Deucravacitinib in psoriasis patients with a history of malignancy: follow-up after 4 years of deucravacitinib treatment in the POETYK PSO program

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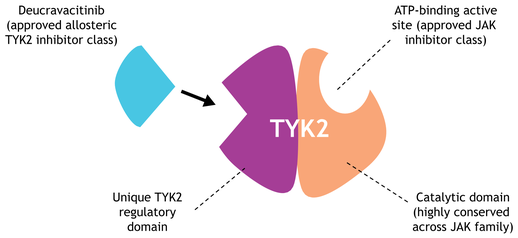
Synopsis

- 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 regulatory domain of TYK2 rather than to the catalytic domain where Janus kinase (JAK) 1,2,3 inhibitors bind (**Figure 1**),[1,7] driving its selectivity for TYK2 and representing the first in a new class of oral drugs

Figure 1. Mechanism of action of deucravacitinib



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

- The global phase 3 POETYK PSO-1 (NCT03624127) and POETYK PSO-2 (NCT03611751) trials of deucravacitinib included patients with moderate to severe plaque psoriasis with a history of malignancy[8,9]
  - Patients with a solid organ or hematologic malignancy or lymphoproliferative disease that occurred >5 years before study entry were eligible
  - Patients with resected cutaneous basal cell carcinoma or squamous cell carcinoma or carcinoma of the cervix in situ who had been treated with no evidence of recurrence were also eligible
- This descriptive analysis examined malignancy events among deucravacitinib-treated patients with a history of malignancy prior to enrolling in the POETYK PSO-1, PSO-2, and long-term extension (LTE) (NCT04036435) trials[10]

Objective

- To provide follow-up assessment after 4 years of deucravacitinib treatment in patients with moderate to severe plaque psoriasis and a history of malignancy excluding those with nonmelanoma skin cancer (NMSC) >5 years prior to enrolling in the POETYK PSO-1, PSO-2, and LTE trials

Methods

Analysis population

- Patients receiving ≥1 dose of deucravacitinib treatment (as-treated population) at any time over 4 years (Week 208; data cutoff, November 1, 2023) in the pooled parent (POETYK PSO-1 and PSO-2) and POETYK LTE trials were screened to identify those with any malignancy >5 years prior to enrolling in the phase 3 parent trials

Assessments

- Baseline patient demographics and clinical characteristics
  - Patient age, sex, race, body mass index, and country
  - Psoriasis duration
  - Prior treatment for psoriasis
- Total deucravacitinib exposure
- Reason for deucravacitinib discontinuation
- Occurrence of malignancy
- Patient narratives of malignancies, including comorbidities and/or other risk factors

Results

Patients with a history of malignancy

- Among 1519 deucravacitinib-treated patients, 19 were identified with a history of malignancy
  - Patients with a history of malignancy were older (mean age, 64.3 vs 46.6 years), had longer psoriasis disease duration (mean, 36.2 vs 18.7 years), and had shorter deucravacitinib exposure (median, 814 vs 1298 days) compared with the overall trial population, respectively

Patients with a history of malignancy excluding NMSC

- 12 of the 19 patients with a history of malignancy had solid organ (n = 10) or hematologic malignancies (n = 2); 7 patients had a history of NMSC and were excluded from further analysis (**Table 1** and **Table 2**)
  - Of the 12 patients with a history of malignancy, 6 discontinued deucravacitinib treatment due to the following reasons: patient withdrawal (n = 2 [17%]), occurrence of malignancy (n = 1 [8%]), adverse events (AEs; n = 1 [8%]), lost to follow-up (n = 1 [8%]), or study site termination by the sponsor (n = 1 [8%])
- Among the 12 patients with a history of solid organ or hematologic malignancy, 1 patient experienced a melanoma (**Table 2**)

Table 1. Baseline patient demographics and clinical characteristics in deucravacitinib-treated patients with a history of solid organ or hematologic malignancy

Patient	Prior malignancy	Age at baseline, y	Sex	Race	Country	Body mass index, kg/m²	Psoriasis duration, y
1	Malignant melanoma	48	Male	White	US	28.2	10.2
2	Prostate cancer	65	Male	White	US	26.1	44.3
3	Prostate cancer	71	Male	White	US	47.8	21.3
4	Ovarian cancer	62	Female	White	Poland	30.0	18.3
5	Uterine cancer	64	Female	White	US	36.4	45.8
6	Cervical carcinoma	59	Female	White	US	38.9	48.8
7	Colon cancer	65	Male	White	US	36.3	57.6
8	Testis cancer	54	Male	White	Germany	28.8	48.5
9	Non-Hodgkin's lymphoma	65	Male	White	Germany	29.1	59.7
10	Malignant melanoma	74	Male	White	Australia	23.9	14.4
11	Hodgkin's disease	68	Male	White	US	33.3	11.2
12	Cervical carcinoma	47	Female	White	Poland	21.9	28.4

Table 2. Outcomes in deucravacitinib-treated patients with a history of solid organ or hematologic malignancy

Patient	Prior malignancy	Initial date or prior malignancy	Prior psoriasis treatment	Total deucravacitinib exposure, d	Reason for discontinuation	Malignancy during phase 3 trials
1	Malignant melanoma	1999	Triamcinolone acetonide	611	Melanoma	Melanoma[a]
2	Prostate cancer	2001	No prior treatment	196	Lost to follow-up	-
3	Prostate cancer	2008	Guselkumab	1618	-	-
4	Ovarian cancer	2001	Adalimumab, brodalumab, guselkumab	1632	-	-
5	Uterine cancer	2012	No prior treatment	268	Site terminated by sponsor	-
6	Cervical carcinoma	1983	Adalimumab, efalizumab, etanercept, methotrexate, ustekinumab	1808	-	-
7	Colon cancer	2004	Ciclosporin, etanercept, methotrexate	54	Adverse event[b]	-
8	Testis cancer	2000	Calcium monoethyl fumarate, dimethyl fumarate, magnesium monoethyl fumarate, zinc ethyl fumarate, secukinumab	1000	Patient withdrawal[c]	-
9	Non-Hodgkin's lymphoma	1997	Adalimumab, methotrexate, secukinumab	1285	-	-
10	Malignant melanoma	1990	Adalimumab	1591	-	-
11	Hodgkin's disease	1997	No prior treatment	616	Patient withdrawal[d]	-
12	Cervical carcinoma	2005	Methotrexate sodium	363	-	-

Dashes denote patients who are ongoing in the POETYK LTE trial and/or did not have a malignancy during the phase 3 trials. [a]Patient had a history of sun exposure and malignant melanoma treated 20 years before study entry. The patient had not received any immunosuppressive medications previously. This patient was randomized to deucravacitinib treatment between Week 0 and Week 84. He was diagnosed with malignant melanoma on the right anterior axilla (stage 1 [T1, N0, M0]), which was considered not related to treatment. No residual melanoma was identified after surgical removal. The patient discontinued treatment due to malignant melanoma per protocol. [b]Decreased glomerular filtration rate. [c]Lack of efficacy. [d]Travel fatigue.

Conclusions

- This is the first analysis evaluating occurrence of malignancy in deucravacitinib-treated patients with moderate to severe plaque psoriasis and a history of malignancy
- Malignancy was infrequent with deucravacitinib treatment in patients with a history of solid organ or hematologic malignancy
  - Among 12 patients with a history of malignancy (excluding those with NMSC), 1 experienced a malignancy
    - This patient, who had multiple risk factors for skin cancer and had received treatment 20 years previously for melanoma, had a melanoma that was considered not related to treatment
- These results are consistent with an analysis of malignancy events in psoriasis patients with a history of malignancy who received guselkumab treatment for 5 years[11]
- Limitations of the current analysis were that a small number of patients were followed for a limited duration (4 years)
  - Analysis of larger patient populations over a longer duration of follow-up using real-world data will help to further characterize the safety of deucravacitinib in regards to adverse events with long latency, such as malignancy

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