Therapeutic Titans:
Battle For Dominance in Psoriasis

South Beach Symposium 2026

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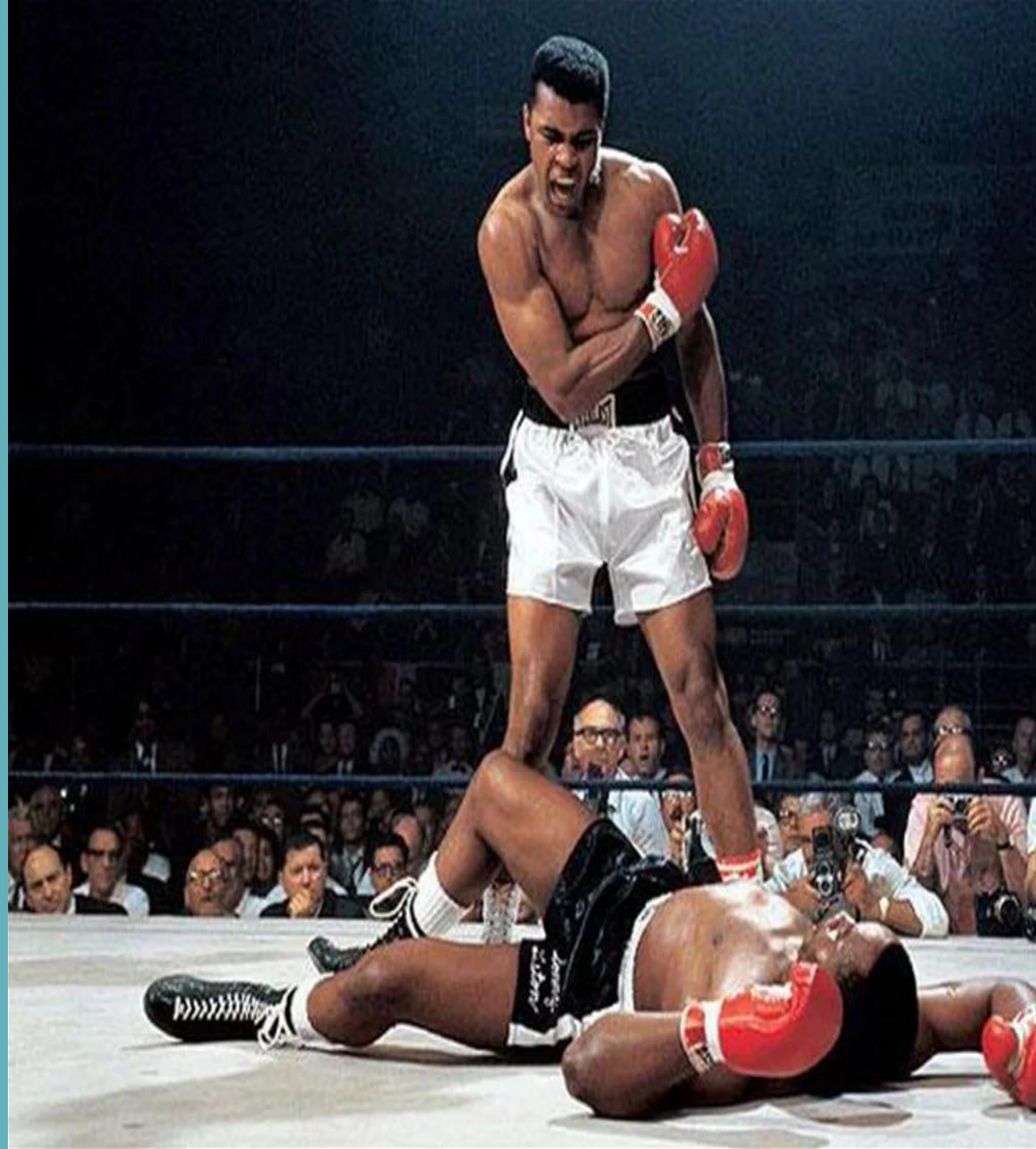
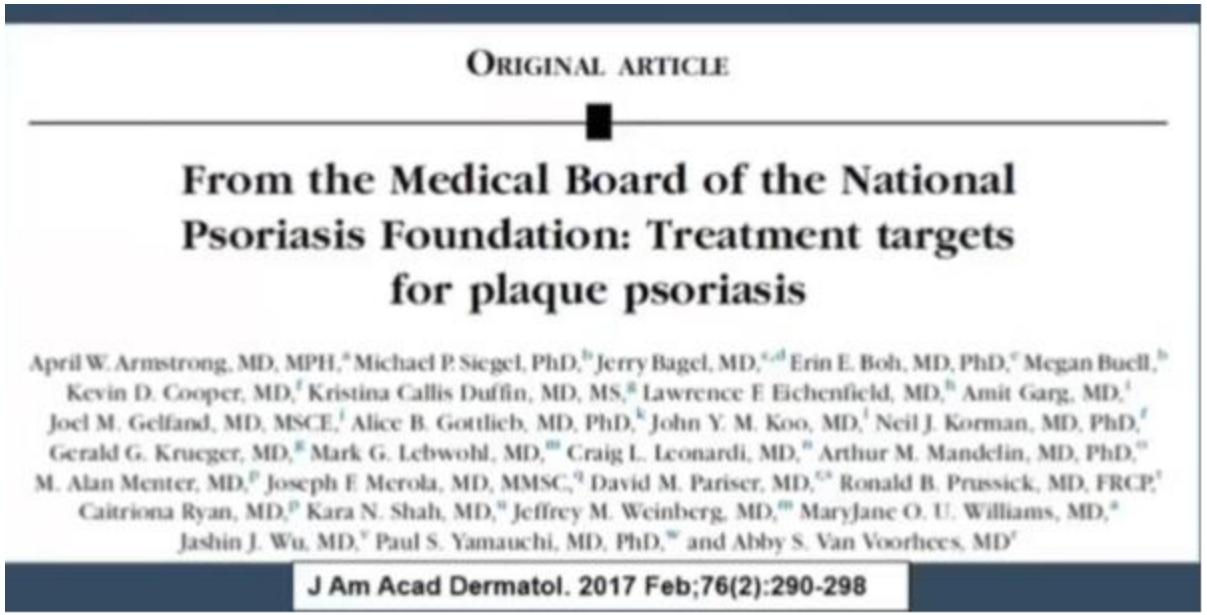


NPF Treat-to-Target Recommendations for Psoriasis



ORIGINAL ARTICLE

From the Medical Board of the National Psoriasis Foundation: Treatment targets for plaque psoriasis

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J Am Acad Dermatol. 2017 Feb;76(2):290-298

- Preferred response: <1% BSA at 3m and during maintenance
- Acceptable response: <3% BSA or >75% BSA improvement

Which Treatments Are Best?

- Included 167 studies, involving 58,912 randomized adult participants, which assessed most outcomes during induction phase (from 8 to 24 weeks after randomization)
- Overall mean PASI score at baseline of 20.4
- 96 trials compared systemic treatment against placebo, 52 were head-to-head trials and 19 had both an active comparator and a placebo
- 18 trials had a co-intervention, mainly phototherapy

Which Treatments Are Best?

- Most effective drugs reaching PASI 90 were infliximab, risankizumab, ixekizumab, and bimekizumab
  - Clinical effectiveness of these drugs was similar when compared against each other
- There was no significant difference between any of the interventions and the placebo for risk of SAEs
- Considering both efficacy and safety, risankizumab and bimekizumab appeared to be best
  - Other highly effective treatments (ixekizumab and infliximab) had more SAEs

Risankizumab vs. Bimekizumab

- RKZ (anti-IL23) became the dominant psoriasis biologic treatment given its convenient dosing schedule, remarkable efficacy and favorable safety profile
- Dosed as 150 mg at week 0, 4 (loading dose) then every 12 weeks (maintenance)
- BKZ (anti-IL17) has become an exciting new therapy given its impressive speed of onset, depth of response and relative convenient dosing schedule for its class
- Dosed as 320 mg at week 0, 4, 8, 12, 16 (loading dose) then every 8 weeks (maintenance)*

  * caveat is PsA data is based on 160 mg every 4 weeks

Early Efficacy – Week 4

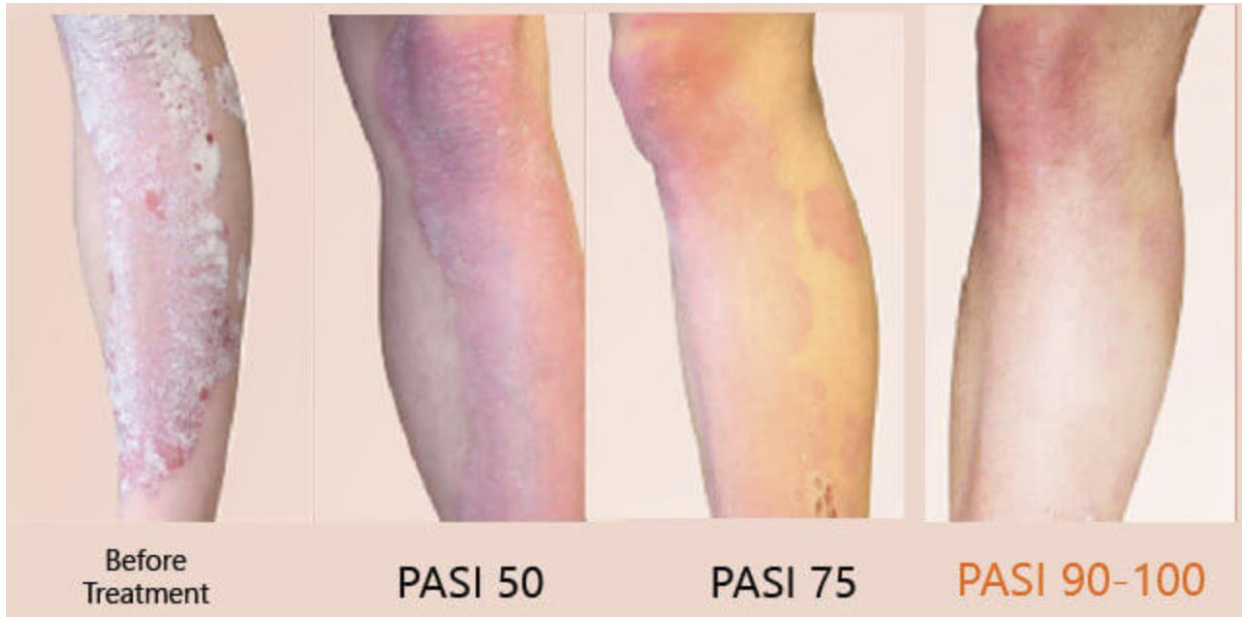
- RKZ with mean PASI improvement of 57%
- PASI 90 of 6%; PASI 100 of 4%
- BKZ with mean PASI improvement of 81%
- PASI 90 of 41%; PASI 100 of 14%

- RKZ with ACR 20 of 26%; ACR 50 of 6%; ACR 70 of 1%
- BKZ with ACR 20 of 42%; ACR 50 of 18%; ACR 70 of 6%

Primary Endpoint – Week 16

- RKZ with PASI 90 of 75%; PASI 100 of 43%
- BKZ with PASI 90 of 89%; PASI 100 of 65%

- RKZ with ACR 20 of 56%; ACR 50 of 26%; ACR 70 of 12%
- BKZ with ACR 20 of 62%; ACR 50 of 44%; ACR 70 of 24%



Later Efficacy – Week 52

- RKZ with PASI 90 of 86%; PASI 100 of 61%
- BKZ with PASI 90 of 86%; PASI 100 of 67%
- RKZ with ACR 20 of 71%; ACR 50 of 44%; ACR 70 of 26%
- BKZ with ACR 20 of 70%; ACR 50 of 54%; ACR 70 of 40%

Early Safety – Week 16

- RKZ with serious TEAE of 2.4% (lower than placebo 4%)
- Serious infection of 0.4% (similar to placebo 0.3%)
- Candida of 0.2% (placebo 0%)
- BKZ with serious TEAE of 1.6% (lower than placebo 2.4%)
- Serious infection of 0.3% (placebo 0%)
- Candida of 9.1% (placebo 0%)

Later Safety – Four To Eight Years

- RKZ with serious AEs of 7.5 per 100 patient years
- Serious infection of 1.2 per 100 patient years
- BKZ with serious AEs of 5.9 per 100 patient years
- Serious infection of 1.3 per 100 patient years

Safety – Events Of Special Interest

BKZ SIB rates are comparable to other psoriasis biologic

Table 2 Comparison of SIB TEAEs across anti-IL-17 and anti-IL-23 clinical development programs in psoriasis

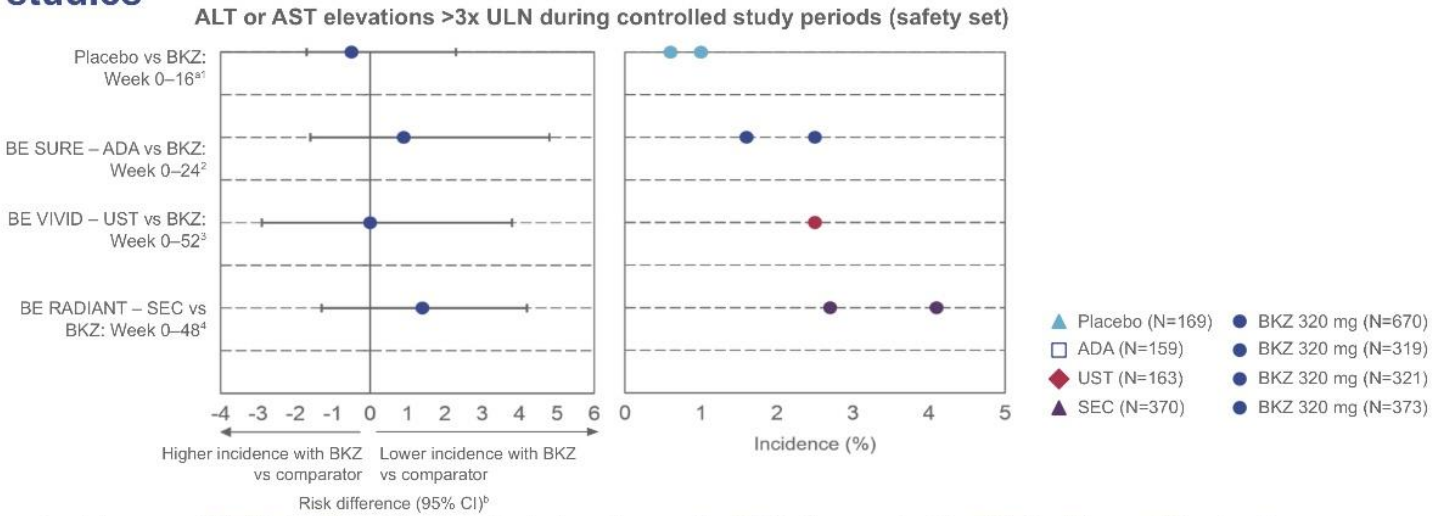
Anti-IL-17A/F | Anti-IL-17A | Anti-IL-17A receptor | Anti-IL-23

	BKZ Total (N=2,480)	SEC[12] (N=5,181)	IXE[15] (N=4,209)	BRO[15] (N=4,464)	RZB[13] (N=3,072)	GUS[14] (N=2,891)	TIL[16] (N=1,994)
Total exposure, PY	7,166	10,417	6,480	9,162	7,927	8,662	4,130
TEAEs, EAIR/100 PY (n)							
SIB[a]	0.13 (9)	0.08[b] (8)	0.14 (9)	0.38 (35)	0.09[b] (7)	0.10 (9)	0.19 (8)
Suicidal behavior	0.06 (4)	0.05[b] (5)	0.14 (9)	0.21 (19)	N/R	0.02[b] (2)	0.07[b] (3)
Suicide attempt	0.04 (3)	0.04[b] (4)	0.14 (9)	0.16 (15)	N/R	0.01[b] (1)	0.02 (1)
Completed suicide	0.01 (1)	0.01[b] (1)	0	0.04 (4)	0	0.01[b] (1)	0.05 (2)

[a]SIB events were adjudicated in the BKZ in psoriasis clinical development program via an independent Neuropsychiatric Adjudication Committee; in the psoriasis development programs for the other treatments shown, SIB events were defined using Standardized MedDRA Query. Inclusion and exclusion criteria, and definitions and monitoring of suicidal ideation, differed between studies, with extensive monitoring in the BKZ studies; therefore, caution should be taken when making comparisons across studies; [b]EAIRs were not reported in the original reference; rates were estimated based on the PY of exposure and number of cases reported in the reference.

Blauvelt A., Armstrong A., Merola J.F., Strober B., Cuyper D., Peterson L., Davies O., Stark J.L., Lebwohl M. Bimekizumab in patients with mod severe plaque psoriasis: Analysis of mental health and associated disorders. Fall Clinical 2023, Oct 19-22, Las Vegas. UCB poster presentatio

Liver transaminase elevations with BKZ, PBO, and comparators in Ph3/3b studies



- **Incidences of TEAE of liver biochemical elevations >3x ULN observed with BKZ in Phase 3/3b studies were comparable to or numerically lower than PBO and active comparators**
- **Elevations of ALT or AST >3xULN may or may not indicate a drug-related event**

“But Doc, I Don’t Want A Shot!”

Psoriasis Therapy Beyond Biologics

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ABSTRACT

Although psoriasis patients have benefited from the advent of biologic treatments over the past two decades, these medications are not appropriate for all patients and can be augmented by additional therapy. Differences among the manifold options can be difficult to parse, though essential for matching treatment with an individual patient. UV-light therapies, including both UV-B and psoralen with UV-A light, continue to play an important role in treatment, as do non-biologic systemic options including methotrexate, cyclosporine, apremilast, and acitretin. Recent years have seen a dramatic expansion in available topical therapies, the most common modality for the treatment of psoriasis, including new foam, spray, lotion, and cream formulations of topical corticosteroids (TCS) and new fixed-dose combination offerings of TCS with tazarotene and calcipotriene. Newer advances, including the oral tyrosine kinase 2 inhibitor deucravacitinib and non-steroidal topicals such as roflumilast, a PDE-4 inhibitor, and tapinarof, a first-in-class non-steroidal small-molecule, will soon provide even more options for treatment. It is vital for clinicians to remain aware of this ever-expanding armamentarium, allowing for more productive shared decision-making with patients, improved satisfaction, and better disease control.

Of note Apremilast is only systemic approved for mild disease

Table 1. Non-biologic systemic therapies for plaque psoriasis

Medication	Treatment success rates*	Advantages
Methotrexate	45.2% at week 12 or 16[3]	Highly effective therapy at low cost
Acitretin	47% at week 12[46]	No immune suppression
Cyclosporine	50-97% at week 10-16[47]	Excellent bridge to alternative therapy for control of severe disease
Apremilast	30-40% at week 16[11-13]	No monitoring needed
Deucravacitinib†	50.3%-53.6% at week 16[16]	Oral dosing with efficacy approaching injectable biologics

*Based on reported PASI75 over multiple studies
†Phase III trials ongoing, application for regulatory approval pending

Early Efficacy – Week 4

- Apremilast with mean PASI improvement of 20%
- PASI 75 of ~6%

- Deucravacitinib with mean PASI improvement of ~50%
- PASI 75 of ~ 8%

Primary Endpoint – Week 16

- Apremilast mean PASI improvement ~52%
- PASI 75 of 35-37%
- PASI 90 of 20%

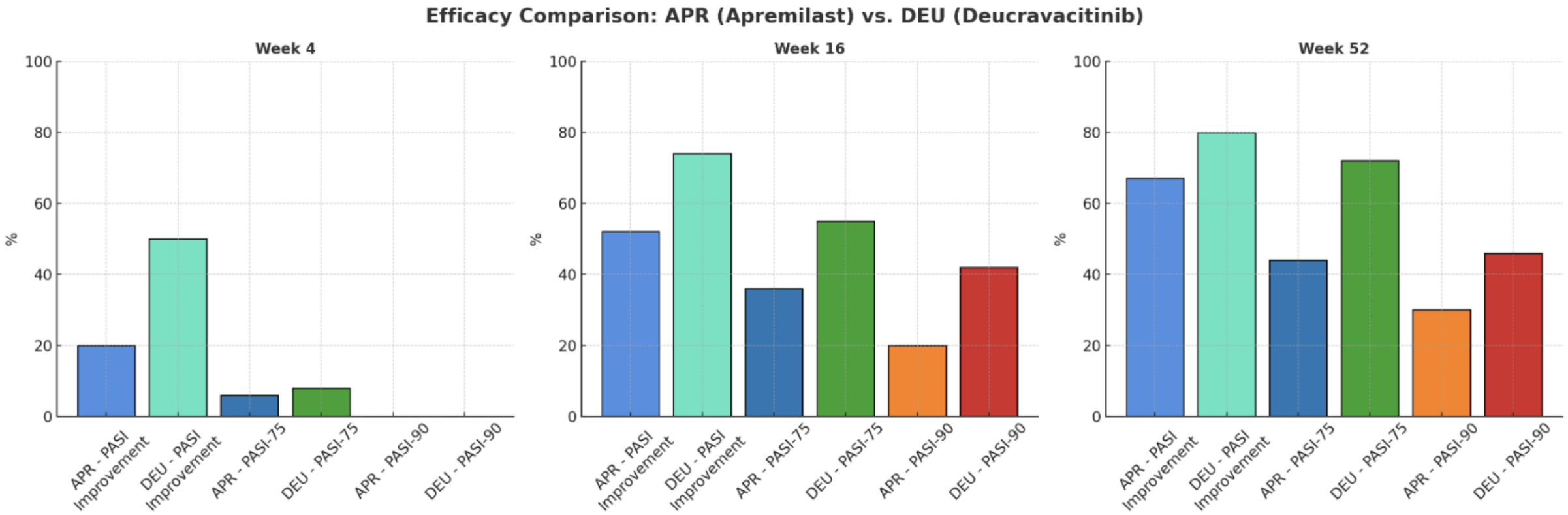
- Deucravacitinib mean PASI improvement ~74%
- PASI 75 of 53-58%
- PASI 90 of 42%

Later Efficacy – Week 52

- Apremilast with mean PASI improvement of 67%
- PASI 75 of 44%; PASI 90 of ~30%

- Deucravacitinib with mean PASI improvement of ~80%
- PASI 75 of 72%; PASI 90 of 46%

Efficacy Summary



Early Safety – Week 16

- Apremilast with nausea/diarrhea of 17% (placebo 6%)
- URI of 9% (placebo 6%)
- Depression of 1% (placebo 0%)
- Folliculitis 1% (placebo 0%)
- Deucravacitinib with nausea/diarrhea of 1.7-4.4%
- URI of 19.2% (placebo 14.8%)
- Folliculitis of 1.7% (placebo 0%)
- HSV of 2% (placebo 0.2%)

Safety profile through Week 16 (≥5%)[2]

AES OCCURRING IN ≥5% OF PATIENTS IN ANY ACTIVE TREATMENT GROUP WEEKS 0-16 FROM POOLED CLINICAL TRIALS (PSO-1 AND PSO-2)[2]

AE category, %	SOTYKTU (n=842)*	Apremilast (n=422)	Placebo (n=419)
Nasopharyngitis	9.0%	8.8%	8.6%
Upper respiratory tract infection	5.5%	4.0%	4.1%
Headache	4.5%	10.7%	4.5%
Diarrhea	4.4%	11.8%	6.0%
Nausea	1.7%	10.0%	1.7%

Later Safety – Five Years

- Apremilast with serious AEs of 4.9 per 100 patient years
- Serious infection of 0.9 per 100 patient years
- MACE of 0.4 per 100 patient years
- Malignancy of 1.4 per 100 patient years

- Deucravacitinib with serious AEs of 5.1 per 100 patient years
- Serious infection of 1.9 per 100 patient years (COVID-19, VZV)
- MACE of 0.3 per 100 patient years
- Malignancy of 0.9 per 100 patient years

Apremilast Label

- No routine lab monitoring recommended

Diarrhea, Nausea, and Vomiting: Cases of severe diarrhea, nausea, and vomiting were associated with the use of Otezla. Most events occurred within the first few weeks of treatment. In some cases, patients were hospitalized. Patients 65 years of age or older and patients taking medications that can lead to volume depletion or hypotension may be at a higher risk of complications from severe diarrhea, nausea, or vomiting. Monitor patients who are more susceptible to complications of diarrhea or vomiting; advise patients to contact their healthcare provider. Consider Otezla dose reduction or suspension if patients develop severe diarrhea, nausea, or vomiting

Depression: Carefully weigh the risks and benefits of treatment with Otezla for patients with a history of depression and/or suicidal thoughts/behavior, or in patients who develop such symptoms while on Otezla. Patients, caregivers, and families should be advised of the need to be alert for the emergence or worsening of depression, suicidal thoughts or other mood changes, and they should contact their healthcare provider if such changes occur

- Plaque Psoriasis: Treatment with Otezla is associated with an increase in depression. During clinical trials in adult patients with moderate to severe plaque psoriasis, 1.3% (12/920) of patients reported depression compared to 0.4% (2/506) on placebo. Depression was reported as serious in 0.1% (1/1308) of patients exposed to Otezla, compared to none in placebo-treated patients (0/506). Suicidal behavior was observed in 0.1% (1/1308) of patients on Otezla, compared to 0.2% (1/506) on placebo. One patient treated with Otezla attempted suicide; one patient on placebo committed suicide

Deucravacitinib Label

- Tuberculosis: Evaluate for TB prior to initiating treatment
- Laboratory Abnormalities: Periodically evaluate serum triglycerides. Evaluate liver enzymes at baseline and thereafter in patients with known or suspected liver disease

J may cause serious side effects, including:

- See **"What is the most important information I should know about ?"**
- **Changes in certain laboratory test results.** Changes in laboratory tests have happened in some people taking Your healthcare provider may do blood tests before you start taking and during treatment with to check for the following:
  - **Increased triglycerides.** Triglycerides are a type of fat found in your blood. Too much fat in your blood can cause problems with your heart.
  - **Increased liver enzymes.** Liver enzymes are found in your blood and help to tell if your liver is functioning normally. If your liver enzymes increase too much, your healthcare provider may need to do additional tests on your liver and may tell you to stop taking if they think tha J is harming your liver.
- **Potential risks from Janus kinase (JAK) inhibition.** is a tyrosine kinase 2 (TYK2) inhibitor. TYK2 is in the JAK family. It is not known whether taking J has the same risks as taking JAK inhibitors. Increased risk of death (all causes) has happened in people who were 50 years of age and older with at least 1 heart disease (cardiovascular) risk factor who were taking a JAK inhibitor used to treat rheumatoid arthritis (RA) compared to people taking another medicine in a class of medicines called TNF blockers. is not for use in people with RA.

The most common side effects of J include:

- common cold, sore throat, and sinus infection (upper respiratory infections)
- cold sores (herpes simplex)
- sores on inner lips, gums, tongue, or roof of the mouth (canker sores)
- inflamed hair pores (folliculitis)
- acne

Who's Up Next?

- Icotrokinra (oral IL-23 inhibitor) being developed by JnJ currently in phase III trials
- Dosed 200mg once daily
- PASI 75 of ~15% at week 4 up to ~69% at week 16 up to 81% at week 24
- PASI 90 of ~50% at week 16 up to 65% at week 24
- Data suggest safety profile mimics injectable drugs in this class

Final Thoughts

- The most effective biologics are much more effective than apremilast and deucravacitinib
- Some patients will want to start with an oral option
- If mild disease or immunocompromised, I favor apremilast
- For moderate to severe and otherwise no major immunocompromise, I favor deucravacitinib
- Efficacy & tolerability data do favor deucravacitinib currently
- Icotrokinra appears poised to be most effective, tolerable, and safe oral therapy in the near future

Final Thoughts Continued

- Both are phenomenal drugs
- In PsO, I often favor RKZ based on convenient dosing profile
- In PsO/PsA or those who want the most rapid improvement, I favor BKZ
- For those prone to yeast infections or with a personal history of IBD, I favor RKZ
- SAEs (MACE, malignancy, infection, SIB, liver injury) are fairly equivalent between the two drugs despite differing warnings in the package insert
- We are clearly in a golden age of the management of psoriatic disease

Thank you