Genetic & Clinical Evidence for TYK2 as a Driver of Psoriasis

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Bristol Myers Squibb™

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Disclosures

Dr. Dominik Straßer is an employee of Bristol Myers Squibb

Presentation objectives

- To review the clinical and genetic rationale for targeting the TYK2 pathway in psoriasis and psoriatic arthritis
- To present the 4-year long-term safety and efficacy data of deucravacitinib, an approved allosteric TYK2 inhibitor for moderate-to-severe plaque psoriasis
- To provide an update on the current management approach to psoriatic arthritis and review the deucravacitinib program in psoriatic arthritis

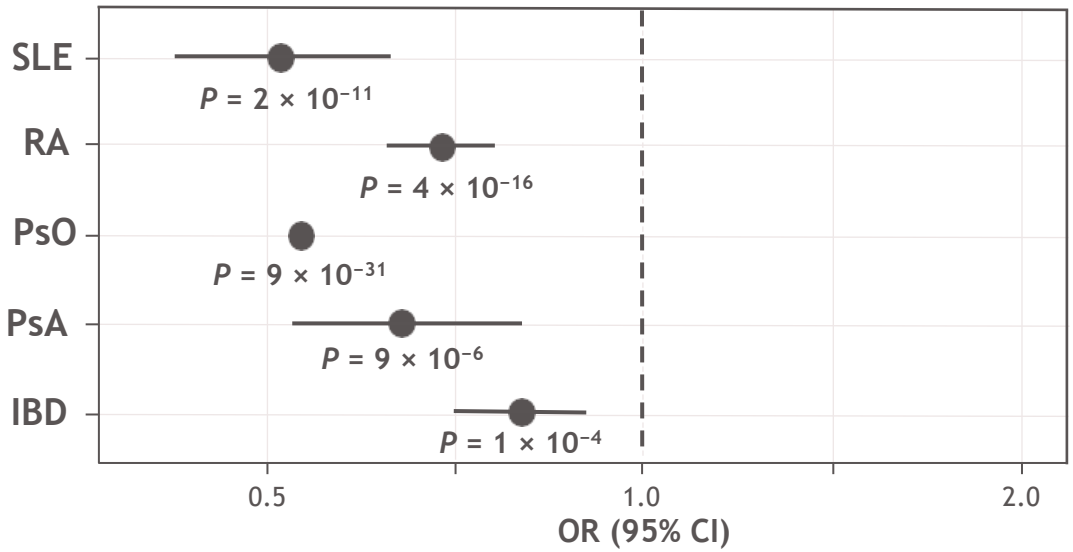
Part 1

Spotlight on the Genetic and Clinical Evidence for TYK2 as a Driver of Psoriasis

Genetic rationale for targeting TYK2

- Genome-wide association studies (**GWAS**) can help in identifying common genetic determinants of disease[1]
  - For example, approximately 148 gene loci are associated with PsO[2,3]
- Gene loci, in turn, can provide insight into the pathogenesis of disease[4]

P1104A associations with select autoimmune diseases[5]

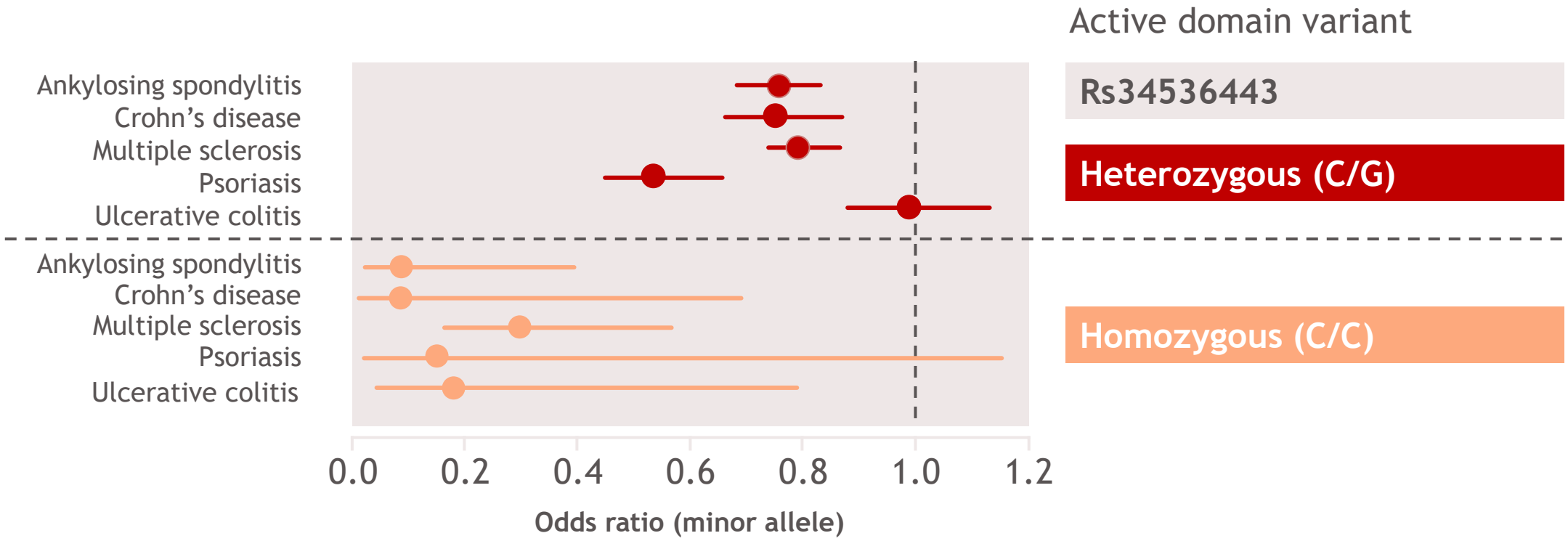


- TYK2 is a nonreceptor kinase enzyme encoded by the *TYK2* gene, which is constitutively expressed in immune cells and keratinocytes[6,7]
- TYK2 P1104A, a partial loss-of-function polymorphism, is associated with:[5,6]
  - Protection against several autoimmune diseases, including PsO
  - Reduction of Type I IFN, IL-12, and IL-23 signaling
  - No increase in the risk of infection, CVD, VTE, mortality, or malignancy (including lymphoma)

Reproduced with permission from Raghupathy N.[3]

1. Price AL et al. *Proc Biol Sci*. 2015;282:20151684. 2. Tsoi LC et al. *Nat Commun*. 2017;8:15382. 3. Dand N et al. *medRxiv* 2023. 4. Patrick MT et al. *Nat Commun*. 2018;9:4178. 5. Raghupathy N et al. Poster presentation at EADV Spring Symposium; May 12–14, 2022; Ljubljana, Slovenia. Poster P110. 6. Dendrou CA et al. *Sci Transl Med*. 2016;8:363ra149. 7. Paige KM et al. *J Invest Dermatol*. 2020;140:1546-1555.e4.

Loss-of-function gene variants in TYK2 were associated with reduced risk of certain immune-mediated diseases in a population study, emphasizing the potential TYK2/inflammation link



Adapted with permission from Dendrou et al.[1]
[a]SNP data in the TYK2 locus was analyzed via Immunochip genotyping from 8726 patients with ankylosing spondylitis, 4017 patients with Crohn's disease, 16,691 patients with multiple sclerosis, 2814 patients with PsO, 3871 patients with ulcerative colities, and 19,738 population controls.
Dendrou CA et al. *Sci Transl Med*. 2016;8:363ra149.

Pathophysiology of Psoriasis

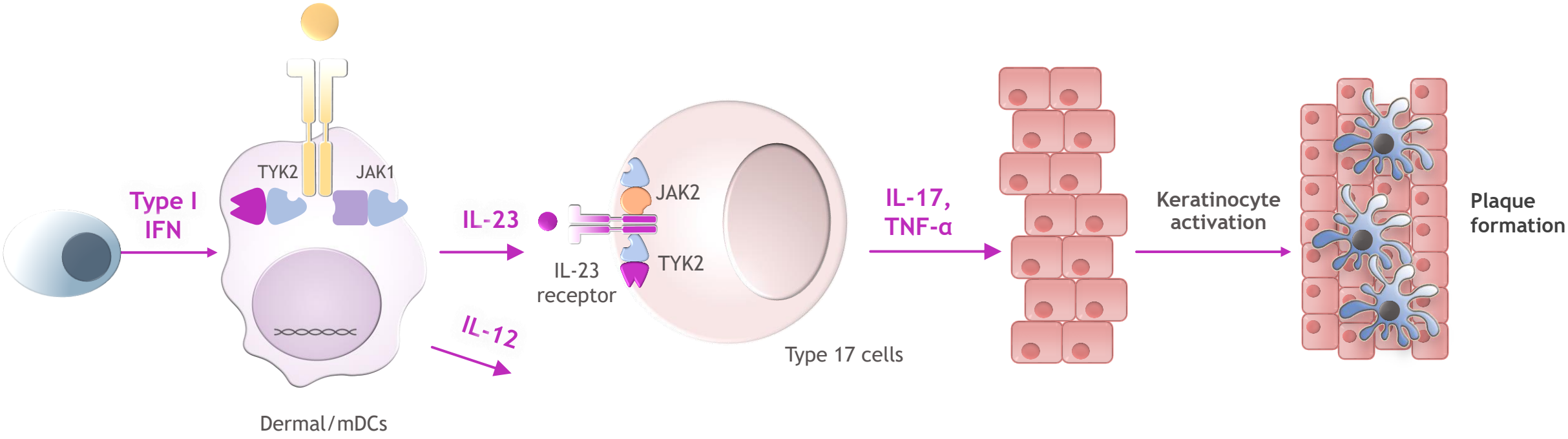
Multiple cytokines, including those mediated by TYK2, are central to the pathology of both early and late PsO[1-3]

Early/acute disease: type I IFN[1,3]

- Flare-ups, unstable lesions
- Erythrodermic PsO
- Paradoxical PsO

Late/chronic disease: IL-23, IL-17, IL-22, TNF-α[1,2]

- Plaque PsO

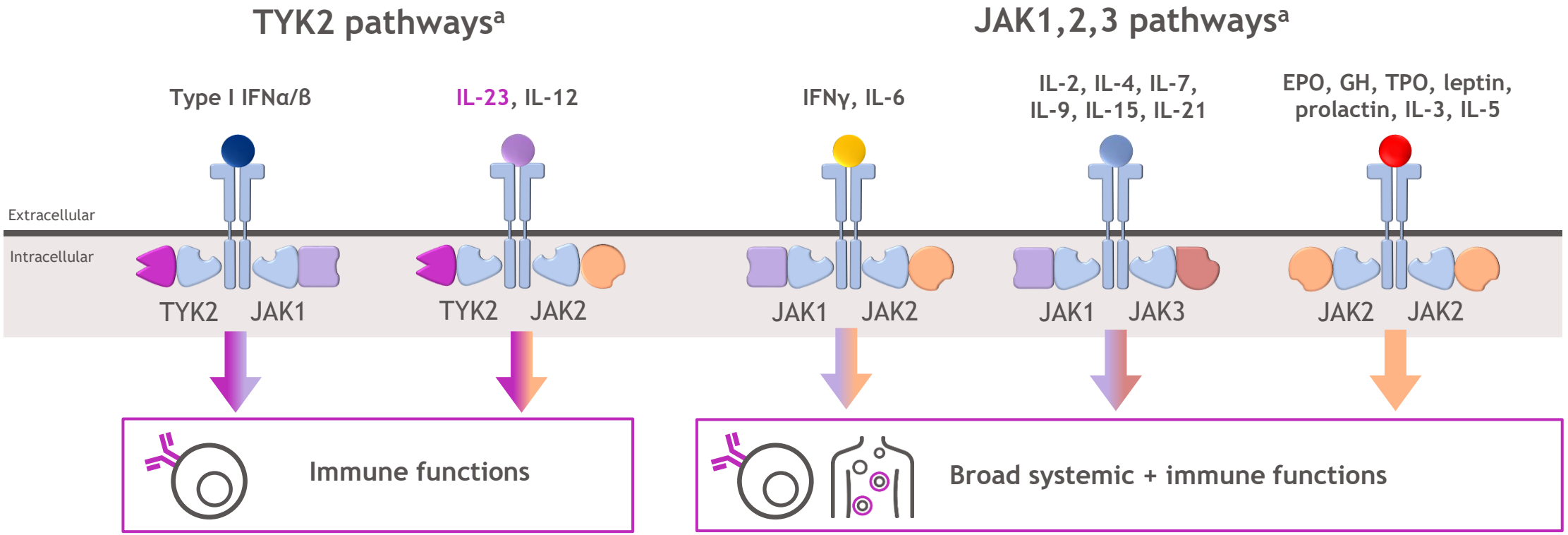


Please note that the pathway discussed is not an extensive diagram and that other cytokines/kinases may be involved within PsO/PsA pathophysiology.

1. Schlapbach C and Conrad C. *J Allergy Clin Immunol*. 2022;149:1936-9. 2. Boutet M-A et al. *Int J Mol Sci*. 2018;19:530. 3. Zhang LJ. *Front Immunol*. 2019;10:1440.

TYK2 as a Target in Psoriasis

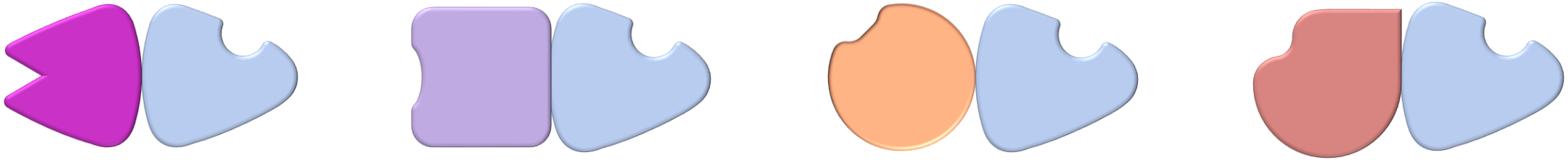
One of the key cytokines for PsO pathophysiology, IL-23, is mediated by TYK2, which transduces immune responses[1-28]



[a]Please note that this list of cytokines modulated by different JAK/JAK and TYK2/JAK pairs is not exhaustive. Certain cytokines might also be mediated by JAK and TYK2 trimers.[1,2]

1. Banerjee S et al. *Drugs*. 2017;77:521-546. 2. Baker KF, Isaacs JD. *Ann Rheum Dis*. 2018;77:175-187. 3. Zhang P et al. *J Exp Med*. 1998;188:1173-1184. 4. Diehl S, Rincón M. *Mol Immunol*. 2002;39:531-536. 5. Kopf M et al. *Nature*. 1994;368:339-342. 6. Glund S, Krook A. *Acta Physiol (Oxf)*. 2008;192:37-48. 7. Gao Y et al. *J Clin Invest*. 2007;117:122-132. 8. Sun L et al. *Oncotarget*. 2017;8:40065-40078. 9. Giliani S et al. *Immunol Rev*. 2005;203:110-126. 10. Karasuyama H et al. *J Exp Med*. 1988;167:1377-1390. 11. Sonoda Y. *Leuk Lymphoma*. 1994;14:231-240. 12. Ebbo M et al. *Nat Rev Immunol*. 2017;17:665-678. 13. Fallon PG et al. *Immunity*. 2002;17:7-17. 14. Kitagawa Y, Sakaguchi S. *Curr Opin Immunol*. 2017;49:64-70. 15. Krolopp JE et al. *Front Physiol*. 2016;7:626. 16. Dougan M et al. *Immunity*. 2019;50:796-811. 17. Zeigler BM et al. *Dis Model Mech*. 2010;3:763-772. 18. Staerk J, Constantinescu SN. *JAKSTAT*. 2012;1:184-190. 19. Lu M et al. *Signal Transduct Target Ther*. 2019;4:3. 20. Jiang L et al. *J Biol Chem*. 2008;283:28066-28073. 21. Simmons DP et al. *J Immunol*. 2012;188:3116-3126. 22. De Groof A et al. *Rheumatology (Oxford)*. 2020;59:668-677. 23. Eloranta ML, Rönnblom L. *J Mol Med (Berl)*. 2016;94:1103-1110. 24. Floss DM et al. *Cells*. 2020;9:2184. 25. Ishizaki M et al. *Int Immunol*. 2014;26:257-267. 26. Aggarwal S et al. *J Biol Chem*. 2003;278:1910-1914. 27. Geremia A et al. *J Exp Med*. 2011;208:1127-1133. 28. Clark JD et al. *J Med Chem*. 2014;57:5023-5038.

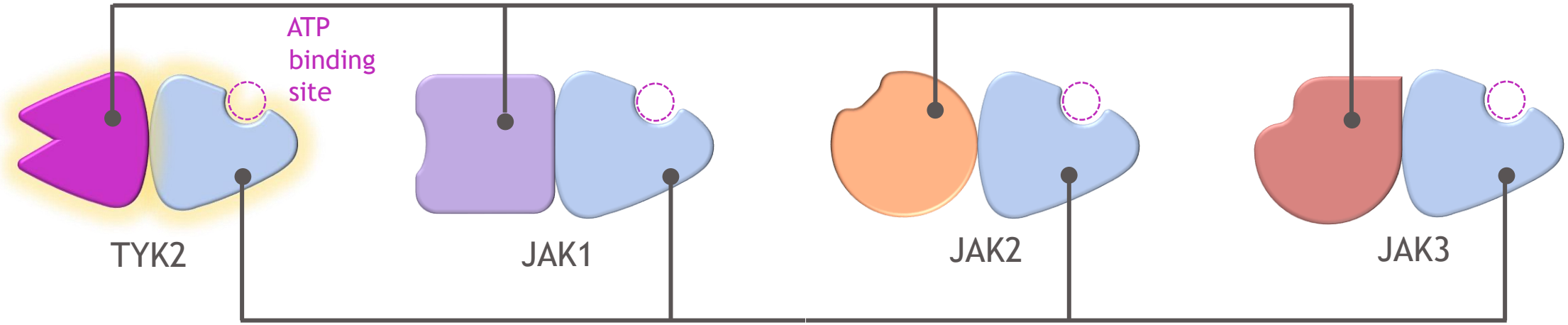
TYK2 is part of the TYK2/JAK family of kinases[1-3]



1. Banerjee S et al. *Drugs*. 2017;77:521–546. 2. Lu X et al. *Angew Chem Int Ed Engl*. 2020;59:13764–13776. 3. Tokarski JS et al. *J Biol Chem*. 2015;290:11061–11074.

TYK2 and JAK1,2,3 have structurally similar active sites, which bind to ATP, and structurally differentiated regulatory domains[1-3]

Regulatory domain: structurally different across family members



Active domain: structurally similar across family members

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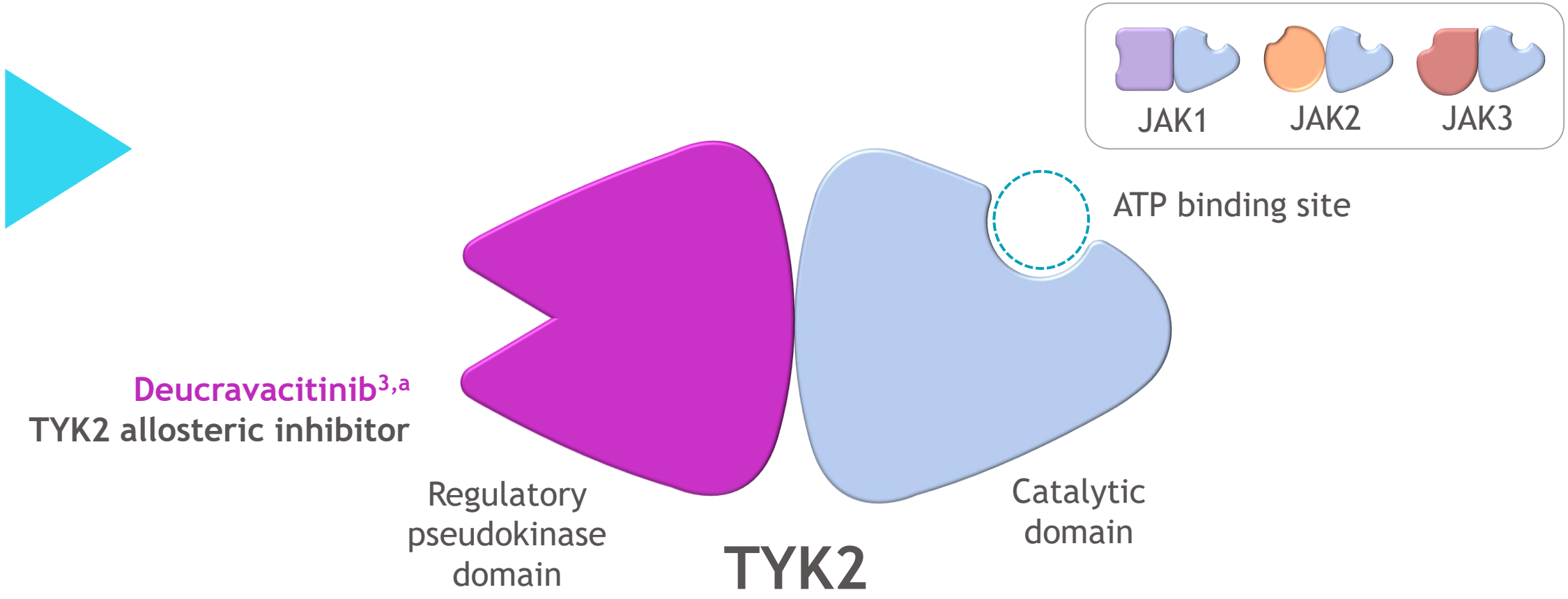
Deucravacitinib is a selective allosteric TYK2 inhibitor, which binds to the regulatory domain[1-3]



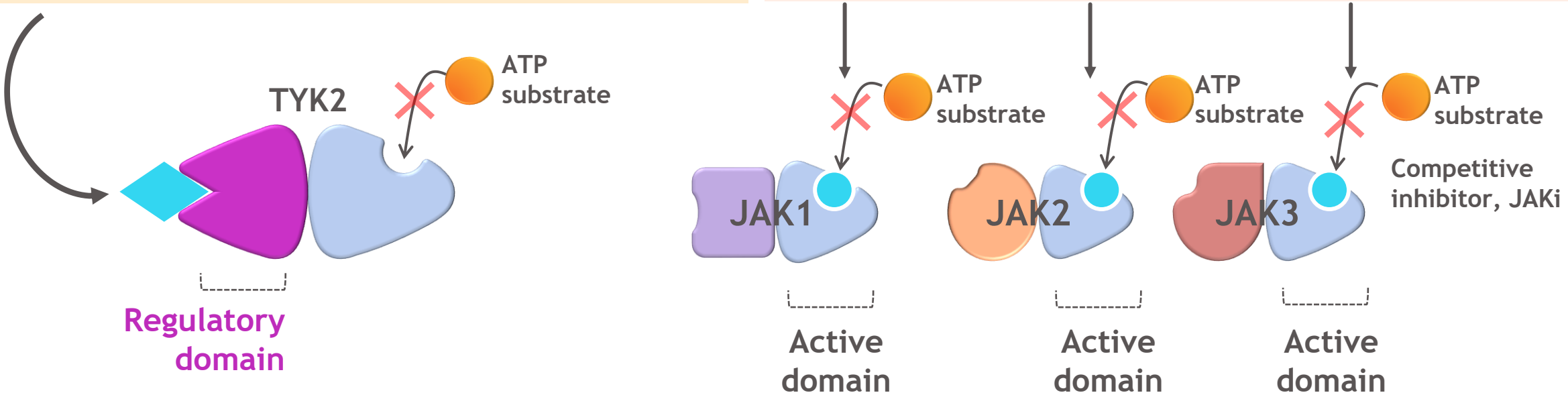
[a]First oral TYK2 allosteric inhibitor approved for the treatment of moderate-to-severe PsO.[3,4]

1. Chimalakonda A et al. *Dermatol Ther (Heidelb)*. 2021;11:1763–1776. 2. Gangolli EA et al. Poster presented at: 2022 SID Annual Meeting, May 18 - 21, 2022; Portland, Oregon. 3. Sotyktu. Summary of Product Characteristics. BMS. 4. Drakos A et al. *Dermatol Ther (Heidlb)*. 2022;12:2715-2730.

What makes allosteric inhibition different from competitive inhibition?

Allosteric inhibitors, such as deucravacitinib, work via **allosteric inhibition of the structurally unique regulatory domain**[1-4]

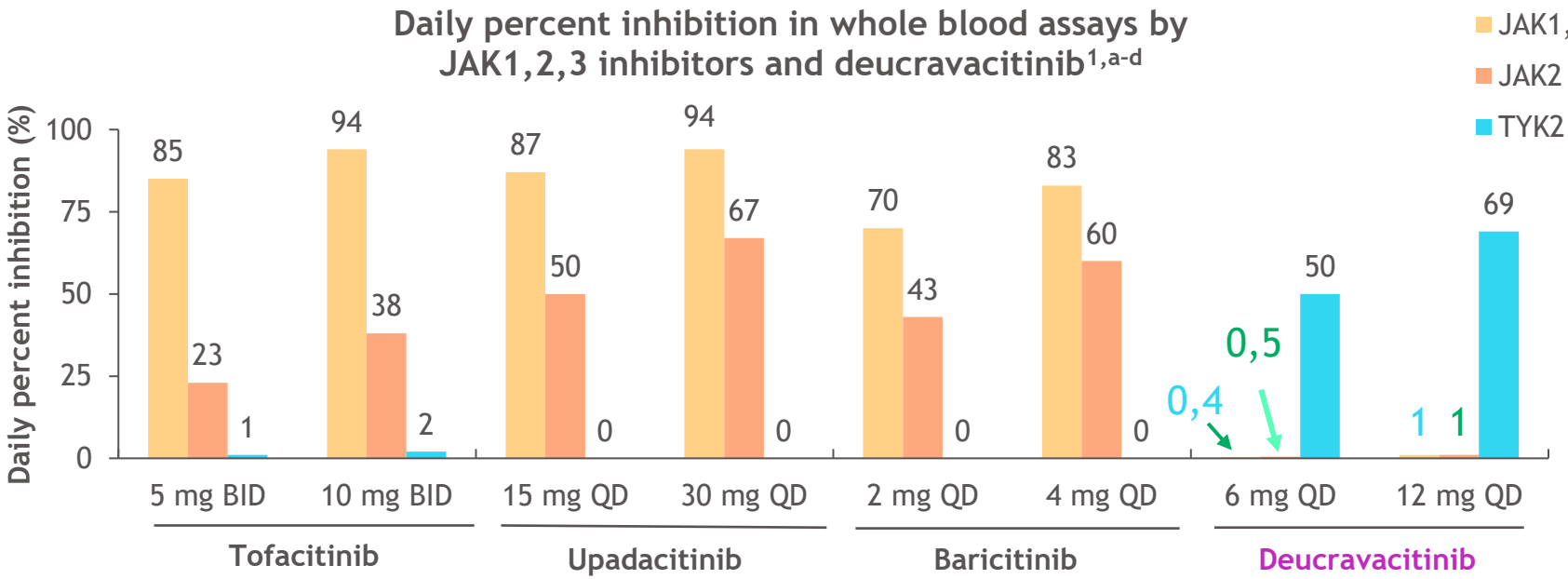
Active domain-targeted JAKis work via competitive inhibition of the highly conserved ATP-binding site[5]



1. Krueger JG et al. *J Amer Acad Dermatol*. 2022;86:148-157. 2. Papp K et al. *N Engl J Med*. 2018;379:1313-1321. 3. Tokarski JS et al. *J Biol Chem*. 2015;290:11061-11074. 4. Gillooly K et al. Poster presentation at ACR/ARHP 2016; November 11-16, 2016; Washington, DC. [or Poster 11L] 5. Virtanen AT et al. *BioDrugs*. 2019;33:15-32.

At clinically relevant doses in *in vitro* assays, deucravacitinib was highly selective for TYK2 vs JAK1,2,3[1]

At clinically relevant doses, deucravacitinib has not been shown to inhibit JAK1,2,3 pathways in *in vitro* assays[1]



	Deucravacitinib IC_{50} (nM) whole blood[1]	Deucravacitinib IC_{50} (nM) cell-based assays[2]
JAK1,3	1646	592
JAK2	>10,000	>10,000
TYK2	42	11

Adapted with permission from Chimalakonda et al.[1] Creative Commons Attribution 4.0 International License (https://creativecommons.org/licenses/by/4.0/).
[a]Not all FDA-approved doses of the JAK inhibitors were included in this analysis. [b]Daily percent inhibition was defined as the average inhibition of TYK2 or JAK1,2,3 activity by these agents over a dosing interval. Average percent inhibition was defined as: percent inhibition = 100 / (1 + [(IC_{50} / X)^H]) where X is the average drug concentration over a dosing interval and H is the Hill coefficient. [c]Reported PK of JAK inhibitors and internal PK profile for deucravacitinib were used. [d]The following were used to measure pathway inhibition: JAK1,3, IL-2–induced STAT5 phosphorylation; JAK2, TPO-induced STAT3 phosphorylation; TYK2, IL-12–induced IFN-γ production. [e]JAK1,3 are grouped together due to IL-2–induced STAT5 phosphorylation in *in vitro* whole-blood assays.
1. Chimalakonda A et al. *Dermatol Ther (Heidelb)*. 2021;11:1763-1776. 2. Burke JR et al. *Sci Transl Med*. 2019;11:eaaw1736.

TYK2 inhibitors affect the pathology of both early and late PsO[1-3]

Early/acute disease: type I IFN[1,3]
- Flare-ups, unstable lesions
- Erythrodermic PsO
- Paradoxical PsO

Late/chronic disease: IL-23, IL-17, IL-22, TNF-α[1,2]
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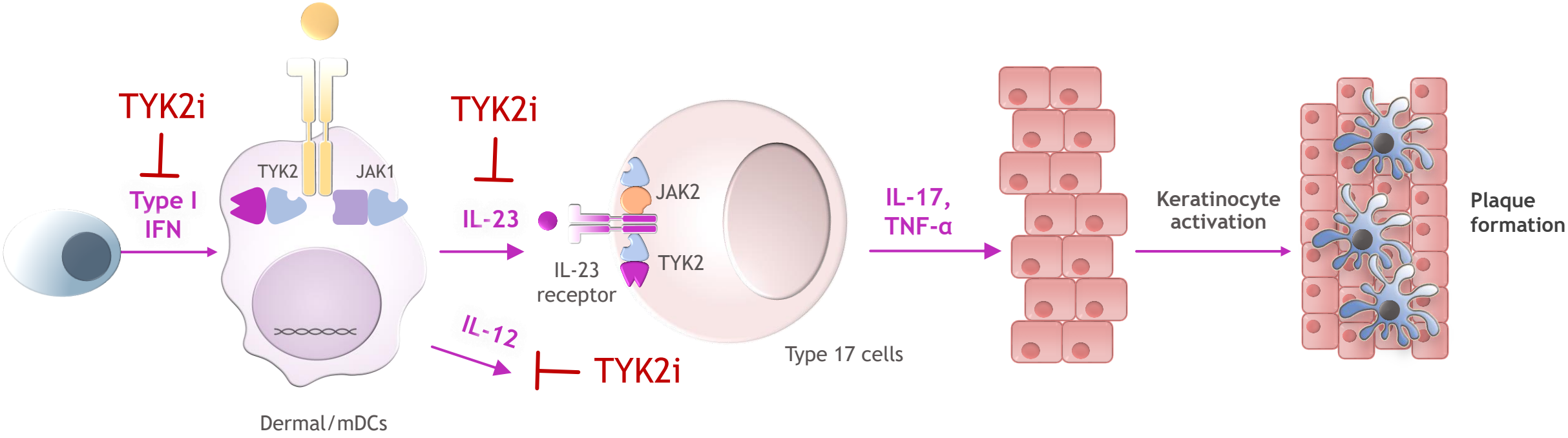

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The current landscape for allosteric TYK2 inhibition in moderate-to-severe plaque psoriasis[1-5]

Two allosteric oral TYK2 inhibitors are progressing to phase 3 clinical trials[3,4]

	Deucravacitinib BMS	Zasocitinib (TAK-279) Takeda	ESK-001 Alumis	VTX958 Ventyx
Status	Approved[1,2]	Two phase 3 trials ongoing[2,3] • EU CTIS 2023-505841-22-00 (NCT06088043) • EU CTIS 2023-505842-24 (NCT06108544)	Two phase 2 trials ongoing[4] • NCT05600036 • NCT05739435 (OLE) Phase 3 to start 2024[4]	Development terminated[5]

1. SOTYKTU. SmPC. 2. Carmona-Rocha et al. *Pharmaceutics*. 2024;16(239):1-36. 3. Takeda Announces Positive Results in Phase 2b Study of Investigational TAK-279, an Oral, Once-Daily TYK2 Inhibitor, in People With Moderate-so-Severe Plaque Psoriasis. 2023. Available at: https://www.takeda.com/newsroom/newsreleases/2023/takeda-announces-positive-results-in-phase-2b-study-of-investigational-tak-279/ Accessed 25 June 2024. 4. Alumis Presents Positive Data From Phase 2 Clinical Trial of ESK-001, an Oral Allosteric TYK2 Inhibitor for the Treatment of Plaque Psoriasis, at AAD Annual Meeting. Available at: https://www.alumis.com/news/press-releases/030924/ Accessed 25 June 2024. 5. Ventyx Biosciences Announces Results From the Phase 2 Trial of VTX958 in Patients with Moderate to Severe Plaque Psoriasis and Provides Corporate Update. 2023. Available at: https://ir.ventyxbio.com/news-releases/news-release-details/ventyx-biosciences-announces-results-phase-2-trial-vtx958. Accessed 25 June 2024. Ventyx Biosciences. VTX958 Phase 2 Plaque Psoriasis Results, Investor Relations. Presented November 6, 2023.

POETYK PSO-1 and PSO-2 and LTE Phase 3 Psoriasis Trials

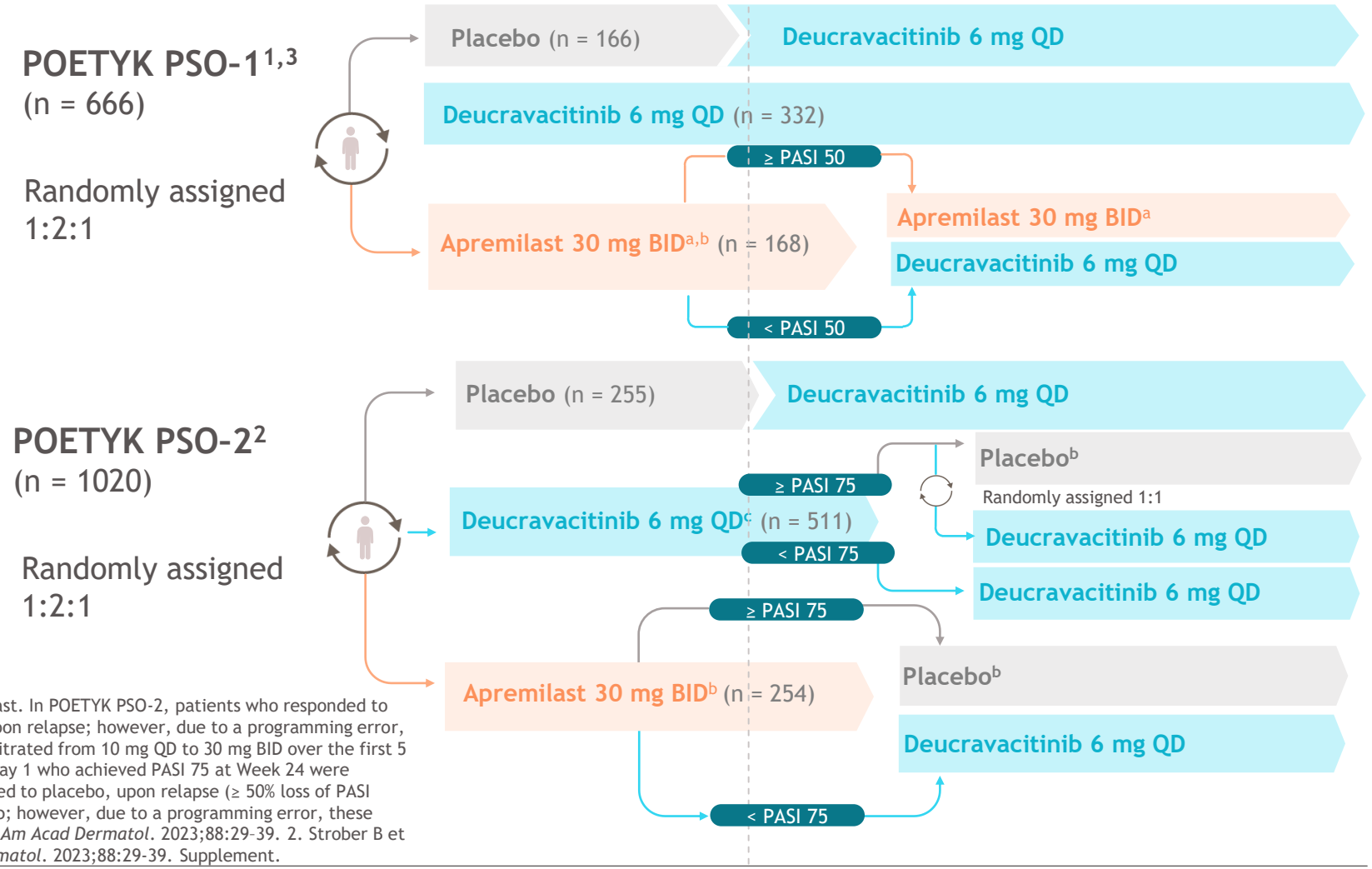
Efficacy

The efficacy and safety of deucravacitinib in PsO was evaluated in two phase 3 trials[1,2]

Double-blind
Multicenter
Moderate-to-severe PsO

Co-primary endpoints (Week 16):[1,2]
- PASI 75
- sPGA 0/1

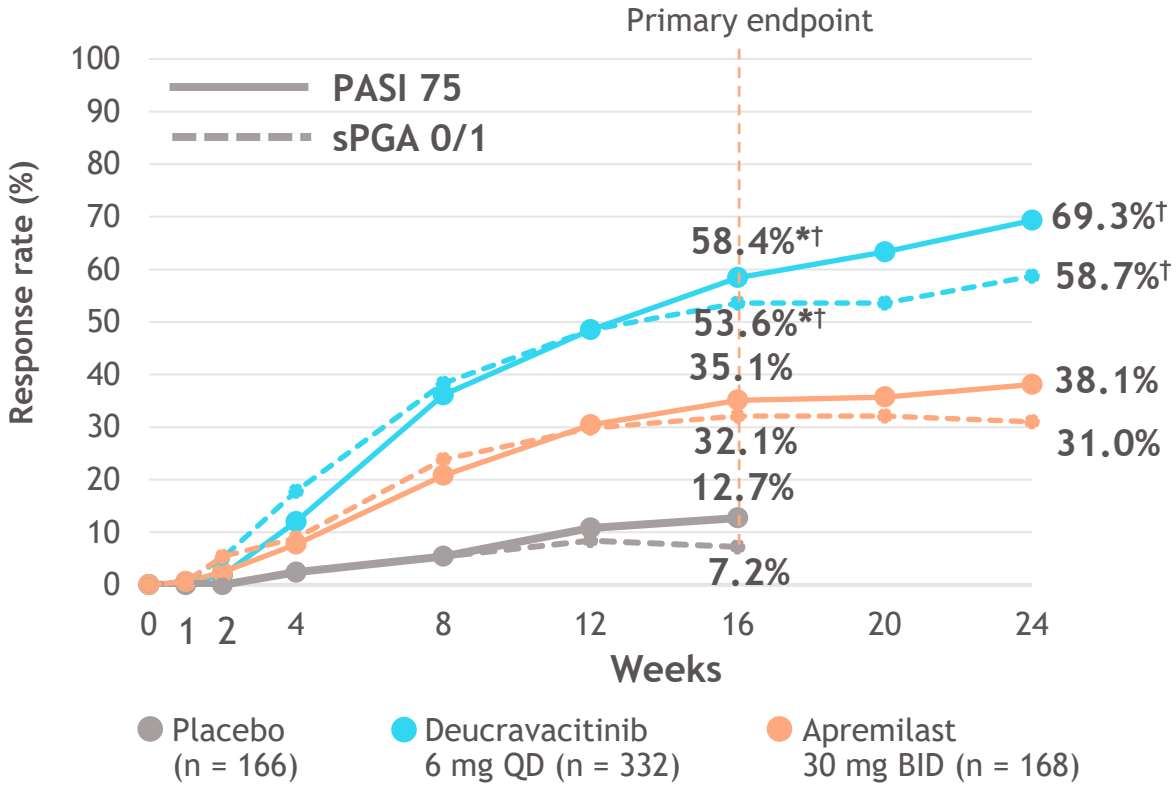
Key inclusion criteria:[1,2]
- ≥ 18 years of age
- Moderate-to-severe PsO (sPGA ≥ 3, PASI ≥ 12, BSA ≥ 10%) for ≥ 6 months before screening



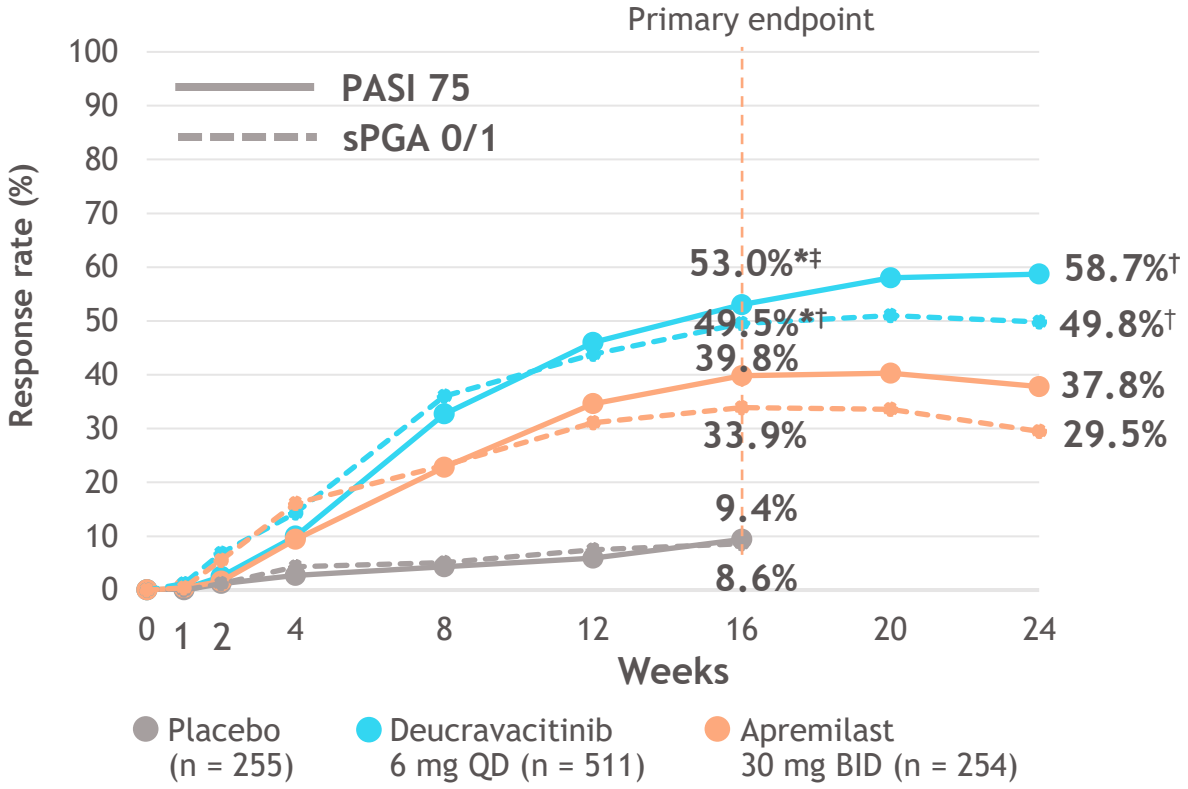
[a]In POETYK PSO-1, patients who responded to apremilast remained on apremilast. In POETYK PSO-2, patients who responded to apremilast crossed over to placebo and were to cross over to deucravacitinib upon relapse; however, due to a programming error, these patients continued to receive placebo until Week 52.[1-3] [b]Apremilast was titrated from 10 mg QD to 30 mg BID over the first 5 days of dosing.[2] [c]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 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.[2] 1. Armstrong AW et al. *J Am Acad Dermatol*. 2023;88:29-39. 2. Strober B et al. *J Am Acad Dermatol*. 2023;88:40-51. 3. Armstrong AW et al. *J Am Acad Dermatol*. 2023;88:29-39. Supplement.

PASI 75 and sPGA 0/1 response rates of deucravacitinib compared with placebo and apremilast[1,2,a,b]

POETYK PSO-1[1]



POETYK PSO-2[2]



Adapted with permission from Armstrong et al.[1]

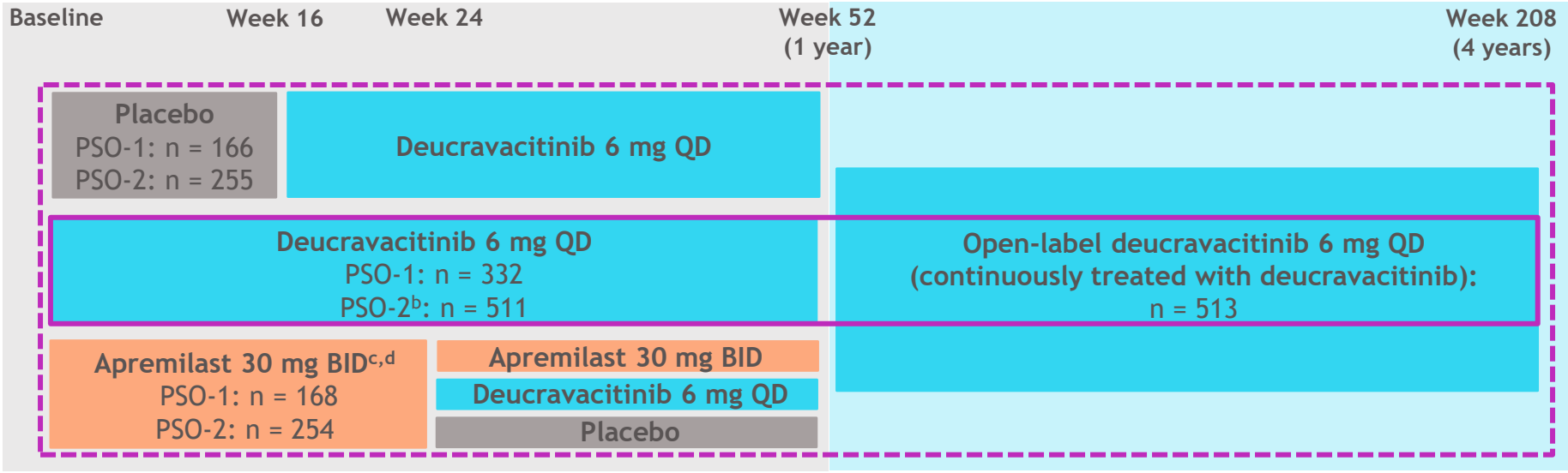
[a]Missing data were imputed using NRI. [b]Response defined as sPGA score of 0 or 1 with a ≥ 2-point improvement from baseline. Missing data were imputed using NRI. *$p<0.0001$ vs placebo. †$p<0.0001$ vs apremilast. ‡$p=0.0004$ vs apremilast.

1. Armstrong AW et al. *J Am Acad Dermatol*. 2023;88:29-39. 2. Strober B et al. *J Am Acad Dermatol*. 2023;88:40-51.

POETYK PSO-1, PSO-2, and PSO-LTE study designs[1,a]

Key eligibility criteria in the parent studies:[1]

- Age ≥ 18 years
- Moderate-to-severe plaque psoriasis:
  - PASI ≥ 12
  - sPGA ≥ 3
  - BSA involvement ≥ 10%



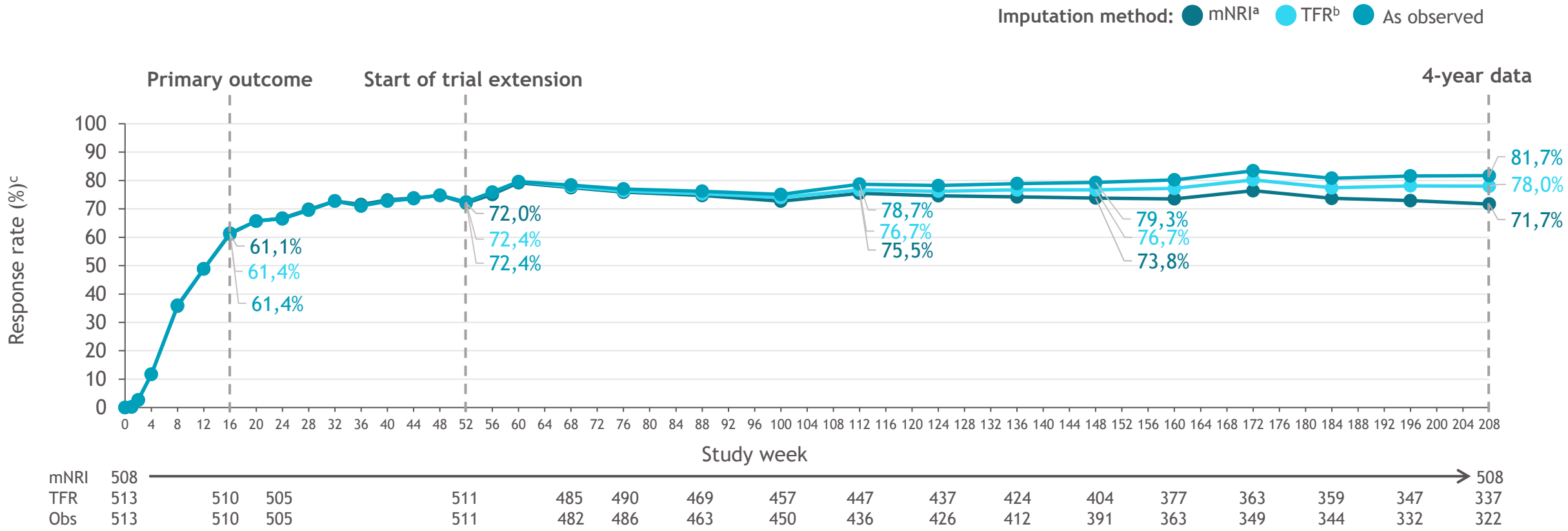
- **Safety population**: Patients in the pooled POETYK PSO-1, PSO-2, and PSO-LTE trials **receiving ≥1 dose of deucravacitinib**[1,e,f]
  - **1519 patients** received ≥1 dose of deucravacitinib across the parent trials (POETYK PSO-1 and PSO-2) and the POETYK PSO-LTE trial

- **Efficacy population**: Patients in the pooled POETYK PSO-1, PSO-2, and PSO-LTE trials who **received continuous deucravacitinib treatment from Day 1** of the parent trials through Week 208[1]
  - **513 patients** were continuously treated with deucravacitinib from Day 1, completed POETYK PSO-1 and PSO-2, and entered the POETYK PSO-LTE trial

[a]Includes patients with ≥1 dose of deucravacitinib 6 mg QD, n = 1519.[1] [b]In POETYK PSO-2, patients randomized to SOTYKTU on Day 1 who achieved PASI 75 at Week 24 were re-randomized to placebo or SOTYKTU; for patients who were re-randomized to placebo, upon relapse (≥ 50% loss of PASI percent improvement from baseline), they were to cross over to SOTYKTU.[2] [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 SOTYKTU upon relapse.[2] [d]Apremilast was titrated from 10 mg QD to 30 mg BID over the first 5 days of dosing.[1] [e]Safety data through 3 years and efficacy data through 148 weeks. Data reported through the cutoff date of June 15, 2022.[2] [f]1178 (77.6%) patients had > 12 months of total SOTYKTU exposure, and 341 (22.4%) patients had > 36 months of total SOTYKTU exposure throughout POETYK PSO-1, PSO-2, and PSO-LTE.[2,3]

1. Armstrong AW et al. Presentation at EADV Spring; May 16-18, 2024; St. Julian's, Malta. 2. Gold LS et al. Poster presentation at the AAD Annual Meeting 2024; March 8-12, 2024; San Diego, CA. 3. Warren RB et al. Poster presentation at the EADV Spring Symposium 2022; May 12-14, 2022; Ljubljana, Slovenia. Poster P465.

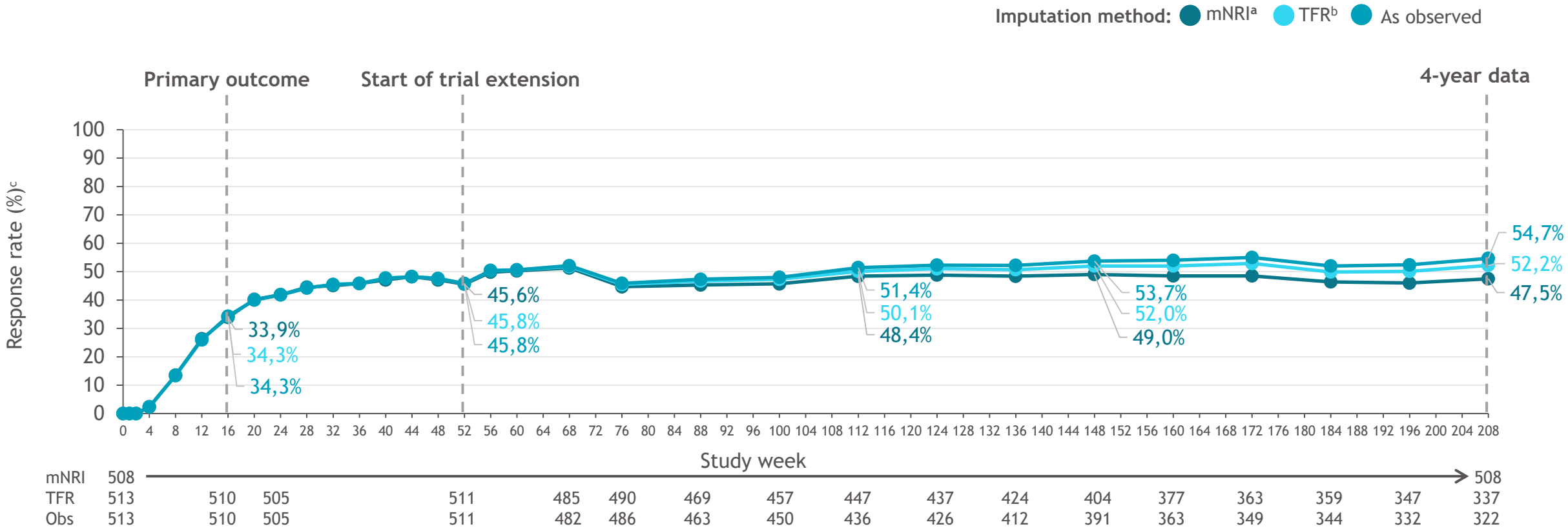
PASI 75 response rates in patients on continuous deucravacitinib treatment through 4 years



[a]For mNRI analyses, at time points where there were no missing data, 95% CI was obtained using the Clopper-Pearson method based on the observed data. [b]TFR analysis captures discontinuations coded as "lack of efficacy." [c]Data callouts represent the response rate (95% CI).

Armstrong AW et al. Presentation at EADV Spring; May 16–18, 2024; St. Julian's, Malta.

PASI 90 response rates in patients on continuous deucravacitinib treatment through 4 years



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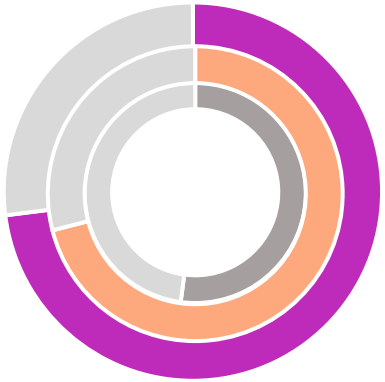
Armstrong AW et al. Presentation at EADV Spring; May 16–18, 2024; St. Julian's, Malta.

POETYK PSO-1 and PSO-2 and LTE Phase 3 Psoriasis Trials

Safety

Deucravacitinib safety profile through Week 52 across two phase 3 trials[1-3]

Incidence of AEs (%, EAIR/100 PY)[1,2,a]

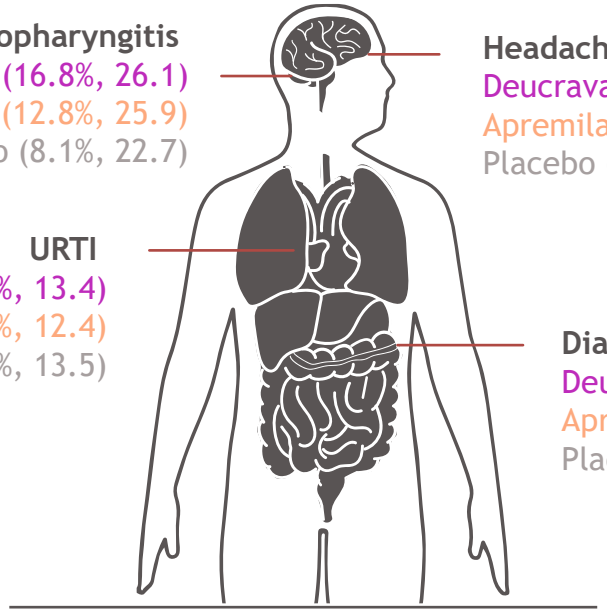


- Deucravacitinib (72.9%, 229.2)
- Apremilast (70.9%, 281.1)
- Placebo (52.1%, 217.9)

Most common AEs (≥ 5%) (%, EAIR/100 PY)[1,2]

Nasopharyngitis
Deucravacitinib (16.8%, 26.1)
Apremilast (12.8%, 25.9)
Placebo (8.1%, 22.7)

URTI
Deucravacitinib (9.1%, 13.4)
Apremilast (6.4%, 12.4)
Placebo (5.0%, 13.5)



Headache
Deucravacitinib (5.9%, 8.5)
Apremilast (12.6%, 26.0)
Placebo (3.2%, 8.6)

Diarrhea
Deucravacitinib (5.1%, 7.3)
Apremilast (12.8%, 26.5)
Placebo (4.2%, 11.5)

AE of interest: nausea
Deucravacitinib (1.5%, 2.1)
Apremilast (11.1%, 22.9)
Placebo (1.5%, 4.1)

SAEs (%, EAIR/100 PY)[1,2]

4.0%, 5.7 in the deucravacitinib group
2.1%, 4.0 in the apremilast group
2.1%, 5.7 in the placebo group

Discontinuations due to AEs (%, EAIR/100 PY)[1,2]

3.2%, 4.4 in the deucravacitinib group
6.2%, 11.6 in the apremilast group
3.5%, 9.3 in the placebo group

An increased risk of MACE, DVT, and PE was not observed in clinical trials with deucravacitinib[3]

[a]The plot refers to % values only.

1. Armstrong A et al. Oral presentation at AAD VMX; April 23–25, 2021; virtual. 2. Alexis A et al. Poster presentation at Winter Clinical Dermatology Conference; January 14–19, 2022; Kauai, HI, and Virtual. 3. Sotyktu. Summary of Product Characteristics. BMS.

Cumulative safety summary through 1 year and 4 years (as-treated population)[1]

- The overall safety profile observed through a total of 4 years was consistent with that observed in the first year[1]
- No new safety signals were observed in the study through Week 208[1]
- No additional laboratory monitoring is required in patients receiving SOTYKTU[2]

AE category	Cumulative through 1 year[a] (POETYK PSO-1 + PSO-2)[1]		Cumulative through 4 years[b] (POETYK PSO-1 + PSO-2 + LTE)[1]	
	Deucravacitinib (n = 1364) Total PY = 969.0		Deucravacitinib (n = 1519) Total PY = 4392.8	
	1-Year cumulative n (%)	EAIR/100 PY (95% CI)	4-Year cumulative n (%)	EAIR/100 PY (95% CI)
AEs	995 (72.9)	**229.2 (215.4-243.9)**	1301 (85.6)	**131.7 (124.6-139.0)**
SAEs	55 (4.0)	**5.7 (4.4-7.4)**	205 (13.5)	**5.0 (4.4-5.8)**
Discontinued treatment due to AEs	43 (3.2)	**4.4 (3.3-5.9)**	97 (6.4)	**2.2 (1.8-2.7)**
Deaths	2 (0.1)[c]	**0.2 (0.1-0.8)**	11 (0.7)[d]	**0.3 (0.1-0.4)**
Most common AEs (EAIR/100 PY ≥ 5)				
Nasopharyngitis	229 (16.8)	**26.1 (23.0-29.8)**	343 (22.6)	**9.7 (8.7-10.8)**
Upper respiratory tract infection	124 (9.1)	**13.4 (11.3-16.0)**	240 (15.8)	**6.1 (5.4-6.9)**
Headache	80 (5.9)	**8.5 (6.8-10.5)**	117 (7.7)	**2.8 (2.3-3.4)**
Diarrhea	69 (5.1)	**7.3 (5.7-9.2)**	99 (6.5)	**2.4 (1.9-2.9)**
Arthralgia	55 (4.0)	**5.7 (4.4-7.4)**	117 (7.7)	**2.8 (2.3-3.4)**
COVID-19[e]	5 (0.4)	**0.5 (0.1-1.2)**	321 (21.1)	**8.3 (7.4-9.3)**

Not all patients were receiving deucravacitinib 6 mg QD continuously throughout this period. Total PY corresponds to the total exposure time to deucravacitinib during the indicated time period. [a]This represents the pooled patient population of POETYK PSO-1 and PSO-2 (Weeks 0-52). [b]This represents the pooled POETYK PSO-1, PSO-2, and LTE population through the cutoff date of November 1, 2023. [c]In POETYK PSO-1 and PSO-2 through 1 year, 1 patient discontinued deucravacitinib after 4 days of treatment due to prohibited medication (leflunomide) and died 9 days later reportedly due to heart failure and sepsis, with no medical records available. Another death occurred between Weeks 16 and 52 and was due to hepatocellular carcinoma in a patient with a history of hepatitis C virus infection and liver cirrhosis. Both deaths were considered unrelated to treatment by the investigator. [d]After Week 52, 7 deaths were due to COVID-19 (all in patients with risk factors for severe disease; 2 deaths were considered related to treatment by the investigator and the other 5 deaths were considered unrelated to treatment by the investigator). One patient with cardiovascular risk factors died due to a ruptured aortic aneurysm, which was considered unrelated to treatment by the investigator. One patient died due to sudden death, which was considered not related to treatment by the investigator. [e]POETYK PSO-1, PSO-2, and LTE trials were conducted during the COVID-19 pandemic.

1. Armstrong AW et al. Presentation at EADV Spring; May 16–18, 2024; St. Julian's, Malta. 2. SOTYTKU (deucravacitinib). SmPC.

Cumulative AEs of interest through 1 year and 4 years (as-treated population)

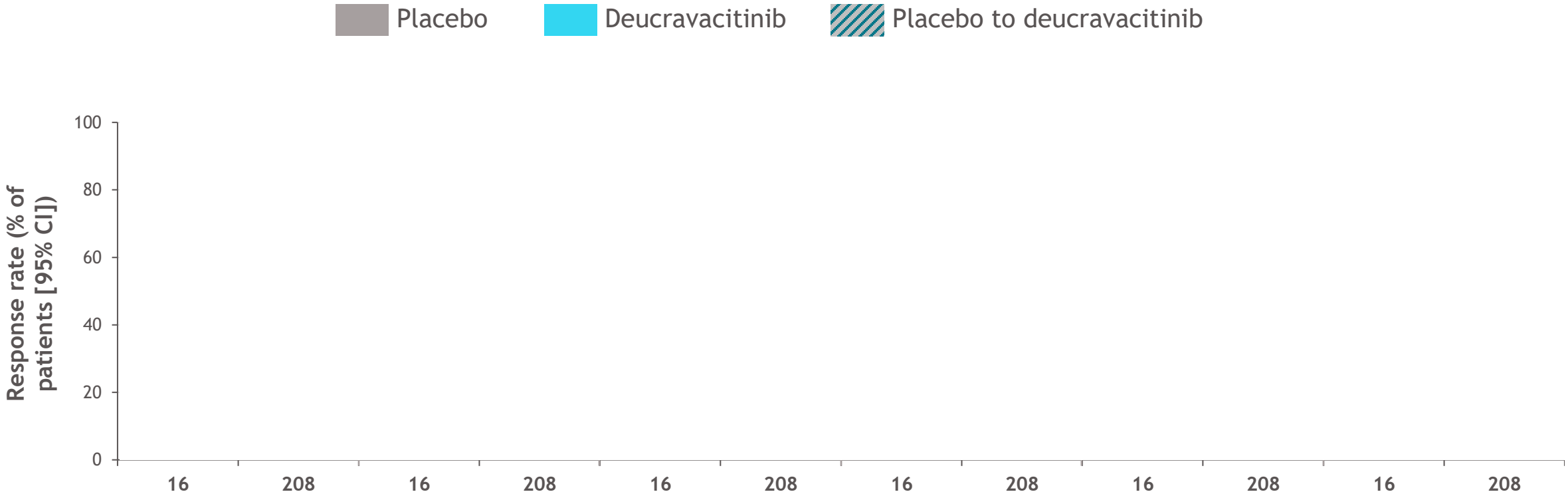
AE category	Cumulative through 1 year[a] (POETYK PSO-1 + PSO-2)		Cumulative through 4 years[b] (POETYK PSO-1 + PSO-2 + LTE)	
	Deucravacitinib (n = 1364) Total PY = 969.0		Deucravacitinib (n = 1519) Total PY = 4392.8	
	1-Year cumulative n (%)	EAIR/100 PY (95% CI)	4-Year cumulative n (%)	EAIR/100 PY (95% CI)
Serious infections[1]	17 (1.2)	**1.7 (1.1-2.8)**	85 (5.6)	**2.0 (1.6-2.5)**
Serious infections excluding COVID-19[1,2]	15 (1.1)	**1.5 (0.9-2.5)**	31 (2.0)	**0.8 (0.6-1.1)**
Herpes zoster (non-serious)[1]				
Herpes zoster[c]	8 (0.6)	**0.8 (0.4-1.6)**	24 (1.6)	**0.6 (0.4-0.8)**
Ophthalmic herpes zoster[d]	1 (0.1)	**0.1 (0.0-0.7)**	1 (0.1)	**0.0 (0.0-0.1)**
MACE[1,e]	3 (0.2)	**0.3 (0.1-0.9)**	14 (0.9)	**0.3 (0.2-0.5)**
VTE[1,f]	2 (0.1)	**0.2 (0.1-0.8)**	3 (0.2)	**0.1 (0.0-0.2)**
Malignancies[1]	10 (0.7)	**1.0 (0.5-1.9)**	39 (2.6)	**0.9 (0.6-1.2)**
NMSC	7 (0.5)	**0.7 (0.3-1.5)**	18 (1.2)	**0.4 (0.2-0.7)**
Basal cell carcinoma	4 (0.3)	**0.4 (0.2-1.1)**	13 (0.9)	**0.3 (0.2-0.5)**
Squamous cell carcinoma[g]	2 (0.1)	**0.2 (0.1-0.8)**	5 (0.3)	**0.1 (0.0-0.3)**
Malignancies excluding NMSC	3 (0.2)	**0.3 (0.1-0.9)**	22 (1.4)[h]	**0.5 (0.3-0.8)**
Lymphoma	1 (0.1)	**0.1 (0.0-0.7)**	3 (0.2)	**0.1 (0.0-0.2)**
Hodgkin's disease	1 (0.1)	**0.1 (0.0-0.7)**	1 (0.1)	**0.0 (0.0-0.1)**
Leukemia	0	**0**	1 (0.1)	**0.0 (0.0-0.1)**

Not all patients were receiving deucravacitinib 6 mg QD continuously throughout this period. Total PY corresponds to the total exposure time to deucravacitinib during the indicated time period. [a]This represents the pooled patient population of POETYK PSO-1 and PSO-2 (Weeks 0-52). [b]This represents the pooled POETYK PSO-1, PSO-2, and LTE population through the cutoff date of November 1, 2023. [c]One patient who was coded as having herpes zoster had corneal/ocular disease related to herpes virus infection diagnosed by an ophthalmologist with a positive qualitative chickenpox virus antigen (epithelial cells). [d]One patient who was coded as having ophthalmic herpes zoster with swelling of eyelids was referred for ophthalmology consultation, which was noted as normal; there was no corneal/ocular disease related to herpes virus infection. [e]MACE were adjudicated and were defined as nonfatal stroke, nonfatal myocardial infarction, or cardiovascular death. MACE in deucravacitinib-treated patients through 1 year: cardiac failure leading to death; cerebrovascular accident; myocardial infarction. Through 4 years: acute myocardial infarction (n = 5), cerebrovascular accident (n = 2), myocardial infarction (n = 2), aortic aneurysm rupture, cardiac arrest, cardiac failure, cerebral hemorrhage, ischemic stroke, sudden death (n = 1 each). [f]VTE was defined as deep vein thrombosis and pulmonary embolism. VTE events in deucravacitinib-treated patients through 1 year: deep vein thrombosis; pulmonary embolism (n = 1 each). Through 4 years: deep vein thrombosis (n = 2), pulmonary embolism (n = 1). The second deep vein thrombosis event occurred in Year 2. [g]Includes preferred terms of squamous cell carcinoma, squamous cell carcinoma of skin, and Bowen's disease. [h]Includes events of breast cancer, lung adenocarcinoma, colon cancer, malignant melanoma (n = 2 each), invasive ductal breast carcinoma, intraductal proliferative breast lesion, metastatic colon cancer, adenocarcinoma of colon, colorectal cancer, pancreatic carcinoma, hepatocellular carcinoma, B-cell lymphoma, nodal marginal zone B-cell lymphoma, Hodgkin's disease, acute promyelocytic leukemia, esophageal carcinoma, prostate cancer, squamous cell carcinoma of the tongue, and squamous cell carcinoma of the oral cavity (n = 1 each).

1. Armstrong AW et al. Presentation at EADV Spring; May 16–18, 2024; St. Julian's, Malta. 2. Data on File. BMS-REF-DEU-0151. Bristol Myers Squibb 2024.

Additional Results

Proportions of patients achieving absolute PASI thresholds through 4 years (mNRI)

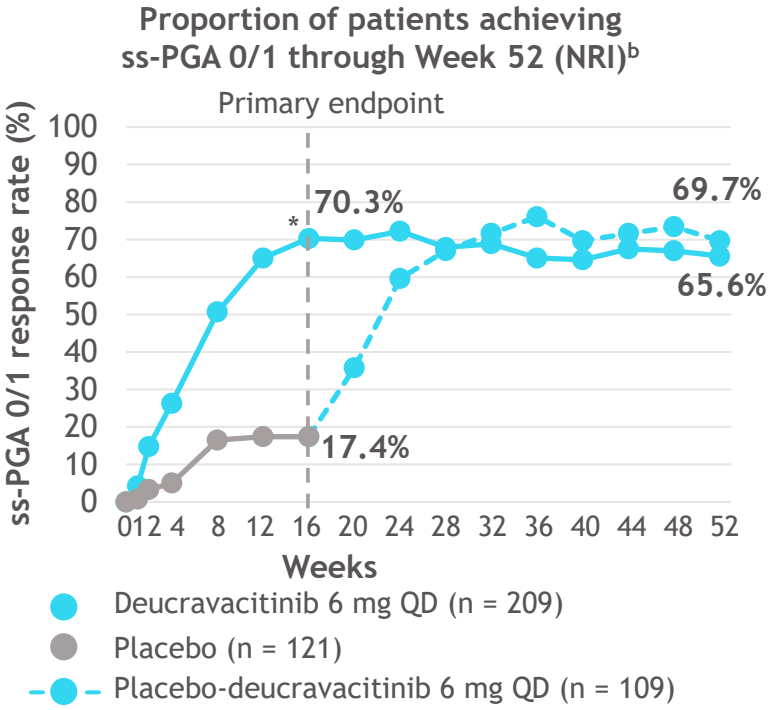


Patients, n												
Placebo	291	291	291	291	291	291	291	291	291	291	291	291
Deucravacitinib	508	508	508	508	508	508	508	508	508	508	508	508

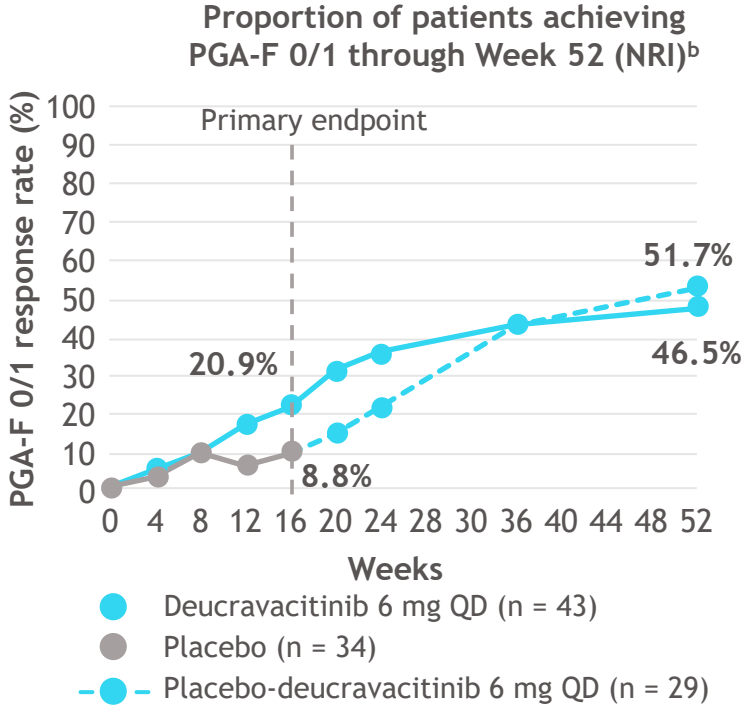
Thaçi D et al. Poster presentation at the EADV Fall Symposium 2024; September 25-28, 2024; Amsterdam, The Netherlands. Poster P3324.

Impact of deucravacitinib in moderate-to-severe scalp, nail, and palmoplantar PsO[1,2]

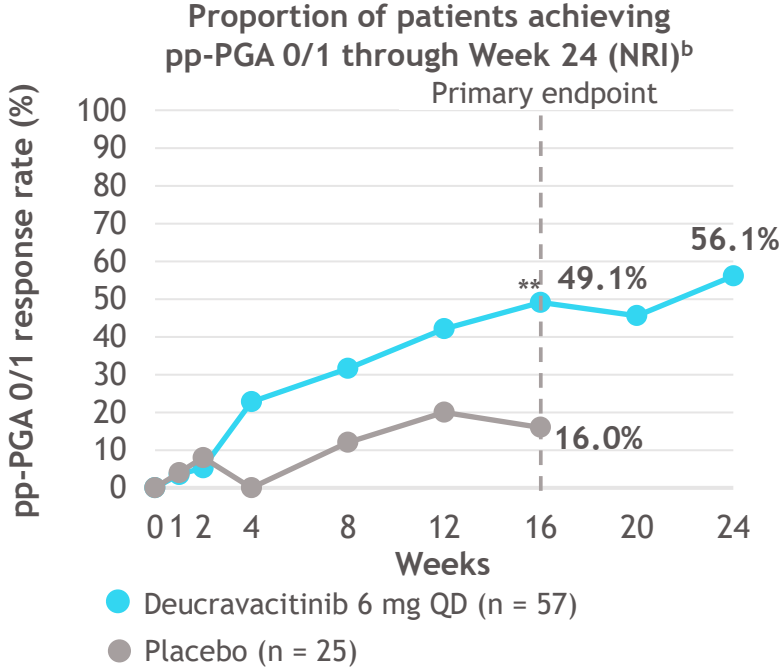
Scalp: ss-PGA 0/1[1,3,4,a]



Fingernail: PGA-F 0/1[1,a]



Palmoplantar: pp-PGA 0/1[2,4,a]



[a]Included patients with a baseline ss-PGA, PGA-F, or pp-PGA score ≥ 3. [b]Missing data were imputed with NRI.
*$p < 0.0001$ vs placebo; **$p = 0.0052$ vs placebo..

1. Blauvelt A et al. Poster presentation at Maui Derm for Dermatologists; January 24-28, 2022; Maui, HI, and virtual. 2. Blauvelt A et al. Poster presentation at Fall Clinical Dermatology Conference; October 20-23, 2022; Las Vegas, NV. 3. Effectiveness and Safety of BMS-986165 Compared to Placebo and Active Comparator in Participants With Psoriasis (POETYK-PSO-1). Accessed May 2023. https://clinicaltrials.gov/ct2/show/NCT03624127
4. An Investigational Study to Evaluate Experimental Medication BMS-986165 Compared to Placebo and a Currently Available Treatment in Participants With Moderate-to-Severe Plaque Psoriasis (POETYK-PSO-2). Accessed May 2023. https://clinicaltrials.gov/ct2/show/NCT03611751

Summary

- TYK2 is a member of the TYK2/JAK family, and plays a key role in PsO pathology[1,2]
- Deucravacitinib works to selectively inhibit TYK2 downstream effects via allosteric inhibition[3]
- PASI 75 and PASI 90 responses were sustained through 4 years in over 500 patients treated continuously with deucravacitinib from Day 1 in the parent trials[4]
- Deucravacitinib demonstrated a consistent safety profile through 4 years with >4000 PY of exposure and with no increases in AE or SAE EAIRs over time and no emergence of any new safety signals, except for increased rates of COVID-19 due to the concurrent global pandemic[4]
  - Rates of serious infections (minus COVID-19), malignancies, and MACE through 4 years were comparable with what has been observed with approved PsO treatments in clinical trials and real-world databases
- These data support the long-term safety and durable efficacy profile through 4 years of treatment with deucravacitinib, a first-in-class TYK2 inhibitor treatment for PsO[3,4]

1. Banerjee S et al. *Drugs*. 2017;77:521–546. 2. Hawkes JE et al. *J Allergy Clin Immunol*. 2017;140:645–653. 3. Burke JR et al. *Sci Transl Med*. 2019;11:eaaw1736. 4. Armstrong AW et al. Presentation at EADV Spring; May 16-18, 2024; St. Julian's, Malta.

Part 2

Current Challenges and Future Outlooks in the Management of Psoriatic Arthritis

Which patients should derms be careful about, and what to look for in patients with PsO?

EULAR Model of Transition[1,2]

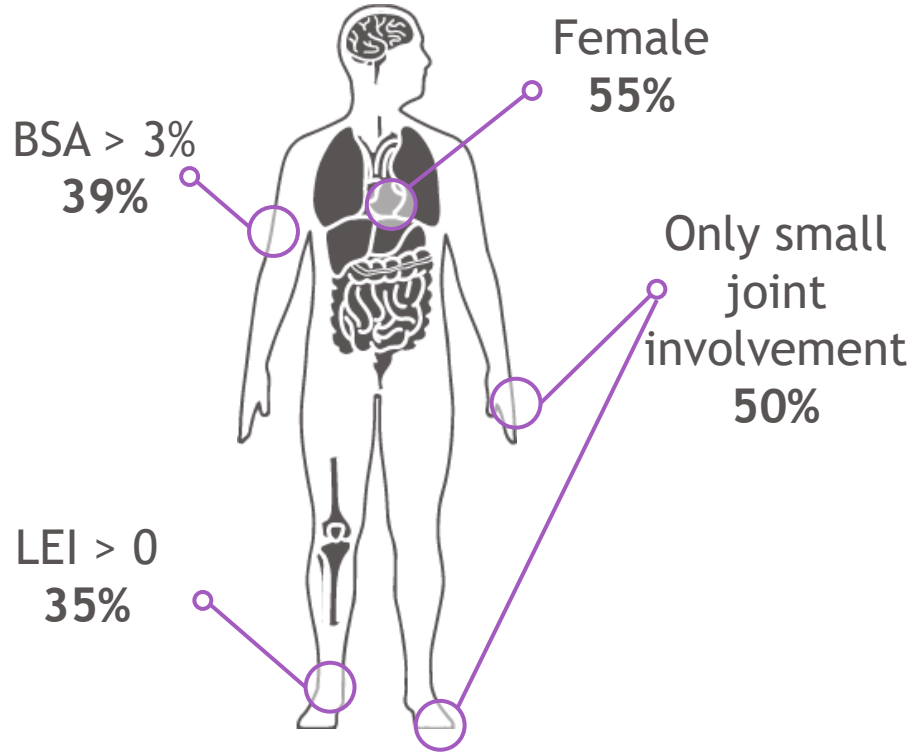
Psoriasis

At higher risk
People with PsO at higher risk of PsA (i.e., severe skin involvement, nail involvement, obesity, familial history)

Subclinical PsA
People with PsO with arthralgia and/or imaging evidence of synovial/ entheseal inflammation without clinical synovitis

Clinical PsA
People with PsO and clinical synovitis

Patient population in FOREMOST, an example study of oligoarticular PsA[3]

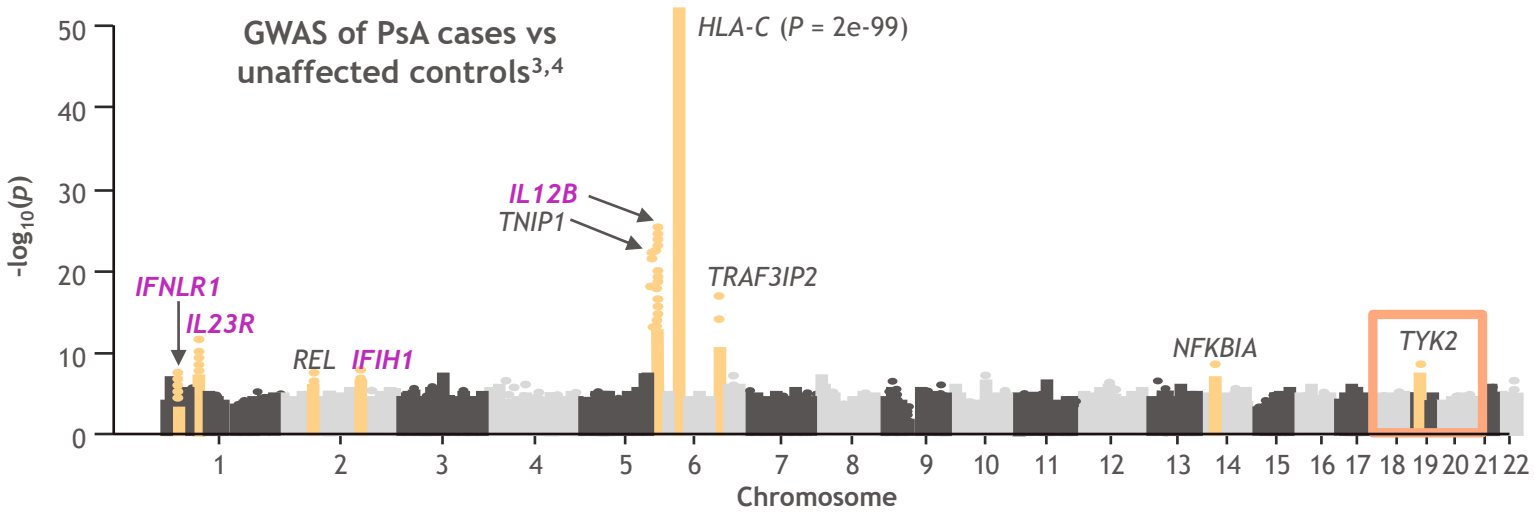


1. Zabotti A et al. *Ann Rheum Dis*. 2023;10.1136/ard-2023-224148. 2. McGonagle DG, et al. *Ann Rheum Dis*. 2022;81(1):7-9. 3. Gossec L et al. *Ann Rheum Dis*. 2024;doi:10.1136/ard-2024-225833.

Pathophysiology of Psoriatic Arthritis

Genetic associations in PsA

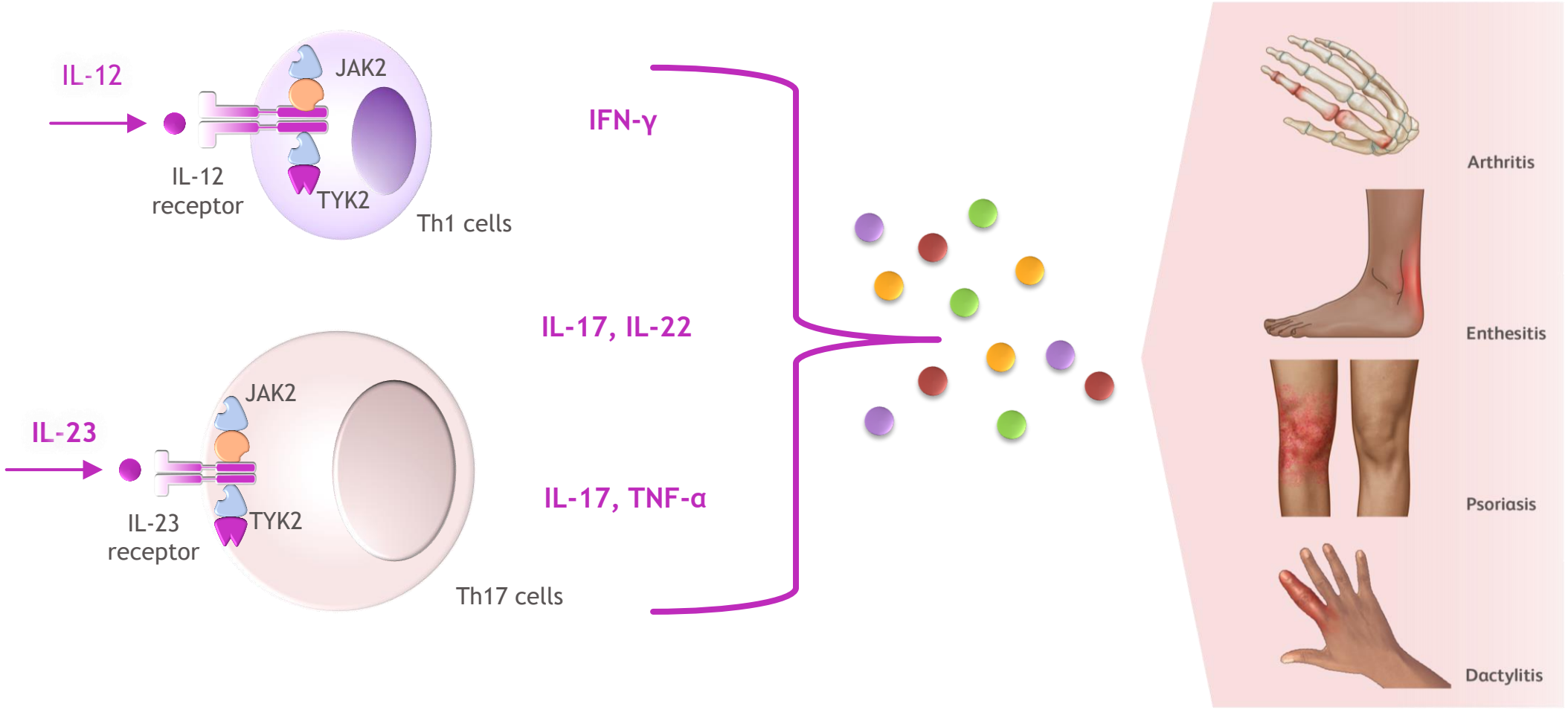
- There is a substantial overlap of susceptibility loci between PsA and PsO, which is indicative of shared pathogenesis[1]
- TYK2 is one of at least 5 susceptibility genes achieving a genome-wide significant association with PsA[1-4]
  - Each of these PsA susceptibility genes has also been associated with PsO[1,3,4]
  - Four out of 10 regions with genome-wide significant association for PsA were associated with the TYK2 pathway: *IL12B*, *IL23R*, *IFNLR1*, and *TYK2*[3-6]



Gene[4]	Marker ID[4]	Alleles (risk/non-risk)[4]	Risk allele frequency (PsA/control)[4]	OR[4,a]	*P*[4,a]
HLA-C	rs13214872	G/C	0.2848/0.1411	2.416	2.3×10^{-99}
TYK2	rs34536443	G/C	0.9750/0.9512	1.934	2.7×10^{-9}
TNIP1	rs8177833	-/C	0.1035/0.0585	1.796	1.8×10^{-23}
TRAF3IP2	rs33980500	T/C	0.1219/0.0772	1.599	1.1×10^{-17}
IL12B	rs918520	G/C	0.2546/0.1900	1.521	3.5×10^{-26}
IFNLR1	rs7540214	C/T	0.8872/0.8621	1.403	1.6×10^{-8}
IL23R	rs12044149	T/G	0.3080/0.2541	1.296	2.5×10^{-12}
NFKBIA	rs12883343	G/C	0.4553/0.4141	1.223	2.6×10^{-9}
IFIH1	rs1990760	T/C	0.6459/0.6049	1.215	1.8×10^{-8}
REL	rs34958906	-/A	0.6164/0.5747	1.208	3.5×10^{-8}

[a]OR and *P* value for fixed effects meta-analysis with inverse variance weighting.[4]
1. Bowes J et al. *Nat Commun*. 2015;6:6406. 2. Budu-Aggrey A et al. *Rheumatology (Oxford)*. 2016;55:25-32. 3. Stuart PE et al. *Am J Hum Genet*. 2015;97:816-836. 4. Stuart PE et al. *Am J Hum Genet*. 2015;97:816-836 [supplementary appendix]. 5. Dand N et al. *Acta Derm Venereol*. 2020;100(3):adv00030. 6. Syedbasha M and Egli A. *Front Immunol*. 2017;8:119.

Multiple cytokines are central to the pathology of both PsO and PsA[1-4]



Please note that the pathway discussed is not an extensive diagram and that other cytokines/kinases may be involved within PsO/PsA pathophysiology.

1. Ritchlin CT et al. *N Engl J Med*. 2017;376:957-970. 2. Veale DJ, Fearon U. *Lancet*. 2018;391:2273-2284. 3. Boutet M-A et al. *Int J Mol Sci*. 2018;19:530. 4. Zhang LJ. *Front Immunol*. 2019;10:1440.

Treatment Landscape in Psoriatic Arthritis

On top of csDMARDs, 6 biologic modes of action and 2 targeted synthetic modes of action available in 2024 in PsA

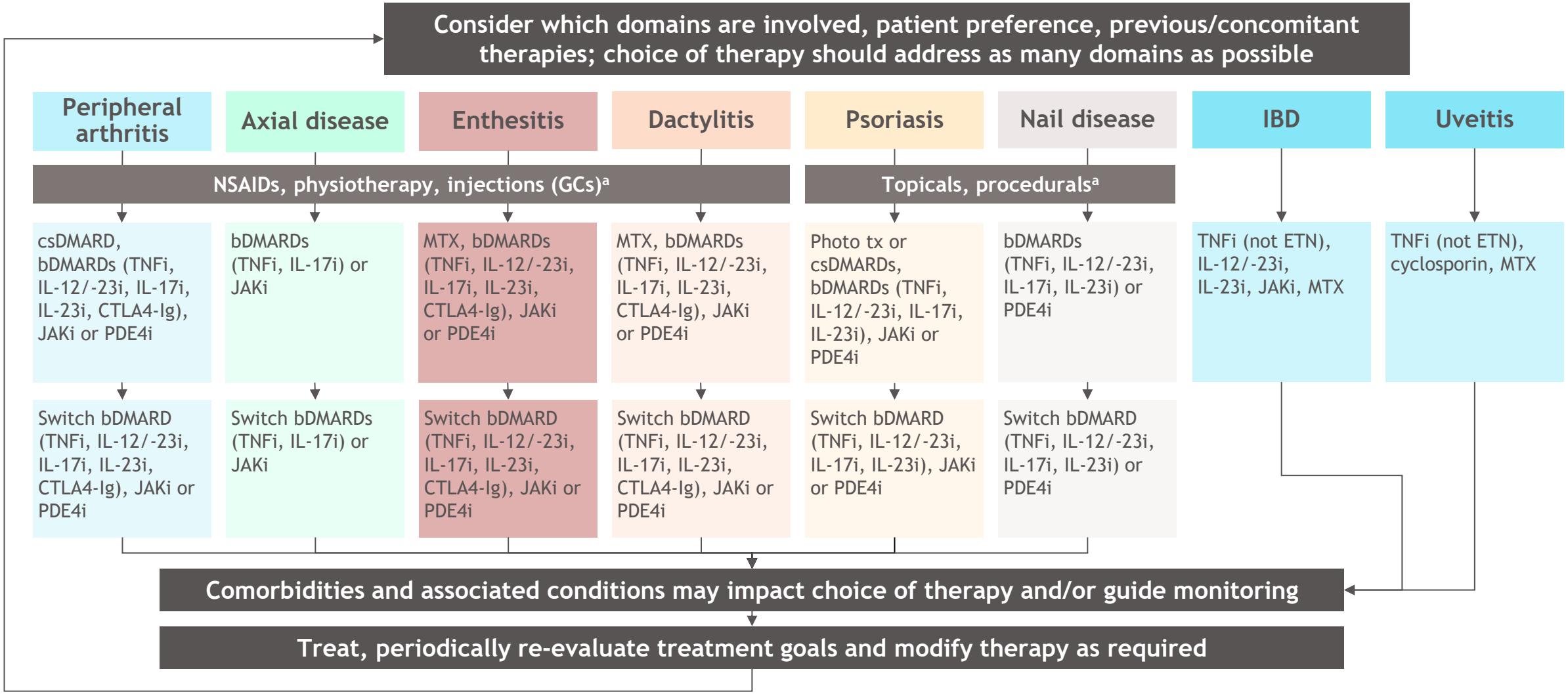
bDMARD mode of action	TNF inhibitor	IL-17A inhibitor	IL-12/-23 inhibitor	IL-23p19 inhibitor	IL-17A/F inhibitor	CTLA4 inhibitor
Drugs	Adalimumab Certolizumab Etanercept Infliximab Golimumab	Ixekizumab Secukinumab	Ustekinumab	Guselkumab Risankizumab	Bimekizumab	Abatacept

tsDMARD mode of action	JAK inhibitor	PDE4 inhibitor
Drugs	Tofacitinib Upadacitinib	Apremilast

Gossec L et al. *Ann Rheum Dis*. 2024;83:706-719.

Note: not all products listed are available in every market

GRAPPA 2021 treatment guidelines



[a]Conditional recommendation based on data from abstracts only. Adapted with permission from Coates et al.

Coates LC, et al. *Nature Reviews Rheumatol*. 2022;18(8):465-479.

Summary view - EULAR 2023 PsA recommendations take into account tissues involved and extra-MSK manifestations

	Arthritis	Entheseal disease	Predominant axial disease
	csDMARD	NSAIDs	NSAIDs
	bDMARD: TNFi, IL-17i, IL-23i, IL-12/-23i	bDMARD: TNFi, IL-17i, IL-23i, IL-12/-23i; (MTX, JAKi)	bDMARD: IL-17Ai, TNFi, IL-17A/Fi; JAKi[a]
	JAKi[a]		
	Specific cases: apremilast		
Skin PsO	IL-17Ai, IL-17A/Fi, IL-23i, IL-12/-23i	IL-17Ai, IL-17A/Fi, IL-23i, IL-12/-23i	IL-17Ai, IL-17A/Fi
Uveitis	TNFi (monoclonal)	TNFi (monoclonal)	TNFi (monoclonal)
IBD	TNFi (monoclonal), IL-12/-23i, IL-23i, JAKi[a]	TNFi (monoclonal), IL-12/23i, IL-23i	TNFi (monoclonal), JAKi[a]

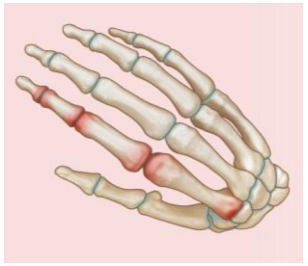
[a]For JAK inhibitors, caution is needed for patients with risk factors, refer to the EMA guidelines.

Gossec L et al. *Ann Rheum Dis*. 2024;83:706-719.

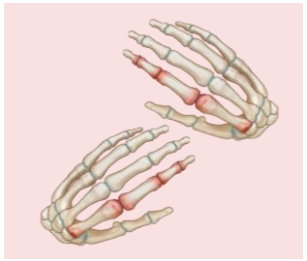
Some PsA-specific challenges compared with PsO (1/2)

Heterogeneity[1,2]

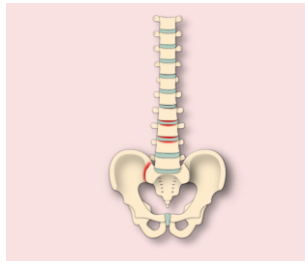
Patterns of PsA may influence management



Asymmetric oligoarticular arthritis



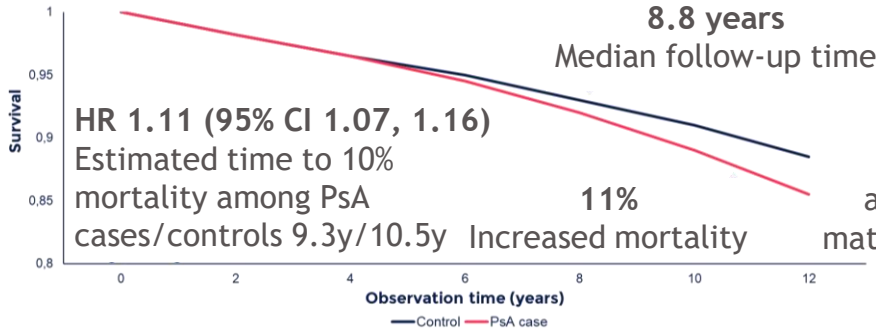
Symmetric oligoarticular arthritis



Axial disease

Severity[3]

PsA leads to an increase in mortality



8.8 years
Median follow-up time

HR 1.11 (95% CI 1.07, 1.16)
Estimated time to 10% mortality among PsA cases/controls 9.3y/10.5y

11%
Increased mortality

33,026
PsA cases
161,094
age and sex matched controls

The increased mortality was most seen in women (IRR 1.27) and patients with longer disease duration (IRR 1.25)

Causes of deaths were similar in PsA and control patients (first causes, CVD, cancer, each 29% in the PsA population)

Outcome measures[4]: No consensus on how best to assess outcomes

Treatment choices[5]: Relative lack of head-to-head trials

Graph adapted with permission from Exarchou et al.[3]

1. Yamamoto T. *Eur J Dermatol*. 2011;21(5):660–666. 2. Mease PJ. *Ann Rheum Dis*. 2011;70(suppl 1):i77–i84. 3. Exarchou S et al. *Ann Rheum Dis*. 2024;83:446-456. 4. Mease PJ, Coates LC. *Semin Arthritis Rheum*. 2018;47:786-796. 5. Kerschbaumer A et al. *Ann Rheum Dis*. 2024;0:1-15.

Some PsA-specific challenges compared with PsO (2/2)

Low proportions of patients with PsA achieve stringent disease activity targets[1,a,b]

- **Prevalence of remission varied 13%-23% in PsA**
- **Prevalence of Low Disease Activity varied 36%-53% in PsA**

PsA patients in "good status" (LDA or remission) (≈ 3/10)

Widespread pain and PsA[2-7]

- **Widespread pain syndrome:**[2-6]
  - Frequent:
    - General population**: 2%-4%**[2]
    - **PsA: 17%-38%**[3-6]
  - Linked to worse outcomes/less remission[7]
- **More frequent in PsA, in women**[6]

43% Women

24% Men

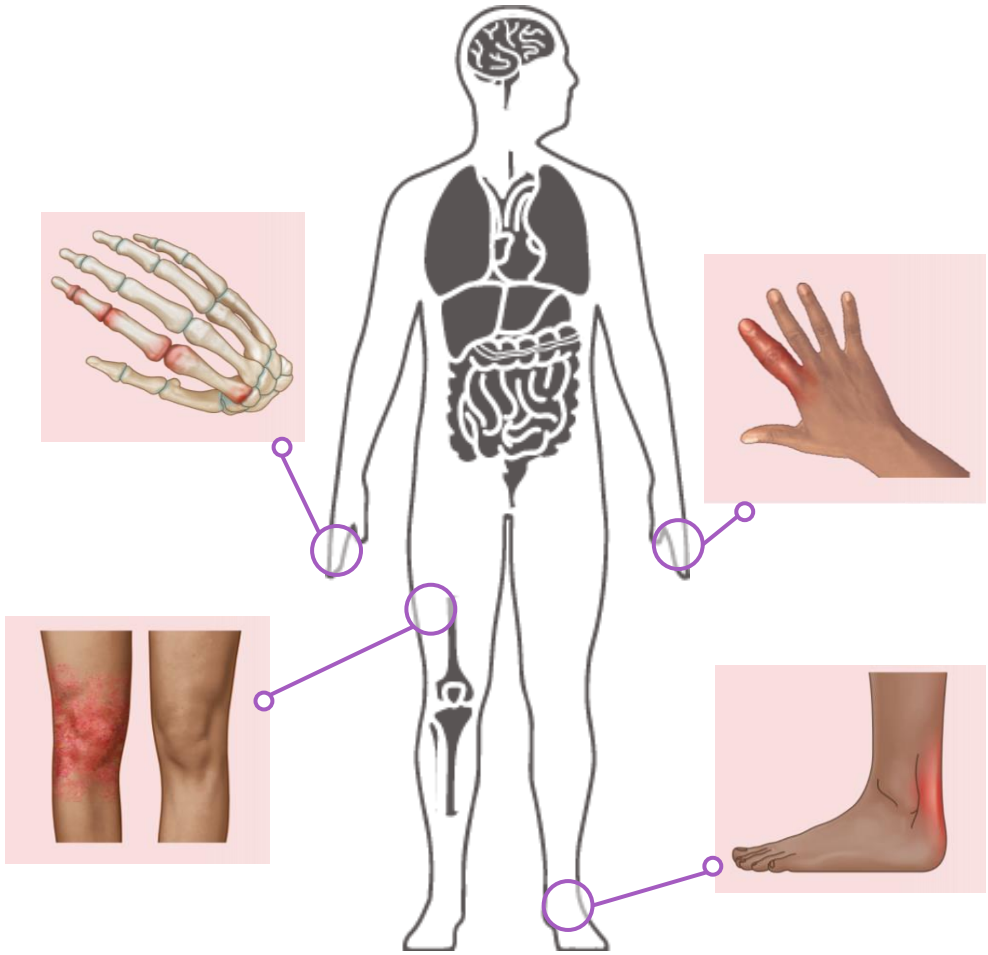
Effect of sex on therapeutic response is currently a subject of interest[6]

[a]Per a systemic literature review of 91 publications.[1] [b]The pooled rate was obtained by random effects meta-analysis.[1]

1. Hagège B, et al. *Rheumatology (Oxford)*. 2020;59(8):1818-1825. 2. Magrey MN, et al. *Arthritis*. 2013;2013:762921. 3. Brikman S, et al. J *Rheumatol*. 2016;43:1749-1754. 4. Ulus Y, et al. *Adv Rheumatol*. 2019;60:1. 5. Elsawy NA, et al. *Int J Rheum Dis*. 2021;24:189-196. 6. Van Kuijk AWR, et al. *Rheumatology (Oxford)*. 2023. 7. Højgaard P, et al. *Arthritis Care Res (Hoboken)*. 2019;71:798-810.

In PsA pivotal trials, ACR improvement criteria are the primary outcome

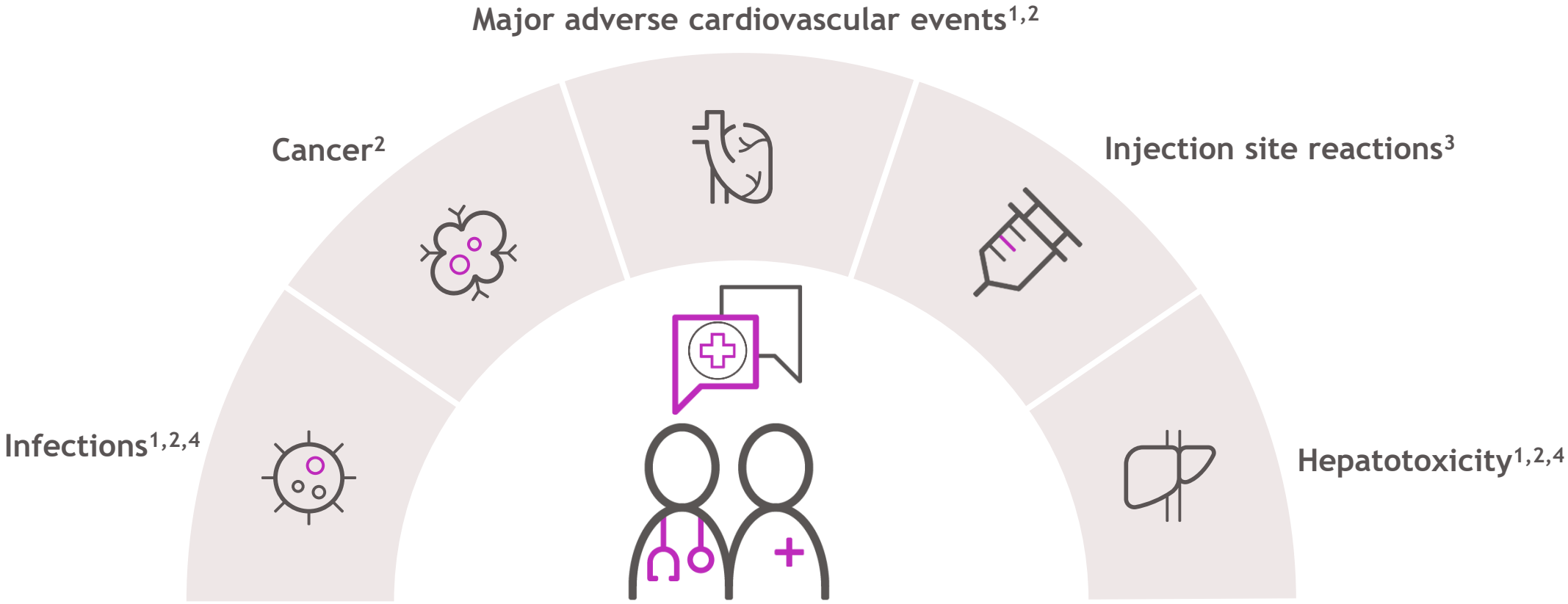
- ✓ Tender joint count
- ✓ Swollen joint count
- ✓ CRP/ESR
- ✓ Function: HAQ-DI
- ✓ Physician Global Assessment
- ✓ Patient assessment of pain
- ✓ Patient Global Assessment



- ⊗ Psoriasis
- ⊗ Enthesitis
- ⊗ Axial disease
- ⊗ Dactylitis
- ⊗ Nail
- ⊗ Fatigue
- ⊗ Impact/QoL

Mease PJ et al. *Ann Rheum Dis*. 2005;64(Suppl II):ii49-ii54.

Taking into account the safety of drugs



For JAKis: EULAR, based on EMA/FDA, states that:[5]

Caution is needed for patients aged 65 years or above, current or past long-time smokers, with a history of atherosclerotic cardiovascular disease or other cardiovascular risk factors or with other malignancy risk factors, and with known risk factors for VTE.

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

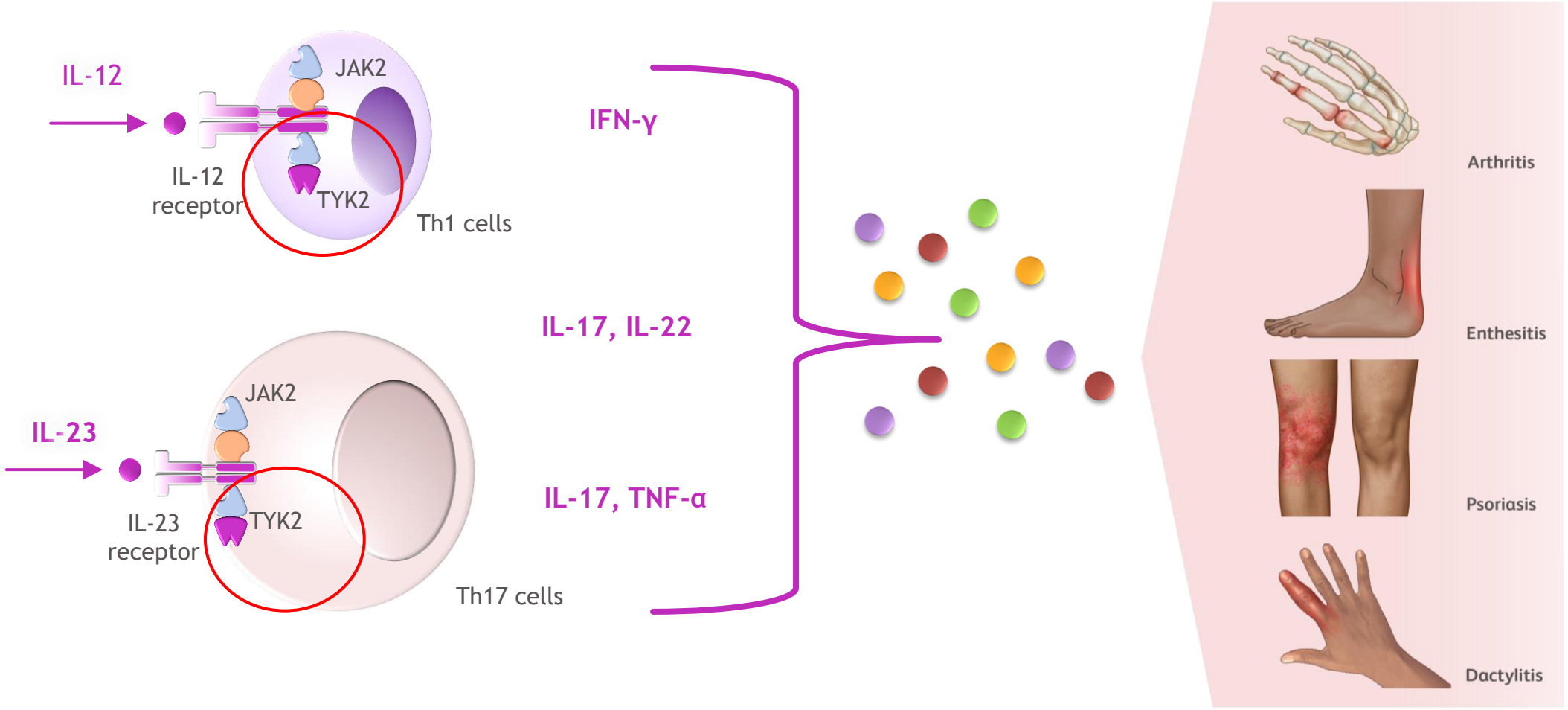
1. Gossec L et al. *Ann Rheum Dis*. 2024;83:706-719. 2. Kerschbaumer A et al. *Ann Rheum Dis*. 2024;doi:10.1136/ard-2024-225534. 3. Kerschbaumer A et al. *Ann Rheum Dis*. 2020;79:778-786. 4. Fiore M et al. *Biomed Res Int*. 2018;2018:3140938. 5. European Medicines Agency. "Janus kinase inhibitors (JAKi) – referral." Available at: https://www.ema.europa.eu/en/medicines/human/referrals/janus-kinase-inhibitors-jaki Accessed Aug 7, 2024.

Exploring TYK2 Inhibition in Psoriatic Arthritis

Note: TYK2 inhibitors, including deucravacitinib, are NOT approved for the treatment of PsA in any country and is an investigative drug still undergoing phase 2 or phase 3 evaluation

Note: Deucravacitinib is NOT approved for the treatment of PsA in any country and is an investigative drug still undergoing phase 3 evaluation

Multiple cytokines, including those mediated by TYK2, are central to the pathology of both PsO and PsA[1-4]



Please note that the pathway discussed is not an extensive diagram and that other cytokines/kinases may be involved within PsO/PsA pathophysiology.

1. Ritchlin CT et al. *N Engl J Med*. 2017;376:957-970. 2. Veale DJ, Fearon U. *Lancet*. 2018;391:2273-2284. 3. Boutet M-A et al. *Int J Mol Sci*. 2018;19:530. 4. Zhang LJ. *Front Immunol*. 2019;10:1440.

The current pipeline for TYK2 inhibition in PsA is encouraging

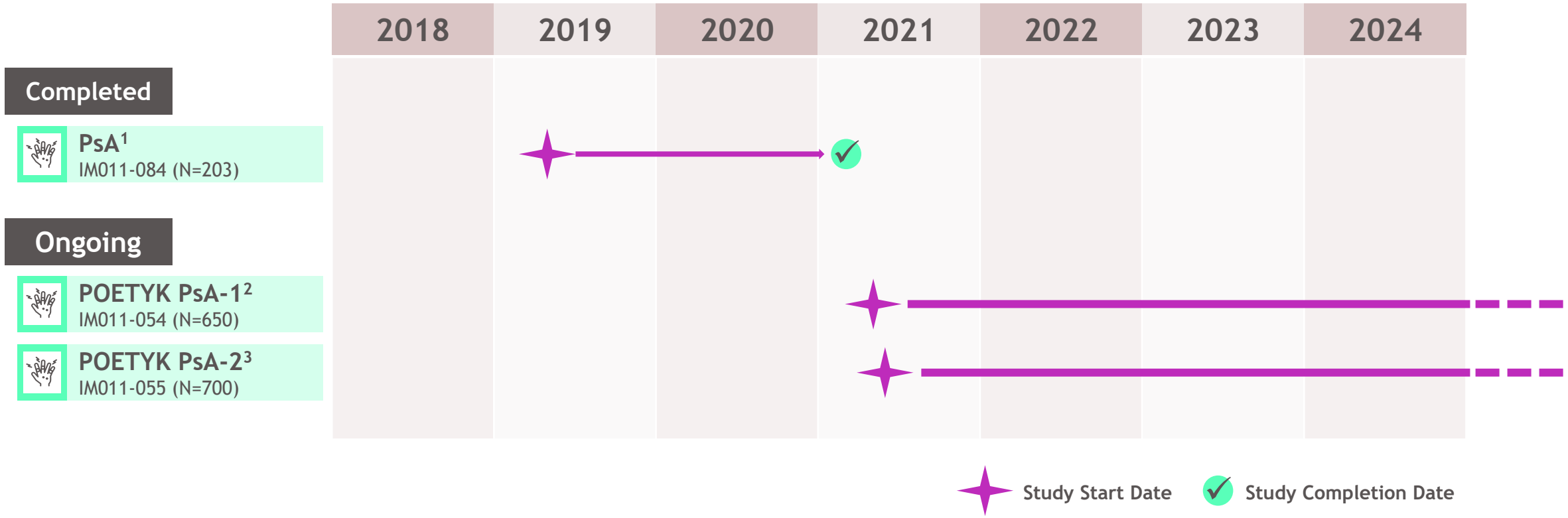
Three oral TYK2 inhibitors with **completed or ongoing phase 2** clinical trials[1-4]

	Zasocitinib (TAK-279) Takeda	HS-10374 Hansoh Pharma	Deucravacitinb BMS
Status	**Completed Phase 2b trial:**[1,2] • EUDRA 2021-005888-52 (NCT05153148) **Phase 3 starting in 2024** • EU CTIS 2024-512496-12	**Phase 2 ongoing:**[3-4] • NCT06176508	**Completed Phase 2b trial:**[5] • EUDRA 2018-004293-10 (NCT03881059) **Phase 3 underway; readouts expected 2024**[6,7]

1. Takeda Announces Positive Topline Results from Phase 2b Study Evaluating TAK-279, a Highly Selective Oral TYK2 Inhibitor, for the Treatment of Active Psoriatic Arthritis. 2023. Available at: https://www.takeda.com/newsroom/newsreleases/2023/Takeda-Announces-Positive-Topline-Results-from-Phase-2b-Study-Evaluating-TAK-279-a-Highly-Selective-Oral-TYK2-Inhibitor-for-the-Treatment-of-Active-Psoriatic-Arthritis. Accessed 29 July 2024. **2.** ClinicalTrials.gov. NCT05153148. 2024. Available at: https://clinicaltrials.gov/study/NCT05153148. Accessed 29 July 2024. 3. ClinicalTrials.gov. NCT06176508. Available at: https://clinicaltrials.gov/study/NCT06176508?cond=HS-10374&rank=3. Accessed 29 July 2024. 4. HS-10374 Basic Information. 2024. Available at: https://data.pharmacodia.com/drugs/details/1377070379905847806. Accessed 29 July 2024. 5. Clinical trials.gov. https://classic.clinicaltrials.gov/ct2/show/NCT03881059. Accessed 06 March 2024. 6. ClinicalTrials.gov. https://clinicaltrials.gov/ct2/show/NCT04908202. Accessed 06 March 2024. 7. ClinicalTrials.gov. https://clinicaltrials.gov/ct2/show/NCT04908189. Accessed 06 March 2024.

Note: Deucravacitinib or other TYK2is are NOT approved for the treatment of PsA in any country and are an investigative drug still undergoing phase 2 or phase 3 evaluation

In PsA, phase 2 data are available and both phase 3 trials have completed enrollment



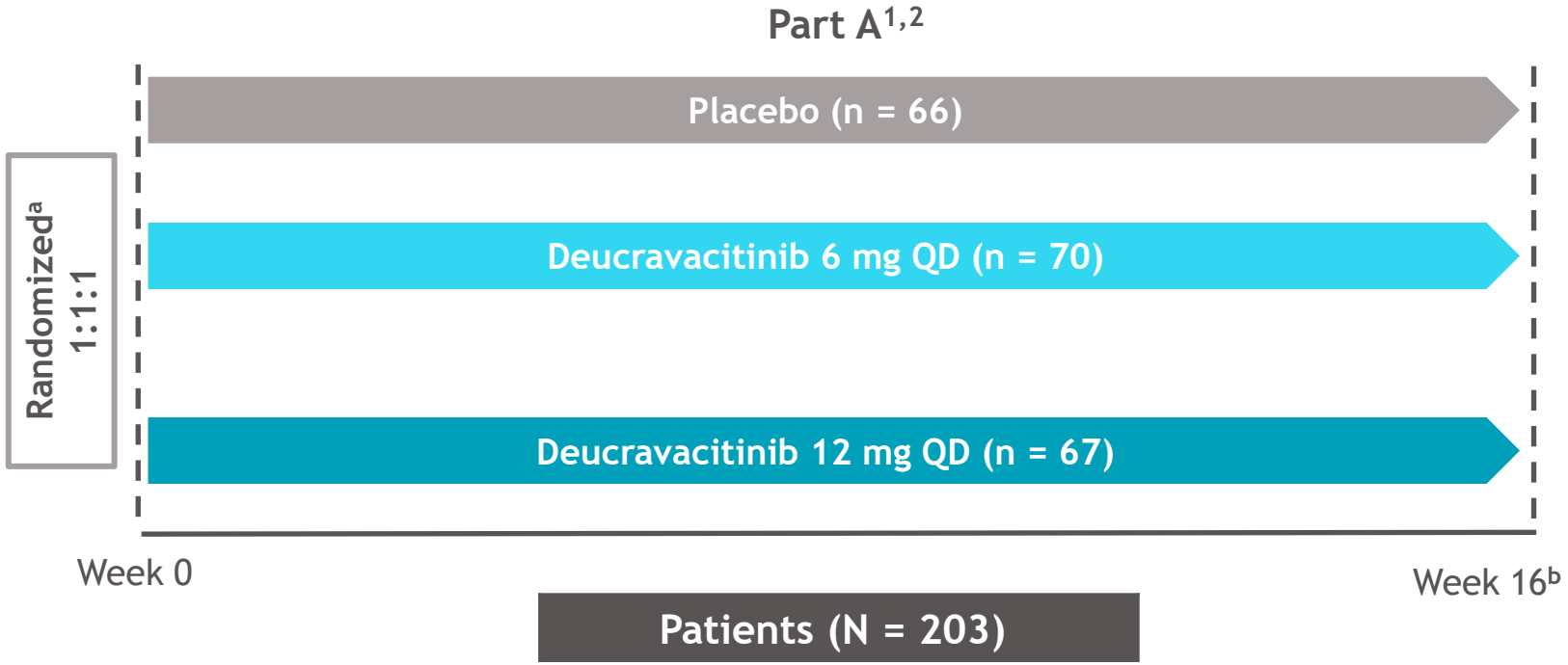
1. ClinicalTrials.gov. https://classic.clinicaltrials.gov/ct2/show/NCT03881059. Accessed 06 March 2024. 2. ClinicalTrials.gov. https://clinicaltrials.gov/ct2/show/NCT04908202. Accessed 06 March 2024.
3. ClinicalTrials.gov. https://clinicaltrials.gov/ct2/show/NCT04908189. Accessed 06 March 2024.

Note: Deucravacitinib is NOT approved for the treatment of PsA in any country and is an investigative drug still undergoing phase 3 evaluation

Efficacy and Safety Results From a Phase 2 Trial of Deucravacitinib in Psoriatic Arthritis

Note: Deucravacitinib is NOT approved for the treatment of PsA in any country and is an investigative drug still undergoing phase 3 evaluation

A phase 2 multicenter study to assess the efficacy and safety of deucravacitinib in patients with active PsA



Primary endpoint[1-4]

- ACR20 at Week 16

Secondary endpoints[1,3,4]

At Week 16:

- HAQ-DI (change from baseline)
- PASI 75
- SF-36 scores (change from baseline)
- ACR50 and ACR70
- MDA
- PROs and composite outcomes
- Enthesitis resolution
- AEs and laboratory parameters

[a]Patients were stratified based on prior exposure to TNF inhibitors and body weight (< 90 vs ≥ 90 kg).[2]
[b]Patients who reached Week 16 were eligible for participation in an optional, blinded, LTE period until Week 52 (part B).[4]

1. Mease PJ et al. *Ann Rheum Dis* 2022;81:815–822. 2. Mease PJ et al. Poster presented at the Virtual ACR Convergence; November 5–9, 2020. Poster L03. 3. ClinicalTrials.gov. Accessed April 2023. https://clinicaltrials.gov/ct2/show/NCT03881059. 4. Mease PJ et al. Poster presented at ACR Convergence 2021. November 6–9, 2021. Poster 1820.

Note: Deucravacitinib is NOT approved for the treatment of PsA in any country and is an investigative drug still undergoing phase 3 evaluation

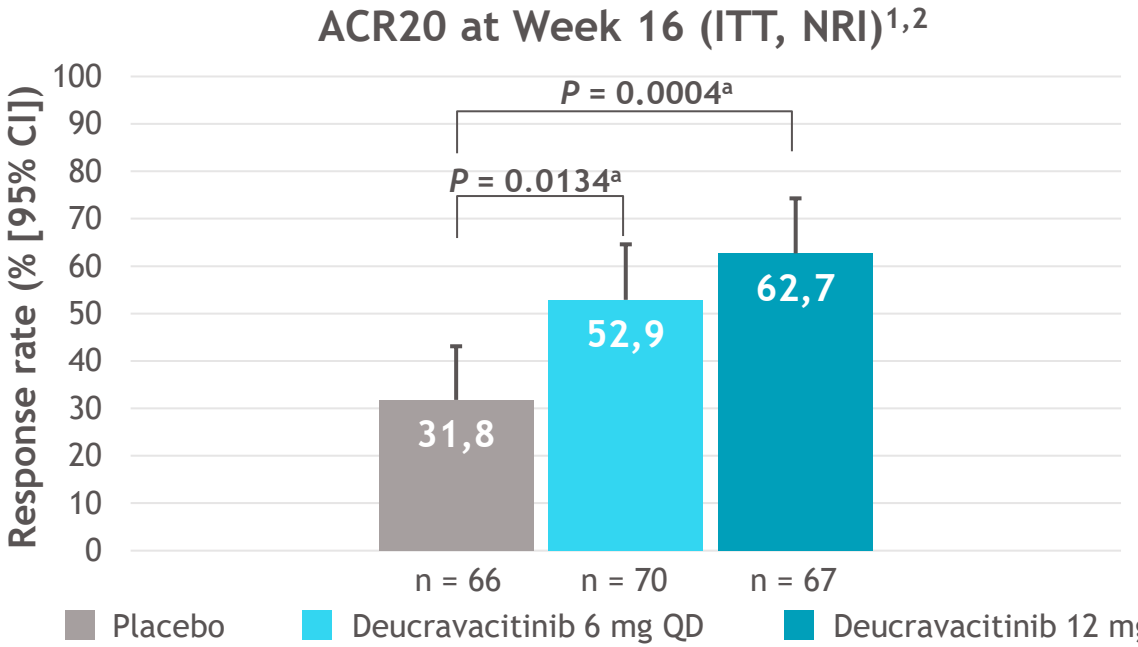
Baseline demographics, clinical, and disease characteristics[1,2]

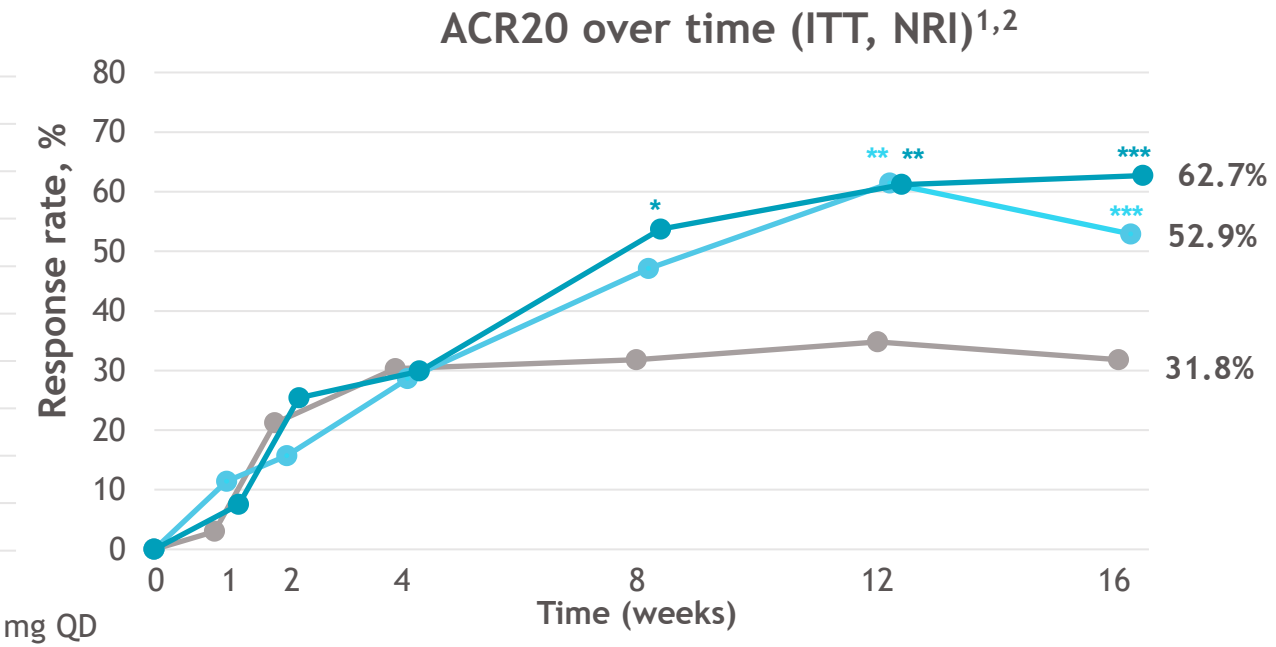
	Placebo (n = 66)	Deucravacitinib 6 mg QD (n = 70)	Deucravacitinib 12 mg QD (n = 67)
Demographics			
Age, years, mean (SD)	48.5 (13.2)	50.5 (13.7)	50.5 (13.8)
Female, n (%)	40 (60.6)	30 (42.9)	34 (50.7)
Baseline BMI, kg/m^2, mean (SD)	31.2 (7.2)	29.6 (5.4)	30.3 (5.4)
Disease duration since diagnosis, years, median (range)	4.5 (0.6-22.9)	5.3 (0.1-42.8)	3.8 (0.6-27.7)
Selected prior/concomitant medications			
Use of csDMARDs at baseline, n (%)	44 (66.7)	45 (64.3)	43 (64.2)
Prior TNF inhibitor use, n (%)	11 (16.7)	12 (17.1)	9 (13.4)
Disease parameters[1]			
Tender joint count, mean (SD)	16.9 (9.79)	18.1 (10.33)	19.4 (11.84)
Swollen joint count, mean (SD)	10.5 (7.74)	11.9 (6.99)	11.3 (8.96)
Pain in mm (VAS), mean (SD)[a]	64.9 (18.2)	63.6 (21.7)	63.8 (15.9)
HAQ-DI, mean (SD)	1.3 (0.56)	1.3 (0.59)	1.3 (0.59)
hsCRP, mg/L, mean (SD)	20.4 (39.1)	17.6 (23.6)	16.5 (21.7)
Psoriasis with BSA ≥ 3%, n (%)	54 (81.8)	59 (84.3)	52 (77.6)
PASI score in patients with BSA ≥ 3%, mean (range)	9.1 (1.2-31.4)	8.5 (1.6-33.8)	7.9 (1.4-31.8)

[a]VAS scale ranges from 0 to 100 mm, with higher values indicating worse pain.
1. Mease PJ et al. *Ann Rheum Dis*. 2022;81:815-822. 2. Mease PJ et al. Poster presentation at Virtual ACR Convergence 2020; November 5-9, 2020. Poster L03.

Note: Deucravacitinib is NOT approved for the treatment of PsA in any country and is an investigative drug still undergoing phase 3 evaluation

ACR20 response and maintenance with deucravacitinib





ACR20 is a key composite assessment score in rheumatology trials.
To achieve ACR20, patients must have ≥ 20% improvement in tender and swollen joint count and 3 of 5 other measures[3,b]

Adapted with permission from Mease PJ.[1] Creative Commons Attribution 4.0 International License (https://creativecommons.org/licenses/by/4.0/).
Nominal *P* values for pairwise comparison vs placebo. *P* values in time course are for odds ratios obtained using a stratified Cochran-Mantel-Haenszel test with stratification factors (body weight and prior TNFi use) per randomization. Missing data were reported using NRI.[1,2]
[a]Statistical analyses of primary and secondary endpoints at Week 16 were adjusted for multiplicity. Additional endpoints were not controlled for multiple comparisons, and nominal *P* values are reported.
[b]Includes VAS scores of patient pain, physician and patient global assessment, a disability measure (HAQ), and an acute phase reactant (ESR or CRP).
*P = 0.0108 (12 mg). **P = 0.0021 (6 mg); P = 0.0021 (12 mg). ***P = 0.0134 (6 mg); P = 0.0004 (12 mg).
1. Mease PJ et al. *Ann Rheum Dis*. 2022;81:815-822. 2. Mease PJ et al. Poster presentation at Virtual ACR Convergence 2020; November 5-9, 2020. Poster L03. 3. Mease PJ et al. *Ann Rheum Dis*. 2005;64(Suppl II):ii49-ii54.

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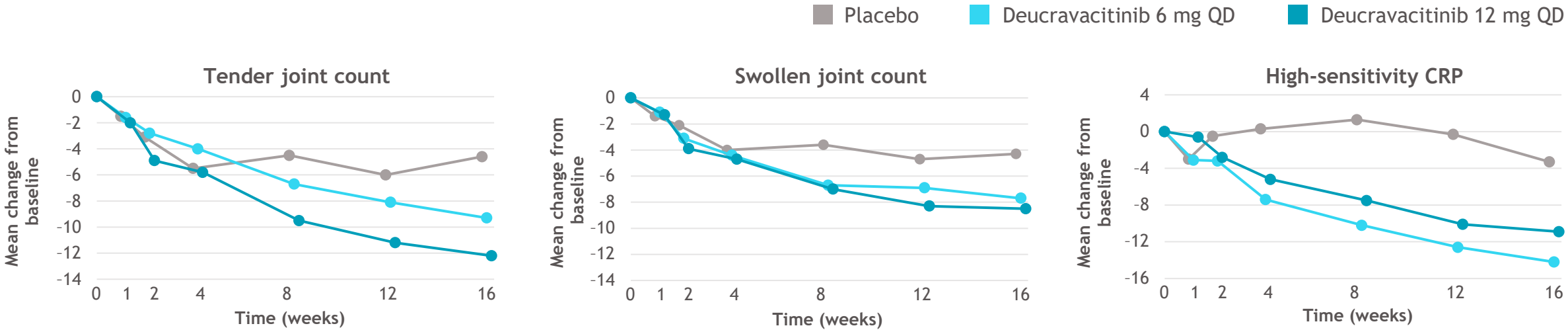
Impact of deucravacitinib on ACR components over 16 weeks[1]

Mean improvements from baseline in each ACR component over time were greater for both deucravacitinib doses vs placebo



The number of tender joints out of 68 tender joints identified in the ACR joint count[2,3]

The number of swollen joints out of 66 swollen joints identified in the ACR joint count[2,3]

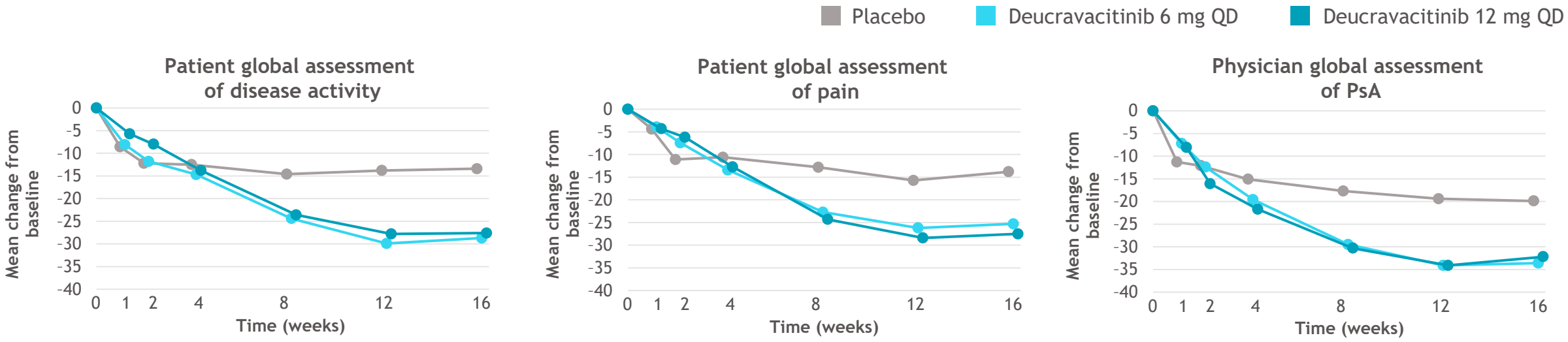
A test to determine levels of C-reactive protein, a biomarker of inflammation[3]

Adapted with permission from Mease PJ et al.[1]
Absolute value changes presented. These analyses were done post hoc using data as observed. Tender joint count baseline values (mean): placebo (16.9), deucravacitinib 6 mg (18.1), deucravacitinib 12 mg (19.4). Swollen joint count baseline values (mean): placebo (10.5), deucravacitinib 6 mg (11.9), deucravacitinib 12 mg (11.3).
1. Mease PJ et al. Oral presentation at Virtual EULAR 2021; June 2–5, 2021. Abstract OP0227. 2. McGagh D and Coates LC. *Rheumatol*. 2020;59:i29-i36. 3. Mease PJ et al. *Ann Rheum Dis*. 2005;64(Suppl II):ii49-ii54.

Note: Deucravacitinib is NOT approved for the treatment of PsA in any country and is an investigative drug still undergoing phase 3 evaluation

Impact of deucravacitinib on ACR components over 16 weeks (cont)[1]

Mean improvements from baseline in each ACR component over time were greater for both deucravacitinib doses vs placebo



Patient uses a VAS scale from excellent (0) to poor (100) to assess how their psoriasis and arthritis impact their life overall[2]

Patient uses a VAS scale (0-100) to assess their level of pain[2]

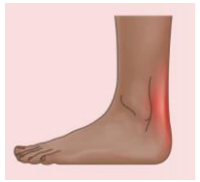
Subjective evaluation by physician of overall severity of psoriasis; numeric scale ranges from clear (0) to severe (100)[2]

Adapted with permission from Mease PJ et al.[1]

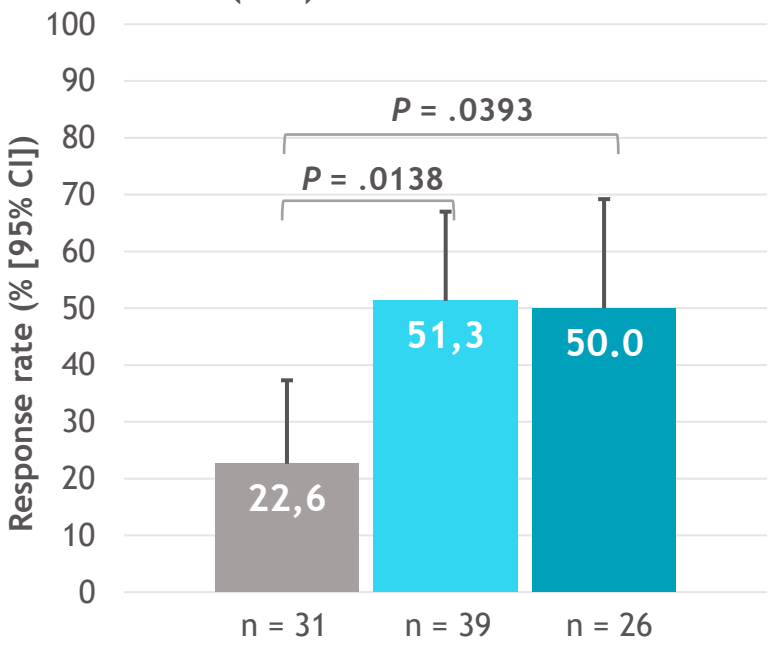
1. Mease PJ et al. Oral presentation at Virtual EULAR 2021; June 2–5, 2021. Abstract OP0227. 2. Ogdie A et al. *Arthritis Care Res (Hoboken)*. 2020;72(Suppl 10):82-109.

Note: Deucravacitinib is NOT approved for the treatment of PsA in any country and is an investigative drug still undergoing phase 3 evaluation

Enthesitis and dactylitis resolution at Week 16



Enthesitis resolution (LEI)[1,2,a]

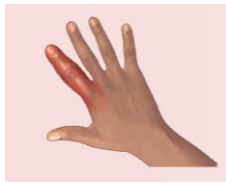


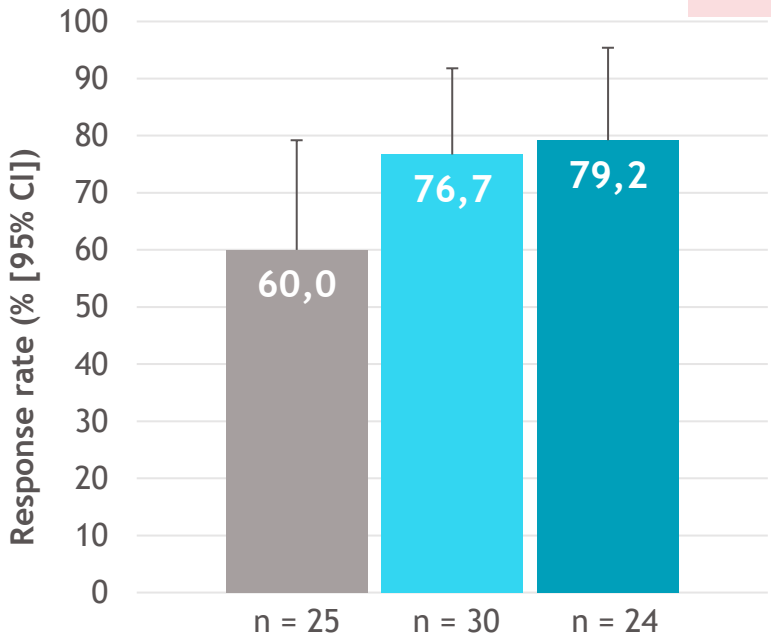
Placebo

Deucravacitinib 6 mg QD

Deucravacitinib 12 mg QD

Dactylitis resolution (LDI)[1]





LEI assesses 6 entheseal sites for presence or absence of tenderness; score of 0 in patients with enthesitis at baseline defined resolution[3,4]

LDI is used to measure size (swelling) and pain of each of 10 fingers and 10 toes on a 0-3 scale for a maximum total score of 60[3]

Adapted with permission from Mease PJ.[2]

[a]Mean (SD) baseline enthesitis LEI scores in patients with LEI ≥ 1 at baseline: placebo = 2.8 (1.7); 6 mg QD = 2.5 (1.6); 12 mg QD = 2.9 (1.4).[2]

1. Mease PJ et al. *Ann Rheum Dis* 2022;81:815-822. 2. Mease PJ, et al. Oral presentation at the European Congress of Rheumatology EULAR 2021; June 2-5, 2021; Virtual. Abstract OP0227. 3. Mease PJ. *Arthritis Care Res (Hoboken)*. 2011;63(S11):S64-S85. 4. Ogdie A et al. *Arthritis Care Res (Hoboken)*. 2020;72(Suppl 10):82-109.

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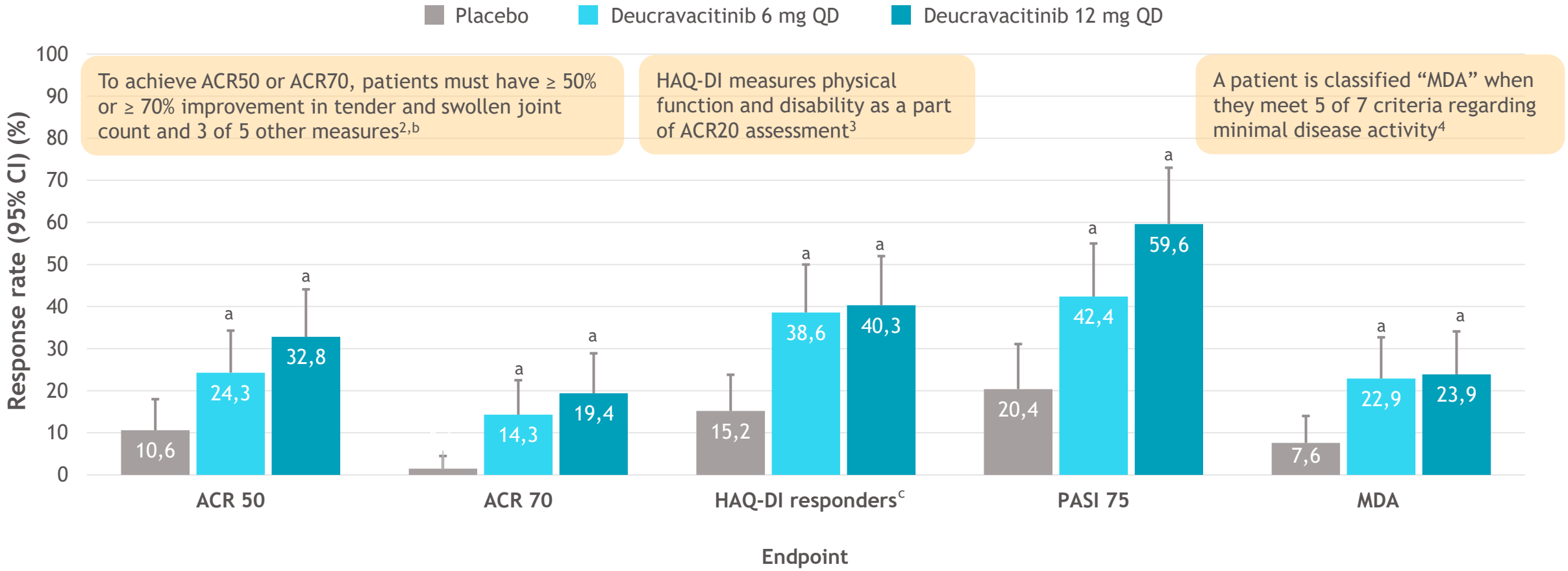
Additional outcomes in patients receiving deucravacitinib[1]



[a]*P* value was significant vs placebo in multiplicity-controlled prespecified analysis. [b]Includes VAS scores of patient pain, physician and patient global assessment, a disability measure (HAQ), and an acute phase reactant (ESR or CRP). [c]Response criteria of ≥ 0.35 improvement from baseline (minimum clinically important difference in PsA).

1. Mease PJ, et al. *Ann Rheum Dis*. 2022;81:815-822. 2. Mease PJ et al. *Ann Rheum Dis*. 2005;64(Suppl II):ii49-ii54. 3. Wan MT. *Rheumatol*. 2021;60:2307-2316. 4. Mease PJ. *Arthritis Care Res (Hoboken)*. 2011;63 suppl 11:S64-S85.

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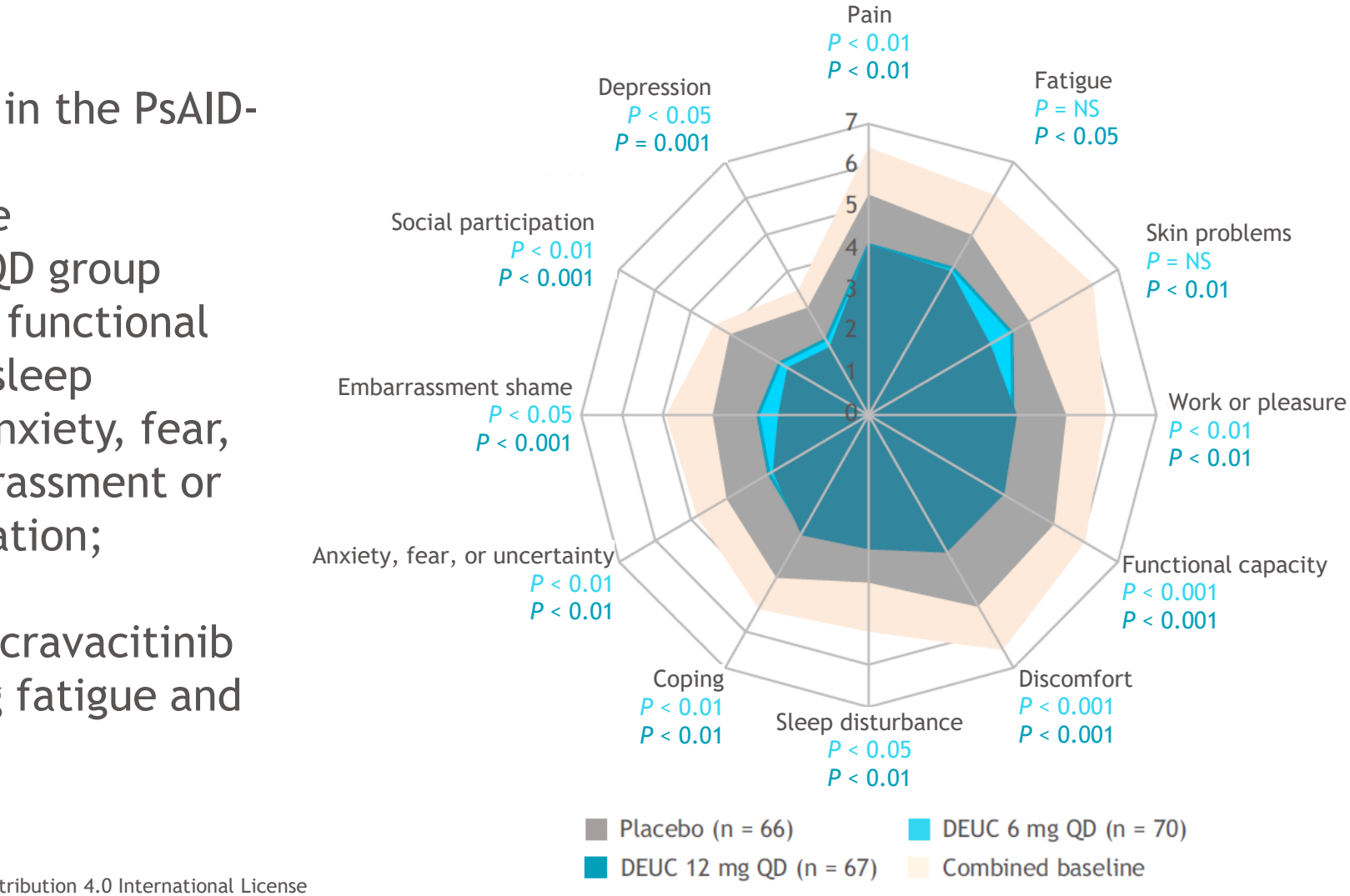
Impact of deucravacitinib on multiple PRO measures

- Adjusted mean CFB scores in the PsAID-12 were improved in:
  - 10 of 12 items with the deucravacitinib 6 mg QD group (pain; work or leisure; functional capacity; discomfort; sleep disturbance; coping; anxiety, fear, or uncertainty; embarrassment or shame; social participation; depression)
  - All 12 items in the deucravacitinib 12 mg group (including fatigue and skin problems)



PsAID-12 item scores at baseline and Week 16

Strand V et al. *Arthritis Care & Res.* 2024:doi:10.1002/acr.25333.

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Safety of deucravacitinib in a phase 2 PsA trial[1,2,a]

Adverse events, n (%)	Placebo n = 66	Deucravacitinib 6 mg QD n = 70	Deucravacitinib 12 mg QD n = 67	Deucravacitinib Total N = 137
AEs	28 (42.4)	46 (65.7)	44 (65.7)	90 (65.7)
Treatment-related AEs	6 (9.1)	22 (31.4)	17 (25.4)	39 (28.5)
Deaths	0	0	0	0
MACE	0	0	0	0
SAEs	1 (1.5)	0	0	0
Discontinued treatment due to AEs[b]	1 (1.5)	3 (4.3)	4 (6.0)	7 (5.1)
AEs ≥ 5%				
Nasopharyngitis	5 (7.6)	4 (5.7)	12 (17.9)	16 (11.7)
Rash	0	3 (4.3)	4 (6.0)	7 (5.1)
Headache	3 (4.5)	5 (7.1)	1 (1.5)	6 (4.4)
Sinusitis	0	0	5 (7.5)	5 (3.6)
Upper respiratory tract infection	0	4 (5.7)	1 (1.5)	5 (3.6)
Bronchitis	1 (1.5)	4 (5.7)	0	4 (2.9)
Diarrhea	0	4 (5.7)	0	4 (2.9)

- No major safety signals appeared in the phase 2 study[1,2]
- There were no incidents of MACE reported[1]

[a]Includes events with a start date between the first dose and the week 16 visit date (inclusive) for patients who continued to part B and events that are reported between first dose and 30 days after last dose of study drug for patients who discontinued early.[1] [b]AEs leading to discontinuation were as follows: placebo (n = 1; PsO); deucravacitinib 6 mg (n = 3; bronchitis, rash, and rosacea); deucravacitinib 12 mg (n = 4; furuncle, urticaria, mouth ulcerations, and 1 patient reporting multiple events [gastroesophageal reflux disease, nausea, dizziness, headache, and blood pressure increase]).[2]
1. Mease PJ et al. *Ann Rheum Dis* 2022;81:815–822. 2. Mease PJ et al. Oral presentation at Virtual EULAR 2021; June 2–5, 2021. Abstract OP0227.

Note: Deucravacitinib is NOT approved for the treatment of PsA in any country and is an investigative drug still undergoing phase 3 evaluation

Summary

- The treatment of PsA rests on conventional DMARDS as well as several targeted drug categories available[1]
- The choice of drug takes into account the type of MSK manifestation, and extra-MSK involvement, as well as safety considerations[1,2]
- In a phase 2 trial in PsA, treatment with deucravacitinib was well tolerated and resulted in clinically relevant efficacy across all or most core domains of PsA[3-5]
  - Larger trials are warranted and ongoing to confirm its safety and efficacy profile

1. Coates LC et al. *Nature Reviews Rheumatol*. 2022;18(8):465-479. 2. Gossec L et al. *Ann Rheum Dis*. 2024;83:706-719. 3. Mease PJ, et al. *Ann Rheum Dis* 2022;81:815–822. 4. Mease PJ et al. Oral presentation at Virtual EULAR 2021; June 2–5, 2021. Abstract OP0227. 5. Strand V et al. *Arthritis Care & Res*. 2024:doi:10.1002/acr.25333.

Note: Deucravacitinib is NOT approved for the treatment of PsA in any country and is an investigative drug still undergoing phase 3 evaluation

Thank you

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