MATERIALS AND METHODS

Study Design and Patient Population

This was a retrospective, pooled, post hoc analysis of four phase 3 clinical trials that randomized patients with moderate-to-severe psoriasis to secukinumab 150 or 300 mg and placebo (ERASURE, FIXTURE, FEATURE, and JUNCTURE) or etanercept (FIXTURE). In the ERASURE study, 738 patients with moderate-to-severe psoriasis were randomized 1:1:1 to receive subcutaneous (SC) secukinumab 150 mg, secukinumab 300 mg, or placebo [16]. In the FIXTURE study, 1,306 patients with moderate-to-severe psoriasis were randomized 1:1:1:1 to receive SC secukinumab 150 mg, secukinumab 300 mg, placebo, or etanercept 50 mg for 52 weeks [16]. In the FEATURE study, 177 patients with moderate-to-severe psoriasis were randomized 1:1:1 to self-administer from prefilled syringes secukinumab 150 mg, secukinumab 300 mg, or placebo for 52 weeks [17]. In the JUNCTURE study, 182 patients with moderate-to-severe psoriasis were randomized 1:1:1 to self-administer from auto-injector/pens secukinumab 150 mg, secukinumab 300 mg, or placebo for 52 weeks [18]. Only patients randomized to the secukinumab 300 mg treatment arm were included in this post hoc analysis.

Study Variables

Patient characteristics were measured at baseline and included demographics (age, sex, body weight, body mass index, and race); clinical characteristics (IGA score, percentage of affected BSA, PASI and DLQI scores, duration and severity of psoriasis, and duration of psoriatic arthritis [PsA; if present]); and treatment history (prior exposure to systemic psoriasis therapy, including use of biologic and nonbiologic systemic therapies).

IGA, percentage of affected BSA, and PASI and DLQI scores were collected at each time point, with weeks 12, 24, and 52 as the primary time points, to determine correlation of IGA × BSA with PASI and 2 definitions of MDA. For this analysis, MDA was defined as achievement of (1) ≥90% improvement in PASI score (PASI 90) and a DLQI score showing no effect on the patient's life (DLQI 0/1), which allows inclusion of both a physician- and

patient-reported outcome measure in the treat-to-target goal, with achievement of PASI 90 predicting a better quality of life as measured by DLQI 0/1 [23]; and (2) PASI score ≤1 or BSA <3% (defined as mild psoriasis), which represents 1 of the 7 criteria used for the definition of MDA in PsA [24]. The 5-point IGA scale (range, 0–4) evaluates the severity of psoriasis, with a value of 0 indicating “clear” and 4 indicating “severe” plaque psoriasis [25]:

- 0 = clear: no signs of psoriasis, although postinflammatory hyperpigmentation may be present
- 1 = almost clear: no thickening, normal to pink coloration, and no to minimal focal scaling
- 2 = mild: slightly detectable to mild thickening, pink to light-red coloration, and predominantly fine scaling
- 3 = moderate: clearly distinguishable to moderate thickening, dull to bright-red coloration, and moderate scaling
- 4 = severe: severe thickening, with hard edges; bright to deep, dark red coloration; and severe/coarse scaling covering almost all or all lesions

Study Outcomes and Data Analysis

The correlation between IGA × BSA and PASI score (percent change from baseline) as well as between IGA × BSA and achievement of ≥75% to <90% improvement from baseline in PASI score was evaluated through Pearson correlation at each time point, with weeks 12, 24, and 52 being the primary time points.

For each definition of MDA, a range of possible cutoff values of IGA × BSA was examined at each time point. The optimal cutoff value was determined using the Youden index (YI), calculated as follows: YI = sensitivity + specificity – 1 [26]. The index balances sensitivity and specificity to maximize values. The YI captures the performance of a diagnostic test, with values ranging from 0 to 1. A value of 0 indicates that the diagnostic test gives the same proportion of positive results for patients with and without the disease, and a value of 1 indicates that there are no false-positive or -negative results. Tests with the same

index value have the same proportion of misclassified tests, as the calculation provides equal weight to sensitivity and specificity and, therefore, false-negative and -positive rates.