An oral, selective tyrosine kinase 2 inhibitor, BMS-986165, improves quality of life in psoriasis: results from a Phase 2 study

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INTRODUCTION

- Psoriasis is a chronic immune-mediated disease, which impairs patients' physical health and worsens their health-related quality of life (QoL).[1–3]
- Improvement in health-related QoL, as measured by the Dermatology Life Quality Index (DLQI),[4] is an important patient-reported outcome in psoriasis trials.
  - The DLQI questionnaire includes 10 questions on how much the skin problem affected life over the previous week.
  - DLQI overall (total) scores range from 0 to 30, with higher scores indicating worse health-related QoL.[4]
- BMS-986165 is an oral, selective inhibitor of tyrosine kinase 2, an intracellular kinase that activates cytokine signaling pathways of interleukin-23 and Type I interferons that are central in the pathophysiology of psoriasis[5,6] and other immune-mediated disorders.[7,8]
- In a 12-week, placebo-controlled, Phase 2 trial (NCT02931838), BMS-986165 was effective and demonstrated acceptable safety in patients with moderate to severe plaque psoriasis.[9]
  - With BMS-986165 at doses ⩾3 mg twice daily (BID), 67–75% of patients achieved Psoriasis Area and Severity Index (PASI) 75 at Week 12 (primary endpoint), versus 7% of those treated with placebo ($P<0.001$).
  - PASI 75 and PASI 90 responses were similar in the highest dose groups (3 mg BID, 6 mg BID, 12 mg once daily [QD]), providing the rationale for combining data from these 3 groups in subsequent analyses.[9]

OBJECTIVE

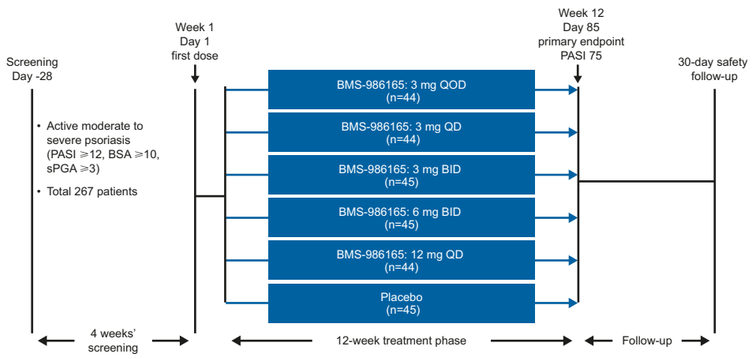
- To evaluate:
  - DLQI responses, both overall and for individual questions, and
  - the time course of DLQI improvements and PASI or static Physicians Global Assessment (sPGA) score of 0 or 1 (0/1) responses

METHODS

Study design, endpoints, and patients

- In this Phase 2 trial, adults with moderate to severe plaque psoriasis were randomized equally to receive 1 of 5 BMS-986165 doses or placebo for 12 weeks (Figure 1).

Figure 1: Study design.



BID=twice daily; BSA=body surface area; PASI=Psoriasis Area and Severity Index; QD=every day; QOD=every other day; sPGA=static Physician Global Assessment.

Analysis of DLQI score

- The proportion of patients achieving DLQI overall score 0/1, indicative of no impact on the patient's health-related QoL,[10] over time to Week 12 was calculated.
- Changes from baseline in DLQI overall score over time to Week 12 were computed.
  - For patients with DLQI overall scores ⩾2 at baseline, scores of 0/1 to individual questions on the 10-question DLQI form (each scored 0–3) were analyzed.
  - In addition, scores of 0 for Question 1 were analyzed in a similar fashion.
- A score of 0 on DLQI Question 1 reflects the effect of the most relevant symptoms of psoriasis (itching, soreness, skin pain, and stinging) on health-related QoL.
- Time courses of PASI 75, PASI 90, sPGA 0/1, and DLQI were analyzed.

RESULTS

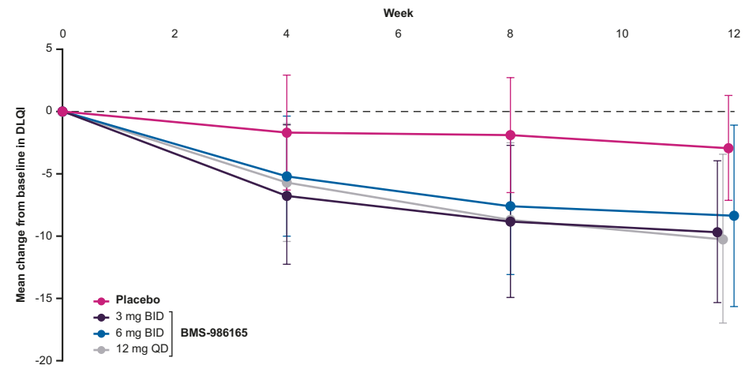
Patients

- Overall, 267 patients were randomized and treated in this study, and 224 (84%) completed the 12-week treatment period.
  - 134 patients were included in the 3 highest dose groups, 3 mg BID (n=45), 6 mg BID (n=45), and 12 mg QD (n=44), which had similar PASI responses; 45 patients were included in the placebo group.
- Patient demographics and disease characteristics, including baseline DLQI scores, were generally comparable across treatment groups.[9]
  - Baseline mean (standard deviation) DLQI scores were as follows: placebo: 12.6 (7.1); 3 mg BID: 12.5 (5.5); 6 mg BID: 11.3 (6.5); 12 mg QD: 13.0 (7.4).

Improvement in the overall DLQI score and individual DLQI questions over time

- Change from baseline over time to Week 12 in the overall DLQI scores were more pronounced with the higher doses of BMS-986165 versus placebo (Figure 2).

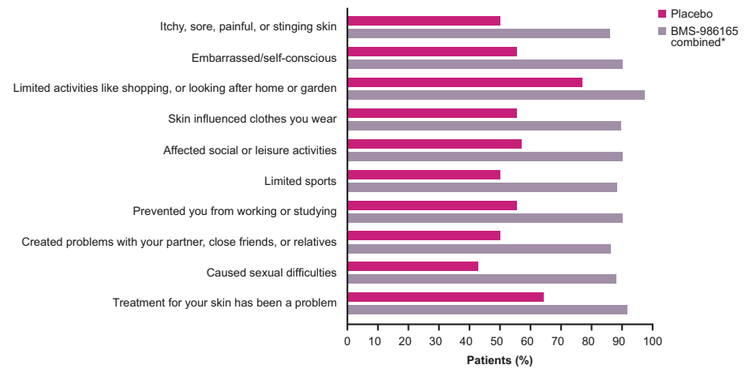
Figure 2: Mean change from baseline in DLQI overall score over time.



Error bars represent SD.
BID=twice daily; DLQI=Dermatology Life and Quality Index; QD=every day; SD=standard deviation.

- In patients with a baseline DLQI score of ⩾2 for an individual question, 85.7–97.4% in the combined dose group versus 42.9–76.9% in the placebo group improved to a score of 0/1 for that question at Week 12 (Figure 3).

Figure 3: Frequency of patients with response of 0/1 on individual DLQI questions at Week 12 among those with response of ⩾2 for that question at baseline (from patients who had DLQI overall score ⩾2 at baseline).

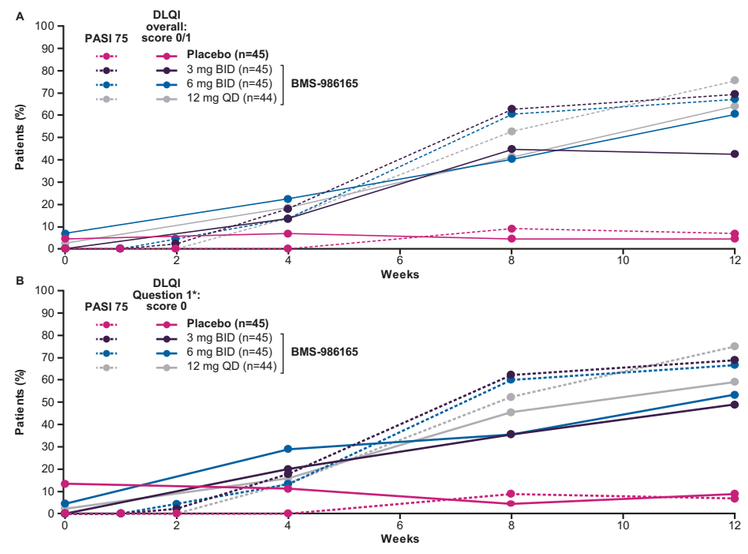


*BMS-986165 3 mg BID, 6 mg BID, and 12 mg QD combined.
BID=twice daily; DLQI=Dermatology Life and Quality Index; QD=every day.

Time course analysis of DLQI, PASI 75, PASI 90, and sPGA 0/1

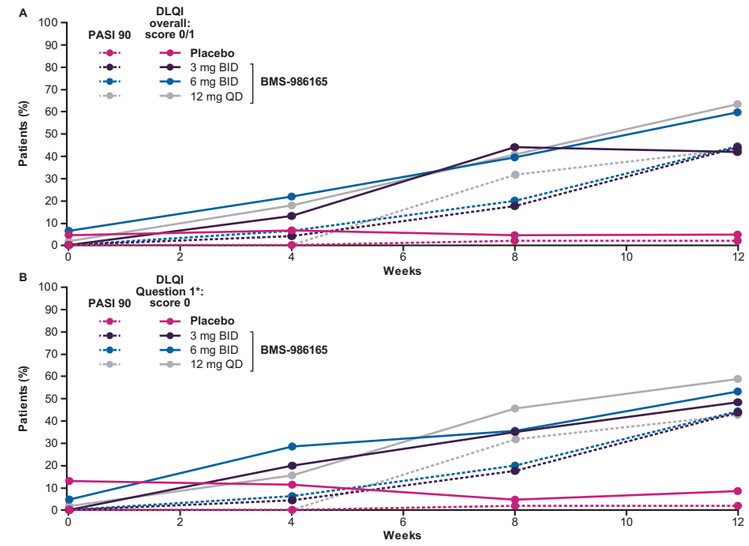
- An improvement as early as Week 4 (earliest time point evaluated) was observed in the proportion of patients attaining scores of 0/1 on DLQI overall (Figures 4A, 5A, and 6A), and a score of 0 ('not at all') on the individual DLQI Question 1 ('*How itchy, sore, painful, or stinging has your skin been?*'), which reflects the most relevant subjective symptoms of psoriasis (Figures 4B, 5B, and 6B).
- At Week 12, the proportion of patients with a score of 0/1 on DLQI overall and 0 on Question 1 was as high as 64% and 59%, respectively, in the combined BMS-986165 dose group versus 4% and 9%, respectively, with placebo.
- Improvements in scores of 0/1 on DLQI overall or 0 on DLQI Question 1 occurred concordantly with improvements in PASI 75 (Figure 4), PASI 90 (Figure 5), and sPGA 0/1 (Figure 6) with each dose over time.

Figure 4: Time course of PASI 75 and (A) DLQI overall or (B) DLQI Question 1* responses.



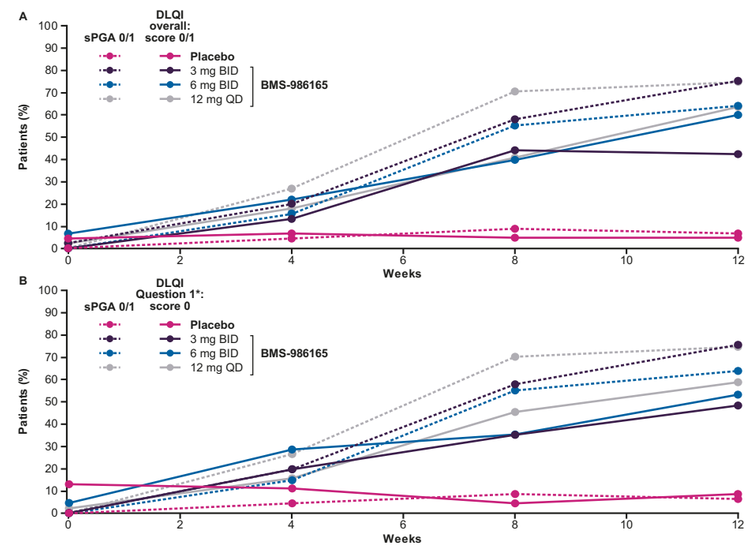
*Question 1 states, '*Over the last week, how **itchy, sore, painful, or stinging** has your skin been?*'
BID=twice daily; DLQI=Dermatology Life and Quality Index; PASI 75=>75% improvement in Psoriasis Area and Severity Index score; QD=every day.

Figure 5: Time course of PASI 90 and (A) DLQI overall or (B) DLQI Question 1* responses.



*Question 1 states, '*Over the last week, how **itchy, sore, painful, or stinging** has your skin been?*'
BID=twice daily; DLQI=Dermatology Life and Quality Index; PASI 90=>90% improvement in Psoriasis Area and Severity Index score; QD=every day.

Figure 6: Time course of sPGA 0/1 and (A) DLQI overall or (B) DLQI Question 1* responses.



*Question 1 states, '*Over the last week, how **itchy, sore, painful, or stinging** has your skin been?*'
BID=twice daily; DLQI=Dermatology Life and Quality Index; QD=every day; sPGA=static Physicians Global Assessment.

CONCLUSIONS

- **Treatment with BMS-986165 improved health-related QoL, as measured by the proportions of patients in whom the disease had no impact on health-related QoL (scores of 0/1 for DLQI overall), as well as those without bothersome subjective symptoms of psoriasis (score of 0 for DLQI Question 1).**
- **Improvements were seen as early as 4 weeks after starting treatment and were concordant with PASI 75, PASI 90, and sPGA 0/1 responses.**
- **Phase 3 studies in psoriasis (POETYK PSO Phase 3 program; NCT03624127, NCT03611751) are ongoing to further assess BMS-986165 in larger groups of patients.**

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Disclosures

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