ORIGINAL ARTICLE

Secukinumab retreatment-as-needed versus fixed-interval maintenance regimen for moderate to severe plaque psoriasis: A randomized, double-blind, noninferiority trial (SCULPTURE)

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Background: Secukinumab has demonstrated high, sustained efficacy in psoriasis to 52 weeks on a fixed-interval regimen.

Objective: We sought to compare a retreatment-as-needed versus a fixed-interval regimen.

Methods: In this double-blind study, adults with moderate to severe plaque psoriasis were randomized 1:1 to subcutaneous secukinumab at 300 mg (n = 484) or 150 mg (n = 482) weekly from baseline until week 4, and at week 8. At week 12, patients achieving 75% or more improvement from baseline Psoriasis Area and Severity Index score (PASI 75) were rerandomized to 2 dose levels of secukinumab retreatment as needed (n = 217, 300 mg; n = 206, 150 mg) or fixed interval (n = 217; n = 203). Primary end point was noninferiority of retreatment as needed versus fixed interval for maintaining PASI 75 to week 52.

Results: Secukinumab induced high responses by week 12 (84.4%-91.1% PASI 75 responders). From week 12 to week 52, more patients on fixed interval (78.2%, 300 mg; 62.1%, 150 mg) maintained PASI 75 versus retreatment as needed (67.7%; 52.4%); statistical noninferiority of retreatment as needed was not

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established. Overall safety, including very low incidences of treatment-emergent anti-drug antibodies (<0.5%), was similar between regimens.

Limitations: The primary end point was developed without any known precedent.

Conclusion: Secukinumab fixed interval showed clear benefit versus the study-specified retreatment-as-needed regimen for maintaining efficacy. Both regimens exhibited safety consistent with previous trials. The potential of retreatment as needed with secukinumab warrants further investigation. (J Am Acad Dermatol http://dx.doi.org/10.1016/j.jaad.2015.04.011.)

Key words: clinical trial; dosing; immunogenicity; noninferiority; psoriasis; retreatment as needed; secukinumab.

Secukinumab (Novartis Pharma AG, Basel, Switzerland), a recombinant, high-affinity, fully human immunoglobulin G1κ monoclonal antibody, selectively binds to and neutralizes the inflammatory mediator interleukin-17A.[1] In phase II and III studies, at subcutaneous doses of 300 mg or 150 mg, secukinumab demonstrated rapid, robust, and durable efficacy in psoriasis and was well tolerated.[2-4] A fixed-interval regimen (every-4-week regular dosing without interruption) of secukinumab maintained high levels of clinical response in the majority of patients to week 52.

CAPSULE SUMMARY

- Individualized treatment is potentially of high value for biologic therapy in psoriasis.
- SCULPTURE was designed to compare a retreatment-as-needed regimen to fixed-interval administration with secukinumab.
- Safety was comparable between both regimens, including low immunogenicity; however, fixed-interval dosing with secukinumab at 300 mg yielded the best sustained efficacy.

The chronic nature of psoriasis makes determining an optimal regimen for long-term maintenance treatment an important clinical consideration. A retreatment-as-needed individualized approach can offer a flexible regimen with lower drug exposure than a fixed-interval regimen. Intermittent, as-needed treatment has been evaluated for approved biologics in psoriasis,[5-8] but no formal noninferiority tests between fixed-interval and retreatment-as-needed regimens have been performed.

SCULPTURE was a phase III study specifically designed to evaluate the noninferiority of maintenance therapy using a retreatment-as-needed regimen versus a fixed-interval regimen at 2 doses (300 mg and 150 mg subcutaneously) of secukinumab in patients with moderate to severe plaque psoriasis. The study was powered to evaluate the primary end point of noninferiority to week 40/52 in terms of maintenance of 75% or more improvement from baseline Psoriasis Area and Severity Index (PASI) score (PASI 75 response).

METHODS

Study population

Patients (age ≥18 years) with moderate to severe chronic plaque psoriasis (PASI score ≥12, static 5-point investigator global assessment [IGA] 2011 modified version[9] score ≥3, and body surface area involvement ≥10%) given a diagnosis 6 months or longer before randomization and inadequately controlled by topical treatments, phototherapy, previous systemic therapy, or a combination of these were eligible.

Study design

This multicenter, randomized, double-blind, parallel-group trial (ClinicalTrials.gov NCT01406938) was conducted at 133 international sites between August 2011 and March 2013.

Eligible patients were randomized (1:1) to secukinumab at 300 mg or 150 mg, administered via two 150-mg subcutaneous injections or one 150-mg subcutaneous and one placebo subcutaneous injection, respectively (Fig 1). Treatment was administered at baseline and weeks 1, 2, 3, 4, and 8. At week 12, patients were classified as PASI 75 responders, partial responders (≥50% but <75% PASI score improvement), or nonresponders (<50% PASI score improvement). PASI 75 responders were rerandomized (1:1) to maintenance therapy on retreatment-as-needed or fixed-interval regimens at the same dose received in the first 12 weeks. For the fixed-interval regimen, patients received secukinumab every 4 weeks from weeks 12 to 48. For the retreatment-as-needed regimen, patients received secukinumab at week 12, then placebo until start of relapse, defined as loss of 20% or more of maximum PASI score improvement