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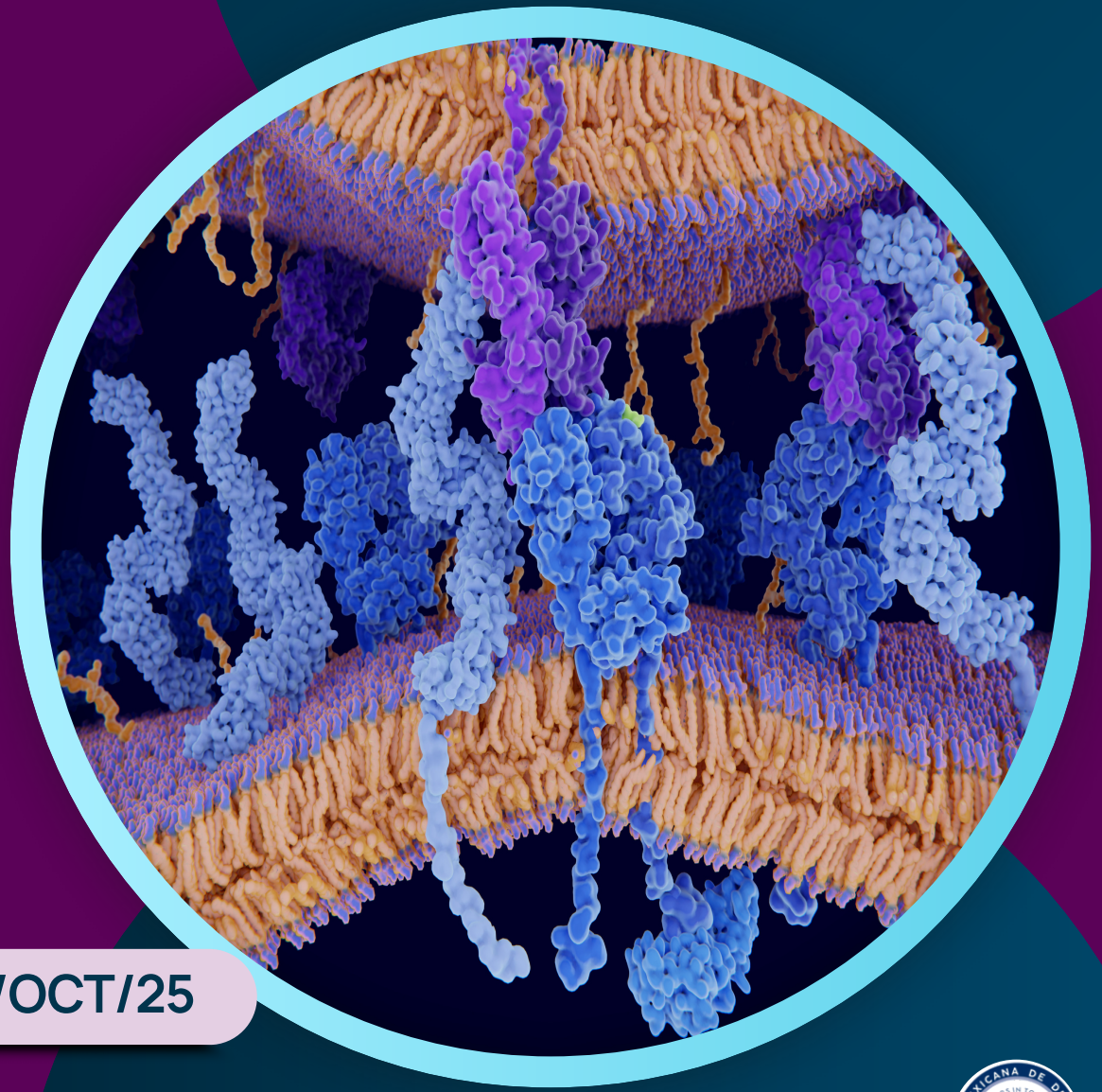
Advancements in Psoriasis Management and Moving Towards IL-23 Inhibitors



INNOVACIÓN & CONEXIONES EN
INMUNODERMATOLOGÍA

Ponente: Dr. Kim Papp

3/OCT/25

Psoriasis: Historical Perspective

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The Greek philosopher and physician Hippocrates (460 to 377 B.C.E.) described inflammatory skin conditions, including psoriasis, using two words: “psora”, meaning itch, and “lopoi”, describing dry, scaly skin.

The first documented use of the term “psoriasis” came centuries laterTrusted Source, from Galen of Pergamon (133 to 220 C.E.), another influential physician.

After the Roman Empire receded, confusion around psoriasis persisted. In Europe, physicians tended to group all inflammatory skin conditions together, and did not understand that only some skin conditions are contagious.

In 1809, an English doctor named Robert Willan produced a simple diagnostic description of several skin conditions, including psoriasis. He also defined some types of psoriasis, including guttate, scalp, and palmar psoriasis

As the 20th century progressed, doctors and researchers learned more about the disease and developed detailed descriptions of various subtypes

In 1973, John M. Moll and Verna Wright made a milestone discovery. They published a paper describing how psoriasis and psoriatic arthritis are part of the same unique disease that is distinct from rheumatoid arthritis.

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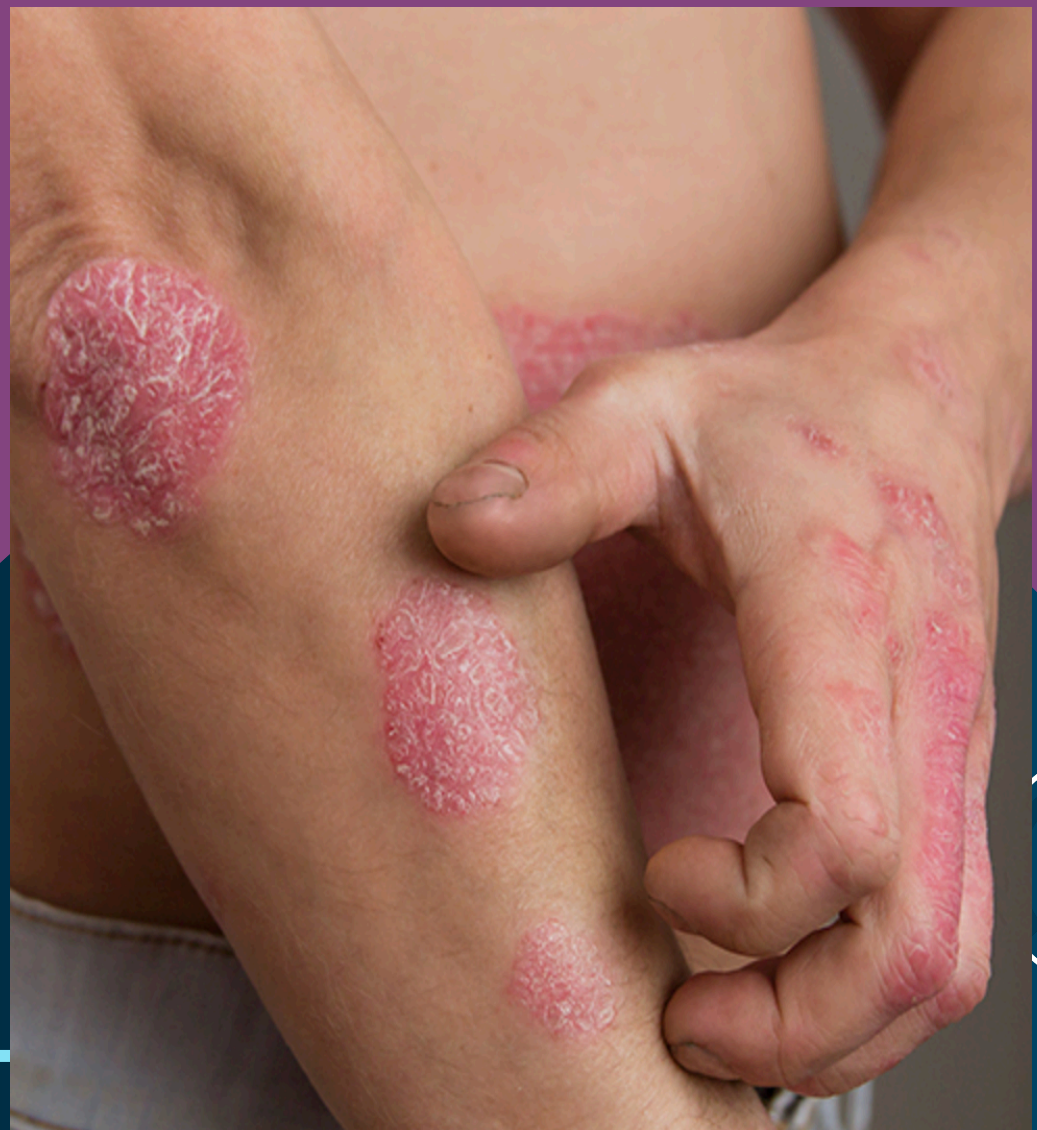
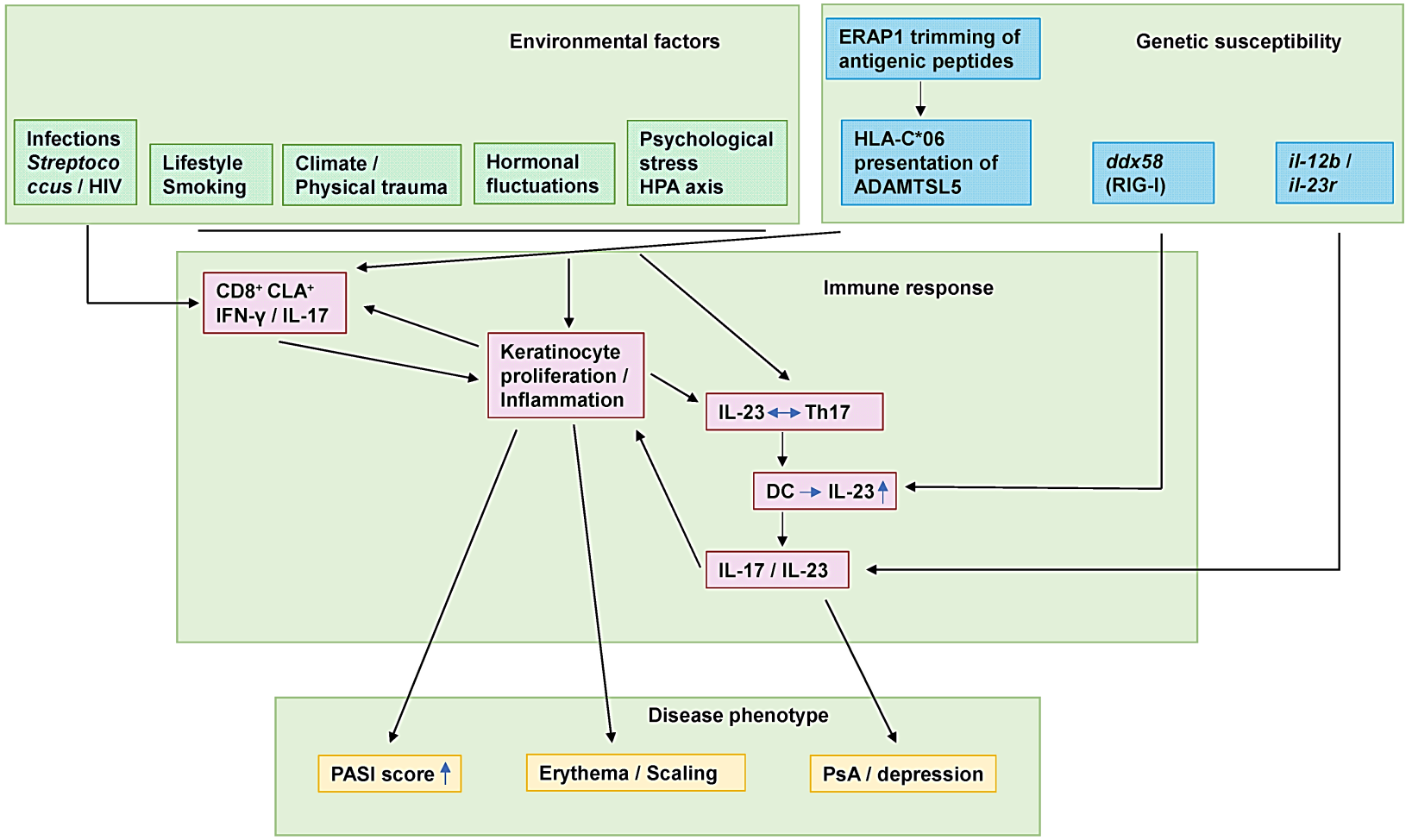
Psoriasis as we know it today

- **Chronic, immune-mediated inflammatory** skin disorder
- Affecting ~2-3% of the global population
- Characterized by erythematous plaques with **silvery scales**, commonly on **extensor surfaces, scalp, and lower back**
- **Associated with multiple comorbidities:**
  - Cardiovascular disease
  - Metabolic syndrome
  - Obesity
  - Depression



Decoding Immune circuits in PsO



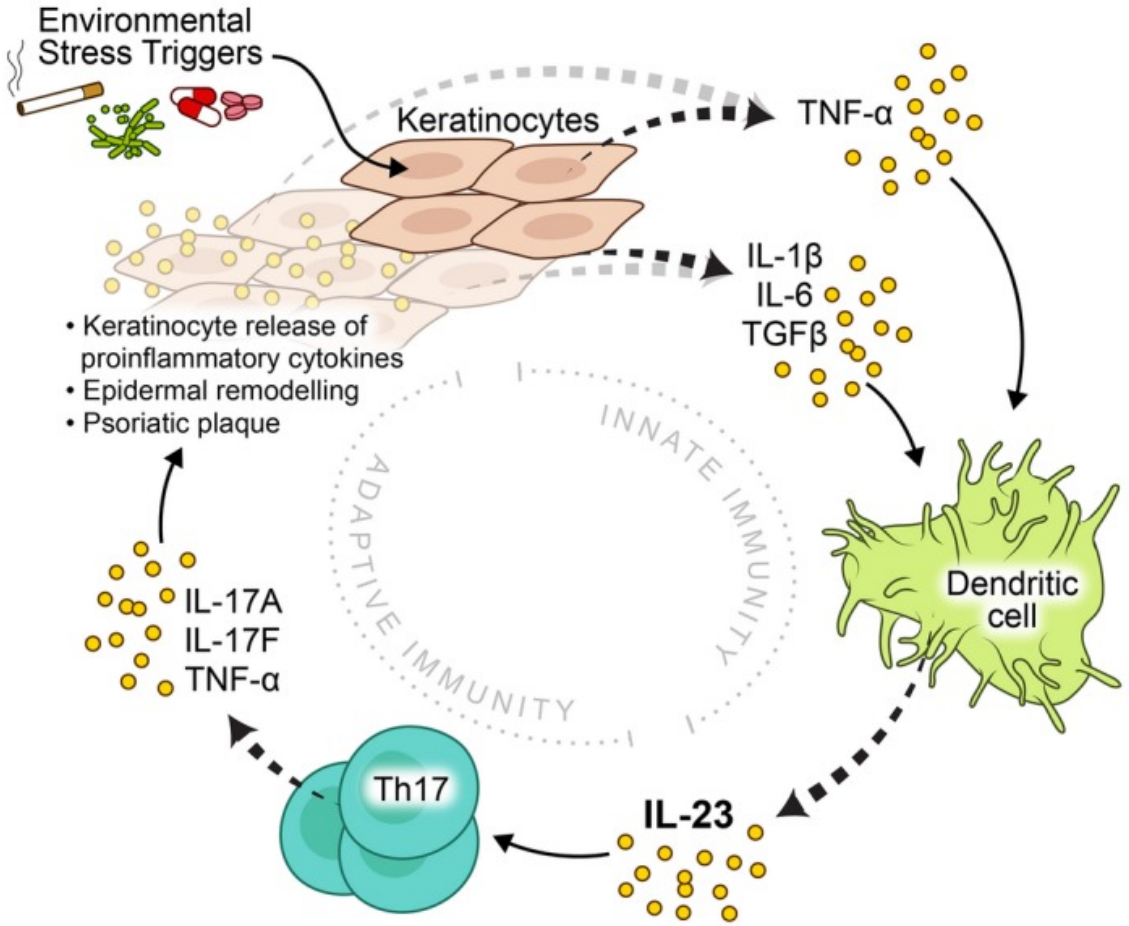
Pathophysiology

- Driven by **immune dysregulation** leading to **keratinocyte hyperproliferation and inflammation**

- Three major cytokine pathways involved:
  - **TNF-α** → Amplifies inflammation and activates dendritic cells.
  - **IL-17** → Directly stimulates keratinocyte hyperproliferation and neutrophil recruitment.
  - **IL-23** → **Master regulator** that **sustains Th17 differentiation**, driving chronic inflammation.

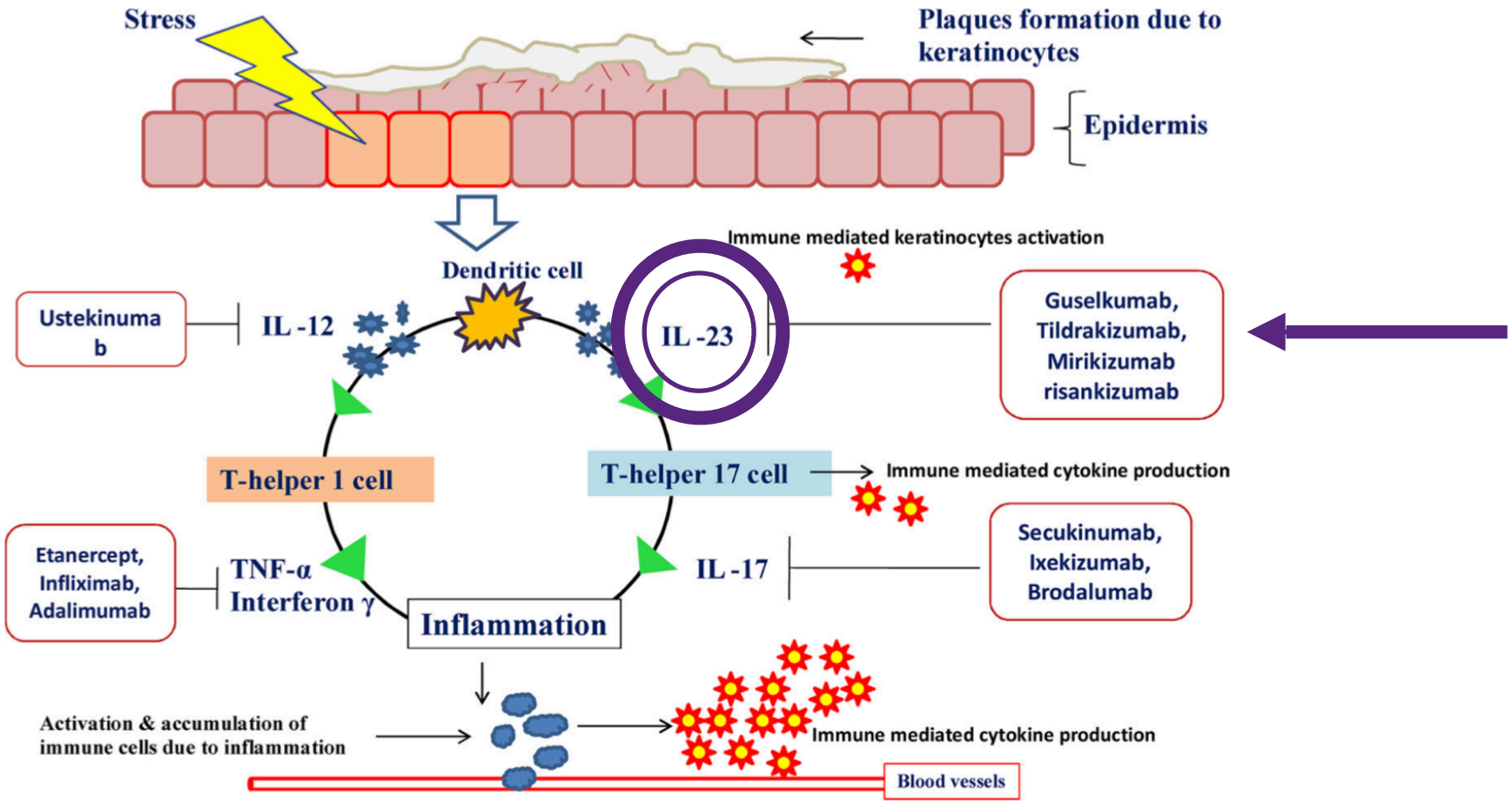
Armstrong AW, Read C. Pathophysiology, Clinical Presentation, and Treatment of Psoriasis: A Review. JAMA. 2020 May 19;323(19):1945-1960. doi: 10.1001/jama.2020.4006.

Assessing the response in circle



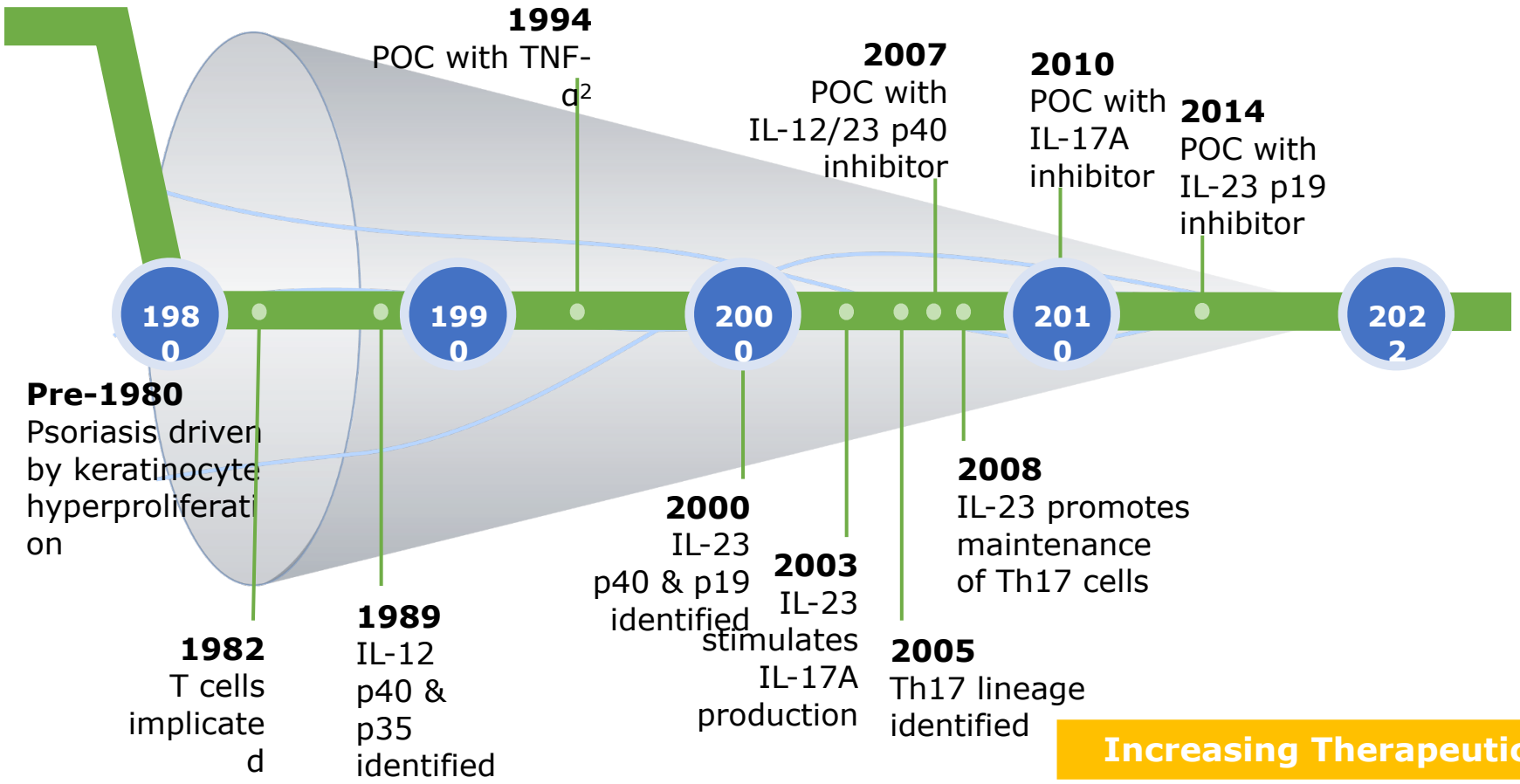
Gooderham MJ, Papp KA, Lynde CW. Shifting the focus - the primary role of IL-23 in psoriasis and other inflammatory disorders. J Eur Acad Dermatol Venereol. 2018 Jul;32(7):1111-1119. doi: 10.1111/jdv.14868.

IL-23: The Master Regulator



Rapalli VK, Singhvi G, Dubey SK, Gupta G, Chellappan DK, Dua K. Emerging landscape in psoriasis management: From topical application to targeting biomolecules. Biomed Pharmacother. 2018 Oct;106:707-713. doi: 10.1016/j.biopha.2018.06.136.

Therapeutic Targeting Has Evolved With Our Understanding of the Pathogenesis of Psoriasis1



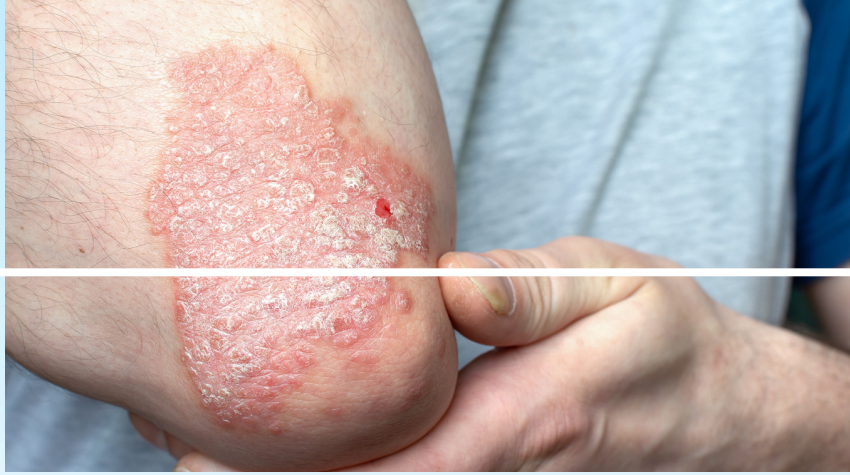
IL, interleukin; POC, proof of concept; Th, T helper; TNF, tumor necrosis factor.

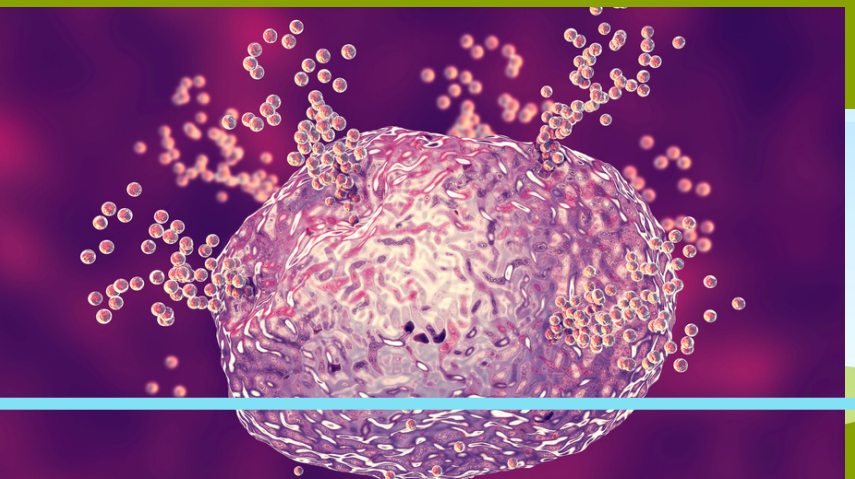
1. Gooderham MJ, et al. J Eur Acad Dermatol Venereol. 2018;32:1111–1119; 2. Maini RN. Arthritis Res Ther. 2004;6:S1–S2.

Biologics in psoriasis

Biologics targeting IL-23 or IL-17 are clinically more beneficial

than IL-12/23 and TNF-alpha inhibitors.





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Efficacy

- **IL-17 inhibitors tend to have a more rapid onset of action** while **IL-23 inhibitors showed progressive improvement during follow-up visits.**

- **IL-23 inhibitors reached a comparable efficacy with IL-17 inhibitors at the end**.

- While initial response rates may vary, **the long-term treatment outcomes of both IL-17 and IL-23 inhibitors are similar**.

Borriello S, Roccuzzo G, Dapavo P, Sciamarrelli N, Macagno N, Leo F, et al. Psoriasis in Childbearing Age: A Real-Life, Retrospective, Single-Center Study on Anti-IL17 and IL-23 Agents. J Clin Med. 2024 Oct 25;13(21):6401. doi: 10.3390/jcm13216401.

Safety

- **The most common adverse effects were found to be similar between IL-17 inhibitors and IL-23 inhibitors.**
  - Nasopharyngitis
  - Upper respiratory tract infections
  - Injection-site reactions

- **IL-17 inhibitors have additional precautions:**
  - Infections with *Candida* species
  - Worsening of inflammatory bowel disease (IBD)

Ghoreschi K, Balato A, Enerbäck C, Sabat R. Therapeutics targeting the IL-23 and IL-17 pathway in psoriasis. Lancet. 2021 Feb 20;397(10275):754-766. doi: 10.1016/S0140-6736(21)00184-7.

Dosing

- **IL-23 inhibitors:**
  (less frequent dosing)
  - **Induction:**
    - ✓ Weeks 0 and 4
  - **Maintenance:**
    - ✓ Every 8 weeks thereafter - Guselkumab
    - ✓ Every 12 weeks thereafter – Tildrakizumab, Risankizumab

- **IL-17 inhibitors:**
  (more frequent dosing)
  - **Induction:**
    - ✓ Every week for the first 5 weeks - Secukinumab
    - ✓ Every 2 weeks for the first 12 weeks – Ixekizumab
  - **Maintenance:**
    - ✓ Every 4 weeks

Ghoreschi K, Balato A, Enerbäck C, Sabat R. Therapeutics targeting the IL-23 and IL-17 pathway in psoriasis. Lancet. 2021 Feb 20;397(10275):754-766. doi: 10.1016/S0140-6736(21)00184-7.

Number of injections

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1-Year Dosing						
IL-23 Inhibitor			IL-17 inhibitor			TNF-alpha inhibitor
Tildrakizumab	Risankizumab	Guselkumab	Secukinumab		Ixekizumab	Adalimumab
6 injections	6 injections	8 injections	17 injections or	34 injections	18 injections	27 injections
ONE 100-mg injection every 12 weeks	ONE 150-mg injection every 12 weeks	ONE 100-mg injection every 8 weeks	ONE 300-mg injection every 4 weeks	TWO 150-mg injection every 4 weeks	ONE 80-mg injection every 4 weeks	ONE 40-mg injection every other week
AFTER one 100-mg injection at weeks 0 and 4	AFTER one 150-mg injection at weeks 0 and 4	AFTER one 100-mg injection at weeks 0-4	AFTER one 300-mg injection or two 150-mg injections at weeks 0, 1, 2, 3 and 4		AFTER two 80-mg injections at week 0, then 80-mg at weeks 2, 4, 6, 8, 10, 12	AFTER one 80-mg injection

Choosing the best biologic for your patient

- IL-17 inhibitors have a higher efficacy during induction therapy with an increased risk of adverse events.

- **IL-23 inhibitors work progressively, with sustained efficacy and consistent safety from induction to maintenance.**

Erichsen CY, Jensen P, Kofoed K. Biologic therapies targeting the interleukin (IL)-23/IL-17 immune axis for the treatment of moderate-to-severe plaque psoriasis: a systematic review and meta-analysis. J Eur Acad Dermatol Venereol. 2020 Jan;34(1):30-38. doi: 10.1111/jdv.15879.

Why choosing IL-23 inhibitors make sense?

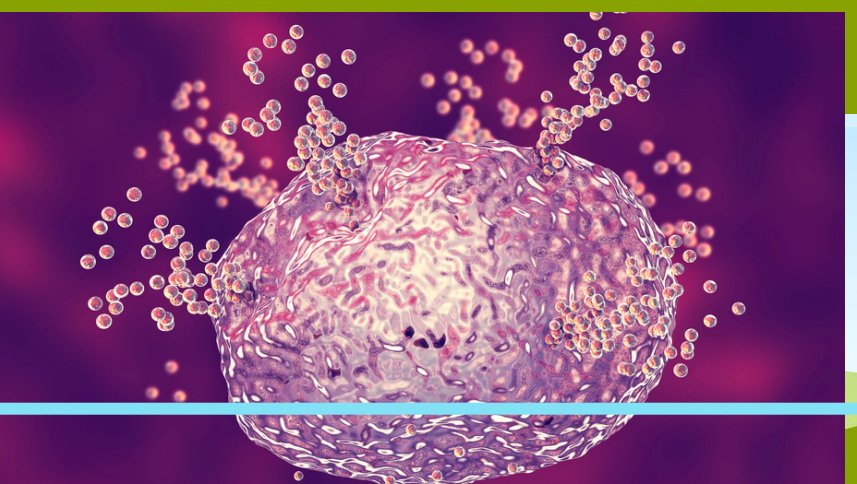
- **IL-23 is critical for maintaining psoriatic inflammation**, making it an optimal therapeutic target.

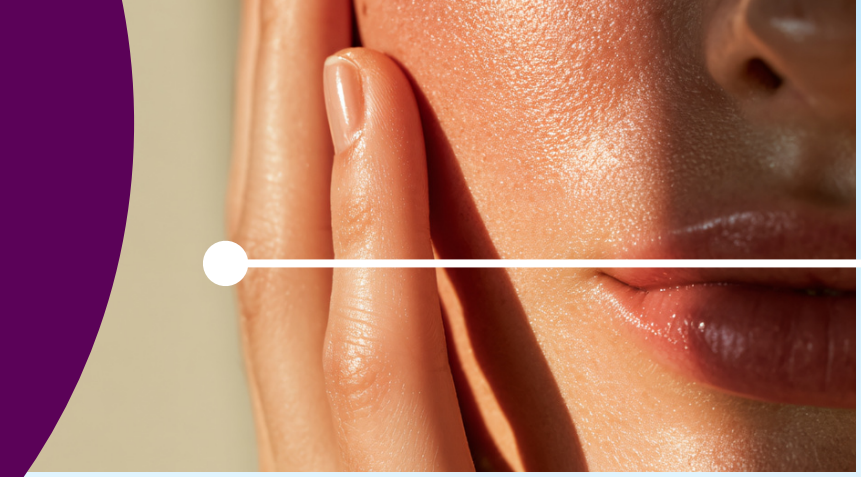
- **IL-23 inhibitors selectively block the p19 subunit**, preventing downstream IL-17 production.

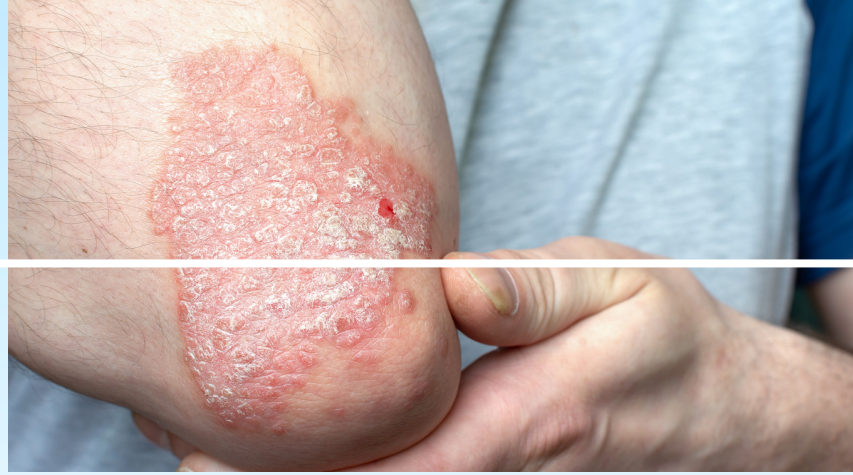
- **Advantages of IL-23 inhibitors over IL-17 inhibitors:**
  - Efficacy: **Sustained remission** with prolonged dosing intervals.
  - Safety:
    - ✓ **Lower risk of candidiasis and other infections**
    - ✓ **More selective immune modulation, sparing systemic immune functions.**

Erichsen CY, Jensen P, Kofoed K. Biologic therapies targeting the interleukin (IL)-23/IL-17 immune axis for the treatment of moderate-to-severe plaque psoriasis: a systematic review and meta-analysis. J Eur Acad Dermatol Venereol. 2020 Jan;34(1):30-38. doi: 10.1111/jdv.15879.

A Systematic Review and Network Meta-analysis







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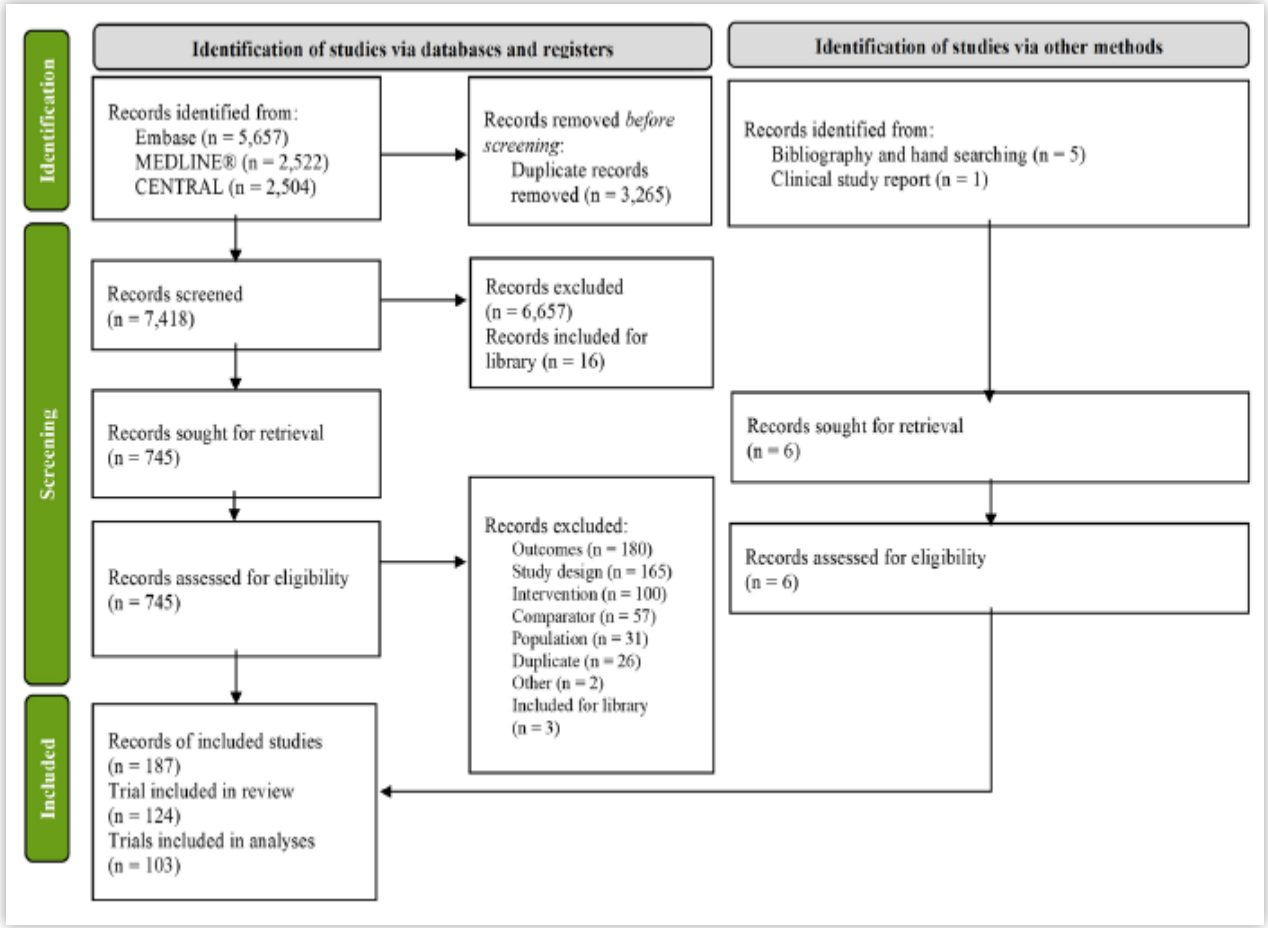
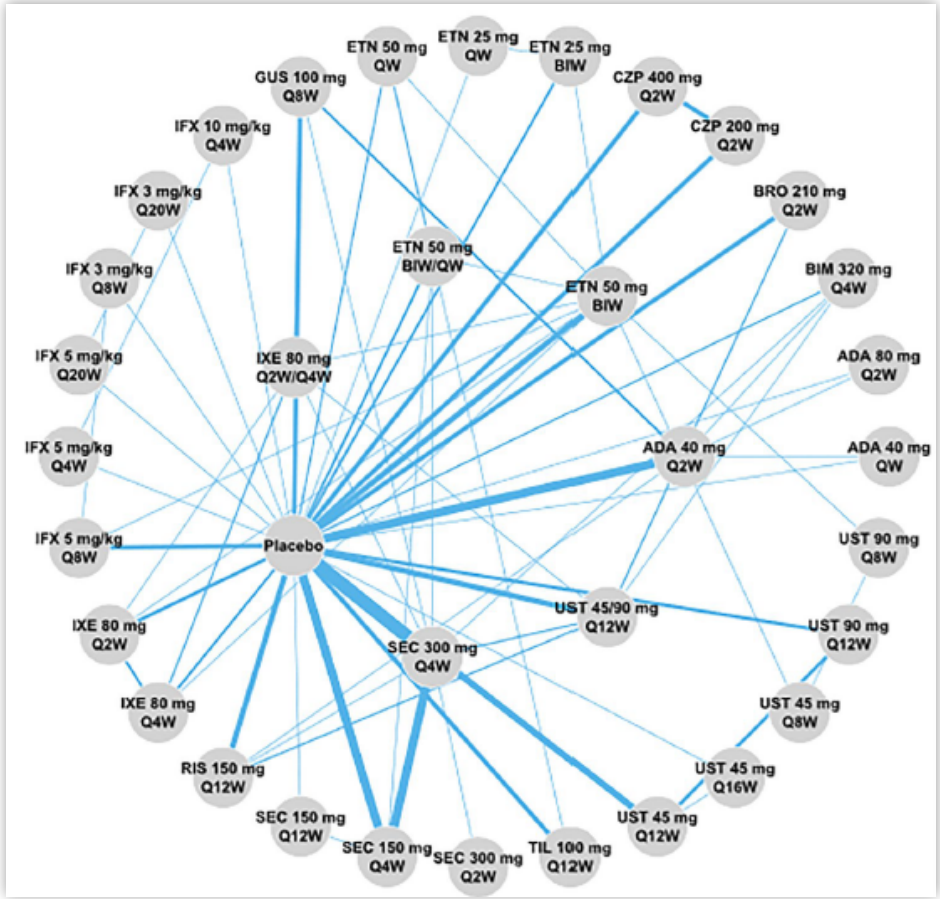
Biologics for the Treatment of Moderate-to-Severe Plaque Psoriasis: A Systematic Review and Network Meta-analysis



Study selection process



Network diagram of included trials and comparisons

Lebwohl MG, Carvalho A, Asahina A, Zhang J, Fazeli MS, Kasireddy E, Serafini P, Ferro T, Gogineni R, Thaçi D. Biologics for the Treatment of Moderate-to-Severe Plaque Psoriasis: A Systematic Review and Network Meta-analysis. Dermatol Ther (Heidelb). 2025 May 6. doi: 10.1007/s13555-025-01423-0. Epub ahead of print. PMID: 40329054.

Results: Summary of risk ratios from NMAs of clinical efficacy outcomes at week 28

Biologic (Dose)	PASI 90 RR (95% CrI)	PASI 100 RR (95% CrI)	PGA 0/1 RR (95% CrI)	DLQI 0/1 RR (95% CrI)
Tildrakizumab 100 mg Q12W	14.09 (11.77–15.50)	10.05 (7.74–12.26)	9.34 (7.79–10.68)	10.19 (7.58–13.49)
Risankizumab 150 mg Q12W	14.81 (13.68–15.73)	20.65 (17.95–22.64)	10.29 (9.53–11.02)	NA
Guselkumab 100 mg Q8W	14.77 (13.64–15.70)	17.99 (15.69–20.11)	10.23 (9.43–11.00)	12.37 (9.22–15.41)
Bimekizumab 320 mg Q4W	14.76 (13.57–15.71)	21.31 (19.19–22.80)	10.24 (9.45–11.00)	11.38 (8.44–14.70)
Ixekizumab 80 mg Q2W/ Q4W	14.14 (12.63–15.36)	17.53 (15.06–19.96)	9.66 (8.67–10.68)	12.52 (8.28–15.67)
Secukinumab 300 mg Q4W	13.58 (12.31–14.77)	16.01 (14.05–17.85)	9.59 (8.80–10.49)	11.89 (9.10–14.74)
Ustekinumab 90 mg Q12W	14.58 (13.01–15.61)	13.53 (11.33–15.84)	10.01 (8.92–10.88)	13.65 (11.11–16.24)
Adalimumab 40 mg Q2W	10.18 (8.69–11.68)	9.99 (8.39–11.50)	7.62 (6.63–8.56)	8.23 (5.61–11.09)
Etanercept 50 mg BIW/QW	8.60 (6.87–10.60)	5.15 (3.73–6.96)	7.76 (5.91–9.58)	7.37 (4.63–11.19)

Lebwohl MG, Carvalho A, Asahina A, Zhang J, Fazeli MS, Kasireddy E, Serafini P, Ferro T, Gogineni R, Thaçi D. Biologics for the Treatment of Moderate-to-Severe Plaque Psoriasis: A Systematic Review and Network Meta-analysis. Dermatol Ther (Heidelb). 2025 May 6. doi: 10.1007/s13555-025-01423-0. Epub ahead of print. PMID: 40329054.

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Thank you!