Deucravacitinib, an Oral, Allosteric Tyrosine Kinase 2 Inhibitor, Reduces Psoriasis Area and Severity Index Component Scores Across Body Regions in Patients With Plaque Psoriasis

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Introduction

- Psoriasis Area and Severity Index (PASI)
  - Evaluates psoriasis disease severity across 4 body regions and 3 scoring components[1]
    - Body regions: head/neck, trunk, upper extremities, and lower extremities
    - Scoring components: erythema, induration, and desquamation
- Tyrosine kinase 2 (TYK2)
  - Intracellular enzyme that mediates key cytokine signaling pathways involved in psoriasis pathogenesis[2]
- Deucravacitinib
  - Novel, oral, selective TYK2 inhibitor with a mechanism of action distinct from other TYK2 or Janus kinase (JAK) inhibitors[2,3]
    - Inhibits TYK2 via an allosteric mechanism by binding to the TYK2-specific regulatory (pseudokinase) domain rather than to the conserved active (adenosine triphosphate-binding) site in the kinase domain[3]
  - In a Phase 2 double-blinded trial in moderate to severe psoriasis (NCT02931838)[2]
    - 67%–75% of patients treated with deucravacitinib at the most efficacious doses (3 mg twice daily [BID], 6 mg BID, or 12 mg once daily [QD]) achieved PASI 75 at Week 12 vs 7% with placebo ($P<0.001$)[2]

Objective

- Post hoc analysis of the Phase 2 trial in moderate to severe plaque psoriasis
  - To compare the efficacy of deucravacitinib vs placebo by PASI scoring component and body region

Methods

- Patient population
  - Adults with moderate to severe plaque psoriasis were randomized equally to 1 of 5 deucravacitinib doses (3 mg every other day to 12 mg QD) or placebo
    - Patients in the 3 highest and most efficacious deucravacitinib doses (3 mg BID, 6 mg BID, 12 mg QD; n=134) and placebo (n=45) groups were compared in this analysis
- Assessments
  - Proportion of patients achieving at least a 75% reduction from baseline in each PASI component by body region at Week 12
  - Mean change from baseline over time in PASI body region and scoring components
- Patients who discontinued early or had a missing value at any timepoint had outcomes imputed as a nonresponse at that timepoint, regardless of response status at the time of discontinuation

Results

- Baseline PASI body region and component scores were similar across study groups (**Table 1**)

Table 1. Baseline PASI body region and component scores

	Mean ± SD baseline PASI body region and component scores			
	Placebo (n=45)	Deucravacitinib 3 mg BID (n=45)	Deucravacitinib 6 mg BID (n=45)	Deucravacitinib 12 mg QD (n=44)
Body region				
Head/neck	16 ± 9	20 ± 13	15 ± 9	14 ± 9
Trunk	16 ± 8	19 ± 12	16 ± 8	15 ± 8
Upper extremities	19 ± 6	19 ± 9	18 ± 8	18 ± 6
Lower extremities	22 ± 10	21 ± 10	21 ± 11	20 ± 6
Scoring component				
Erythema	7 ± 2	7 ± 3	6 ± 2	6 ± 2
Induration	6 ± 2	6 ± 3	6 ± 2	6 ± 2
Desquamation	6 ± 2	6 ± 2	6 ± 2	6 ± 2

BID, twice daily; PASI, Psoriasis Area and Severity Index; QD, once daily.

- The proportion of patients achieving a 75% reduction in each PASI body region (≥68% vs ≤30%) and scoring component (≥68% vs ≤18%) at Week 12 was higher among patients receiving deucravacitinib vs placebo (**Table 2**)

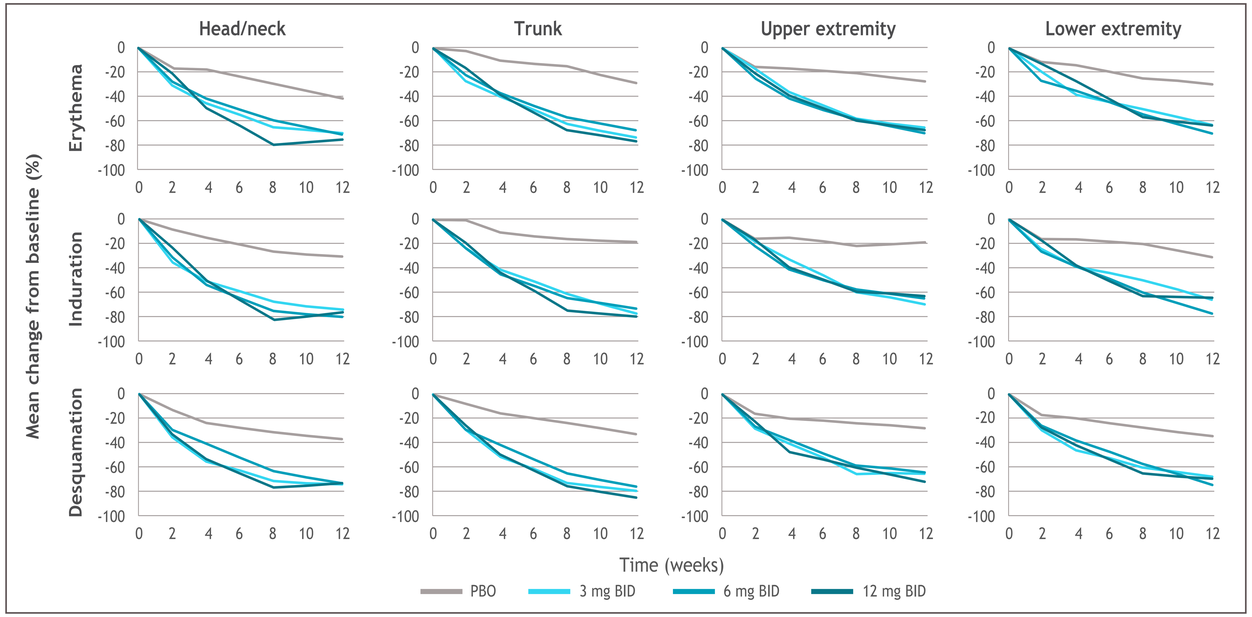
Table 2. Proportion of patients achieving ≥75% reductions from baseline in PASI body region and scoring components at Week 12

	Patients achieving ≥75% reductions from baseline, %			
	Placebo (n=45)	Deucravacitinib 3 mg BID (n=45)	Deucravacitinib 6 mg BID (n=45)	Deucravacitinib 12 mg QD (n=44)
Body region				
Head/neck	30.3	73.2	68.4	73.2
Trunk	20.6	74.4	70.0	87.8
Upper extremities	8.8	69.8	72.5	72.1
Lower extremities	23.5	79.5	75.0	76.7
Scoring component				
Erythema	8.8	68.2	70.0	76.7
Induration	17.6	70.5	80.0	76.7
Desquamation	14.7	68.2	72.5	76.7

BID, twice daily; PASI, Psoriasis Area and Severity Index; QD, once daily.

- Regardless of body region or scoring component, numerically greater reductions in mean percent change from baseline were observed over time with deucravacitinib vs placebo (**Figure 1**)
- Numerical differences between deucravacitinib and placebo in mean percent change from baseline in most body regions and scoring components were observed by Week 2 and maintained through Week 12

Figure 1. Mean percentage change from baseline in PASI body region and scoring components over time



BID, twice daily; PASI, Psoriasis Area and Severity Index; QD, once daily.

Conclusions

- Deucravacitinib treatment was associated with consistent improvements in erythema, induration, and desquamation across all body regions in adults with plaque psoriasis
  - Improvements occurred early and increased over time
- Five Phase 3 trials are evaluating the efficacy and safety of deucravacitinib over a longer treatment duration in larger cohorts of patients with plaque psoriasis
  - POETYK PSO-1 (NCT03624127) and POETYK PSO-2 (NCT03611751) – recently completed
  - POETYK PSO-3 (NCT04167462), POETYK PSO-4 (NCT03924427), and POETYK PSO-LTE (NCT04036435) – currently ongoing

References

1. Walsh JA et al. *J Am Acad Dermatol*. 2013;69:931-937.
2. Papp K et al. *N Engl J Med*. 2018;379:1313-1321.
3. Burke JR et al. *Sci Transl Med*. 2019;11:1-16.

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