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### Assessing clinical response and defining minimal disease activity in plaque psoriasis with the Physician Global Assessment and body surface area (PGA × BSA) composite tool: An analysis of apremilast phase 3 ESTEEM data



To the Editor: The product of Physician Global Assessment (PGA) and body surface area (BSA) (PGA × BSA) is a simple tool for assessing psoriasis severity and clinical response to treatment. PGA × BSA scores have demonstrated sensitivity to therapeutic change and concordance with Psoriasis

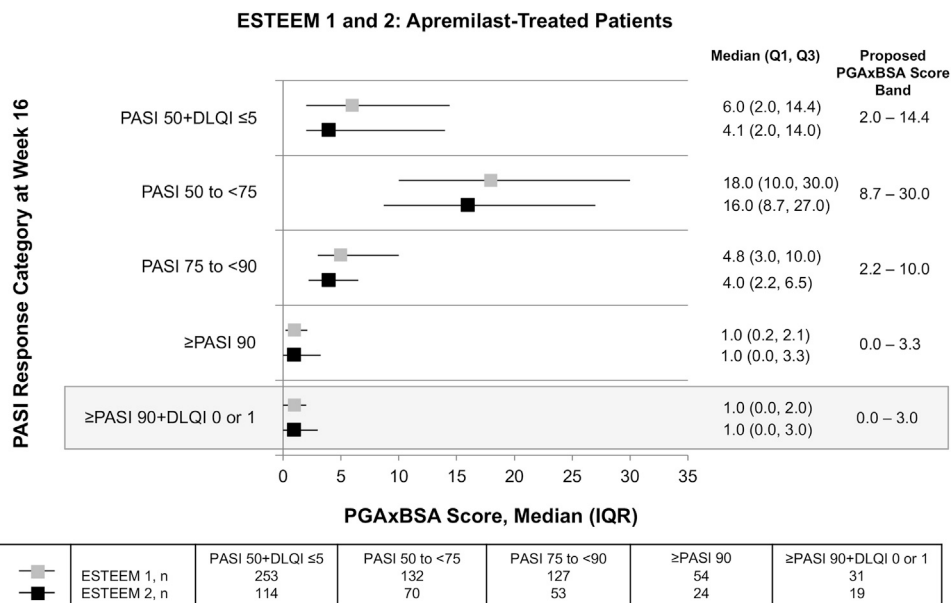
Area and Severity Index (PASI)-based clinical response.<sup>1,2</sup>

We report the results of a post hoc analysis of data from the ESTEEM 1 and 2 trials that defines bands and minimal disease activity (MDA) for the PGA × BSA scale using accepted PASI and Dermatology Life Quality Index (DLQI) response categories as anchors. The analyses were performed with week 16 data, as observed and sufficient for evaluation with no imputation for missing values, from 836 patients who were randomized to receive apremilast, 30 mg twice daily, at baseline in ESTEEM 1 (N = 562) and ESTEEM 2 (N = 274).<sup>3,4</sup> Detailed study design and assessment procedures have been published.<sup>2-4</sup> Patients provided written informed consent before study-related procedures were performed, and the protocol and consent were approved by institutional review boards or ethics committees at all investigational sites. The studies were conducted in accordance with the principles of Good Clinical Practice and the Declaration of Helsinki.

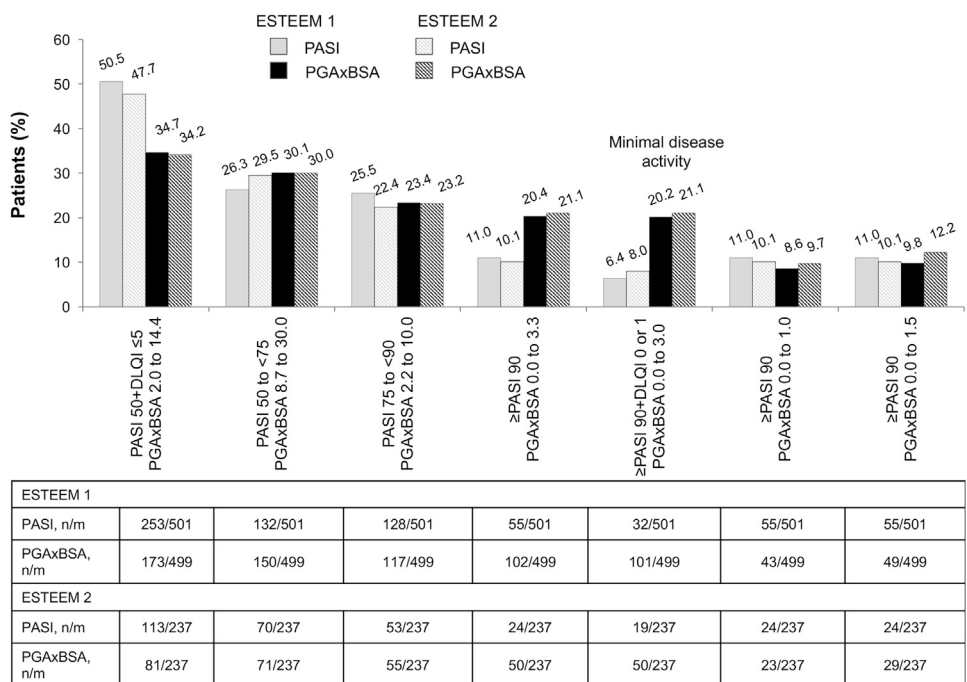
Mean percent change in PGA × BSA was significantly correlated with percent change in PASI (*r* range, 0.915-0.943; all *P* < .001) and mean change in DLQI (*r* range, 0.303-0.407; all *P* < .008), regardless of baseline PASI score category (12-19 or ≥20).

The PGA × BSA absolute median and interquartile range (IQR) scores observed in subgroups of patients who achieved PASI and/or DLQI “anchor” responses (eg, PASI 90 or PASI 90 plus DLQI score of 0 or 1 [PASI 90+DLQI 0 or 1]) at week 16 are illustrated in Fig 1. With increasing levels of clinical improvement as defined by PASI or PASI/DLQI response, median (IQR) PGA × BSA scores decreased in a distinct stepwise fashion.

To establish reproducibility of the proposed bands, the defined PGA × BSA IQR score ranges were subsequently used as treatment target values, and response rates were determined. These PGA × BSA response rates were generally similar to those observed with the corresponding PASI or PASI/DLQI anchors, particularly for the most widely achieved PASI response categories (PASI 50 to <75 and PASI 75 to <90) (Fig 2). Discrepant response rates, however, were observed for the proposed PGA × BSA MDA criterion of 3 or lower versus the corresponding anchor of PASI 90+DLQI 0 or 1 for ESTEEM 1 (20.2% vs 6.4%) and ESTEEM 2 (21.1% vs 8.0%) (Fig 2). Additional ad hoc analyses demonstrated that when a PGA × BSA MDA of 1 or lower or 1.5 or lower was used, the response rates better aligned with those for PASI 90 and PASI 90+DLQI 0 or 1.



**Fig 1.** Product of Physician Global Assessment (PGA) and body surface area (BSA) (PGA × BSA) (median [interquartile range (IQR)]), by Psoriasis Area and Severity Index (PASI) response category at week 16. Boxes indicate PGA × BSA median; horizontal lines indicate IQR (quarter 1 [Q1], Q3). *DLQI*, Dermatology Life Quality Index; *PASI 50*, 50% or greater reduction from baseline in PASI score; *PASI 75*, 75% or greater reduction from baseline in PASI score; *PASI 90*, 90% or greater reduction from baseline in PASI score.



**Fig 2.** Patients (%) achieving response at week 16, by Psoriasis Area and Severity Index (PASI) or product of Physician Global Assessment (PGA) and body surface area (BSA) (PGA × BSA) criteria in ESTEEM 1 and ESTEEM 2. *DLQI*, Dermatology Life Quality Index; *n/m*, number of patients achieving response/total number of patients with evaluable data; *PASI 50*, 50% or greater reduction from baseline in PASI score; *PASI 75*, 75% or greater reduction from baseline in PASI score; *PASI 90*, 90% or greater reduction from baseline in PASI score.

The proposed PGA × BSA MDA score of 1.0 or lower may be appropriate for patients who wish to achieve complete or nearly complete skin clearance, whereas higher PGA × BSA bands may be appropriate for patients with psoriasis who report good quality of life despite some remaining skin involvement.

In sum, these findings show that the PGA × BSA composite tool can be used to measure clinical response and to assess MDA in patients with psoriasis. The current post hoc banding analysis, using PASI and DLQI response categories as clinically relevant “anchors,” identified PGA × BSA bands that provide clinically useful criteria for treat-to-target strategies. Because ESTEEM enrolled only patients with moderate to severe plaque psoriasis, the criteria require further investigation in patients with all levels of psoriasis severity. Recently, the PGA × BSA composite tool was successfully used to assess efficacy of apremilast in patients with moderate disease (BSA 5% to 10%).<sup>5</sup>

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