BMS-986165, an Oral, Selective TYK2 Inhibitor, in the Treatment of Moderate to Severe Psoriasis as Assessed by the Static Physician's Global Assessment (sPGA)/Body Surface Area (BSA) Composite Tool (sPGA×BSA), a Clinically Useful Alternative to PASI

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Introduction

- The Psoriasis Area and Severity Index (PASI), sPGA, and percentage of BSA involvement are all instruments for the assessment of disease activity in psoriasis, although each has limitations[1,2]
  - PASI is a composite measure requiring a complex multistep formula that restricts its routine use in the clinic; the sPGA assesses erythema, desquamation, and induration of psoriatic plaques independent of the extent of BSA involved with the lesions, while the BSA does not assess the severity of psoriatic lesions[1,2]
- Several studies have shown that measures that combine some form of investigator global assessment with BSA, such as the product of sPGA and BSA (sPGA×BSA), strongly correlate with PASI in the assessment of moderate to severe psoriasis[2-5]
- Tyrosine kinase 2 (TYK2) activates intracellular signal transducer and activator of transcription (STAT)-dependent signaling pathways of specific cytokines, including interleukin (IL)-23, IL-12, and Type I interferons, that are involved in the pathogenesis of psoriasis and other immune-mediated disorders[6-10]
- BMS-986165 is an oral, selective TYK2 inhibitor with a unique mode of binding to the regulatory pseudokinase domain of the enzyme, which provides high functional selectivity for TYK2, rather than the active kinase domain targeted by other tyrosine kinase inhibitors[7,11]
- In a 12-week, Phase 2 trial (NCT02931838) in adults with moderate to severe plaque psoriasis, BMS-986165 demonstrated a dose-dependent improvement in PASI 75 response and a favorable safety profile[12]
  - At Week 12, PASI 75 responses were highest (67–75%) at doses from 3 mg twice daily (BID) up to 12 mg once daily (QD) versus placebo (7%; *P*<0.001; primary endpoint)

Objective

- This post hoc analysis of the Phase 2 trial evaluated the composite sPGA×BSA score compared with PASI score to assess clinical response to BMS-986165 in patients with moderate to severe plaque psoriasis

Methods

Patient population and study design

- The Phase 2 trial included adult patients with plaque psoriasis for ≥6 months and a body mass index of 18–40 kg/m^2 who were eligible for phototherapy or systemic therapy and had moderate to severe disease as defined by affected BSA ≥10%, PASI score ≥12, and sPGA score ≥3[12]
- Patients were randomized to 1 of 5 oral doses of BMS-986165 (3 mg every other day, 3 mg QD, 3 mg BID, 6 mg BID, 12 mg QD) or placebo[12]
- The treatment period was 12 weeks, with an additional 30-day off-treatment follow-up period for safety[12]

Efficacy assessments and outcomes

- Key efficacy assessments included PASI, sPGA, BSA, and the Dermatology Life Quality Index (DLQI) questionnaire
  - The primary endpoint was PASI 75 at Week 12
- Percentage mean change from baseline to Week 12 in sPGA×BSA and PASI score was assessed for the placebo group and all BMS-986165 dose groups
- Spearman correlation coefficients were used to assess the relationship between sPGA×BSA and PASI or DLQI scores at Week 12, as well as between percentage change from baseline in sPGA×BSA and PASI or DLQI scores at Week 12 for all treatment groups. Agreement was based on concordance rates
- The proportion of patients achieving 75% improvement in sPGA×BSA (sPGA×BSA 75) or achieving PASI 75 and the percent improvement from baseline in PASI or sPGA×BSA were calculated for patients receiving placebo and for the combined group of patients receiving doses of BMS-986165 that were most effective (≥3 mg BID)

Results

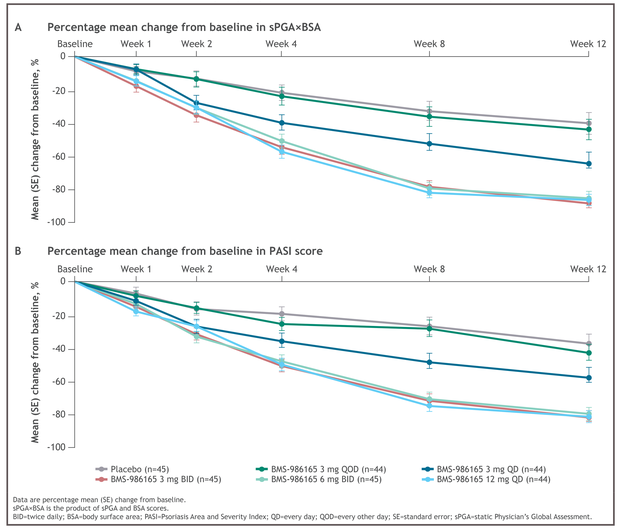
Patient population

- This post hoc analysis included all 267 patients who were randomized and treated in the Phase 2 trial
- Patient demographics and baseline disease characteristics were generally similar across treatment groups[12]

Outcomes

- The trend in percentage mean change from baseline to Week 12 across all BMS-986165 treatment groups and the placebo group was similar for sPGA×BSA (**Figure 1A**) and PASI (**Figure 1B**)

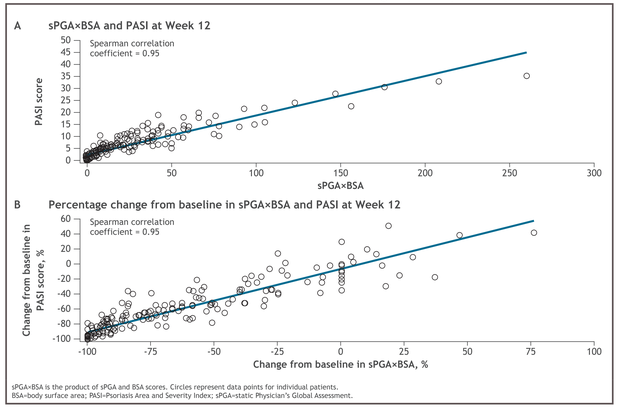
Figure 1. Percentage mean change from baseline by visit in (A) sPGA×BSA and (B) PASI score in patients with moderate to severe plaque psoriasis treated with BMS-986165 or placebo (N=267)



Data are percentage mean (SE) change from baseline.
sPGA×BSA is the product of sPGA and BSA scores.
BID=twice daily; BSA=body surface area; PASI=Psoriasis Area and Severity Index; QD=every day; QOD=every other day; SE=standard error; sPGA=static Physician's Global Assessment.

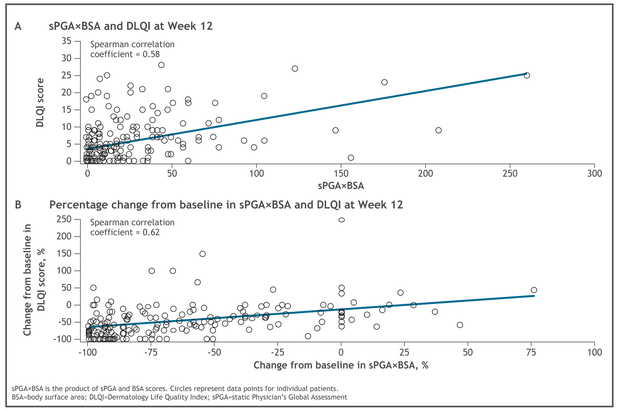
- At Week 12 there was a strong correlation between sPGA×BSA and PASI (**Figure 2A**; Spearman correlation coefficient = 0.95) and between percent change from baseline in sPGA×BSA and PASI (**Figure 2B**; Spearman correlation coefficient = 0.95)
- At Week 12 there was a moderate correlation between sPGA×BSA and DLQI (**Figure 3A**; Spearman correlation coefficient = 0.58) and between percent change from baseline in sPGA×BSA and DLQI (**Figure 3B**; Spearman correlation coefficient = 0.62)
- A similar proportion of patients achieved sPGA×BSA 75 and PASI 75 at Week 12 (**Figure 4A**)
- The percent improvement from baseline to Week 12 for BMS-986165 (≥3 mg BID dose groups combined) and placebo was similar for sPGA×BSA and PASI (**Figure 4B**)

Figure 2. Correlation between (A) sPGA×BSA and PASI and (B) percentage change from baseline in sPGA×BSA and PASI at Week 12 for all BMS-986165 treatment groups and placebo (N=267)



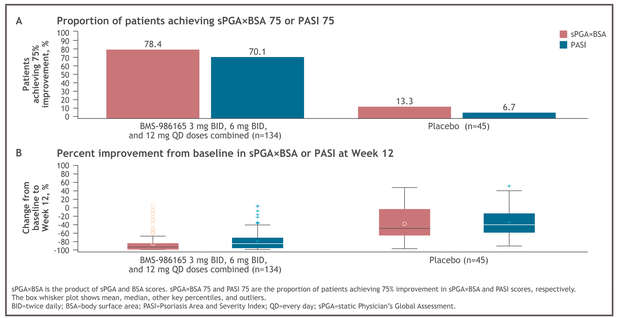
sPGA×BSA is the product of sPGA and BSA scores. Circles represent data points for individual patients.
BSA=body surface area; PASI=Psoriasis Area and Severity Index; sPGA=static Physician's Global Assessment.

Figure 3. Correlation between (A) sPGA×BSA and DLQI and (B) percentage change from baseline in sPGA×BSA and DLQI at Week 12 for all BMS-986165 treatment groups and placebo (N=267)



sPGA×BSA is the product of sPGA and BSA scores. Circles represent data points for individual patients.
BSA=body surface area; DLQI=Dermatology Life Quality Index; sPGA=static Physician's Global Assessment

Figure 4. (A) Proportion of patients achieving 75% improvement and (B) percent improvement from baseline in sPGA×BSA or PASI scores at Week 12 for the combined group of patients receiving the 3 most effective BMS-986165 doses (3 mg BID, 6 mg BID, and 12 mg QD) (n=134) vs placebo (n=45)



sPGA×BSA is the product of sPGA and BSA scores. sPGA×BSA 75 and PASI 75 are the proportion of patients achieving 75% improvement in sPGA×BSA and PASI scores, respectively. The box whisker plot shows mean, median, other key percentiles, and outliers.
BID=twice daily; BSA=body surface area; PASI=Psoriasis Area and Severity Index; QD=every day; sPGA=static Physician's Global Assessment.

Conclusions

- The sPGA×BSA offers more information on the nature of a patient's disease — ie, on plaque quality and severity as well as BSA — than either measure alone. Cutoffs defining minimal disease activity for sPGA×BSA have been published[13]
- In patients with moderate to severe psoriasis treated with BMS-986165 or placebo for 12 weeks, similar trends were observed for sPGA×BSA and PASI for all measures evaluated, including percentage mean change and percent improvement from baseline and the proportion of patients achieving sPGA×BSA 75 or PASI 75
- There was a strong correlation between sPGA×BSA and PASI score at Week 12 for all BMS-986165 treatment groups and placebo, and a moderate correlation was observed between sPGA×BSA and DLQI score
- These data further support sPGA×BSA as a simple, accurate, and convenient alternative to PASI that can be used in both clinical trial and practice settings[2-5]

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