Deucravacitinib in plaque psoriasis: immune response to and safety of pneumococcus and tetanus toxoid vaccines in the POETYK LTE trial

Joanna Narbutt,[1] Shahram Jacobs,[2] Kim A. Papp,[3] Alessandra Alió,[4] Yi Luo,[4] Yanqiu Shao,[4] Victoria Berger,[4] Carolin Daamen,[4] Kevin Winthrop[5]

[1]Medical University of Łódź and Dermoklinika Medical Centre, Łódź, Poland; [2]Unison Clinical Trials, Sherman Oaks, CA, USA; [3]Alliance Clinical Trials and Probity Medical Research, Waterloo, and the Temerty Faculty of Medicine, University of Toronto, Toronto, ON, Canada; [4]Bristol Myers Squibb, Princeton, NJ, USA; [5]Oregon Health & Science University, Portland, OR, USA

Synopsis

- Deucravacitinib, an oral, selective, allosteric tyrosine kinase 2 (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[1-3]
- The global, 52-week, phase 3, randomized, double-blinded POETYK PSO-1 (NCT03624127) and POETYK PSO-2 (NCT03611751) trials demonstrated that deucravacitinib 6 mg once daily (QD) was significantly more efficacious than placebo and apremilast at Week 16 and was well tolerated in patients with moderate to severe plaque psoriasis[4-7]
  - Patients who completed POETYK PSO-1 or PSO-2 could enroll in the POETYK long-term extension (LTE) (NCT04036435) trial and receive open-label deucravacitinib 6 mg QD[8]
- Clinical efficacy and safety were maintained through 4 years in deucravacitinib-treated patients in the ongoing POETYK LTE trial[8]
- Vaccines are a cornerstone of public health
- A retrospective analysis has demonstrated that patients with psoriasis receiving deucravacitinib treatment developed serologic response to SARS-CoV-2 vaccines and/or infection[9]
- The effect of deucravacitinib treatment on immune response to non-live vaccines has not been prospectively evaluated with or without treatment interruption
- Pneumococcal (T-cell independent) and tetanus toxoid (T-cell dependent) vaccines are clinically relevant immunizations for patients with psoriasis and thus were chosen for this substudy

Objective

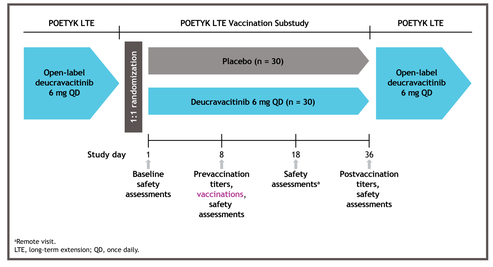
- To evaluate the immune response to and safety of non-live pneumococcus (T-cell independent) and tetanus toxoid (T-cell dependent) vaccines in patients who received continuous deucravacitinib treatment compared with those who interrupted treatment in the POETYK LTE trial

Methods

Substudy design

- This was a phase 3b, prospective, multicenter, randomized, placebo-controlled, double-blinded substudy of the POETYK LTE trial (**Figure 1**)
- Patients in the vaccine substudy were previously enrolled in POETYK PSO-1 or PSO-2 and had completed ≥1 year of treatment in the POETYK LTE trial

Figure 1. Study design



[a]Remote visit.
LTE, long-term extension; QD, once daily.

Outcome measures

- Coprimary endpoints:
  - Pneumovax 23 (pneumococcus): the proportion of patients achieving at least a 2-fold increase in immunoglobulin G (IgG) titers of ≥6 of 13 selected pneumococcal serotypes (out of 23 serotypes) at Day 36 postvaccination
  - Boostrix (tetanus): the proportion of patients achieving serological response at Day 36 postvaccination; serological response was defined as follows:
    - For prevaccination IgG titer ≤0.1 IU/mL → postvaccination titer level ≥0.4 IU/mL
    - For prevaccination IgG titer >0.1 IU/mL and ≤2.7 IU/mL → postvaccination titer level of at least a 4-fold increase
    - For prevaccination IgG titer >2.7 IU/mL → postvaccination titer level of at least a 2-fold increase
- Secondary endpoints:
  - Immune responses elicited by Pneumovax 23 measured by opsonophagocytic activity (OPA) in patients on deucravacitinib vs placebo
  - The proportion of patients achieving seroconversion in tetanus toxoid-specific antibody titers in patients on deucravacitinib vs placebo
    - Seroconversion responder was defined as IgG serologic response to tetanus toxoid with at least a 4-fold increase in antibody concentration at Study Day 36
  - The proportion of patients achieving seroprotection in tetanus toxoid-specific antibody titers in patients on deucravacitinib vs placebo
    - Seroprotection responder was defined as anti-tetanus toxoid IgG concentration >0.1 IU/mL at Study Day 36
  - Safety and tolerability of Pneumovax 23 and Boostrix vaccines while on deucravacitinib

Analysis populations

- **All evaluable patients:** all patients who were compliant with study treatment and who do not have any relevant protocol deviations that may impact the coprimary endpoints assessments
- **Safety analysis set:** all randomized patients who received at least 1 dose of blinded study treatment

Statistical analysis

- The proportional difference in response rate for each vaccine and its associated 2-sided 95% confidence interval (CI) were determined for deucravacitinib vs placebo using the Newcombe-Wilson score method
- Adjusted geometric mean titer ratio of serotype-specific IgG antibody titers and OPA titers were based on the analysis of covariance model with prevaccination titers as a covariate and treatment group as a fixed effect

Results

Patients

- A total of 59 patients were randomized
  - 30 patients received deucravacitinib and 28 (93.3%) completed treatment
    - 1 patient discontinued prior to vaccination due to an adverse event (AE) (influenza) and 1 patient discontinued due to noncompliance with protocol
  - 29 patients received placebo and 27 (93.1%) completed treatment
    - 1 patient withdrew due to discomfort in receiving vaccines and 1 patient met exclusion criteria
- Baseline patient demographics and clinical characteristics were similar between treatment groups (**Table 1**)

Table 1. Baseline patient demographics and clinical characteristics (all evaluable patients)

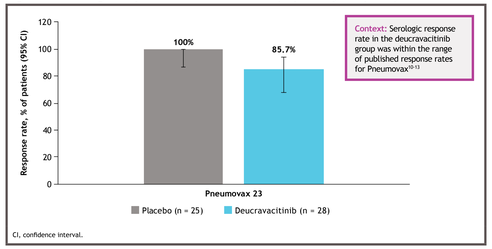
Parameter	Placebo (n = 25)[a]	Deucravacitinib (n = 28)	Total (N = 53)
Age,[b] mean (SD), y	44.9 (11.1)	46.4 (9.5)	45.7 (10.3)
Male, n (%)	13 (52.0)	16 (57.1)	29 (54.7)
Weight,[c] mean (SD), kg	88.2 (15.5)	86.2 (13.9)	87.1 (14.5)
≥90 kg, n (%)	11 (44.0)	13 (46.4)	24 (45.3)
Body mass index,[c] mean (SD), kg/m²	29.8 (4.7)	29.5 (4.6)	29.6 (4.6)
Geographic region, n (%)			
Poland	20 (80.0)	20 (71.4)	40 (75.5)
United States	3 (12.0)	7 (25.0)	10 (18.9)
Canada	2 (8.0)	1 (3.6)	3 (5.7)
Age at disease onset,[b] mean (SD), y	21.2 (10.9)	26.3 (13.1)	23.9 (12.3)
Duration of disease,[d] mean (SD), y	24.9 (14.4)	21.4 (12.4)	23.1 (13.4)
sPGA score 0-2,[c] n (%)	24 (96.0)	27 (96.4)	51 (96.2)
PASI,[c,e] mean (SD)	2.2 (2.8)	1.8 (2.3)	2.0 (2.5)

[a]Evaluable patients; 2 of the 27 patients who had completed treatment were excluded due to lack of compliance with study treatment and/or relevant protocol deviations that may impact the coprimary endpoint assessments. [b]Baseline in parent studies. [c]Baseline in substudy at Day 1. [d]Last visit in parent studies. [e]One patient in the deucravacitinib arm did not have PASI data.
PASI, Psoriasis Area and Severity Index; SD, standard deviation; sPGA, static Physician Global Assessment.

Pneumovax 23

- The proportion of patients meeting serological response criteria to pneumococcus was high in the deucravacitinib group and numerically lower compared with placebo (difference [95% CI] vs placebo, -14.3 [-31.5, 1.6]) (**Figure 2**)

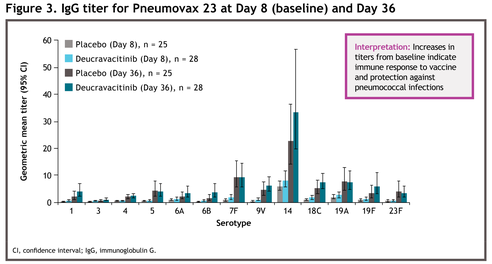
Figure 2. Serologic response to Pneumovax 23 (coprimary endpoint)



CI, confidence interval.

- Baseline (Day 8) Pneumovax 23 IgG antibody titers tended to be higher across all serotypes for deucravacitinib vs placebo; Day 36 IgG antibody titers were comparable across both treatment groups (**Figure 3**)
  - After adjusting for prevaccination titers, antibody geometric mean titers at Day 36 were generally similar across both treatment groups

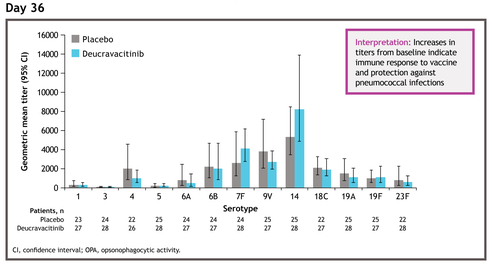
Figure 3. IgG titer for Pneumovax 23 at Day 8 (baseline) and Day 36



CI, confidence interval; IgG, immunoglobulin G.

- OPA at Day 36 for all serotypes was generally similar across treatment groups (**Figure 4**)
  - OPA is a measure of bacteria-killing functions of vaccine-induced antibodies in patients and indicates the success of the pneumococcal vaccine
    - During opsonophagocytosis, bacteria coated with antibodies are engulfed by phagocytes; this is the main mechanism by which antibodies facilitate the killing and clearance of bacteria[14]
  - After adjusting for prevaccination levels, OPA confirmed similar responses in both treatment groups

Figure 4. Geometric mean titer of serotype-specific OPA for Pneumovax 23 at Day 36

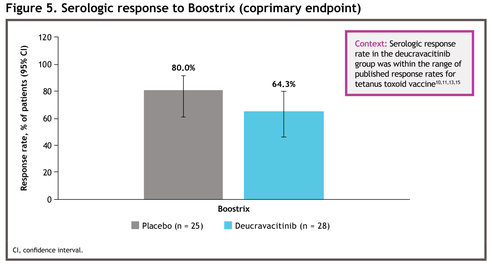


CI, confidence interval; OPA, opsonophagocytic activity.

Boostrix

- The proportion of patients meeting serological response criteria to tetanus toxoid antigen was high in the deucravacitinib group and numerically lower compared with placebo (difference [95% CI] vs placebo, -15.7 [-37.3, 8.6]) (**Figure 5**)

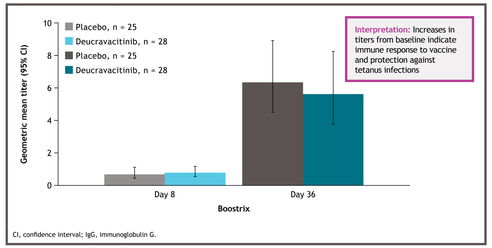
Figure 5. Serologic response to Boostrix (coprimary endpoint)



CI, confidence interval.

- Baseline (Day 8) and Day 36 Boostrix IgG antibody titers were similar across both treatment groups (**Figure 6**)
  - After adjusting for prevaccination titers, antibody geometric mean titers at Day 36 were generally similar across both treatment groups

Figure 6. Boostrix IgG titer



CI, confidence interval; IgG, immunoglobulin G.

- Seroconversion for tetanus toxoid-specific antibody titers was high in the deucravacitinib group (64.3% [95% CI, 45.8-79.3]) and numerically lower compared with placebo (76.0% [95% CI, 56.6-88.5]) (difference [95% CI], -11.7 [-34.0, 12.8])

Context: Seroconversion is the ability to mount immune responses and produce antibodies against pathogens after vaccination

- Seroprotection was achieved in both treatment groups for tetanus toxoid-specific antibody titers (deucravacitinib, 100% [95% CI, 87.9-100]; placebo, 100% [95% CI, 86.7-100])

Context: Seroprotection is the ability to achieve protective levels of antibodies against a pathogen

Safety

- No serious AEs were reported; AE rates were infrequent and comparable across treatment groups (**Table 2**)
- One patient in the deucravacitinib group reported an AE of interest (influenza prior to vaccination); no other AEs of interest occurred during the substudy
- No clinically meaningful changes in hematology, chemistry, or lipid laboratory parameters related to study treatment were observed
- Psoriasis flares were not observed in patients who remained on deucravacitinib treatment and received vaccinations
  - Flare was defined as having at least 1 of the following:
    - Psoriasis Area and Severity Index (PASI) ≥12 at Day 36
    - Static Physician Global Assessment (sPGA) ≥3 with a ≥2-point increase from baseline at Day 36
    - AE of worsening psoriasis from Day 1 to Day 36 of the substudy
  - 2 patients in the placebo group experienced flares (1 patient had sPGA ≥3 with a ≥2-point increase from baseline; 1 patient had AE of worsening psoriasis on the arms and chest)

Table 2. Overall safety summary[a]

AE category, n (%)	Placebo (n = 28)	Deucravacitinib (n = 30)	Total (N = 58)
AEs	3 (10.7)	4 (13.3)	7 (12.1)
Serious AEs	0	0	0
Local vaccine-related AEs[b]	11 (39.3)	13 (43.3)	24 (41.4)
Systemic vaccine-related AEs[b]	3 (10.7)	3 (10.0)	6 (10.3)
Discontinued treatment due to AEs[c]	0	0	0

[a]No deaths were reported during the substudy. [b]Local and systemic vaccine-related AEs were mild or moderate in severity; no severe events were reported. [c]One patient in the deucravacitinib 6 mg QD group discontinued treatment prior to vaccination due to AE of influenza (they only completed 1 day of the study); this patient did not have relevant information captured in an AE case report form.
AE, adverse event; QD, once daily.

Conclusions

- In patients with plaque psoriasis, continuing deucravacitinib treatment did not impact humoral responses to the non-live Pneumovax 23 (T-cell independent) and Boostrix (T-cell dependent) vaccines
  - Serologic response rates in the deucravacitinib group were high for both Pneumovax 23 and Boostrix and were within the range of published response rates for these vaccines in patients with psoriasis and in healthy human volunteers[10-13,15]
    - Serologic response is a binary measure; while serologic response rates were numerically lower in the deucravacitinib group compared with the placebo group, the protection provided by the vaccines, as measured by IgG titers, was generally similar in the deucravacitinib and placebo groups
  - Functional immune responses, as measured by OPA, were comparable in the deucravacitinib and placebo groups for Pneumovax 23 serotypes
  - Seroconversion and seroprotection were achieved in both treatment groups for tetanus toxoid-specific antibody titers
- No serious AEs or AEs of interest were reported after vaccination
  - Patients who remained on deucravacitinib treatment did not experience flares/worsening of psoriasis, but psoriasis flares were observed in patients who had their treatment withheld
- Our data suggest that withholding deucravacitinib treatment at the time of these vaccinations is not required
  - These data further support recent clinical recommendations that deucravacitinib treatment should be continued without interruption in patients with psoriasis receiving non-live vaccines[16]

References

1. Sotyktu [package insert]. Princeton, NJ, USA: Bristol Myers Squibb; September 2022. **2.** Sotyktu [summary of product characteristics]. Dublin, Ireland: Bristol Myers Squibb EEIG; December 2023. **3.** Sotyktu [package insert]. Tokyo, Japan: Bristol Myers Squibb K.K.; September 2022. **4.** Sotyktu [product monograph]. Montreal, QC, Canada: Bristol Myers Squibb Canada Co.; November 2022. **5.** Sotyktu [product information]. Mulgrave, VIC, Australia: Bristol Myers Squibb Australia Pty. Ltd.; December 2022. **6.** Armstrong AW, et al. *J Am Acad Dermatol*. 2023;88:29-39. **7.** Strober B, et al. *J Am Acad Dermatol*. 2023;88:40-51. **8.** Armstrong AW, et al. Presented at: the EADV Symposium; 16-18 May 2024; St. Julians, Malta. **9.** Winthrop K, et al. Presented at the 33rd EADV Congress; 25-28 September 2024; Amsterdam, Netherlands. **10.** Brodmerkel C, et al. *J Drugs Dermatol*. 2013;12:1122-1129. **11.** Gomez EV, et al. *BioDrugs*. 2017;31:545-554. **12.** Winthrop KL, et al. *Ann Rheum Dis*. 2016;75:687-695. **13.** Chiricozzi A, et al. *Vaccines (Basel)*. 2020;8:769. **14.** Schuerman L, et al. *Clin Vacc Immunol*. 2011;18:2161-2167. **15.** Winthrop KL, et al. *J Am Acad Dermatol*. 2018;78:1149-1155. **16.** Chat VS, et al. *J Am Acad Dermatol*. 2024;90:1170-1181.

Acknowledgments

- This study was sponsored by Bristol Myers Squibb
- Writing and editorial assistance was provided by Ann Marie Fitzmaurice, PhD, of Peloton Advantage, LLC, an OPEN Health company, funded by Bristol Myers Squibb

Disclosures

- **JN:** Honoraria and/or grants, consultant, and investigator: AbbVie, Amgen, Almirall, Boehringer Ingelheim, Bristol Myers Squibb, Celltrion, Eli Lilly, Galderma, Janssen, Leo Pharma, Novartis, Pfizer, Sanofi-Aventis/Genzyme, Sandoz, Takeda, and UCB
- **SJ:** Clinical trial site investigator: Bristol Myers Squibb
- **KAP:** Honoraria and/or grants, consultant, investigator, or scientific officer: AbbVie, Acelyrin, Akros, Alumis, Amgen, Arcutis, Bausch Health/Valeant, Boehringer Ingelheim, Bristol Myers Squibb, Can-Fite Biopharma, Celltrion, Concert Pharmaceuticals, Dermavant, Dermira, DICE Therapeutics, Eli Lilly, Evelo Biosciences, Forbion, Galderma, Horizon Therapeutics, Incyte Corporation, Janssen, Kymab, Kyowa Hakko Kirin, Leo Pharma, Meiji Seika Pharma, Mitsubishi Pharma, Nimbus Therapeutics, Novartis, Pfizer, Reistone, Sanofi-Aventis/Genzyme, Sandoz, Sun Pharma, Takeda, Tarsus Pharmaceuticals, UCB Pharma, and Zai Lab
- **AA, YL, YS, VB,** and **CD:** Employees and shareholders: Bristol Myers Squibb
- **KW:** Consultant: AbbVie, AstraZeneca, Bristol Myers Squibb, Eli Lilly, Galapagos, Gilead, GlaxoSmithKline, Novartis, Pfizer, Regeneron, Roche, Sanofi, and UCB; Research support: Bristol Myers Squibb and Pfizer

Presented at the Winter Clinical Dermatology Conference - Hawaii®; February 14-19, 2025; Waikoloa, HI

Email: joanna.narbutt@umed.lodz.pl