# Assessment of Pain Outcomes in a Phase 2 Trial of a Selective, Allosteric Tyrosine Kinase 2 Inhibitor, Deucravacitinib, in Patients With Active PsA

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## Background

- Pain is commonly cited by patients with PsA as affecting their daily activities and quality of life, and perceptions of pain can be different in male and female patients[1-3]
- Pain signaling involves a variety of cytokines, such as interleukin (IL)-17, interferon gamma (IFNγ), and IL-6[4,5]
- Tyrosine kinase 2 (TYK2) mediates signaling of key cytokines involved in PsA pathogenesis, such as IL-23 (and its downstream effectors including IL-17), IL-12, and type 1 interferons[6]
- Deucravacitinib is a first-in-class, oral, selective, allosteric TYK2 inhibitor
  - Approved in multiple countries for the treatment of adults with plaque psoriasis[7]
  - Under investigation for the treatment of PsA, systemic lupus erythematosus, cutaneous lupus erythematosus, Sjögren's disease, and alopecia areata
- Deucravacitinib was efficacious vs placebo in a phase 2 trial in patients with active PsA[8]
  - Cytokine levels were reduced with deucravacitinib treatment vs placebo, including IL-17A, as expected by IL-23 inhibition, and other cytokines that reflect downstream indirect anti-inflammatory effects of TYK2 inhibition, including IL-6 and tumor necrosis factor alpha[9]

## Objective

- To characterize the effect of deucravacitinib on pain assessed by different instruments, alignment across pain instruments, and sex-specific differences in reported pain in patients in the phase 2 PsA trial (NCT03881059)

## Methods

### Trial design

- This was a phase 2, 1-year, randomized, double-blind, placebo-controlled (initial 16 weeks [part A]) trial in patients with active PsA
- Patients (N = 203) were randomized 1:1:1 to placebo, deucravacitinib 6 mg once daily (QD), or deucravacitinib 12 mg QD (**Figure 1**)
- Three instruments were used to assess pain (**Figure 2**)
  - Patient Global Assessment of Pain visual analog scale (Pain VAS), scored from 0-100
  - Psoriatic Arthritis Impact of Disease instrument pain question (PsAID Pain), scored from 0-10
  - 36-Item Short Form Survey (SF-36), bodily pain question (question 7 of SF-36 instrument), in which patients rated their pain on a 6-item scale from "none" to "very severe"; this scale was then converted into a numerical scale from 1-6 for the purposes of these analyses

### Analyses

- Pain scores reported by male vs female patients
- Baseline and change from baseline in pain scores using different instruments
- Correlation between pain scores and disease efficacy measures
- Proportion of patients who reported meaningful improvements in pain

**Figure 1. Phase 2 PsA trial design**

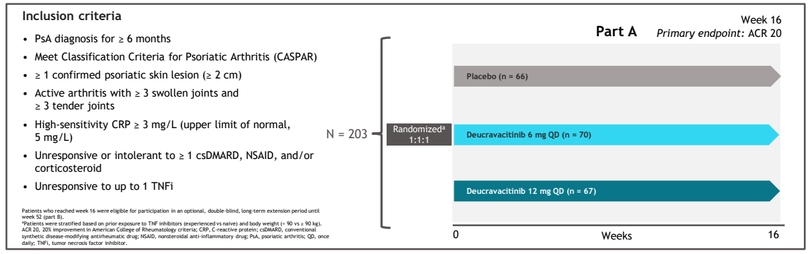
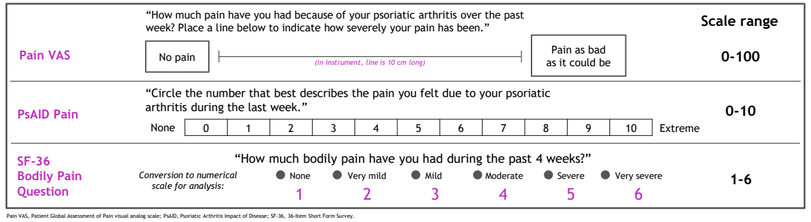



**Figure 2. Assessments to measure pain**




Pain VAS, Patient Global Assessment of Pain visual analog scale; PsAID, Psoriatic Arthritis Impact of Disease; SF-36, 36-Item Short Form Survey.

## Results

### Baseline pain and correlation of pain to disease activity

- Baseline mean pain scores were generally similar across treatment groups and between male and female patients (**Table 1**)

**Table 1. Baseline pain characteristics**

| Instrument | | Placebo | | | Deucravacitinib 6 mg QD | | | Deucravacitinib 12 mg QD | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | All (N = 66) | Male (n = 26) | Female (n = 40) | All (N = 70) | Male (n = 40) | Female (n = 30) | All (N = 67) | Male (n = 33) | Female (n = 34) |
| Pain VAS (0-100 cm) | Mean (SD) | 64.9 (18.23) | 63.0 (19.85) | 66.2 (17.24) | 63.6 (21.67) | 59.8 (25.39) | 68.7 (14.31) | 63.8 (15.93) | 64.1 (13.73) | 63.5 (18.01) |
| | Median | 68.0 | 69.0 | 67.5 | 67.0 | 61.0 | 72.0 | 62.0 | 62.0 | 63.0 |
| PsAID Pain (0-10 NRS) | Mean (SD) | 6.6 (1.76) | 6.7 (1.72) | 6.5 (1.81) | 6.3 (2.04) | 5.9 (2.43) | 6.8 (1.21) | 6.4 (1.53) | 6.6 (1.48) | 6.2 (1.57) |
| | Median | 7.0 | 7.0 | 7.0 | 7.0 | 6.5 | 7.0 | 6.0 | 6.0 | 6.0 |
| SF-36 bodily pain question (1-6 Likert scale) | Mean (SD) | 4.5 (0.75) | 4.4 (0.76) | 4.5 (0.75) | 4.4 (0.83) | 4.3 (0.97) | 4.6 (0.57) | 4.4 (0.74) | 4.5 (0.67) | 4.3 (0.81) |
| | Median | 5.0 | 4.5 | 5.0 | 5.0 | 4.0 | 5.0 | 4.0 | 4.0 | 4.0 |

NRS, numerical rating scale; Pain VAS, Patient Global Assessment of Pain visual analog scale; PsAID, Psoriatic Arthritis Impact of Disease; QD, once daily; SD, standard deviation; SF-36, 36-Item Short Form Survey.

- At baseline, all assessments of pain strongly correlated with Psoriatic Arthritis Disease Activity Score and Patient Global Assessment of Disease Activity (**Table 2**)

**Table 2. Baseline correlations between pain assessments and disease activity**

| | Pain measurements | | | Disease activity measurements | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Pain VAS | PsAID Pain | SF-36 bodily pain | PASDAS | PtGA | DAPSA | DAS28 | HAQ-DI | TJC | SJC | PGA | CRP | Dactylitis[a] | SPARCC enthesitis[a] | LEI[a] |
| Pain VAS | NA | 0.746 | 0.655 | 0.618[b] | 0.653[b] | 0.495[b] | 0.466[b] | 0.423[b] | 0.351[b] | 0.305[b] | 0.367[b] | 0.190[b] | 0.197 | 0.213 | 0.072 |
| PsAID Pain | 0.746 | NA | 0.703 | 0.602 | 0.643 | 0.505 | 0.495 | 0.468 | 0.349 | 0.349 | 0.265 | 0.297 | 0.220 | 0.246 | 0.184 |
| SF-36 bodily pain | 0.655 | 0.703 | NA | 0.511 | 0.535 | 0.361 | 0.401 | 0.472 | 0.196 | 0.262 | 0.204 | 0.289 | 0.173 | 0.157 | 0.060 |

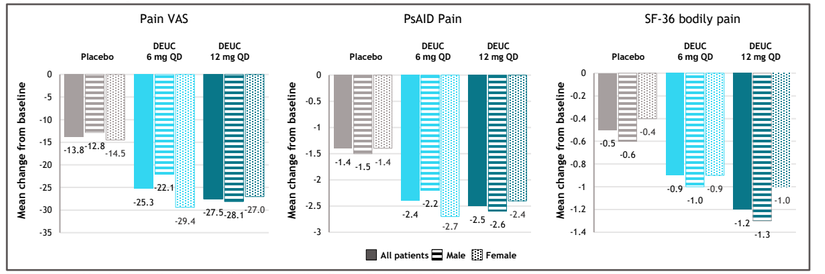
Strength of association: ☐ None: 0.0-0.1 ■ Weak: 0.1-0.3 ■ Medium: 0.3-0.5 ■ Strong: 0.5-1.0

Spearman rank correlation coefficient was used unless otherwise noted.
[a]Only in patients with a score of > 0 at baseline; [b]Pearson rank correlation coefficient.
CRP, C-reactive protein; DAPSA, Disease Activity in Psoriatic Arthritis; DAS28, Disease Activity Score - 28 joint; HAQ-DI, Health Assessment Questionnaire - Disability Index; LEI, Leeds Enthesitis Index; NA, not applicable; Pain VAS, Patient Global Assessment of Pain visual analog scale; PASDAS, Psoriatic Arthritis Disease Activity Score; PGA, Physician's Global Assessment; PsAID, Psoriatic Arthritis Impact of Disease; PtGA, Patient Global Assessment of Disease Activity; SF-36, 36-Item Short Form Survey; SJC, swollen joint count; SPARCC, Spondyloarthritis Research Consortium of Canada; TJC, tender joint count.

### Efficacy in pain instruments at week 16

- At week 16, mean improvements in pain were greater in patients treated with deucravacitinib compared with placebo with all 3 pain instruments, with no clear dose dependence (**Figure 3**)
- No consistent differences were reported between male vs female patients in mean improvements in pain

**Figure 3. Mean change from baseline in pain at week 16: sex-specific differences**

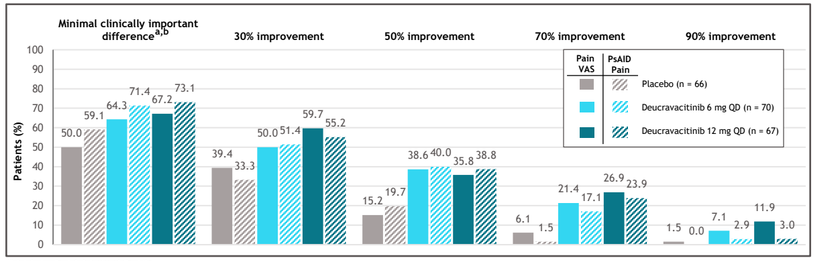



DEUC, deucravacitinib; Pain VAS, Patient Global Assessment of Pain visual analog scale; PsAID, Psoriatic Arthritis Impact of Disease; QD, once daily; SF-36, 36-Item Short Form Survey.

### Pain VAS vs PsAID Pain: improvement in pain with different thresholds at week 16

- Pain VAS and PsAID Pain (NRS) ask similar questions, while SF-36 bodily pain is an ordinal Likert scale that investigates pain using a slightly different approach than the other 2 scales
  - Different thresholds in percent pain improvements were assessed with these 2 instruments
- A greater percentage of patients treated with deucravacitinib reported improvements in Pain VAS thresholds at week 16 compared with placebo (**Figure 4**)
  - Percentages of patients who reported improvements in both Pain VAS and PsAID Pain were greater with deucravacitinib treatment compared with placebo
  - Achievement of improvements in Pain VAS and PsAID Pain were generally similar with no clear dose dependence

**Figure 4. Pain VAS and PsAID Pain improvement at week 16**

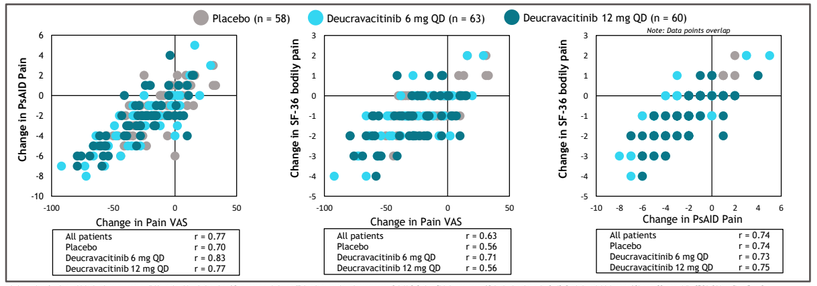



Missing values were imputed using nonresponder imputation.
[a]For Pain VAS, MCID is defined as a ≥ 10-point reduction in change from baseline or ≥ 15% reduction in percent change from baseline on a scale of 0-100; [b]For PsAID Pain, MCID is defined as a ≥ 1-point reduction in change from baseline or ≥ 15% reduction in percent change from baseline on a scale of 0-10.
MCID, minimal clinically important difference; Pain VAS, Patient Global Assessment of Pain visual analog scale; PsAID, Psoriatic Arthritis Impact of Disease; QD, once daily.

### Correlation of pain assessments at week 16

- Changes from baseline in pain assessments at week 16 were strongly correlated (**Figure 5**)
  - However, divergent responses to pain questions were reported by a few participants (top-left and bottom-right quadrants)

**Figure 5. Correlation of pain assessments: change from baseline to week 16**




n is the number of patients with both pain assessments available at the visit; r is the value of Spearman correlation coefficient between the pain assessments. Pain VAS, Patient Global Assessment of Pain visual analog scale; PsAID, Psoriatic Arthritis Impact of Disease; QD, once daily; SF-36, 36-Item Short Form Survey.

## Conclusions

- Reduction of pain (eg, joint pain or bodily pain) is an important treatment target in patients with PsA
- A greater proportion of patients treated with deucravacitinib reported clinically meaningful improvements in pain compared with placebo, regardless of the instrument used
  - Reported improvements in pain were similar between male and female patients across instruments
  - There was no clear dose dependence in responses to deucravacitinib
- Patient-reported improvements in pain were well correlated across instruments; however, a few patients had divergent pain responses when answering pain questions via different instruments for reasons unclear at present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