

Psoriasis Patients With PASI 90 Response Achieve Greater Health-Related Quality of Life Improvements Than Those With PASI 75-89 Response

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BACKGROUND

- Secukinumab, a fully human monoclonal antibody that selectively targets interleukin (IL)-17A, has been demonstrated in phase 3 studies to be highly efficacious in the treatment of moderate to severe plaque psoriasis, with a rapid onset of action, a sustained effect, and an acceptable safety profile.^{1,2}
- Previous research indicates that patients with moderate to severe plaque psoriasis who achieved an objective skin clearing, defined by a Psoriasis Area and Severity Index (PASI) 90 response, had a significantly higher rate of achieving a Dermatology Life Quality Index (DLQI) response (0/1), indicating the disease has no effect at all on their lives, than the patients who achieved a PASI 75-89 response.³
 - PASI 75-89 response is defined as a 75% to 89% improvement from baseline on PASI score; PASI 90 response is defined as 90% improvement or more from baseline on PASI score.

OBJECTIVE

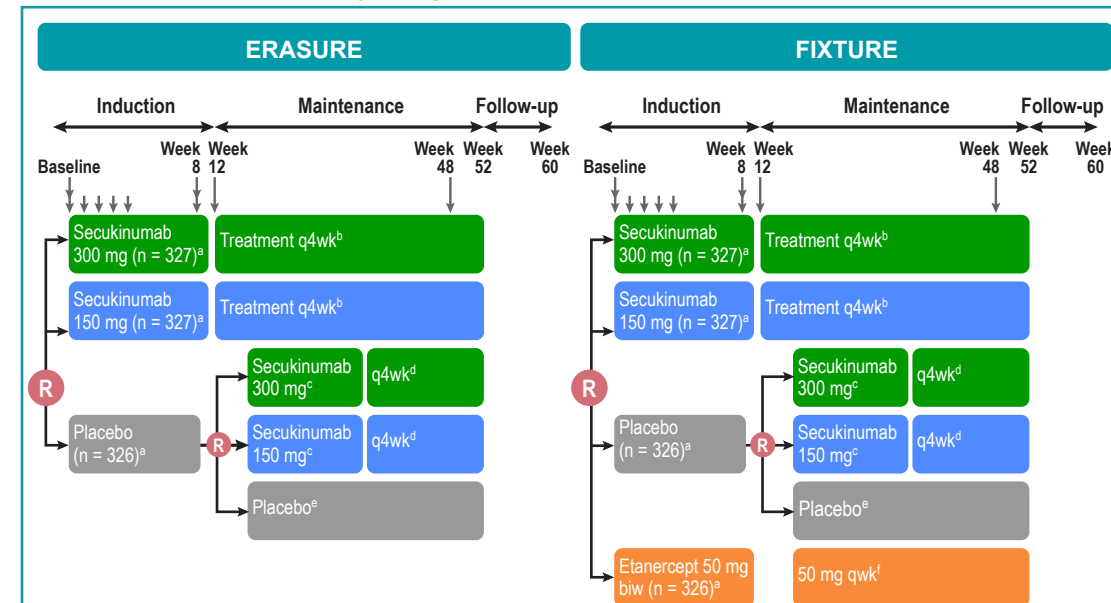
- To evaluate the additional benefit of achieving improvements in objective skin clearing on patient-reported outcome (PRO) responses in patients with moderate to severe plaque psoriasis.

METHODS

Study Design

- ERASURE and FIXTURE, two multicenter phase 3 trials, were used in this pooled analysis.
- Subjects aged 18 years and older were randomized 1:1:1 in ERASURE to subcutaneous treatment groups (secukinumab 150 mg, secukinumab 300 mg, and placebo) and 1:1:1 in FIXTURE (including an etanercept 50 mg twice-weekly group).

ERASURE and FIXTURE Study Designs



b/w = twice weekly; q4wk = every 4 weeks; qwk = every week; R = randomization; wk = week.
^a Treatment or placebo at baseline and weeks 1, 2, 3, 4, and 8; short arrows indicate time points at which doses were given during induction period.
^b Maintenance treatment starts at week 12 and continues q4wk until week 48.
^c Treatment at weeks 12, 13, 14, and 15.
^d Treatment q4wk from week 16 until week 48.
^e Placebo at weeks 12, 13, 14, and 15, then q4wk from week 16 until week 48.
^f Treatment qwk from week 12 until week 51.

Assessments

Clinical Outcomes

Clinical outcomes were assessed by investigators at screening, baseline, and each scheduled visit after randomization using the following:

- PASI
 - PASI score is calculated using the following formula:

$$PASI = 0.1 (Eh + Ih + Dh) Ah + 0.2 (Eu + Iu + Du) Au + 0.3 (Et + It + Dt) At + 0.4 (El + Il + Dl) Al,$$
 where *E, I, D,* and *A* denote erythema, induration, desquamation, and area, respectively, and *h, u, t,* and *l* denote head, upper extremities, trunk, and lower extremities, respectively.
 - Scores range from 0 (no signs of psoriasis) to 72 (maximal severity). Eligible subjects must have had a score of 12 or higher prior to randomization.
- Investigator's Global Assessment (IGA) modified 2011
 - Scores range from 0 (no symptoms) to 4 (severe symptoms).

Patient-Reported Outcomes

Patient-reported outcomes were assessed at baseline and weeks 4, 8, 12, 24, 36, and 52 using the following:

- DLQI
 - This 10-item general dermatology disability index was designed to assess health-related quality of life in adult patients with skin diseases.
 - The DLQI includes domains of daily activities, leisure, personal relationships, symptoms and feelings, treatment, and work/school, with each item responses ranging from 0 (not at all) to 3 (very much).
 - Total scores range from 0 to 30; higher scores indicate greater impairment (worse health).
 - Scores of 0 to 1 indicate that the disease has no effect at all on the patient's life.
- EuroQol 5-Dimension Health Status Questionnaire (EQ-5D) visual analog scale (VAS)
 - EQ-5D was designed to assess health status in adults.
 - These self-rated (global) health status questions utilize a vertically oriented VAS; 100 represents the "best possible health state" and 0 represents the "worst possible health state."

Definition of Response

- Subjects had to have a baseline and at least one postbaseline score to be included in the analyses.
- The percentage of subjects identified as achieving clinical response (based on PASI 75-89 and PASI 90 and PRO response (on the DLQI and EQ-5D VAS) were compared using the chi-square test.

Definition of Response

| Measure | Definition of Response |
|-------------|--|
| DLQI | Total score of 0 or 1 at week 12 |
| EQ-5D VAS | Increase of > 7 points from baseline to week 12 |
| PASI 75-89 | 75%-89% improvement from baseline to week 12 on PASI score |
| PASI 90-100 | ≥ 90% improvement from baseline to week 12 on PASI score |

DLQI = Dermatology Life Quality Index; EQ-5D = EuroQol 5-Dimension Health Status Questionnaire; PASI = Psoriasis Area and Severity Index; VAS = visual analog scale.

RESULTS

Subject Characteristics

- 1,470 subjects were randomized to active treatment (150 mg, n = 572; 300 mg, n = 572, etanercept, n = 326).
- Given similarity across groups, active treatment arms were combined.

Baseline Demographic and Disease Characteristics

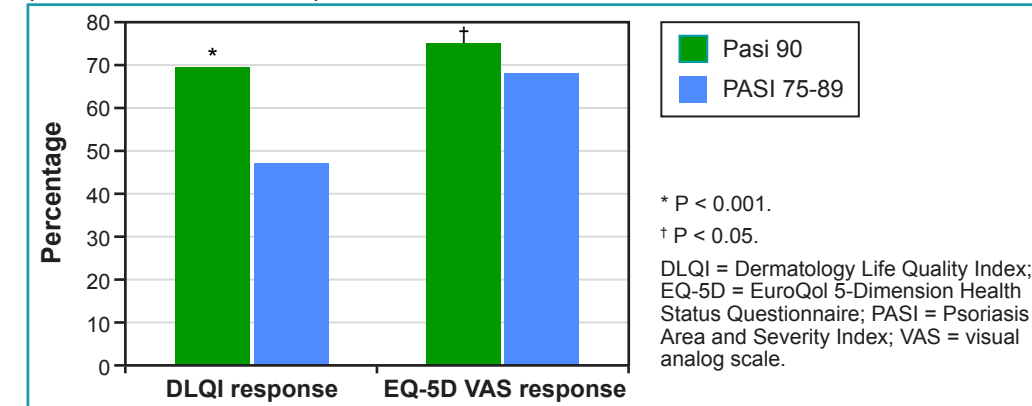
| Demographics and Characteristics | Secukinumab 300 mg (n = 572) | Secukinumab 150 mg (n = 572) | Etanercept (FIXTURE ONLY) (n = 326) | Overall Active Treatment (n = 1,470) |
|----------------------------------|------------------------------|------------------------------|-------------------------------------|--------------------------------------|
| Male, n (%) | 393 (68.7) | 404 (70.6) | 232 (71.2) | 1,029 (70.0) |
| Age in years, mean (SD) | 44.5 (13.5) | 44.8 (13.0) | 42.9 (12.9) | 44.3 (13.2) |
| Body weight, mean (SD) | 85.5 (22.8) | 85.1 (21.5) | 84.6 (20.5) | 85.1 (21.8) |
| BSA score, mean (SD) | 33.7 (19.2) | 34.0 (19.3) | 33.6 (18.0) | 33.8 (19.0) |
| PASI score, mean (SD) | 23.3 (9.7) | 23.1 (10.2) | 23.2 (9.8) | 23.2 (9.9) |
| IGA mod 2011, n (%) | | | | |
| Moderate (level = 3) | 357 (62.4) | 367 (64.2) | 195 (59.8) | 919 (62.5) |
| Severe (level = 4) | 215 (37.6) | 205 (35.8) | 131 (40.2) | 551 (37.5) |
| PRO measures, mean (SD) | | | | |
| DLQI Total score | 13.6 (7.3) | 13.4 (7.1) | 13.4 (7.3) | 13.5 (7.2) |
| EQ-5D VAS | 61.4 (23.6) | 61.7 (23.0) | 62.6 (22.1) | 61.8 (23.0) |

BSA = body surface area; DLQI = Dermatology Life Quality Index; EQ-5D = EuroQol 5-Dimension Health Status Questionnaire; IGA = Investigator's Global Assessment modified 2011 (based on a scale of 0-4); PASI = Psoriasis Area and Severity Index; PRO = patient-reported outcomes; SD = standard deviation; VAS = visual analog scale.

Response at Week 12

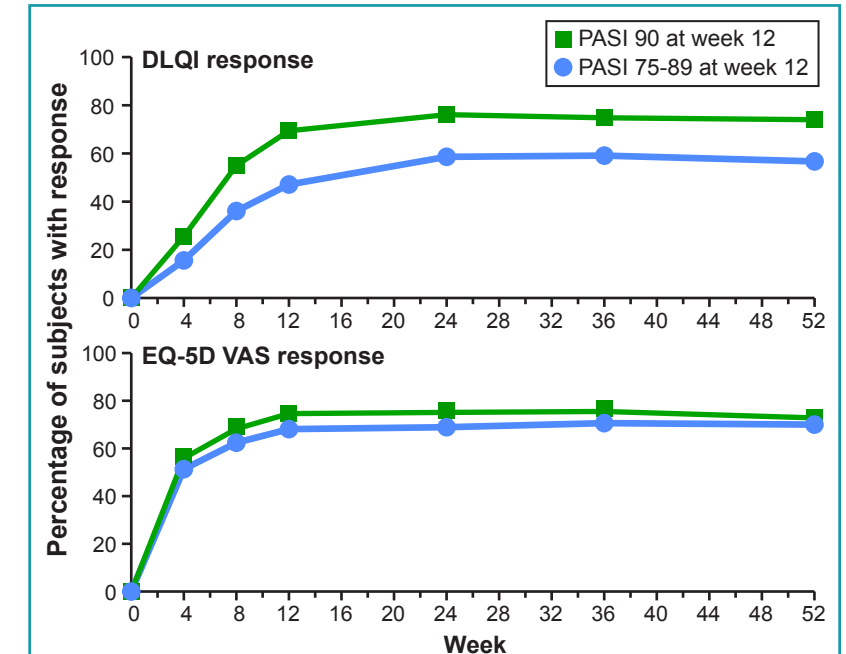
- Among the 1,144 subjects randomized to secukinumab (150 mg, n = 572; 300 mg, n = 572), 550 (48.3%) were PASI 90 responders, and 292 (25.5%) were PASI 75-89 responders at week 12.
- Rates of subjects achieving both clinical response and DLQI response were significantly higher among the PASI 90 responders compared with PASI 75-89 responders at week 12 (70.0% vs. 48.1%; *P* < 0.05).
- Significantly more subjects achieved both PASI 90 response and DLQI or EQ-5D VAS response than both PASI 75-89 response and DLQI or EQ-5D VAS response.
- The response rates were similar between PASI 90 and PASI 75-89 responders (73.8% vs. 70.9%; *P* > 0.05) who achieved EQ-5 D VAS response at week 12.

Percentage of DLQI and EQ-5D VAS Responders by PASI Response Status at Week 12 (Pooled Active Treatment)



- Subjects who achieved PASI 90 response were more likely to achieve DLQI and EQ-5D VAS response than those who achieved PASI 75-89 response.
- Through week 52, differences in proportion of PRO responders between PASI 75-89 and PASI 90 response was greater for the DLQI.

Percentage of DLQI and EQ-5D VAS Responders by Week 12 PASI Response Status Over Time (Pooled Active Treatment)



DLQI = Dermatology Life Quality Index; EQ-5D = EuroQol 5-Dimension Health Status Questionnaire; PASI = Psoriasis Area and Severity Index; VAS = visual analog scale.

DISCUSSION

- Psoriasis skin clearing is related to improvements in some measures of HRQOL and health status.
- The benefit of PASI 90 over PASI 75-89 is more pronounced for a disease-specific measure (DLQI) than a general health status (EQ-5D VAS) measure.

CONCLUSION

- Psoriasis skin clearing is related to improvements in some measures of HRQOL and health status, with a meaningful reduction of the DLQI associated with better improvements in objective skin clearing (PASI 90 response vs. PASI 75-89 response).

REFERENCES

- Langley RG, et al. *New Engl J Med.* 2014; 371:326-38.
- Mrowietz U, et al. Oral presentation at: 22nd EADV Congress; October 2-6, 2013. Istanbul, Turkey.
- Torii H, et al. *J Dermatol.* 2012; 39(3):253-59.

