Secukinumab Provides Complete or Almost-complete Psoriasis Clearance in Moderate-to-Severe Plaque Psoriasis: Pooled Analysis of 4 Phase 3 Trials

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ABSTRACT

- **Introduction:** Investigator's Global Assessment modified 2011 (IGA mod 2011) is a more robust measure of psoriasis clearance than traditional IGA and Physician's Global Assessment scales. Secukinumab, a fully human monoclonal antibody that selectively neutralizes interleukin-17A, has significant efficacy in moderate-to-severe psoriasis and psoriatic arthritis, demonstrating a rapid onset of action and sustained responses with a favorable safety profile. This post hoc analysis evaluates IGA mod 2011 0 (clear) and IGA (mod 2011) 0/1 (clear or almost clear) response rates over 1 year following treatment with secukinumab pooled from 4 phase 3 trials (ERASURE, FIXTURE, FEATURE, and JUNCTURE) involving patients with moderate-to-severe plaque psoriasis.
- **Methods:** Secukinumab (300 mg or 150 mg) or placebo was administered at Baseline, Weeks 1, 2 and 3, and then every 4 weeks from Week 4 to 48. In FIXTURE, etanercept (50 mg) was administered twice weekly for 12 weeks, then once weekly.
- **Results:** Of 2396 patients, 691, 692, 326, and 687 were randomized to secukinumab 300 mg, secukinumab 150 mg, etanercept, and placebo, respectively. Significantly more patients receiving secukinumab 300 mg compared with placebo achieved IGA (mod 2011) 0/1 (clear or almost clear) responses as early as Week 2 (after 2 doses of secukinumab) and IGA (mod 2011) 0 (clear) responses as early as Week 8 (after 5 doses of secukinumab). A significantly greater proportion of patients achieved IGA (mod 2011) 0/1 (clear or almost clear) responses at Week 12 (after 6 doses of secukinumab) with secukinumab 300 mg (65.0%) and secukinumab 150 mg (51.4%) compared with etanercept (27.2%) and placebo (2.2%; P <0.0001 for both secukinumab doses vs. etanercept and placebo). IGA (mod 2011) 0/1 (clear or almost clear) responses were sustained at Week 52 for secukinumab 300 mg (64.9%), secukinumab 150 mg (47.4%), and etanercept (37.2%; P <0.0001 for secukinumab 300 mg vs. etanercept). At Week 12, a significantly greater proportion of patients achieved IGA (mod 2011) 0 (clear) responses with secukinumab 300 mg (29.9%) and secukinumab 150 mg (15.1%) compared with etanercept (5.3%) and placebo (0.3%; P <0.0001 for both secukinumab doses vs. etanercept and placebo). IGA (mod 2011) 0 (clear) responses were sustained at Week 52 for secukinumab 300 mg (37.8%), secukinumab 150 mg (21.6%), and etanercept (9.6%; P <0.0001 for secukinumab 300 mg vs. etanercept).
- **Conclusion:** Secukinumab 300 mg provides early and sustained complete or near-complete skin clearance in up to 65% of patients with moderate-to-severe plaque psoriasis.

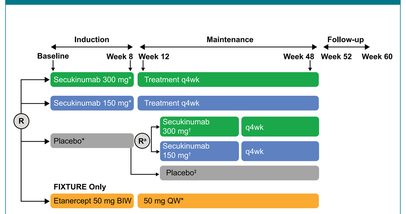
INTRODUCTION

- 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[1–3]
- Psoriasis clearance shortly after treatment initiation is important so that patients can experience improved quality of life early during treatment
  - Greater levels of psoriasis clearance are associated with a greater quality-of-life benefit[4]
- IGA modified 2011 (IGA mod 2011) is a more robust measure of psoriasis clearance than traditional IGA and Physician's Global Assessment scales[5]
  - For example, evaluation of induration requires "no thickening" for a score of 1 with IGA mod 2011 compared with "minimal plaque elevation" in other scales[5]
- In this post hoc analysis, we evaluated IGA mod 2011 0 (clear) and IGA mod 2011 0/1 (clear or almost clear) response rates over 1 year of secukinumab treatment, pooled from 4 phase 3 trials (ERASURE, FIXTURE, FEATURE, and JUNCTURE) of patients with moderate-to-severe plaque psoriasis

METHODS

- This pooled analysis included data from 4 phase 3 randomized, double-blinded, clinical trials of patients with moderate-to-severe plaque psoriasis (details of these trials have been previously published)
  - ERASURE (NCT01365455)[1]
  - FIXTURE (NCT01358578)[1]
  - FEATURE (NCT01555125)[6]
  - JUNCTURE (NCT01636687)[7]
- In all trials, patients received subcutaneous (SC) secukinumab (300 mg or 150 mg) or placebo at Baseline, Weeks 1, 2, and 3, and then every 4 weeks from Week 4 to 48 (**Figure 1**)
  - In the FIXTURE study, etanercept 50 mg was administered as per label twice weekly from Baseline to Week 12, then once weekly to Week 51
  - At Week 12, patients initially randomized to placebo who did not achieve a Psoriasis Area and Severity Index (PASI) response of 75 were re-randomized to secukinumab 300 mg or secukinumab 150 mg

Figure 1. Study Design



*Treatment or placebo at Baseline and Weeks 1, 2, 3, 4, and 8 to Week 48; in FIXTURE, etanercept or placebo BIW to Week 12
†Treatment at Weeks 12, 13, 14, and 15
‡Placebo at Weeks 12, 13, 14, and 15, then q4wk from Week 16 until Week 48; in FIXTURE, etanercept placebo QW to Week 51
BIW, twice weekly; QW, every week; q4wk, every 4 weeks; PASI, Psoriasis Area and Severity Index;
R, randomization; R†, subjects on placebo who did not achieve a PASI 75 response were re-randomized

- In each study, the co-primary endpoints were PASI 75 and IGA mod 2011 responses of 0/1 (clear or almost clear) at Week 12
  - An IGA mod 2011 score of 0 indicates no signs of psoriasis, although postinflammatory hyperpigmentation may be present. An IGA mod 2011 score of 1 indicates almost clear skin, with no thickening, normal-to-pink coloration, and no-to-minimal focal scaling[5]
  - IGA scales correlate well with PASI[5]
- Missing values were analyzed by nonresponder imputation in this analysis

RESULTS

- Demographic and baseline disease characteristics were well balanced across treatment groups (**Table 1**)

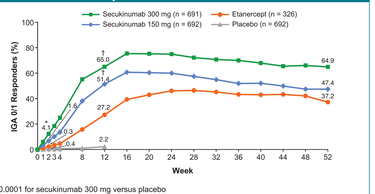
Table 1. Patient Demographic and Baseline Disease Characteristics

Parameter	Secukinumab 300 mg SC (n = 691)	Secukinumab 150 mg SC (n = 692)	Etanercept (n = 326)	Placebo (n = 692)
Sex (male), n (%)	477 (69.0)	485 (70.1)	232 (71.2)	484 (69.9)
Age (years), mean (SD) Range	44.9 (13.3) 18–83	45.1 (13.4) 18–83	43.8 (13.0) 18–79	44.7 (12.8) 18–82
Race/ethnicity, n (%) White Asian Black Other	 505 (73.1) 129 (18.7) 9 (1.3) 48 (6.9)	 499 (72.1) 129 (18.6) 13 (1.9) 51 (7.4)	 219 (67.2) 74 (22.7) 0 33 (10.1)	 509 (73.6) 121 (17.5) 13 (1.9) 49 (7.1)
Height (cm), mean (SD) Range	171.2 (9.6) 145.0–198.5	171.3 (10.2) 145.0–197.0	171.2 144.0–198.0	171.6 (10.2) 141.0–200.7
Weight (kg), mean (SD) Range	86.6 (23.2) 45.0–219.1	86.6 (23.2) 43.1–215.0	84.6 (20.5) 42.0–175.6	86.0 (22.6) 42.0–191.9
BMI (kg/m²), mean (SD) Range	29.4 (6.9) 17.4–67.4	29.4 (7.0) 16.5–79.7	28.7 (5.9) 15.4–58.3	29.1 (6.9) 16.2–71.2
PASI, mean (SD) Range	22.7 (9.4) 11.2–72.0	22.8 (10.0) 12.0–69.6	23.2 (9.8) 12.0–54.5	22.5 (9.7) 10.6–72.0
IGA modified 2011 score, n (%) 3 (Moderate disease) 4 (Severe disease)	 436 (63.1) 255 (36.9)	 439 (63.4) 253 (36.6)	 195 (59.8) 131 (40.2)	 424 (61.3) 268 (38.7)
Time since first psoriasis diagnosis (years), mean (SD) Range	17.0 (12.0) 0.5–61.5	17.9 (12.5) 0.5–69.0	16.4 (12.0) 0.6–57.2	17.5 (12.2) 0.5–68.1
Previous exposure to systemic psoriasis therapy (Yes), n (%)	438 (63.4)	447 (64.6)	214 (65.6)	420 (60.7)
Previous exposure to biologic systemic psoriasis therapy (Yes), n (%)	146 (21.1)	161 (23.3)	45 (13.8)	147 (21.2)
Previous exposure to nonbiologic systemic psoriasis therapy (Yes), n (%)	373 (54.0)	393 (56.8)	204 (62.6)	363 (52.5)

BMI, body mass index; IGA, Investigator's Global Assessment; PASI, Psoriasis Area and Severity Index; SC, subcutaneous; SD, standard deviation

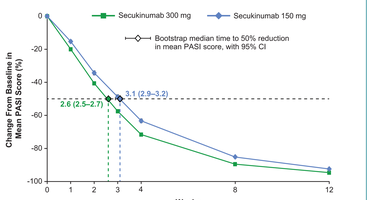
- IGA mod 2011 0/1 (clear or almost clear) response rates to Week 52 are presented in **Figure 2**
  - Significantly greater improvements with secukinumab 300 mg compared with placebo were observed beginning at Week 2, after 2 doses of secukinumab (4.1% versus 0.4%; P < 0.0001)
  - At Week 12 (after 6 doses of secukinumab), significantly more patients achieved IGA mod 2011 0/1 responses with secukinumab 300 mg (65.0%) and secukinumab 150 mg (51.4%) compared with etanercept (27.2%) and placebo (2.2%; P < 0.0001 for both secukinumab doses versus etanercept and versus placebo)
  - IGA mod 2011 0/1 response rates were sustained at Week 52 and were significantly greater for secukinumab 300 mg compared with etanercept (P < 0.0001)
- In patients achieving IGA 0/1 at any time up to 12 weeks, median time to a 50% decrease from Baseline in mean PASI was 2.6 weeks with secukinumab 300 mg and 3.1 weeks with secukinumab 150 mg (**Figure 3**)

Figure 2. IGA Mod 2011 0/1 (Clear/Almost Clear) Response Rates Over Time



*P < 0.0001 for secukinumab 300 mg versus placebo
†P < 0.0001 for both secukinumab doses versus etanercept and placebo
IGA mod 2011 0/1, Investigator's Global Assessment, 2011 modified version, improvement to scores of 0 or 1 (clear or almost clear skin)

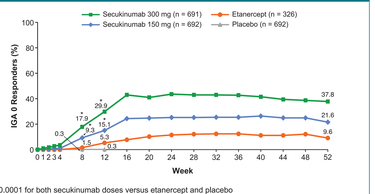
Figure 3. Speed of Response in IGA Mod 2011 0/1 (Clear/Almost Clear) Responders at Any Time Up to 12 Weeks



A repeated-measures, mixed-effects model was used to analyze the mean percent change from Baseline in PASI
The median time to a 50% reduction in mean PASI was estimated from parametric bootstrap samples with the use of linear interpolation between time points
CI, confidence interval; IGA mod 2011 0/1, Investigator's Global Assessment, 2011 modified version, improvement to scores of 0 or 1 (clear or almost clear skin); PASI, Psoriasis Area and Severity Index

- IGA mod 2011 0 (clear) response rates to Week 52 are presented in **Figure 4**
  - Beginning at Week 8 (after 5 doses of secukinumab), significantly greater response rates were observed with secukinumab 300 mg (17.9%) and secukinumab 150 mg (9.3%) compared with etanercept (1.5%) and placebo (0.3%; P < 0.0001 for both secukinumab doses versus etanercept and placebo)

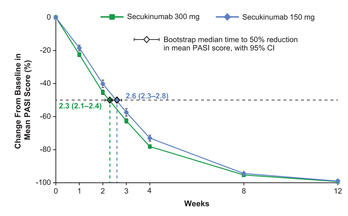
Figure 4. IGA Mod 2011 0 (Clear) Response Rates Over Time



*P < 0.0001 for both secukinumab doses versus etanercept and placebo
IGA mod 2011 0, Investigator's Global Assessment, 2011 modified version, improvement to scores of 0 (clear skin)

- Similarly, significantly more patients achieved IGA mod 2011 0 (clear) responses at Week 12 with secukinumab 300 mg (29.9%) and secukinumab 150 mg (15.1%) compared with etanercept (5.3%) and placebo (0.3%) (P < 0.0001 for both secukinumab doses versus etanercept and placebo)
  - IGA mod 2011 0 (clear) response rates were sustained at Week 52 and were significantly greater for secukinumab 300 mg compared with etanercept (37.8% versus 9.6%, respectively; P < 0.0001)
- In patients achieving IGA mod 2011 0 at any time up to 12 weeks, median time to a 50% decrease from Baseline in mean PASI was 2.3 weeks with secukinumab 300 mg and 2.6 weeks with secukinumab 150 mg (**Figure 5**)

Figure 5. Speed of Response in IGA Mod 2011 0 (Clear) Responders at Any Time Up to 12 Weeks



A repeated-measures, mixed-effects model was used to analyze the mean percent change from Baseline in PASI
The median time to a 50% reduction in mean PASI was estimated from parametric bootstrap samples with the use of linear interpolation between time points
CI, confidence interval; IGA mod 2011 0, Investigator's Global Assessment, 2011 modified version, improvement to score 0 (clear skin); PASI, Psoriasis Area and Severity Index

- At Week 12, the Spearman correlation coefficient between IGA and Dermatology Life Quality Index responses was 0.43 for secukinumab 300 mg and 0.45 for secukinumab 150 mg

Safety

- Rates of adverse events and serious adverse events were similar across all treatment groups (**Table 2**)

Table 2. Summary of Adverse Events at Week 52

Preferred term, n (%)	Secukinumab 300 mg SC (n = 690)	Secukinumab 150 mg SC (n = 692)	Etanercept (n = 323)
Discontinuation due to adverse event	21 (3.0)	25 (3.6)	12 (3.7)
Any serious adverse event	48 (7.0)	48 (6.9)	20 (6.2)
Any adverse event	575 (83.3)	562 (81.2)	253 (78.3)
Most common adverse events (> 5%)			
Nasopharyngitis	172 (24.9)	164 (23.7)	86 (26.6)
Headache	79 (11.4)	65 (9.4)	40 (12.4)
Diarrhea	54 (7.8)	45 (6.5)	22 (6.8)
Upper respiratory tract infection	53 (7.7)	64 (9.2)	18 (5.6)
Cough	45 (6.5)	21 (3.0)	12 (3.7)
Back pain	37 (5.4)	30 (4.3)	26 (8.0)
Hypertension	35 (5.1)	37 (5.3)	14 (4.3)
Arthralgia	34 (4.9)	38 (5.5)	23 (7.1)

SC, subcutaneous

CONCLUSIONS

- Secukinumab provides early and sustained skin clearance for patients with moderate-to-severe psoriasis
  - Up to 65% of patients achieved complete or near-complete clearance of psoriasis after 1 year of treatment as measured by IGA mod 2011 0/1
- The safety profile of secukinumab remained favorable and comparable to that of etanercept
- In patients receiving secukinumab, response rates were similar between IGA mod 2011 0 and PASI 100 and between IGA mod 2011 0/1 and PASI 90 groups
  - At Week 52, with secukinumab 300 mg, IGA mod 2011 0 was achieved by 37.8% of patients and PASI 100 was achieved by 40.8% of patients; similarly, IGA 0/1 was achieved by 64.9% of patients and PASI 90 was achieved by 68.1% of patients[8]

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DISCLOSURES

A Blauvelt: Scientific adviser and clinical study investigator for AbbVie, Amgen, Boehringer-Ingelheim, Celgene, Dermira, Genentech, GlaxoSmithKline, Janssen, Lilly, Merck, Novartis, Pfizer, Regeneron, Sandoz, Sanofi Genzyme, Sun Pharmaceutical Industries, UCB, Valeant; paid speaker for Lilly, Regeneron, Sanofi Genzyme. **A Armstrong:** Investigator and/or adviser to AbbVie, Amgen, Celgene, Janssen, Merck, Lilly, Novartis, Pfizer. **P Rich:** Consultant, investigator, speaker, and/or adviser for, and/or received travel and/or research grants from Lilly, Novartis, Boehringer-Ingelheim, Janssen, Pfizer, Merck, Amgen, AbbVie. **R Kisa, A Guana, X Meng:** Employees of Novartis Pharmaceuticals Corporation. **K Callis Duffin:** Grant/research support from Amgen, Lilly, Janssen, Stiefel, AbbVie, BMS, Celgene, Novartis; consultant for Amgen, Lilly, Janssen, Stiefel, AbbVie, BMS, Celgene, Pfizer, Novartis.

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