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

INTRODUCTION

Psoriasis is a chronic immune-mediated disease, which impairs patients’ physical health and worsens their health-related quality of life (QoL).1,2 Improvement in health-related QoL, as measured by the Dermatology Life Quality Index (DLQI),3 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 psoriasis5,6 and other immune-mediated disorders.7,8
- In a 12-week, placebo-controlled, Phase 2 trial (NCT02915836), 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.10

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.

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,11 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 score ≥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 (itchy, sore, painful, or stinging skin) 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.4
- Baseline mean (standard deviation) DLQI scores were as follows: placebo: 12.6 (7.1); 3 mg BID: 12.5 (5.6); 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.

- Table 1: Proportion of patients achieving DLQI overall score 0/1 and Question 1 score 0.

<table>
<thead>
<tr>
<th>Group</th>
<th>Overall score 0/1 (%)</th>
<th>Question 1 score 0 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo</td>
<td>7%</td>
<td>1%</td>
</tr>
<tr>
<td>3 mg BID</td>
<td>22%</td>
<td>7%</td>
</tr>
<tr>
<td>6 mg BID</td>
<td>34%</td>
<td>11%</td>
</tr>
<tr>
<td>12 mg QD</td>
<td>41%</td>
<td>14%</td>
</tr>
</tbody>
</table>

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

Table 2: Proportion of patients achieving PASI 75 and PASI 90.

<table>
<thead>
<tr>
<th>Group</th>
<th>PASI 75 (%)</th>
<th>PASI 90 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo</td>
<td>3%</td>
<td>2%</td>
</tr>
<tr>
<td>3 mg BID</td>
<td>11%</td>
<td>9%</td>
</tr>
<tr>
<td>6 mg BID</td>
<td>14%</td>
<td>14%</td>
</tr>
<tr>
<td>12 mg QD</td>
<td>18%</td>
<td>17%</td>
</tr>
</tbody>
</table>

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

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 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.

References


Disclosures

The data are owned by Sanofi Genzyme. Sanofi Genzyme is a wholly owned subsidiary of Sanofi. Takeda, UCB, Valeant, Novartis, Regeneron, Roche, Sanofi Genzyme, Takeda, UCB, Valeant; honoraria: AbbVie, Akros, Amgen, Baxter, Boehringer Ingelheim, Celgene, Coherus, Eli Lilly, Forward Pharma, Galderma, GlaxoSmithKline, Janssen, Kyowa Hakko Kirin, Merck

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

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

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Figure 7: Time course of PASI 90 and (A) DLQI overall or (B) DLQI Question 1* responses.

Figure 8: Time course of sPGA 0/1 and (A) DLQI overall or (B) DLQI Question 1* responses.