# Deucravacitinib in moderate to severe plaque psoriasis: comorbidities and use of prior and concomitant medication in patients enrolled in the phase 3 POETYK PSO-1 and PSO-2 trials

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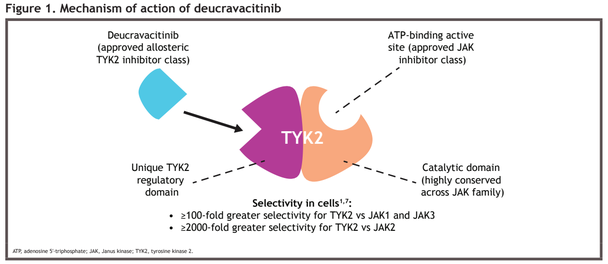
## Synopsis

- Tyrosine kinase 2 (TYK2) is an intracellular enzyme that mediates signaling of select inflammatory cytokines (eg, interleukin [IL]-23, IL-12, Type I interferons [IFNs])[1]
  - IL-23 and Type I IFNs are involved in psoriasis pathogenesis[1]
- Deucravacitinib, an oral, selective, allosteric TYK2 inhibitor, is approved in the US, EU, and other countries for the treatment of adults with moderate to severe plaque psoriasis who are candidates for systemic therapy[2-6]
- Deucravacitinib uniquely binds to the TYK2 regulatory domain rather than to the catalytic domain where Janus kinase (JAK) 1,2,3 inhibitors bind[1,7] (**Figure 1**), driving its selectivity for TYK2 and representing the first in a new class of oral drugs
- Deucravacitinib demonstrated a robust efficacy and safety profile in the global phase 3 POETYK PSO-1 (NCT03624127) and POETYK PSO-2 (NCT03611751) trials in patients with moderate to severe plaque psoriasis[8,9]

**Figure 1. Mechanism of action of deucravacitinib**




ATP, adenosine 5′-triphosphate; JAK, Janus kinase; TYK2, tyrosine kinase 2.

- Psoriasis is a systemic inflammatory disease and is associated with significant risk of comorbidities, including:
  - Cardiovascular disease
  - Metabolic syndrome, including diabetes, hypertension, and dyslipidemia[10-13]
- It is important that the phase 3 trials reflect the real-world populations of patients with plaque psoriasis to the greatest extent possible

## Objective

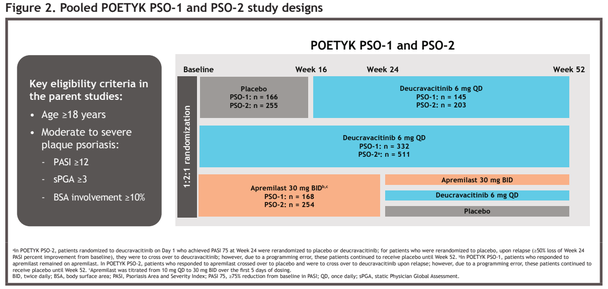
- To evaluate the baseline comorbidities and use of prior and concomitant medications in the pooled POETYK PSO-1 and PSO-2 trial populations to more comprehensively describe the medical history of individuals who participated in the deucravacitinib phase 3 trials

## Methods

### POETYK PSO-1 and PSO-2 study designs

- POETYK PSO-1 (NCT03624127) and POETYK PSO-2 (NCT03611751) were global, 52-week, phase 3, double-blinded trials that randomized adults with moderate to severe plaque psoriasis 1:2:1 to oral placebo, deucravacitinib 6 mg once daily (QD), or apremilast 30 mg twice daily (BID) (**Figure 2**)
  - Patients randomized to placebo crossed over to deucravacitinib at Week 16
  - Patients randomized to apremilast who failed to meet study-specific efficacy thresholds (≥50% reduction from baseline Psoriasis Area and Severity Index [PASI 50] in POETYK PSO-1; ≥75% reduction from baseline in PASI [PASI 75] in POETYK PSO-2) switched to deucravacitinib at Week 24
- At Week 52, eligible patients were able to enroll in the POETYK long-term extension (LTE) (NCT04036435) trial and receive open-label deucravacitinib 6 mg QD

**Figure 2. Pooled POETYK PSO-1 and PSO-2 study designs**




[a]In POETYK PSO-2, patients randomized to deucravacitinib on Day 1 who achieved PASI 75 at Week 24 were rerandomized to placebo or deucravacitinib; for patients who were rerandomized to placebo, upon relapse (≥50% loss of Week 24 PASI percent improvement from baseline), they were to cross over to deucravacitinib; however, due to a programming error, these patients continued to receive placebo until Week 52. [c]In POETYK PSO-1, patients who responded to apremilast remained on apremilast. In POETYK PSO-2, patients who responded to apremilast crossed over to placebo and were to cross over to deucravacitinib upon relapse; however, due to a programming error, these patients continued to receive placebo until Week 52. Apremilast was titrated from 10 mg QD to 30 mg BID over the first 5 days of dosing.
BID, twice daily; BSA, body surface area; PASI, Psoriasis Area and Severity Index; PASI 75, ≥75% reduction from baseline in PASI; QD, once daily; sPGA, static Physician Global Assessment.

### Outcomes

- The proportion of patients reporting comorbidities at baseline by system organ class and preferred term
  - System organ class and preferred term are coded according to the Medical Dictionary for Regulatory Activities (MedDRA; version 23.1)
- The proportion of patients reporting prior and concomitant medications at baseline by medication category
  - Prior medications are defined as medications with a stop date prior to the first dose of study treatment
  - Concomitant medications are defined as medications that are ongoing at the start of study treatment or with a start date on or after the first dose date
  - Medication categories were coded according to the WHODrug Global Dictionary
- Outcomes are reported for the pooled POETYK PSO-1 and PSO-2 populations

## Results

### Baseline patient demographics and clinical characteristics

- Baseline patient demographics and clinical characteristics, including PASI, static Physician Global Assessment (sPGA), and body surface area (BSA) involvement, were similar across treatment groups (**Table 1**)
- Medical histories were also similar across the treatment groups (**Table 2**)
  - Metabolism, nutrition, and vascular disorders were the most commonly reported histories across treatment groups

**Table 1. Baseline patient demographics and clinical characteristics**

| Parameter | Pooled POETYK PSO-1 and PSO-2 | | | |
|---|---|---|---|---|
| | Placebo (n = 419) | Deucravacitinib (n = 842) | Apremilast (n = 422) | Total (N = 1683) |
| Age, mean (SD), y | 47.6 (13.7) | 46.5 (13.5) | 45.7 (12.8) | 46.6 (13.4) |
| Weight, mean (SD), kg | 90.7 (21.1) | 90.5 (21.9) | 91.1 (22.0) | 90.7 (21.7) |
| Female, n (%) | 127 (30.3) | 276 (32.8) | 155 (36.7) | 558 (33.2) |
| Race, n (%) | | | | |
| White | 359 (85.7) | 740 (87.9) | 368 (87.2) | 1467 (87.2) |
| Asian | 41 (9.8) | 83 (9.8) | 40 (9.5) | 164 (9.7) |
| Black or African American | 12 (2.9) | 10 (1.2) | 10 (2.4) | 32 (1.9) |
| Other | 7 (1.7) | 9 (1.1) | 4 (0.9) | 20 (1.2) |
| Disease duration, mean (SD), y | 18.9 (12.9) | 18.6 (12.8) | 18.5 (12.1) | 18.7 (12.6) |
| Prior systemic therapy, n (%) | | | | |
| Biologic | 146 (34.8) | 295 (35.0) | 145 (34.4) | 586 (34.8) |
| Non-biologic | 183 (43.7) | 326 (38.7) | 183 (43.4) | 692 (41.1) |
| No prior systemic therapy, n (%) | 173 (41.3) | 369 (43.8) | 173 (41.0) | 715 (42.5) |
| PASI, mean (SD) | 21.0 (8.6) | 21.1 (8.0) | 21.6 (8.6) | 21.2 (8.3) |
| sPGA, n (%) | | | | |
| 3 (moderate) | 344 (82.1) | 664 (78.9) | 335 (79.4) | 1343 (79.8) |
| 4 (severe) | 75 (17.9) | 178 (21.1) | 87 (20.6) | 340 (20.2) |
| BSA involvement, %, mean (SD) | 25.3 (16.2) | 26.4 (15.8) | 27.6 (16.4) | 26.5 (16.1) |
| Psoriatic arthritis, n (%) | 71 (16.9) | 163 (19.4) | 76 (18.0) | 310 (18.4) |
| Smoking status, n (%) | | | | |
| Smoker | 116 (27.7) | 223 (26.5) | 116 (27.5) | 455 (27.0) |
| Non-smoker | 303 (72.3) | 619 (73.5) | 306 (72.5) | 1228 (73.0) |

BSA, body surface area; PASI, Psoriasis Area and Severity Index; SD, standard deviation; sPGA, static Physician Global Assessment.

**Table 2. Medical history at baseline: system organ classes of interest**

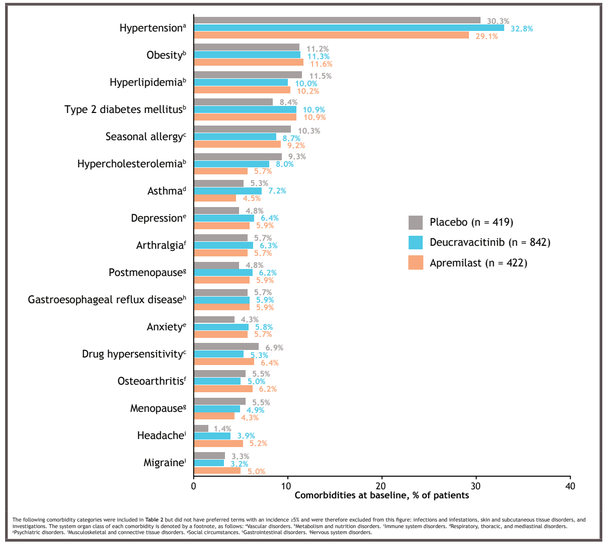
| Category | Pooled POETYK PSO-1 and PSO-2 | | | |
|---|---|---|---|---|
| | Placebo (n = 419) n (%) | Deucravacitinib (n = 842) n (%) | Apremilast (n = 422) n (%) | Total (N = 1683) n (%) |
| Metabolism and nutrition disorders | 179 (42.7) | 330 (39.2) | 162 (38.4) | 671 (39.9) |
| Vascular disorders | 141 (33.7) | 294 (34.9) | 134 (31.8) | 569 (33.8) |
| Musculoskeletal and connective tissue disorders | 90 (21.5) | 195 (23.2) | 102 (24.2) | 387 (23.0) |
| Gastrointestinal disorders | 64 (15.3) | 154 (18.3) | 74 (17.5) | 292 (17.3) |
| Infections and infestations | 79 (18.9) | 143 (17.0) | 77 (18.2) | 299 (17.8) |
| Respiratory, thoracic, and mediastinal disorders | 69 (16.5) | 138 (16.4) | 50 (11.8) | 257 (15.3) |
| Immune system disorders | 80 (19.1) | 129 (15.3) | 71 (16.8) | 280 (16.6) |
| Psychiatric disorders | 59 (14.1) | 114 (13.5) | 64 (15.2) | 237 (14.1) |
| Nervous system disorders | 49 (11.7) | 110 (13.1) | 58 (13.7) | 217 (12.9) |
| Social circumstances[a] | 55 (13.1) | 110 (13.1) | 51 (12.1) | 216 (12.8) |
| Cardiac disorders | 44 (10.5) | 93 (11.0) | 36 (8.5) | 173 (10.3) |
| Skin and subcutaneous tissue disorders | 45 (10.7) | 87 (10.3) | 44 (10.4) | 176 (10.5) |
| Investigations[b] | 43 (10.3) | 85 (10.1) | 45 (10.7) | 173 (10.3) |

Categories are system organ class level terms and are sorted in descending order of frequency in the deucravacitinib group.
[a]The social circumstances category included postmenopause; menopause; tobacco or ex-tobacco user; substance use; non-consumption; use of corrective lens, cardiac assistance device; orthosis; or breast, dental, or joint prosthesis.
[b]This category included abnormal blood or urine laboratory test findings; screenings including colonoscopy, endoscopy, mammogram, and biopsies; and abnormal cardiac or vascular test findings.

### Baseline comorbidities

- Hypertension was the most common comorbidity across the treatment groups, occurring in up to 32.8% of patients (**Figure 3**)
- Obesity, hyperlipidemia, type 2 diabetes mellitus, and seasonal allergy were reported in at least 10% of patients in any treatment group

**Figure 3. Comorbidities at baseline with an incidence ≥5% in any treatment group**

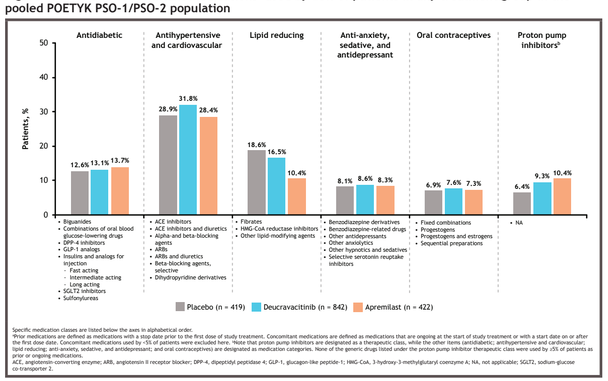



The following comorbidity categories were included in **Table 2** but did not have preferred terms with an incidence ≥5% and were therefore excluded from this figure: infections and infestations, skin and subcutaneous tissue disorders, and investigations. The system organ class of each comorbidity is denoted by a footnote, as follows: [a]Vascular disorders. [b]Metabolism and nutrition disorders. [c]Immune system disorders. [d]Respiratory, thoracic, and mediastinal disorders. [e]Psychiatric disorders. [f]Musculoskeletal and connective tissue disorders. [g]Social circumstances. [h]Gastrointestinal disorders. [i]Nervous system disorders.

### Prior and concomitant medication use

- Antihypertensive and cardiovascular medications were the most commonly reported therapies in each treatment group (**Figure 4**)
- Antidiabetic and lipid-reducing therapies were also reported by at least 10% of patients in each treatment group

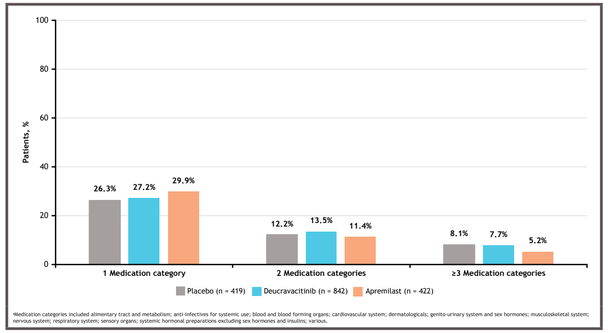
**Figure 4. Prior and concomitant medications[a] used by ≥5% of patients in any treatment group in the pooled POETYK PSO-1/PSO-2 population**




Specific medication classes are listed below the axes in alphabetical order.
[a]Prior medications are defined as medications with a stop date prior to the first dose of study treatment. Concomitant medications are defined as medications that are ongoing at the start of study treatment or with a start date on or after the first dose date. Concomitant medications used by <5% of patients were excluded here. [b]Note that proton pump inhibitors are designated as a therapeutic class, while the other items (antidiabetic; antihypertensive and cardiovascular; lipid reducing; anti-anxiety, sedative, and antidepressant; and oral contraceptives) are designated as medication categories. None of the generic drugs listed under the proton pump inhibitor therapeutic class were used by ≥5% of patients as prior or ongoing medications.
ACE, angiotensin-converting enzyme; ARB, angiotensin II receptor blocker; DPP-4, dipeptidyl peptidase 4; GLP-1, glucagon-like peptide-1; HMG-CoA, 3-hydroxy-3-methylglutaryl coenzyme A; NA, not applicable; SGLT2, sodium-glucose co-transporter 2.

- Up to 30% of patients reported prior or concomitant treatments from at least 1 medication category, with up to 8% reporting therapies from ≥3 medication categories (**Figure 5**)
  - Rates of medication use were similar across treatment groups

**Figure 5. Number of medication categories[a] used by the pooled POETYK PSO-1/PSO-2 population**




[a]Medication categories included alimentary tract and metabolism; anti-infectives for systemic use; blood and blood forming organs; cardiovascular system; dermatologicals; genito-urinary system and sex hormones; musculoskeletal system; nervous system; respiratory system; sensory organs; systemic hormonal preparations excluding sex hormones and insulins; various.

## Conclusions

- The phase 3 POETYK PSO-1 and PSO-2 studies enrolled patients with moderate to severe psoriasis with a range of comorbidities, consistent with the real-world population of patients with psoriasis[10-13]
  - Medical histories and use of concomitant medications were similar across treatment arms in the pooled POETYK PSO-1/PSO-2 population
  - The medication classes being used by patients were consistent with the comorbidities reported at baseline in both trials
- Concomitant medication usage reflects the standard management of common psoriasis comorbidities[13]

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