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

Jerry Bagel[1], John Nia[2], Peter Hashim[2], Manmath Patekar[3], Ana de Vera[3], Sophie Hugot[3], Kuan Sheng[4], Summer Xia[5], Elisa Muscianisi[4], Andrew Blauvelt[6], Mark Lebwohl[2]

[1]Psoriasis Treatment Center of Central New Jersey, East Windsor, NJ, USA; [2]Icahn School of Medicine at Mount Sinai, New York, NY, USA; [3]Novartis Pharma AG, Basel, Switzerland; [4]Novartis Pharmaceuticals Corporation, East Hanover, NJ, USA; [5]Novartis Beijing Novartis Pharma Co. Ltd, Shanghai, China; [6]Oregon Medical Research Center, Portland, OR, USA

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.

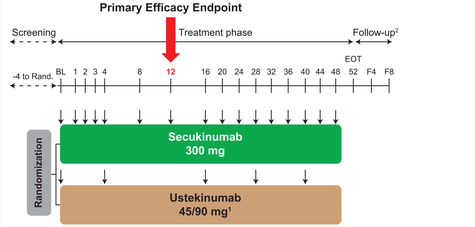
INTRODUCTION

- 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

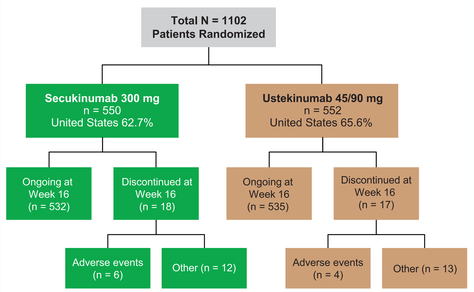


1 = ustekinumab dose is based on body weight at baseline; 45 mg for patient ≤ 100 kg; 90 mg for patient > 100 kg
2 = for patients with premature treatment discontinuation only
Follow-up visit F4 is approximately 4 weeks after the EOT visit. Follow-up visit F8 is approximately 8 weeks after the EOT visit
ǂ = 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

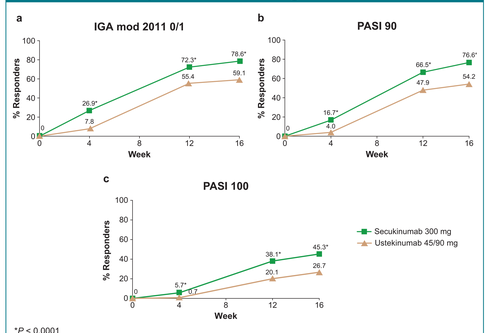
Parameter	Secukinumab 300 mg (n = 550)	Ustekinumab 45/90 mg (n = 552)
Mean age, years (SD)	45 (14.1)	45 (14.2)
Sex, male, n (%)	356 (64.7)	376 (68.1)
Race, white, n (%)	414 (75.3)	410 (74.3)
Mean weight, kg (SD)	91.0 (24.88)	93.0 (24.85)
> 100 kg, n (%)	189 (34.4)	188 (34.1)
Mean PASI score (SD)	20.8 (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.

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