Deucravacitinib long-term efficacy with continuous treatment in plaque psoriasis: 2-year results from the phase 3 POETYK PSO study program

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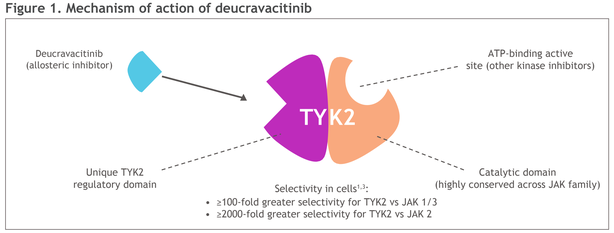
Introduction

- Tyrosine kinase 2 (TYK2) is an intracellular enzyme that mediates signaling of cytokines (eg, interleukin-23, Type I interferons) involved in psoriasis pathogenesis[1]
- Deucravacitinib, an oral, selective, allosteric TYK2 inhibitor, is approved by the US Food and Drug Administration for the treatment of adults with moderate to severe plaque psoriasis who are candidates for systemic therapy or phototherapy[2]
- Deucravacitinib binds to the TYK2 regulatory domain rather than to the more conserved catalytic domain where Janus kinase 1/2/3 inhibitors bind[1] (**Figure 1**)

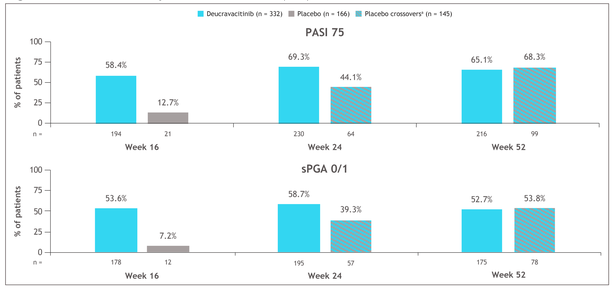
Figure 1. Mechanism of action of deucravacitinib



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

- Deucravacitinib was studied at 6 mg once daily in two global phase 3 pivotal trials, POETYK PSO-1 (NCT03624127) and PSO-2 (NCT03611751)[4,5]
  - Only POETYK PSO-1 included a continuous deucravacitinib treatment arm from Day 1 to Week 52
  - Placebo patients crossed over to deucravacitinib at Week 16 in both trials
- POETYK PSO-1 demonstrated (**Figure 2**[6]):
  - Significantly greater response rates for ≥75% reduction from baseline in Psoriasis Area and Severity Index (PASI 75) and static Physician's Global Assessment score of 0 (clear) or 1 (almost clear) with a ≥2-point improvement from baseline (sPGA 0/1) at Week 16 with deucravacitinib vs placebo and apremilast[4]
  - Clinical efficacy that was maintained through Week 52 with continuous deucravacitinib treatment[7]
- Patients completing the POETYK PSO-1 trial could enroll in the POETYK long-term extension (LTE) trial and receive open-label deucravacitinib 6 mg once daily
- The 2-year safety profile of deucravacitinib in the POETYK LTE trial was consistent with that observed from Weeks 0–52 of the POETYK PSO-1 and PSO-2 trials, and there were no emerging safety signals[8]

Figure 2. Clinical efficacy in POETYK PSO-1 (NRI)[6]



[a]Patients initially randomized to placebo crossed over to deucravacitinib at Week 16.
NRI, nonresponder imputation; PASI 75, ≥75% reduction from baseline in Psoriasis Area and Severity Index; sPGA 0/1, static Physician's Global Assessment score of 0 (clear) or 1 (almost clear) with a ≥2-point improvement from baseline.

Objectives

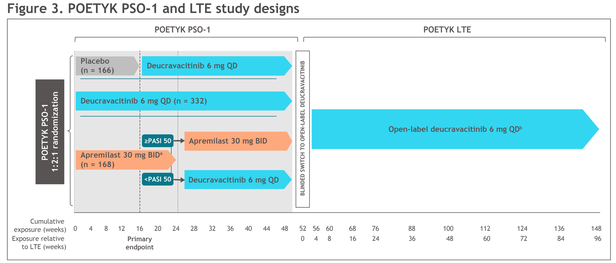
- To examine long-term efficacy responses in POETYK PSO-1 patients who:
  - Received continuous deucravacitinib treatment from Day 1 and entered the POETYK LTE
  - Achieved PASI 75 on deucravacitinib at Week 16, continued on deucravacitinib, and entered the POETYK LTE

Methods

Study designs and analysis populations

- The study designs for the POETYK PSO-1 and LTE trials are illustrated in **Figure 3**
- Patients meeting the following criteria were eligible to enroll in the study:
  - Age ≥18 years
  - Diagnosis of moderate to severe plaque psoriasis
    - Baseline PASI ≥12, sPGA ≥3, and body surface area involvement ≥10%
- Patient randomization in POETYK PSO-1 was stratified by geographic region, body weight, and prior biologic use
- Analysis populations were defined as:
  - **Continuous deucravacitinib treatment from baseline:** patients who received continuous deucravacitinib from Day 1 (Week 0) and entered the POETYK LTE
    - Since results with nonresponder imputation (NRI) were shown earlier from Weeks 0-52,[4,5] only Weeks 52–112 results are shown here
  - **Continuous deucravacitinib Week 16 PASI 75 responders:** patients who received continuous deucravacitinib from Day 1, achieved PASI 75 at Week 16, and entered the POETYK LTE

Figure 3. POETYK PSO-1 and LTE study designs



[a]Apremilast was titrated from 10 mg QD to 30 mg BID over the first 5 days of dosing. [b]Data reported through the 120-day LTE cutoff date of October 1, 2021.
BID, twice daily; LTE, long-term extension; PASI 50, ≥50% reduction from baseline in Psoriasis Area and Severity Index; QD, once daily.

Outcome measures

- Efficacy was assessed in patients with up to 112 weeks (=2 years) of continuous deucravacitinib exposure as of the cutoff date of October 1, 2021
  - PASI 75
  - ≥90% reduction from baseline in PASI (PASI 90)
  - sPGA 0/1
- In addition to the as-observed analysis, 2 methods of imputation for missing data were used to evaluate long-term efficacy:
  - **Treatment failure rule (TFR)[9]:** patients who discontinued treatment or the study due to worsening of psoriasis or lack of efficacy were imputed as nonresponders
  - **Modified NRI (mNRI)[10]:** multiple imputation analysis was used for imputation of missing values, and patients who discontinued due to worsening of psoriasis were imputed as nonresponders
    - Only patients who discontinued or had reached Week 112 by the cutoff date of October 1, 2021, were included

Results

Baseline patient demographics and disease characteristics

- Baseline demographics and disease characteristics for POETYK PSO-1 patients randomized to deucravacitinib who rolled over to the POETYK LTE are presented in **Table 1**
- A total of 332 patients were randomized to deucravacitinib
  - 265 patients completed the study and entered the POETYK LTE
  - 173 PASI 75 responders at Week 16 entered the POETYK LTE

Table 1. Baseline patient demographics and disease characteristics

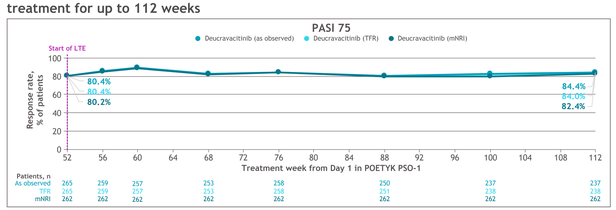
	Patients randomized to deucravacitinib entering POETYK LTE	
Parameter	Total (N = 265)	Week 16 PASI 75 responders (n = 173)
Age, mean (SD), y	46.0 (13.7)	45.2 (14.0)
Weight, mean (SD), kg	87.0 (22.2)	84.7 (22.4)
Female, n (%)	87 (32.8)	58 (33.5)
Race, n (%)		
White	211 (79.6)	133 (76.9)
Asian	51 (19.2)	37 (21.4)
Black or African American	1 (0.4)	1 (0.6)
Other	2 (0.8)	2 (1.2)
Age at disease onset, mean (SD), y	29.8 (15.1)	29.8 (15.1)
Disease duration, mean (SD), y	17.0 (12.2)	16.2 (11.8)
PASI, mean (SD)	21.8 (8.3)	22.6 (8.9)
sPGA, n (%)		
3 (moderate)	208 (78.5)	129 (74.6)
4 (severe)	57 (21.5)	44 (25.4)
BSA involvement, mean (SD), %	27.2 (15.6)	28.3 (15.6)

BSA, body surface area; LTE, long-term extension; PASI, Psoriasis Area and Severity Index; PASI 75, ≥75% reduction from baseline in PASI; sPGA, static Physician's Global Assessment.

PASI 75 and PASI 90 outcomes

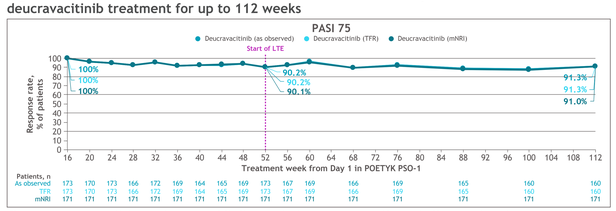
- Overall, PASI 75 responses were consistent from Weeks 52–112 in all patients with continuous deucravacitinib treatment (**Figure 4**)
- PASI 75 response rates were maintained from Weeks 16–112 in Week 16 PASI 75 responders (**Figure 5**)
- Overall, PASI 90 responses were consistent from Weeks 52–112 (**Figure 6**)
- PASI 90 response rates were maintained from Weeks 16–112 in Week 16 PASI 75 responders (**Figure 7**)

Figure 4. PASI 75 response from Week 52 in all patients with continuous deucravacitinib treatment for up to 112 weeks



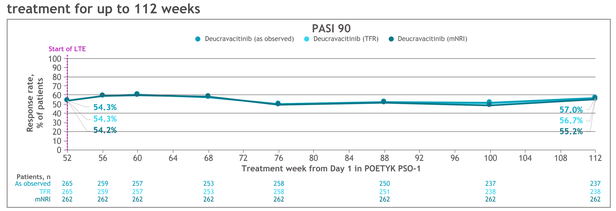
LTE, long-term extension; mNRI, modified nonresponder imputation; PASI 75, ≥75% reduction from baseline in Psoriasis Area and Severity Index; TFR, treatment failure rule.

Figure 5. Maintenance of PASI 75 response in Week 16 PASI 75 responders with continuous deucravacitinib treatment for up to 112 weeks



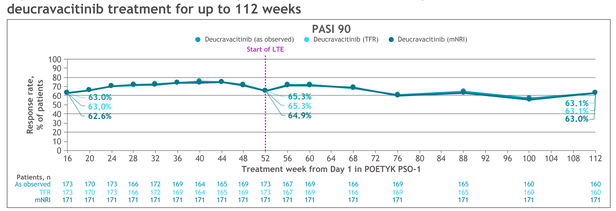
LTE, long-term extension; mNRI, modified nonresponder imputation; PASI 75, ≥75% reduction from baseline in Psoriasis Area and Severity Index; TFR, treatment failure rule.

Figure 6. PASI 90 response from Week 52 in all patients with continuous deucravacitinib treatment for up to 112 weeks



LTE, long-term extension; mNRI, modified nonresponder imputation; PASI 90, ≥90% reduction from baseline in Psoriasis Area and Severity Index; TFR, treatment failure rule.

Figure 7. Maintenance of PASI 90 response in Week 16 PASI 75 responders with continuous deucravacitinib treatment for up to 112 weeks

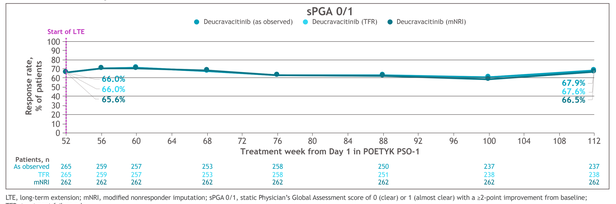


LTE, long-term extension; mNRI, modified nonresponder imputation; PASI 75/90, ≥75%/≥90% reduction from baseline in Psoriasis Area and Severity Index; TFR, treatment failure rule.

sPGA 0/1 outcomes

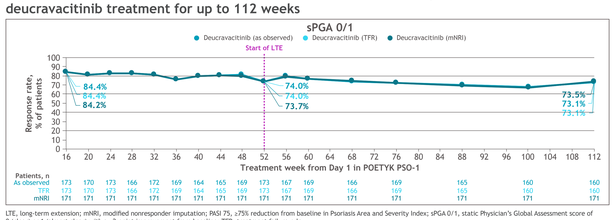
- Overall, sPGA 0/1 responses were consistent from Weeks 52–112 (**Figure 8**)
- sPGA 0/1 responses were maintained from Weeks 16–112 in Week 16 PASI 75 responders (**Figure 9**)

Figure 8. sPGA 0/1 response from Week 52 in all patients with continuous deucravacitinib treatment for up to 112 weeks



LTE, long-term extension; mNRI, modified nonresponder imputation; sPGA 0/1, static Physician's Global Assessment score of 0 (clear) or 1 (almost clear) with a ≥2-point improvement from baseline; TFR, treatment failure rule.

Figure 9. Maintenance of sPGA 0/1 response in Week 16 PASI 75 responders with continuous deucravacitinib treatment for up to 112 weeks



LTE, long-term extension; mNRI, modified nonresponder imputation; PASI 75, ≥75% reduction from baseline in Psoriasis Area and Severity Index; sPGA 0/1, static Physician's Global Assessment score of 0 (clear) or 1 (almost clear) with a ≥2-point improvement from baseline; TFR, treatment failure rule.

Conclusions

- Continuous treatment with deucravacitinib for up to 112 weeks resulted in durable efficacy
  - High efficacy responses in patients from the POETYK PSO-1 study who received continuous deucravacitinib from Day 1 to Week 52 have been previously reported[3]
  - Clinical outcomes were consistent from Weeks 52–112 in these patients who entered the POETYK LTE
  - Clinical efficacy responses were maintained well through Week 112 among those who achieved PASI 75 at Week 16 with deucravacitinib treatment
- Deucravacitinib, a once-daily oral drug, has the potential to become a treatment of choice and new standard of care for patients who require systemic therapy for their moderate to severe plaque psoriasis

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10. Papp K, et al. *Br J Dermatol.* 2021;185:1135–1145.

Acknowledgments

- This study was sponsored by Bristol Myers Squibb
- Writing and editorial assistance was provided by Liz Rockstein, PhD, of Peloton Advantage, LLC, an OPEN Health company, Parsippany, NJ, USA, funded by Bristol Myers Squibb
- The authors also acknowledge Julie Scotto, BS, MPH, for her contributions to this analysis

Disclosures

- **ML:** Research funds on behalf of Mount Sinai: AbbVie, Amgen, Arcutis, Avotres, Boehringer Ingelheim, Dermavant, Eli Lilly, Incyte, Janssen, Ortho Dermatologics, Regeneron, and UCB; Consultant: Aditum Bio, Almirall, AltruBio, Anaptysbio, Arcutis, Arena, Aristea, Arrive Technologies, Avotres, BiomX, Boehringer Ingelheim, Brickell Biotech, Bristol Myers Squibb, Cara Therapeutics, Castle Biosciences, CorEvitas' (Corrona) Psoriasis Registry, Dermavant, Dr Reddy's Laboratories, Evelo Biosciences, Evommune, Forte Biosciences, Helsinn Therapeutics, Hexima, Leo Pharma, MeiJi Seika Pharma, Mindera, Pfizer, Seanergy, and Verrica
- **RBW:** Research grants: AbbVie, Almirall, Amgen, Celgene, Janssen, Eli Lilly, Leo Pharma, Novartis, Pfizer, and UCB; Consulting fees: AbbVie, Almirall, Amgen, Astellas, Boehringer Ingelheim, Celgene, DICE, Eli Lilly, GlaxoSmithKline, Janssen, Leo Pharma, Novartis, Pfizer, Sanofi, UCB, UNION, and XenoPort
- **HS:** Clinical investigator: AbbVie, Amgen, Boehringer Ingelheim, Bristol Myers Squibb, Eli Lilly, Janssen, Leo Pharma, Novartis, and Sun Pharma
- **SI:** Grants and personal fees: AbbVie, Eisai, Kyowa Kirin, Janssen, Leo Pharma, Maruho, Sun Pharma, Taiho Yakuhin, Tanabe Mitsubishi, and Torii Yakuhin; Personal fees: Amgen (Celgene), Boehringer Ingelheim, Bristol Myers Squibb, Daiichi Sankyo, Eli Lilly, Novartis, and UCB
- **CP:** Grants and consultant: AbbVie, Almirall, Amgen, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Eli Lilly, Janssen, Leo Pharma, Merck, Mylan, Novartis, Pfizer, Sandoz, and UCB
- **JCS:** Advisory board member/consultant: AbbVie, Leo Pharma, Novartis, Pierre-Fabre, Sanofi Genzyme, and Trevi; Speaker: AbbVie, Eli Lilly, Janssen-Cilag, Leo Pharma, Novartis, and Sanofi Genzyme; Investigator: AbbVie, Amgen, Bristol Myers Squibb, Galapagos, Galderma, Incyte, InflaRx, Janssen-Cilag, Mento Therapeutics, Merck, Novartis, Pfizer, Regeneron, UCB, and Trevi
- **LS:** Consultant, paid investigator, and/or speaker: AbbVie, Amgen, Anacor, Ascend, Astellas, AstraZeneca, Blaze Bioscience, Bristol Myers Squibb, Boehringer Ingelheim, Botanix, Celgene, Dermira, Eli Lilly, Galderma, Genentech, GlaxoSmithKline, Hexima, Janssen, Leo Pharma, Mayne, Medimmune, Merck (MSD), Merck-Serono, Novartis, Otsuka, Pfizer, Phosphagenics, Photon MD, Regeneron, Roche, Samumed, Sanofi Genzyme, SHR, Sun Pharma ANZ, Trius, UCB, and Zai Lab
- **TP:** Advisory board and consulting fees: AbbVie, Almirall, Amgen, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Eli Lilly, Galderma, Incyte, Janssen, Leo Pharma, Novartis, Pfizer, Sanofi Genzyme, Sun Pharma, and UCB
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- **DT:** Grant/research support, consultant, scientific advisory board speakers bureau: AbbVie, Almirall, Amgen, Biogen Idec, Boehringer Ingelheim, Bristol Myers Squibb, Eli Lilly, Galapagos, Galderma, Janssen-Cilag, Leo Pharma, Novartis, Pfizer, Regeneron, Roche, Sandoz-Hexal, Sanofi, Target Solution, and UCB
- **AB:** Speaker (with honoraria): AbbVie, Arcutis, Bristol Myers Squibb, Eli Lilly, Pfizer, Regeneron, Sanofi, and UCB; Scientific adviser (with honoraria): AbbVie, Abcentra, Affibody, Aligos, Almirall, Alumis, Amgen, Anaptysbio, Arcutis, Arena, Aslan, Athenex, Bluefin Biomedicine, Boehringer Ingelheim, Bristol Myers Squibb, Cara Therapeutics, Dermavant, EcoRI, Eli Lilly, Excient, Evelo, Evommune, Forte Biosciences, Galderma, Highlight Therapeutics, Incyte, InnoventBio, Janssen, Landos, Leo Pharma, Merck, Novartis, Pfizer, Rapt, Regeneron, Sanofi Genzyme, Spherix Global Insights, Sun Pharma, TLL Pharmaceutical, TriaDSpark, UCB, Vitiligone, and Xoncor; Clinical study investigator (institution has received clinical study funds): AbbVie, Acelyrin, Almirall, Amgen, Arcutis, Athenex, Boehringer Ingelheim, Bristol Myers Squibb, Concert, Dermavant, Eli Lilly, Evelo, Evommune, Galderma, Incyte, Janssen, Leo Pharma, Merck, Novartis, Pfizer, Regeneron, Sun Pharma, and UCB

Presented at the Dermatology Innovation Symposium (DIS) 2022; October 14-16, 2022; Anaheim, CA
This is an encore of the 2022 31st EADV Congress presentation

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