Secukinumab Is Superior to Ustekinumab in Clearing Skin of Patients With Moderate to Severe Plaque Psoriasis: CLARITY, a Randomized, Controlled, Phase 3b Trial

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ABSTRACT

- **Introduction:** Secukinumab, a fully human anti-interleukin-17A monoclonal antibody, has previously demonstrated superior efficacy to ustekinumab in the phase 3b CLEAR study of moderate to severe plaque psoriasis.[1,2] Here, we report 16-week results from CLARITY, the second head-to-head trial comparing secukinumab with ustekinumab.
- **Methods:** In this ongoing multicenter, head-to-head, double-blind, parallel-group, phase 3b study (NCT02826603), patients were randomized 1:1 to receive subcutaneous secukinumab 300 mg or ustekinumab per label. The co-primary objectives are to demonstrate the superiority of secukinumab over ustekinumab at Week 12 in relation to the proportion of patients with (1) 90% or more improvement from Baseline Psoriasis Area and Severity Index (PASI 90) and (2) a score of 0/1 (clear/almost clear) on the Investigator's Global Assessment (IGA mod 2011 0/1). Key secondary objectives include demonstrating the superiority of secukinumab over ustekinumab with respect to PASI 75 at Week 4; PASI 75 and 100 at Week 12; PASI 75, 90, 100; and IGA mod 2011 0/1 at Week 16. Missing values were handled by multiple imputation.
- **Results:** At Week 12, both co-primary objectives were met, secukinumab 300 mg (n = 550) was significantly superior to ustekinumab (n = 552) for the proportion of patients achieving both PASI 90 (66.5% vs. 47.9%; $P < 0.0001$) and IGA mod 2011 0/1 (72.3% vs 55.4%; $P < 0.0001$) response rates. Additionally, all key secondary objectives were met. At Week 4, PASI 75 response rates were significantly superior with secukinumab 300 mg compared to ustekinumab (40.2% vs 16.3%; $P < 0.0001$). At Week 16, secukinumab 300 mg demonstrated significantly superior response rates compared to ustekinumab for PASI 75 (91.7% vs 79.8%; $P < 0.0001$), PASI 90 (76.6% vs 54.2%; $P < 0.0001$), PASI 100 (45.3% vs 26.7%; $P < 0.0001$), and IGA mod 2011 0/1 (78.6% vs 59.1%; $P < 0.0001$). Furthermore, at Week 12, patients receiving secukinumab 300 mg compared to ustekinumab had significantly greater PASI 75 (88.0% vs 74.2%; $P < 0.0001$) and PASI 100 (38.1% vs 20.1%; $P < 0.0001$) responses. Safety findings were consistent with the known safety profile of secukinumab.
- **Conclusions:** Secukinumab demonstrated superior results with greater improvements compared to ustekinumab across all study outcomes at Week 4, 12, and 16 in patients with moderate to severe plaque psoriasis.

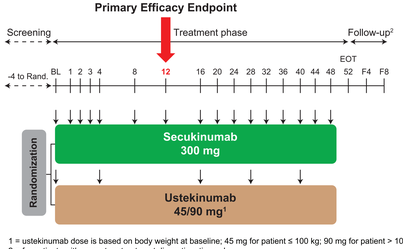
INTRODUCTION

- Secukinumab, a fully human monoclonal antibody that inhibits interleukin (IL)-17A, has been shown to have significant efficacy in the treatment of moderate to severe psoriasis and psoriatic arthritis, demonstrating sustained high levels of efficacy with a favorable safety profile[3–5]
  - Secukinumab has also shown efficacy in dedicated trials of scalp, nail, and palmoplantar psoriasis[6–8]
  - Additionally, secukinumab has previously demonstrated superior efficacy to ustekinumab in the phase 3b CLEAR study of moderate to severe plaque psoriasis[1]
- Here, we report 16-week results from CLARITY, the second head-to-head trial comparing secukinumab with ustekinumab

METHODS

- CLARITY (NCT02826603) is a multicenter, double-blinded, parallel-group, phase 3b study
- Patients were required to have moderate to severe psoriasis at Baseline defined as:
  - Psoriasis Area and Severity Index (PASI) score of ≥12 **and**
  - Body Surface Area (BSA) affected by plaque-type psoriasis ≥10% **and**
  - Investigator's Global Assessment, 2011 modification (IGA mod 2011) ≥3 (based on a scale of 0–4)
- Patients were randomized 1:1 to subcutaneous secukinumab 300 mg at Baseline, Weeks 1, 2, and 3, and then every 4 weeks from Week 4 to 48 or subcutaneous ustekinumab (45 mg for patient weighing ≤100 kg or 90 mg for patient weighing >100 kg) at Baseline, Week 4, and then every 12 weeks (**Figure 1**)
- Coprimary objectives of the study are to demonstrate the superiority of secukinumab compared to ustekinumab with respect to:
  - PASI 90 at Week 12
  - IGA mod 2011 0/1 (clear or almost clear skin) at Week 12
- Key secondary objectives will be assessed sequentially by a hierarchical testing strategy, and include measures testing the superiority of secukinumab compared to ustekinumab with respect to the following (shown in hierarchical order):
  1. PASI 75 at Week 12
  2. PASI 75 at Week 4
  3. PASI 90 at Week 16
  4. PASI 100 at Week 16
  5. IGA mod 2011 0/1 at Week 16
  6. PASI 100 at Week 12
  7. PASI 75 at Week 16
- Missing values were handled by multiple imputation in this analysis

Figure 1. Study Design

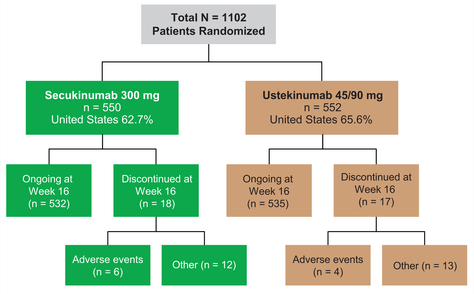


1 = ustekinumab dose is based on body weight at baseline; 45 mg for patient ≤ 100 kg; 90 mg for patient > 100 kg
2 = for patients with premature treatment discontinuation only
Follow-up visit F4 is approximately 4 weeks after the EOT visit. Follow-up visit F8 is approximately 8 weeks after the EOT visit
↓ = active dose administration; in order to keep the blind, patients will receive placebo administrations at several time points (not shown in this study design figure)
BL, Baseline; EOT, end of treatment phase

RESULTS

- A total of 1102 patients were randomized: 550 to receive secukinumab 300 mg and 552 to receive ustekinumab (**Figure 2**)
  - The rate of discontinuation was low and balanced between treatment arms

Figure 2. Patient Disposition



- Demographic and baseline disease characteristics were well balanced across patients receiving secukinumab 300 mg and ustekinumab 45/90 mg (**Table 1**)

Table 1. Patient Demographic and Baseline Disease Characteristics

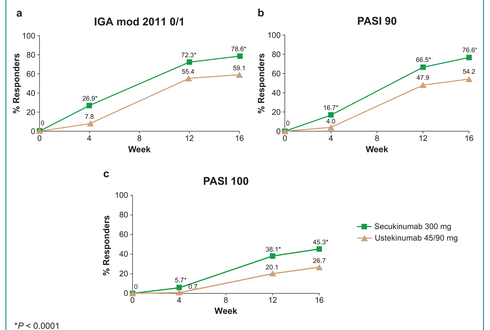
Parameter	Secukinumab 300 mg (n = 550)	Ustekinumab 45/90 mg (n = 552)
Mean age, years (SD)	45 (14.1)	45 (14.2)
Sex, male, n (%)	356 (64.7)	376 (68.1)
Race, white, n (%)	414 (75.3)	410 (74.3)
Mean weight, kg (SD)	91.0 (24.88)	93.0 (24.85)
> 100 kg, n (%)	189 (34.4)	188 (34.1)
Mean PASI score (SD)	20.8 (8.95)	21.3 (9.19)
Score > 20, n (%)	210 (38.2)	226 (40.9)
BSA affected, % (SD)	29.2 (17.93)	29.5 (17.69)
IGA mod 2011 score; severe disease, n (%)	209 (38.0)	239 (43.3)
Mean time since first diagnosis of plaque-type psoriasis, years (SD)	16.8 (11.88)	17.3 (13.34)
Previous exposure to biologic psoriasis therapy: Yes, n (%)	110 (20.0)	130 (23.6)

BSA, body surface area, IGA mod 2011, Investigator's Global Assessment, 2011 modification; PASI, Psoriasis Area and Severity Index; SD, standard deviation

Efficacy

- Both coprimary objectives were met:
  - Secukinumab 300 mg was superior to ustekinumab for the proportion of patients that achieved PASI 90 responses at Week 12 (66.5% vs 47.9%; $P < 0.0001$)
  - Secukinumab 300 mg was also superior to ustekinumab for the proportion of patients that achieved IGA mod 2011 0/1 responses at Week 12 (72.3% vs 55.4%; $P < 0.0001$)
- Secukinumab demonstrated statistical superiority compared with ustekinumab at Week 4 and maintained superiority to Week 16 (**Figure 3 a-c**)

Figure 3. IGA mod 2011 0/1 (a), PASI 90 (b), and PASI 100 (c) Response Rates Through Week 16



*$P < 0.0001$
IGA mod 2011 0/1, Investigator's Global Assessment, 2011 modification, clear (0) or almost clear (1) score; PASI 90/100, Psoriasis Area and Severity Index 90%/100% improvement vs Baseline

- Additionally, all key secondary objectives were met in the hierarchical testing strategy (**Table 2**)

Table 2. Hierarchical Efficacy Analysis of Key Secondary Objectives

Objectives (shown in order of hierarchical testing strategy)	Secukinumab 300 mg (n = 550)	Ustekinumab 45/90 mg (n = 552)	*P* value
PASI 75 at Week 12	88.0%	74.2%	< 0.0001
PASI 75 at Week 4	40.2%	16.3%	< 0.0001
PASI 90 at Week 16	76.6%	54.2%	< 0.0001
PASI 100 at Week 16	45.3%	26.7%	< 0.0001
IGA mod 2011 0/1 at Week 16	78.6%	59.1%	< 0.0001
PASI 100 at Week 12	38.1%	20.1%	< 0.0001
PASI 75 at Week 16	91.7%	79.8%	< 0.0001

IGA mod 2011 0/1, Investigator's Global Assessment, 2011 modification, clear (0) or almost clear (1); PASI, Psoriasis Area and Severity Index

Safety

- The safety profile of secukinumab was similar to that reported in previous secukinumab clinical trials
  - To prevent unblinding of treatment groups, detailed safety results are not presented
  - Complete safety data will be presented upon completion of the study

CONCLUSIONS

- Both coprimary objectives were met with secukinumab demonstrating superiority to ustekinumab for PASI 90 and IGA mod 2011 0/1 response rates at Week 12
- Additionally, secukinumab demonstrated robust superiority with greater improvements compared with ustekinumab across all study objectives up to Week 16
- The safety of secukinumab was consistent with the known secukinumab safety profile

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DISCLOSURES

J Bagel: Investigator and consultant for AbbVie, Amgen, Boehringer-Ingelheim, Sun, Janssen, Leo, Novartis, Celgene, Eli Lilly; consultant and speaker for Valiant; speakers' bureau for AbbVie, Eli Lilly, Janssen, Leo, Novartis. **J Nia** and **P Hashim:** nothing to disclose. **M Patekar**, **A de Vera**, **S Hugot:** Employees of Novartis Pharma AG. **K Sheng**, **E Muscianisi:** Employees of Novartis Pharmaceuticals Corporation. **S Xia:** Employee of Novartis Beijing Novartis Pharma Co. Ltd. **A Blauvelt:** Scientific adviser and clinical study investigator for AbbVie, Aclaris, Allergan, Almirall, Amgen, Boehringer-Ingelheim, Celgene, Dermavant, Dermira, Inc., Eli Lilly, Genentech/Roche, GlaxoSmithKline, Janssen, Leo, Meiji, Merck Sharp & Dohme, Novartis, Pfizer, Purdue Pharma, Regeneron, Sandoz, Sanofi Genzyme, Sienna Pharmaceuticals, Sun Pharma, UCB Pharma, Valeant, Vidac; paid speaker for Eli Lilly, Janssen, Regeneron, Sanofi Genzyme. **M Lebwohl:** Employee of Mount Sinai, which receives research funds from Amgen, Anacor, Boehringer–Ingelheim, Celgene, Lilly, Janssen Biotech, Kadmon, LEO Pharmaceuticals, Medimmune, Novartis, Pfizer, Sun Pharmaceuticals, and Valeant.

ACKNOWLEDGEMENTS

The authors thank the patients and their families and all investigators and their staff for participation in this study. Oxford PharmaGenesis, Inc., Newtown, PA, provided assistance with editing, layout, and printing the poster; this support was funded by Novartis Pharmaceuticals Corporation, East Hanover, NJ.

This research was sponsored by Novartis Pharma AG, Basel, Switzerland. The authors had full control of the contents of this poster.

Poster presented at: 13th Annual Winter Clinical Dermatology Conference, Maui, HI, USA; January 12–17, 2018.

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