Psoriatic disease: Defining a new era for patients and physicians

Fall Clinical Dermatology Conference 2022 Las Vegas

UCB Educational Symposium

October 22, 2022

Inspired by **patients.**
Driven by **science.**

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Welcome and introduction

Bruce Strober

Inspired by **patients.**
Driven by **science.**

Affiliation and disclosures

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Disclosures:

- Consultant (honoraria): AbbVie, Alumis, Almirall, Amgen, Arcutis, Arena, Aristea, Asana, Boehringer Ingelheim, Immunic Therapeutics, Bristol-Myers-Squibb, Connect Biopharma, Dermavant, EPI Health, Evelo Biosciences, Janssen, Leo, Eli Lilly, Maruho, Meiji Seika Pharma, Mindera Health, Novartis, Pfizer, UCB Pharma, Sun Pharma, Regeneron, Sanofi-Genzyme, Union Therapeutics, Ventyxbio, vTv Therapeutics
- Stock Options: Connect Biopharma, Mindera Health
- Speaker: AbbVie, Eli Lilly, Incyte, Janssen, Regeneron, Sanofi-Genzyme
- Scientific Co-Director (consulting fee): CorEvitas (formerly Corrona) Psoriasis Registry
- Investigator: Dermavant, AbbVie, CorEvitas Psoriasis Registry, Dermira, Cara, Novartis
- Editor-in-Chief (honorarium): Journal of Psoriasis and Psoriatic Arthritis

Learning objectives

Understand the patient journey and unmet needs of psoriatic disease, appreciating the role of the dermatologist in recognizing and managing the condition

Explore the evolving therapeutic landscape

Highlight the current understanding of the pathobiology of psoriatic disease and how advances in this understanding can lead to more targeted therapies

Meeting agenda

Time (PT)	Presentation
1:05–1:06 p.m.	Welcome and introduction
1:06–1:16 p.m.	The psoriatic disease patient journey: present and future
1:16–1:26 p.m.	Psoriatic disease: understanding the pathobiology and journey to targeted therapies
1:26–1:33 p.m.	Q&A
1:33–1:35 p.m.	Meeting close

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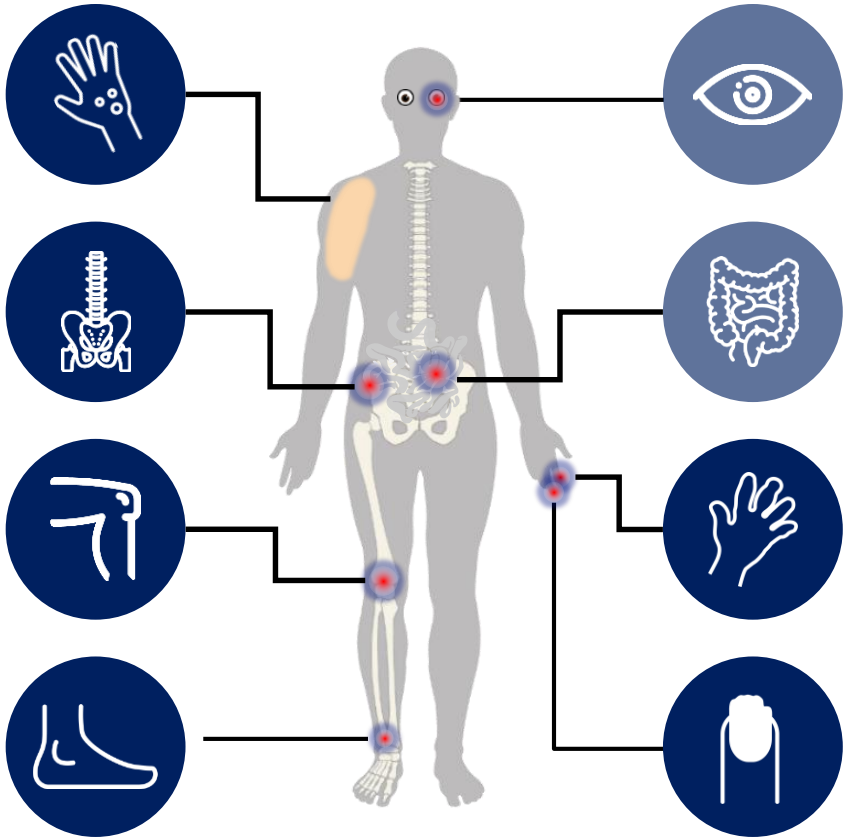
The psoriatic disease patient journey: present and future

Psoriatic disease is a chronic inflammatory systemic disease with multiple manifestations that may involve skin, nails and joints[1]



Skin disease[3]
- 94% prevalence

Axial Disease[5]
- 20–50% prevalence

Peripheral arthritis[8–12]
- ≤100% prevalence

Enthesitis[13,14]
- 35–57% prevalence

Uveitis[2]
- 7–18% prevalence

IBD[4]
- 4% prevalence

Dactylitis[6]
- 16–48% prevalence

Nail disease[7]
- ≤80% prevalence

IBD, inflammatory bowel disease.

1. Coates et al. Nat Rev Rheumatol. 2022;18:465–79; 2. Chen H and Chou C. Curr Rheumatol Rev. 2008;4:111–4; 3. Kane et al. Rheumatology. 2003;42:1460–8; 4. Williamson L et al. J Rheumatol. 2004;31:1469–70; 5. McGagh & Coates. Rheumatology. 2020;59:i29–36; 6. Helliwell et al. J Rheumatol. 2005;32:1745–50; 7. Sobolewski et al. Reumatologia. 2017;55:131–5; 8. Moll & Wright. Semin Arthritis Rheum. 1973;3:55–78; 9. Torre Alonso et al. Br J Rheumatol. 1991;30:245–50; 10. Helliwell & Taylor. Ann Rheum Dis. 2005;64(Suppl 2):ii3–8; 11. Gladman. Ann Rheum Dis. 2006;65(Suppl 3):iii22–4; 12. Acosta Felquer & FitzGerald. Clin Exp Rheumatol. 2015;33(Suppl 93):S26–30; 13. Kaeley et al. Semin Arthritis Rheum. 2018;48:35–43; 14. D'Agostino et al. Arthritis Rheum. 2003;48:523–33.

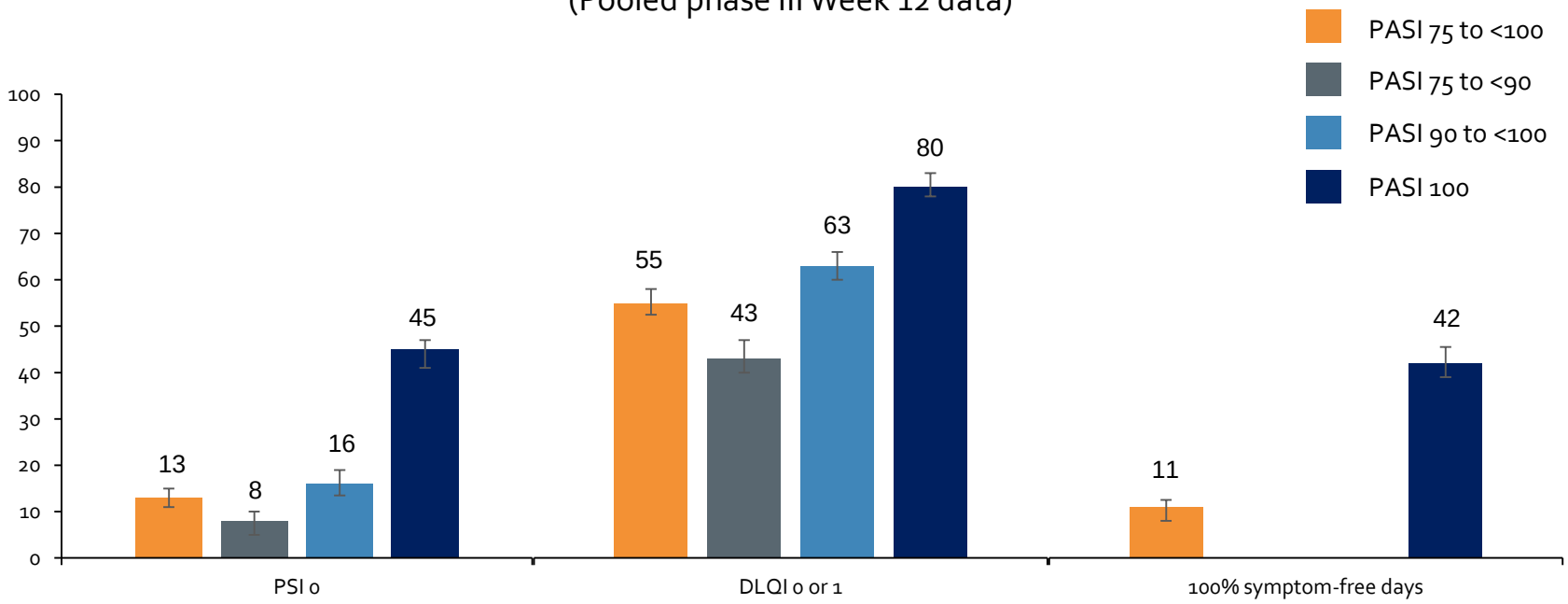
Complete skin clearance represents a clinically meaningful endpoint and outcome for patients with psoriasis[1]

Complete clearance means that patients are more likely to benefit from…

- No psoriasis symptoms
- No impairment on health-related quality of life

Achieving clear skin (PASI 100) correlates with better outcomes compared with PASI 75 or PASI 90 to <100

(Pooled phase III Week 12 data)



P<0.001 for all comparisons between PASI response without clearance groups (N=1,549) and the PASI 100 group (N=1,095).
DLQI, Dermatology Life Quality Index; PASI75/90/100, Psoriasis Area and Severity Index 75%/90%/100% improvement criteria; PSI, Psoriasis Symptom Inventory.

1. Strober et al. J Am Acad Dermatol. 2016;75:77–82.

However, most patients in the US do not achieve PASI 100

Aim: *To explore real-world, geographic variations in the use of biologic classes and outcomes within the CorEvitas registry*[1]

Methods

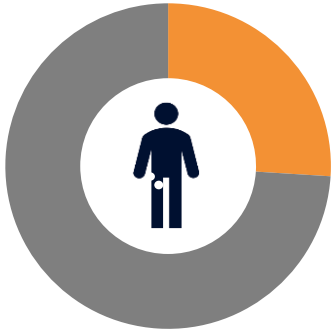
248 US sites were active in CorEvitas registry

737 biologic initiations with a 6-month follow-up visit

Patients could initiate >1 biologic in a year

Results

Among 717 patients across the US



26%

patients with PsO in the US achieve a PASI 100 response six months after initiation with a biologic

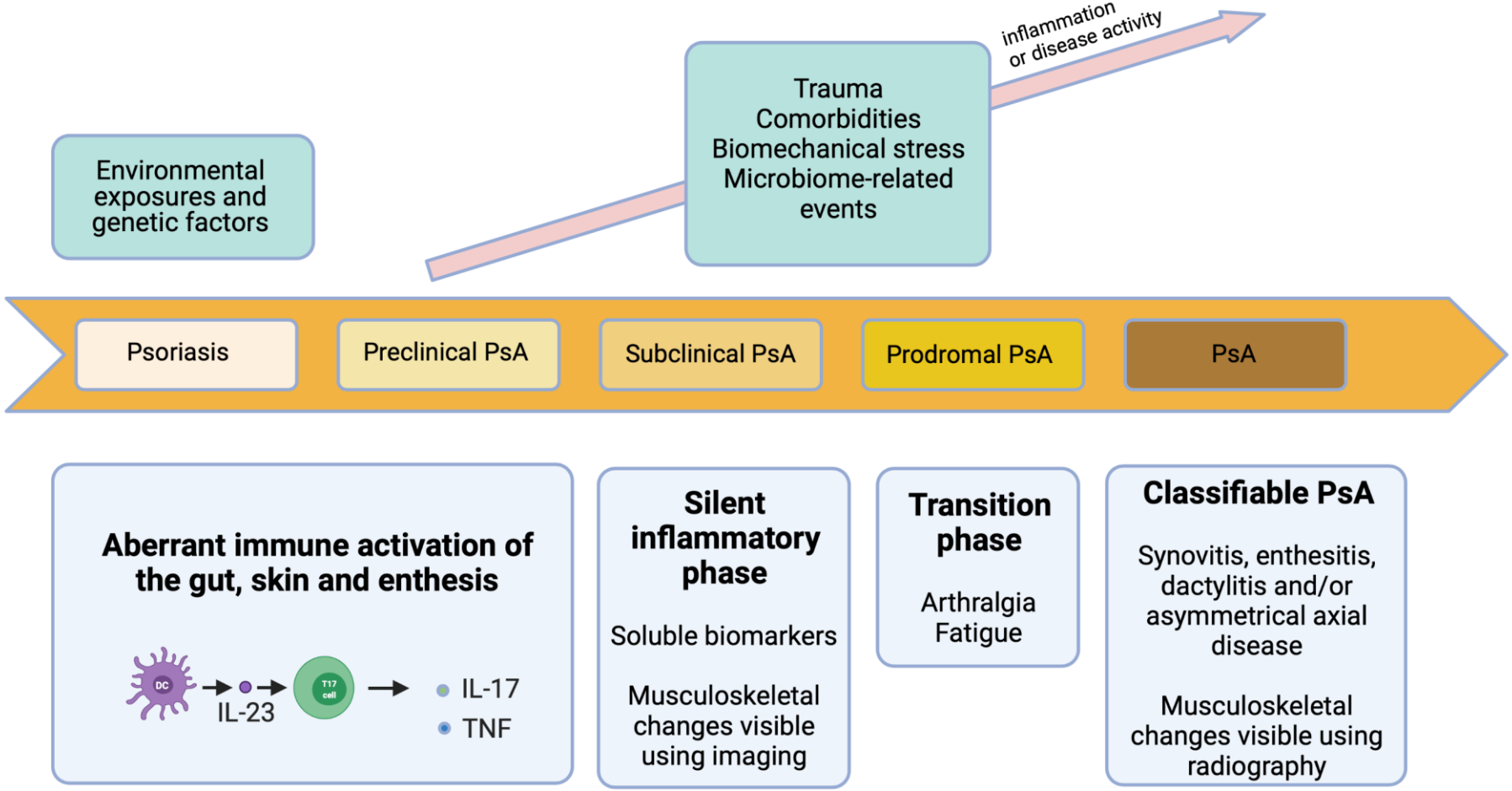
PASI 100, Psoriasis Area and Severity Index 100% improvement criteria; PsO, psoriasis.

1. Enos et al. JID Innov. 2021;1:100025.

Over 30% of patients with psoriasis will eventually develop PsA[1]

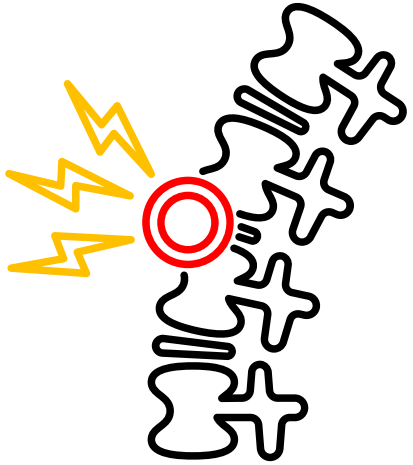
In patients with psoriasis, time to onset of PsA is **7–12 years**, and prevalence of PsA increases with psoriasis duration[2]

As skin symptoms often precede PsA, dermatologists are well placed to identify and treat patients with PsA[3]

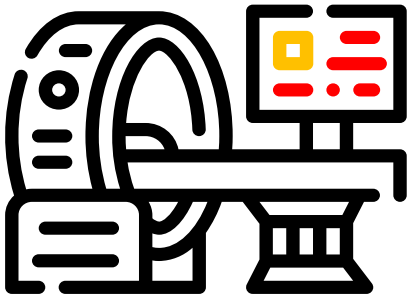


IL, interleukin; PsA, psoriatic arthritis; TNF, tumor necrosis factor.
Figure adapted from Ref. 2.
1. Mease et al. Drugs. 2014;74:423–41; 2. Scher et al. Nat Rev Rheumatol. 2019;15:153–66; 3. Gottlieb & Merola. J Am Acad Dermatol. 2021;84:92–101.

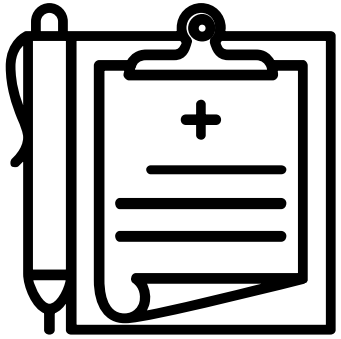
Patients with PsA may also develop axial disease[1]



Axial disease is present in **20–50% of patients with PsA**; axial PsA may sometimes involve the **spine** and not the sacroiliac joints[2]



Axial disease in PsA is often **not diagnosed**[3]

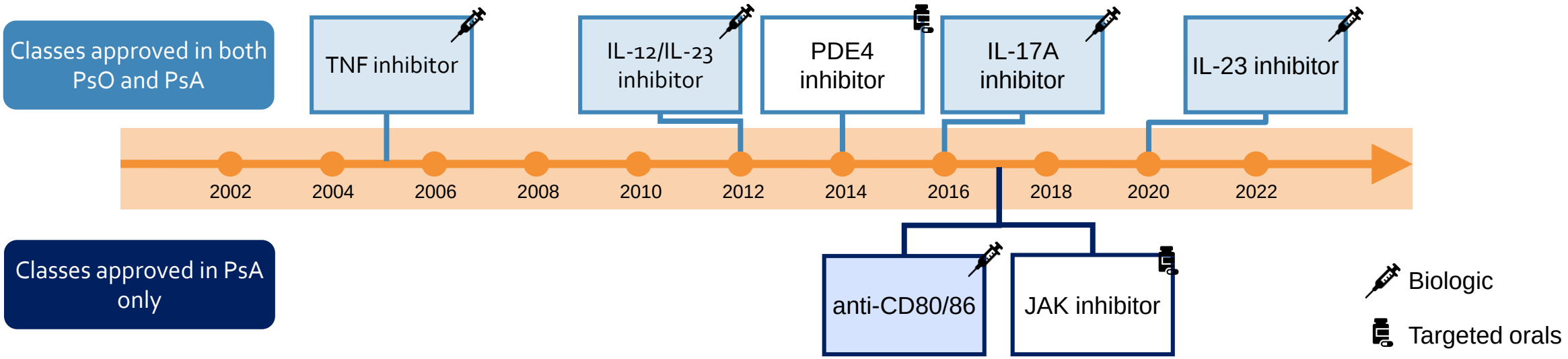


It is critical for dermatologists to be aware of the **signs of axial involvement in PsA**, especially inflammatory back pain[4]

ASDAS, Ankylosing Spondylitis Disease Activity score; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BASFI, Bath Ankylosing Spondylitis Functional Index; MRI, magnetic resonce imaging; PRO, patient-reported outcome; PsA, psoriatic arthritis.

1. Käding et al. Ann Rheum Dis. 2022;81:19–20; 2. McGagh & Coates. Rheumatology. 2020;59:i29–36; 3. Giovannini et al. J Clin Med. 2021;10:2845; 4. Gottlieb & Merola. J Am Acad Dermatol. 2021;84:92–101.

Standard of care in PsA has evolved to include biologics and targeted orals[1]



Compared with conventional immunosuppressants, biologics have several advantages[2]

Targeted immunosuppression

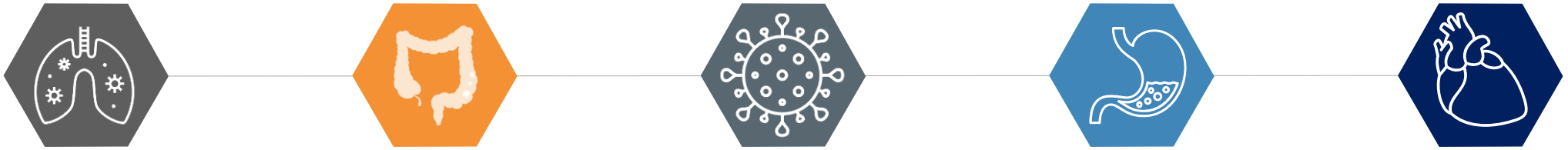
Less frequent dosing

Improved understanding of the pathogenesis of psoriatic disease has allowed the development of targeted agents[3]

Not all IL-17 or IL-23 inhibitors are approved in both PsO and PsA.
CD, cluster of differentiation; IL, interleukin; JAK, Janus kinase; PDE4, phosphodiesterase-4; PsA, psoriatic arthritis; PsO, psoriasis; TNF, tumor necrosis factor.
1. Gossec et al. Ann Rheum Dis. 2020;79:700–12; 2. Brownstone et al. Biologics. 2021;15:39–51; 3. Chimenti et al. Biologics. 2020;14:53–75.

Modern therapies in psoriatic disease generally have a tolerable safety profile[1]

However, some adverse events are associated with certain classes



TNF inhibitors	IL-17 inhibitors	IL-23 inhibitors	PDE4 inhibitors	JAK inhibitors
• Serious infection, tuberculosis, paradoxical reaction, lupus, and infusion reaction[1,2]	• Exacerbation of inflammatory bowel disease and oral candidiasis[3,4]	• Nasopharyngitis, upper respiratory tract infections and headache[5]	• Gastrointestinal-related adverse events[6]	• Infectious events, embolism and thrombosis and malignancies[7]

IL, interleukin; JAK, Janus kinase; PDE4, phosphodiesterase-4; TNF, tumor necrosis factor.

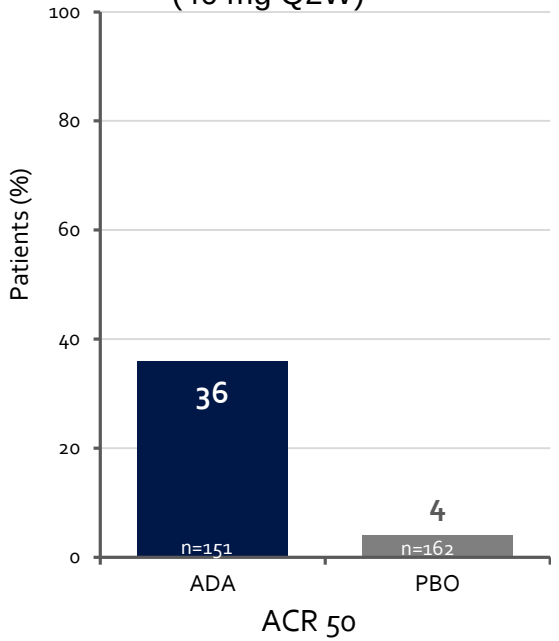
1. Kamata & Tada. Int J Mol Sci. 2020;21:1690; 2. Sivamani et al. Clinic Rev Allerg Immunol. 2013;44:121–40; 3. Schreiber et al. Ann Rheum Dis. 2019;78:473–9; 4. Armstrong et al. Dermatol Ther. 2022;12:787–800; 5. Yang et al. Am J Clin Dermatol. 2021;22:173–92; 6. Gooderham & Papp. BioDrugs. 2015;29:327–39; 7. Hoisnard et al. Sci Rep. 2022;12:7140.

Currently available bDMARDS have demonstrated efficacy in biologic naïve patients with PsA

Only licensed doses for PsA are shown

TNF[a]

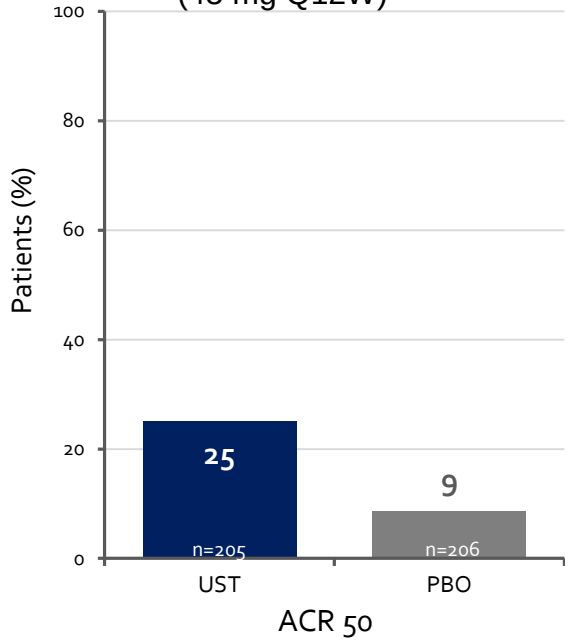
ADEPT: Adalimumab Week 12 (40 mg Q2W)[1]



Primary endpoint ACR20 at Week 12: 58% of patients achieved the primary endpoint with 40 mg Q2W ADA

IL-12/IL-23

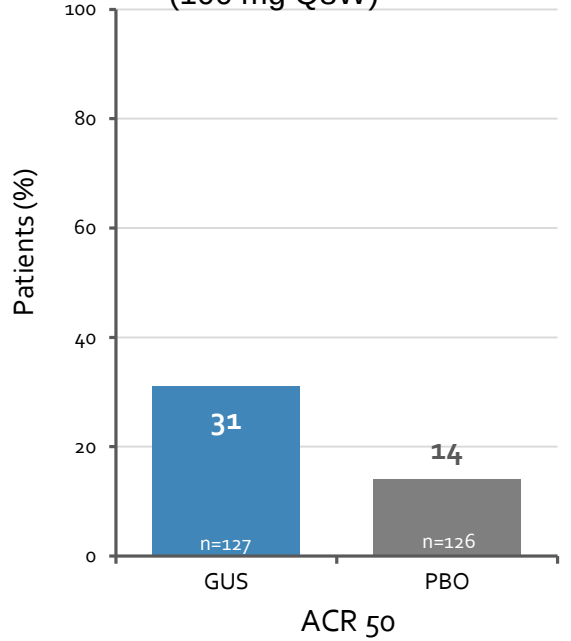
PSUMMIT-1: Ustekinumab Week 24 (45 mg Q12W)[2]



Primary endpoint ACR20 at Week 24: 42% of patients achieved the primary endpoint with 45 mg Q12W UST

IL-23[b]

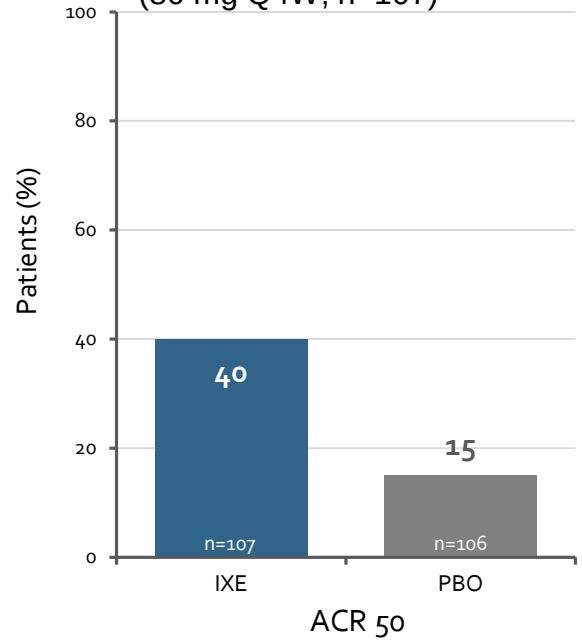
DISCOVER-2: Guselkumab Week 24 (100 mg Q8W)[3,†]



Primary endpoint ACR20 at Week 24: 64% of patients achieved the primary endpoint with 100 mg Q8W GUS

IL-17A[b]

SPIRIT-P1: Ixekizumab Week 24 (80 mg Q4W; n=107)[4]



Primary endpoint ACR20 at Week 24: 58% of patients achieved the primary endpoint with 80 mg Q4W IXE

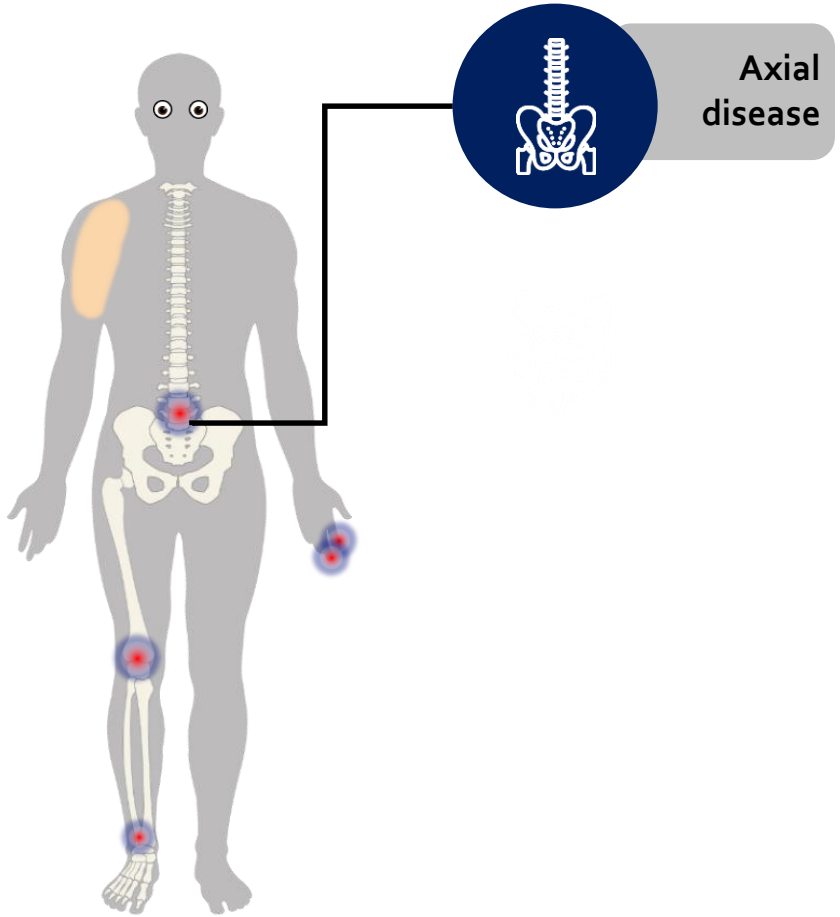
For illustrative purposes only – other bDMARDs are available

No head-to-head comparisons: Results of individual studies cannot be directly compared, nor conclusions inferred

aNot an exhaustive list, other TNF inhibitors, IL-23 inhbitiors and IL-17A inhibitors are available. †For patients with a high risk of radiographic progression, GUS 100 mg Q4W is recommended.

1. Mease PJ, et al. Arthritis & Rheum. 2005;52(10):3279–89; 2. McInnes IB, et al. Lancet. 2013;382:780–89; 3. Mease PJ, et al. Lancet 2020; 395: 1126–36; 4. Mease PJ, et al. Ann Rheum Dis 2017;76:79–87; 5. Ritchlin C, et al. Ann Rheum Dis 2014;73:990–99

IL-17 or TNF inhibitors are the preferred biologics in axial disease across major PsA guidelines[1–3]



GRAPPA guidelines 2021[1]

As TNF and IL-17 inhibitors have demonstrated efficacy in radiographic and non-radiographic axSpA, they are recommended for **axial PsA**

EULAR guidelines 2019[2]

- TNF or IL-17 inhibitors strongly recommended in **all domains**
- IL-23 inhibitors recommended in all domains **except axial disease**

ACR guidelines 2018[3]

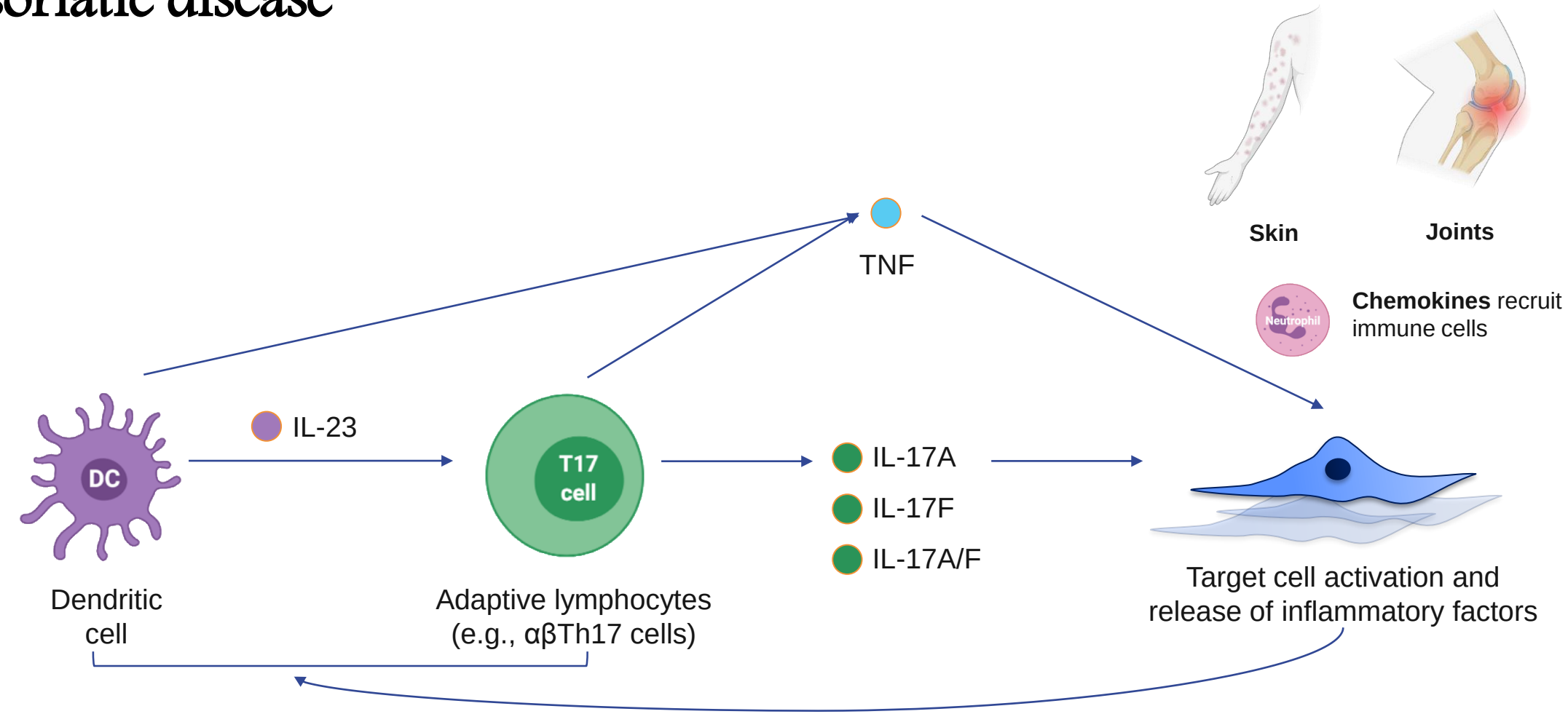
In patients with **axial PsA,** TNF inhibitors are preferred — except patients with severe skin manifestations or a contraindication, where IL-17 inhibitors may be used

ACR, American College of Rheumatology; EULAR, European Alliance of Associations for Rheumatology; GRAPPA, Group for Research and Assessment of Psoriasis and Psoriatic Arthritis; PsA, psoriatic arthritis; IL, interleukin; TNF, tumor necrosis factor.

1. Coates et al. Nat Rev Rheumatol. 2022;18:465–79; 2. Gossec et al. Ann Rheum Dis. 2020;79:700–12; 3. Singh et al. Arthritis Rheumatol. 2019;71:5–32.

Psoriatic disease: understanding the pathobiology and journey to targeted therapies

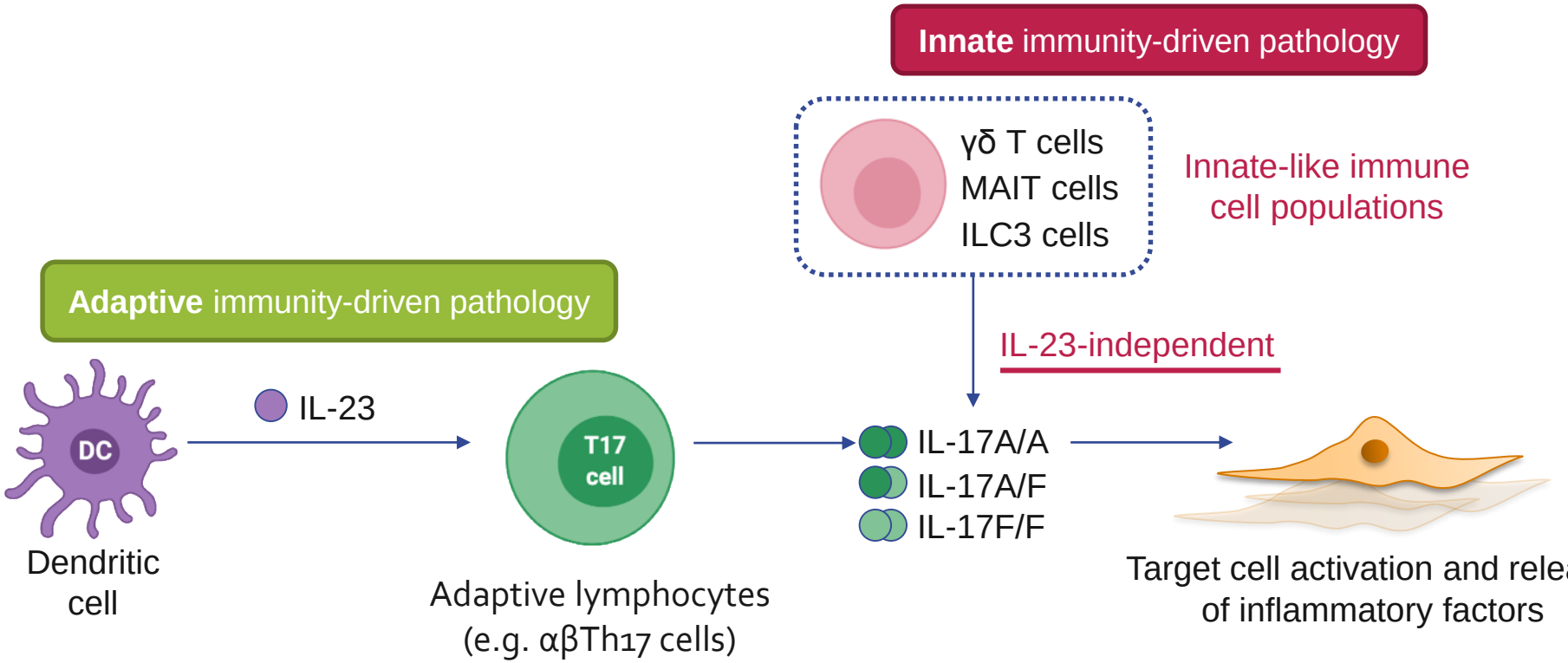
In synergy with TNF, the IL–17/23 axis is central to the pathobiology of psoriatic disease[1]



Inflammatory factors secreted by target cell drive the release of more inflammatory factors

Example cell types are shown; not an exhaustive list.
IL, interleukin; Th, T-helper; TNF, Tumor necrosis factor.
1. Lynde et al. J Am Acad Dermatol. 2014;71:141–50.

Innate immune cells may be important targets in disease domains, such as axial disease[1–5]



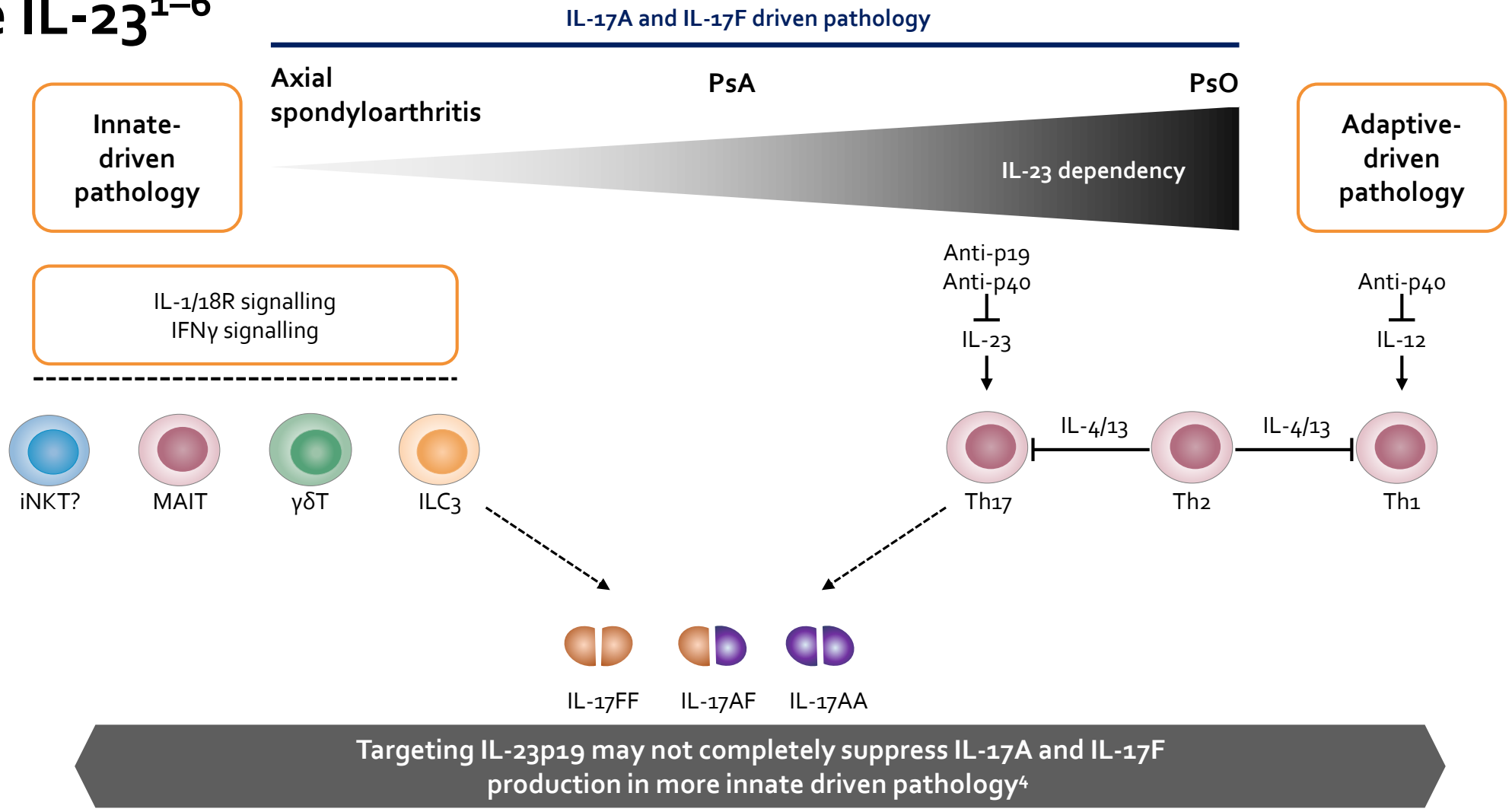
Hypothesis: IL-17 producing innate immune cells may be more relevant in axial disease and even peripheral joint inflammation

*Immunohistochemical analysis of IL-17+ cells was performed on the facet joints of 33 AS patients and compared with data from 20 OA patients.

AS, ankylosing spondylitis; IL, interleukin; MAIT, mucosal-associated invariant T cell; OA, osteoarthritis; Th17, T helper 17 cell; TNF, tumor necrosis factor; γδT, gamma delta T cell.

1. Rosine & Miceli-Richard. Front Immunol. 2021;11:553742; 2. Cole et al. Front Immunol. 2020;11:585134; 3. Zhang et al. Front Immunol.2022;13:818413; 4. Appel et al. Arthritis Res Ther. 2011;13:R95; 5. Gracey et al. Ann Rheum Dis. 2016;75:2124–32.

Pathological IL-17 production may not always require IL-23[1–6]



IFNγ; Interferon gamma; IL, interleukin; ILC, innate lymphoid cells; iNKT, invariant natural killer T cells; MAIT, mucosal associated invariant T cells; PsA, psoriatic arthritis; PsO, psoriasis; Th17: T-helper 17 cells; γδT: Gamma delta T cells.

1. Patel and Kuchroo. Immunity. 2015;43:1040–51; 2. Appel et al. Arthritis Res Ther. 2011;13:R95; 3. Sieper et al. Nat Rev Rheumatol. 2019;15:747–57; 4. Cole et al. Front Immunol. 2020;11:585134; 5. Al-Mossawi et al. Nat Commun. 2017;8:1510; 6. Gracey et al. Ann Rheum Dis. 2016;75:2124–32.

Conclusions

Psoriatic disease is a spectrum of chronic, inflammatory, systemic diseases with multiple manifestations, all representing a quality of life burden for patients

Dermatologists are ideally placed to recognize and manage early psoriatic arthritis and work collaboratively with colleagues in rheumatology to optimize outcomes

Innate sources of IL-17 may contribute to pathobiology in some disease domains, such as axial disease and in peripheral joints, and could explain the lack of efficacy demonstrated by IL-23 inhibitors

Inhibition of both IL-17A and IL-17F may result in effective suppression of inflammation driven by the innate and adaptive immune response

Thank you for your attention!

UCB would love to hear your feedback on this symposium, which will help to improve similar sessions in the future

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