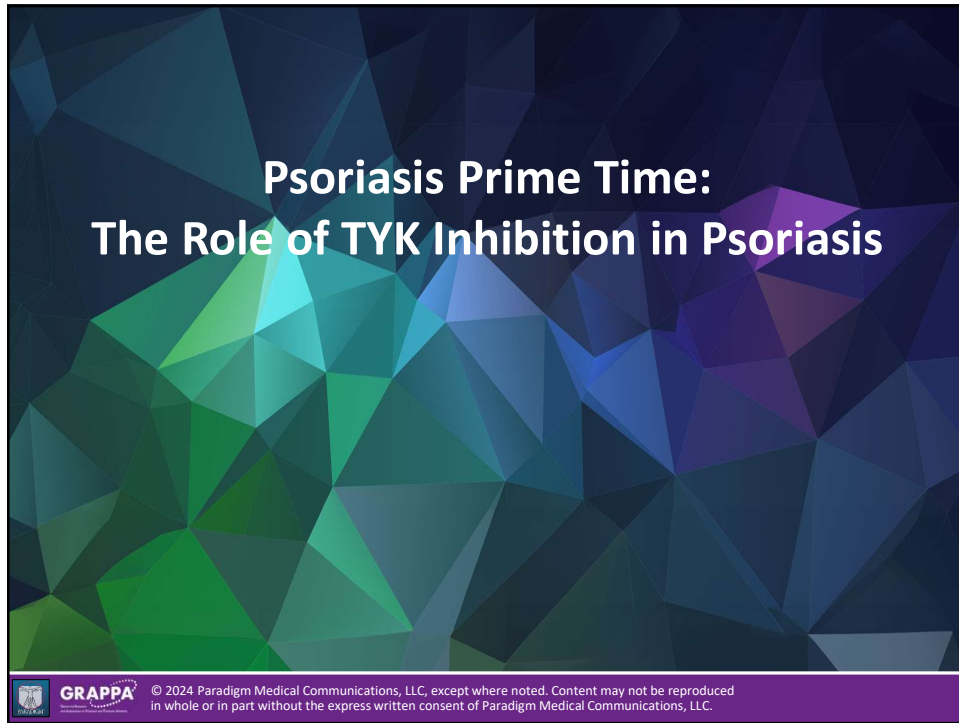
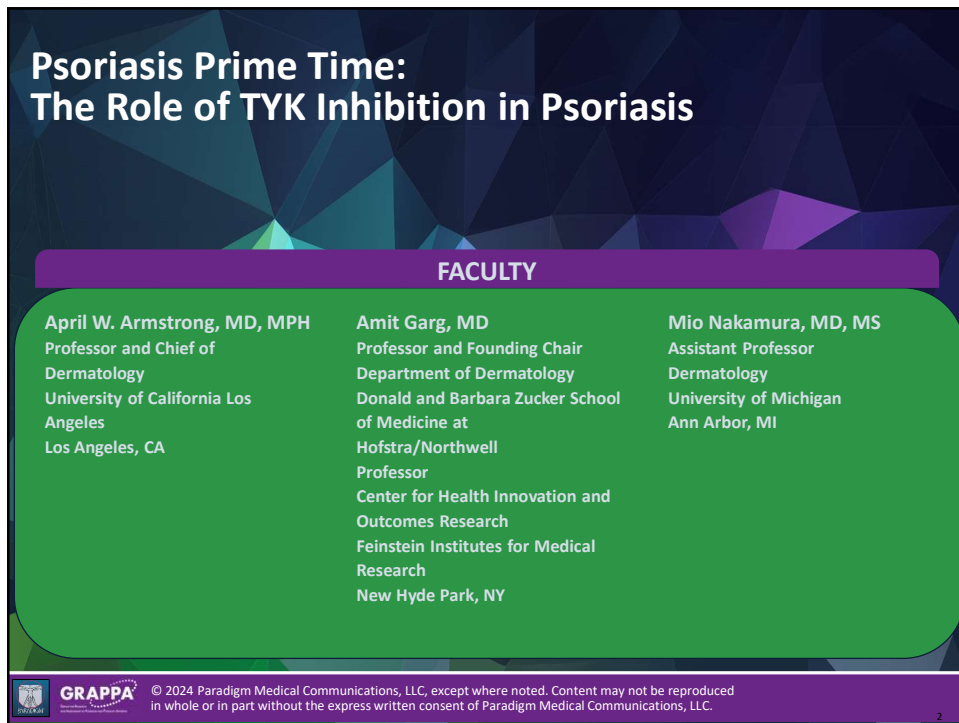


**Psoriasis Prime Time:
The Role of TYK Inhibition in Psoriasis**
www.paradigmmc.com/1284-1



1



2

© 2024 Paradigm Medical Communications, LLC, except where noted. Content may not be reproduced in whole or in part without the express written consent of Paradigm Medical Communications, LLC.

**Psoriasis Prime Time:
The Role of TYK Inhibition in Psoriasis**
www.paradigmmc.com/1284-1

**63-Y-Old Man With Longstanding
Plaque Psoriasis**

Past 4 mo

- Progressive increases in BSA and itch

BSA, body surface area

3

3

**63-Y-Old Man With Longstanding
Plaque Psoriasis**

Past treatment history:

- Topical steroids
- Methotrexate 15 mg/wk
 - ◆ 4 mo with inadequate response

4

4

**Psoriasis Prime Time:
The Role of TYK Inhibition in Psoriasis**
www.paradigmmc.com/1284-1

**63-Y-Old Man With Longstanding
Plaque Psoriasis**

Past medical history:

- Hyperlipidemia
- Type 2 diabetes
- Fatty liver disease
- Cardiomyopathy
 - ◆ Class III congestive heart failure

5

**63-Y-Old Man With Longstanding
Plaque Psoriasis**

Family history:

- Brother and paternal uncle with Crohn's disease

6

**Psoriasis Prime Time:
The Role of TYK Inhibition in Psoriasis**
www.paradigmmc.com/1284-1

**63-Y-Old Man With Longstanding
Plaque Psoriasis**

- Exam: Well demarcated, red, erythematous, indurated plaques with silvery scale on scalp, trunk, and extremities, BSA 12%



Images courtesy of Amit Garg, MD

Images used with permission. ©2024 Amit Garg, MD. All rights reserved.

7

7

**63-Y-Old Man With Longstanding
Plaque Psoriasis**



Images courtesy of Amit Garg, MD

Images used with permission. ©2024 Amit Garg, MD. All rights reserved.

8

8

© 2024 Paradigm Medical Communications, LLC, except where noted. Content may not be reproduced in whole or in part without the express written consent of Paradigm Medical Communications, LLC.

Psoriasis Prime Time: The Role of TYK Inhibition in Psoriasis

www.paradigmmc.com/1284-1

63-Y-Old Man With Longstanding Plaque Psoriasis



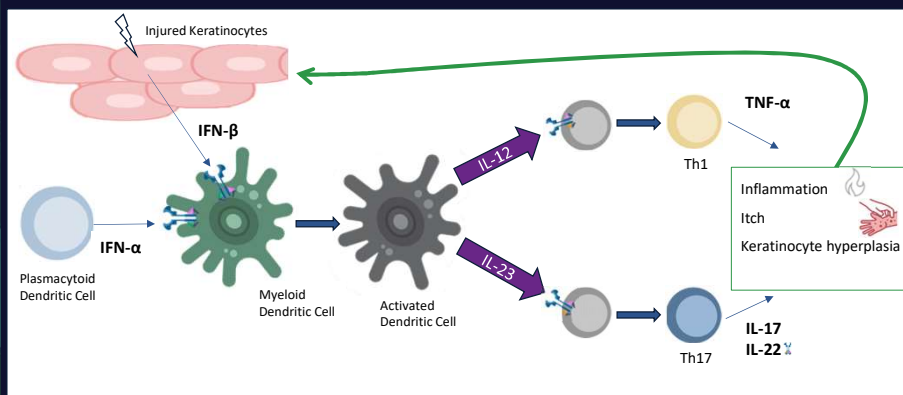
Images courtesy of Amit Garg, MD

Images used with permission. ©2024 Amit Garg, MD. All rights reserved.

9

9

IL-23/IL-17 Pathway



IFN, interferon
Armstrong AW et al. *JAMA*. 2020;323(19):1945-1960. Alwan W et al. *Clin Exp Rheumatol*. 2015;33(5 Suppl 93):S2-S6.
Dudakov JA et al. *Annu Rev Immunol*. 2015;33:747-785.

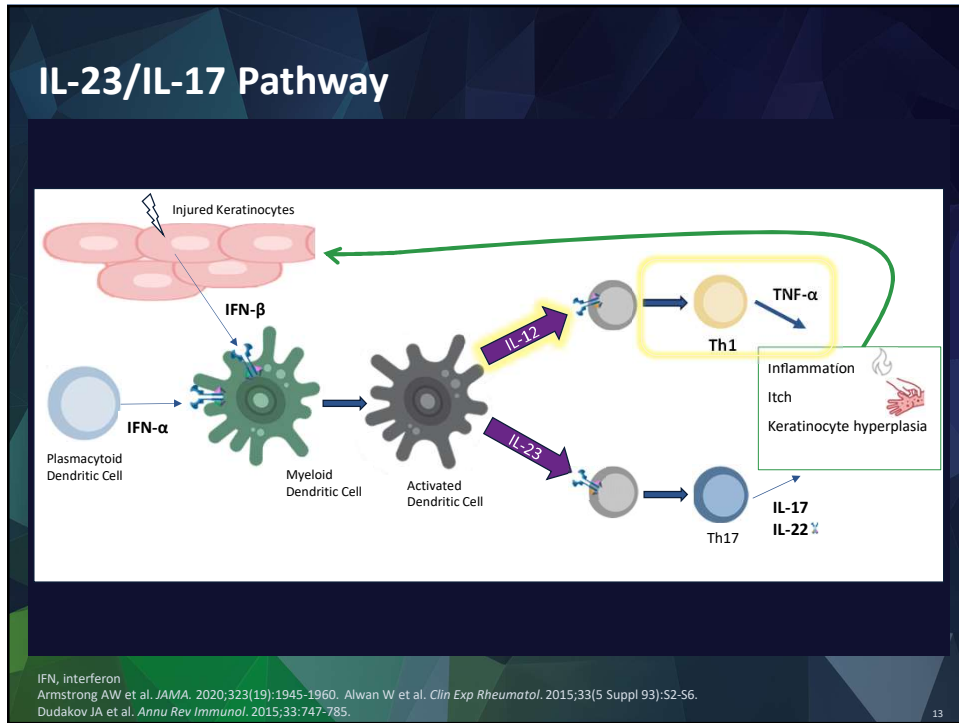
12

12

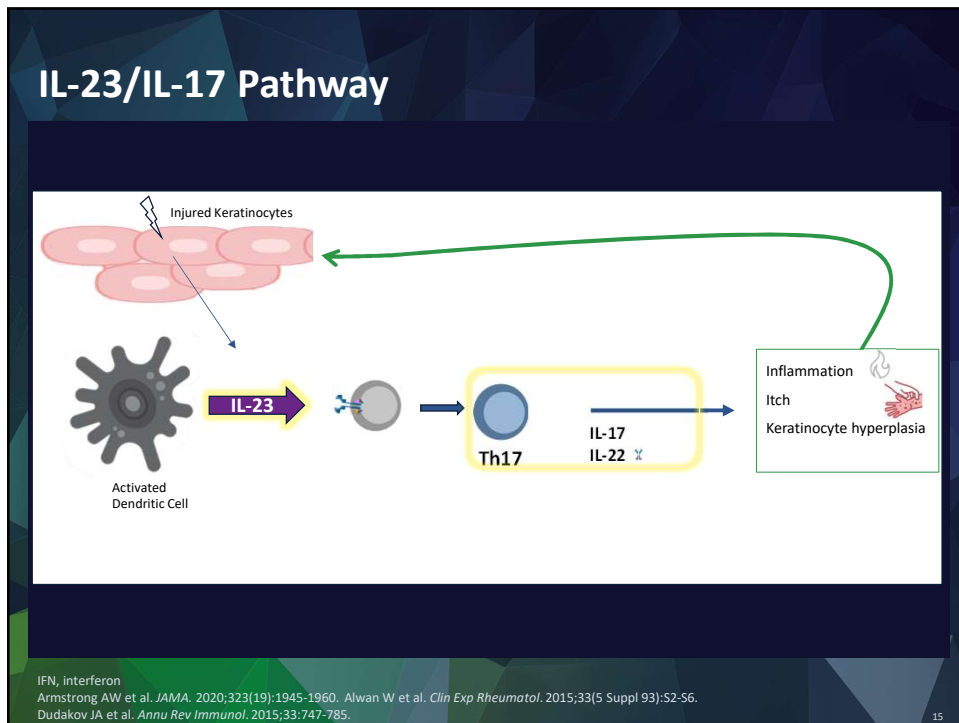
© 2024 Paradigm Medical Communications, LLC, except where noted. Content may not be reproduced in whole or in part without the express written consent of Paradigm Medical Communications, LLC.

Psoriasis Prime Time: The Role of TYK Inhibition in Psoriasis

www.paradigmmc.com/1284-1



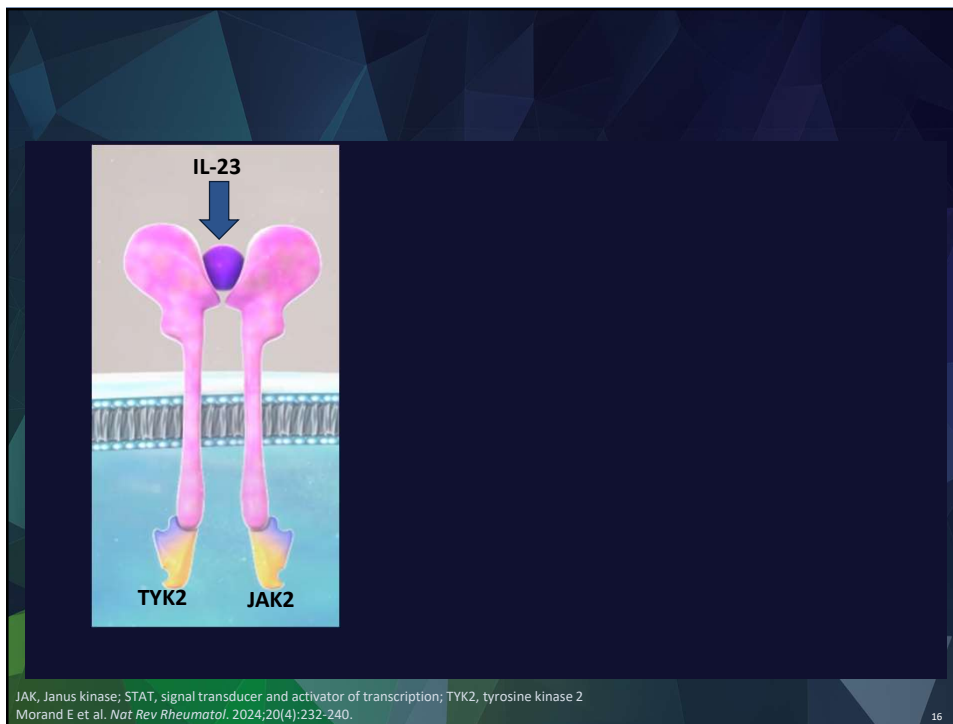
13



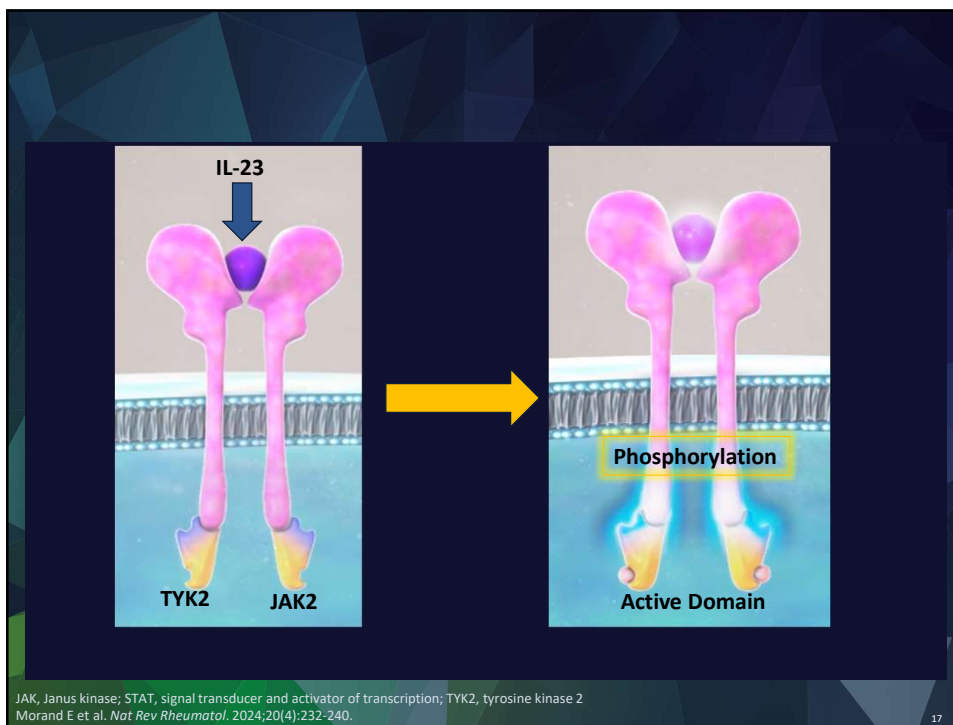
15

Psoriasis Prime Time: The Role of TYK Inhibition in Psoriasis

www.paradigmmc.com/1284-1



16

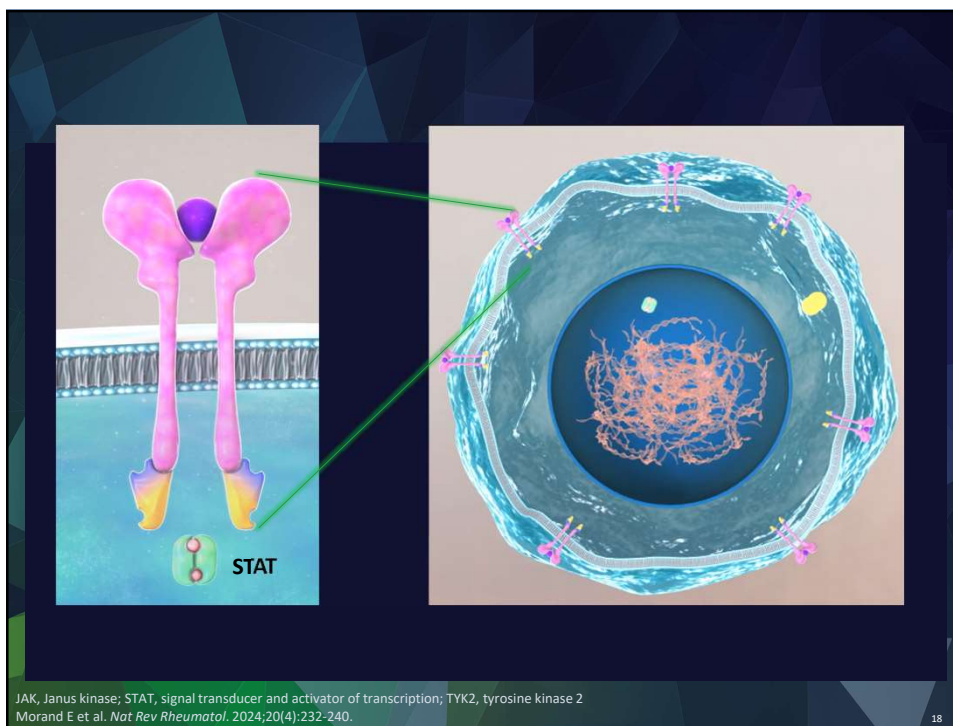


17

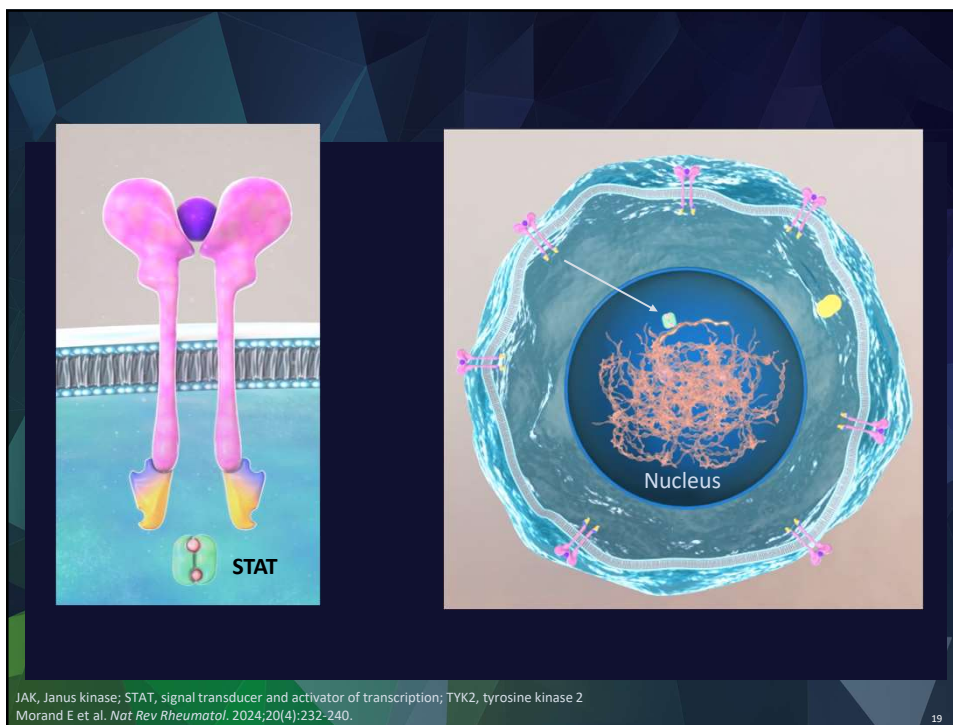
© 2024 Paradigm Medical Communications, LLC, except where noted. Content may not be reproduced in whole or in part without the express written consent of Paradigm Medical Communications, LLC.

Psoriasis Prime Time: The Role of TYK Inhibition in Psoriasis

www.paradigmmc.com/1284-1



18

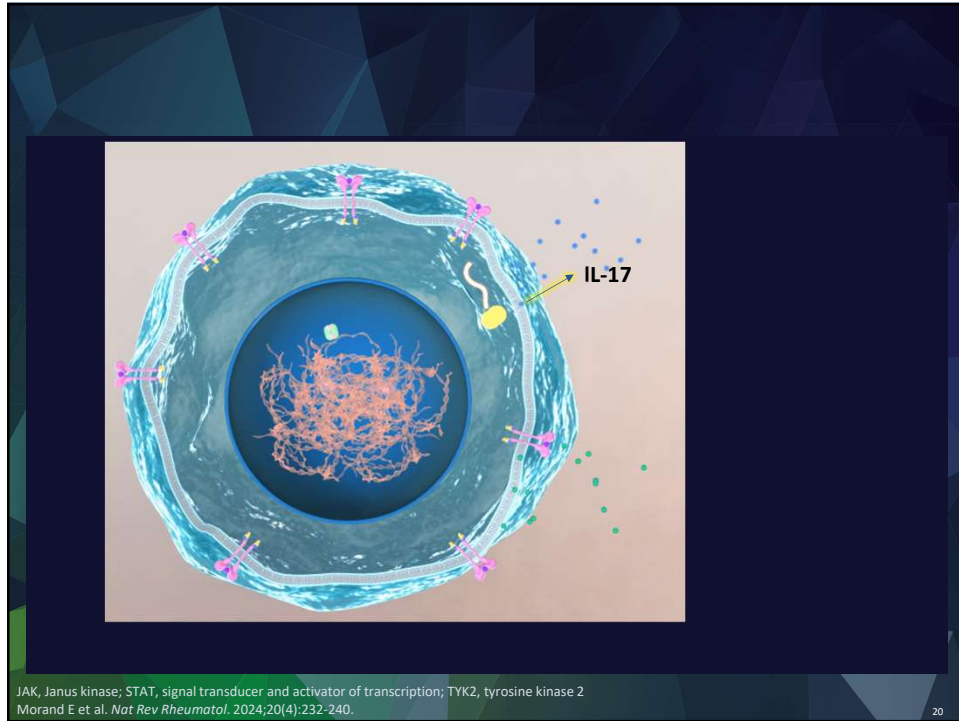


19

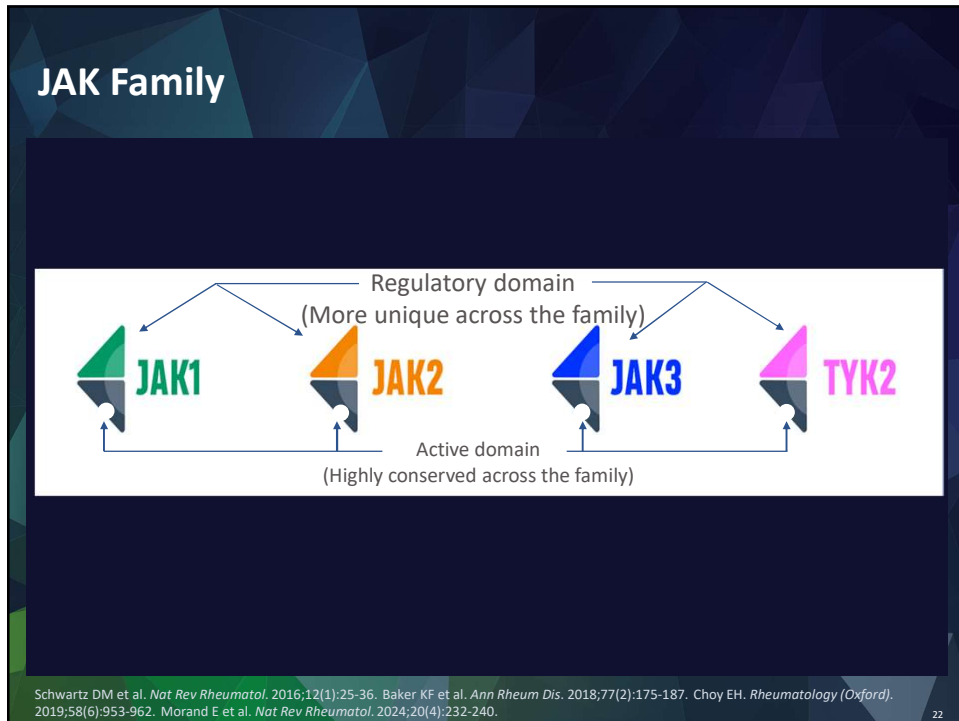
© 2024 Paradigm Medical Communications, LLC, except where noted. Content may not be reproduced in whole or in part without the express written consent of Paradigm Medical Communications, LLC.

Psoriasis Prime Time: The Role of TYK Inhibition in Psoriasis

www.paradigmmc.com/1284-1



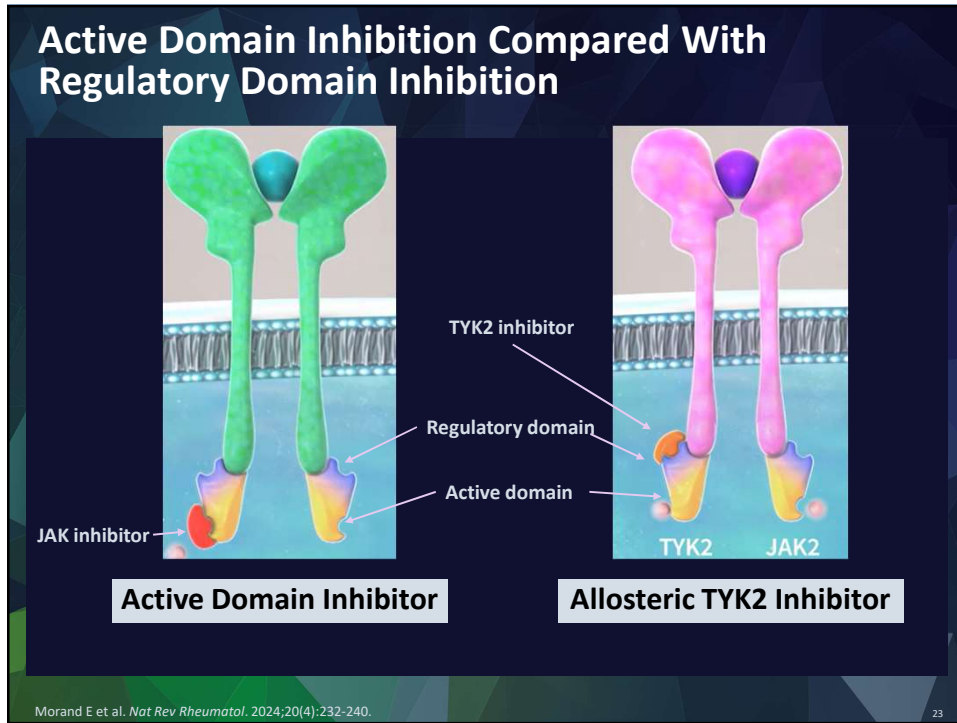
20



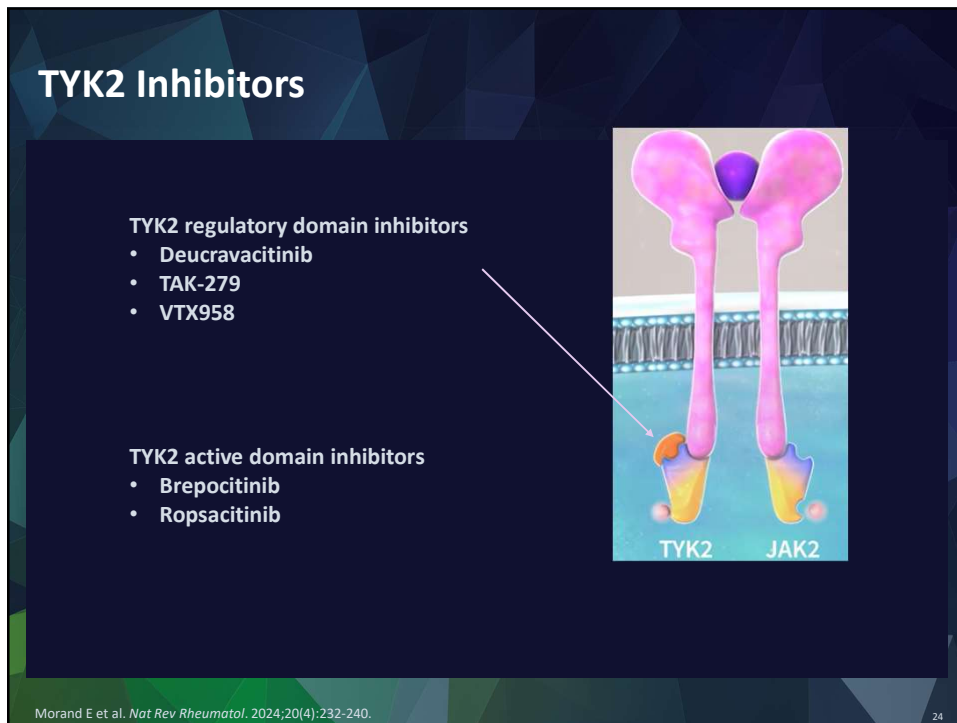
22

© 2024 Paradigm Medical Communications, LLC, except where noted. Content may not be reproduced in whole or in part without the express written consent of Paradigm Medical Communications, LLC.

Psoriasis Prime Time:
The Role of TYK Inhibition in Psoriasis
www.paradigmmc.com/1284-1



23



24

© 2024 Paradigm Medical Communications, LLC, except where noted. Content may not be reproduced in whole or in part without the express written consent of Paradigm Medical Communications, LLC.

Psoriasis Prime Time: The Role of TYK Inhibition in Psoriasis

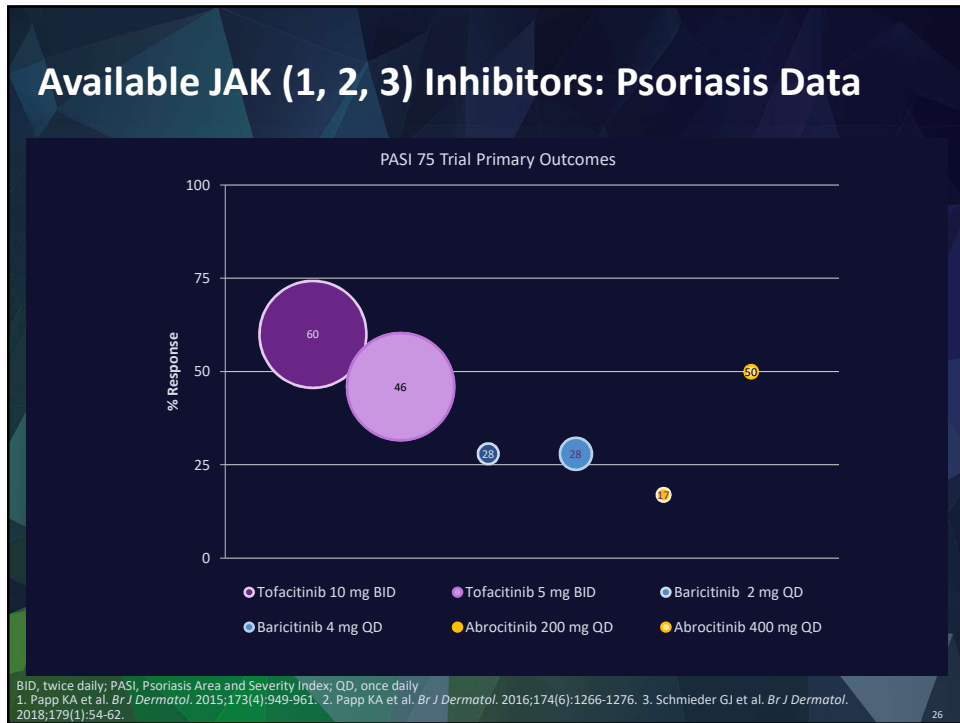
www.paradigmmc.com/1284-1

Selectivity Profiles of JAK/TYK2 Inhibitors

IC ₅₀ (nM)	JAK1	JAK2	JAK3	TYK2 Active Site (JH1)	TYK2 Pseudokinase Site (JH2)
Tofacitinib	15	77	55	489	—
Baricitinib	4	7	787	61	—
Upadacitinib	47	120	2304	4690	—
Abrocitinib	29	803	>15,000	1250	—
TYK2 Inhibitors					
Brepocitinib	17	77	6494	23	—
Ropsacitinib PF-06826647	383	74	>10,000	17	—
Deucravacitinib	>10,000	>10,000	>10,000	>10,000	0.2

Wroblewski ST et al. J Med Chem. 2019;62(20):8973-8995.

25

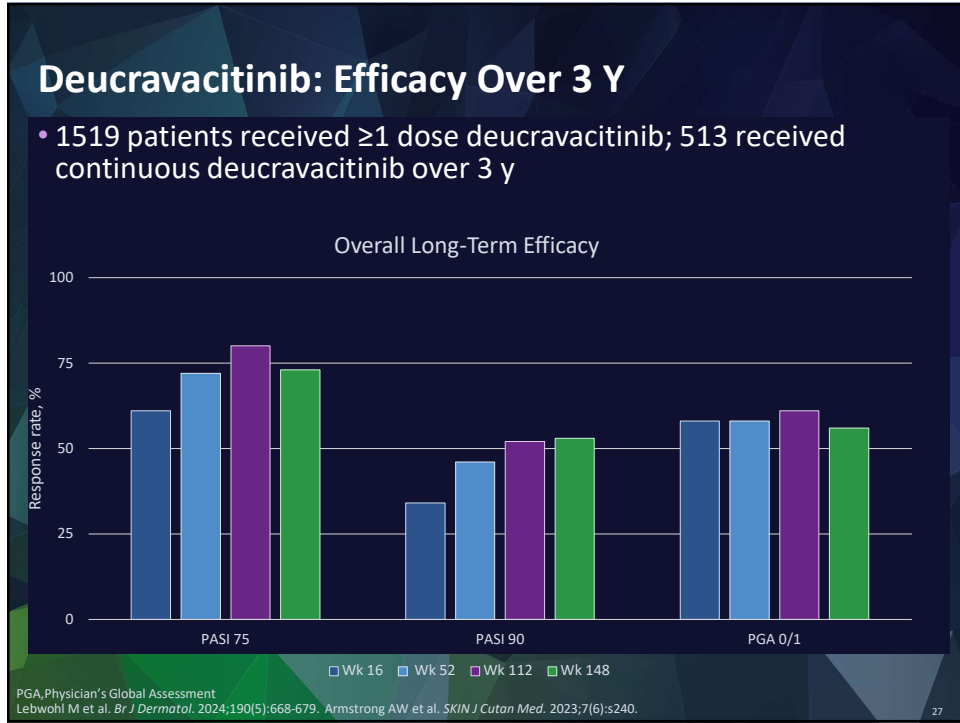


26

© 2024 Paradigm Medical Communications, LLC, except where noted. Content may not be reproduced in whole or in part without the express written consent of Paradigm Medical Communications, LLC.

Psoriasis Prime Time: The Role of TYK Inhibition in Psoriasis

www.paradigmmc.com/1284-1



27

Deucravacitinib: Long-Term Safety

AE, EAIRs/100 PY	Y1	Y2	Y3
Nasopharyngitis	26.1	12.9	11.4
URI	13.4	6.5	
COVID-19	0.2	5.1	6.5
Herpes zoster	0.9	0.7	0.6
MACE	1.2	0.4	0.3
VTE	0.2	0.1	0.1
Malignancies	1.0	0.9	0.9
Lymphoma	0.1	0.1	
Acne	2.9	1.3	
Folliculitis	2.8	1.3	

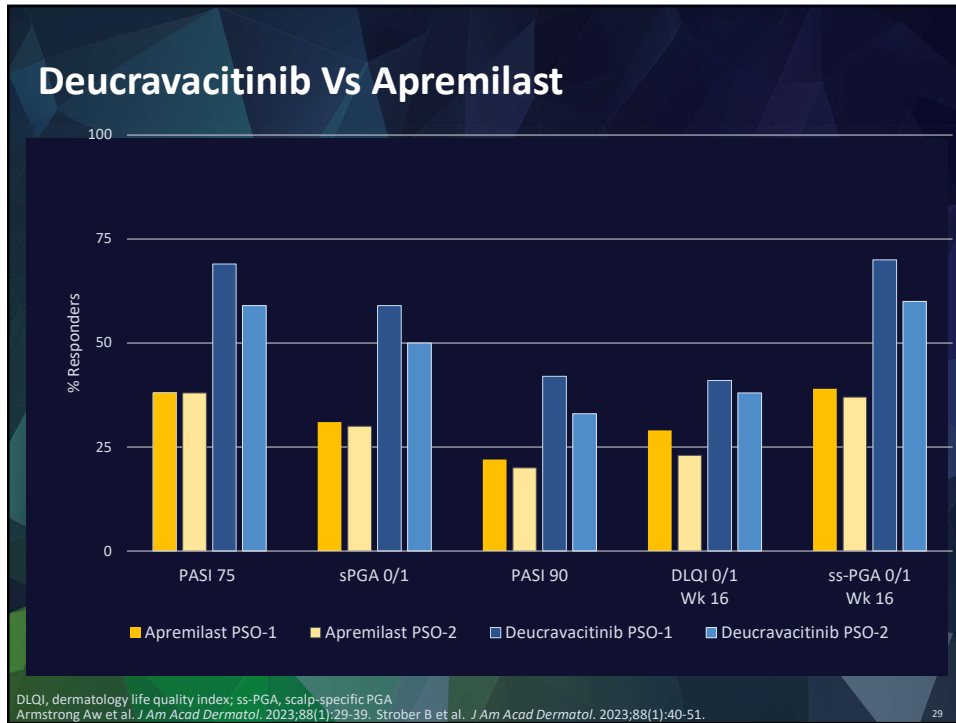
AE, adverse event; EAIR, exposure-adjusted incidence rate; MACE, major adverse cardiovascular events; PY, patient years; URI, upper respiratory infection; VTE, venous thromboembolism
Lebwohl M et al. *Br J Dermatol.* 2024;190(5):668-679. Armstrong AW et al. *SKIN J Cutan Med.* 2023;7(6):s240.

28

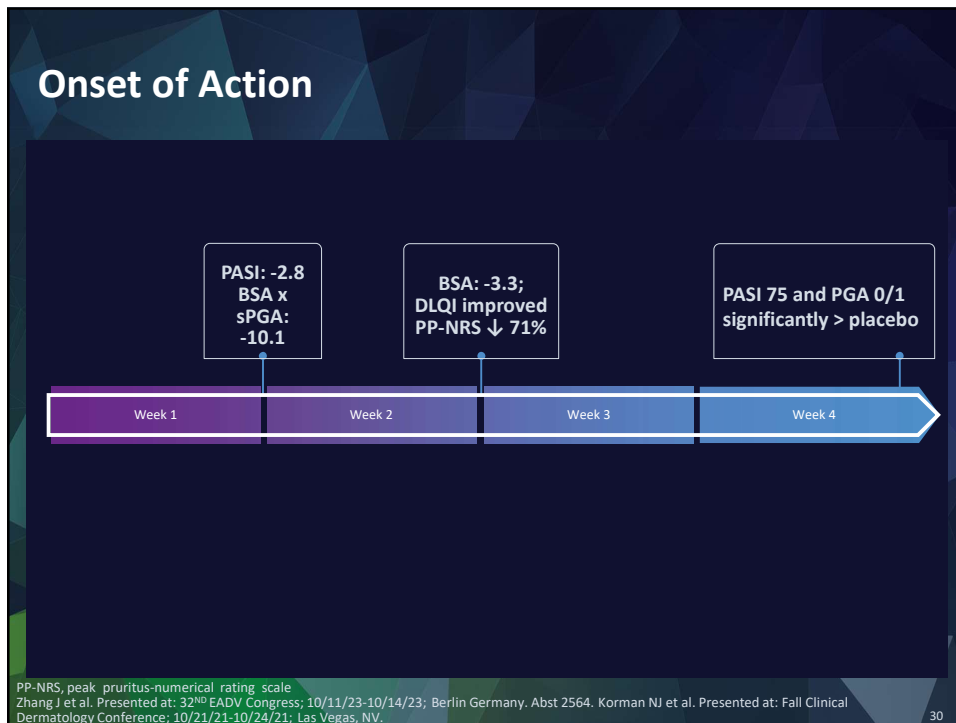
© 2024 Paradigm Medical Communications, LLC, except where noted. Content may not be reproduced in whole or in part without the express written consent of Paradigm Medical Communications, LLC.

Psoriasis Prime Time: The Role of TYK Inhibition in Psoriasis

www.paradigmmc.com/1284-1



29

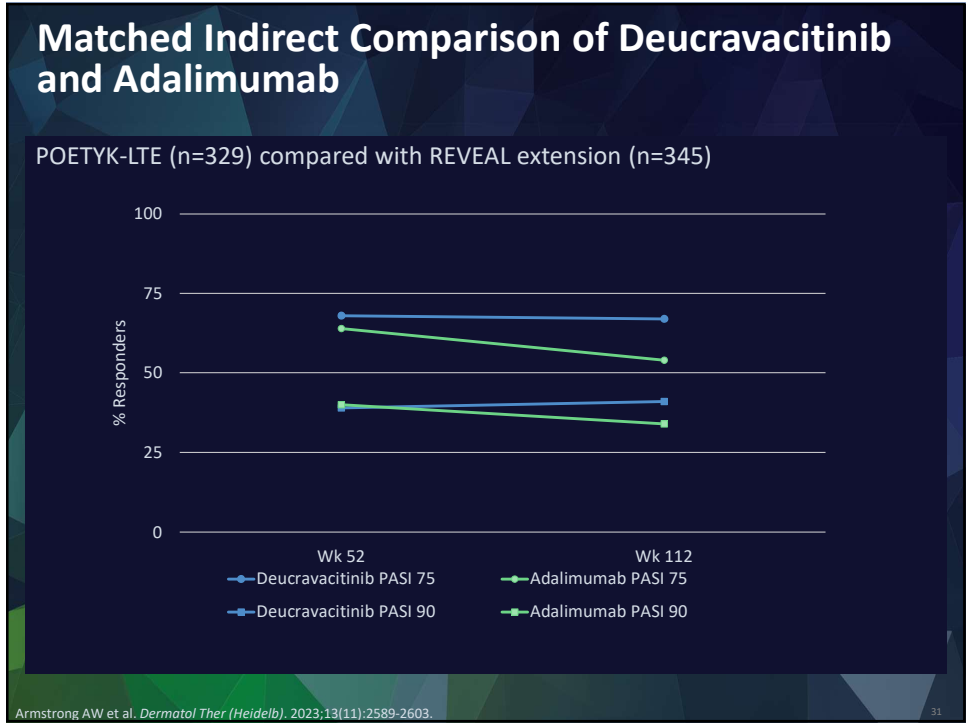


30

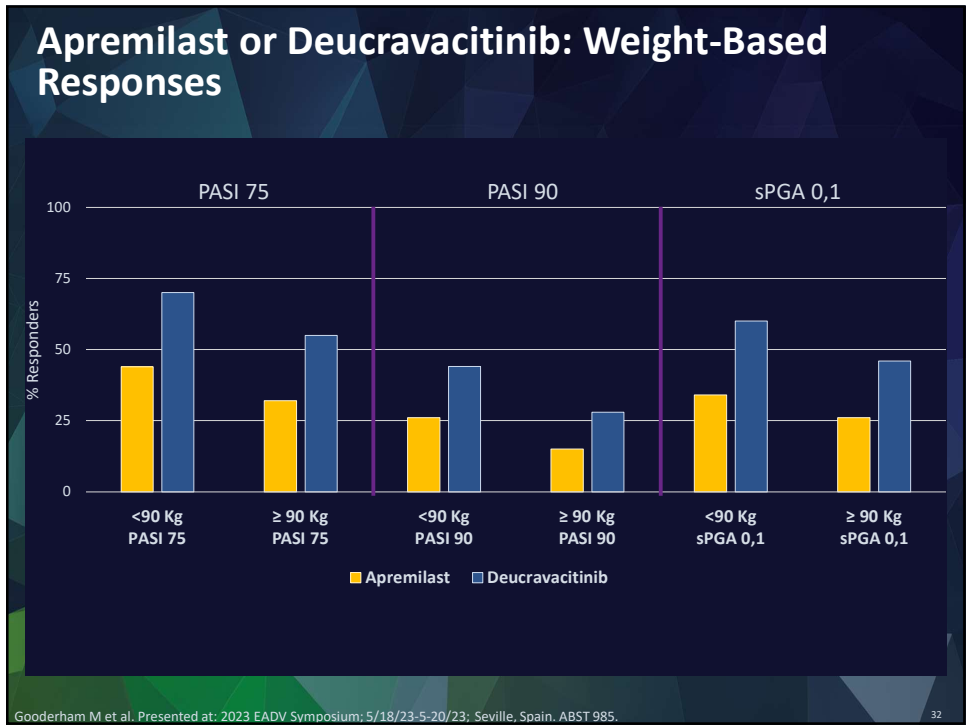
© 2024 Paradigm Medical Communications, LLC, except where noted. Content may not be reproduced in whole or in part without the express written consent of Paradigm Medical Communications, LLC.

Psoriasis Prime Time: The Role of TYK Inhibition in Psoriasis

www.paradigmmc.com/1284-1



31

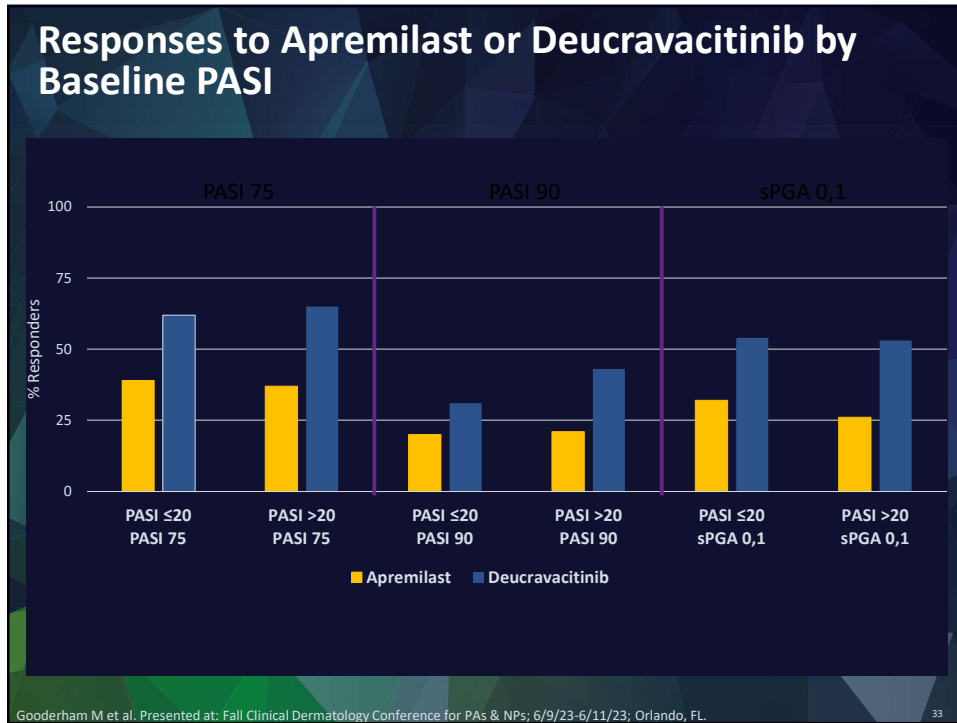


32

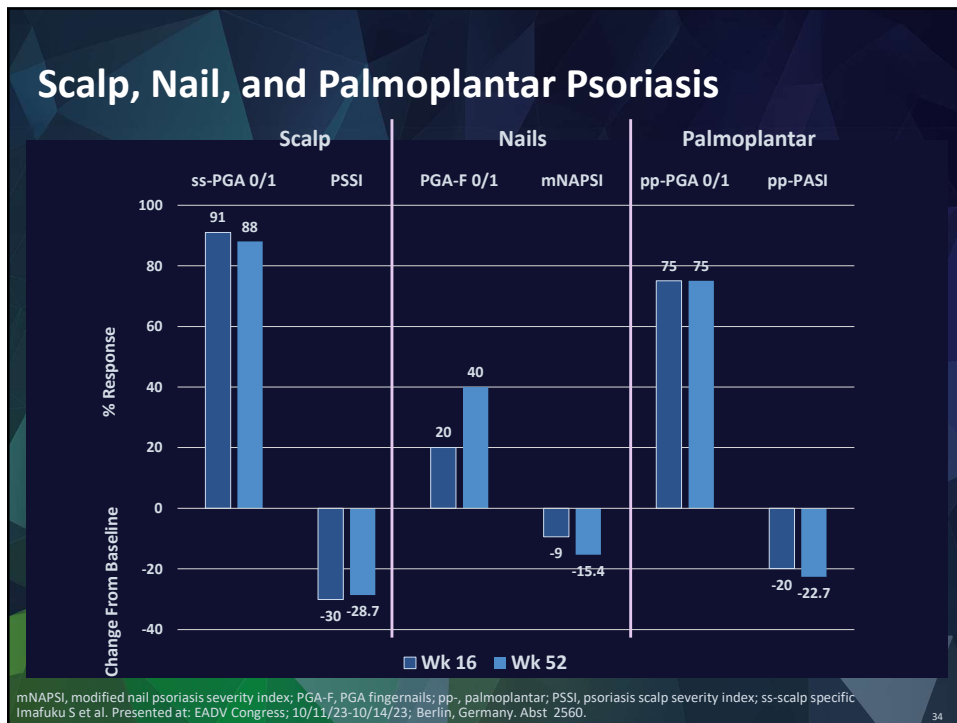
© 2024 Paradigm Medical Communications, LLC, except where noted. Content may not be reproduced in whole or in part without the express written consent of Paradigm Medical Communications, LLC.

Psoriasis Prime Time: The Role of TYK Inhibition in Psoriasis

www.paradigmmc.com/1284-1



33

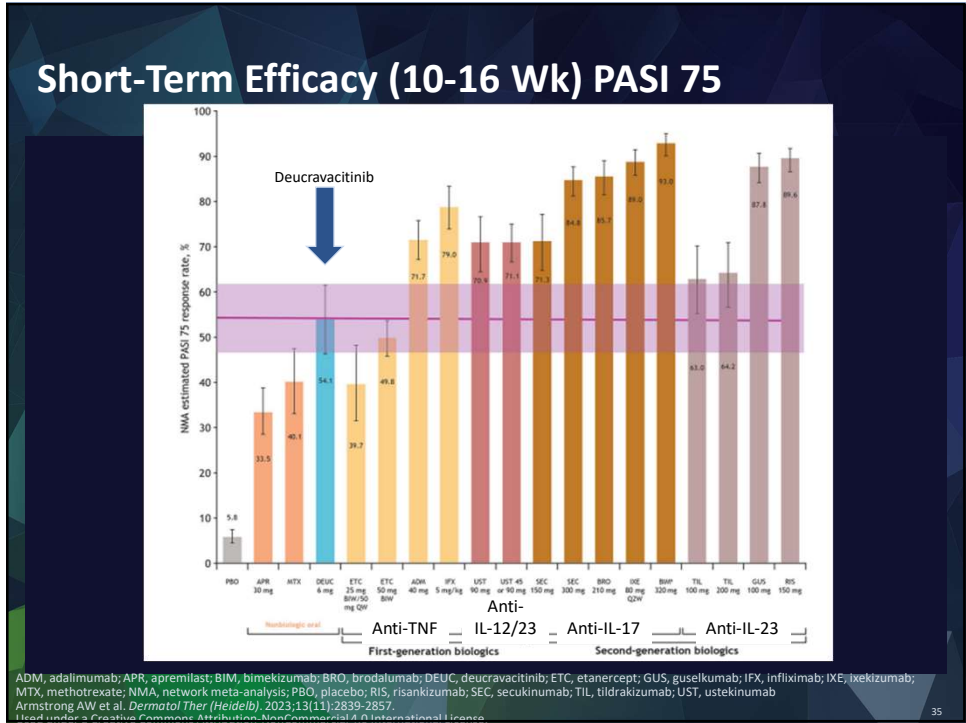


34

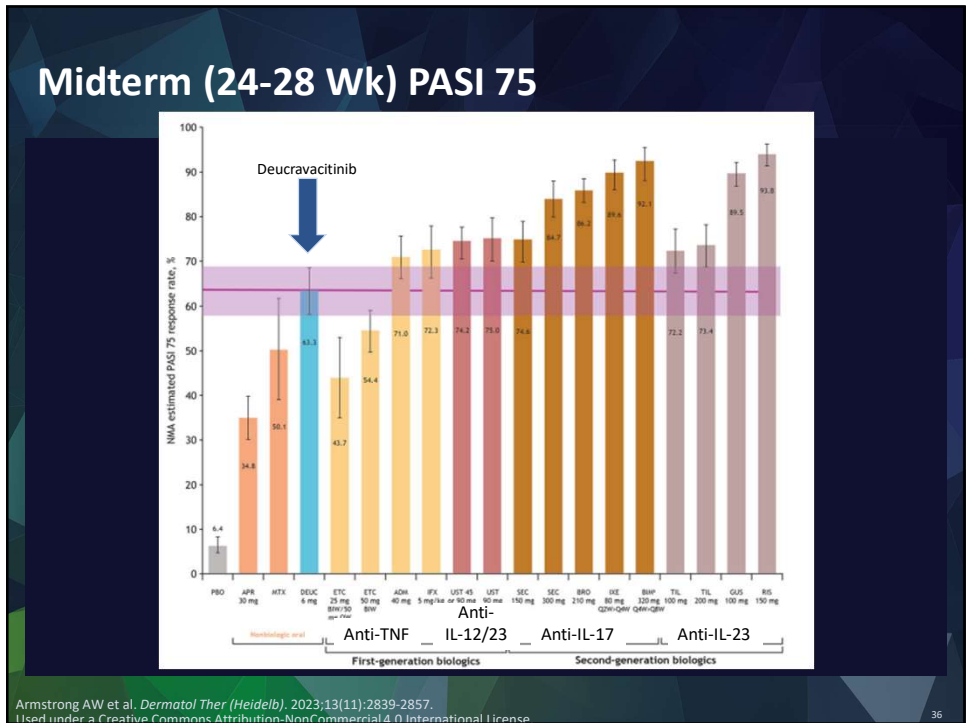
© 2024 Paradigm Medical Communications, LLC, except where noted. Content may not be reproduced in whole or in part without the express written consent of Paradigm Medical Communications, LLC.

Psoriasis Prime Time: The Role of TYK Inhibition in Psoriasis

www.paradigmmed.com/1284-1



35

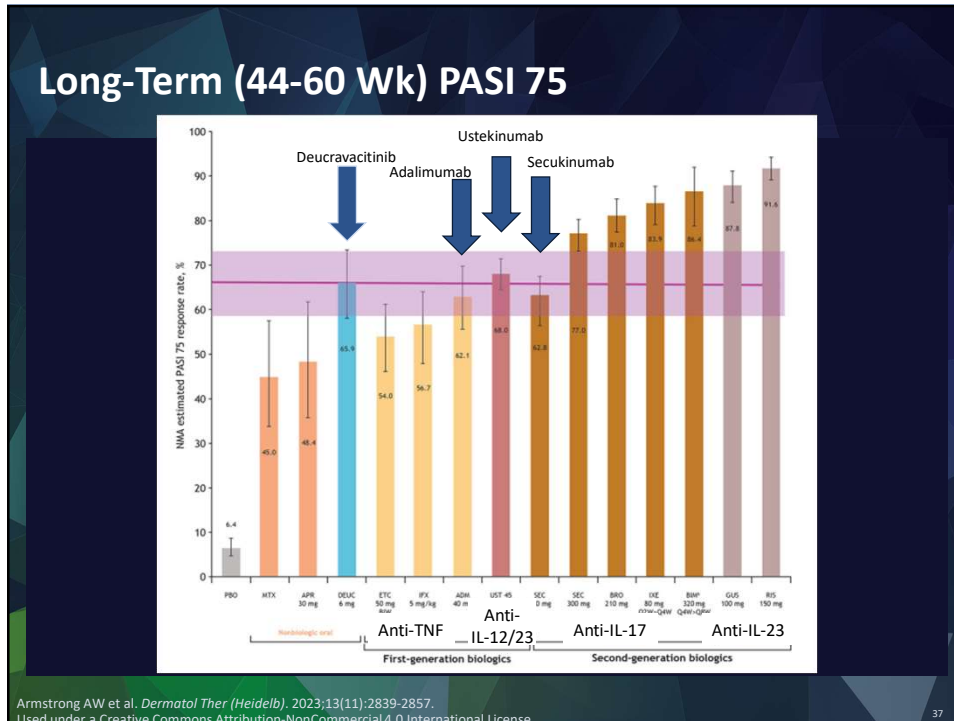


36

© 2024 Paradigm Medical Communications, LLC, except where noted. Content may not be reproduced in whole or in part without the express written consent of Paradigm Medical Communications, LLC.

Psoriasis Prime Time: The Role of TYK Inhibition in Psoriasis

www.paradigmmc.com/1284-1



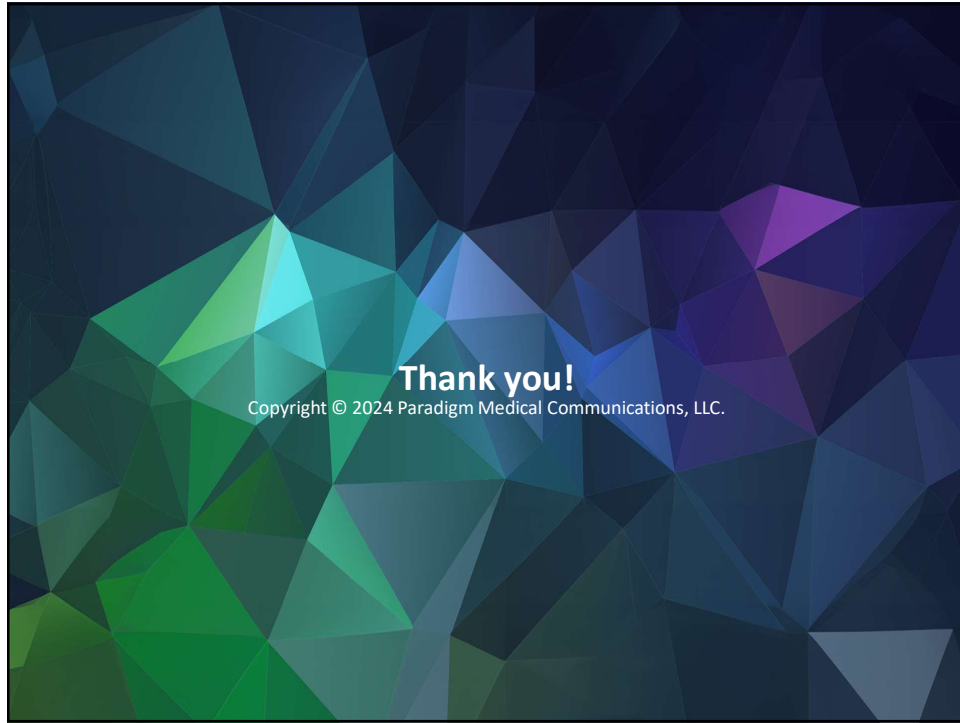
37

Summary Wrap-Up

- The IL-23/Th17 pathway is active in psoriasis, making IL-23 and IL-17 attractive treatment targets
- Proinflammatory cytokines can be inhibited through kinase inhibition of the JAK-STAT signaling pathway
 - ▶ Inhibition of the active kinase site is effective, but there is cross-reactivity due to conserved homology in the active sites of JAKs 1,2,3 and TYK2
 - ▶ Allosteric inhibition of the TYK2 regulatory site shows greater selectivity for TYK2 and reduction of TYK2-mediated cytokines
- Clinical data for deucravacitinib show superiority compared with apremilast and comparable efficacy in meta-analysis to 1st generation biologics, particularly with long-term use, with good safety and tolerability

38

**Psoriasis Prime Time:
The Role of TYK Inhibition in Psoriasis**
www.paradigmmc.com/1284-1



39