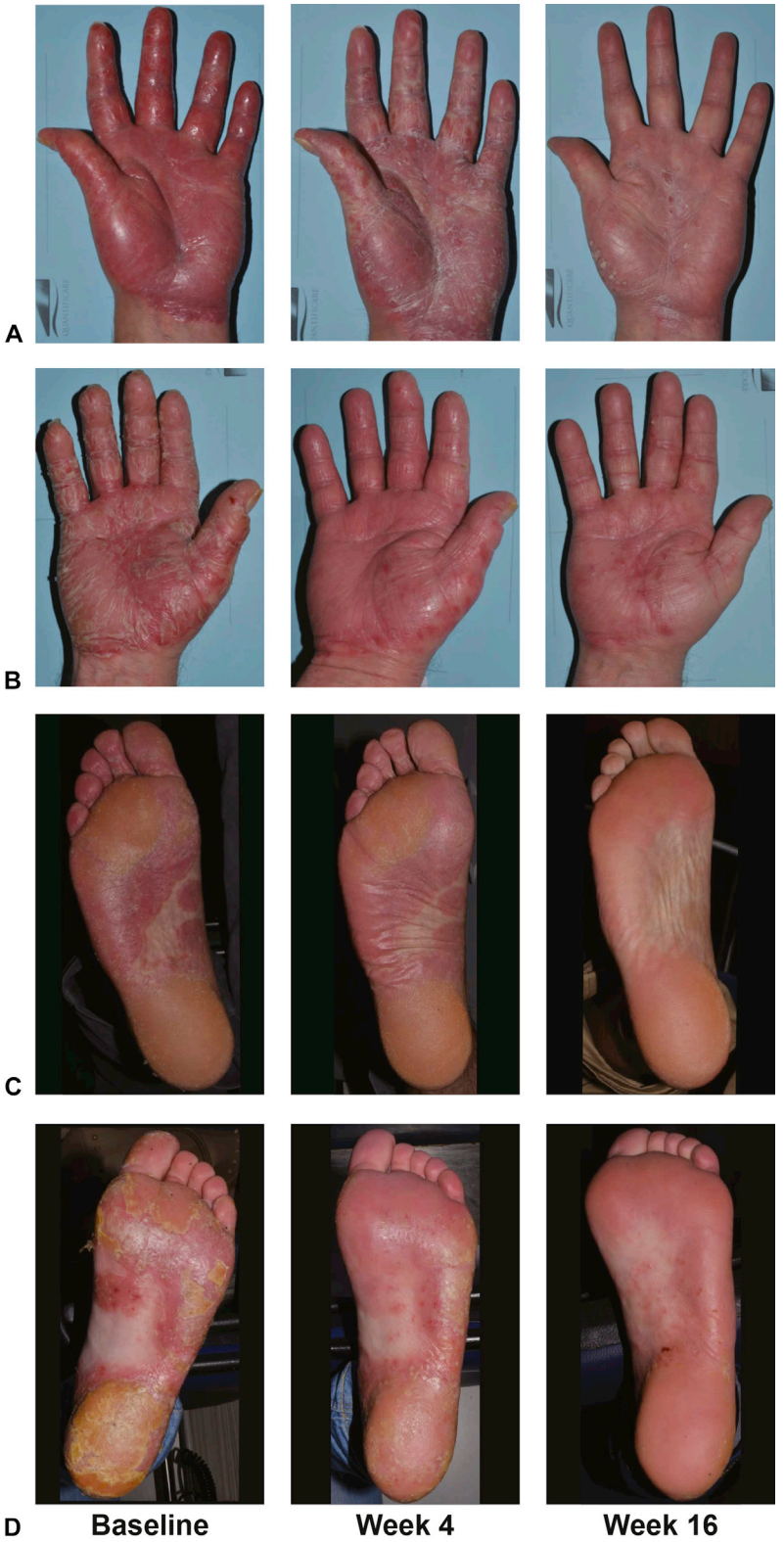

Fig 5. Photographs of the palms and soles from the GESTURE study. The images of the palms are from two different subjects (**A** and **B**) and the soles are from 2 different subjects (**C** and **D**). **A**, Man in his early fifties with a 3-year palmoplantar psoriasis history who had previously failed several topicals and phototherapy. His ppPASI score was reduced by 66% at week 16. At baseline he reported moderate difficulty with hand dexterity, burning sensations, and inability to work, as well as feeling embarrassed and less confident due to hands. He reported

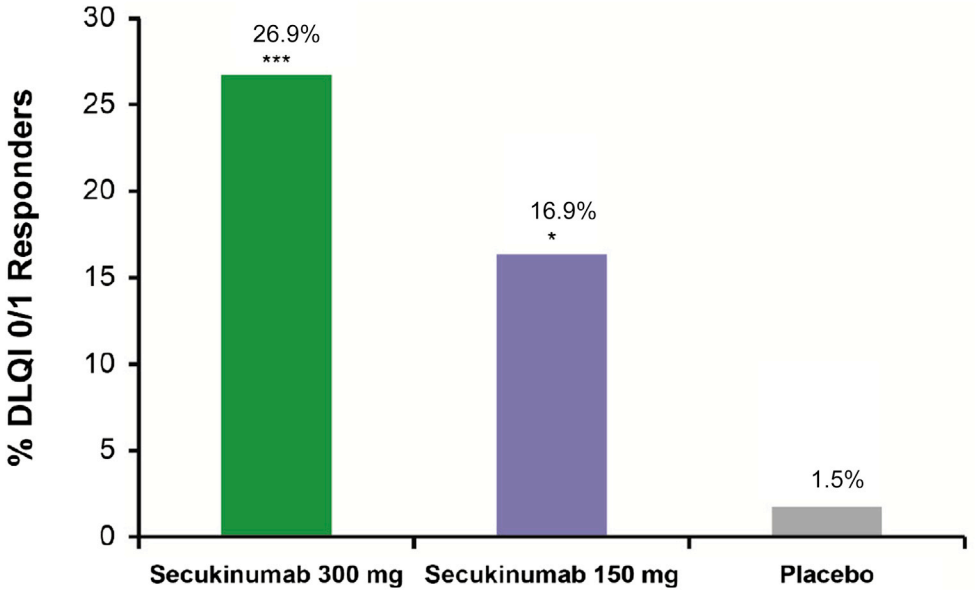

Fig 6. Percentage of DLQI 0/1 responders at week 16. *$P < .01$ vs placebo; ***$P < .0001$ vs placebo. *DLQI*, Dermatology Life Quality Index.

Overall, cross-study comparison of treatments is difficult and even more so in this patient population in which results obtained thus far are limited by small sample size and different/heterogeneous study populations.[12-15] Previously, the strongest evidence came from a study with adalimumab in moderate-to-severe palmoplantar psoriasis. In this study, adalimumab treatment resulted in 15 of 49 subjects (31%) achieving clear or almost clear palms and soles versus 1 of 23 (4%) on placebo.[13] However, some subjects had psoriasis on the backs of their hands and feet rather than on the palms and soles, and the study allowed concomitant use of low-to-mid potency topical corticosteroids. In another smaller, controlled trial, 3 of 12 (25%) patients on infliximab and 1 of 12 (8.3%) on placebo had clear or almost clear palms and soles at week 14.[12] Ustekinumab in an open-label, single-center study involving 20 patients showed a 35% Palmoplantar Physician Global Assessment (ppPGA) 0/1 response at week 16, but the study was not placebo-controlled.[14] In addition to these studies, there are several subgroup/post-hoc analyses, which are limited by the fact that palmoplantar psoriasis was not the primary focus of the trials. In the largest post-hoc analysis of apremilast, 22 of 57 patients (38.6%) versus 8 of 26 (30.8%) with placebo achieved a ppPGA 0/1 response at week 16.[15] This placebo response is unusually high given the slowly progressing natural course of palmoplantar psoriasis.

almost no difficulty with hand dexterity, reduced/mild/slight burning of palms and work limitation, as well as no longer being embarrassed and less confident at week 16. **B**, Man in his sixties with 7-month palmoplantar psoriasis history (overall 44 years of psoriasis history) who previously failed phototherapy. After 16 weeks, palm psoriasis improved by almost three quarters (by ppPASI). From severe hand pain, burning and itching, moderate hand dexterity impairment, being very limited in work, and feeling embarrassed due to his palms at baseline, he reported almost no hand dexterity impairment, mild pain, burning and itching, slight impact on work, and no longer being embarrassed at week 16. **C**, Man in his early sixties with a 10-year palmoplantar psoriasis history who had previously failed topical and ciclosporin therapy. Sole lesions completely cleared at week 16. From moderate difficulty walking and walking fast/running at baseline, he reported absence of any limitations at week 16. **D**, Woman in her twenties with a 1-year palmoplantar psoriasis history who had previously failed topicals. Psoriasis of the soles was improved by 66% (by ppPASI) at week 16. From severe difficulty and extreme pain while walking, moderate impact on work, extreme interference with life and in doing what she wanted, resulting in her frequently staying indoors at baseline. She reported no pain, no difficulty walking, and no impact on her work and life at week 16. *ppPASI*, Palmoplantar Psoriasis Area and Severity Index.

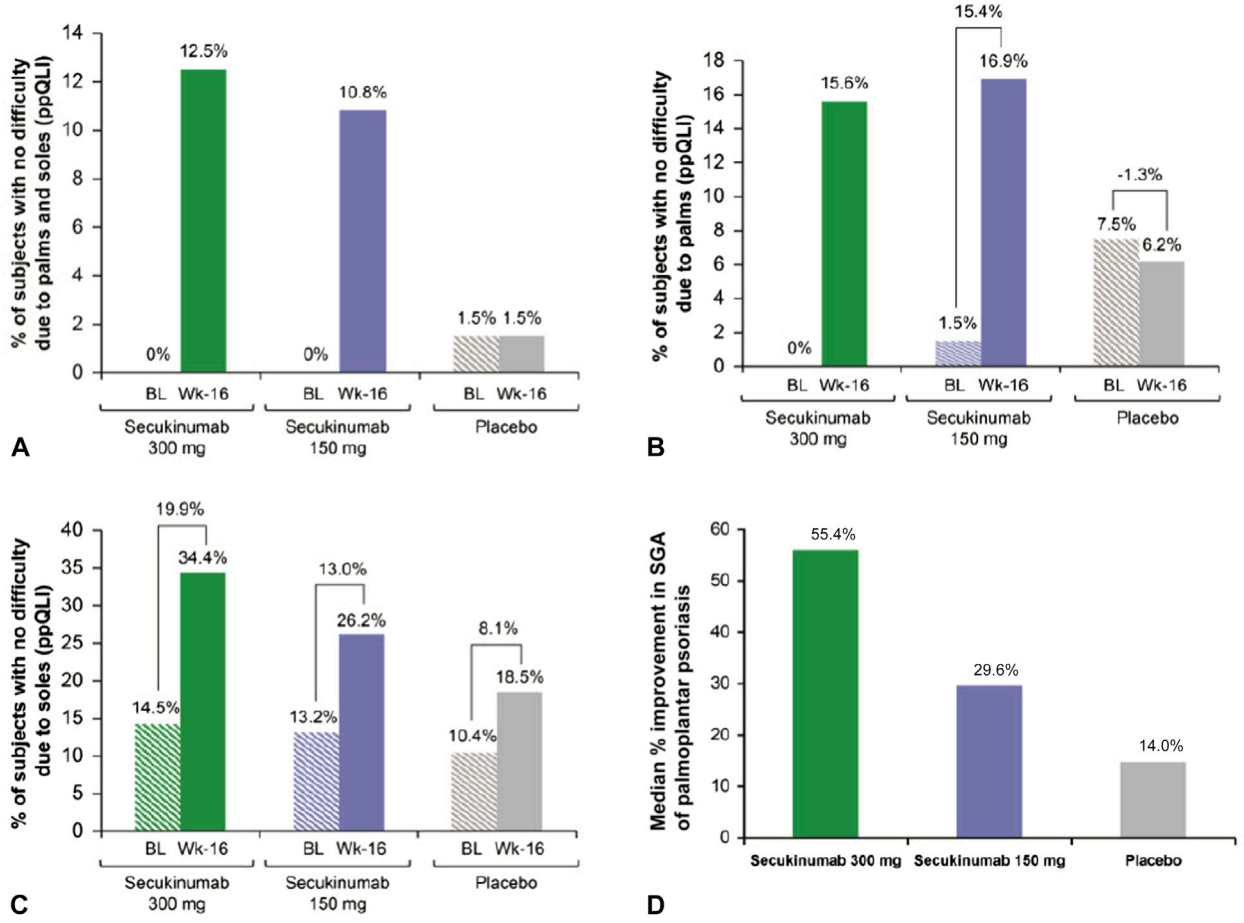

Fig 7. Palmoplantar psoriasis—specific QoL. ppQLI in subjects at baseline and week 16 (**A**-**C**). The percentage of subjects who experienced no difficulty due to palms and soles (**A**), palms (**B**), or soles (**C**) as assessed using the ppQLI. **D**, SGA of palmoplantar psoriasis after 16 weeks of treatment. *BL*, Baseline; *ppQLI*, palmoplantar Quality-of-Life Instrument; *QoL*, quality of life; *SGA*, Subject Global Assessment.

The above overview of results reinforces the difficult-to-treat nature of palmoplantar psoriasis compared with psoriasis on other locations of the body where higher rates of efficacy are more readily achieved. Furthermore, it highlights the need for more research given the paucity of randomized controlled studies dedicated to palmoplantar psoriasis to date. In this context, given the large sample size, homogeneous target patient population, and the prospective, placebo-controlled study design, GESTURE provides the best evidence for high efficacy of a therapy in this population, with the efficacy of secukinumab appearing better than that seen with other therapies in the initial 16-week period. Furthermore, GESTURE confirmed the favorable safety profile of secukinumab,[18-22] with no new safety concerns in subjects with palmoplantar psoriasis.

The study included placebo; however, it is limited by the absence of an active comparator. The study is ongoing with results up to 132 weeks expected in the future.

GESTURE provides the most robust data in subjects with palmoplantar psoriasis to date and significantly contributes to the body of evidence that may be used to inform treatment decisions and guidelines for this rarely studied population. Secukinumab demonstrated significant efficacy in palmoplantar psoriasis with a favorable safety profile, thus offering a valuable new treatment option for plaque psoriasis in difficult-to-treat locations.

The authors would like to thank the subjects who are participating in the study and the study investigators across numerous international sites: Australia (J. Sullivan, L.J. Spelman, R.D. Sinclair, and P.A. Foley), Belgium (P.D. Ghislain and A.F. Nikkels), Canada (K. Papp, K. Barber, W.D. Carey, L. Guenther, and R.A. Kunynetz), Finland (R. Pasternack and T. Mälkönen), Hungary (A. Vajda, Z. Károlyi, L. Kemény, and É. Remenyik), Israel (R. Tal, M. Ziv, H. Matz, and M. David),

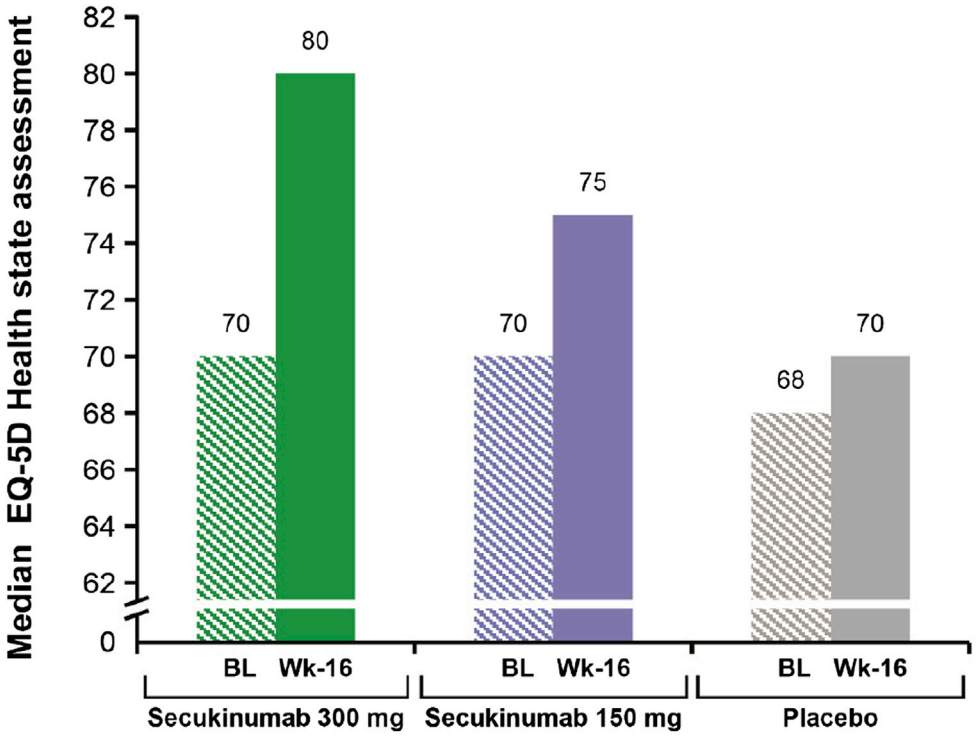

Fig 8. EQ-5D health state assessment at baseline and at week 16. *BL*, Baseline; *EQ-5D*, Euro Quality-of-Life 5-Dimension Health Status Questionnaire.

Table II. Summary of adverse events

	Secukinumab 300 mg (n = 69)	Secukinumab 150 mg (n = 68)	Placebo (n = 68)
Exposure to study treatment, days mean (SD)	109.8 (21.6)	112.7 (9.6)	111.3 (15.3)
Any AEs, n (%)	40 (58.0)	44 (64.7)	34 (50.0)
Death, n (%)	0 (0.0)	0 (0.0)	0 (0.0)
Nonfatal SAEs, n (%)	2 (2.9)	4 (5.9)	2 (2.9)
Discontinuations due to AEs, n (%)	2 (2.9)	1 (1.5)	2 (2.9)
Most common AEs, n (%)*			
Headache	7 (10.1)	4 (5.9)	6 (8.8)
Nasopharyngitis	2 (2.9)	5 (7.4)	4 (5.9)
Upper respiratory tract infection	3 (4.3)	4 (5.9)	3 (4.4)

AE, Adverse event; *SAE*, serious adverse event; *SD*, standard deviation.
*Expressed by preferred term and occurring at an incidence ≥5% in any secukinumab group. AEs are listed in descending order of frequency.

Netherlands (M. B. van Doorn, P.I. Spuls, and W.J.A. de Kort), Norway (T. Ternowitz), Portugal (P. Filipe, H. Oliveira, T. Torres, S.M. Magina, and J.M. Silva), Russia (A. Kubanov, M.N. Potekaev, A.V. Samtsov, and I.K. Minullin), Slovakia (K. Drotarova, J. Jautova, and H. Zelenkova), Spain (C. Ferrandiz, L.J. Spertino, and N. Santana), Turkey (Y. Tüzün, M.A Gürer, H.S. Inalöz, and N. Onsun), United Kingdom (A. Bewley and E. Ladoyanni), and USA (A. Gottlieb, S. Jazayeri, L.H. Kircik, J.M. Krell, K.H. Loven, R. Nossa, Z.D. Draelos, and K.W. Dawes).The authors also acknowledge the contributions of Felicity Telang (Clinical Manager); Pascaline Regnault (Global Trial Leader); Bhushan Valanju (Clinical Data Manager), Irene Edson (Clinical Trial Manager and Study Protocol Author), Priyanka Pujari (Research Programmer), Stephanie Harbers (Senior Medical Communications Leader); and David Bergin and Gillian Brodie (Expert Medical Writers) at Novartis for providing writing and editorial assistance (funded by Novartis).

REFERENCES

1. Kumar B, Saraswat A, Kaur I. Palmoplantar lesions in psoriasis: a study of 3065 patients. *Acta Derm Venereol*. 2002;82:192-195.
2. Pettey AA, Balkrishnan R, Rapp SR, Fleischer AB, Feldman SR. Patients with palmoplantar psoriasis have more physical disability and discomfort than patients with other forms of psoriasis: implications for clinical practice. *J Am Acad Dermatol*. 2003;49:271-275.

3. Melwani PM, Penate Y, Guillermo N, Soler E, Hernandez-Machin B, Borrego L. Leflunomide in the treatment of palmoplantar pustulosis. *Arch Dermatol*. 2009;145:1224-1226.
4. Elahmed HH. Rapid improvement of palmoplantar psoriasis after cessation of smoking. *Sultan Qaboos Univ Med J*. 2013;13:188-189.
5. Chung J, Callis Duffin K, Takeshita J, et al. Palmoplantar psoriasis is associated with greater impairment of health-related quality of life compared with moderate to severe plaque psoriasis. *J Am Acad Dermatol*. 2014;71:623-632.
6. Van Voorhees A, Feldman SR, Koo JKM, Lebwohl MG, Menter A. *The psoriasis and psoriatic arthritis pocket guide: treatment algorithms and management option*. Available at: https://www.psoriasis.org/sites/default/files/accessing-health-care/FY10_Pocket_Guide_WEB.pdf/. Accessed September 22, 2016.
7. Au SC, Madani A, Alhaddad M, Alkofide M, Gottlieb AB. Comparison of the efficacy of biologics versus conventional systemic therapies in the treatment of psoriasis at a comprehensive psoriasis care center. *J Drugs Dermatol*. 2013;12:861-866.
8. Gelfand JM, Wan J, Callis Duffin K, et al. Comparative effectiveness of commonly used systemic treatments or phototherapy for moderate to severe plaque psoriasis in the clinical practice setting. *Arch Dermatol*. 2012;148:487-494.
9. Takahashi H, Iinuma S, Tsuji H, Honma M, Iizuka H. Biologics are more potent than other treatment modalities for improvement of quality of life in psoriasis patients. *J Dermatol*. 2014;41:686-689.
10. Frankel AJ, Goldenberg G. Insights into treating palmoplantar psoriasis. *Skin and Aging*. 2010;18.
11. Strober BE, Griffiths CE, O'Dell SJ, Tebbey PW, Barker JN, International Psoriasis C. Prioritizing the global research agenda in psoriasis: an International Psoriasis Council Delphi consensus exercise. *Br J Dermatol*. 2016;174:212-215.
12. Bissonnette R, Poulin Y, Guenther L, Lynde CW, Bolduc C, Nigen S. Treatment of palmoplantar psoriasis with infliximab: a randomized, double-blind placebo-controlled study. *J Eur Acad Dermatol Venereol*. 2011;25:1402-1408.
13. Leonardi C, Langley RG, Papp K, et al. Adalimumab for treatment of moderate to severe chronic plaque psoriasis of the hands and feet: efficacy and safety results from REACH, a randomized, placebo-controlled, double-blind trial. *Arch Dermatol*. 2011;147:429-436.
14. Au SC, Goldminz AM, Kim N, et al. Investigator-initiated, open-label trial of ustekinumab for the treatment of moderate-to-severe palmoplantar psoriasis. *J Dermatolog Treat*. 2013;24:179-187.
15. Robert Bissonnette; Jennifer Cather; Phoebe Rich; Alan Menter; Carlos Ferrandiz; Mark Goodfield; ChiaChi Hu ERMDMS. Efficacy of apremilast, an oral phosphodiesterase 4 inhibitor, for palmoplantar psoriasis in patients with moderate to severe plaque psoriasis in phase 2 and phase 3 (ESTEEM) trials. 73rd Annual Meeting of the American Academy of Dermatology. San Francisco, CA 2015.
16. Hueber W, Patel DD, Dryja T, et al. Effects of AIN457, a fully human antibody to interleukin-17A, on psoriasis, rheumatoid arthritis, and uveitis. *Sci Transl Med*. 2010;2:52ra72.
17. Ivanov S, Linden A. Interleukin-17 as a drug target in human disease. *Trends Pharmacol Sci*. 2009;30:95-103.
18. Papp KA, Langley RG, Sigurgeirsson B, et al. Efficacy and safety of secukinumab in the treatment of moderate-to-severe plaque psoriasis: a randomized, double-blind, placebo-controlled phase II dose-ranging study. *Br J Dermatol*. 2013;168:412-421.
19. Rich P, Sigurgeirsson B, Thaci D, et al. Secukinumab induction and maintenance therapy in moderate-to-severe plaque psoriasis: a randomized, double-blind, placebo-controlled, phase II regimen-finding study. *Br J Dermatol*. 2013;168:402-411.
20. Langley RG, Elewski BE, Lebwohl M, et al. Secukinumab in plaque psoriasis—results of two phase 3 trials. *N Engl J Med*. 2014;371:326-338.
21. Paul C, Lacour JP, Tedremets L, et al. Efficacy, safety, and usability of secukinumab administration by autoinjector/pen in psoriasis: a randomized, controlled trial (JUNCTURE). *J Eur Acad Dermatol Venereol*. 2015;29:1082-1090.
22. Pariser DM, Bagel J, Gelfand JM, et al. National Psoriasis Foundation clinical consensus on disease severity. *Arch Dermatol*. 2007;143:239-242.
23. Thaci D, Blauvelt A, Reich K, et al. Secukinumab is superior to ustekinumab in clearing skin of subjects with moderate to severe plaque psoriasis: CLEAR, a randomized controlled trial. *J Am Acad Dermatol*. 2015;73:400-409.
24. Paul C, Reich K, Gottlieb AB, et al. Secukinumab improves hand, foot, and nail lesions in moderate-to-severe plaque psoriasis: subanalysis of a randomized, double-blind, placebo-controlled, regimen-finding phase 2 trial. *J Eur Acad Dermatol Venereol*. 2014;28:1670-1675.
25. Langley RG, Feldman SR, Nyirady J, van de Kerkhof P, Papavassilis C. The 5-point Investigator's Global Assessment (IGA) Scale: aA modified tool for evaluating plaque psoriasis severity in clinical trials. *J Dermatolog Treat*. 2015;26:23-31.
26. Fredriksson T, Pettersson U. Severe psoriasis—oral therapy with a new retinoid. *Dermatologica*. 1978;157:238-244.
27. Weisman S, Pollack CR, Gottschalk RW. Psoriasis disease severity measures: comparing efficacy of treatments for severe psoriasis. *J Dermatolog Treat*. 2003;14:158-165.
28. Finlay AY, Khan GK. Dermatology Life Quality Index (DLQI)—a simple practical measure for routine clinical use. *Clin Exp Dermatol*. 1994;19:210-216.
29. Farley E, Masrour S, McKey J, Menter A. Palmoplantar psoriasis: a phenotypical and clinical review with introduction of a new quality-of-life assessment tool. *J Am Acad Dermatol*. 2009;60:1024-1031.
30. Brooks R. EuroQol: the current state of play. *Health Policy*. 1996;37:53-72.
31. EuroQol G. EuroQol—a new facility for the measurement of health-related quality of life. *Health Policy*. 1990;16:199-208.