Immunology

Introduction to deucravacitinib

August 2023

Bristol Myers Squibb™

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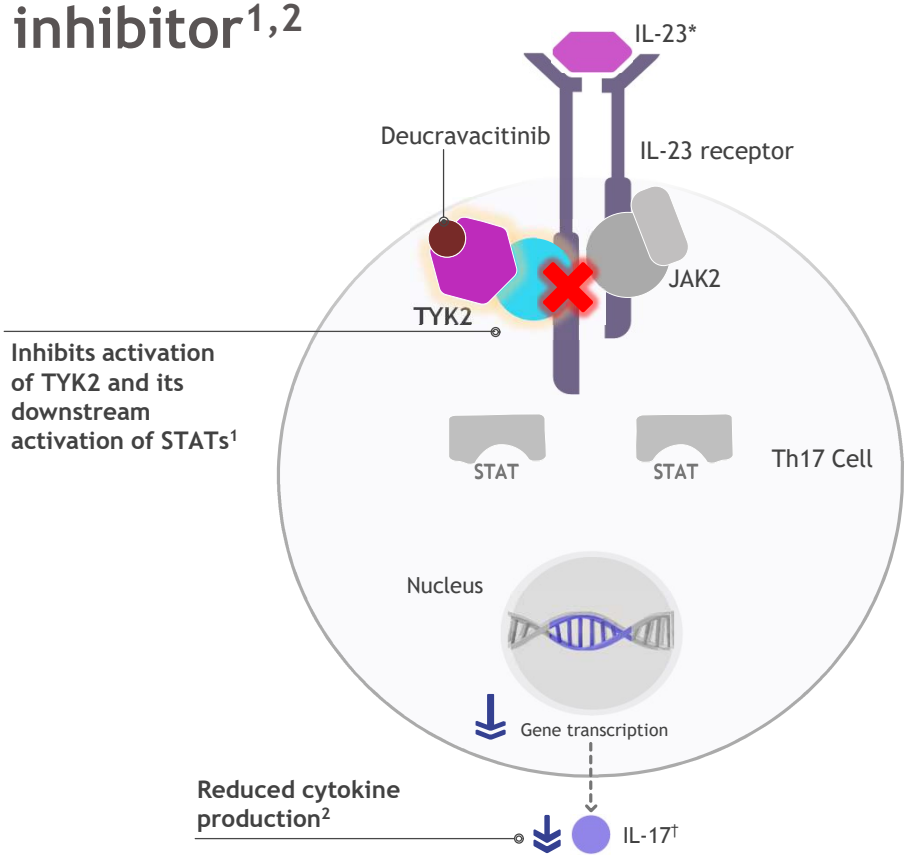
- Please refer to the approved Product Information before prescribing any products referred to in any of the presentations at this event. Product Information is available at www.ebs.tga.gov.au
- Should you have any questions or require further information about BMS Medicine SOTYKTU™ (deucravacitinib), please contact Medical Information on 1800 067 567 or medinfo.australia@bms.com or your BMS representative.

Deucravacitinib is indicated for the treatment of moderate-to-severe plaque psoriasis in adults who are candidates for systemic therapy or phototherapy[1]

TYK2, tyrosine kinase 2.

1. SOTYKTU Product Information. 2. Australian Register of Therapeutic Goods. Available at: https://www.ebs.tga.gov.au/. Accessed August 2023.

Deucravacitinib: First-in-class and only selective allosteric TYK2 inhibitor[1,2]



TYK2 pairs with JAK1 or JAK2 to mediate multiple cytokine pathways such as **IL-23**, which results in the production of proinflammatory cytokines including **IL-17**.[1,3]

Deucravacitinib is an **oral, selective, allosteric TYK2 inhibitor**.[1,4]

The precise mechanism linking inhibition of TYK2 enzyme to therapeutic effectiveness in the treatment of adults with moderate-to-severe plaque psoriasis is not currently known.[1]

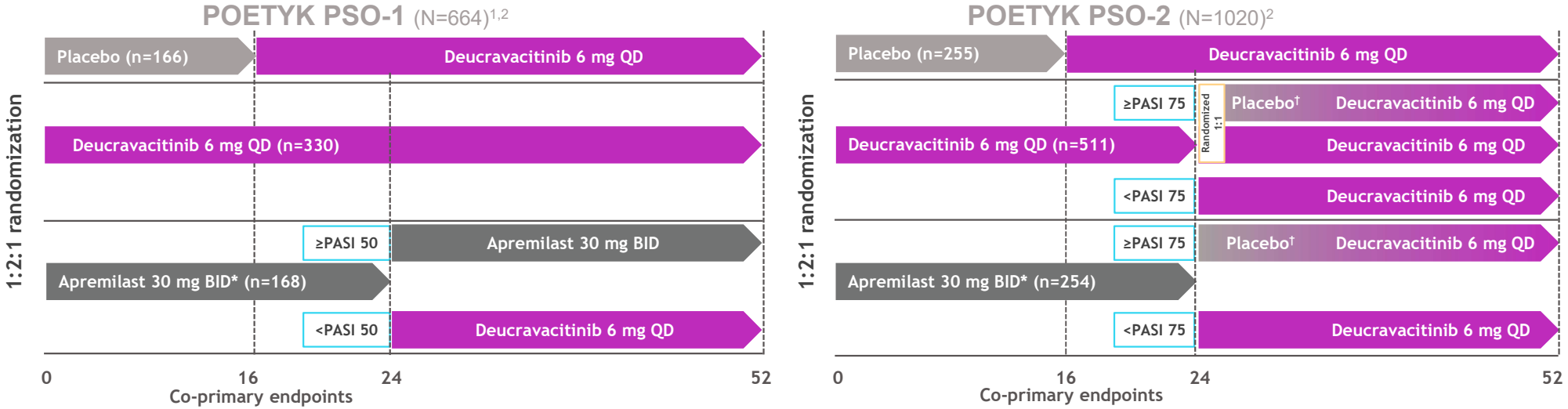
*TYK2 is a member of the Janus kinase family. Deucravacitinib reduced psoriasis-associated gene expression in psoriatic skin in a dose dependent manner, including reductions in IL-23-pathway and Type I IFN pathway-regulated genes.[1] †In Phase 3 studies, IL-17A, IL-19, and beta-defensin were reduced by deucravacitinib treatment by 47%–50%, 72%, and 81%–84% respectively.[1]
The relationship between these pharmacodynamic markers and the mechanism(s) by which deucravacitinib exerts its clinical effects is unknown.[1]

IFN, interferon; IL, interleukin; JAK, Janus kinase; STAT, signal transducer and activator of transcription; Th17, helper T cell, subtype 17; TYK2, tyrosine kinase 2.

1. SOTYKTU Product Information. 2. Australian Register of Therapeutic Goods. Available at: https://www.ebs.tga.gov.au/. Accessed August 2023. 3. Di Cesare A *et al. J Invest Dermatol*. 2009;129(6):1339-1350. 4. Chimalakonda A *et al. Dermatol Ther (Heidelb)*. 2021;11:1763-1776.

Phase 3 head-to-head trials of deucravacitinib vs placebo and apremilast

Multicentre, randomised, double-blind, placebo- and active-controlled clinical trials[1,2]



Key eligibility criteria[1]

- Adults with moderate-to-severe plaque psoriasis who were eligible for systemic therapy or phototherapy
- PASI ≥12, sPGA ≥3, BSA involvement ≥10%

Co-primary endpoints[1]

Proportion of patients who achieve the following responses vs placebo at Week 16:

- sPGA score of 0 (clear) or 1 (almost clear)
- At least a 75% improvement in PASI scores from baseline (PASI 75)

Select secondary endpoints[1,2]

Proportion of patients who achieve the following responses vs apremilast:

- At Week 16 and Week 24: PASI 75, PASI 90, sPGA score of 0 (clear) or 1 (almost clear)
- At Week 16: ss-PGA score of 0 (clear) or 1 (almost clear)

Proportion of patients who achieve the following responses vs placebo:

- At Week 16: PASI 100, ss-PGA score of 0 (clear) or 1 (almost clear), PSSD symptom score of 0

Statistical significance was not met for the following secondary endpoints:

- PGA-F 0/1 (PGA-F score of clear or minimal disease) vs placebo (BL ≥3) at Week 16, PSSD symptom score of 0 vs apremilast (BL ≥1) at Week 16

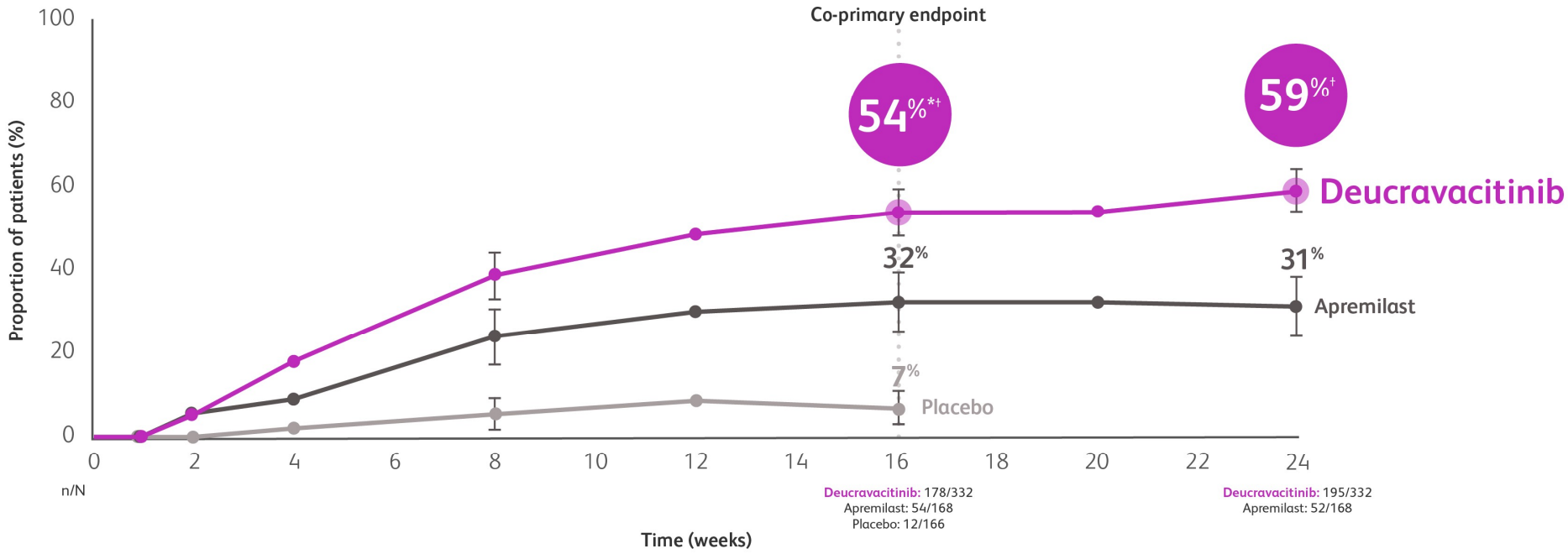
*Apremilast was titrated from 10 mg QD to 30 mg BID over the first 5 days of dosing.[2]

†Upon relapse (≥50% loss of Week-24 PASI percentage improvement from baseline), patients were switched to deucravacitinib 6 mg QD; due to a programming error, however, these patients continued on placebo until Week 52.[2,3]

BID, twice daily; BL, baseline; BSA, body surface area; PASI, Psoriasis Area and Severity Index; PASI 50, 50% improvement from baseline in PASI score; PASI 75, 75% improvement from baseline in PASI score; PASI 90, 90% improvement from baseline in PASI score; PASI 100, 100% improvement from baseline in PASI score; PGA-F, Physician's Global Assessment of Fingernail Psoriasis; PSSD, Psoriasis Symptoms and Signs Diary; QD, once daily; sPGA, static Physician's Global Assessment; ss-PGA, scalp-specific Physician's Global Assessment.

1. SOTYKTU Product Information. 2. Armstrong AW *et al. J Am Acad Dermatol* 2023;88(1):29-39. 3. Strober B *et al. J Am Acad Dermatol* 2023;88(1):40-51.

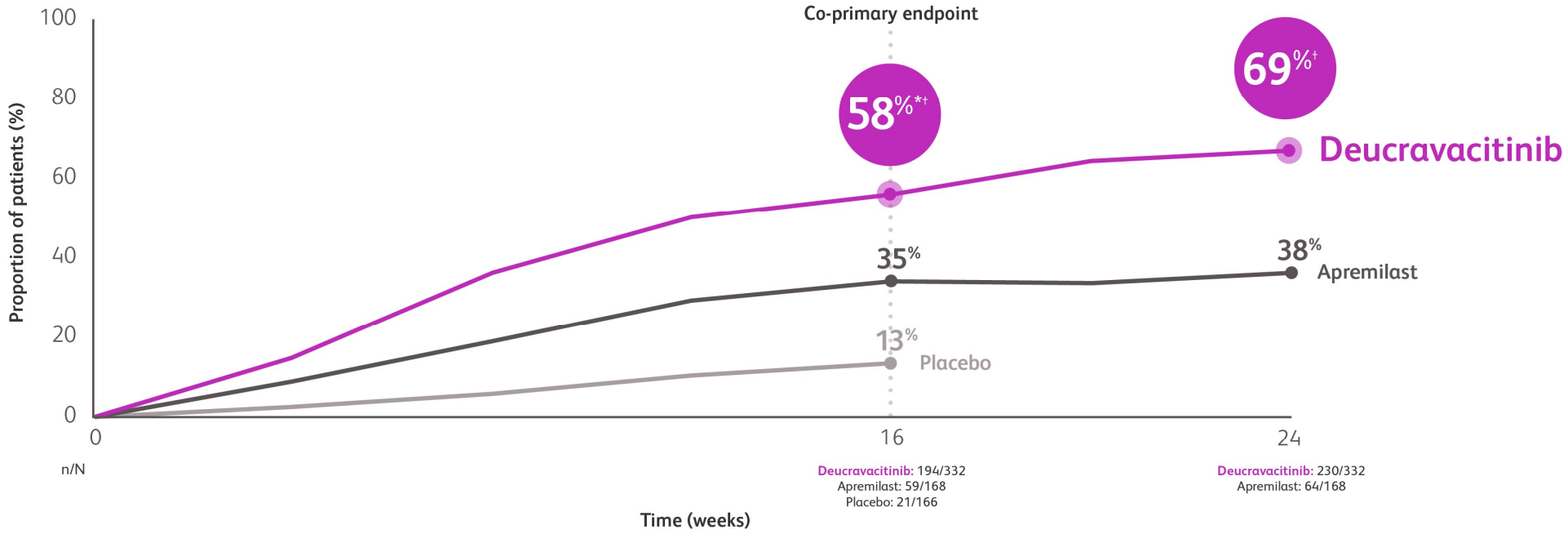
POETYK PSO-1: Superior sPGA 0/1 (clear or almost clear skin) response rates vs placebo and apremilast[1,2]



Adapted from SOTYKTU Product Information[1] and Armstrong *et al*, 2022.[2]
*p<0.0001 for deucravacitinib vs placebo at Week 16. †p<0.0001 for deucravacitinib vs apremilast at Weeks 16 and 24.
Percentage of patients achieving an sPGA score of 0 or 1 with a ≥2-point improvement from baseline (non-responder imputation).

BID, twice daily; QD, once daily; sPGA, static Physician's Global Assessment.
1. SOTYKTU Product Information. 2. Armstrong AW *et al*. *J Am Acad Dermatol* 2023;88(1):29-39.

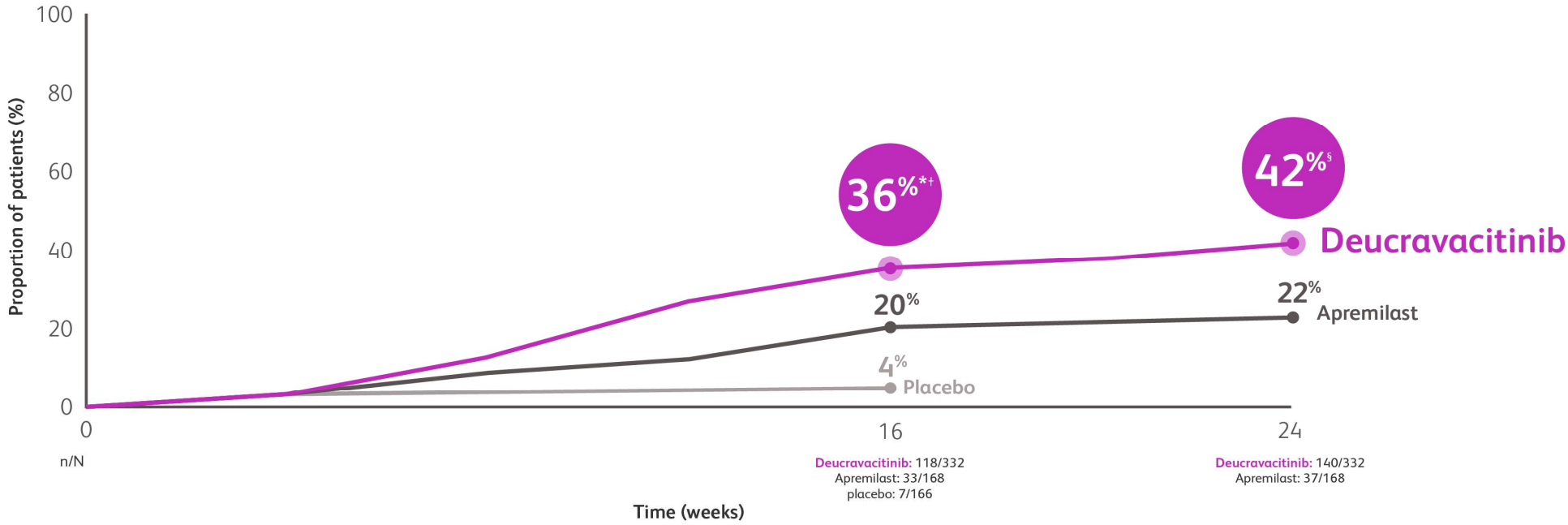
POETYK PSO-1: Superior PASI 75 response rate vs placebo and apremilast[1,2]



Adapted from SOTYKTU Product Information[1] and Armstrong *et al*, 2022.[2]
*p<0.0001 for deucravacitinib vs placebo at Week 16. †p<0.0001 for deucravacitinib vs apremilast at Weeks 16 and 24.
Non-responder imputation.

BID, twice daily; PASI, Psoriasis Area and Severity Index; QD, once daily.
1. SOTYKTU Product Information. 2. Armstrong AW *et al*. *J Am Acad Dermatol* 2023;88(1):29-39.

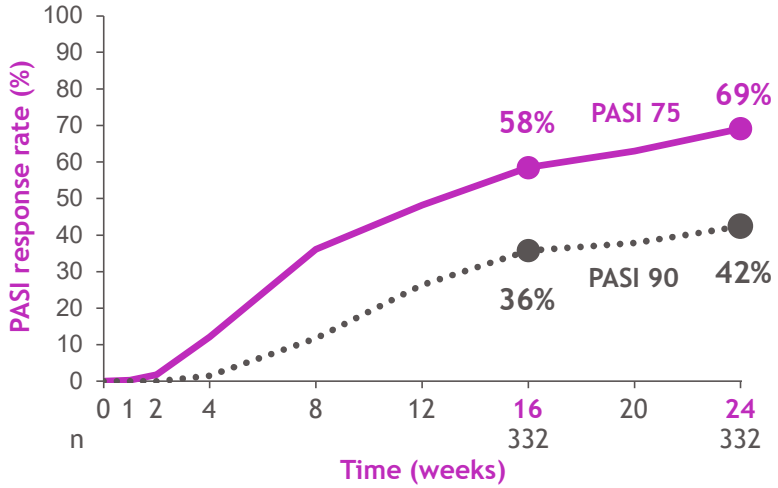
POETYK PSO-1: Superior PASI 90 response rates vs placebo and apremilast[1,2]



Adapted from SOTYKTU Product Information[1] and Armstrong *et al*, 2022 & Supplementary Appendix.[2] Non-responder imputation.
*p=0.0002 for deucravacitinib vs apremilast at Week 16. †p<0.0001 for deucravacitinib vs placebo at Week 16. §p<0.0001 for deucravacitinib vs apremilast at Week 24.

BID, twice daily; PASI, Psoriasis Area and Severity Index; QD, once daily.
1. SOTYKTU Product Information. 2. Armstrong AW *et al. J Am Acad Dermatol* 2023;88(1):29-39. 3. Strober B *et al. J Am Acad Dermatol* 2023;88(1):40-51.

POETYK PSO-1: Maintenance of PASI 75 and PASI 90 response at Week 52 in patients on deucravacitinib[1,2]



Among patients who achieved **PASI 75** at Week 24:

81% (n=186/230) **MAINTAINED AT 1 YEAR**

Among patients who achieved **PASI 90** at Week 24:

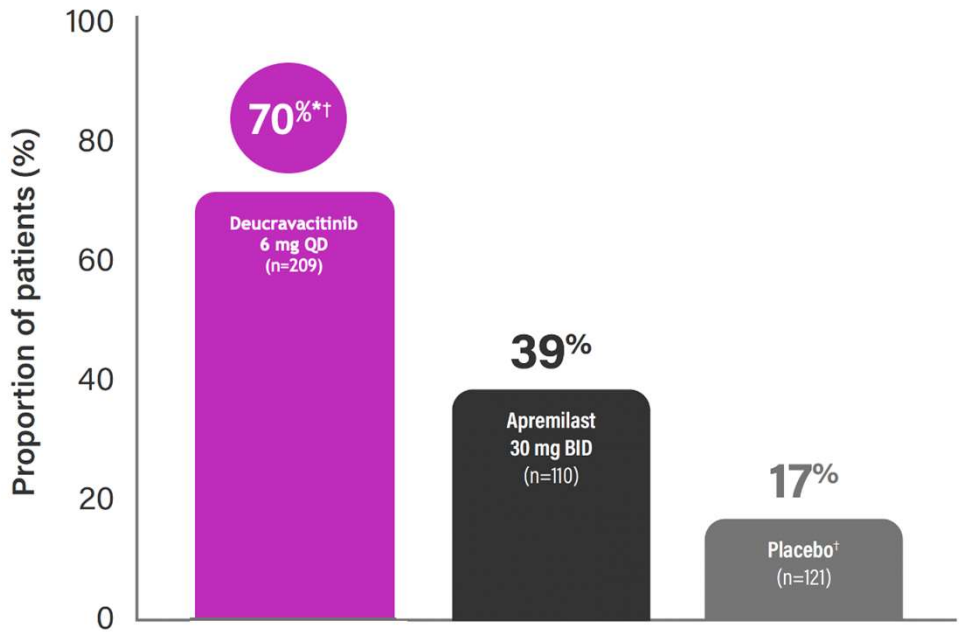
74% (n=103/140) **MAINTAINED AT 1 YEAR**

Adapted from SOTYKTU Product Information[1] and Armstrong *et al*. 2022.[2] Non-responder imputation.

PASI, Psoriasis Area and Severity Index.

1. SOTYKTU Product Information. 2. Armstrong AW *et al*. *J Am Acad Dermatol* 2023;88(1):29-39.

POETYK PSO-1: Clear or almost clear scalp – ss-PGA 0/1 response rates at Week 16[1,2]



A greater portion of patients achieved **clear or almost clear scalp** at Week 16 vs apremilast and placebo*†[1,2]

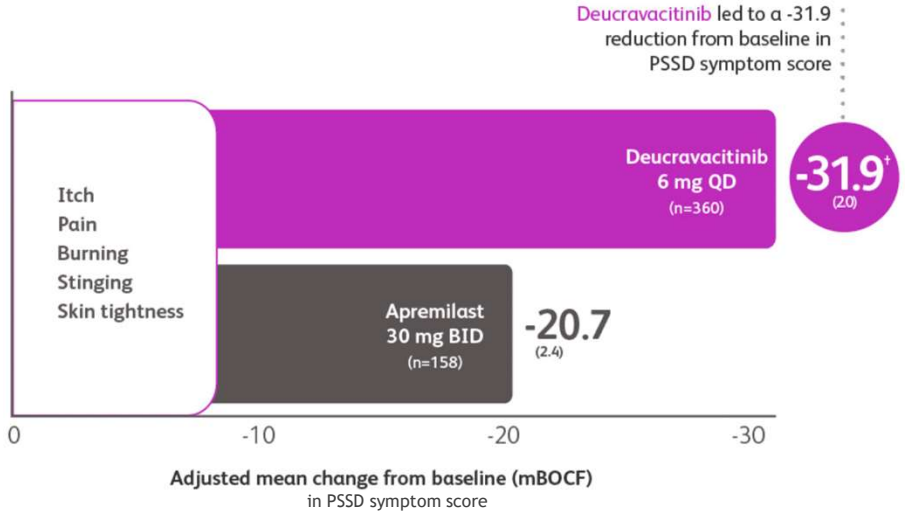
Response rates with deucravacitinib were 72.2% at Week 24 (vs 42.7% for apremilast; p=0.0001)[1,2]

Adapted from SOTYKTU Product Information[1] and Armstrong et al, 2022.[2]
*p<0.0001 for deucravacitinib vs apremilast.
†p<0.0001 for deucravacitinib vs placebo.
ss-PGA, scalp-specific Physician's Global Assessment.
Results in these tabs are from the POETYK PSO-1 study. For results from the POETYK PSO-2 study, please refer to the Product Information.[1]
1. SOTYKTU Product Information. 2. Armstrong AW *et al. J Am Acad Dermatol* 2023;88(1):29-39 & Supplementary Appendix. 3. Strober B *et al. J Am Acad Dermatol* 2023;88(1):40–51.

POETYK PSO-1: Superior patient-reported outcomes vs apremilast[1-3]

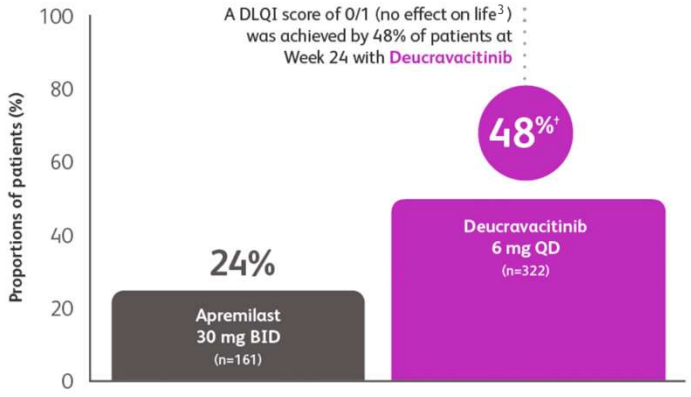
Secondary endpoints

Adjusted mean change (SE) in PSSD symptom score from baseline to Week 24[1,2]



Adapted from SOTYKTU Product Information[1] and Armstrong *et al*. 2022.[2]
†p<0.0001 for deucravacitinib vs apremilast.

Proportion of patients with DLQI score 0/1 at Week 24[2]



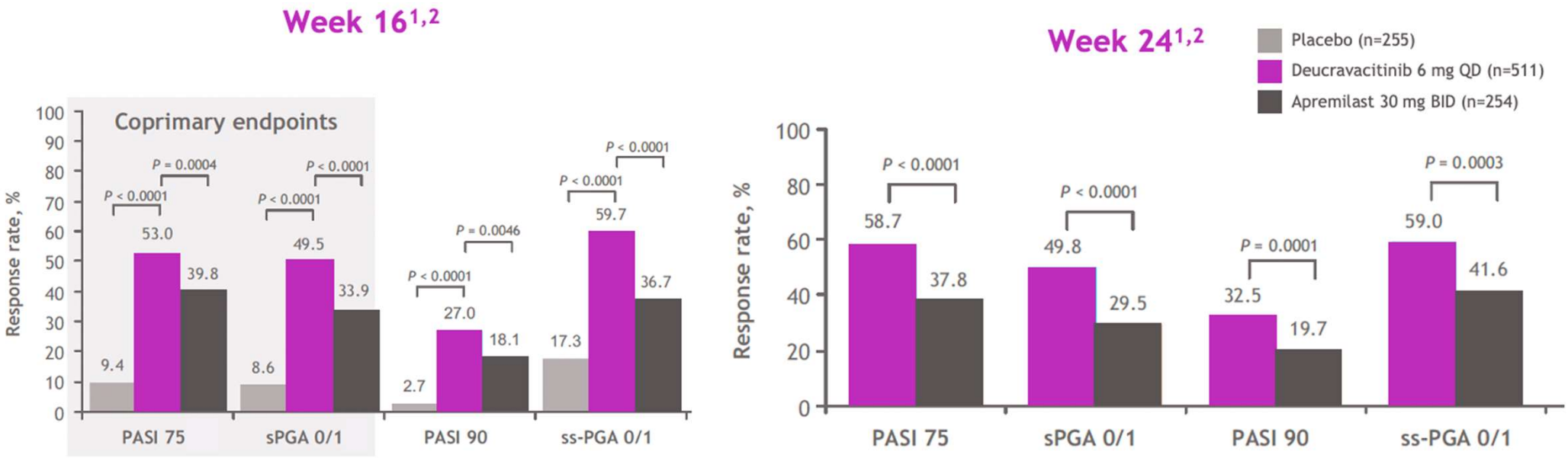
Adapted from Armstrong *et al*, 2022.[2]
†p<0.0001 for deucravacitinib vs apremilast.

- A greater proportion of patients treated with deucravacitinib (8%) compared to placebo (1%) achieved a PSSD symptom score of 0 at Week 16[1,2]

DLQI, Dermatology Life Quality Index; mBOCF, modified baseline observation carried forward; PSSD, Psoriasis Symptoms and Signs Diary; SE, standard error.

1. SOTYKTU Product Information. 2. Armstrong AW *et al*. *J Am Acad Dermatol* 2023;88(1):29-39.

POETYK PSO-2: Superior efficacy vs placebo and apremilast[1,2]

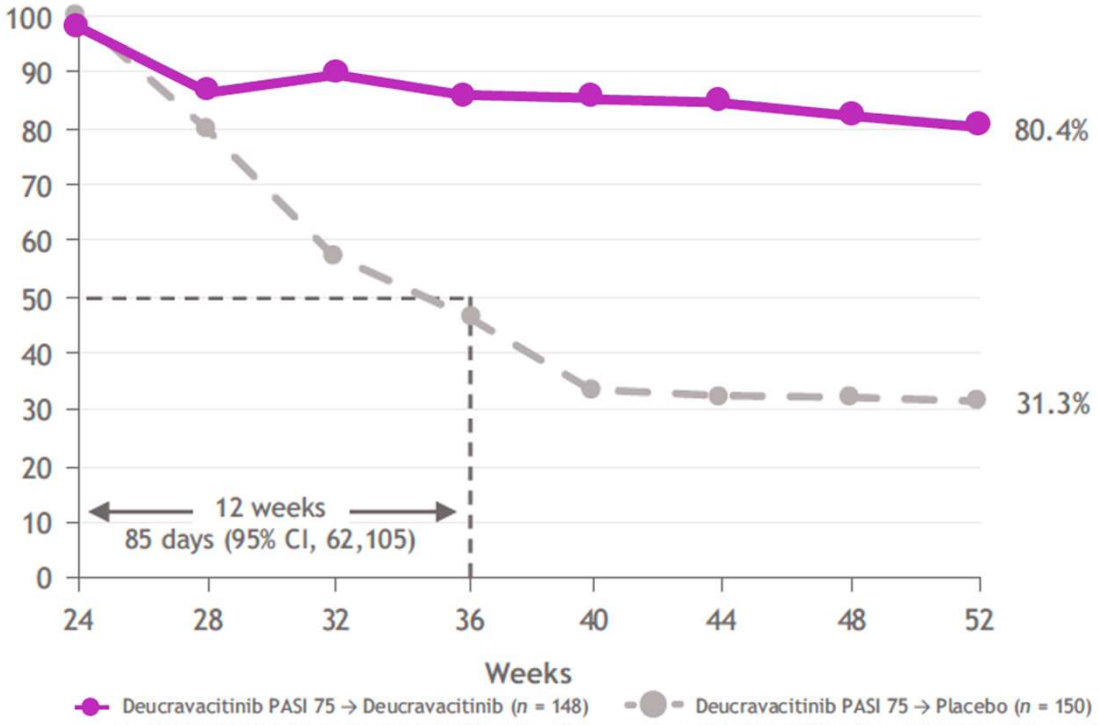


Adapted from SOTYKTU Product Information[1] and Strober *et al*. 2023.[2] Non-responder imputation.

BID, twice daily; PASI, Psoriasis Area and Severity Index; QD, once daily; sPGA, static Physician's Global Assessment; ss-PGA, scalp-specific Physician's Global Assessment.

1. SOTYKTU Product Information. 2. Strober B *et al*. *J Am Acad Dermatol* 2023;88(1):40-51.

POETYK PSO-2: Maintenance of PASI 75 response at Week 52 in patients on deucravacitinib[1,2]



Among patients who achieved **PASI 75** at Week 24:

80.4% (n=148) **MAINTAINED AT 1 YEAR**

Adapted from SOTYKTU Product Information[1] and Strober *et al*. 2023.[2] Non-responder imputation.

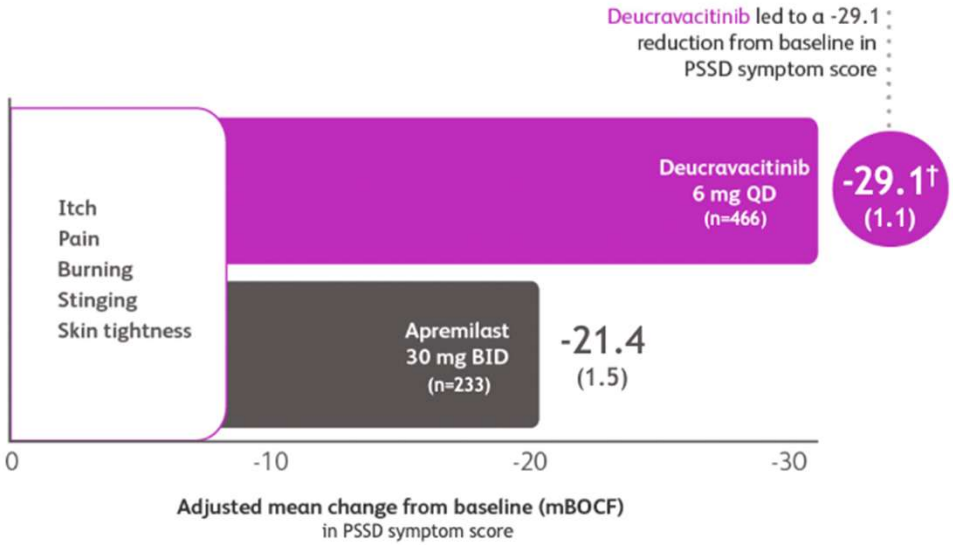
BID, twice daily; PASI, Psoriasis Area and Severity Index; QD, once daily; sPGA, static Physician's Global Assessment; ss-PGA, scalp-specific Physician's Global Assessment.

1. SOTYKTU Product Information. 2. Strober B *et al*. *J Am Acad Dermatol* 2023;88(1):40-51.

POETYK PSO-2: Superior patient-reported outcomes vs apremilast[1,2]

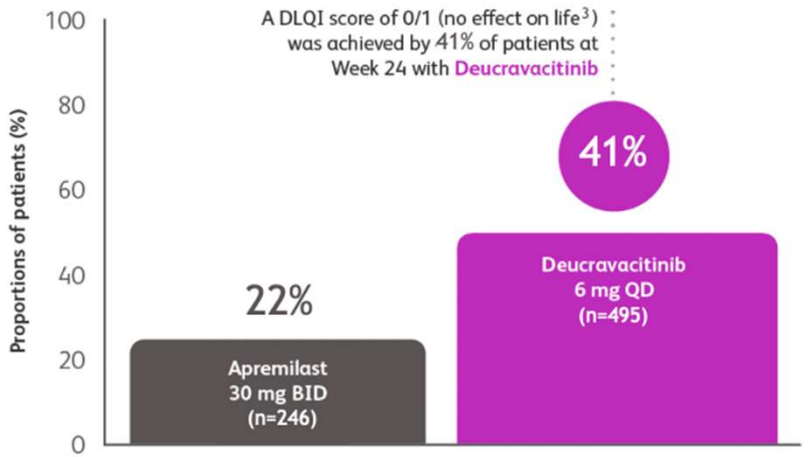
Secondary endpoints

Adjusted mean change (SE) in PSSD symptom score from baseline to Week 24[2]



Adapted from SOTYKTU Product Information[1] and Strober *et al*. 2023.[2]
†p<0.0001 for deucravacitinib vs apremilast.

Proportion of patients with DLQI score 0/1 at Week 24[2]



Adapted from Strober *et al*, 2023.[2]
†p<0.0001 for deucravacitinib vs apremilast.

- A greater proportion of patients treated with deucravacitinib (8%) compared to placebo (1%) achieved a PSSD symptom score of 0 at Week 16[1,2]

DLQI, Dermatology Life Quality Index; mBOCF, modified baseline observation carried forward; PSSD, Psoriasis Symptoms and Signs Diary; SE, standard error.

1. SOTYKTU Product Information. 2. Strober B *et al*. *J Am Acad Dermatol* 2023;88(1):40-51.

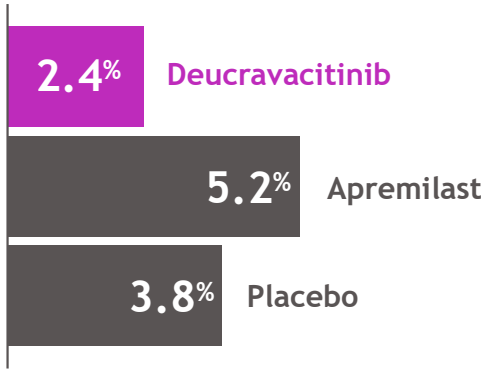
Through Week 16: safety analysis[1]

POETYK PSO-1 and POETYK PSO-2 (pooled safety)

n (%)	Placebo n=419	Deucravacitinib n=842*	Apremilast n=422
AEs occurring in ≥5% of patients in any treatment group			
Nasopharyngitis	36 (8.6)	76 **(9.0)**	37 (8.8)
Upper respiratory tract infection	17 (4.1)	46 **(5.5)**	17 (4.0)
Headache	19 (4.5)	38 **(4.5)**	45 (10.7)
Diarrhoea	25 (6.0)	37 **(4.4)**	50 (11.8)
Nausea	7 (1.7)	14 **(1.7)**	42 (10.0)

Deucravacitinib was associated with a low rate of GI adverse events, similar to placebo and lower than apremilast

Discontinuation rates due to AEs at Week 16[1]



Through Week 52, no new AEs were identified with deucravacitinib and the incidence rates of common AEs did not increase compared to those observed during the first 16 weeks of treatment

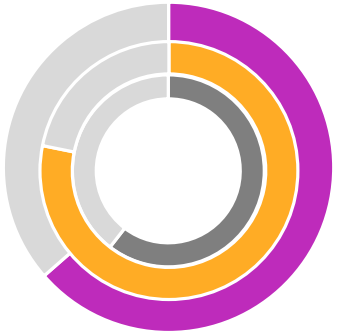
Studies were not designed to compare the safety of apremilast to deucravacitinib. Some of the observed safety rates for apremilast may differ from those previously reported. Please refer to the apremilast full Product Information.

*Includes 2 patients in the deucravacitinib arm who were excluded from primary and secondary endpoint analyses.[1] AE, adverse event.

1. SOTYKTU Product Information.

Deucravacitinib had a favourable safety profile across two phase 3 trials through week 52[1-6]

Incidence of AEs[1]

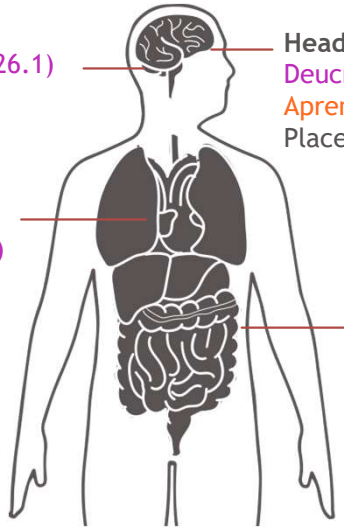


- Deucravacitinib (229.2 EAIR/100 PY)
- Apremilast (281.1 EAIR/100 PY)
- Placebo (217.4 EAIR/100 PY)

Most common AEs (≥5%) in the deucravacitinib treatment group (EAIR/100 PY)[1,2]

Nasopharyngitis
Deucravacitinib (26.1)
Apremilast (25.9)
Placebo (22.7)

URTI
Deucravacitinib (13.4)
Apremilast (12.4)
Placebo (13.5)



Headache
Deucravacitinib (8.5)
Apremilast (26.0)
Placebo (8.6)

Diarrhoea
Deucravacitinib (7.3)
Apremilast (26.5)
Placebo (11.5)

SAEs[1,2]
4.0% with deucravacitinib
2.1% with apremilast
2.1% with placebo

Discontinuations because of AEs[1,2]
3.2% with deucravacitinib
6.2% with apremilast
3.5% with placebo

- An increased risk of MACE, DVT, and PE was not observed in clinical trials with deucravacitinib[6]
- Long-term safety evaluations for deucravacitinib are ongoing

AE, adverse event; DVT, deep vein thrombosis; EAIR, exposure-adjusted incidence rate; MACE, major adverse cardiac events; PE, pulmonary embolism; PY, patient-years; SAE, serious adverse event; URTI, upper respiratory tract infection.

1. Armstrong AW et al. Oral presentation at AAD VMX 2021; April 23-25, 2021; virtual. 2. Alexis A et al. Poster presentation at Winter Clinical Dermatology Conference 2022; January 14-19, 2022; Koloa, HI.
3. Armstrong AW *et al. J Am Acad Dermatol* 2023;88(1):29-39. 4. Strober B *et al. J Am Acad Dermatol* 2023;88(1):40-51. 5. SOTYKTU Product Information. 6. Gooderham MJ et al. Skin Therapy Lett 2022;27:1-5.

Deucravacitinib: Once-daily dosing[1]

A first-in-class TYK2 inhibitor[1,2] with:

- **NO** DOSE TITRATION & ADJUSTMENTS
- **NO** KNOWN DRUG-TO-DRUG INTERACTIONS
  (Avoid use with live vaccines)
- CAN BE TAKEN **WITH OR WITHOUT** FOOD
  (Do not crush, cut or chew the tablet)

TYK2, tyrosine kinase 2.

1. SOTYKTU Product Information. 2. Australian Register of Therapeutic Goods. Available at: https://www.ebs.tga.gov.au/. Accessed August 2023.

Deucravacitinib is effective in a range of patient types[1-3]

Dom, aged 32 years*

Moderate-to-severe plaque psoriasis;
no prior systemic therapy

Anna, aged 48 years*

Moderate-to-severe plaque psoriasis;
taking Otezla® (apremilast)
but experiencing GI tolerability issues

Deucravacitinib has demonstrated effectiveness across multiple patient profiles regardless of:[1-3]

- AGE
- RACE
- PRIOR SYSTEMIC/BIOLOGIC TREATMENT
- GENDER
- DISEASE SEVERITY
- BODY WEIGHT

POETYK PSO-1 and POETYK PSO-2 enrolled patients aged ≥18 years with moderate-to-severe plaque psoriasis who were eligible for systemic therapy or phototherapy.[1]
Patients had BSA involvement ≥10%, PASI score >12, and sPGA ≥3 (moderate or severe) on a 5-point scale of overall disease severity.[1]

*Hypothetical patients.
BSA, body surface area; GI, gastrointestinal; PASI, Psoriasis Area and Severity Index; sPGA, static Physician's Global Assessment.
Otezla® is a registered trademark of Amgen Australia Pty Ltd.
References: 1. SOTYKTU Product Information. 2. Armstrong AW *et al. J Am Acad Dermatol* 2023;88(1):29-39. 3. Strober B *et al. J Am Acad Dermatol* 2023;88(1):40–51 & supplementary materials.

Dom, aged 32 years*

Moderate-to-severe plaque psoriasis; no prior systemic therapy

*Hypothetical patient

- Married man with one child who emigrated from China 10 years ago
- Diagnosed with moderate-to-severe plaque psoriasis 5 years ago
- PASI 14
- Smokes and drinks 1–2 beers daily
- Currently treated with topical therapy and phototherapy; has not previously received systemic therapy
- States that he feels increasingly depressed about his psoriasis flares

PASI, Psoriasis Area and Severity Index

Anna, aged 48 years*

Moderate-to-severe plaque psoriasis; taking Otezla® (apremilast) but experiencing GI tolerability issues

*Hypothetical patient

- Married with two teenaged children
- Diagnosed with moderate-to-severe plaque psoriasis 10 years ago
- PASI 12
- Obese (BMI 30 kg/m^2)
- Taking apremilast but experiencing GI tolerability issues
- Upon questioning, she states that her psoriasis is negatively impacting her work and social life

BMI, body mass index; GI, gastrointestinal; PASI, Psoriasis Area and Severity Index.
Otezla® is a registered trademark of Amgen Australia Pty Ltd.

PBS Information: SOTYKTU is not listed on the PBS.

Before prescribing, please refer to the approved Product Information available at https://medsinfo.com.au/product-information/document/Sotyktu_PI or by contacting Bristol Myers Squibb Australia Medical Information, telephone: 1800 067 567, email: MedInfo.Australia@bms.com

▼ This medicinal product is subject to additional monitoring in Australia. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse events at www.tga.gov.au/reporting-problems.

NAME OF THE MEDICINE: SOTYKTU™ (deucravacitinib) **THERAPEUTIC INDICATION:** Treatment of adult patients with moderate-to-severe plaque psoriasis who are candidates for systemic therapy or phototherapy. **DOSE AND METHOD OF ADMINISTRATION:** 6 mg once daily taken orally, with or without food. Do not crush, cut, or chew the tablet. **CONTRAINDICATIONS:** Hypersensitivity to the active substance or to any of the excipients. **SPECIAL WARNINGS AND PRECAUTIONS FOR USE:** Hypersensitivity; Infections including viral reactivation; Pretreatment Evaluation for Tuberculosis; Malignancies; Immunisations; Potential risks of JAK inhibition; Laboratory abnormalities including elevated CPK and rhabdomyolysis, Triglyceride Elevations and Liver Enzyme Elevations; Use in Elderly; Paediatric Use. Pregnancy: Category B1. Refer to the Product Information (PI) for further details of the Warnings and Precautions. **INTERACTIONS:** Deucravacitinib is eliminated via multiple pathways with no single pathway predominantly responsible for elimination, major drug interactions via inhibition or induction of a pathway are not anticipated. **ADVERSE EVENTS:** Common (≥1 to <10%): Nasopharyngitis; Upper respiratory tract infection; Headache; Diarrhoea; Blood creatine phosphokinase increased; Arthralgia; Hypertension; Psoriasis; Nausea; Back pain. Refer to the PI for a full list of adverse events and further details. Date of preparation: December 2022.