Deucravacitinib (BMS-986165), an Oral, Allosteric Tyrosine Kinase 2 Inhibitor, Reduces Body Surface Area Involvement and Improves Quality of Life in Patients With Psoriasis

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Introduction

- In patients with psoriasis, assessment of body surface area (BSA) involvement is a common measure of disease severity[1,2]
  - An acceptable response to treatment after 3 months is defined by the National Psoriasis Foundation as BSA ≤3%, whereas the target response to treatment at 3 months is defined as BSA ≤1%[3]
- Deucravacitinib (BMS-986165) is a novel, oral, allosteric inhibitor that selectively inhibits intracellular signaling by cytokines involved in psoriasis pathogenesis by binding to tyrosine kinase 2 (TYK2) at its pseudokinase domain rather than to the conserved active site in the kinase domain[4,5]
- In a Phase 2 double-blind trial in patients with moderate to severe plaque psoriasis (PsO; NCT02931838), 67%-75% of patients treated with deucravacitinib at dosages of 3 or 6 mg twice daily (BID) or 12 mg once daily (QD) achieved Psoriasis Area and Severity Index 75 (PASI 75; ≥75% reduction from baseline PASI) at Week 12 vs 7% of patients who received placebo (P<0.001)[5]
  - Additionally, more patients in the Phase 2 trial treated with 3 mg BID, 6 mg BID, or 12 mg QD deucravacitinib reported normal or near-normal quality of life (QoL) than placebo recipients (42%, 60%, and 64%, respectively, vs 4%)[5]

Objective

- The objective of this post hoc analysis of data from the Phase 2 trial was to evaluate BSA changes over time as well as the relationship between BSA reductions and improvements in QoL at Week 12

Methods

Patient population

- Adults with moderate to severe PsO were randomized equally to 1 of 5 deucravacitinib dosages (3 mg every other day to 12 mg QD) or placebo
  - Patients in the 3 most efficacious dose groups (3 mg BID [n=45], 6 mg BID [n=45], 12 mg QD [n=44]) and in the placebo group (n=45) were included in this analysis

Assessments

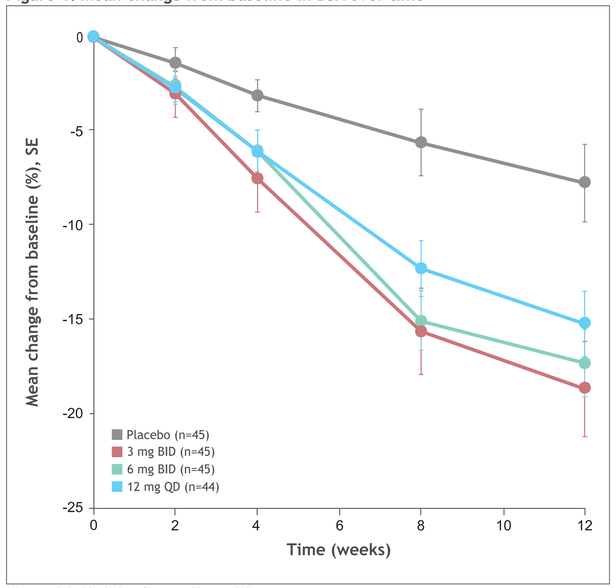
- Mean change from baseline in BSA over time
  - Measurement of BSA involvement with skin lesions was estimated using the handprint method, with the size of a patient's handprint representing ~1% of BSA involvement
- Percentage of patients who achieved BSA of ≤1% and ≤3% at Week 12
- Dermatology Life Quality Index (DLQI; range, 0–30, with higher scores indicating worse QoL) at Week 12 in subgroups of patients with BSA ≤1% or ≤3%
- Patients who discontinued the trial early or had a missing value at any time point had outcomes imputed as a nonresponse at that time point, regardless of the status of response at the time of discontinuation

Results

Change from baseline in BSA over time

- At baseline, BSA involvement was generally comparable across deucravacitinib dosage groups and the placebo group (mean [SD]: 3 mg BID (n=45), 24.5% [15.5%]; 6 mg BID (n=45), 24.8% [13.0%]; 12 mg QD (n=44), 20.6% [12.0%]; and placebo (n=45), 24.2% [13.3%])
- Substantial improvements from baseline in mean BSA were observed over time with deucravacitinib treatment, with similar improvements observed in each of the 3 deucravacitinib dosage groups (**Figure 1**)

Figure 1. Mean change from baseline in BSA over time

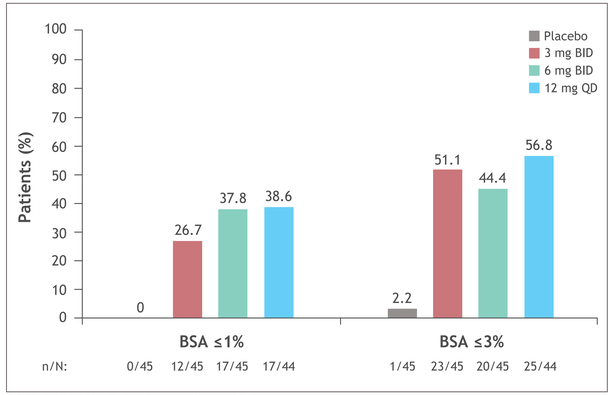


BID, twice daily; BSA, body surface area; QD, once daily.

Percentage of patients who achieved BSA of ≤1% and ≤3% at Week 12

- BSA ≤1% was achieved by approximately one-third of patients receiving deucravacitinib vs 0% of those receiving placebo (**Figure 2**)
  - Additionally, BSA ≤3% was achieved by approximately one-half of patients receiving deucravacitinib vs 2.2% receiving placebo
- Nearly 40% of patients achieved BSA ≤1 and nearly 60% achieved BSA ≤3 in the highest-responding deucravacitinib 12 mg QD group

Figure 2. Percentage of patients with BSA involvement of ≤1% or ≤3% at Week 12

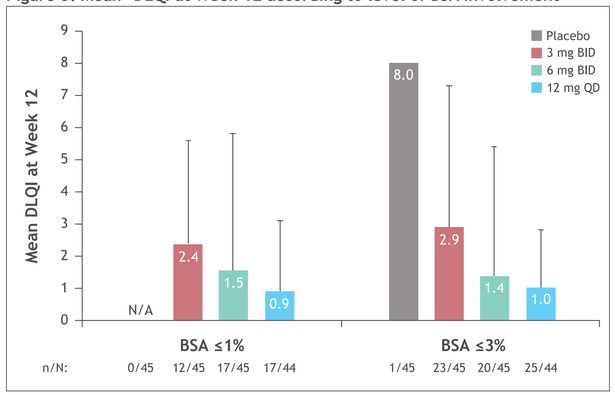


BID, twice daily; BSA, body surface area; QD, once daily.

DLQI at Week 12 according to level of BSA involvement

- Mean DLQI at Week 12 was lower among patients with BSA ≤1% and ≤3% who received deucravacitinib compared with the placebo recipient with BSA ≤3% (**Figure 3**)
  - Mean DLQI at Week 12 was also numerically lower in those patients who received a daily dose of 12 mg deucravacitinib (ie, 6 mg BID and 12 mg QD groups) than in those who received 6 mg daily doses (ie, 3 mg BID; **Figure 3**)

Figure 3. Mean* DLQI at Week 12 according to level of BSA involvement



BID, twice daily; BSA, body surface area; DLQI, Dermatology Life Quality Index; N/A, not applicable; QD, once daily.
*Error bars are SDs.

Conclusions

- This post hoc analysis indicates that deucravacitinib is associated with clinically meaningful decreases in BSA over time, and that clinically meaningful DLQI values were reported in patients who achieved BSA ≤1% and ≤3%
- A substantial number of patients treated with deucravacitinib at the 3 highest tested doses achieved absolute and acceptable treat-to-target BSA values established by the National Psoriasis Foundation[3]
- Five Phase 3 trials in PsO (NCT03624127, NCT03611751, NCT04167462, NCT03924427, and NCT04036435) are currently evaluating the efficacy and safety of deucravacitinib in larger patient cohorts over a longer treatment period

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