Updates in Psoriasis Care

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Conflicts

- No conflicts of interest to disclose

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Teaching Point

- Biologic treatment for psoriasis is complex
- Critical to recognize underlying patient comorbid conditions

Outline

- Brief overview of psoriasis pathophysiology and targets
- Review comorbid conditions and preferred biologic agent
- What's new and coming
  - Bimekizumab
  - Deucravacitinib
  - Precision medicine

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Overview of Psoriasis

- Affects up to 3.2% of US adults
  - PsA >25%
- Multisystem inflammatory disorder
  - Recognition of extra-cutaneous disease critical in optimizing care
- Treatment should consider individual patient characteristics

Rachakonda et al, JAAD 2014
Kaushik et al, JAAD 2019

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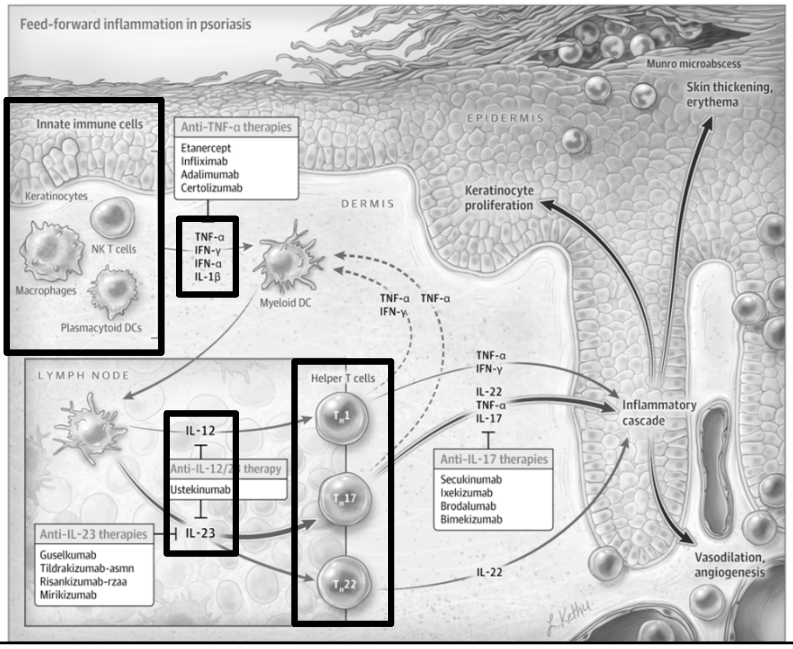
Pathophysiology



Biologic Targets

- TNF-α inhibitors
- IL-12/23 inhibitors
- IL-23 inhibitors
- IL-17 inhibitors
- T-cell inhibitors
- JAK inhibitors

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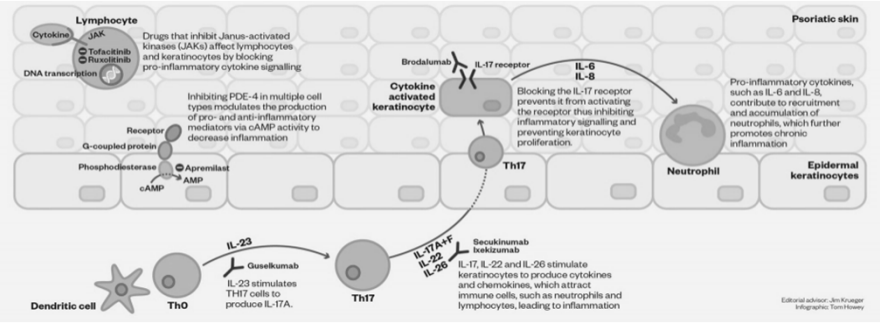
Treatment

- Treatment associated with improved QOL
- 2016 National Psoriasis Foundation: Treat to target
  - 3 months: BSA ≤1% or improved by 75% from baseline



Gordon et al, JEADV 2018
Menter et al, JAAD, 2019

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Biological agent	Suggested dose-escalation/interval-reduction strategy
Adalimumab 40 mg every other week	Adalimumab 40 mg weekly
Certolizumab pegol 200 mg every 2 weeks	Certolizumab pegol 400 mg every 2 weeks
Etanercept 50 mg once weekly	Etanercept 50 mg twice weekly
Infliximab 5 mg kg^{-1} every 8 weeks	[a]Infliximab 5 mg kg^{-1} every 6 weeks
Ixekizumab 80 mg every 4 weeks	[a]Ixekizumab 80 mg every 2 weeks
Tildrakizumab 100 mg every 12 weeks	Tildrakizumab 200 mg every 12 weeks (high disease burden or ≥ 90 kg)
Ustekinumab 45 mg every 12 weeks (≤ 100 kg)	[a]Ustekinumab 90 mg every 8 or 12 weeks (≤ 100 kg)
Ustekinumab 90 mg every 12 weeks (> 100 kg)	[a]Ustekinumab 90 mg every 8 weeks (> 100 kg)

Smith et at, Br J Dermatol 2020

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Monitoring

- Baseline
  - CBC, CMP
  - TB
  - Hepatitis B/C
  - TNF inhibitors
    - Black box warning: contraindicated in active infection or sepsis
- Annual Monitoring
  - Latent TB if high risk
  - Total body skin exam
- Vaccines
  - Dead vaccines may be administered
  - Live vaccines: discontinue 2-3 half lives or 1 month before and 1-2 weeks after

Menter et al, JAAD, 2019

Comorbidities

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Psoriatic Arthritis

- **TNF-α inhibitors** inhibit progressive structural damage
  - May be superior to Ustekinumab in treating joints
- **IL-17 and 23 inhibitors** similar efficacy to anti-TNF-α in joints
- T-cell inhibitor: Abatacept modest skin improvement

Kaushik, et al JAAD 2019
Fagerli et al, Ann Rheum Dis 2014
Bonifati et al, Deratol Ther 2016
Mease et al, Arthitis Rheum 2011
Mease et al, Ann Rheum Dis 2020
Smolen, Ann Rheum Dis 2020
McInnes et al, Lancet 2020
Ogfie et al, Rheum 2020
Mease et al, Rheum 2021

Obesity

- Overall obesity reduces odds of achieving PASI 75, PASI 90 by 25-30%
  - Weight loss improves efficacy
  - Conflicting data
    - Reduced response to TNFi and IL-17i
    - **IL-12/23i and IL-23i** appear efficacious
- Weight based dosing
  - Infliximab and Ustekinumab

Iannone et al, Autoimmune Rev 2016
Feldman et al, Intl Society for Pharmacoeconomics and Outcomes 2019
Reich et al, Br J Dermatol 2020
Von Stebut et al, Front Immunol 2021
Lebwohl et al, J Am Acad Dermatol 2021
Lebwohl et al, J Am Acad Dermatol 2020
Reich et al, J Eur acad Dermatol Venereol 2017
Enos et al, J Am Acad Dermatol 2022

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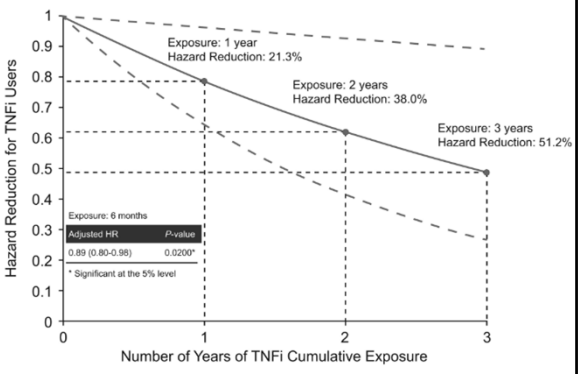
Cardiovascular Disease

- American College of Cardiology
  - **Additional RCT to determine if treatment reduces CVD risk**
- Biologics ↓ inflammation ↓incidence of CVD
  - Conflicting evidence looking at vascular inflammation
- Meta-analysis: No ↑ MACE with TNF-α, IL-17, IL 12/23 inhibitors
  - Ustekinumab: Initial concern MACE not found in longitudinal studies



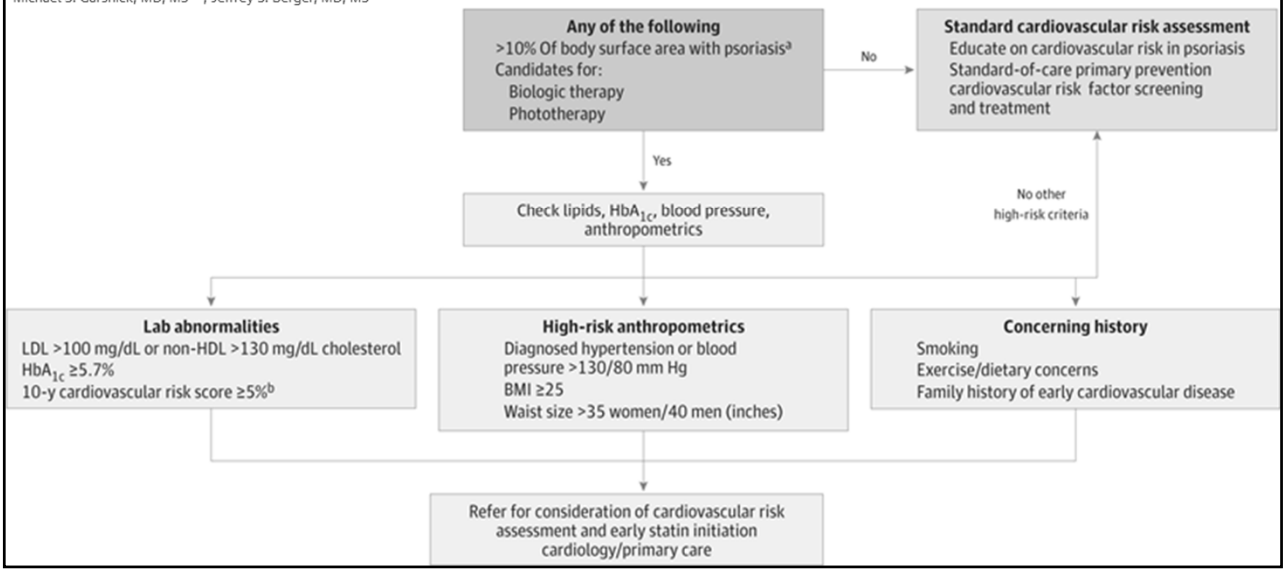
Wu et al, JAAD 2017

Garshick et al, JACC 2021
Wu et al, JAAD 2017
Bissonette et al, J Invest Dermatol, 2017
Champs et al, RMD 2019
Rungapiromnan et al, Br Jr Dermatol 2017
Papp et al, J Drugs Dermatol 2015

January 19, 2022

Psoriasis and Cardiovascular Disease—An Ounce of Prevention Is Worth a Pound of Cure

Michael S. Garshick, MD, MS[1,2]; Jeffrey S. Berger, MD, MS[1,2,3,4]



Congestive Heart Failure

- TNF-α inhibitors contraindicated in NYHA Class III and IV CHF
  - Avoid with EF <50%
  - Discontinue TNF-α inhibitors with new onset CHF
  - Echo before TNF-α inhibitors in CHF Class I/II
- **No CHF exacerbation with IL-17, IL-12/23, or IL-23 inhibitor use**

Desai et al, Best Pract Res Clin Rheumatol, 2006
Menter et al, JAAD 2008

Cancer

- TNF-α inhibitors: No overall increased risk cancer
  - Reports of up to 80% increased risk cSCC
  - Avoid in malignancy or hx malignancy
- **Ustekinumab**: Low to no increased risk malignancy
  - Initial concern increased risk cSCC in animal studies
- **IL 17/23 inhibitors**: Low rates cSCC and lymphoma
  - Still awaiting longer term data

Asgari et al, JAAD 2017
Bonovas et al, Expert Opin Drug Saf 2016
Gordon et al, JAAD 2012
Papp et al, Br J Dermatol 2013
Fiocentino et al, JAAD 2017
Van de Kerkhof et al, JAAD 2016
Strober et al, JAAD 2016
Gottleib et al, Am J Clin Dermatol 2020
Bachelez et al, J Eur Acad Dermatol Venereol 2019
Reich et al, Br J Dermatol 2020
Gordon et al, Lancet 2018
Reich et al, JAAD 2017
Blauvelt et al, JAAD 2017

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Inflammatory Bowel Disease

- **TNF-α inhibitors**:
  - FDA: Adalimumab (UC/CD), infliximab (UC/CD), certolizumab (CD)
  - **Etanercept de novo CD and UC**
- **IL-12/23**: Ustekinumab FDA approved for CD/UC
- IL-17 inhibitors: FDA warns against use in IBD
  - No direct causal relationship
- IL-23 inhibitors: Risankizumab now FDA for CD
  - No IBD cases reported

Korzenik et al, Aliment Pharmacol Ther 2019
O'Toole et al, Dig Dis Sci 2016
Sandborn et al, Aliment Pharmacol Ther 2018
Sads et al, N Engl J Med 2019
Fieldhouse et al, Drugs Context 2020

Lupus

- TNF-α inhibitors: Concern for de novo and LE flare
  - Anti-TNF-α induced lupus
- IL-12/23: Ustekinumab did not show efficacy in treating LE but no flare
- IL-17/23 inhibitors: Limited data
  - No new cases or flare reported

Spillane et al, JAAD 2007

Williams et al, Rheumatology 2009
Varada et al, JAAD 2015
De Brandt et al, Arthritis Res Ther 2005
Winchester et al, Lupus 2012

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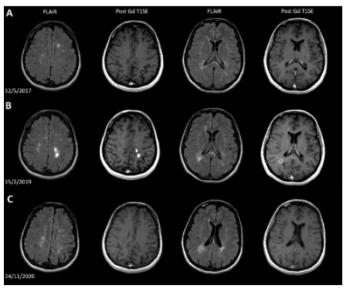
Multiple Sclerosis



- TNF-α inhibitors not recommended in MS
  - Includes those with 1st degree relatives
- **IL-17 inhibitors** appear safe
  - Secukinumab phase II RCT reduced active MS lesions
- **IL-12/23 and IL-23 inhibitors**: No reported MS progression

Hong et al, J Invest Dermatol 2016
Mansouri et al, J Drugs Dermatol 2015
Havrdova et al, J Neurol 2016
Kougkas et al, Neuroim Reports 2022
Leonardi et al, Lancet 2008
Blauvelt et al, Br HJ Dermatol 2018
Gordon et al, Lancet 2018
Reich et al, JAAD 2017

Latent TB

- TNF-α and IL-12/23 inhibitors: INH prophylaxis for 1 month
  - WHO Black box warning for risk TB/serious infection with TNFi
- IL-17/23 inhibitors: Safe in LTBI
- Guidelines for biologics with LBTI not updated since 2008

Doherty et al, JAAD 2008
Soung, Cliical Focus 2020

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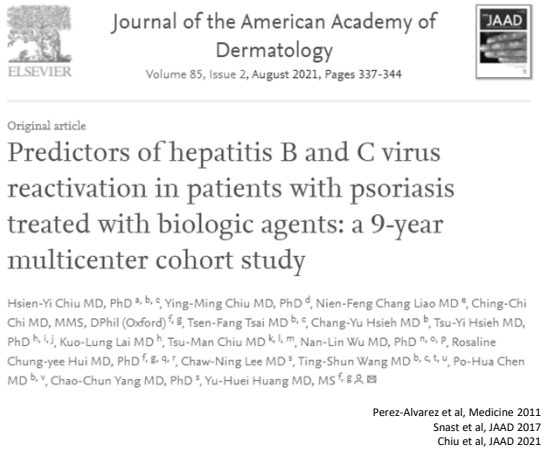
Hepatitis

- Biologics may be cautiously used in chronic or resolved hepatitis
  - Collaboration with GI
- Reactivation risk:
  - HbsAg+, HbeAg+, TNFi use
  - HBV antiviral prophylaxis reduced risk



Journal of the American Academy of Dermatology
Volume 85, Issue 2, August 2021, Pages 337-344

Original article

Predictors of hepatitis B and C virus reactivation in patients with psoriasis treated with biologic agents: a 9-year multicenter cohort study

Hsien-Yi Chiu MD, PhD [a, b, c], Ying-Ming Chiu MD, PhD [d], Nien-Feng Chang Liao MD [e], Ching-Chi Chi MD, MMS, DPhil (Oxford) [f, g], Tsen-Fang Tsai MD [b, c], Chang-Yu Hsieh MD [b], Tsu-Yi Hsieh MD, PhD [h, i, j], Kuo-Lung Lai MD [h], Tsu-Man Chiu MD [k, l, m], Nan-Lin Wu MD, PhD [n, o, p], Rosaline Chung-yee Hui MD, PhD [f, g, q, r], Chaw-Ning Lee MD [s], Ting-Shun Wang MD [b, c, t, u], Po-Hua Chen MD [b, v], Chao-Chun Yang MD, PhD [s], Yu-Huei Huang MD, MS [f, g]

Perez-Alvarez et al, Medicine 2011
Snast et al, JAAD 2017
Chiu et al, JAAD 2021

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Agent	PsA	Obesity	IBD	CVD	CHF	Cancer	Lupus	MS	Latent TB	Hepatitis
Anti-TNF										
Adalimumab	+	+	+	+	x	-	-	x	+ w/ppx	-
Certolizumab	+	+	+	+	x	-	-	x	+ w/ppx	-
Etanercept	+	+	x	+	x	-	-	x	+ w/ppx	-
Infliximab	+	+	+	+	x	-	-	x	+ w/ppx	-
Anti-12/23										
Ustekinumab	+	+	+	+	+	+	+	+	+ w/ ppx	+
Anti-17										
Ixekizumab	+	+	x	+	+	+	+	+	+	+
Brodalumab	+	+	x	+	+	+	+	+	+	+
Secukinumab	+	+	x	+	+	+	+	+	+	+
Anti-23										
Guselkumab	+	+	+	+	+	+	+	+	+	+
Risankizumab	+	+	+	+	+	+	+	+	+	+
Tildrakizumab	+	+	+	+	+	+	+	+	+	+

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A 30 year old patient with a history of Crohn's disease presents with extensive plaque psoriasis (>10%BSA). Which of the following biologics should be avoided in this patient?

A. Adalimumab
B. Etanercept
C. Infliximab
D. Certolizumab
E. Ustekinumab

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A 53 year old with plaque psoriasis (BSA>20%) presents to discuss Ustekinumab given the easy dosing schedule. He failed topical and light therapy. He has a positive quantiferon gold but negative chest x-ray. Which is the appropriate management?

A. Biologics are contraindicated
B. He must take multidrug therapy for at least 12 months prior to treatment
C. He can start the medication right away since his CXR is negative
D. He must take prophylaxis for 1 month, but can then begin injections

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Dermatol Ther (Heidelb) (2021) 11:885–905
https://doi.org/10.1007/s13555-021-00511-1

ORIGINAL RESEARCH

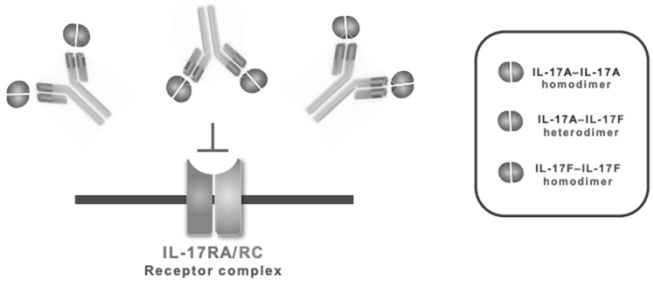
Comparative Efficacy and Relative Ranking of Biologics and Oral Therapies for Moderate-to-Severe Plaque Psoriasis: A Network Meta-analysis

April W. Armstrong · Ahmed M. Soliman · Keith A. Betts · Yan Wang · Yawen Gao · Luis Puig · Matthias Augustin

- Short term: Ixekizumab, risankizumab, brodalumab
- Long term: Risankizumab

What's Coming?

- Bimekizumab
  - Monoclonal IgG1 antibody blocking **IL-17F** and IL-17A
  - Dose: 320mg subQ week 0,4,8,12,16 then every 8 weeks



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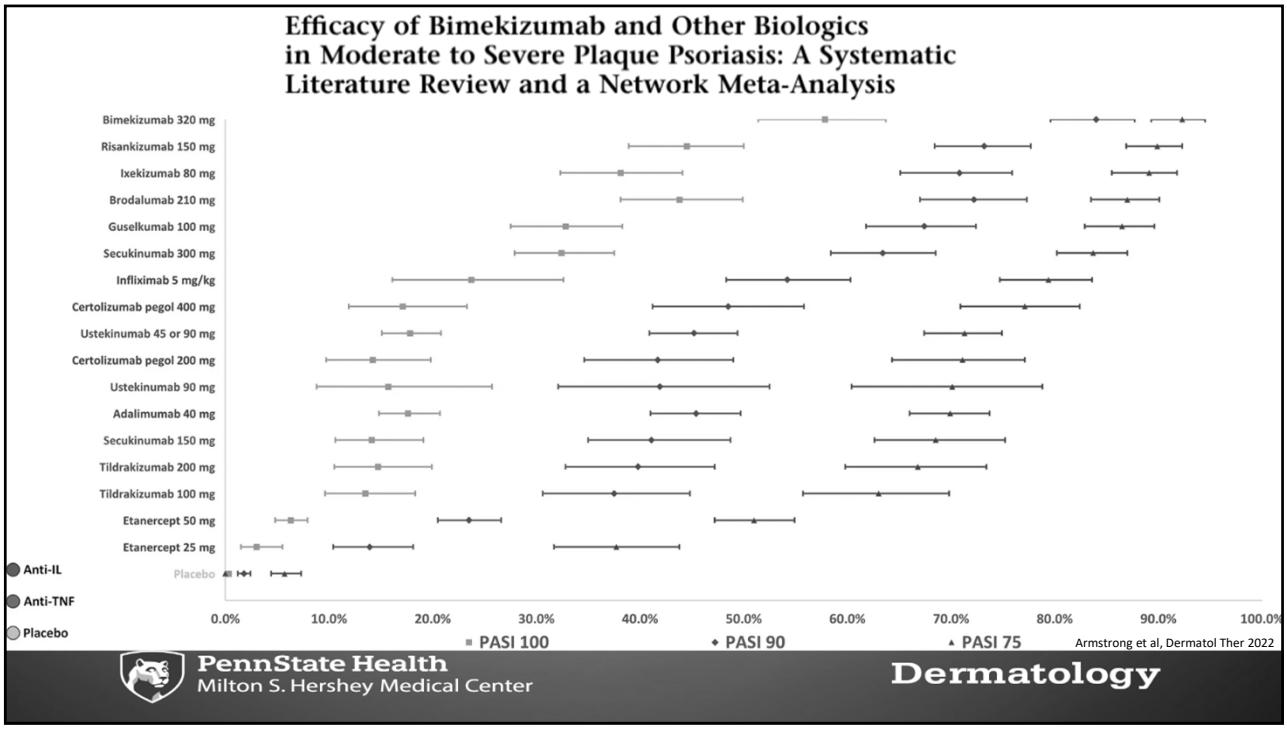
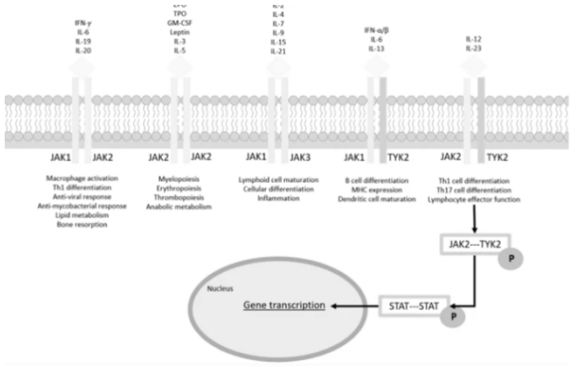


What's Coming?

- Deucravacitinib
  - Oral tyrosine kinase 2 inhibitor
    - Mediates signaling IL-23, IL-12 and type 1 interferon
  - Dose: 6mg daily



Le et al, Am J Clin Dermatol 2022

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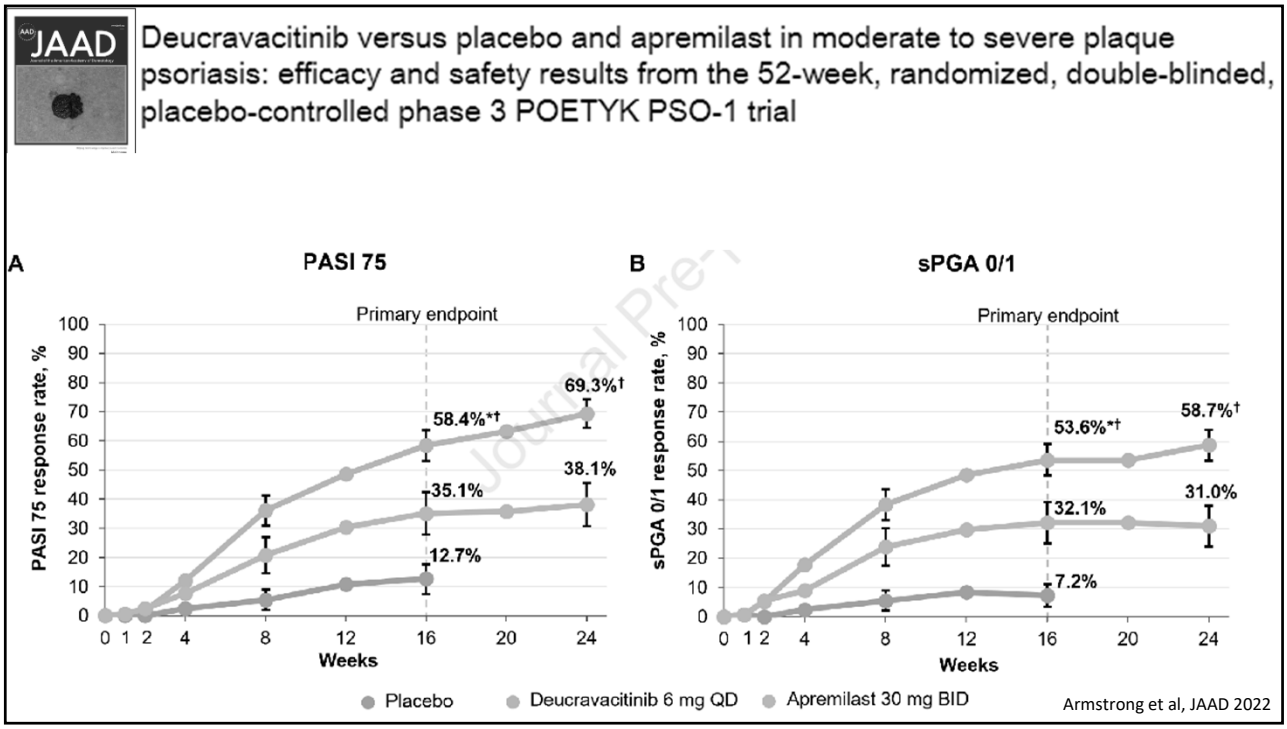
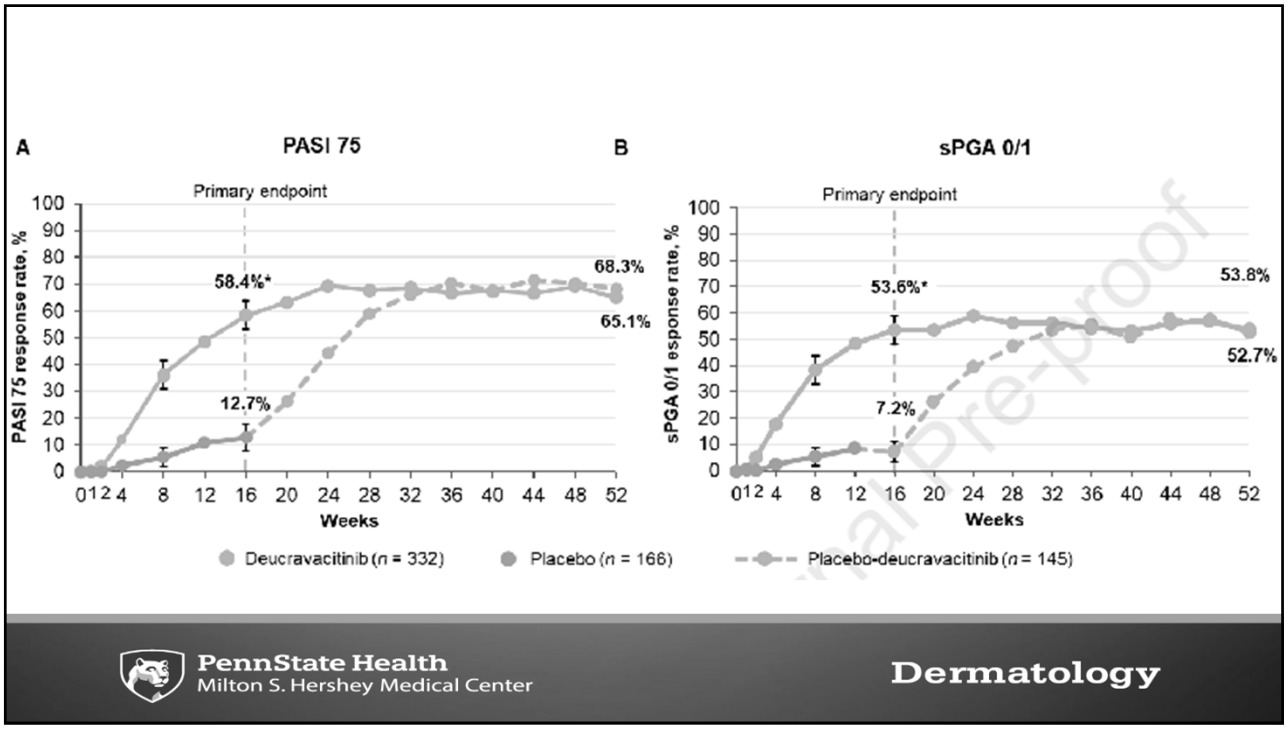


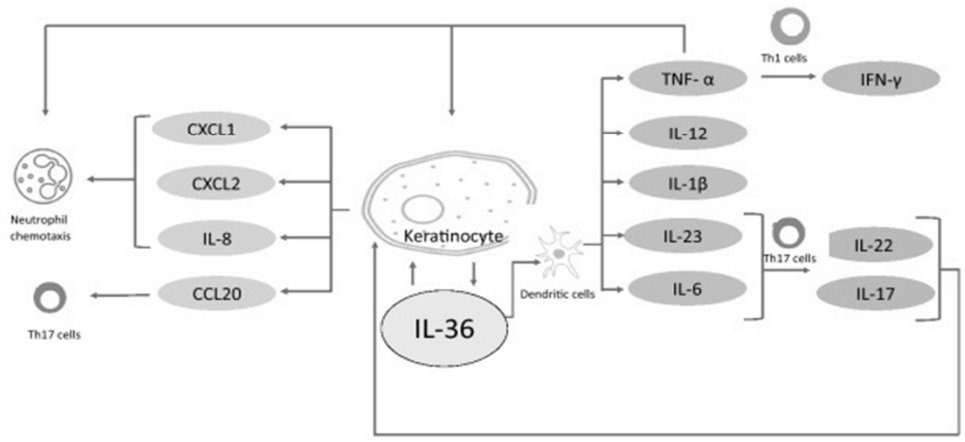


Precision Medicine

- AAD-NPF: Identify biomarkers to predict biologic response
  - 3 year persistence ~40%
- Mindera Health: Mind.Px
  - Dermal biomarker patch
    - Extracts RNA and uses nextgen sequencing to evaluate biomarkers
  - PPV 91% for patient response to class

FDA approves the first treatment option for generalized pustular psoriasis flares in adults

- More than half of patients treated with SPEVIGO® (spesolimab-sbzo) injection, for intravenous use showed no visible pustules one week after receiving treatment
- Spesolimab is a monoclonal antibody that inhibits interleukin-36 (IL-36) signaling



Suguira, K, Dermatol Ther 2022

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Teaching Point

- Biologic treatment for psoriasis is complex
- Critical to take into account underlying comorbid conditions

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