斑塊性乾癬之新型生物製劑綜論

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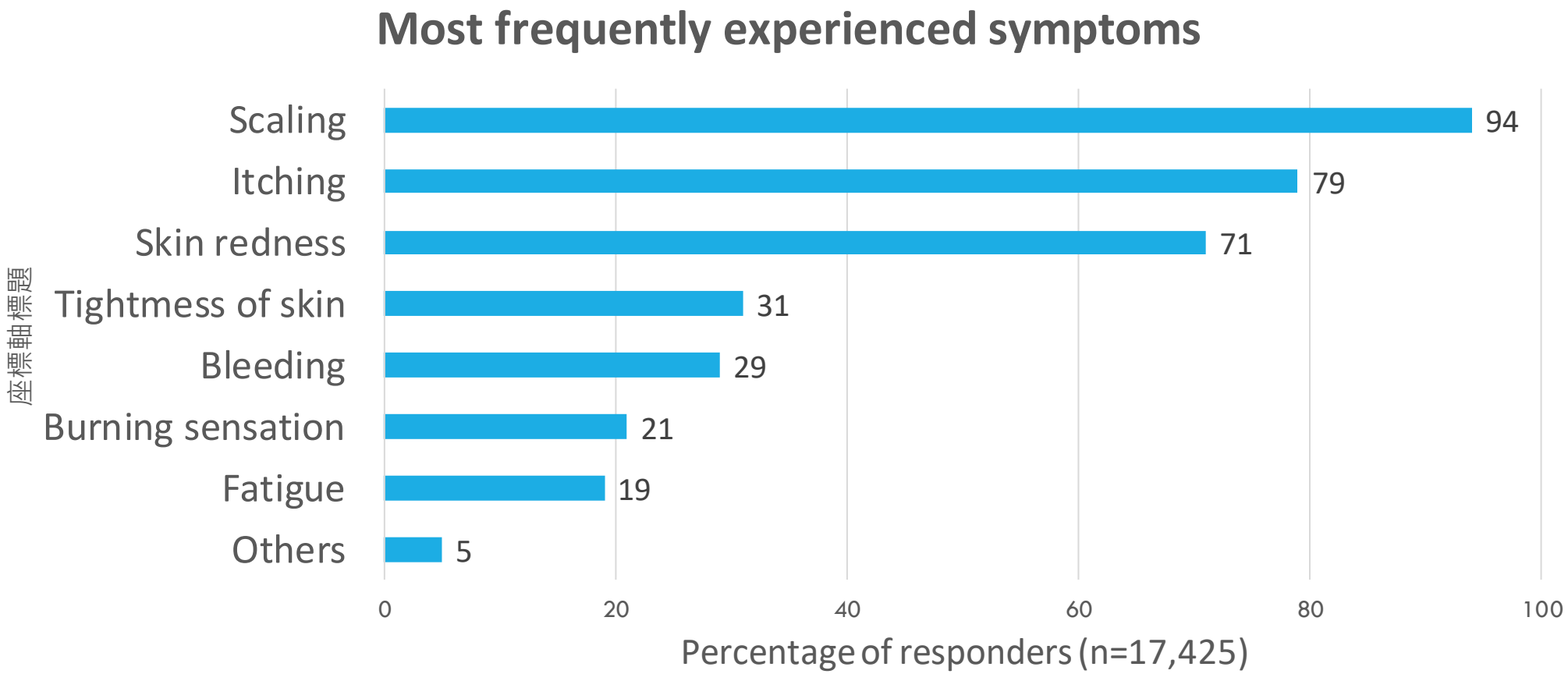
乾癬簡介
Introduction of Psoriasis

What is psoriasis?

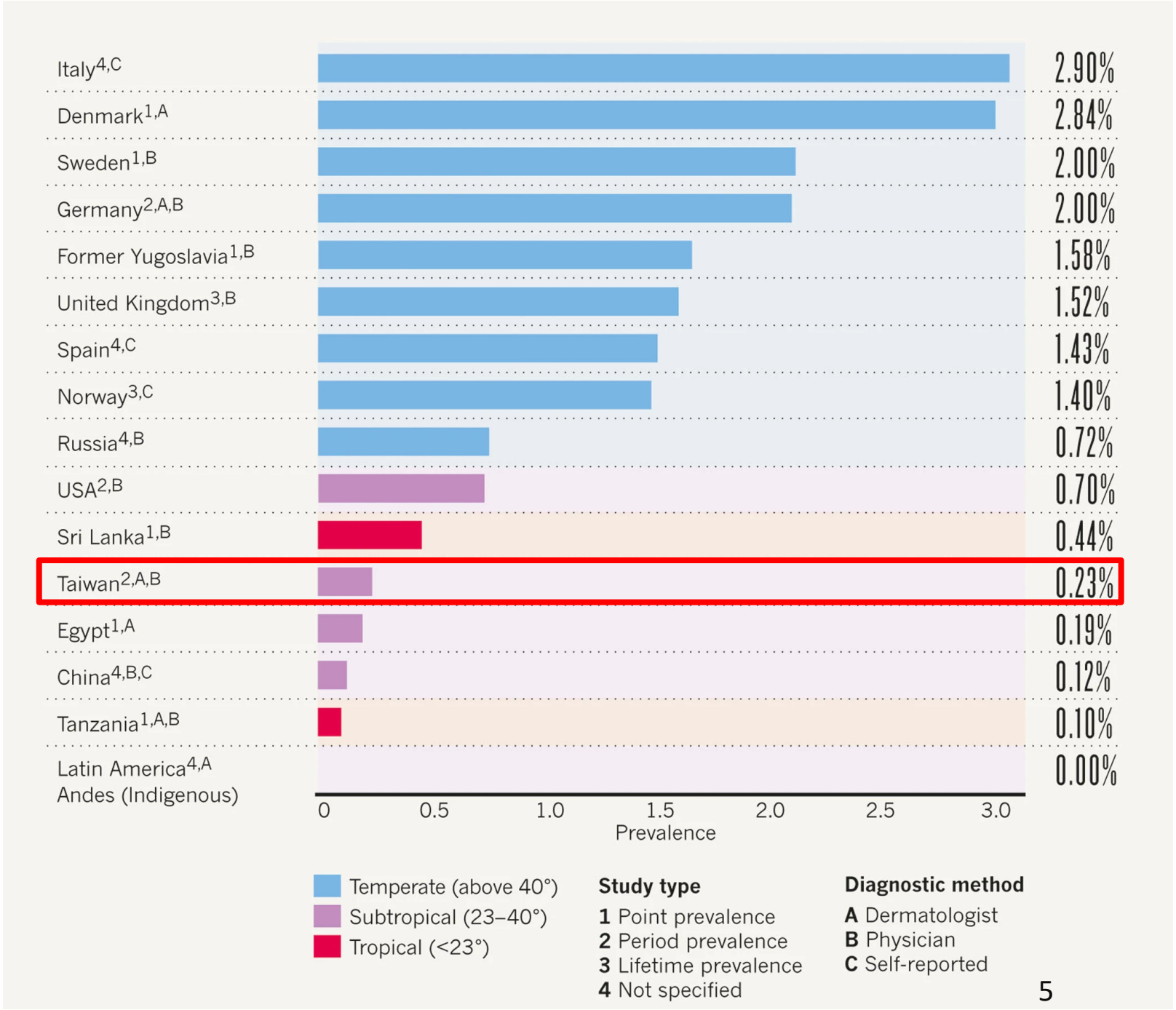
- Psoriasis is a chronic cutaneous inflammatory disease manifesting as erythematous, raised, well-demarcated plaques with adherent scales

Symptoms of Psoriasis



Krueger G, Koo J, Lebwohl M, Menter A, Stern RS, Rolstad T. The Impact of Psoriasis on Quality of Life: Results of a 1998 National Psoriasis Foundation Patient-Membership Survey. *Arch Dermatol.* 2001;137(3):280–284. doi:10-1001/pubs.Arch Dermatol.-ISSN-0003-987x-137-3-dst0024

Epidemiology of Psoriasis



Crow, J. Psoriasis uncovered. *Nature* **492,** S50–S51 (2012). https://doi.org/10.1038/492S50a

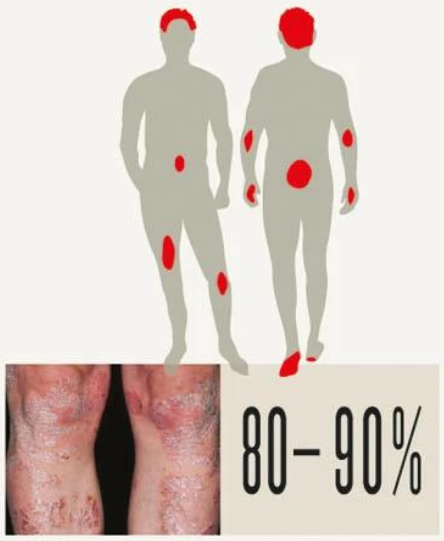
Risk Factors of Psoriasis

- Genetic factors appear to play a strong role
- Environmental factors
  - Medications: beta blockers, lithium
  - Obesity
  - Infection?
  - Stress?

Chronic Plaque Psoriasis

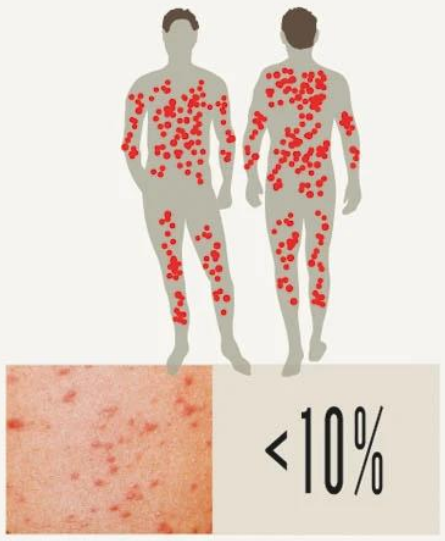
- The most common form of psoriasis
- Characterized by raised patches called lesions or plaques which are covered by silvery white scale
  - Scalp, extensor elbows, knees, and gluteal cleft

Classification of Psoriasis



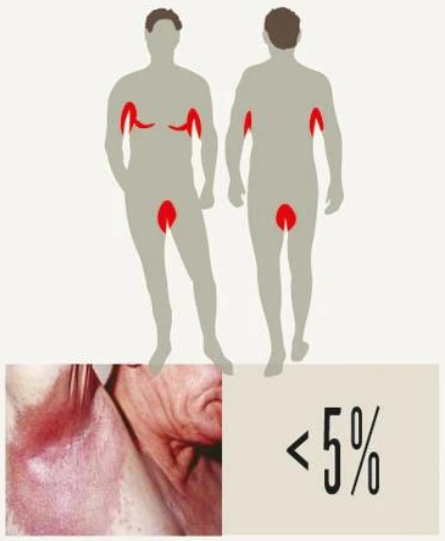
Chronic plaque psoriasis

Red, scaly plaques in discrete patches. The extent of body surface area covered varies widely from patient to patient.



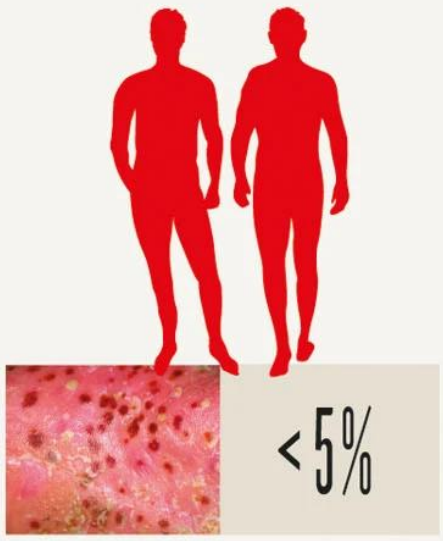
Guttate psoriasis

Multiple small, red spots, usually on the trunk and limbs.



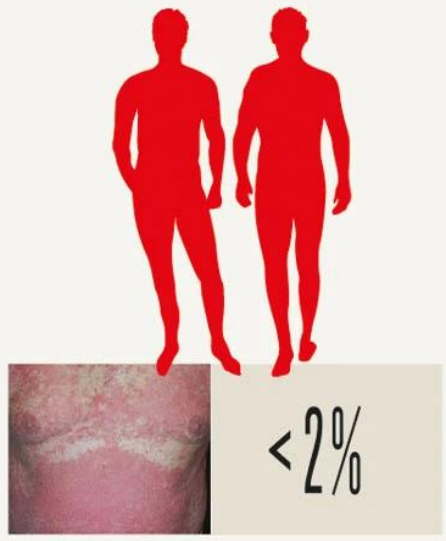
Inverse/flexural psoriasis

Very red scale-free lesions that form in skin folds.



Pustular psoriasis

White blisters surrounded by red skin, which may be localized to a particular area, but which can also cover the whole body.

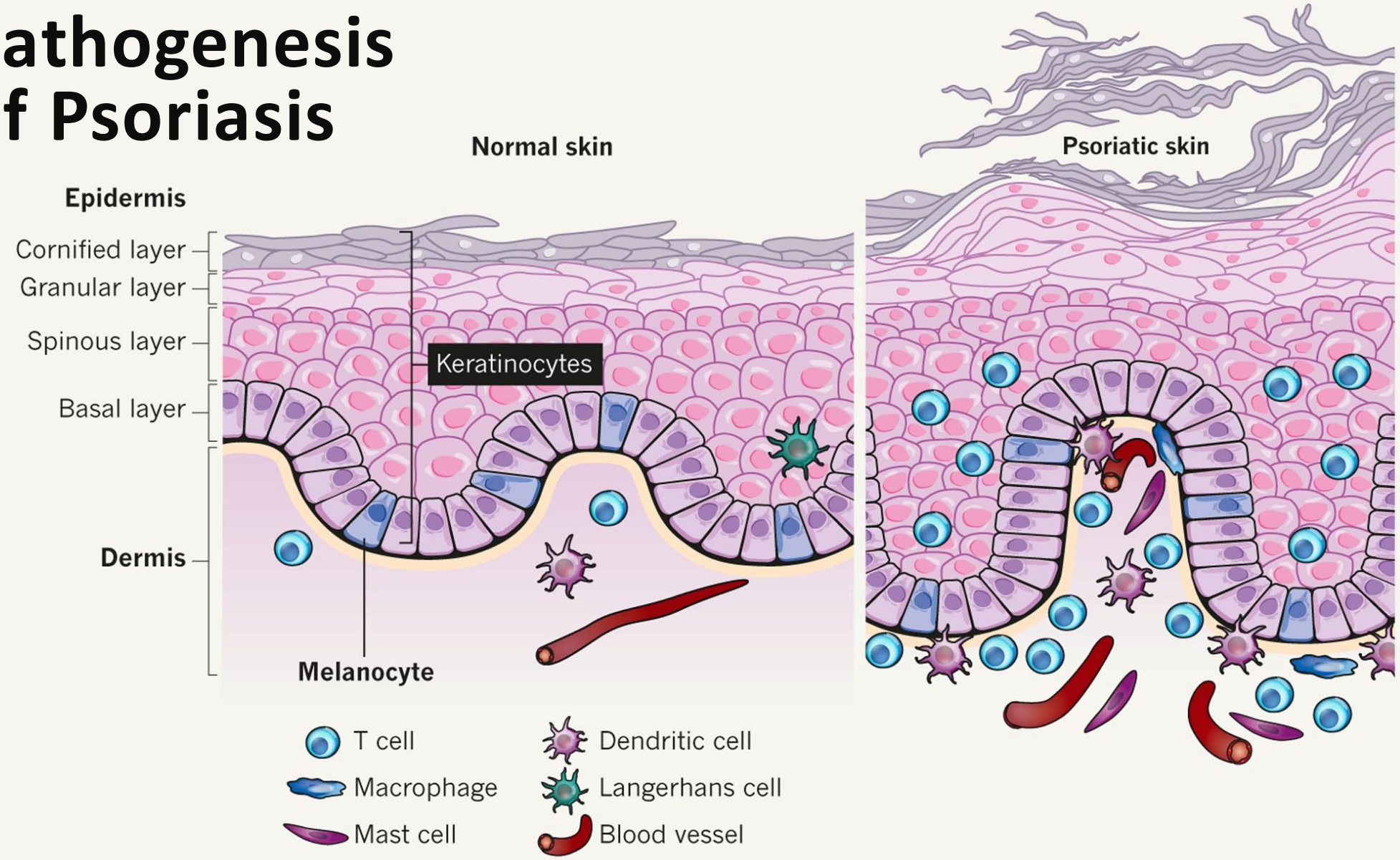


Erythrodermic psoriasis

Severe red inflammation and skin shedding covering most of the body. A rare but dangerous form of the disease that can cause patients to lose excessive amounts of heat through the skin.

Crow, J. Psoriasis uncovered. *Nature* **492,** S50–S51 (2012). https://doi.org/10.1038/492S50a

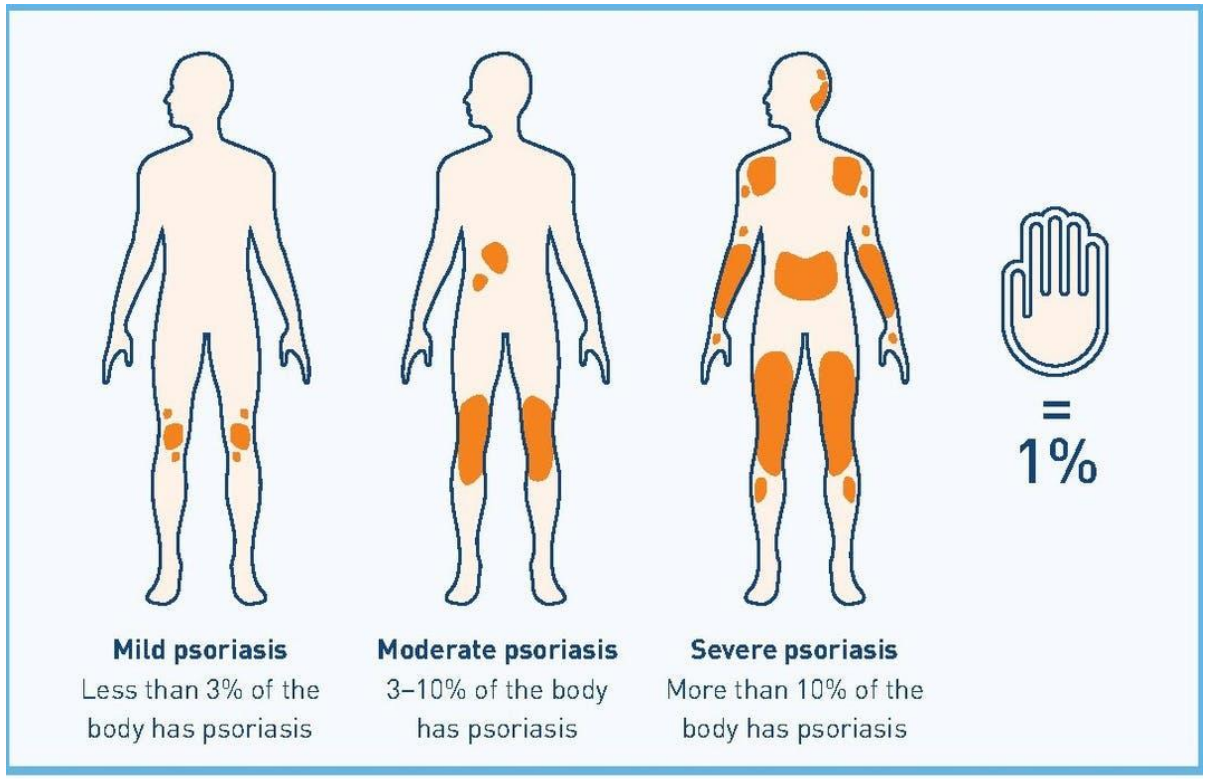
Pathogenesis of Psoriasis



Crow, J. Psoriasis uncovered. *Nature* **492,** S50–S51 (2012). https://doi.org/10.1038/492S50a

Severity Evaluation of Psoriasis

- **Body surface area (BSA)**
  - Mild-to-moderate: <5%
  - Moderate-to-severe: ≥5%; hands, feet, face, or genitals
  - 80% mild to moderate disease
  - 20% moderate to severe disease

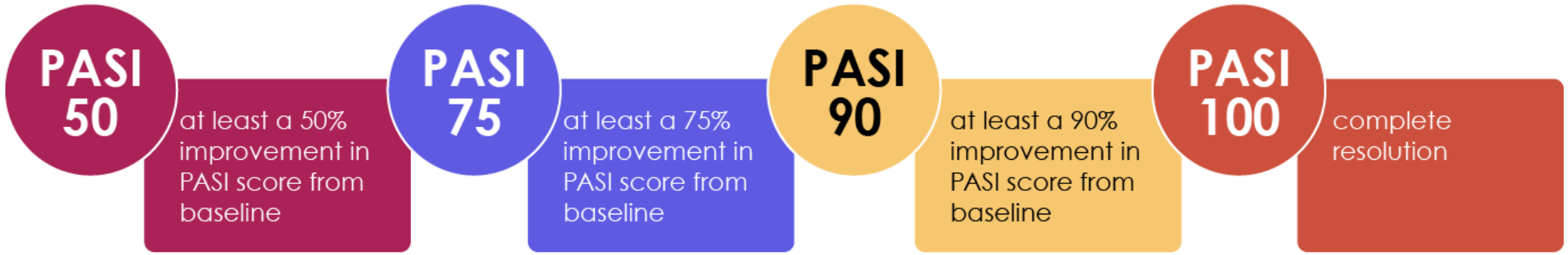


Severity Evaluation of Psoriasis

- **Psoriasis Area and Severity Index (PASI)**
  - Used in clinical trials to assess efficacy of treatment
  - Measure of overall psoriasis severity and coverage
    - ✓ body surface area (BSA)
    - ✓ erythema
    - ✓ induration
    - ✓ Scaling
  - Score ranges from 0 (no disease) to 72 (maximal disease)

Severity Evaluation of Psoriasis

- **Psoriasis Area and Severity Index (PASI)**



https://www.medthority.com/psoriasis/diagnosis/

Severity Evaluation of Psoriasis

- **Dermatology Life Quality Index (DLQI)**
  - Questionnaire used to assess the impact of a skin condition on quality of life
  - Moderate-to-severe: >10, regardless of the PASI score

DLQI score	Impact on QoL[6]
0–1	No effect at all
2–5	Small effect
6–10	Moderate effect
11–20	Very large effect
21–30	Extremely large effect

https://www.medthority.com/psoriasis/diagnosis/

乾癬治療綜論

Overview of Psoriasis Treatment

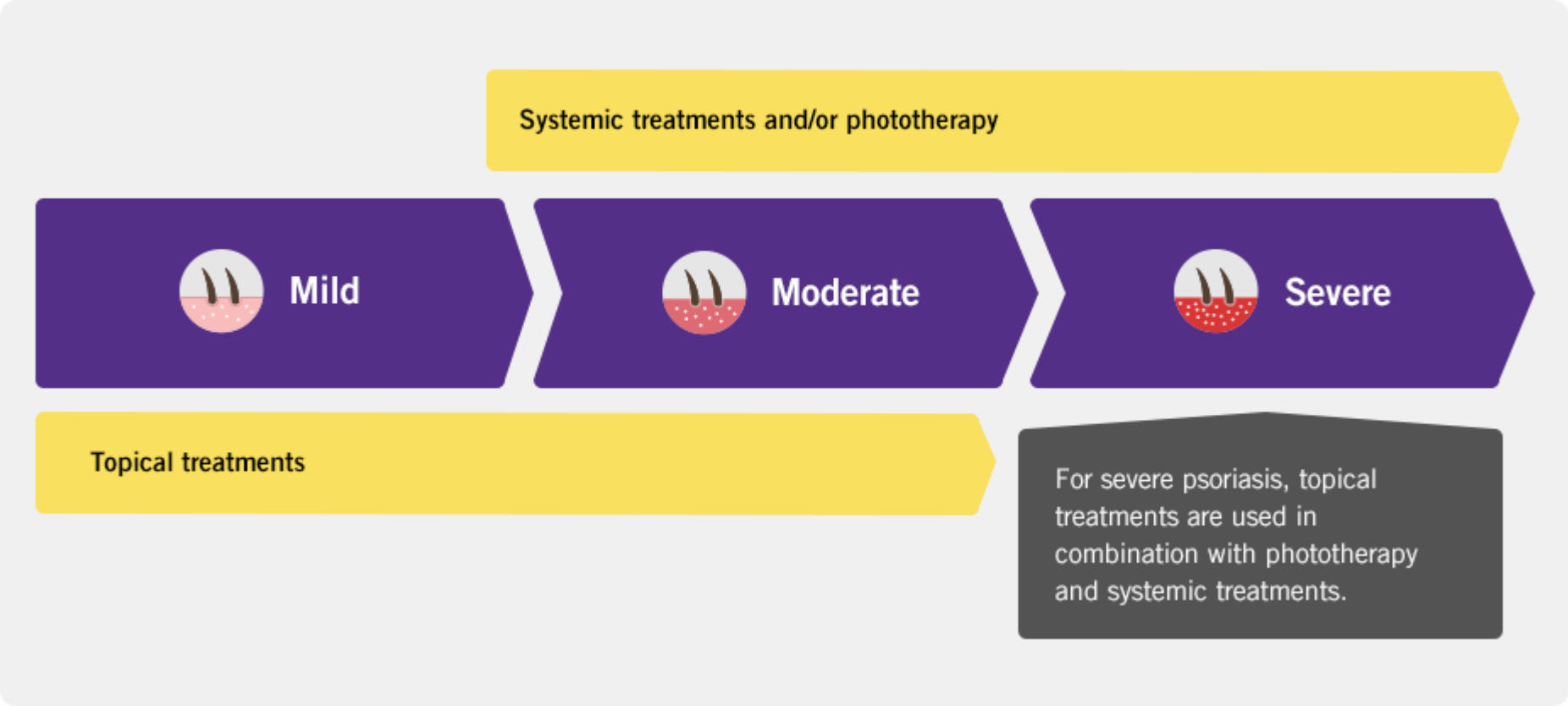
Goal of Treatment

- Primary goal is control of disease rather than cure
- Minimize extent and severity of psoriasis
- Prevent substantial disruption of patient’s quality of life
- Identify and treat psoriatic arthritis and other comorbid diseases

Treatment Overview

- Stewardship approach
- Consider patient preferences, severity of disease, and ability to adhere to treatment

Pharmacologic Therapy



https://www.getpsorted.com.au/treating-psoriasis/treating-psoriasis-pasi

Treatment Options for Psoriasis

- **Topical therapy**
  - Topical corticosteroids
  - Vitamin D analogs
- **Phototherapy**
- **Systemic therapy**
  - Methotrexate, Cyclosporine, Acitretin
  - Biologic agents
  - Small molecule inhibitor: Apremilast

Topical Therapy

- **Topical corticosteroids**
  - Mainstay of topical psoriasis treatment
  - Consider application site
    - ✓ Scalp → Solution, foam
    - ✓ Face and intertriginous → low potency
  - Minimize adverse effects
    - ✓ Transition to less potent agents after clinical improvement, intermittent usage

Topical Therapy

- **Topical vitamin D analogs**
  - Hypoproliferative effect on keratinocytes
  - Enhance the efficacy of topical corticosteroids
  - Calcipotriene: <100g/week
  - Calcitriol: <200g/week
  - Minimal side effect; hypercalcemia

Phototherapy

- Indicated for generalized psoriasis (BSA >10%) and in pregnancy
  - Narrowband UVB (311-320 nm) > broadband UVB
  - Systemic Psoralen Plus Ultraviolet A (PUVA)
- Typically takes 15-20 treatments to achieve clearance
- Photoaging; increased risk of skin cancer after prolonged treatment

Agents for the Treatment of Severe Psoriasis

Treatment Modality	Advantages	Disadvantages
Methotrexate	Effective for both skin lesions and arthritis	Hepatotoxicity; bone marrow toxicity; folic acid protects against stomatitis; contraindicated during pregnancy and lactation
Cyclosporine	Toxicities and short-lived remissions; used in patients with extensive disease who are unresponsive to other agents	Renal impairment; suppressive therapy; increased risk of skin cancer, lymphomas, and solid tumors; hypertension, hyperuricemia, hyperkalemia, acute infections
Acitretin	Not as effective as other systemic agents; efficacy enhanced if given with PUVA or UVB	Teratogenic (contraception required); contraindicated with liver or renal dysfunction, hypertriglyceridemia

治療斑塊性乾癬之生物製劑

Biologic Agents for Treatment of Plaque Psoriasis

Table 1. Summary of various national guidelines for consideration of biologic agents for moderate-to-severe psoriasis

American Academy of Dermatology[2]	BSA ≥5%
British Association of Dermatologists[9]	BSA >10% or PASI >10 + DLQI >10 + Unable to use or failed standard systemic Rx
European Academy of Dermatology & Venereology[10]	DLQI >10 + Unable to use or failed standard
Malaysian Clinical Practice Guidelines[11]	Criteria A (Severe Disease): 1. PASI ≥20 OR 2. BSA ≥30% OR 3. DLQI ≥18 + Criteria B (Clinical Categories): 1. Contraindications to standard 2. Intolerance to standard system 3. Failed standard systemic treat
Singapore Clinical Practice Guidelines[12]	Moderate-to-severe psoriasis an failure of phototherapy or stand unstable life-threatening disease ("standard systemic therapy" is defined as cyclosporine 2-5 mg/kg/day for 12 weeks, methotrexate 15 mg-25 mg weekly for 12 weeks, acitretin 25-50 mg daily for 12-24 weeks)

BSA >10%
PSAI >10
DLGI >10%

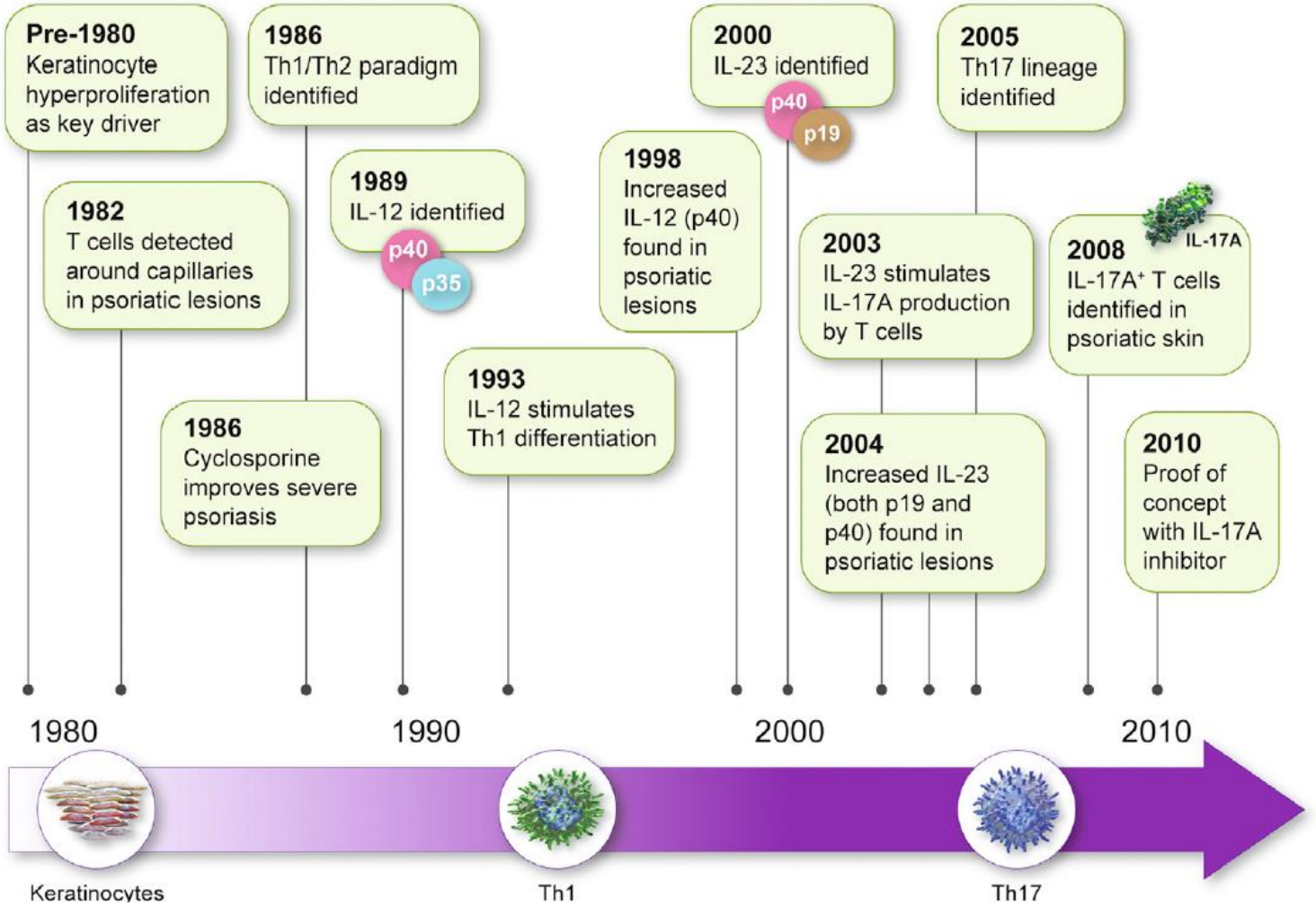
Face, scalp, palms, soles, flexures and genitals

•. 2007 Sep;6(8):515-9. doi: 10.1016/j.autrev.2006.12.002. Epub 2007 Jan 9

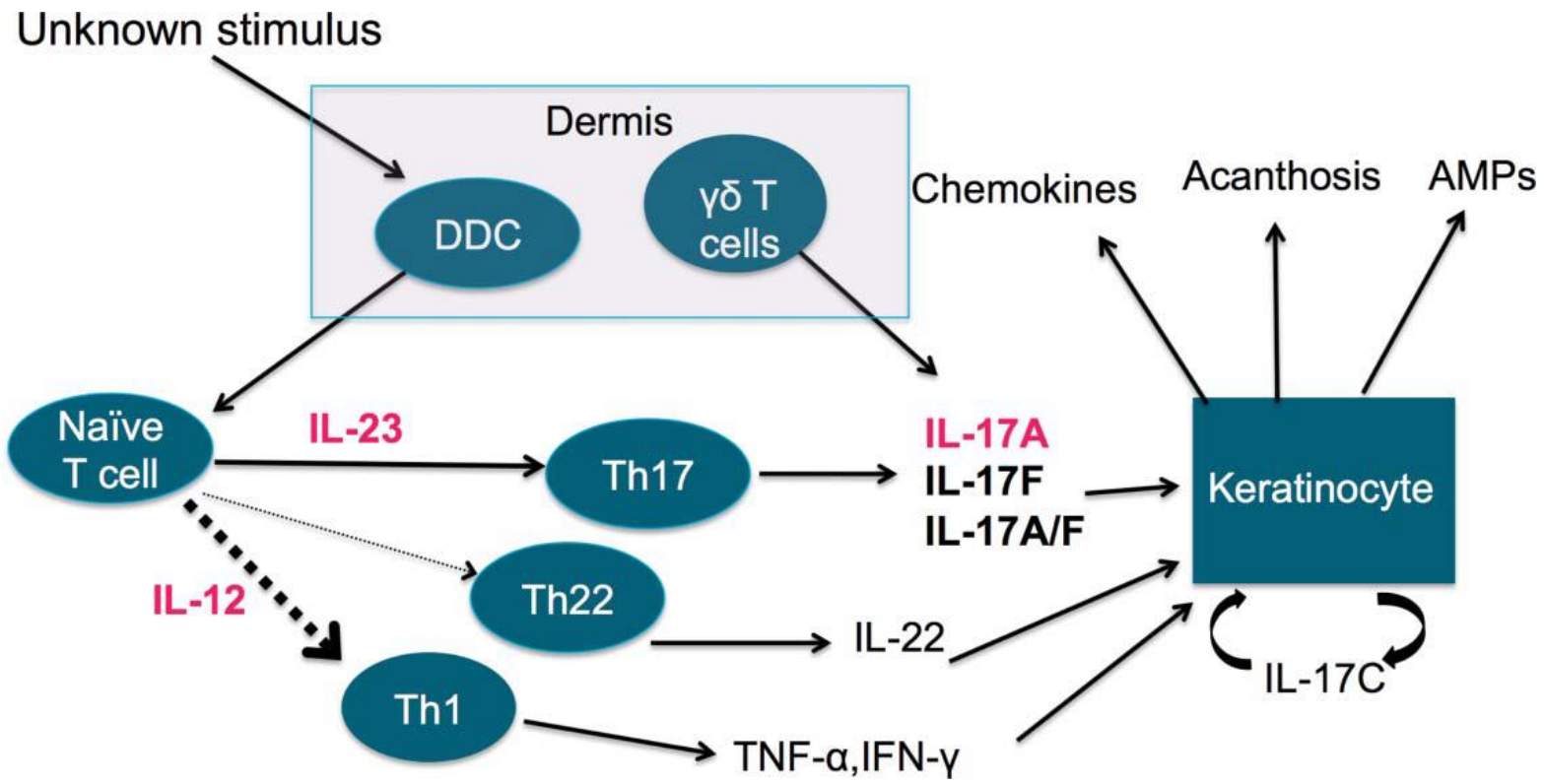
Biologic Agents in Plaque Psoriasis

Class/target pathway	Generic drug name	Year of approval for psoriasis by FDA
TNF-α inhibition	Etanercept (Enbrel® 恩博)	2004
	Infliximab (Remicade®類克)	2006
	Adalimumab (Humira® 復邁)	2008
IL-12/23 inhibition	Ustekinumab (Stelara® 喜達諾)	2008
Direct inhibition of IL-17	Secukinumab (Cosentyx® 可善挺)	2015
	Ixekizumab (Taltz® 達癬治)	2017
	Brodalumab (Lumicef® 立美西膚)	2017
IL-23 blocker	Guselkumab (Tremfya®特諾雅)	2017
	Risankizumab (Skyrizi®喜開悅)	2020

Timeline of Evolving Concepts in Psoriasis Pathophysiology

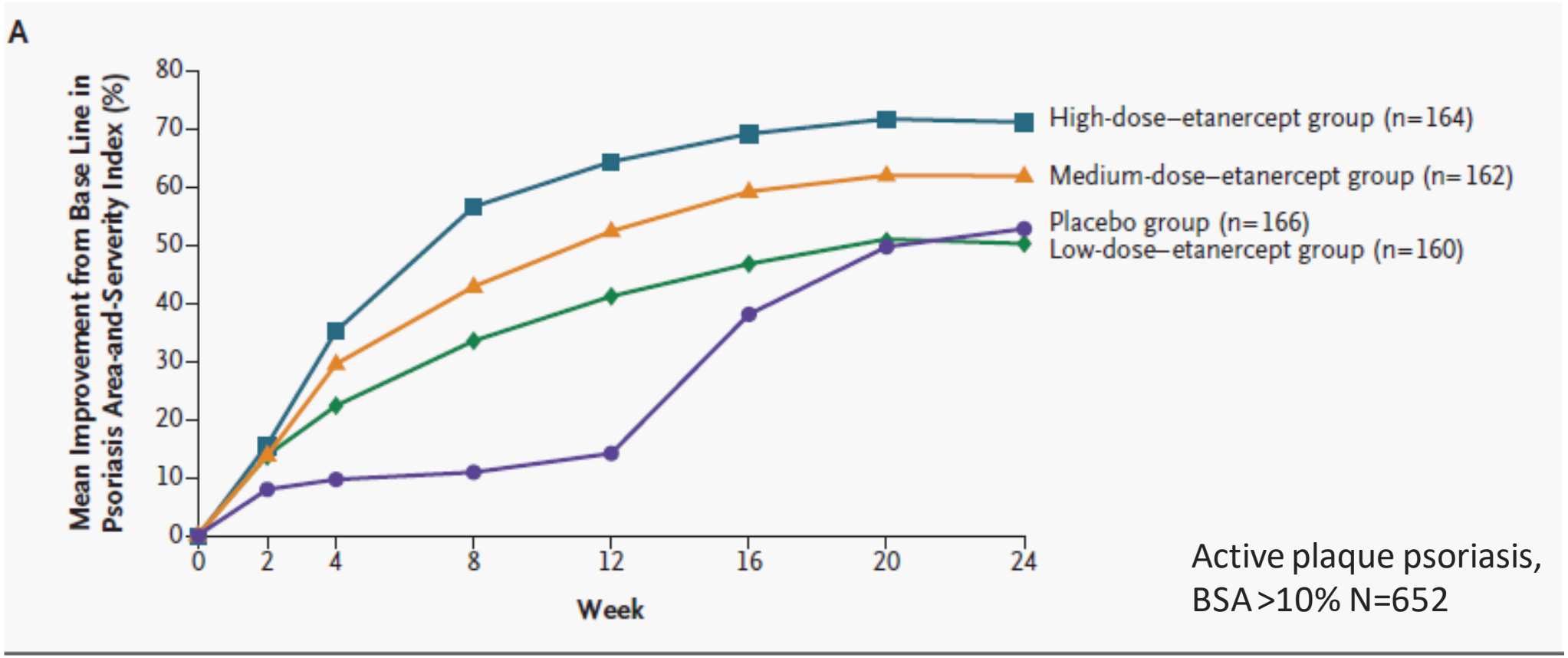


Pathogenesis of Psoriasis



Human vaccines & immunotherapeutics 2017, vol. 13, no. 10, 2247–2259

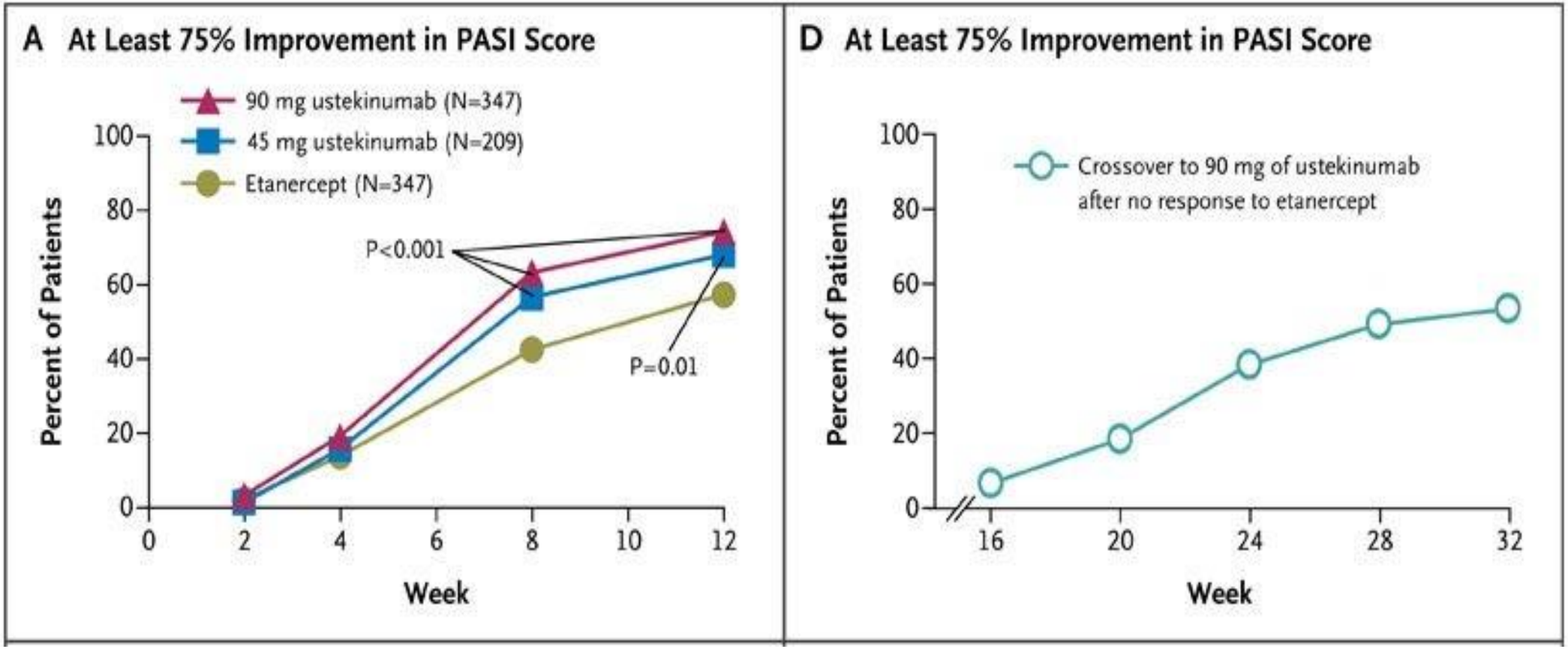
Etanercept Reduces Psoriasis Severity over a Period of 24 Weeks



Active plaque psoriasis, BSA >10% N=652

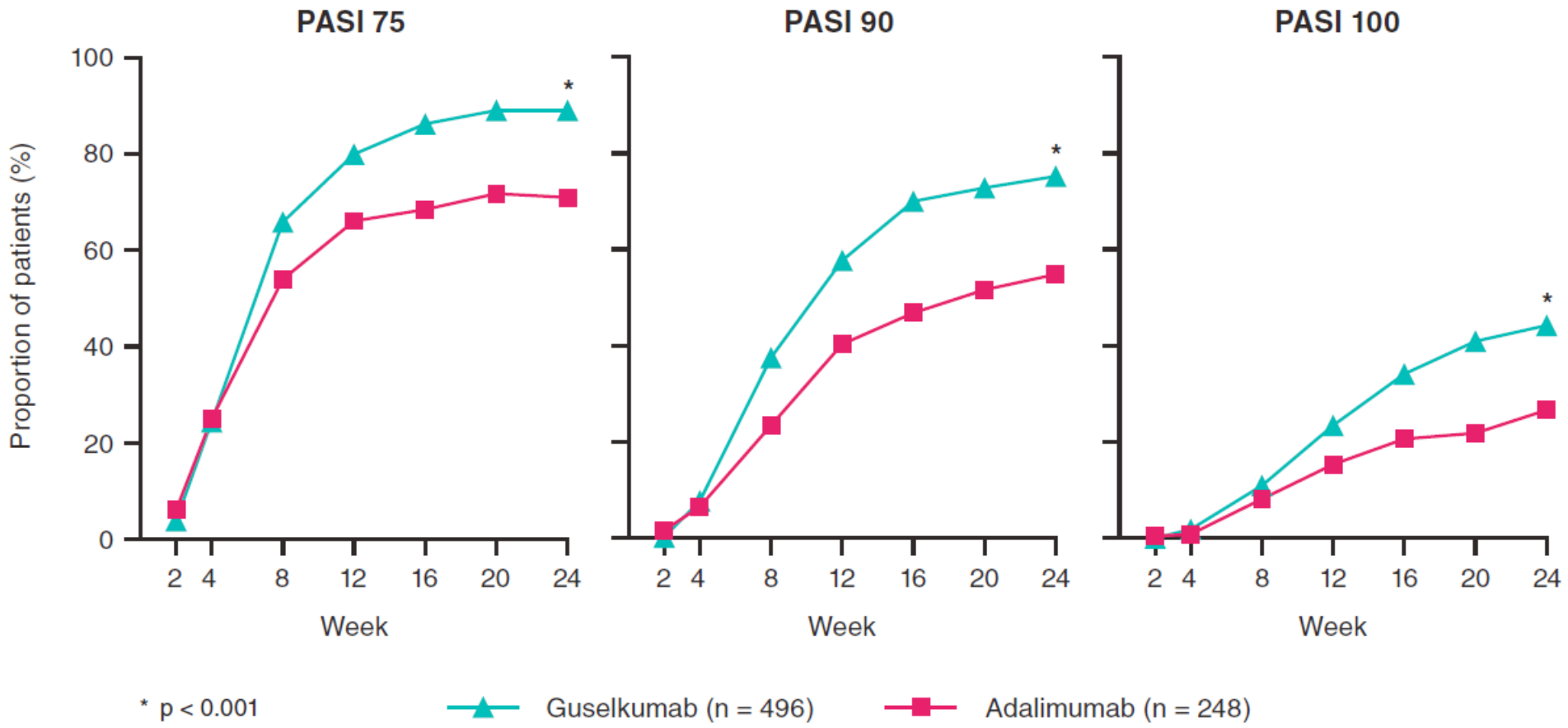
N Engl J Med 2003 Nov 20;349(21):2014

Efficacy of Ustekinumab is Superior to Etanercept



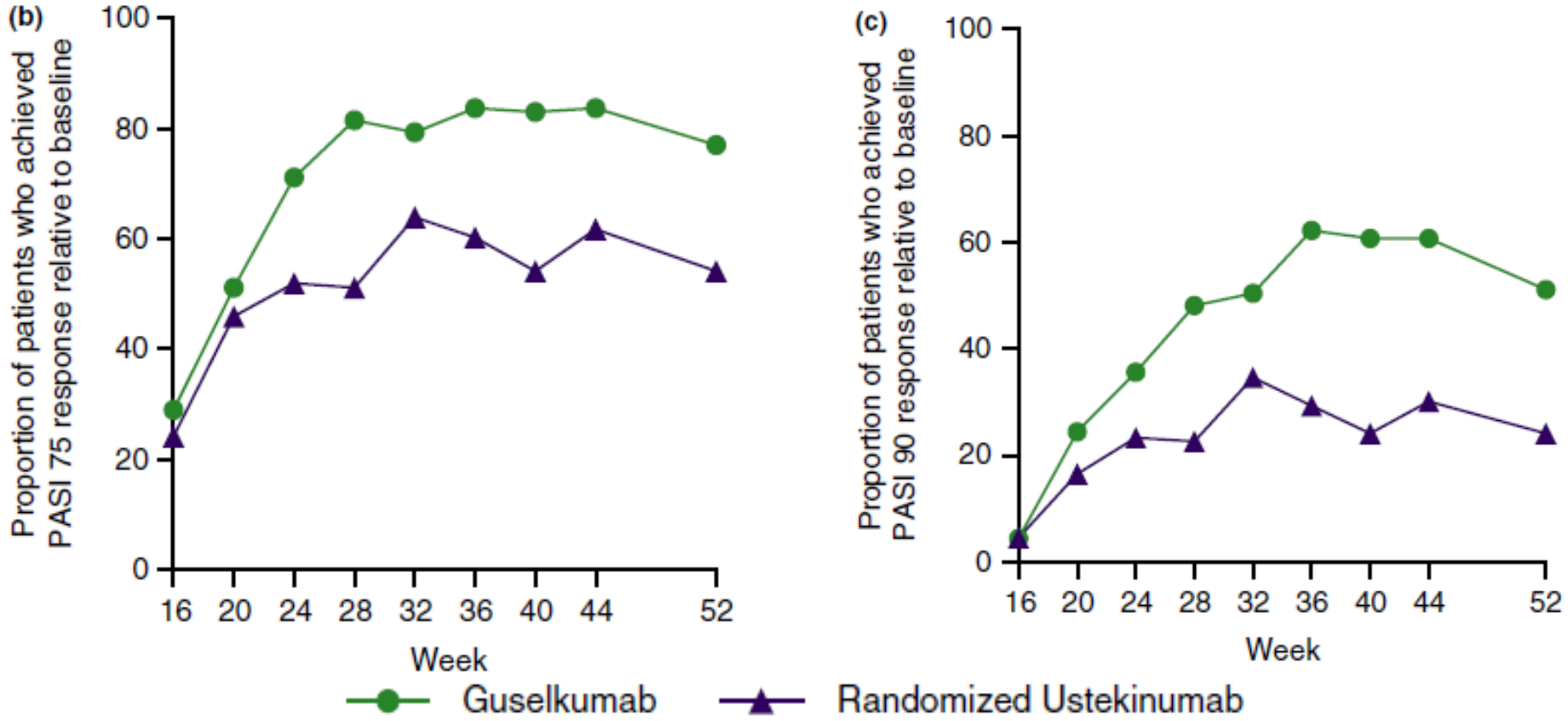
Griffiths CE et al. N Engl J Med 2010;362:118-128.

Guselkumab Reduces Psoriasis Severity Compared to Adalimumab



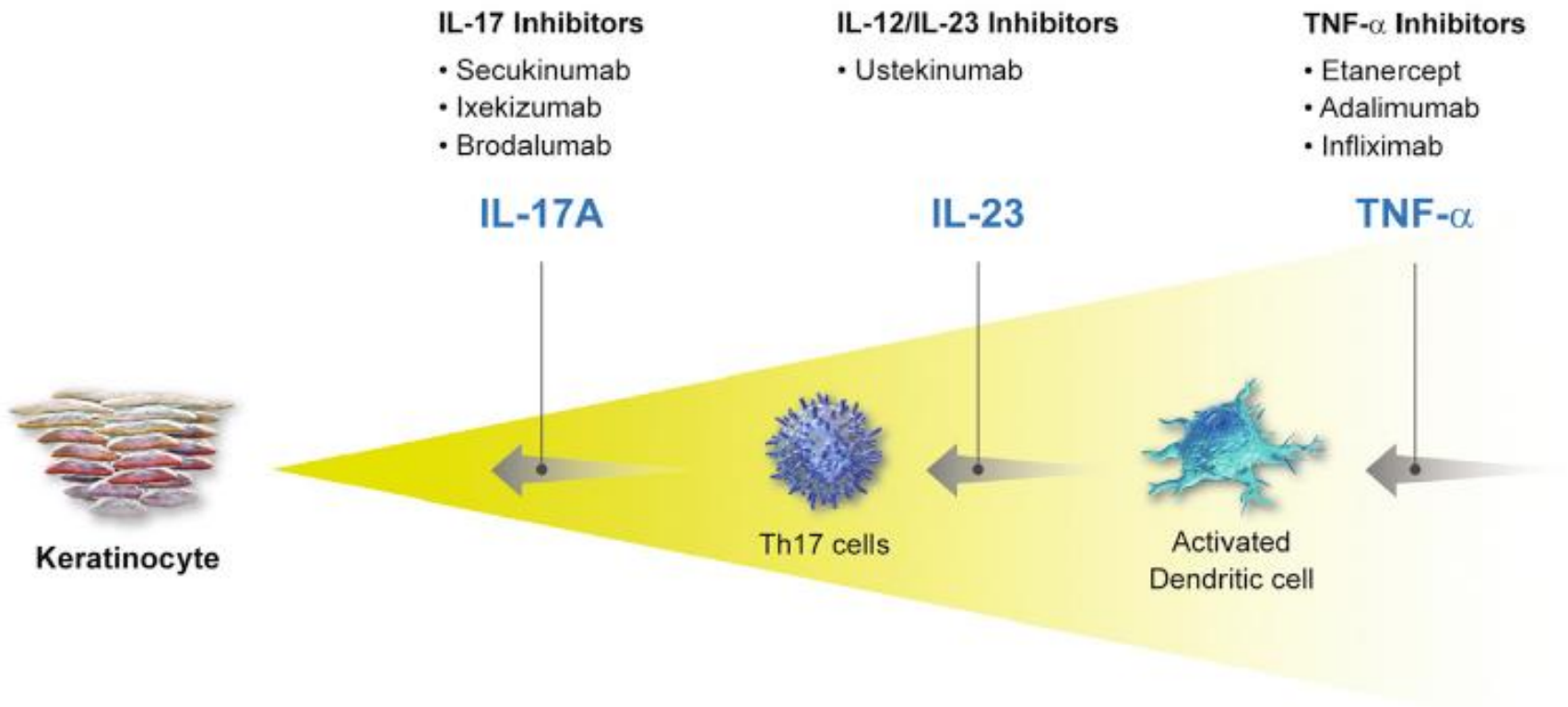
J Am Acad Dermatol. 2017 Mar;76(3):418-431

Guselkumab Reduces Psoriasis Severity in Patients with Inadequate Response to Ustekinumab



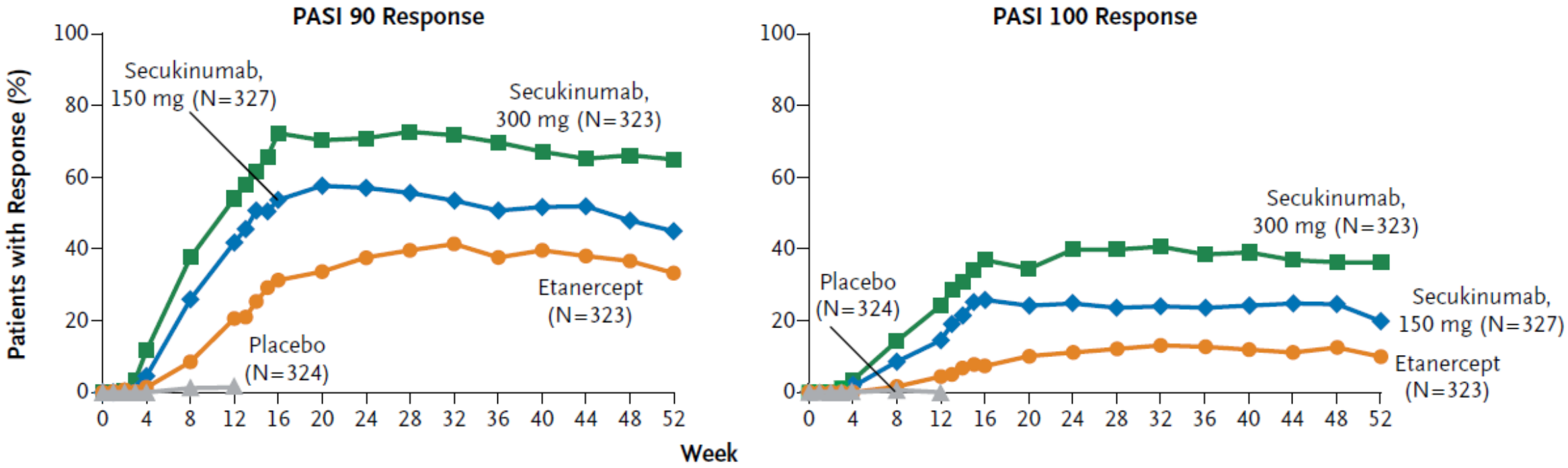
Br J Dermatol 2018 Jan;178(1):114

Key Cytokine Targets in Psoriasis



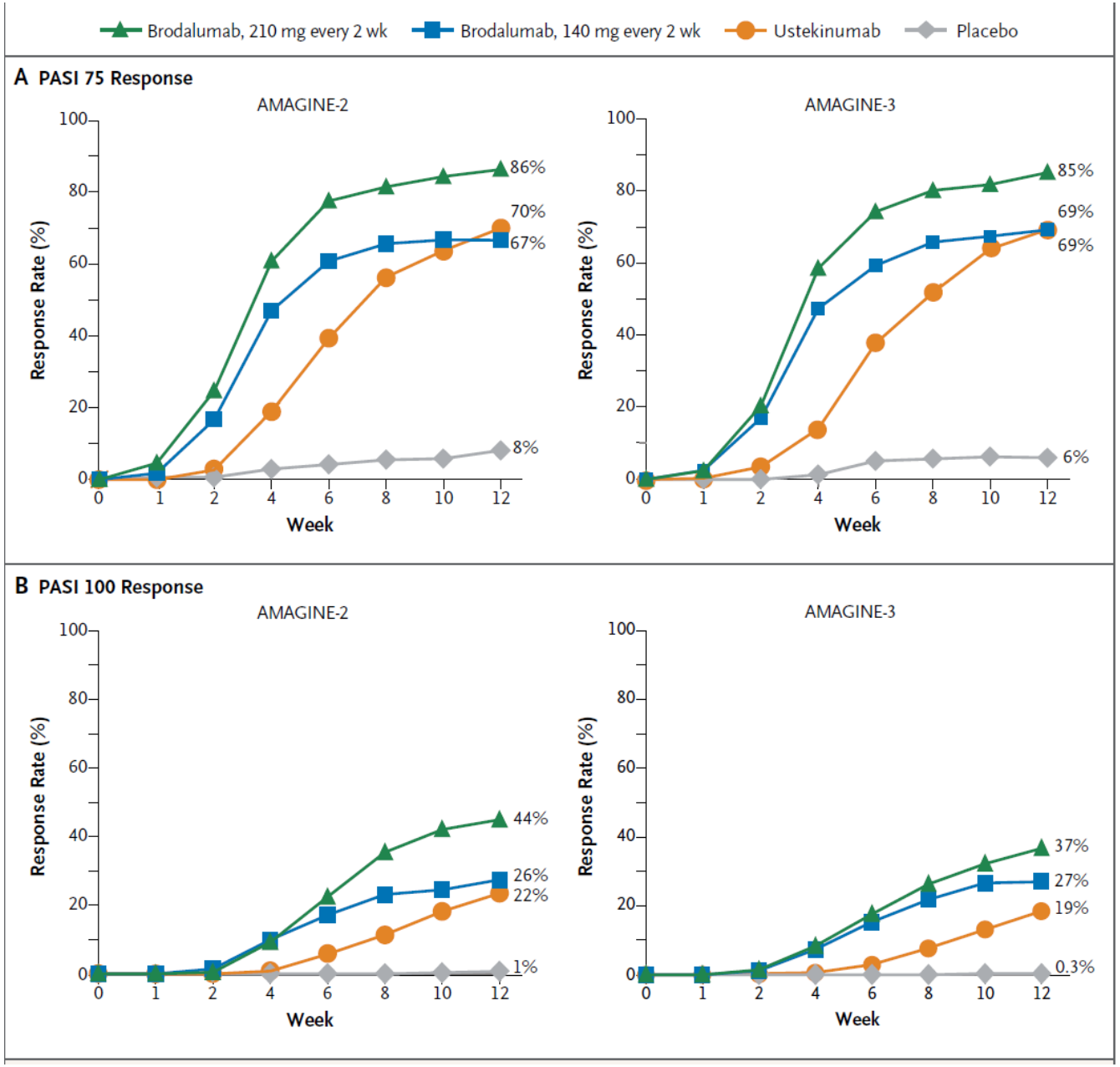
. 2014 Jul;71(1):141-50. doi: 10.1016/j.jaad.2013.12.036. Epub 2014 Mar 18.

Secukinumab Reduces Psoriasis Severity Compared to Etanercept in Poor Disease Control



N Engl J Med. 2014 Jul 24;371(4):326-38.

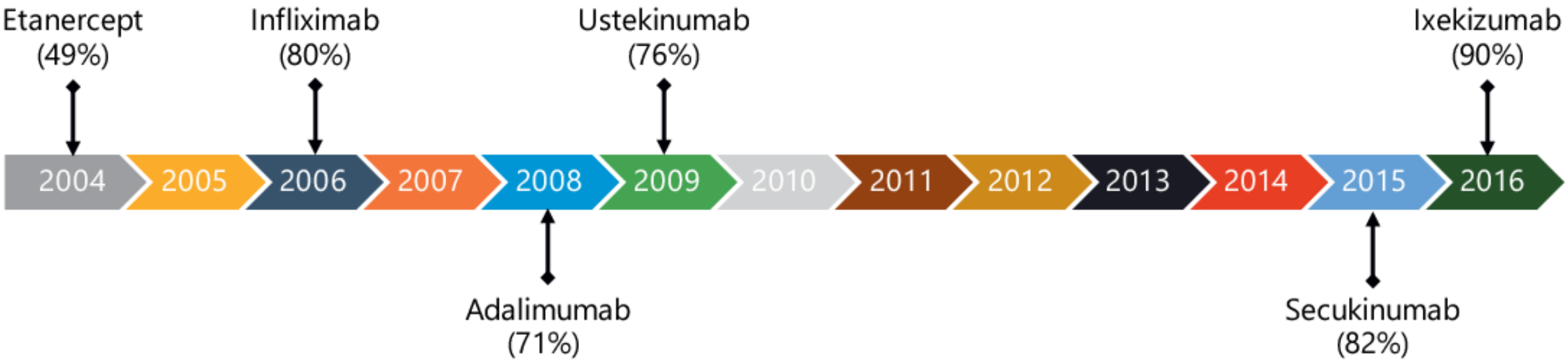
Brodalumab Improves Moderate-to-severe Plaque Psoriasis



N Engl J Med. 2015 Oct;373(14):1318-28

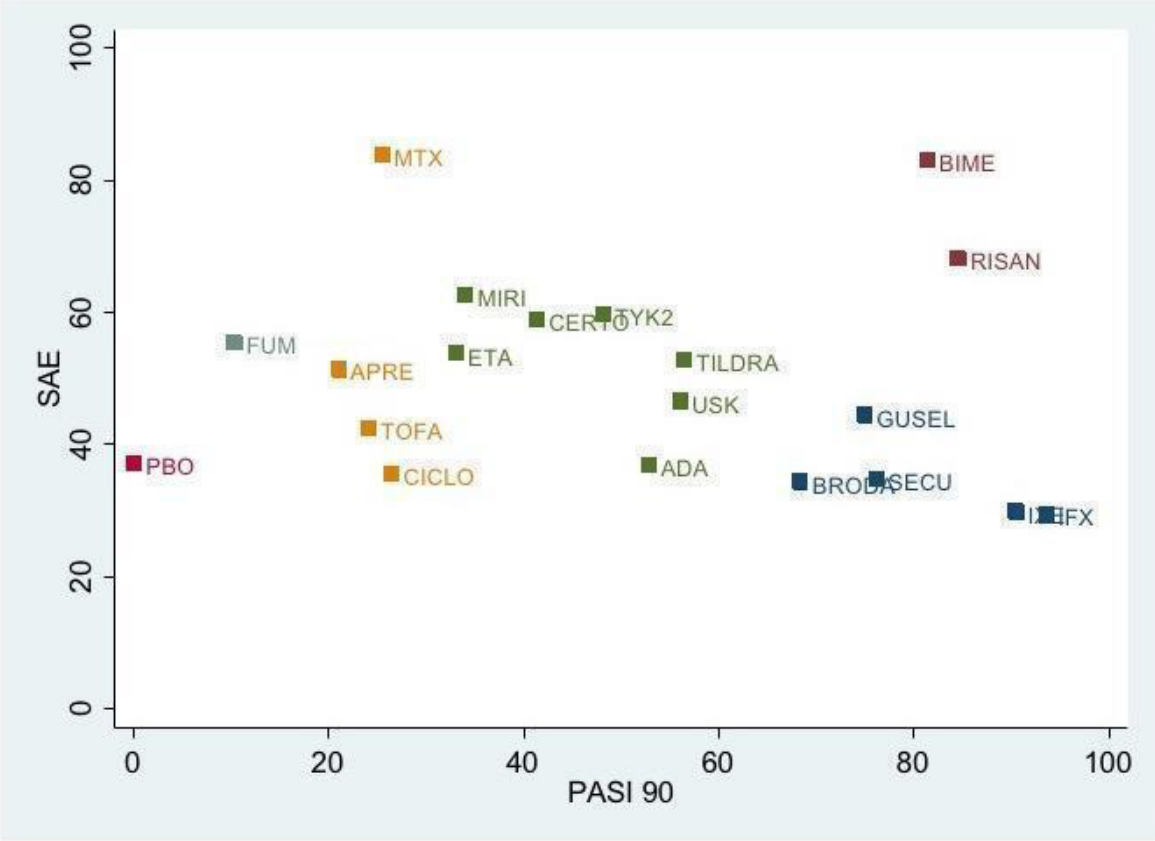
Timeline of Approved Biologics

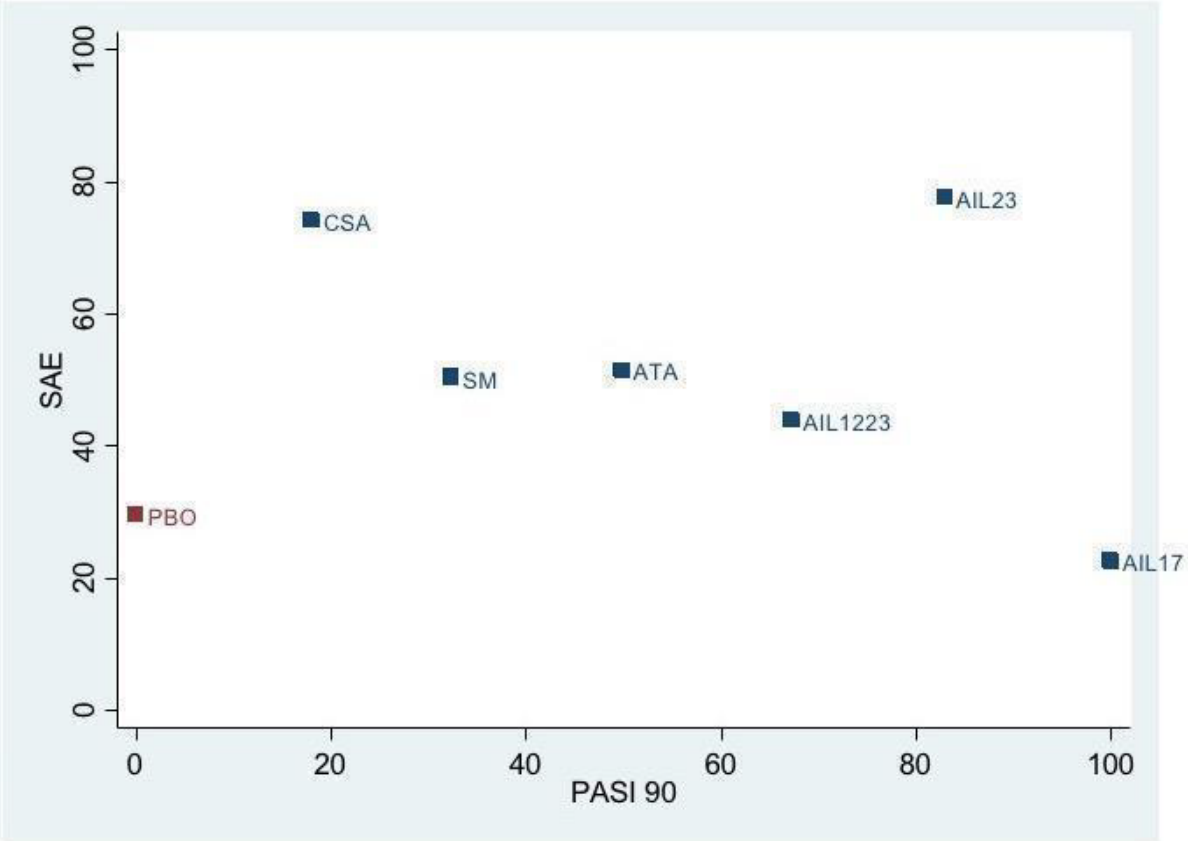
Approved biologics for adult plaque psoriasis (PASI 75 response rate) at approximately 3 month endpoint



Lockwood, S., Prens, L.M., & Kimball, A.B. (2018). Adverse Reactions to Biologics in Psoriasis. *Current problems in dermatology, 53*, 1-14.

Comparisons of Systemic Pharmacological Treatments by Network Meta-analysis





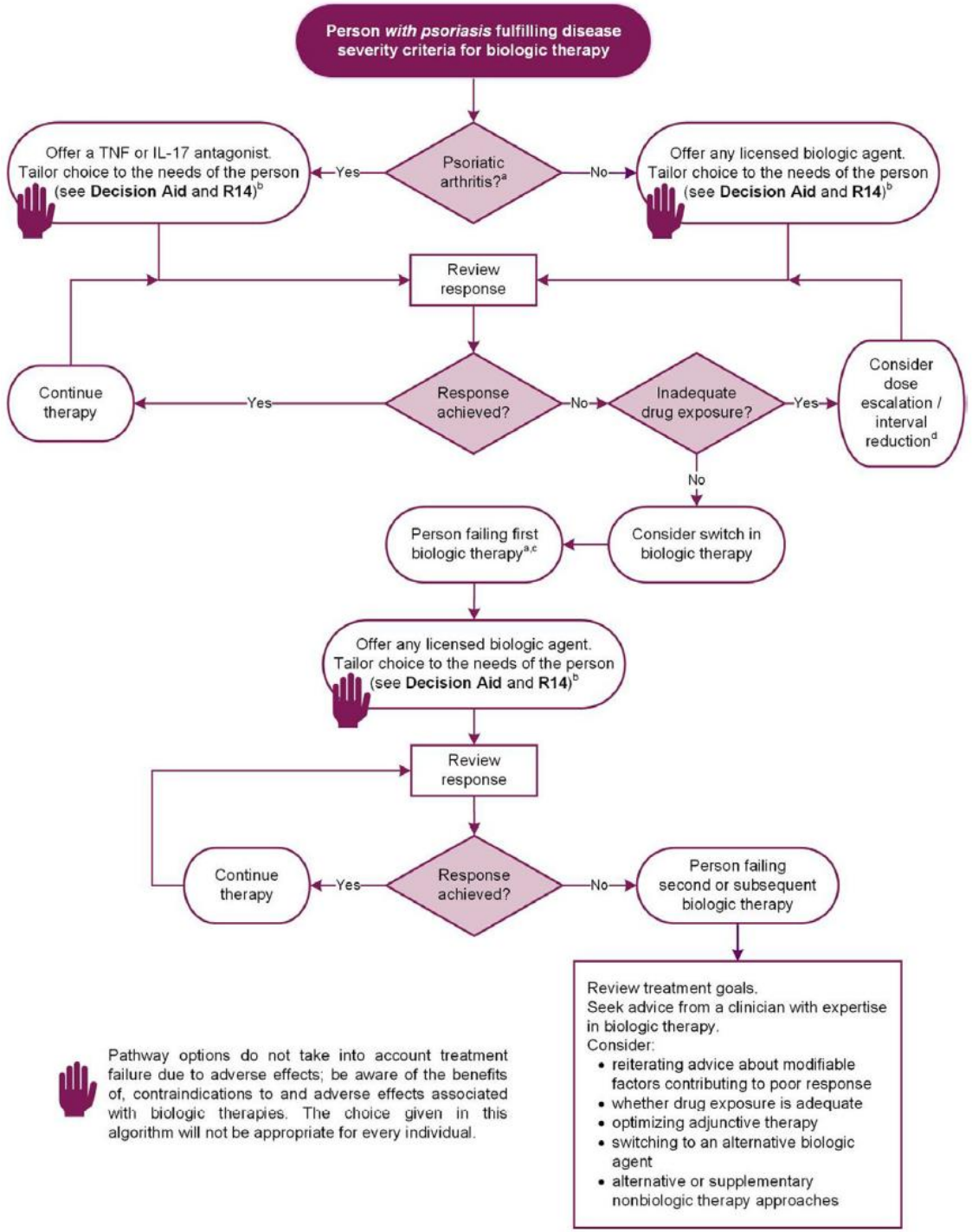
Nat Med. 2015 Jul;21(7):719-29.

Adverse Events of Biologic Agents

- Serious infection
- Hepatitis B and C virus reactivation
- Immunogenicity

Adverse Events of Biologic Agents

- TNF-a inhibitors
  - Reactivation of latent TB infection
  - Malignancies
- IL-12/23 inhibitors
  - Major adverse cardiovascular event
- IL-17 inhibitors
  - Candidiasis
  - Neutropenia
  - Inflammatory bowel disease
  - Depression and risk of suicide (Brodalumab)



Br J Dermatol. 2020 Oct;183(4):628-637

Consideration of Selecting Biologic Agents

Situations	Consider
Psoriatic arthritis	TNF antagonist; IL-17 antagonist (except for Brodalumab)
Severe disease and rapid onset required	Infliximab
Children and young people	Adalimumab (age ≥ 4 years), etanercept (≥ 6 years) or ustekinumab (≥ 12 years)