Complete Skin Clearance is Associated with the Greatest Benefits to Health-Related Quality of Life and Perceived Symptoms for Patients with Psoriasis

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ABSTRACT

Introduction: With newer biologics, the achievement of complete skin clearance has become an attainable treatment goal for patients with plaque psoriasis. We evaluate how improvements in Psoriasis Area and Severity Index (PASI) responses, particularly at incremental improvements approaching complete skin clearance (PASI 100), translate into improvements in health-related quality of life (HRQoL) and patient-perceived symptoms.

Methods: Data from the BE RADIANT phase 3b trial (NCT03536884) and its open-label extension (OLE), pooled across all study visits and treatments over 16 weeks (randomised patients) and 2 years (patients entering the OLE), were analysed using mixed-effects logistic regression models. Proportions of patients achieving a Dermatology Life Quality Index (DLQI) of 0/1, DLQI item scores of 0, and Psoriasis Symptoms

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and Impacts Measure (P-SIM) item scores of 0 for itching, scaling, and skin pain at specific PASI improvement levels were estimated.

Results: Seven hundred and forty-three patients were randomised to treatment; 654 entered the OLE. Using 16-week pooled data, there were incremental improvements in the proportions of patients estimated by our model to achieve DLQI 0/1 with PASI 100 compared with 95% (PASI = 95%) and 90% (PASI = 90%) improvements in PASI (93.0%, 89.3%, and 83.8% achieving DLQI 0/1, respectively). Estimated proportions achieving DLQI item scores of 0 had the greatest increases at higher PASI improvement levels for Items 1 (itchy, sore, painful, or stinging skin), 2 (embarrassment), and 4 (choice of clothing). Estimated proportions of patients achieving P-SIM = 0 were also higher for PASI 100 (itching: 61.7%; scaling: 82.2%; skin pain: 96.9%) than for PASI = 95% (50.8%; 72.3%; 95.7%) and PASI = 90% (39.8%; 59.5%; 94.0%). Similar benefits of incremental PASI improvements were estimated using 2-year data.

Conclusions: Complete skin clearance translated into the greatest benefits to HRQoL and patient-perceived symptoms, over and above skin clearance between 90% and 100%, highlighting the importance of targeting PASI 100 as a treatment outcome for patients with psoriasis.

Trial Registration Number: NCT03536884.

Keywords: Biologics; Clinical trials; Psoriasis; Quality of life

Key Summary Points

Why carry out this study?

The introduction of newer biologic therapies has made the achievement of complete skin clearance an attainable goal for a growing number of patients.

Improvement of health-related quality of life (HRQoL) is a major objective in the management of psoriasis and should be considered alongside clinical efficacy parameters such as skin clearance.

In this analysis we evaluated how improvements in Psoriasis Area and Severity Index (PASI) responses, particularly at incremental improvements approaching complete skin clearance (PASI 100), translate into improvements in HRQoL and patient-perceived symptoms.

What was learned from the study?

Incremental PASI improvements corresponded with more patients achieving benefits in HRQoL and perceived symptoms, including at the highest levels of skin clearance between 90% (PASI 90) and 100% (PASI 100).

These findings indicate that patients can experience further benefits to HRQoL and perceived symptoms even beyond those achieved at the commonly used PASI 90 treatment goal and highlight the importance of complete skin clearance, or PASI 100, as a treatment outcome for patients with plaque psoriasis.

DIGITAL FEATURES

This article is published with digital features, including a video to facilitate understanding of the article. To view digital features for this article go to https://doi.org/10.6084/m9.figshare.26780089.

INTRODUCTION

Plaque psoriasis is a chronic, systemic, inflammatory skin disease resulting in debilitating physical symptoms, such as itchy, sore, painful, and scaly skin, and is associated with increased rates of psoriatic arthritis and cardiometabolic diseases [1, 2]. For patients with mild psoriasis,

topical agents, including corticosteroids, vitamin D analogues, and calcineurin inhibitors, as well as phototherapy, remain the mainstay of treatment, whilst for moderate to severe psoriasis biologics are recommended as the first-line treatment option [1]. Over the past 2 decades, there have been major advances in the treatment of plaque psoriasis; the introduction of newer biologic therapies, which target and modify the underlying dysregulated inflammatory response, has made the achievement of complete skin clearance (PASI 100; 100% improvement from baseline in Psoriasis Area and Severity Index) an attainable goal for a growing number of patients [3].

In addition to physical symptoms of psoriasis, patients can experience stigmatisation, embarrassment, and psychological strain, all of which impact their emotional well-being and overall health-related quality of life (HRQoL) [4]. The combination of physical and psychological impairment can accumulate over the course of patients' lives and may have a significant impact during critical periods, such as adolescence or early adulthood, when patients are consolidating their personality, establishing social contacts, and planning for higher education or their career [5, 6]. As a result, improvement of HRQoL is a major objective in the management of psoriasis and should be considered alongside clinical efficacy parameters such as skin clearance to provide a comprehensive view of treatment outcomes [4, 7–9]. Understanding the relationship between different levels of clinical response and HRQoL is important in determining whether psoriasis treatments that lead to physical disease control further translate into patient-perceived improvements in their daily life and well-being [4, 9].

Patient-reported outcome measures, such as the Dermatology Life Quality Index (DLQI), have been developed to assess HRQoL in patients with dermatological conditions. This measure, however, is not specific to psoriasis and may not fully capture all relevant aspects of patient experiences for this disease [10, 11]. Psoriasis-specific tools also exist, such as the Psoriasis Symptoms and Impacts Measure (P-SIM), a valid, reliable, well-defined patient-reported outcome tool that was developed to capture key signs, symptoms

(including itching, scaling, and skin pain), and impacts of psoriasis [9, 12].

A previous review has highlighted the advantages of complete skin clearance compared to high levels of efficacy without complete skin clearance; additional benefits of complete skin clearance included greater improvements in patient-reported symptoms of psoriasis, a higher proportion of symptom-free days, and significant improvements in HRQoL [3]. Furthermore, up to 95% of patients consider clear skin as a 'highly important' outcome of their treatment [13, 14]. This indicates the value of complete skin clearance to patients over other key treat-to-target outcomes, such as PASI 90 and absolute PASI ≤ 2 [8]. However, the exact relationship between very high levels of skin clearance and resulting improvements in HRQoL has not been described.

Here, we evaluated how improvements in PASI responses, in particular incremental improvements at very high levels of response between 90 and 100% improvement from baseline, translate into improvements in HRQoL and patient-perceived symptoms specific to psoriasis, irrespective of treatment received. We report analyses using data over up to 2 years from patients with moderate to severe plaque psoriasis from the BE RADIANT phase 3b clinical trial of bimekizumab, a dual inhibitor of IL-17A and IL-17F which has demonstrated substantial efficacy in treating psoriasis [15, 16].

METHODS

In this post hoc analysis, we used mixed-effects logistic regression models to assess the relationship between incremental improvements in skin clearance and improvements in HRQoL, irrespective of treatment received by patients. Inputs for the models were taken from all treatment arms of the BE RADIANT (NCT03536884) phase 3b trial of bimekizumab in psoriasis.

Patients

Data from the first 96 weeks of the BE RADIANT trial were analysed. Full inclusion and

exclusion criteria for BE RADIANT have been published previously [15, 16]. Eligible patients were ≥ 18 years of age with moderate to severe plaque psoriasis at baseline (defined as absolute PASI ≥ 12, body surface area [BSA] affected by psoriasis ≥ 10%, and Investigator's Global Assessment [IGA] score ≥ 3) and were eligible for systemic psoriasis therapy and/or phototherapy.

Study Design

The full study design for the 48-week double-blinded period of BE RADIANT, which compared bimekizumab versus secukinumab, and the first 48 weeks of its open-label extension (OLE), has been reported previously [15, 16]. Patients were initially randomised to bimekizumab or secukinumab. Patients randomised to bimekizumab received 320 mg dosed every 4 weeks (Q4W) to Week 16, then Q4W or every 8 weeks (Q8W) to Week 48; patients randomised to secukinumab received 300 mg weekly to Week 4, then Q4W to Week 48 (Fig. 1).

The OLE began at Week 48, in which all patients received open-label bimekizumab 320 mg dosed Q4W or Q8W. Dose frequency in the OLE was dependent on PASI response at Week 48 and treatment and dose frequency at the end of the double-blinded period. Following a protocol amendment, all patients receiving bimekizumab 320 mg Q4W were switched to bimekizumab Q8W at Week 64 or the next scheduled clinic visit.

Fig. 1 BE RADIANT study design. [a]SEC 300 mg was administered at baseline, Weeks 1, 2, 3, and 4, then Q4W for the remainder of the double-blinded treatment period; [b]re-randomisation at Week 16 was due to a protocol amendment; some patients had already passed Week 16 at the time of protocol amendment implementation; [c]following a protocol amendment, all patients receiving BKZ 320 mg Q4W in the OLE period were switched to BKZ 320 mg Q8W at Week 64 or the next scheduled clinic visit. *BKZ* bimekizumab, *OLE* open-label extension, *PASI 90* ≥ 90% improvement from baseline in Psoriasis Area and Severity Index, *Q4W* every 4 weeks, *Q8W* every 8 weeks, *SEC* secukinumab

The study was conducted in accordance with the principles of the Declaration of Helsinki and approved by an Independent Review Board and Independent Ethics Committee. All participants provided informed written consent.

Outcomes

The PASI is a clinician-evaluated tool commonly used to assess the severity of psoriasis, measuring the average redness, thickness, and scaliness of psoriatic lesions weighted by area of involvement [17]. PASI divides the body into four regions (head and neck, trunk, upper limbs, and lower limbs), which are individually scored before being combined to give the weighted overall score from 0 to 72 [18]. Relative PASI (the percentage improvement in PASI from baseline) is also used to define disease activity endpoints, such as PASI 100, which represents a 100% improvement in PASI from baseline, or complete skin clearance [8].

The DLQI consists of ten items asking patients questions regarding how their skin disease impacts various aspects of their daily life. Each item is scored by the patient from 0, indicating 'not at all' (all items) or 'not relevant' (items 3–10 only), to 3, indicating 'very much' or 'prevented' (item 7 only) [19]. In some cases, an item score of 'not relevant' may mean that the activity in question is not possible, sometimes due to severe disease, rather than there being no impact of disease on the activity. The DLQI ranges from 0–30, with a total score of 0 or 1 defined as 'no impact of skin disease on a patient's life' [20]. The DLQI, however, is not specific to psoriasis and aspects captured by each item may differ in terms of how burdensome they are to patients with psoriasis. Therefore, in addition to the total score, all item scores are considered individually in these analyses. DLQI Item 1 ('over the last week, how itchy, sore, painful, or stinging has your skin been') is specific to skin symptoms commonly seen in psoriasis and so was considered to be of particular relevance for analysis here.

The 14-item P-SIM is a novel, reliable, well-defined patient-reported outcome tool developed to capture key signs, symptoms, and life impacts specific to plaque psoriasis. Items are scored on an 11-point numeric rating scale from 0 to 10 by patients, with 0 meaning 'no sign, symptom, or impact' and 10 meaning 'very severe sign, symptom, or impact' [9, 12]. In the BE RADIANT trial, 3 of the 14 P-SIM items were assessed and are therefore reported in these analyses (itching, scaling, and skin pain). P-SIM items were scored based on symptoms experienced in the 24 h prior to the visit at which it was assessed. Data collection schedules are available in Table S1.

Statistical Analysis

We used mixed-effects logistic regression models to assess the relationship between skin clearance (measured via PASI) and achievement of DLQI 0/1, DLQI item scores of 0, or a score of 0 in P-SIM itching, scaling, and skin pain items. The models included PASI percentage change from baseline and baseline DLQI, DLQI item scores, or P-SIM item scores as covariates, respectively, with a patient-level random intercept to account for repeated observations at the patient level.

Data to be inputted into the models were first taken from all randomised patients pooled across all study visits up to Week 16, regardless of whether they were treated with bimekizumab or secukinumab. Models were also then run using data pooled across all study visits and treatments over 2 years (up to Week 96) for patients who received ≥ 1 dose of study treatment in the OLE. Model analyses used observed case data from the relevant patient population.

Using observed patient data, the models estimated the proportions of patients who achieve DLQI 0/1, DLQI item scores of 0, and a P-SIM score of 0 for the itching, scaling, and skin pain items at specific PASI improvement levels (e.g. PASI = 75%, PASI = 90%). The model estimates are presented here alongside 95% confidence intervals (CIs). In this report, PASI improvement levels correspond with discrete levels of PASI achievement rather than bands of improvement (e.g., when reporting results for PASI = 90%, this refers to exactly 90% improvement in PASI from baseline rather than ≥ 90% improvement).

Model estimates for proportions of patients achieving DLQI 0/1, DLQI item scores of 0, and P-SIM item scores of 0 were obtained with the value of the covariate corresponding to the baseline scores for each measure set equal to the baseline median for the respective population, therefore reflecting a typical patient enrolled in BE RADIANT and its OLE.

RESULTS

Patient Disposition and Baseline Characteristics

In BE RADIANT, 743 patients were randomised to treatment: 373 to bimekizumab and 370 to secukinumab. Mean and median DLQI were both 11.0; mean and median DLQI Item 1 scores were both 2.0. Mean and median baseline P-SIM scores were 6.7 and 7.0, respectively, for itching; 6.7 and 7.0 for scaling; and 4.6 and 5.0 for skin pain.

Six hundred and fifty-four of 743 randomised patients entered the OLE (336 bimekizumab-randomised; 318 secukinumab-randomised). Baseline DLQI and P-SIM scores for this group were similar to those for all randomised patients (Table 1).

DLQI 0/1 at Different PASI Improvement Levels

Using data pooled over 16 weeks, our model estimated the proportion of patients achieving DLQI 0/1 to be 93.0% (95% CI: 90.7%, 94.8%) with PASI 100, 89.3% (86.4%, 91.6%) with PASI = 95%, 83.8% (80.3%, 86.8%) with PASI = 90%, and 55.7% (49.6%, 61.6%) with PASI = 75% (Fig. 2A). Estimates were similar using data pooled over 2 years (Fig. 2B).

DLQI Item Scores = 0 at Different PASI Improvement Levels

DLQI Item 1 ('over the last week, how itchy, sore, painful, or stinging has your skin been')

is specific to skin symptoms commonly seen in psoriasis. Using data pooled over 16 weeks, our model estimated the proportion of patients achieving DLQI Item 1 = 0 to be 76.2% (95% CI: 71.9%, 80.0%) with PASI 100, 68.4% (63.9%, 72.5%) with PASI = 95%, 59.3% (54.7%, 63.8%) with PASI = 90%, and 31.0% (26.0%, 36.4%) with PASI = 75% (Fig. 3A). Estimates were similar using data pooled over 2 years (Fig. 3B).

At PASI = 75%, our model estimated proportions of patients achieving DLQI item scores of 0 were lowest for Items 1, 2 (embarrassment), and 4 (choice of clothing), indicating that these items are most burdensome to patients with psoriasis. The greatest increases in model estimates at higher PASI improvement levels were seen for these items too; estimates were consistently high for all other DLQI items, even at PASI = 75%, demonstrating that changes in achievement of DLQI 0/1 were driven by changes in scores for Items 1, 2, and 4 (Figure S1).

P-SIM Item Scores = 0 at Different PASI Improvement Levels

For the itching P-SIM item, large incremental improvements in model estimates for proportions of patients achieving P-SIM = 0 were seen at high levels of skin clearance, indicating the high importance of complete skin clearance for relief of itching in patients with psoriasis. Using data pooled across the first 16 weeks, our model estimated the proportion of patients achieving P-SIM = 0 to be 61.7% (95% CI: 56.0%, 67.1%) with PASI 100, 50.8% (45.3%, 56.2%) with PASI = 95%, 39.8% (34.8%, 45.1%) with PASI = 90%, and 14.8% (11.4%, 19.0%) with PASI = 75% (Fig. 4A). Using data pooled over up to 2 years, at higher levels of PASI improvement, estimated achievement of P-SIM = 0 for itching was numerically higher compared with data pooled over 16 weeks (Fig. 4B).

For scaling, our model estimated that the proportions of patients achieving P-SIM = 0 also saw large increases at the highest levels of skin clearance, with 82.2% (78.6%, 85.4%) achieving P-SIM = 0 with PASI 100, 72.3% (68.1%, 76.1%)

Table 1 Baseline characteristics

	BE RADIANT randomised patients[a] (N = 743)	BE RADIANT OLE patients[b] (N = 654)
Age (years), mean ± SD	45.0 ± 14.5	45.0 ± 14.4
Male, n (%)	486 (65.4)	436 (66.7)
White, n (%)	695 (93.5)	613 (93.7)
Weight (kg), mean ± SD	89.5 ± 20.7	89.7 ± 20.3
Duration of psoriasis (years), mean ± SD	17.8 ± 12.7	18.0 ± 12.6
PASI, mean ± SD	20.0 ± 7.1	19.9 ± 7.0
IGA score, n (%)		
3: Moderate	508 (68.4)	448 (68.5)
4: Severe	233 (31.4)	204 (31.2)
BSA (%), mean ± SD	24.3 ± 14.9	24.2 ± 14.8
DLQI, mean ± SD	11.0 ± 6.9	11.0 ± 7.0
DLQI, median	11.0	10.0
DLQI (Item 1), n (%)		
0	20 (2.7)	18 (2.8)
1	171 (23.0)	156 (23.9)
2	314 (42.3)	275 (42.0)
3	238 (32.0)	205 (31.3)
DLQI item scores, median		
1: Itchy, sore, painful, or stinging	2.0	2.0
2: Embarrassed	2.0	2.0
3: Shopping, gardening	1.0	1.0
4: Choice of clothing	2.0	2.0
5: Social or leisure activities	1.0	1.0
6: Sport	0.0	0.0
7: Prevent/problem with working or studying	0.0	0.0
8: Problems with partners or friends	1.0	1.0
9: Sexual difficulties	0.0	0.0
10: Treatment	1.0	1.0
P-SIM item score, mean ± SD		
Itching	6.7 ± 2.7	6.7 ± 2.8

Table 1 continued

	BE RADIANT randomised patients[a] (N = 743)	BE RADIANT OLE patients[b] (N = 654)
Scaling	6.7 ± 2.4	6.7 ± 2.4
Skin pain	4.6 ± 3.2	4.6 ± 3.2
P-SIM item score, median		
Itching	7.0	7.0
Scaling	7.0	7.0
Skin pain	5.0	5.0
Any prior systemic therapy, n (%)	540 (72.7)	478 (73.1)
Prior biologic therapy, n (%)	245 (33.0)	219 (33.5)

BSA body surface area, *DLQI* Dermatology Life Quality Index, *IGA* Investigator's Global Assessment, *OLE* open-label extension, *PASI* Psoriasis Area and Severity Index, *P-SIM* Psoriasis Symptoms and Impacts Measure, *Q4W* every 4 weeks, *Q8W* every 8 weeks, *SD* standard deviation

[a]Patients were initially randomised to bimekizumab 320 mg Q4W to Week 16, then Q4W or Q8W to Week 48, or to secukinumab 300 mg weekly to Week 4, then Q4W to Week 48

[b]BE RADIANT OLE patients completed the double-blinded maintenance treatment period and received ≥ 1 dose of bimekizumab treatment in the OLE

with PASI = 95%, 59.5% (54.9%, 63.8%) with PASI = 90%, and 20.7% (16.7%, 25.4%) with PASI = 75% (Fig. 5A); at higher PASI improvement levels, estimates using data pooled over 2 years were numerically higher than the 16-week estimates, although the difference was smaller than observed with the itching item (Fig. 5B).

For skin pain, improvements in estimated proportions of patients achieving P-SIM = 0 were also seen with incremental improvements in skin clearance, although these estimates were consistently higher than for the itching and scaling items using both data pooled over 16 weeks and 2 years (Fig. 6).

DISCUSSION

In these analyses, we showed that incremental improvements in skin clearance at the highest levels of PASI improvement between 90 and 100% translated into additional benefits in HRQoL and patient-perceived symptoms specific to psoriasis, with the greatest benefits seen with complete skin clearance (PASI 100), using estimates from mixed-effects logistic regression models looking across all treatment arms in BE RADIANT.

Moderate incremental improvements in model estimates for the attainment of DLQI 0/1 (no impact on patient's life) were seen at the highest levels of skin clearance between 90% and 100%, using data pooled over both 16 weeks and 2 years. These results are in line with previous studies, indicating that complete skin clearance is highly valued by patients over and above near-complete skin clearance for its impact on HRQoL. Indeed, incremental improvement from near-complete (PASI 90–< 100) to complete skin clearance (PASI 100) has previously been demonstrated to result in 11%–18% differences in proportions of patients reporting DLQI 0/1 [21, 22].

The DLQI is not specific to psoriasis, and for many of the items analysed here, estimated proportions of patients with DLQI item score = 0 were high regardless of PASI improvement level. Meanwhile, estimated proportions of patients achieving scores of 0 for DLQI Items 1, 2, and 4, considered of particular relevance for
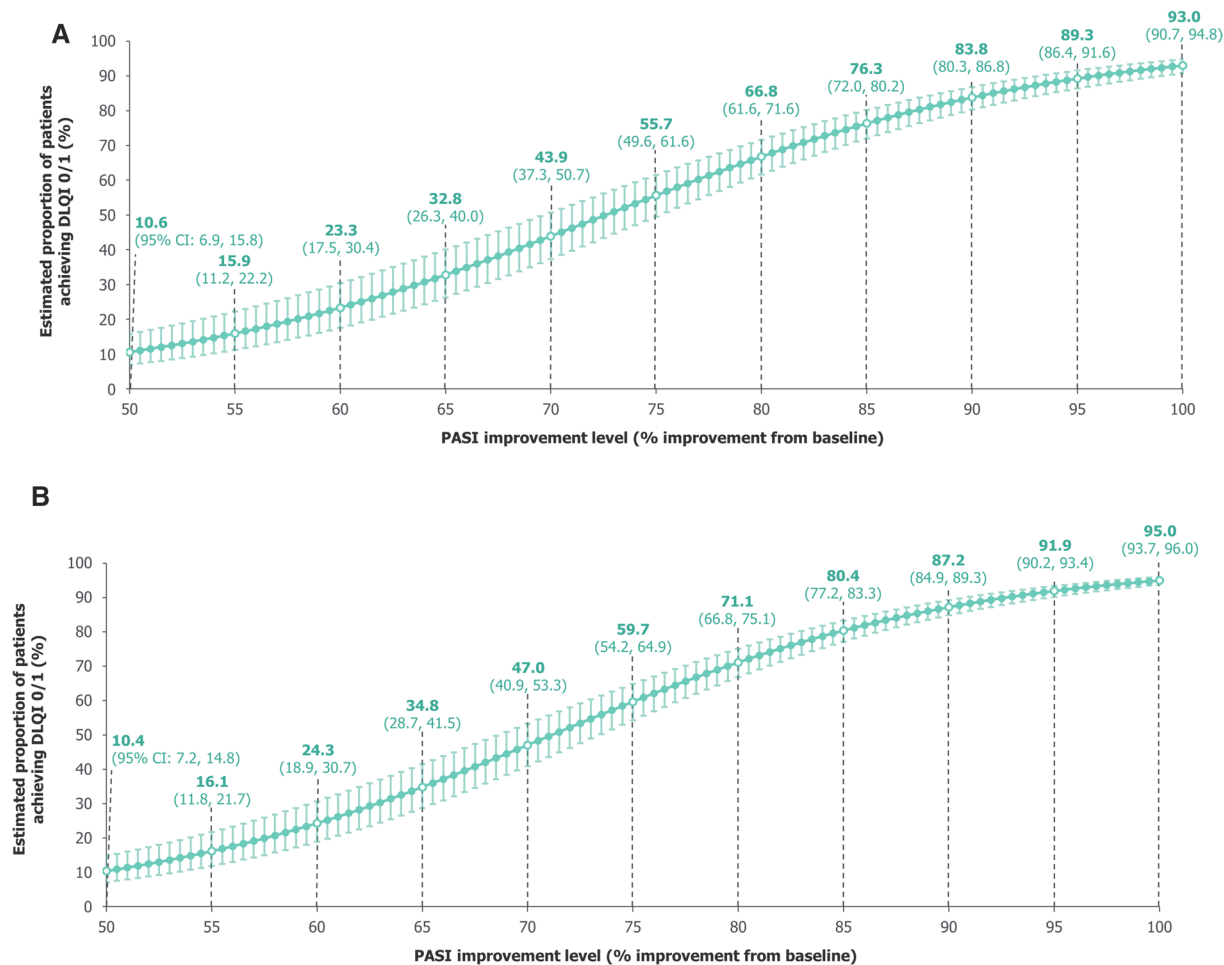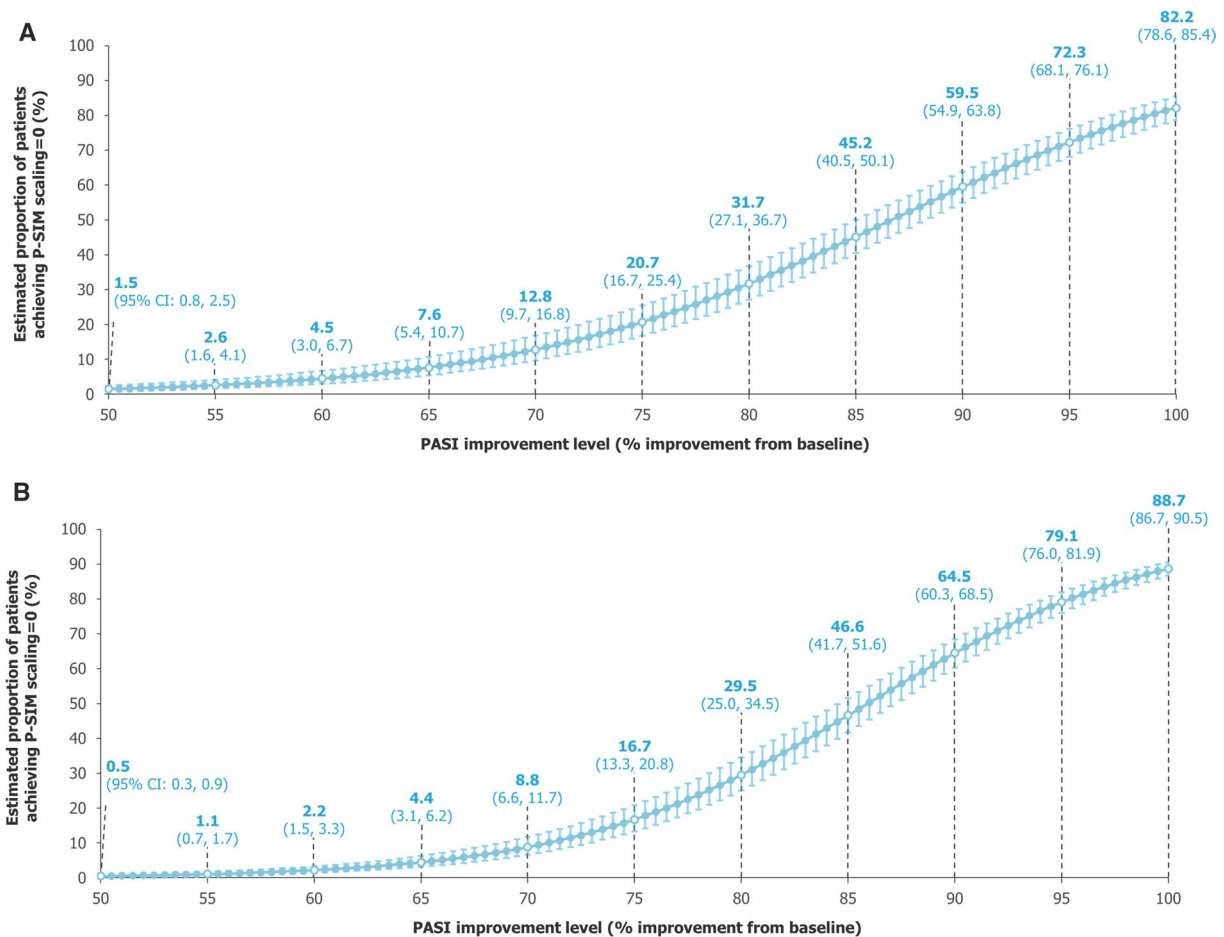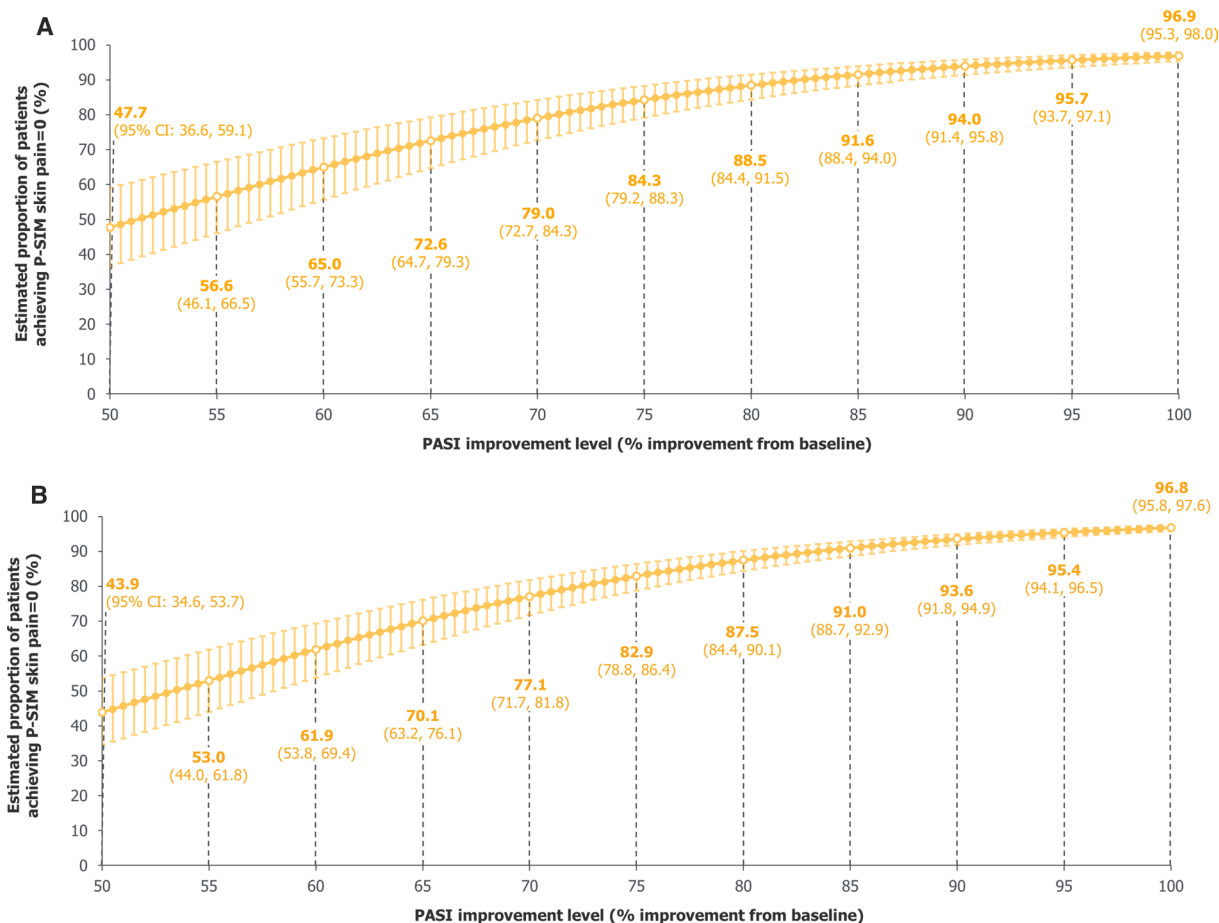
Fig. 2 Model-estimated proportions of patients achieving DLQI 0/1. **A** Over 16 weeks. **B** Over 2 years. A mixed-effects logistic regression model used data pooled across all trial visits and treatments over **A** 16 weeks and **B** 2 years of BE RADIANT to estimate the proportions of patients achieving DLQI 0/1 at specific PASI improvement levels. Error bars correspond to 95% CIs. The curves correspond to model estimates calculated with baseline DLQI equal to the baseline median for the respective populations (16 weeks: 11.0 [all randomised patients]; 2 years: 10.0 [patients who entered the OLE]). *CI* confidence interval, *DLQI* Dermatology Life Quality Index, *OLE* open-label extension, *PASI* Psoriasis Area and Severity Index

psoriasis, substantially increased at higher PASI improvement levels. Importantly, these results indicate that Items 1, 2, and 4 have the highest impact on changes to HRQoL for patients with psoriasis. DLQI Item 1 (itchy, sore, painful, or stinging skin) had the greatest incremental improvements at higher PASI improvement levels; however, even with complete skin clearance (PASI 100), the model-estimated proportion of patients reporting no symptom impact was 76.2%, indicating that about a quarter of patients still report itching, soreness, pain, or stinging despite clear skin, in line with the P-SIM itching item results reported here and DLQI results in other studies [23].

Although 60%–75% of patients were estimated by our model to achieve itch resolution alongside complete skin clearance, estimated proportions of patients achieving P-SIM = 0 for the itching item were relatively low at high PASI improvements compared with other items, aligned with the high baseline scores
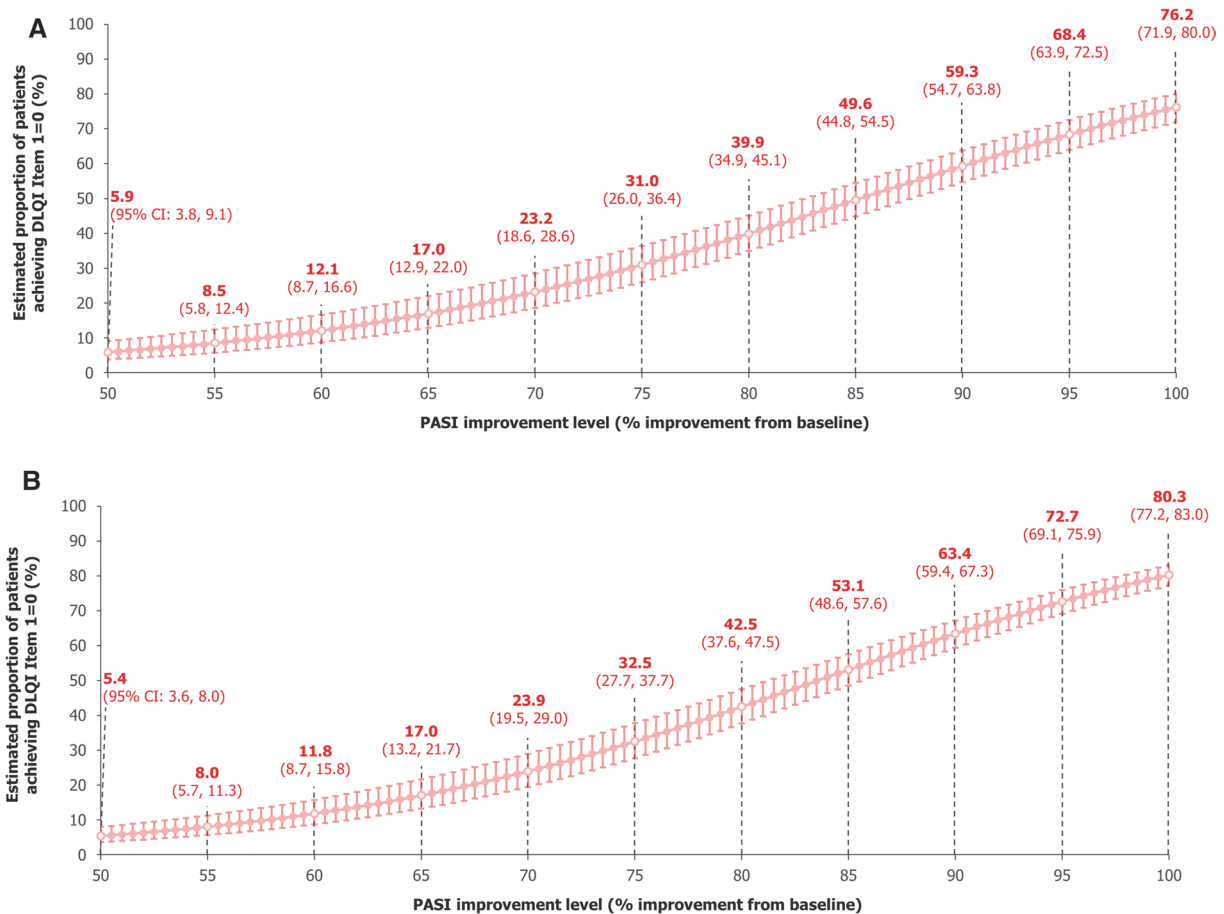
Fig. 3 Model-estimated proportions of patients achieving DLQI Item 1 (itchy, sore, painful, or stinging skin)[a] = 0. **A** Over 16 weeks. **B** Over 2 years, a mixed-effects logistic regression model used data pooled across all trial visits and treatments over **A** 16 weeks and **B** 2 years of BE RADIANT to estimate the proportions of patients achieving DLQI Item 1 = 0 at specific PASI improvement levels. Error bars correspond to 95% CIs. The curves correspond to model estimates calculated with baseline DLQI Item 1 score equal to the baseline median for the respective populations (16 weeks: 2.0 [all randomised patients]; 2 years: 2.0 [patients who entered the OLE]). [a]Question: 'over the last week, how itchy, sore, painful, or stinging has your skin been'; answer: 'not at all' (0), 'a little' (1), 'a lot' (2), or 'very much' (3). *CI* confidence interval, *DLQI* Dermatology Life Quality Index, *OLE* open-label extension, *PASI* Psoriasis Area and Severity Index

in this item. The large increases in estimated proportions achieving P-SIM = 0 observed with incremental PASI improvements are consistent with previous reports that itching is the most important factor contributing to disease severity for patients [24]. Furthermore, using 2-year pooled data including later visits where subjects may have had sustained periods of skin clearance, higher estimated proportions achieving P-SIM = 0 for itching with complete skin clearance were reported compared with 16-week pooled data (75.6% vs 61.7%). Nevertheless, these data suggest that residual itching persists over time, even with complete skin clearance, in about 25% of patients. Future research should explore why itching persists in some patients even after complete skin clearance is achieved and seek granularity on the sub-components of itching that persist.

For the skin pain P-SIM item, the curves produced from the model estimates were flatter and consistently higher than those for itching or
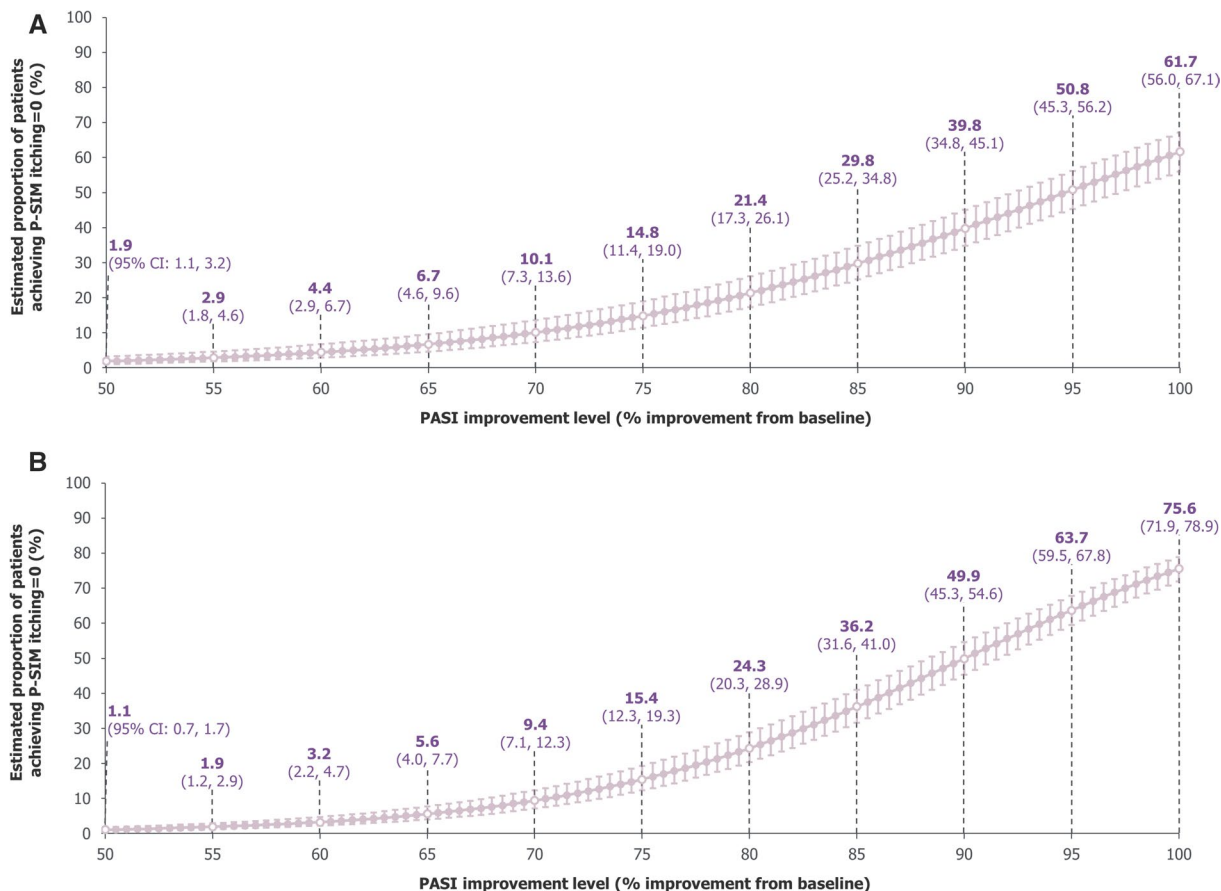
Fig. 4 Model-estimated proportions of patients achieving P-SIM itching = 0. **A** Over 16 weeks. **B** Over 2 years. A mixed-effects logistic regression model used data pooled across all trial visits and treatments over **A** 16 weeks and **B** 2 years of BE RADIANT to estimate the proportions of patients achieving P-SIM itching = 0 at specific PASI improvement levels. Error bars correspond to 95% CIs. The curves correspond to model estimates calculated with baseline P-SIM itching score equal to the baseline median for the respective populations (16 weeks: 7.0 [all randomised patients]; 2 years: 7.0 [patients who entered the OLE]). *CI* confidence interval, *OLE* open-label extension, *PASI* Psoriasis Area and Severity Index, *P-SIM* Psoriasis Symptoms and Impacts Measure

scaling, potentially owing to the lower median score at baseline, which was used in the model to calculate the estimates. This ultimately suggests that, for a typical patient in these populations, pain was less burdensome than itching or scaling; hence, the level of skin clearance at which patients are estimated to experience no effect of the symptom was lower. This may be due to pain resulting more directly from inflammation rather than skin symptoms themselves; however, it is acknowledged that skin pain is complex and poorly defined [25] and requires further investigation to understand the differential quantitative and qualitative attributes that define pain.

PASI 90 has become widely accepted as the current universal treatment goal in psoriasis [26]. The ability of novel biologics such as bimekizumab to provide rapid, complete skin clearance, which is maintained with long-term use, represents an opportunity to raise treatment expectations for patients with psoriasis. Bimekizumab has previously demonstrated superior efficacy versus placebo, secukinumab, adalimumab, and ustekinumab in phase 3/3b trials. In these trials, bimekizumab treatment also led to greater proportions of patients

Fig. 5 Model-estimated proportions of patients achieving P-SIM scaling = 0. **A** Over 16 weeks. **B** Over 2 years. A mixed-effects logistic regression model used data pooled across all trial visits and treatments over **A** 16 weeks and **B** 2 years of BE RADIANT to estimate the proportions of patients achieving P-SIM scaling = 0 at specific PASI improvement levels. Error bars correspond to 95% CIs. The curves correspond to model estimates calculated with baseline P-SIM scaling score equal to the baseline median for the respective populations (16 weeks: 7.0 [all randomised patients]; 2 years: 7.0 [patients who entered the OLE]). *CI* confidence interval, *OLE* open-label extension, *PASI* Psoriasis Area and Severity Index, *P-SIM* Psoriasis Symptoms and Impacts Measure

achieving PASI 100 at Week 16 versus placebo- (68.2% vs 1.2%), secukinumab- (61.7% vs 48.9%), adalimumab- (60.8% vs 23.9%), and ustekinumab-treated patients (58.6% vs 20.9%), respectively (non-responder imputation [NRI]) [16, 27–29]. These high levels of skin clearance have been demonstrated to be durable over 3 years [30]. Taken together with the data presented here, this suggests that higher treatment goals, including PASI 100, could be used routinely in clinical practice to

provide additional benefits for patients with psoriasis.

The large sample size, using model estimates with up to 2 years of data, represents a strength of this study. Additionally, the modelling approaches used here were relatively simple, aiding ease of interpretation of the results. However, this simplicity may not provide as good a fit as other, more complex models. Limitations of these analyses include that data were not equally available for each incremental level of PASI improvement; greater availability

Fig. 6 Model-estimated proportions of patients achieving P-SIM skin pain = 0. **A** Over 16 weeks. **B** Over 2 years. A mixed-effects logistic regression model used data pooled across all trial visits and treatments over **A** 16 weeks and **B** 2 years of BE RADIANT to estimate the proportions of patients achieving P-SIM skin pain = 0 at specific PASI improvement levels. Error bars correspond to 95% CIs. The curves correspond to model estimates calculated with baseline P-SIM skin pain score equal to the baseline median for the respective populations (16 weeks: 5.0 [all randomised patients]; 2 years: 5.0 [patients who entered the OLE]). *CI* confidence interval, *OLE* open-label extension, *PASI* Psoriasis Area and Severity Index, *P-SIM* Psoriasis Symptoms and Impacts Measure

of data at high levels of PASI improvement may have impacted the strength of the trend seen here. Furthermore, the 2-year analyses only included patients who entered the OLE as opposed to all randomised patients in the 16-week analyses; patients who responded less well to study treatments may have opted not to enrol in the OLE, and patients remaining in the study into the OLE may have been more likely to report higher levels of skin clearance, contributing to the unequal distribution of data for different PASI response levels; this patient population may also reflect patients who are more optimistic that their disease will improve, which may lead to higher rates of patient-reported benefits to their HRQoL and perceived symptoms. Moreover, these models made predictions with the covariate corresponding to the baseline score of the outcome measure set equal to the baseline median, therefore reflecting a typical patient enrolled in BE RADIANT and its OLE in terms of their perceived symptoms and HRQoL at baseline. As such, these

findings may be limited in their generalisability to real-world populations because of stringent patient eligibility criteria.

CONCLUSION

Incremental PASI improvements corresponded with more patients achieving benefits in HRQoL and perceived symptoms; this trend was seen at the highest levels of skin clearance between 90 and 100%, indicating that patients can experience further benefits in HRQoL and patient-perceived symptoms beyond those achieved at the commonly used PASI 90 treatment goal. These findings highlight the importance of complete skin clearance, or PASI 100, as a treatment outcome for patients with plaque psoriasis to achieve the greatest benefits to HRQoL and perceived symptoms.

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Ethical Approval. The study was conducted in accordance with the principles of the Declaration of Helsinki and approved by an Independent Review Board and Independent Ethics Committee. All participants provided informed written consent.

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