Secukinumab is superior to ustekinumab in clearing skin of subjects with moderate to severe plaque psoriasis: CLEAR, a randomized controlled trial

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Background: Secukinumab, a fully human anti-interleukin-17A monoclonal antibody, has shown superior efficacy to etanercept with similar safety in moderate to severe plaque psoriasis (FIXTURE study).

Objective: We sought to directly compare efficacy and safety of secukinumab versus ustekinumab.

Methods: In this 52-week, double-blind study (NCT02074982), 676 subjects were randomized 1:1 to subcutaneous injection of secukinumab 300 mg or ustekinumab per label. Primary end point was 90% or more improvement from baseline Psoriasis Area and Severity Index (PASI) score (PASI 90) at week 16.

Results: Secukinumab (79.0%) was superior to ustekinumab (57.6%) as assessed by PASI 90 response at week 16 ($P < .0001$). The 100% improvement from baseline PASI score at week 16 was also significantly greater with secukinumab (44.3%) than ustekinumab (28.4%) ($P < .0001$). The 75% or more improvement from baseline PASI score at week 4 was superior for secukinumab (50.0%) versus ustekinumab (20.6%) ($P < .0001$). Percentage of subjects with the Dermatology Life Quality Index score 0/1 (week 16) was significantly higher with secukinumab (71.9%) than ustekinumab (57.4%) ($P < .0001$). The safety profile of secukinumab was comparable with ustekinumab and consistent with pivotal phase III secukinumab studies.

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Limitations: The study was not placebo-controlled and of short-term duration.

Conclusions: Secukinumab is superior to ustekinumab in clearing skin of subjects with moderate to severe psoriasis and improving health-related quality of life with a comparable safety profile over 16 weeks. (J Am Acad Dermatol 2015;73:400-9.)

Key words: clear or almost clear skin; clinical trial; head to head; plaque psoriasis; secukinumab; superiority; ustekinumab; 90% or more improvement in baseline Psoriasis Area and Severity Index.

CAPSULE SUMMARY

- Secukinumab previously demonstrated superior efficacy to etanercept in psoriasis, with similar safety.
- CLEAR study demonstrates secukinumab is superior to ustekinumab in clearing skin of subjects with moderate to severe plaque psoriasis and improving quality of life with comparable safety.
- These head-to-head results are important to inform treatment decisions for psoriasis.

Targeted biologic therapies—such as tumor necrosis factor (TNF)-α inhibitors infliximab, etanercept, and adalimumab and the interleukin (IL)-12/IL-23 antagonist ustekinumab—have greatly improved the treatment of moderate to severe plaque psoriasis. In randomized controlled trials, approximately 50% to 80% of subjects receiving these biologics achieved 75% or more improvement from baseline Psoriasis Area and Severity Index (PASI) score (PASI 75) after 10 to 16 weeks of treatment.[1-8] A 90% improvement from baseline PASI score, however, is now defined as the threshold of treatment success per the European Medicines Agency[9] and a "measure of optimal response" by the American Academy of Dermatology.[10] Of note, 90% or more improvement from baseline PASI score (PASI 90) response was only achieved by approximately 20% of patients treated with etanercept,[1,2] and approximately 40% to 50% with infliximab,[3,4] adalimumab,[5,6] and ustekinumab.[7,8]

Achieving PASI 90 response in patients with psoriasis is highly clinically relevant, given the direct relationship between PASI score improvement and health-related quality of life (HRQoL).[11-13] In 1 study, 44.3% of subjects achieving PASI 90 to less than 100% improvement from baseline PASI score response and 65.1% achieving 100% improvement from baseline PASI score (PASI 100) response at week 16 reported no impact of their skin problems on HRQoL, versus 24.3% of those with PASI 75 to less than PASI 90 response.[11] These results support the importance of achieving PASI 90 to PASI 100 responses in patients with psoriasis for the maximal improvement in HRQoL.

Secukinumab (Cosentyx, Novartis Pharma AG, Basel, Switzerland), recently approved for the treatment of adult patients with moderate to severe plaque psoriasis, is a fully human IgG1κ monoclonal antibody that selectively targets IL-17A.[14] IL-17A is a key pathogenic cytokine in psoriasis and acts directly on keratinocytes to stimulate the secretion of proinflammatory mediators; the action of IL-23 on keratinocytes is more remote but ultimately depends on inducing IL-17A.[15,16] The clinical benefit of TNF-α inhibition has been linked to the suppression of the IL-23/IL-17 axis.[16,17] The importance of IL-17A in psoriasis pathogenesis has been validated by the clinical efficacy of secukinumab in pivotal 52-week phase III trials; secukinumab was shown to be superior to placebo and to etanercept in achieving a strong and sustained response with a favorable safety profile.[18-22] PASI 90 responses were obtained by 70% to 72% of subjects treated with secukinumab 300 mg at week 16 and sustained in the majority of subjects at week 52.[18] The magnitude of improvement after 16 weeks of treatment with secukinumab[18] is higher than that reported in phase III studies for etanercept,[1,2] infliximab,[3,4] adalimumab,[5,6] and ustekinumab.[7,8]

Comparative efficacy among therapies is best evaluated in rigorous head-to-head randomized trials. CLEAR, the second head-to-head trial of secukinumab, directly compared the efficacy and safety of secukinumab with ustekinumab in subjects with moderate to severe plaque psoriasis. Ustekinumab is a human monoclonal antibody directed against cytokines IL-12 and IL-23, the latter of which, by activating T-helper 17 cells, functions upstream of IL-17A in driving psoriasis pathogenesis.[15,16] Like secukinumab, ustekinumab has shown superiority to etanercept in achieving PASI 75 responses in a phase III study.[23] The CLEAR study, presented here, was designed with the primary objective of demonstrating superiority of secukinumab to ustekinumab in achieving PASI 90 response, a high-threshold clinical response that to our knowledge has not been used as the primary end

Abbreviations used:

AE:	adverse event
DLQI:	Dermatology Life Quality Index
HRQoL:	health-related quality of life
IGA:	investigator global assessment
IGA mod 2011:	investigator global assessment 2011 modified version
IL:	interleukin
MedDRA:	Medical Dictionary for Regulatory Activities
PASI:	Psoriasis Area and Severity Index
PASI 75:	75% or more improvement from baseline Psoriasis Area and Severity Index score
PASI 90:	90% or more improvement from baseline Psoriasis Area and Severity Index score
PASI 100:	100% improvement from baseline Psoriasis Area and Severity Index score
SAE:	serious adverse event
TNF:	tumor necrosis factor

point in previous phase III psoriasis trials. CLEAR is an ongoing 52-week study; week-16 primary end point results are reported here.

METHODS

Study population

Subjects (age ≥18 years) with moderate to severe plaque psoriasis (as defined previously[18]) were eligible. Subjects had a diagnosis of psoriasis at least 6 months before randomization and had been inadequately controlled by topical treatments, phototherapy, and/or previous systemic therapy. Key exclusion criteria included previous exposure to any biologics directly targeting IL-17A/IL-17 receptor A or IL-12/IL-23.

Study design

This 52-week, randomized, double-blind, active comparator, parallel-group, superiority phase IIIb study was conducted in accordance with ethical principles of the Declaration of Helsinki at 134 sites worldwide. US sites maintained compliance with Health Insurance Portability and Accountability Act regulations. The study was initiated in February 2014 (first subject, first visit), and last subject, last visit for the week-16 primary efficacy analysis occurred in October 2014.

Eligible subjects were randomized 1:1 via an interactive response technology system to subcutaneous injection of secukinumab 300 mg or ustekinumab (dosing per label[24]: 45 mg for subjects ≤100 kg at baseline; 90 mg for subjects >100 kg at baseline). Randomization was stratified by body weight (≤100 kg and >100 kg). Secukinumab was administered at baseline and weeks 1, 2, and 3, then every 4 weeks from week 4 to week 48; ustekinumab at baseline and week 4, then every 12 weeks from week 16 to week 40. To maintain blinding, placebo injections matching the secukinumab regimen were given to subjects in the ustekinumab group (Fig 1).

The analyses presented here were performed after all subjects completed the primary end point visit (week 16 [predose]). Full analysis of all data collected up to week 52 will be performed after all subjects have completed the week-52 visit. The designated sponsor team performing the 16-week analysis was unblinded after the 16-week database lock, whereas the sponsor team in charge of data review, and investigators, site personnel who evaluated subjects, and subjects, remain blinded to individual treatment allocation (blinding in place until after final database lock at week 52).

Study objectives

The primary objective was to demonstrate superiority of secukinumab versus ustekinumab with respect to PASI 90 response at week 16. Secondary objectives were to demonstrate superiority of secukinumab versus ustekinumab in achieving PASI 75 response at week 4 and PASI 90 response at week 52 (week-52 data will be analyzed and reported at a later date). The efficacy of secukinumab versus ustekinumab, with respect to PASI 75/90/100 and investigator global assessment (IGA) 2011 modified version (IGA mod 2011) 0/1 (defined as IGA score of 0 [clear] or 1 [almost clear] and improvement of ≥2 points vs baseline[25]) responses over time, was also evaluated.

Subjects self-assessed symptoms of pain, itching, or scaling on an 11-point numeric rating scale (range, 0-10 points, higher scores indicate worse symptoms), and reported on HRQoL using the Dermatology Life Quality Index (DLQI). DLQI has been validated for dermatologic conditions (range, 0-30 points, higher scores indicate greater impact on HRQoL).[26] Safety and tolerability were evaluated by adverse event (AE), laboratory and vital sign assessments, and physical examinations. AEs were coded using the Medical Dictionary for Regulatory Activities (MedDRA) terminology. The study protocol and its amendments were reviewed by the independent ethics committee or institutional review board for each participating center.

Statistical analyses

Efficacy variables were assessed in the full analysis set according to the treatment assigned at randomization. A sequentially rejective testing

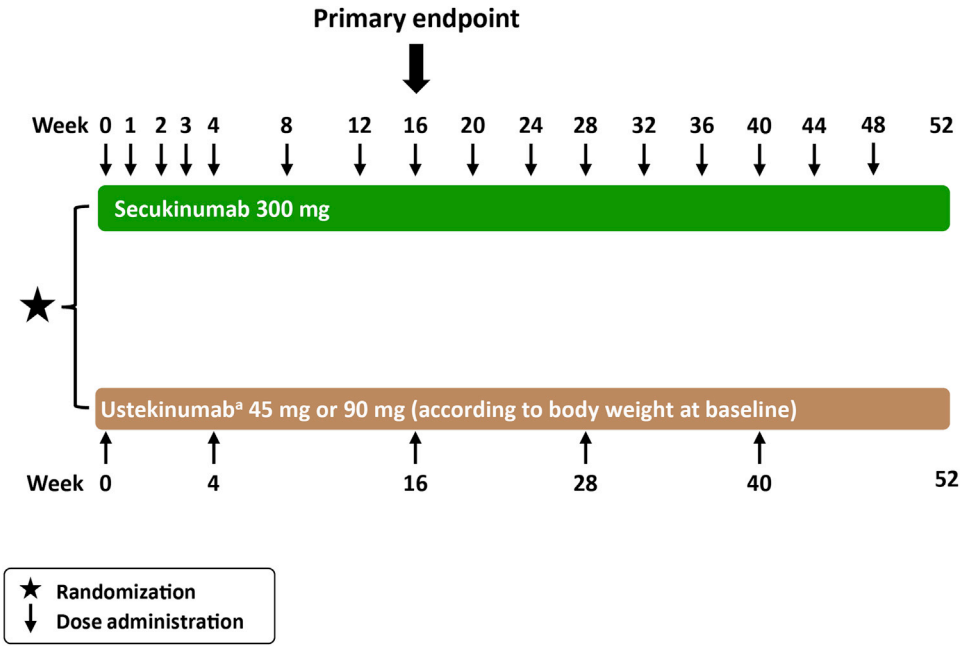

Fig 1. Study design. [a]To maintain blinding, placebo injections matching the secukinumab regimen were given to subjects in the ustekinumab group.

procedure[27] was used to evaluate study hypotheses for primary and secondary efficacy variables. Between-treatment comparisons of clinical responses were made using a logistic regression model with treatment group, randomized strata, and baseline PASI score as explanatory variables. Missing values with respect to response variables based on PASI and IGA mod 2011 scores were imputed as nonresponse (nonresponder imputation). Missing values for these response variables were also imputed using a multiple imputation method. Fisher exact test was used to compare DLQI 0/1 responses between treatments; analysis of covariance was used for absolute change from baseline in subjects' assessment of pain, itching, and scaling. For patient-reported outcomes, last observation carried forward was used to manage missing data.

A sample size of 320 subjects per group was calculated for greater than 99% power to show PASI 90 response of 71% at week 16 in the secukinumab group, assuming PASI 90 response of 51% at week 16 in the ustekinumab group,[7,8] based on a 2-group χ^2 test of equal proportions.

RESULTS

Study population

Baseline demographic and disease characteristics were similar between treatment arms, although there was a slight numeric imbalance in subjects with psoriatic arthritis (20.5% and 15.9% in the secukinumab and ustekinumab groups, respectively) (Table I). A total of 676 subjects were randomized. Among these, 675 subjects were included in the full analysis set for primary efficacy analyses (1 subject was excluded [informed consent was obtained the day after study-related procedure]); 671 subjects received at least 1 dose of study treatment and were included in the safety analysis (subject disposition in Fig 2).

Efficacy

Both the primary and secondary objectives evaluated within 16 weeks in the testing procedure were met (Table II). Secukinumab was superior to ustekinumab with respect to the primary end point of the study, with 79.0% of subjects in the secukinumab group and 57.6% of subjects in the ustekinumab group achieving a PASI 90 response at week 16 ($P < .0001$). The proportion of subjects achieving a PASI 100 response (clear skin) at week 16 was significantly greater with secukinumab (44.3%) compared with ustekinumab (28.4%) ($P < .0001$). Significantly higher efficacy of secukinumab over ustekinumab was also observed for PASI 75 and IGA mod 2011 0/1 responses at week 16 (Table II).

Secukinumab was superior to ustekinumab with respect to efficacy in the initial treatment period, with the proportion of subjects achieving the secondary end point of a PASI 75 response at week 4: 50.0% in the secukinumab versus 20.6% in the

Table I. Baseline demographic and clinical characteristics

Characteristic	Secukinumab 300 mg (n = 337)	Ustekinumab (n = 339)
Age, y	45.2 ± 13.96	44.6 ± 13.67
Male gender	229 (68.0)	252 (74.3)
Race		
Caucasian	299 (88.7)	288 (85.0)
Other	38 (11.3)	51 (15.0)
Weight, kg	87.4 ± 19.95	87.2 ± 22.11
BMI, kg/m^2	29.1 ± 5.87	29.0 ± 6.69
Time since psoriasis diagnosis, y	19.6 ± 12.90	16.1 ± 11.24
PASI score	21.7 ± 8.50	21.5 ± 8.07
Body surface area involved, %	32.6 ± 17.78	32.0 ± 16.80
IGA mod 2011 score		
4 (Severe disease)*	130 (38.6)	125 (36.9)
Psoriatic arthritis reported	69 (20.5)	54 (15.9)
Previous systemic psoriasis treatment		
Any	225 (66.8)	231 (68.1)
Conventional agent†	218 (64.7)	223 (65.8)
Biologic agent	48 (14.2)	44 (13.0)
Failed biologic agent	36 (10.7)	34 (10.0)

PASI scores range from 0 (no disease) to 72 (maximal disease).
IGA mod 2011 scores range from 0 (clear skin) to 4 (severe disease).
Data are given as n (%) or mean ± SD.
BMI, Body mass index; *IGA mod 2011*, investigator global assessment 2011 modified version; *PASI*, Psoriasis Area and Severity Index.
*All other subjects had a score of 3 (moderate disease), with the exception of 2 subjects who were recorded at baseline as having a score of 2 (mild disease), which was corrected to a score of 3 after the wk-16 database lock.
†Included methotrexate, cyclosporine, corticosteroids, and fumaric acid esters.

ustekinumab groups ($P < .0001$). The proportions of subjects achieving PASI 90, PASI 100, or IGA mod 2011 0/1 responses at week 4 were also significantly greater with secukinumab compared with ustekinumab (Table II).

Overall, secukinumab achieved consistently higher PASI 75/90/100 and IGA mod 2011 0/1 responses versus ustekinumab at each assessed time point throughout 16 weeks of treatment (Fig 3, *A* to *D*). Analyses of clinical responses using the multiple imputation method (Table III) produced numerically comparable results as those from the primary, nonresponder imputation method.

Subject-reported outcomes

Subjects in the secukinumab group reported greater improvement in pain, itching, and scaling compared with the ustekinumab group (Table II). The percentage of subjects achieving a DLQI score of 0/1, indicating no impairment of HRQoL because of skin problems, was significantly higher with secukinumab than with ustekinumab at each assessed time point through 16 weeks (week 16: 71.9% vs 57.4%, respectively; $P < .0001$) (Fig 3, *E*, and Table II).

Safety

Both groups had similar duration of exposure to study treatment. The proportion of subjects experiencing at least 1 AE was 64.2% in the secukinumab group and 58.3% in the ustekinumab group. AEs in the system organ class of "Infections and Infestations" were reported most often (29.3% for secukinumab and 25.3% for ustekinumab); however, most infectious AEs were nonserious, of mild to moderate severity, easily manageable, and did not lead to study drug discontinuation. The most common AEs by MedDRA preferred term were headache and mild to moderate nasopharyngitis in both groups (Table IV).

No deaths occurred during the 16-week treatment period. The incidence of serious AEs (SAEs) was low: 3.0% of subjects in each group. To maintain blinding until after the final database lock at week 52, the distributions of rare AEs across study treatments are not presented in this report. A total of 20 subjects experienced SAEs up to the 16-week database lock, including 3 cases of infections (appendicitis, diverticulitis, scrotal abscess), 2 cardiac events (unstable angina, myocardial infarction), 1 case of embolic stroke, 1 malignancy (lung adenocarcinoma), 1 injection-related reaction with nausea/vomiting, and 2 hepatic events (toxic hepatitis, acute hepatitis). Both cases of hepatic SAEs were confounded by concomitant isoniazid therapy and improved/resolved after interruption of study treatment and isoniazid. No cluster of SAEs was observed and all SAEs were single events.

Among AEs of special interest, 12 cases of nonserious, localized mucosal or cutaneous *Candida* infections and 10 cases of oral herpes infections were reported; all were mild or moderate and none led to treatment discontinuation. There were no AE reports of neutropenia, inflammatory bowel disease, or tuberculosis.

DISCUSSION

Results of this study demonstrate that secukinumab was superior to ustekinumab at week 16 in clearing the skin of subjects with moderate to severe plaque psoriasis and achieving a better HRQoL improvement with a comparable safety profile. Comparative effectiveness research, as done

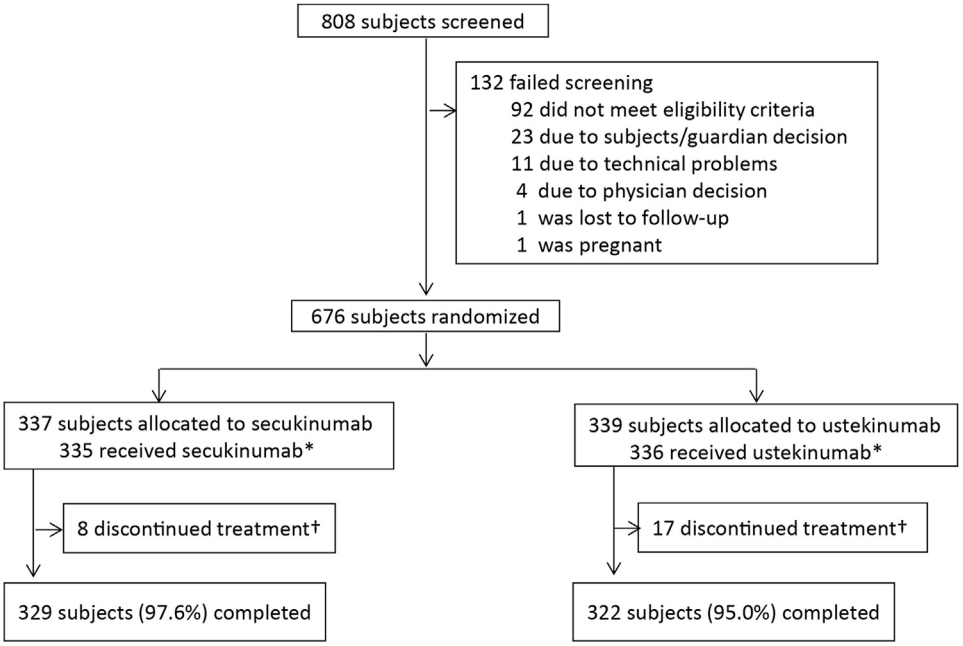

Fig 2. Subject disposition. *Four subjects did not receive study treatment (2 withdrew consent; 1 because of technical problem; and 1 because of physician decision) and discontinued the study at randomization; 1 subject was excluded from all analyses because the informed consent form was obtained the day after study-related procedure. †In all, 25 subjects discontinued study treatment because of adverse event (7); lost to follow-up (3); protocol deviation (5); subject/guardian decision (7); physician decision (1); noncompliance with study treatment (1); and technical problem (1).

here, is important to aid in therapy selection. However, evidence on comparative efficacy among biologics in psoriasis is poor because of the limited number of head-to-head trials. The CLEAR study reported here included the IL-12/IL-23 inhibitor ustekinumab, an agent with a different mechanism of action and higher efficacy than etanercept,[23] as the active biologic comparator with secukinumab.

The CLEAR study shows that secukinumab was superior to ustekinumab in achieving PASI 90 (primary end point) response at week 16; PASI 100 response was also statistically significantly greater in the secukinumab group. Clinical responses with secukinumab occurred earlier and were greater than those with ustekinumab at each visit throughout the 16-week treatment period. Consistent with its higher clinical efficacy, secukinumab also achieved significantly greater improvement in subject-reported symptoms and with HRQoL (DLQI 0/1 response), compared with ustekinumab. Secukinumab is currently the only biologic for which superiority versus both anti-IL-12/IL-23 and an anti—TNF treatment has been demonstrated in plaque psoriasis. These results provide dermatologists important head-to-head comparison information for consideration when choosing an appropriate therapy for patients with plaque psoriasis.

The threshold for treatment success in psoriasis has been defined as a PASI 90 response. This goal, however, was considered a "very stringent requirement and a target not always possible to obtain in clinical practice."[9] Importantly, the current findings with secukinumab show that a PASI 90 response was achieved in 79% of subjects and PASI 100 response in 44.3% of subjects after 16 weeks of treatment. Thus, with secukinumab, these data show that a PASI 90 response is now an achievable goal in a majority of subjects.

No new or unexpected safety signals were identified for secukinumab during the 16-week treatment period. Secukinumab exhibited a safety profile similar to that of ustekinumab and consistent with that seen in secukinumab pivotal phase III trials.[18-20] The duration of the current primary analysis (16 weeks) may not be long enough to detect all rare AEs or AEs with long latency. In addition, details of rare AEs were not reported in this article according to the treatment arms in the current analysis to maintain blinding. In previously published studies, comprehensive and long-term safety data for both secukinumab and ustekinumab

Table II. Efficacy end points

	Secukinumab 300 mg	Ustekinumab	*P* value
PASI and IGA mod 2011 0/1 responses based on nonresponder imputation method			
PASI 100 response, no./N (%)			
Wk 16	148/334 (44.3)	95/335 (28.4)	<.0001
Wk 12	130/334 (38.9)	86/335 (25.7)	.0003
Wk 4	14/334 (4.2)	3/335 (0.9)	.0139
PASI 90 response, no./N (%)			
Wk 16 (primary end point)	264/334 (79.0)	193/335 (57.6)	<.0001
Wk 12	243/334 (72.8)	179/335 (53.4)	<.0001
Wk 4	70/334 (21.0)	18/335 (5.4)	<.0001
PASI 75 response, no./N (%)			
Wk 16	311/334 (93.1)	277/335 (82.7)	.0001
Wk 12	304/334 (91.0)	265/335 (79.1)	<.0001
Wk 4 (secondary end point)	167/334 (50.0)	69/335 (20.6)	<.0001
IGA mod 2011 0/1,* no./N (%)			
Wk 16	277/334 (82.9)	226/335 (67.5)	<.0001
Wk 12	270/334 (80.8)	218/335 (65.1)	<.0001
Wk 4	126/334 (37.7)	41/335 (12.2)	<.0001
Subject-reported outcomes			
DLQI 0/1, no./N (%)			
Wk 16	238/331 (71.9)	191/333 (57.4)	<.0001
Wk 12	219/331 (66.2)	188/333 (56.5)	.0109
Wk 4	111/325 (34.2)	70/331 (21.1)	.0002
Subject-reported symptoms			
Pain, mean score			.0414
Baseline	4.1	3.8	
Wk 16	0.8	1.0	
Absolute change	−3.3	−2.8	
Itching, mean score			.0053
Baseline	6.3	6.2	
Wk 16	1.2	1.6	
Absolute change	−5.0	−4.6	
Scaling, mean score			.0001
Baseline	6.5	6.5	
Wk 16	0.8	1.3	
Absolute change	−5.7	−5.2	

DLQI, Dermatology Life Quality Index; *IGA mod 2011*, investigator global assessment 2011 modified version; *N*, the number of evaluable subjects; *no.*, the number of subjects with a response; *PASI*, Psoriasis Area and Severity Index; *PASI 75*, 75% or more improvement from baseline Psoriasis Area and Severity Index score; *PASI 90*, 90% or more improvement from baseline Psoriasis Area and Severity Index score; *PASI 100*, 100% improvement from baseline Psoriasis Area and Severity Index score.

*IGA mod 2011 score of 0 (clear) or 1 (almost clear) and an improvement of ≥2 points from baseline.

have been reported.[18,28] The CLEAR study is ongoing and results over the entire 52 weeks will be reported at a later date.

The study does not have a placebo arm, which might explain the slightly higher response rates observed with secukinumab and ustekinumab when compared with the corresponding rates reported in previous placebo-controlled studies.[7,8,18-20] Cross-study comparisons, however, must be viewed with caution. In addition, both biologic treatments have previously shown superior efficacy compared with placebo in phase III trials, making the inclusion of a placebo arm of questionable ethical and scientific value.

In conclusion, the head-to-head CLEAR study demonstrates that secukinumab is superior to ustekinumab in clearing skin of subjects with moderate to severe plaque psoriasis with similar safety. Greater clinical efficacy with secukinumab is accompanied by significantly greater improvement in HRQoL, compared with ustekinumab. IL-17A is a key cytokine in the pathophysiology of psoriasis, and selectively inhibiting IL-17A with secukinumab

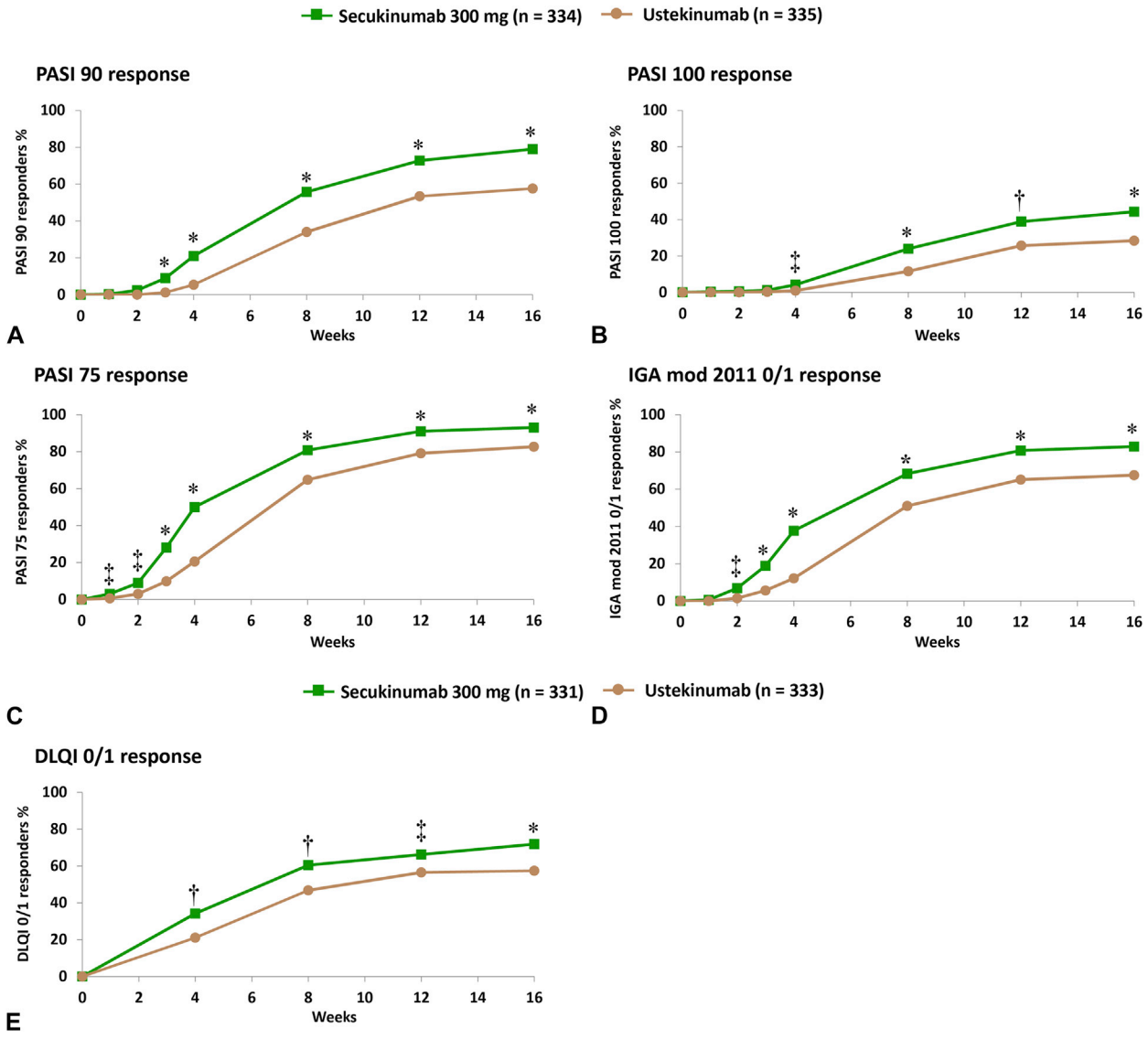

Fig 3. Efficacy over time to week 16. Improvement from baseline Psoriasis Area and Severity Index (PASI) score of 90% or more (*PASI 90*) (**A**), 100% (*PASI 100*) (**B**), or 75% or more (*PASI 75*) (**C**). **D**, Investigator global assessment 2011 modified version (IGA mod 2011) 0/1 response. **E**, Dermatology Life Quality Index (*DLQI*) 0/1 response. $^{*}P \leq .0001$, $^{\dagger}P < .001$, $^{\ddagger}P < .05$. Missing values for PASI score response variables and IGA mod 2011 0/1 response were imputed as nonresponses (nonresponder imputation). Only subjects who could be evaluated for a response were included (subjects who had missed all postbaseline values were excluded for that response variable). Missing values for DLQI were handled using last observation carried forward.

has proven superiority over both anti-IL-12/IL-23 and anti—TNF therapies in clinical trials. Results from the CLEAR study add to the evidence from the pivotal phase III program supporting that secukinumab can better deliver clear or almost clear skin and improved HRQoL when compared with other existing therapies, making it the new reference standard treatment for patients with moderate to severe plaque psoriasis.

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Table III. Psoriasis Area and Severity Index and investigator global assessment 2011 modified version 0/1 responses based on the multiple imputation method

	Secukinumab 300 mg	Ustekinumab	*P* value
PASI 100 response, no./N (%)			
Wk 16	150/334 (45.0)	98/335 (29.3)	<.0001
Wk 12	131/334 (39.3)	87/335 (26.0)	.0003
Wk 4	14/334 (4.2)	3/335 (0.9)	.0174
PASI 90 response, no./N (%)			
Wk 16 (primary end point)	268/334 (80.1)	199/335 (59.5)	<.0001
Wk 12	246/334 (73.5)	182/335 (54.4)	<.0001
Wk 4	70/334 (21.0)	18/335 (5.5)	<.0001
PASI 75 response, no./N (%)			
Wk 16	315/334 (94.3)	283/335 (84.5)	.0001
Wk 12	307/334 (91.8)	272/335 (81.1)	.0001
Wk 4 (secondary end point)	168/334 (50.3)	70/335 (20.9)	<.0001
IGA mod 2011 0/1,* no./N (%)			
Wk 16	281/334 (84.1)	233/335 (69.5)	<.0001
Wk 12	273/334 (81.7)	224/335 (66.9)	<.0001
Wk 4	127/334 (38.0)	42/335 (12.4)	<.0001

IGA mod 2011, Investigator global assessment 2011 modified version (IGA mod 2011); *N*, the number of evaluable subjects; *no.*, the number of subjects with a response; *PASI 75*, 75% or more improvement from baseline Psoriasis Area and Severity Index score; *PASI 90*, 90% or more improvement from baseline Psoriasis Area and Severity Index score; *PASI 100*, 100% improvement from baseline Psoriasis Area and Severity Index score.

*IGA mod 2011 score of 0 (clear) or 1 (almost clear) and an improvement of ≥2 points from baseline.

Table IV. Adverse events during the 16-wk treatment period of CLEAR study

	Secukinumab 300 mg (n = 335)	Ustekinumab (n = 336)
Exposure to study treatment, d	111.1 ± 10.21	110.3 ± 14.76
Subjects with any AE	215 (64.2)	196 (58.3)
Death	0	0
Nonfatal serious AE	10 (3.0)	10 (3.0)
Discontinuations because of AE	3 (0.9)	4 (1.2)
Infections and infestations	98 (29.3)	85 (25.3)
Most common AE*		
Headache	26 (7.8)	27 (8.0)
Nasopharyngitis	23 (6.9)	34 (10.1)
Diarrhea	14 (4.2)	12 (3.6)
Fatigue	14 (4.2)	9 (2.7)
Arthralgia	13 (3.9)	14 (4.2)

Data are given as n (%) or mean ± SD.

AE, Adverse events.

*Expressed by preferred term and occurring at an incidence of ≥4% in either treatment arm during the 16-wk treatment period. AEs are listed in decreasing order of frequency in the secukinumab arm.

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