JAKI: ELEVATING STANDARDS OF CARE IN AD

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DISCLOSURES

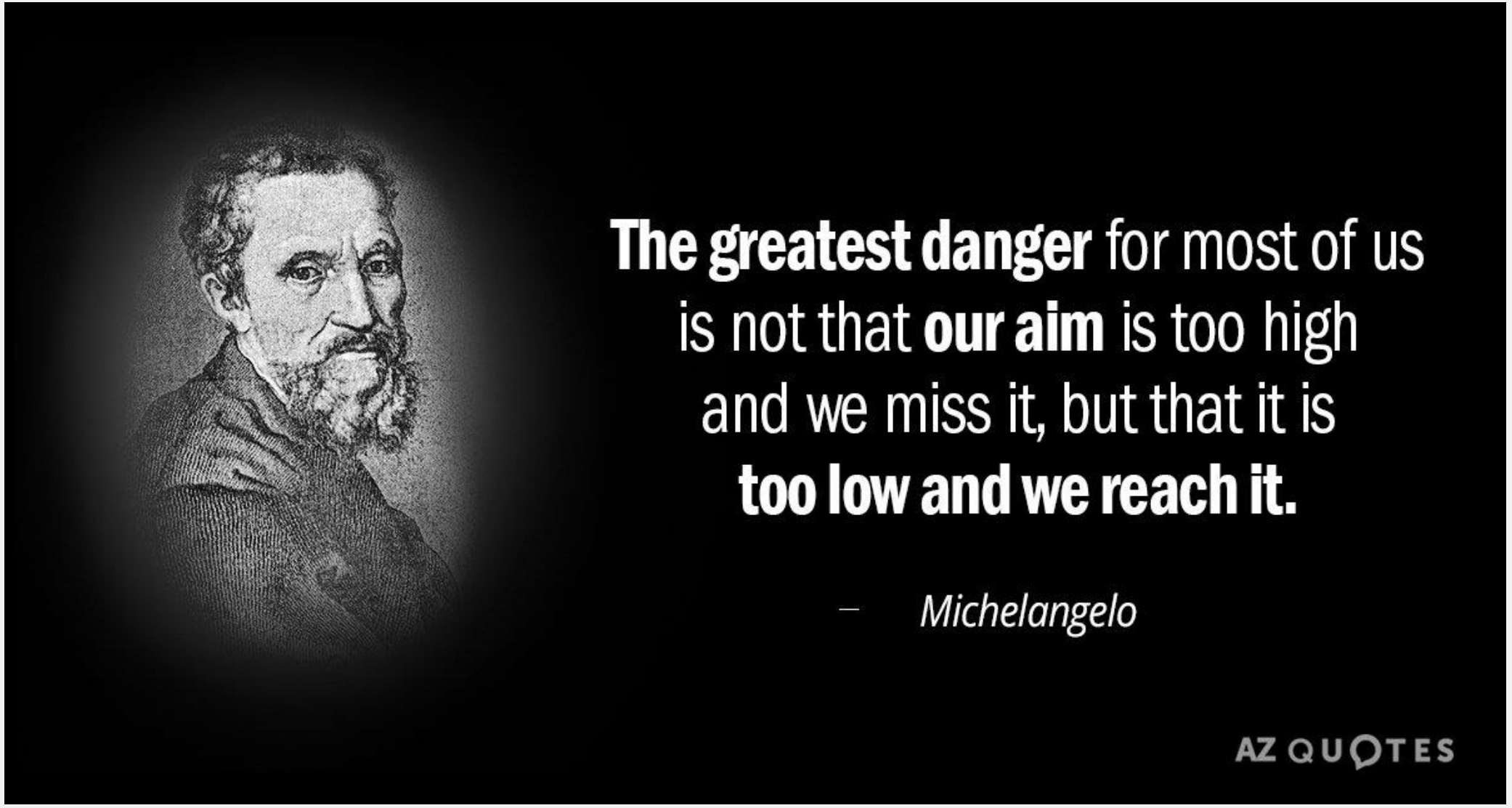
- Speaker
  - Abbvie
  - Arcutis
  - Boehringer-Ingelheim
  - Bristol Myers Squibb
  - Castle
  - Dermavant
  - DermTech
  - Galderma
  - Journey
  - LEO
  - Sanofi
  - Regeneron
  - UCB

- Advisor/ Consultant
  - Abbvie
  - Alumis
  - Arcutis
  - Boehringer-Ingelheim
  - Bristol Myers Squibb
  - Castle Biosciences
  - Dermavant
  - DermTech
  - GLG
  - Jansen
  - LEO
  - Novartis
  - Pfizer
  - Sanofi
  - ReachRx
  - Regeneron
  - UCB

- Investigator
  - Abbvie
  - Adelphi
  - Almirall
  - Castle Biosciences
  - Cellgene
  - COREVITAS
  - Eli Lilly
  - Galderma
  - LEO
  - Nektar Therapeutics
  - Novartis
  - Pulse Biosciences
  - PROSE
  - Sanofi
  - Thermo Fisher Scientific
  - Regeneron

OBJECTIVES

- Define optimal treatment targets for Atopic Dermatitis – AHEAD Recommendations
- Discuss the positioning of Jak inhibitors amidst the current treatment landscape
- Analyze efficacy and safety profiles of Jak inhibitors for atopic dermatitis
- Introduce recent molecular tools to help aid in treatment selection


The greatest danger for most of us is not that our aim is too high and we miss it, but that it is too low and we reach it.
– Michelangelo
AZ QUOTES

AHEAD RECOMMENDATION:

ACHIEVE OPTIMAL TREATMENT TARGETS WITHIN 3-6 MONTHS FOR ATOPIC DERMATITIS

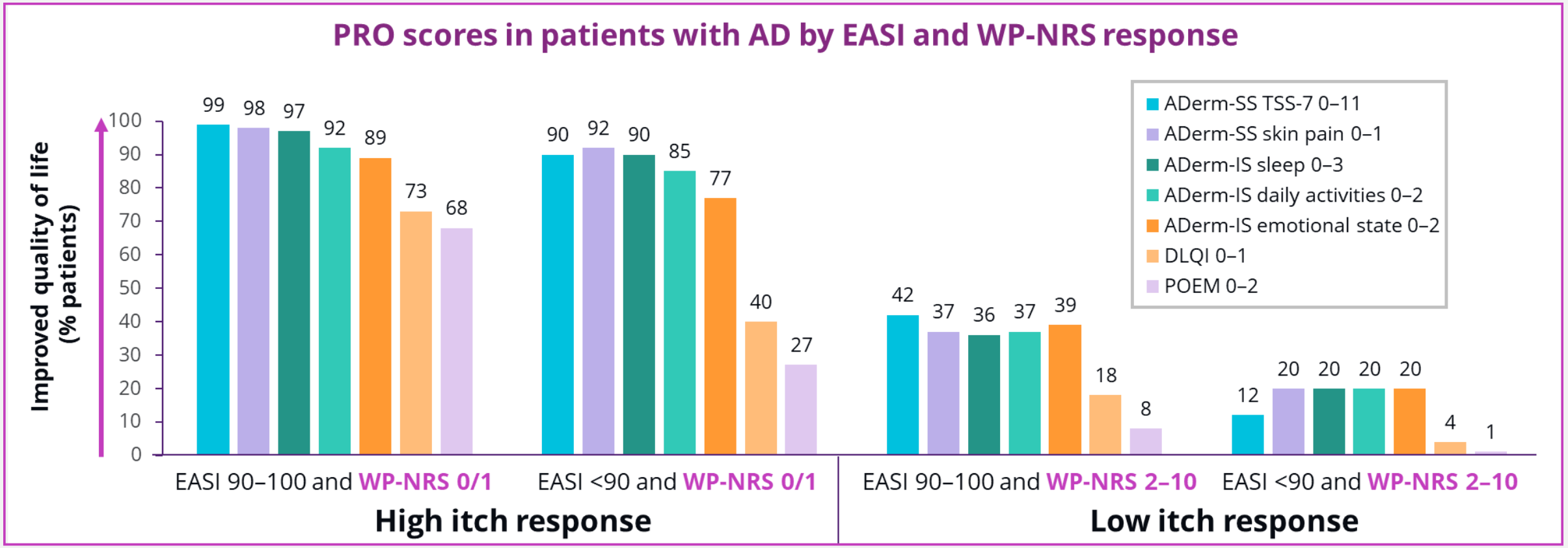
Practical Approach to Achieve MDA		
Measure	**Optimal Outcome**	**Meaning**
SKIN	✓ EASI-90, or IGA 0/1 & BSA ≤2%	**Clear or almost clear skin**
ITCH	✓ NRS 0/1	**Little or no itch**

Clinician-reported Measure	Moderate Target	Optimal Target
EASI	EASI-75 or EASI ≤7	EASI-90 or EASI ≤3
SCORAD	SCORAD 50 or SCORAD ≤24	SCORAD 75 or SCORAD ≤10
IGA and BSA	IGA≤2 and 50% BSA Improvement	IGA 0/1 and BSA ≤2%
Patient-reported Measure	**Moderate Target**	**Optimal Target**
Itch NRS	≥4-point improvement	0/1
DLQI (impact on daily life)	≥4-point improvement	0/1
Sleep NRS (for sleep disturbance)	≥3-point improvement	0/1
POEM	≥4-point improvement	≤2
HADS (for mental health)	<11	<8
Pain NRS (for skin pain)	≥3-point improvement	0/1

AHEAD, Aiming High in Eczema/Atopic Dermatitis; AD, atopic dermatitis; BSA, body surface area; DLQI, Dermatology Life Quality Index; EASI, Eczema Area and Severity Index; IGA, Investigator Global Assessment; MDA, minimal disease activity; NRS, Numeric Rating Scale; POEM, Patient-Oriented Eczema Measure; SCORAD, SCORing Atopic Dermatitis.

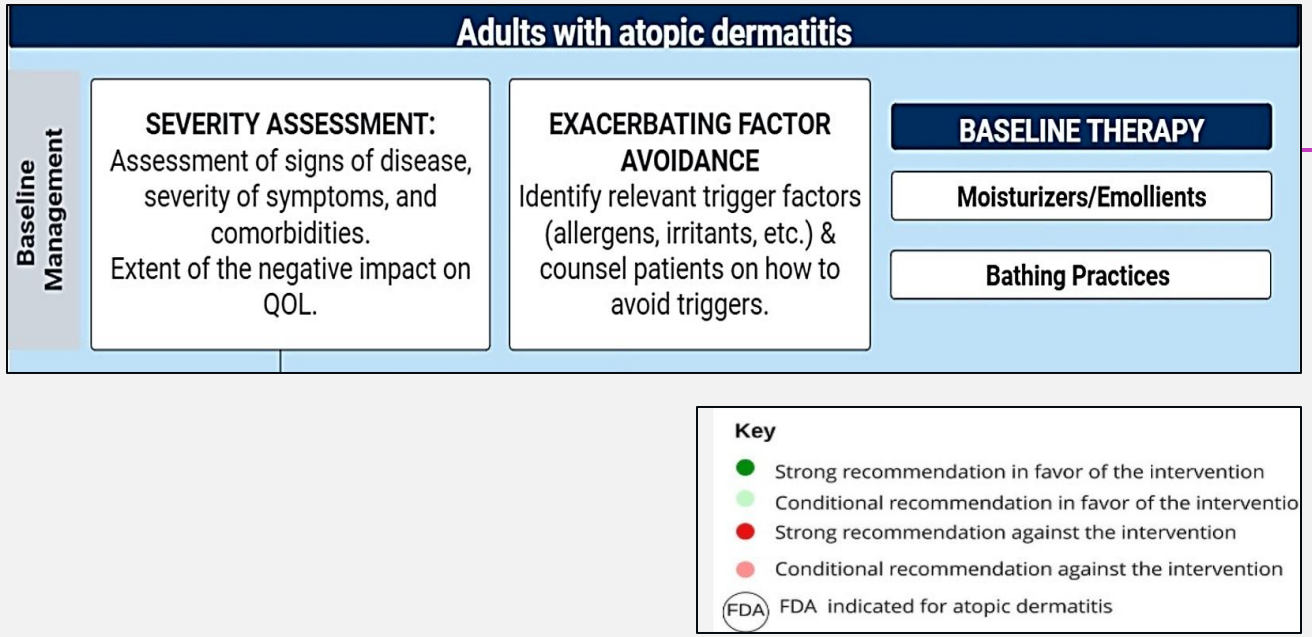
Silverberg JI, et al. *J Eur Acad Dermatol Venereol.* 2024;00:1-10

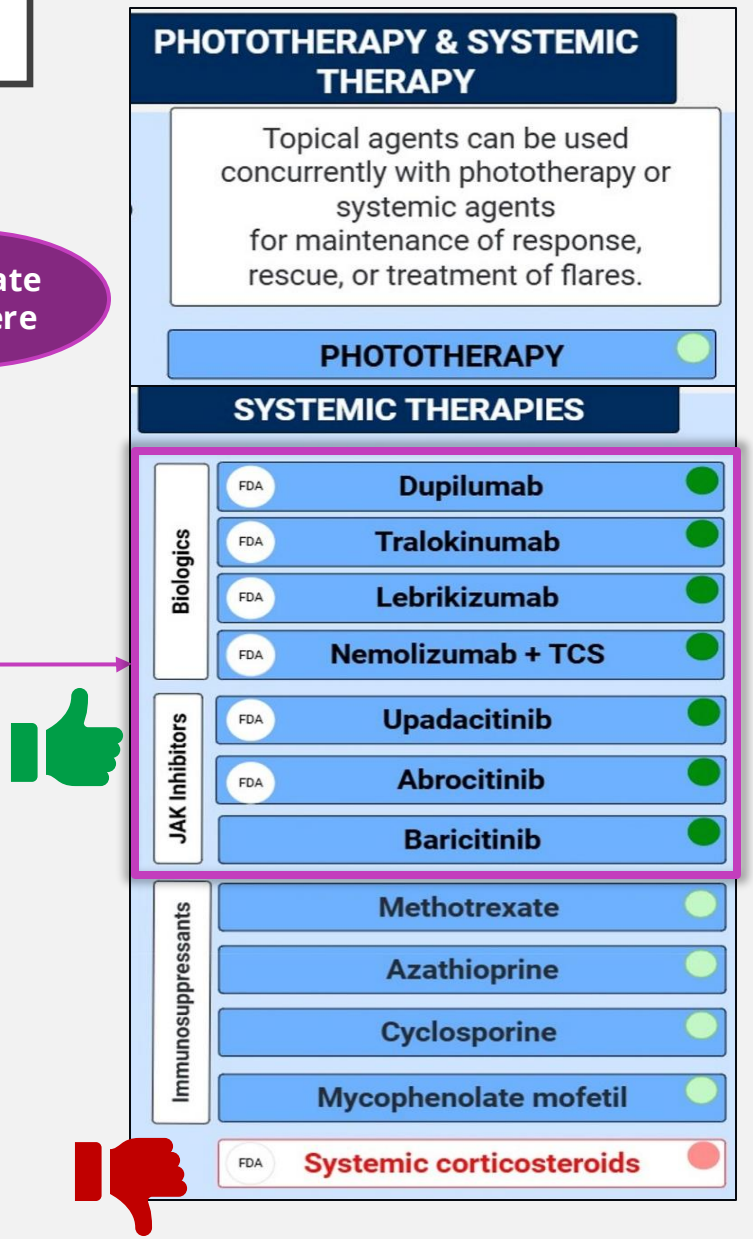
WHY BOTH MATTER



AD, atopic dermatitis; ADerm-IS, Atopic Dermatitis Impact Scale; ADerm-SS, Atopic Dermatitis Symptom Scale; DLQI, Dermatology Life Quality Index; EASI, Eczema Activity and Severity Index; POEM, Patient-Oriented Eczema Measure; PRO, patient-reported outcome;
TSS-7, 7-Item Total Symptom Score; WP-NRS, Worst Pruritus Numerical Rating Scale.
Reich K et al. J Eur Acad Dermatol Venereol. 2023;37(8):1634–1641.

AMERICAN ACADEMY OF DERMATOLOGY (AAD) GUIDELINES, 2025





Strong Recommendation in favor of biologics and JAK inhibitors approved for atopic dermatitis

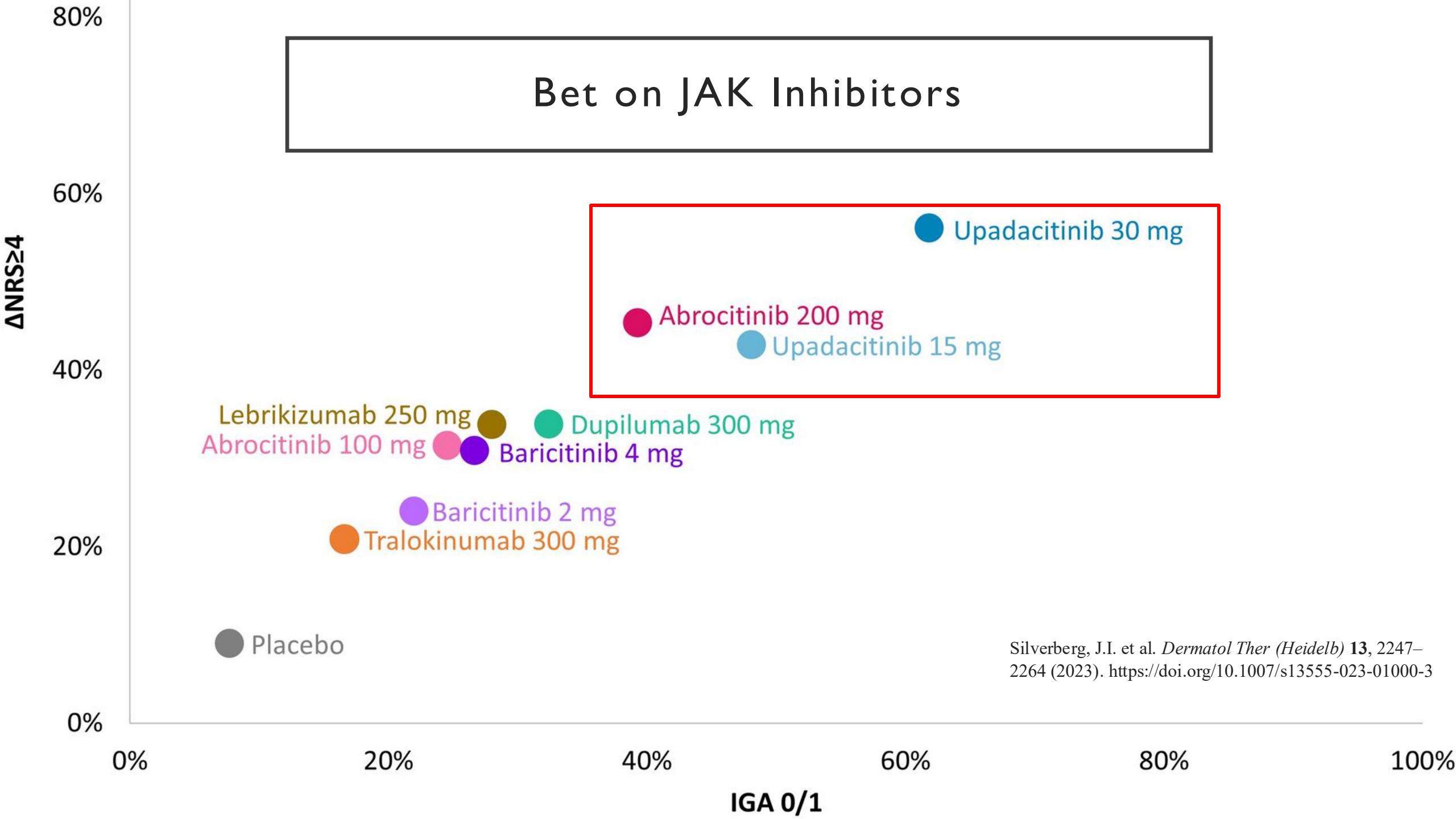
FDA, Food and Drug Administration; JAK, Janus kinase; QoL, quality of life; TCS, topical corticosteroid

Davis DMR, et al. *J Am Acad Dermatol.* 2025;93(3):745.e1-745.e7.


HOW DO I CHOOSE?

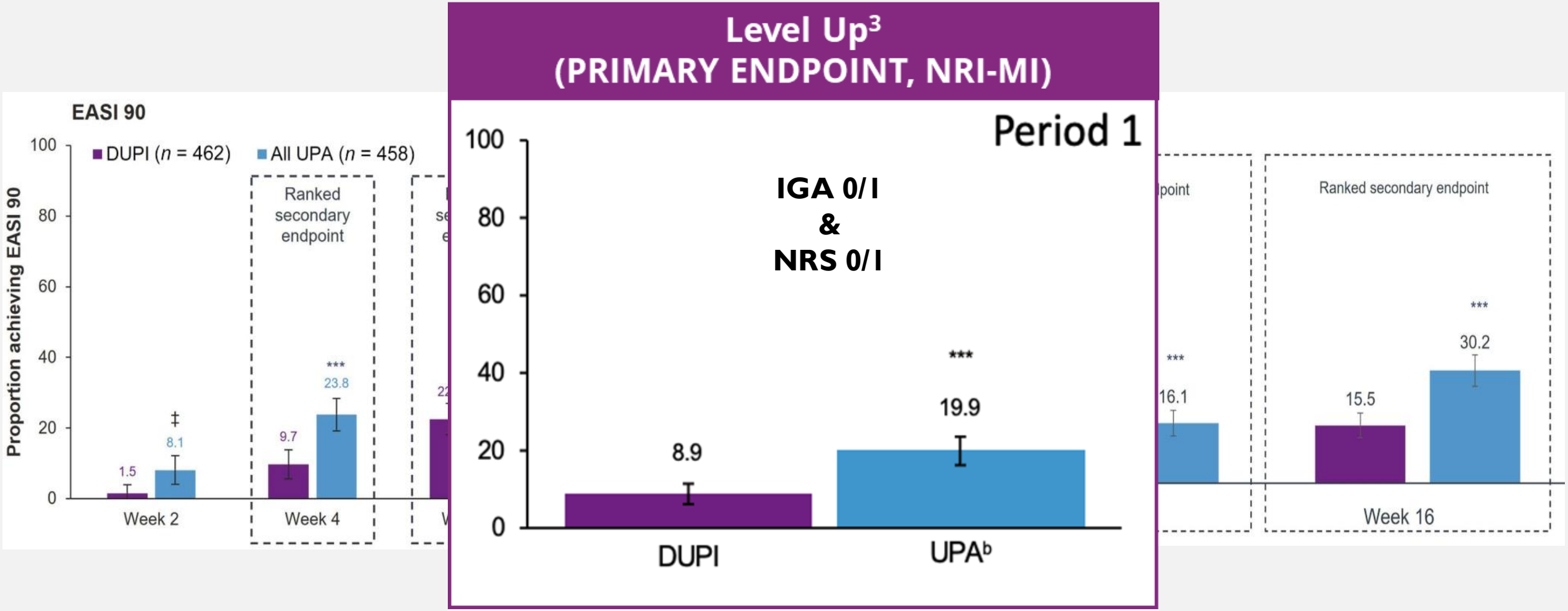
PLAY THE ODDS

Bet on JAK Inhibitors



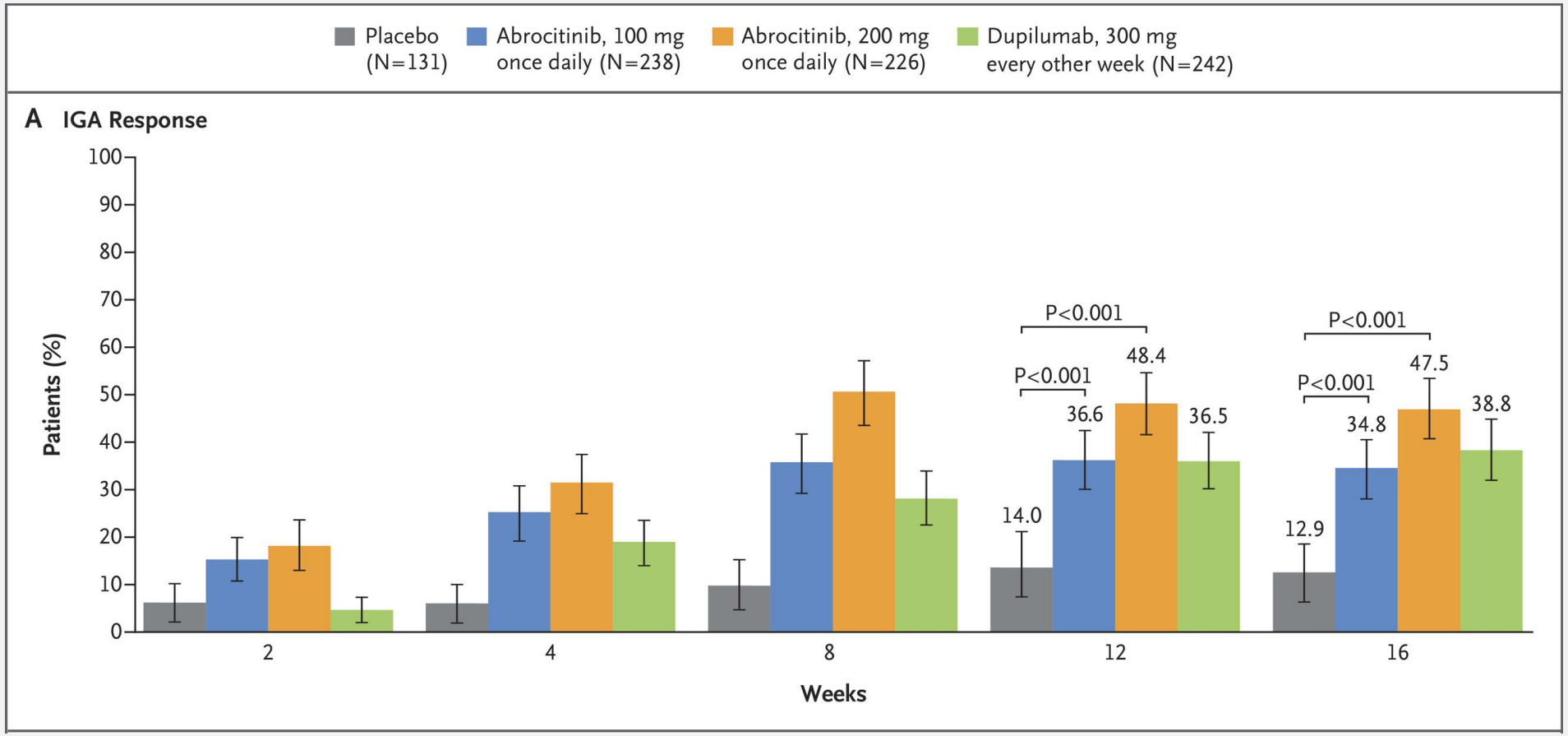
Silverberg, J.I. et al. *Dermatol Ther (Heidelb)* **13**, 2247–2264 (2023). https://doi.org/10.1007/s13555-023-01000-3

LEVEL UP:
Upadacitinib Versus Dupilumab



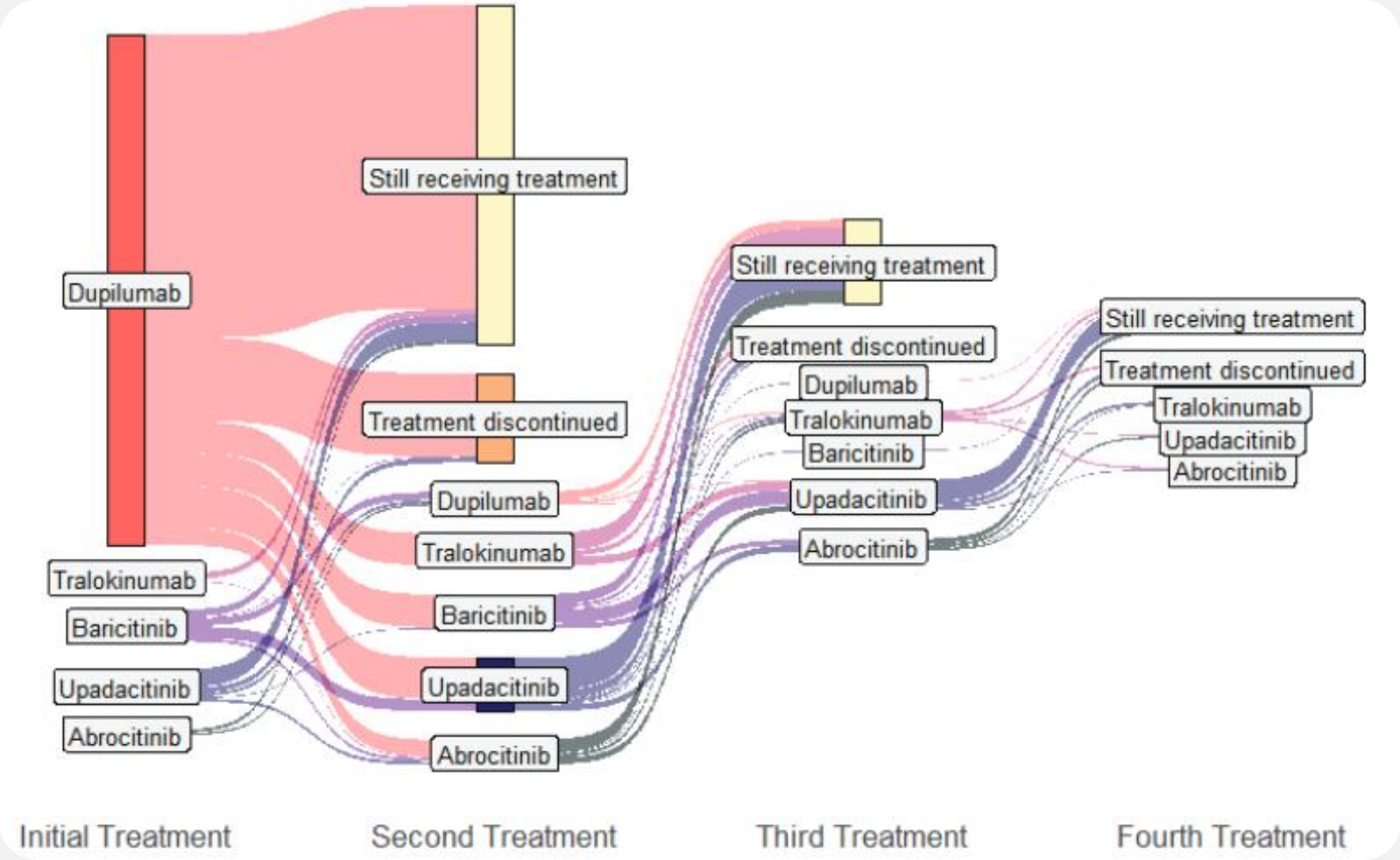
Silverberg JI, et al. *Br J Dermatol*. 2024 Dec 23;192(1):36-45

JADE COMPARE:
Abrocitinib Versus Dupilumab



Bieber T, Simpson EL, Silverberg JI, et al. *N Engl J Med.* 2021;384(12):1101-1112.

REAL WORLD AD TREATMENT PATTERNS



~ 90% of patients were initially treated with Th2-targeted therapy

41% of Th2 targeted treatment courses were discontinued, mainly due to ineffectiveness

<30% of patients received a JAK inhibitor at any treatment sequence

Schlosser, AR, et al. Acta Derm VenerEol 2025

WHY?

- Two Birds, One Stone?
- Perceived Safety Advantage?
- No Lab Monitoring?
- Difficulty Discussing Jaki's?

Uncontrolled Moderate-to-Severe

Atopic Dermatitis

For Patients **Ages 6+ Months**

Chronic Spontaneous Urticaria

For Patients **Ages 12+ Years** Who Remain Symptomatic Despite H1 Antihistamine Treatmen

Limitations of Use: [redacted] is not indicated for other forms of urticaria.

Prurigo Nodularis

For Patients **Ages 18+ Years**

Bullous Pemphigoid

For Patients **Ages 18+ Years**

Add-on Maintenance for Moderate-to-Severe

Asthma

For Patients **Ages 6+ Years** With an Eosinophilic Phenotype or OCS Dependent

Limitations of Use: [redacted] is not indicated for the relief of acute bronchospasm or status asthmaticus.

Add-on Maintenance for Inadequately Controlled

Chronic Obstructive Pulmonary Disease

For Patients **Ages 18+ Years** With an Eosinophilic Phenotype

Limitations of Use: [redacted]T is not indicated for the relief of acute bronchospasm.

Add-on Maintenance for Inadequately Controlled

Chronic Rhinosinusitis with Nasal Polyps

For Patients **Ages 12+ Years**

Eosinophilic Esophagitis

For Patients **Ages 1+ Years**, Weighing at Least 15 kg

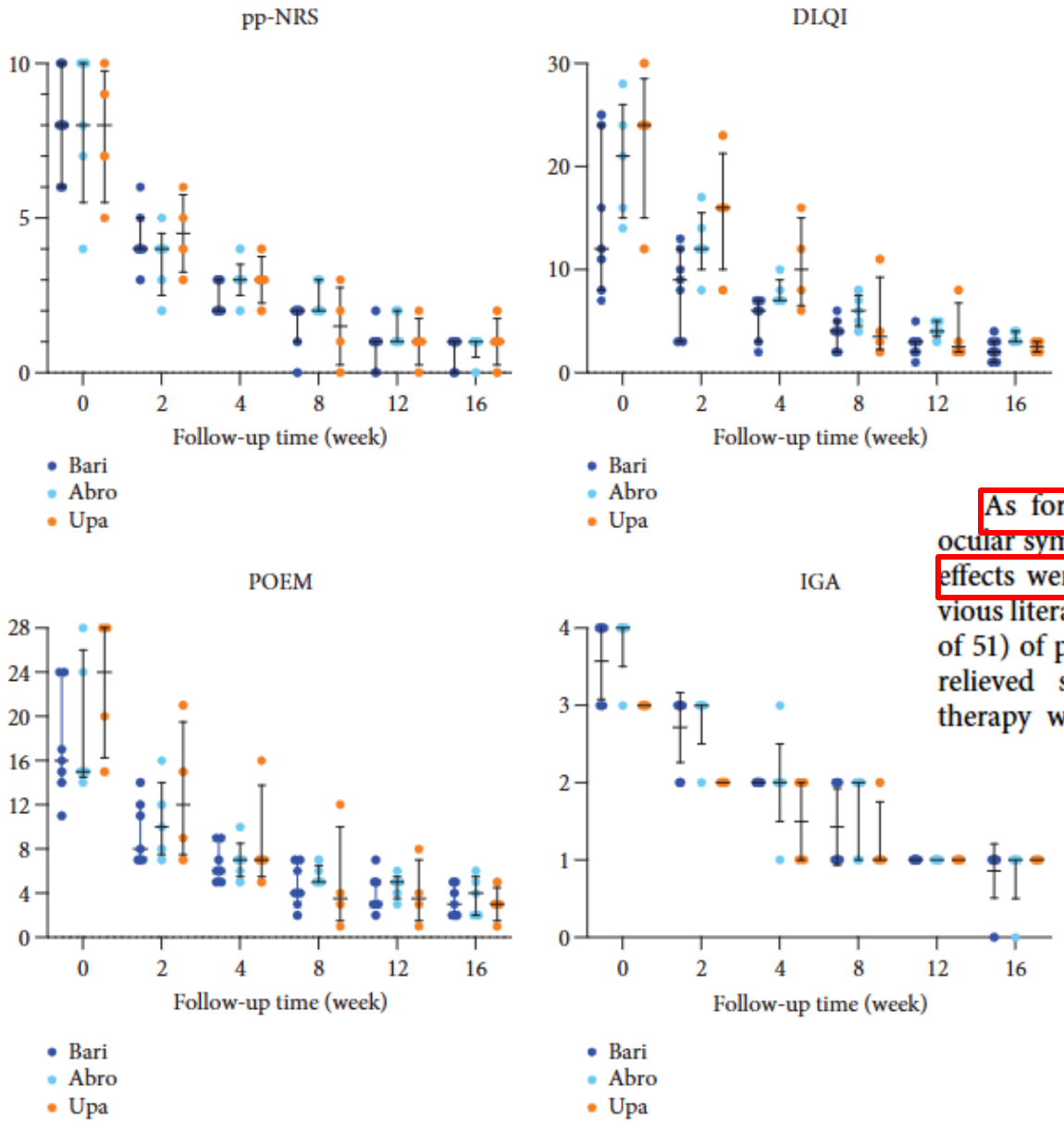
Research Article | Open Access

Dupilumab in Combination With JAK Inhibitor for Refractory Moderate-to-Severe Atopic Dermatitis

Xiaoting Song, Bo Liu, Chengyue Peng, Yen Tan, Zuotao Zhao

First published: 13 December 2024 | https://doi.org/10.1155/dth/9515524 | VIEW METRICS

OK TO ADD A JAKI



As for safety profile, only one patient reported mild ocular symptom in our patient. No significant systemic side effects were observed, which was consistent with the previous literature [7, 9, 10]. Yang et al. [7] observed only 8% (4 of 51) of patients developed mild conjunctivitis, which was relieved spontaneously. All the reported combination therapy was short term (2–6 months), which showed an

Figure 2: The scores of pp-NRS, DLQI, POEM, and IGA through 16 weeks Bari, dupilumab in combination with baricitinib 2 mg daily ($n = 7$); Abro, dupilumab in combination with abrocitinib 100 mg daily ($n = 5$); Upa, dupilumab in combination with upadacitinib 15 mg daily ($n = 4$); pp-NRS, peak pruritus numeric rating scale; DLQI, dermatology life quality index; POEM, patient-oriented eczema measure; IGA, investigator global assessment. The pp-NRS, DLQI, POEM, and IGA scores at each time point were shown as medians and interquartile range. Compared with the scores at baseline, the scores at week 2, 4, 8, 12, and 16 were significantly improved ($p < 0.05$, Wilcoxon matched-pair signed-rank test).

JAK-inhibitors as rescue therapy in dupilumab-refractory severe atopic dermatitis: A case series of 6 patients

Neda Shahriari, MD,[a] Bruce Strober, MD, PhD,[b,c] and Mona Shahriari, MD[b,c]

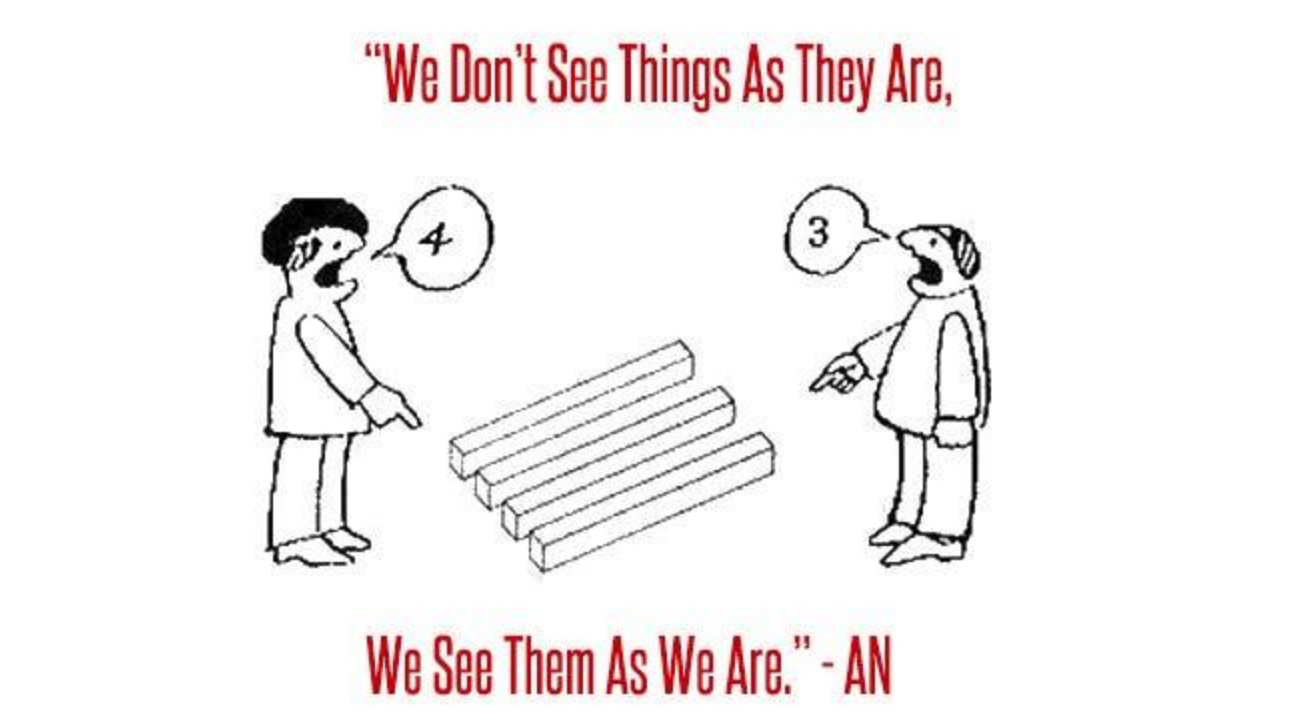
Table I. Patient with atopic dermatitis characteristics and clinical response to combination treatment with dupilumab and a JAK-I

Pt	Age, sex, ethnicity	Comorbidities	Baseline BSA involvement (%)	Baseline IGA	Duration of treatment on dupilumab (300 mg QOW) until flare	IGA preflare	BSA during flare (%)	IGA during flare	Post-JAK-I BSA (%), after 4 wks	Post-JAK-I IGA, after 4 wks	Duration of JAK-I treatment until discontinuation	JAK-I used
1	62, Male, White	HTN CVD with stent placement, no history of clotting	30%	4	6 mo	1	10%	3	2	1	6 mo	Tofacitinib 5 mg daily
2	19, Male, Indian	None	10%	3	8 mo	0	3%	2	0	0	4 mo	Upadacitinib 15 mg daily
3	22, Male, White	None	40%	4	6 mo	1	15%	4	4	1	3 mo	Tofacitinib 5 mg twice daily
4	48, Female, White	CVA	20%	3	7 mo	1	6%	3	1	1	2 mo	Upadacitinib 15 mg daily
5	83, Female, White	HTN, CKD, HLD	40%	4	1.5 y	1	20%	4	1	1	2 mo	Upadacitinib 15 mg daily
6	56, Female, White	None	15%	3	6 mo	0	10%	3	0	0	6 mo	Upadacitinib 15 mg daily

BSA, Body surface area; *CKD*, chronic kidney disease; *CVA*, cerebrovascular accident; *CVD*, cardiovascular disease; *HLD*, hyperlipidemia; *HTN*, hypertension; *IGA*, investigator's global assessment; *Pt*, patient.

Shahriari N, Strober B, Shahriari M. JAAD Case Rep. 2023 Feb 4;33:81-83. doi: 10.1016/j.jdcr.2023.01.020. PMID: 36873051; PMCID: PMC9982443.

PERCEIVED SAFETY ADVANTAGE



5-Year Safety of Oral JAK Inhibitors in Moderate to Severe Atopic Dermatitis

	AD: Phase 3 Long-term Measure Up 1/Measure Up 2/AD UP (Up to 5 yrs)		AD Phase 3 Long-term JADE MONO-1,2; JADE TEEN, JADE DARE, JAKE COMPARE, JADE EXTENDE, JAGE REGIMEN (Up to 4 years)	
	UPA 15 mg QD[1] (N=1337)	UPA 30 mg QD[1] (N=1346)	Abro 100 mg QD[2] (N=1023)	Abro 200 mg QD[2] (N=1981)
	Events Per 100 Patient Years (E/100 PY)			
Serious infections	2.2	2.6	2.2	2.7
Eczema herpeticum	1.5	2.0	1.6	0.9
Active tuberculosis	<0.1	<0.1	0	0.04
Herpes zoster	3.1	5.5	2.1	4.7
NMSC[a]	0.4	0.3	0.4	0.1
Adverse events leading to death	<0.1	<0.1	0.1	0.2

[a]Rates shown are n/100 PY=number of subjects with at least one event per 100 PY

AD, atopic dermatitis; MACE, major adverse cardiovascular event; NMSC, non-melanoma skin cancer; PY, patient year; TB, tuberculosis; UPA, Upadacitinib; VTE, venous thromboembolic event.

Bunick C et al. *Br J Dermatol*. 2024;190(Suppl 2):ii35-6.; Simpson EL, et al. *Am J Clin Dermatol*. 2024;25(4):639-654.

Incidence Rates of Malignancy, MACE, and VTE Reflect Background Rates in AD Population

Incidence rate per 100 PY (95% CI)	Upadacitinib 15 mg QD n=1,337 (PY=3,823)[1]	Upadacitinib 30 mg QD n=1,346 (PY=4,077)[1]	Abrocitinib 100 mg QD n=1,023 (PY=1,507)[2]	Abrocitinib 200 mg QD n=1,981 (PY=2,173)[2]	AD general population
Malignancy[a], excluding NMSC	0.3 (0.1, 0.5)	0.4 (0.2, 0.7)	0.2 (0.0, 0.4)	0.3 (0.2, 0.6)	0.33 (0.30, 0.36)[c 3] [N=66,258]
Adjudicated MACE[b]	0.2 (0.1, 0.3)	<0.1 (0.0, 0.2)	0.3 (0.1, 0.7)	0.3 (0.1, 0.5)	0.63 (0.51, 0.78)[d 4] [N=2,527]
Adjudicated VTE[b]	0.1 (0.0, 0.3)	0.1 (0.1, 0.3)	0.1 (0.0, 0.3)	0.3 (0.1, 0.5)	0.31 (0.29, 0.34)[e 5] [N=113,927]

[a]Excluding NMSC; [b]Adjudicated; [c]N=66,258, UK patients of all ages with mild-to-severe AD, patients with AD were identified by the presence of at least 2 correlative codes of AD, or by the presence of AD codes entered by a specialist; [d]N=2,527, all Danish citizens 15 years of age or older with moderate-to-severe AD, moderate/severe AD was identified using systemic therapy for AD as a proxy measure including azathioprine, methotrexate, cyclosporine, and/or mycophenolate mofetil; [e]N=113,927, US adults (≥18 years of age) with moderate-to-severe AD, moderate-to-severe AD was identified using prescription dispensing as a proxy measure, including high- or ultra-high-potency topical corticosteroids, systemic corticosteroids, systemic immunosuppressants, phototherapies, or biologics used at any time after AD diagnosis (including index date).

AD, atopic dermatitis; CI, confidence interval; PY, patient years; NMSC, non-melanoma skin cancer; QD, once daily

1. Bunick C, et al. *Revolutionizing Atopic Dermatitis (RAD),* Virtual, 10 December 2023. Oral; 2. Simpson EL, et al. *Am J Clin Dermatol* 2024;25(4):639–654; 3. Arana A, et al. *BJD*. 2010;163:1036–43; 4. Anderson YMF, et al. *J Allergy Clin Immunol*. 2016;138(1):310–12; 5. Meyers KJ, et al. *Dermatol Ther (Heidelb)*. 2021;11:1041–52.

Cross-Trial Long-Term Safety Data

	Oral JAK-1 Selective Inhibitor	
AESI	**UPA 15 mg (≤5 yrs) N=1337; PY=3823.0 (IR per 100 PY)**	**UPA 30 mg (≤5 yrs) N=1346; PY=4076.9 (IR per 100 PY)**
MACE	**0.2** (0.1–0.3)	**<0.1** (0.0–0.2)
VTE (combined)	**0.1** (0.0–0.3)	**0.1** (0.1–0.3)
Pulmonary embolism (PE)	(included in VTE)	(included in VTE)
Deep-vein thrombosis (DVT)	(included in VTE)	(included in VTE)
Malignancy (excluding NMSC)	**0.3** (0.1–0.5)	**0.4** (0.2–0.7)
Non-melanoma skin cancer (NMSC)	**0.4** (0.3–0.7)	**0.3** (0.2–0.6)

Do these events happen in patients treated with biologics?

IRs are exposure-adjusted incidence rates per 100 patient-years. 95% CIs shown when available from the source datasets. † Tralokinumab VTE is derived as PE + DVT over total PYE; CI by exact Poisson.

- Bunick C, Chovatiya R, Guttman E, Shahriari M, Boguniewicz M, Gao X, Greiwe J, Blauvelt A, Schuttelaar ML, Irvine AD, Levy GF. 533-Long-term 5-year safety of upadacitinib in moderate-to-severe atopic dermatitis: an integrated analysis including over 7000 patient-years of exposure. British Journal of Dermatology. 2024 Feb;190(Supplement_2):ii35-6.
- Reich K, Langley RG, Salvador JF, Staumont-Sallé D, Costanzo A, Pink AE, Paller AS, Katoh N, Wollenberg A, Warren RB, Blauvelt A. Safety of tralokinumab in patients with moderate-to-severe atopic dermatitis followed for up to 4.5 years: an integrated analysis of 8 clinical trials. British Journal of Dermatology. 2025 Aug 29:ljaf309.

Cross-Trial Long-Term Safety Data

	Oral JAK-1 Selective Inhibitor		IL-13 Injectable Biologic
AESI	**UPA 15 mg (≤5 yrs) N=1337; PY=3823.0 (IR per 100 PY)**	**UPA 30 mg (≤5 yrs) N=1346; PY=4076.9 (IR per 100 PY)**	**Tralokinumab (≤4.5 yrs) N=2693; PYE=5320.2 (IR per 100 PYE)**
MACE	**0.2** (0.1–0.3)	**<0.1** (0.0–0.2)	**0.25** (0.15–0.43)
VTE (combined)	**0.1** (0.0–0.3)	**0.1** (0.1–0.3)	**0.06** (0.01–0.16)†
Pulmonary embolism (PE)	(included in VTE)	(included in VTE)	0.04 (0.01–0.15)
Deep-vein thrombosis (DVT)	(included in VTE)	(included in VTE)	0.02 (0.00–0.14)
Malignancy (excluding NMSC)	**0.3** (0.1–0.5)	**0.4** (0.2–0.7)	**0.35** (0.22–0.54)
Non-melanoma skin cancer (NMSC)	**0.4** (0.3–0.7)	**0.3** (0.2–0.6)	**0.42** (0.27–0.64)

IRs are exposure-adjusted incidence rates per 100 patient-years. 95% CIs shown when available from the source datasets. † Tralokinumab VTE is derived as PE + DVT over total PYE; CI by exact Poisson.

- Bunick C, Chovatiya R, Guttman E, Shahriari M, Boguniewicz M, Gao X, Greiwe J, Blauvelt A, Schuttelaar ML, Irvine AD, Levy GF. 533-Long-term 5-year safety of upadacitinib in moderate-to-severe atopic dermatitis: an integrated analysis including over 7000 patient-years of exposure. British Journal of Dermatology. 2024 Feb;190(Supplement_2):ii35-6.
- Reich K, Langley RG, Salvador JF, Staumont-Sallé D, Costanzo A, Pink AE, Paller AS, Katoh N, Wollenberg A, Warren RB, Blauvelt A. Safety of tralokinumab in patients with moderate-to-severe atopic dermatitis followed for up to 4.5 years: an integrated analysis of 8 clinical trials. British Journal of Dermatology. 2025 Aug 29:ljaf309.

LAB MONITORING

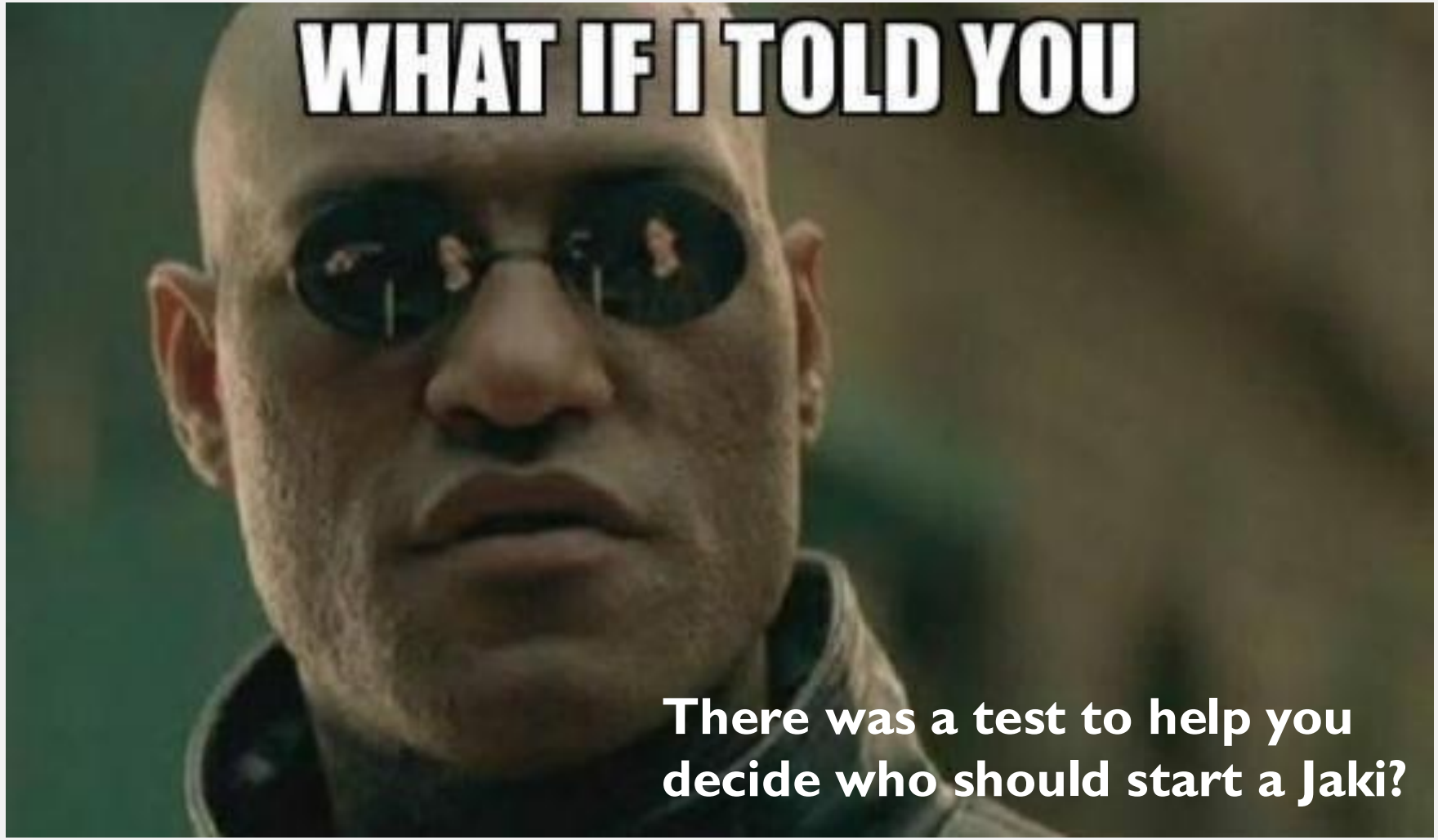
Table 1 Laboratory and vaccine monitoring recommendations for Janus kinase inhibitor treatment of atopic dermatitis

	Pretreatment	4–12 weeks after initiation[a]	Every 3–6 months
TB screening[b]	×		
Pregnancy[c]	×	×	×
HBV[d]/HCV	×		
HIV[e]	×		
CBC with differential	×	×	×
CMP	×	×	×
HDL cholesterol, LDL-cholesterol, TG	×	×	Annually
Vaccination	Comments		
Inactivated pneumococcal vaccine	Recommended for patients aged> 18 years		
Influenza	Recommended annually		
S[illegible]ix – recombinant zoster vaccine	Recommended for patients aged> 18 years; two doses separated by 2–6 months		

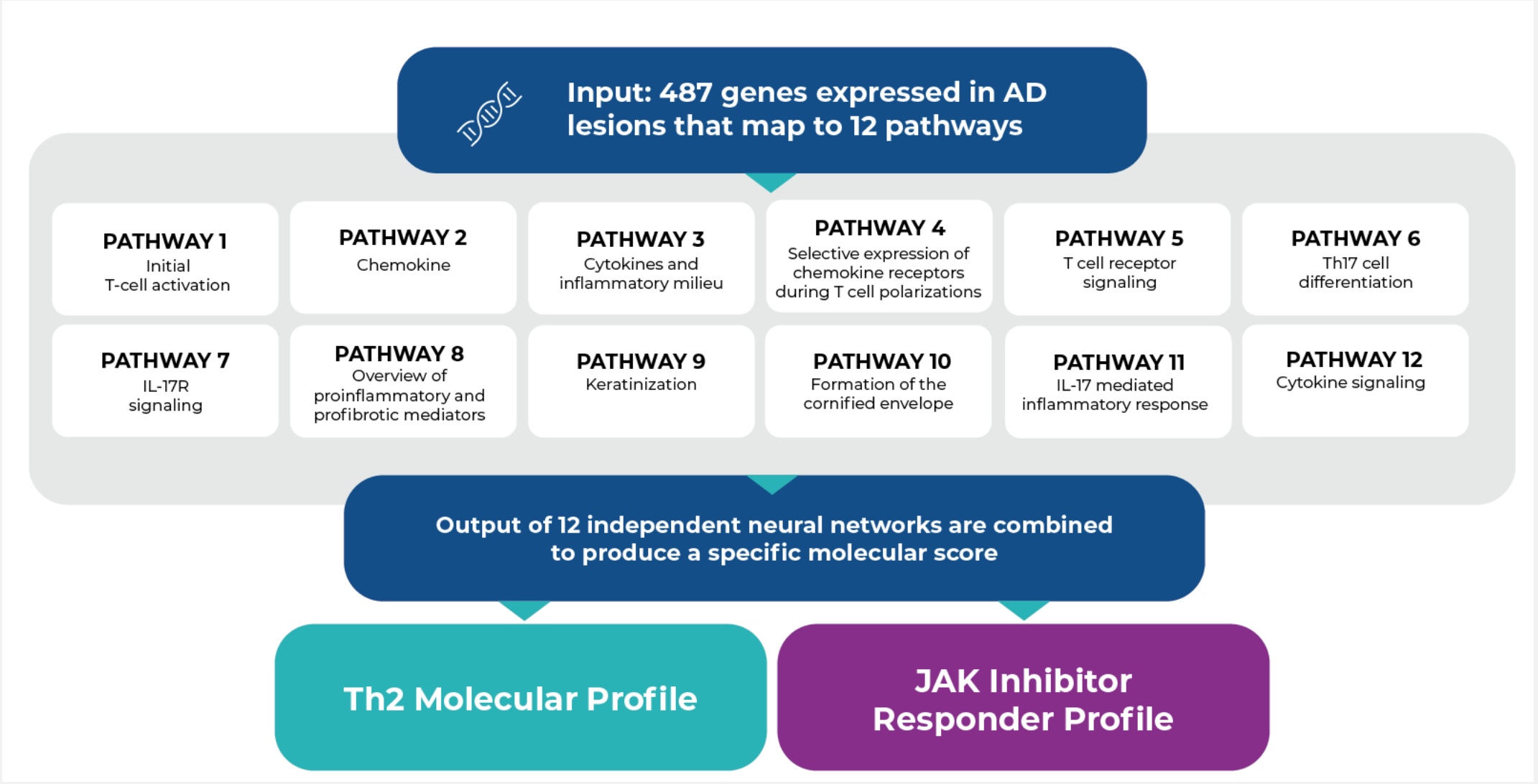
A practical guide to using oral Janus kinase inhibitors for atopic dermatitis from the International Eczema Council. Br J Dermatol. 2024 Dec 23;192(1):135-143. doi: 10.1093/bjd/ljae342. PMID: 39250758.

PERFECT YOUR PITCH

- So you have tough eczema…
- Would you like something to help level the playing field?
- The most effective medicines are pills that you take once daily – they are called Jak inhibitors
- They work fast and provide a lot of relief
- When we use Jak inhibitors to treat eczema, they are safe, but we have to check a few things before we start
- If you google them…
- But when we use them to treat eczema, we don't see those scary events.

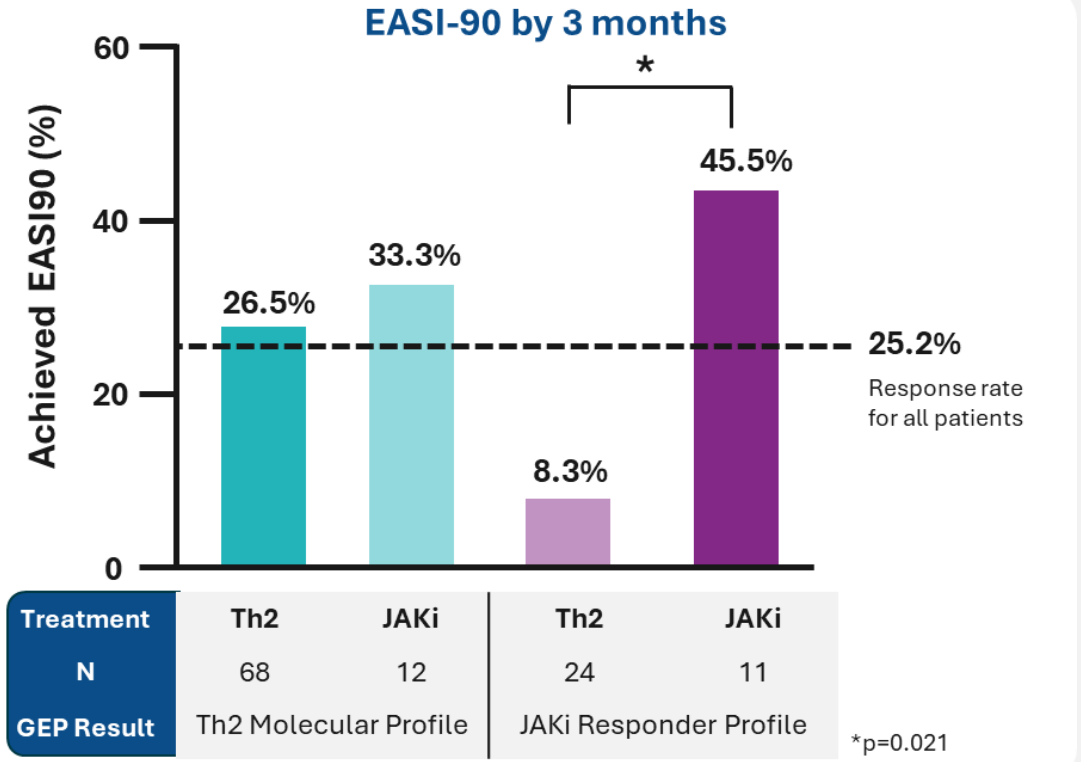

WHAT IF I TOLD YOU
There was a test to help you decide who should start a Jaki?

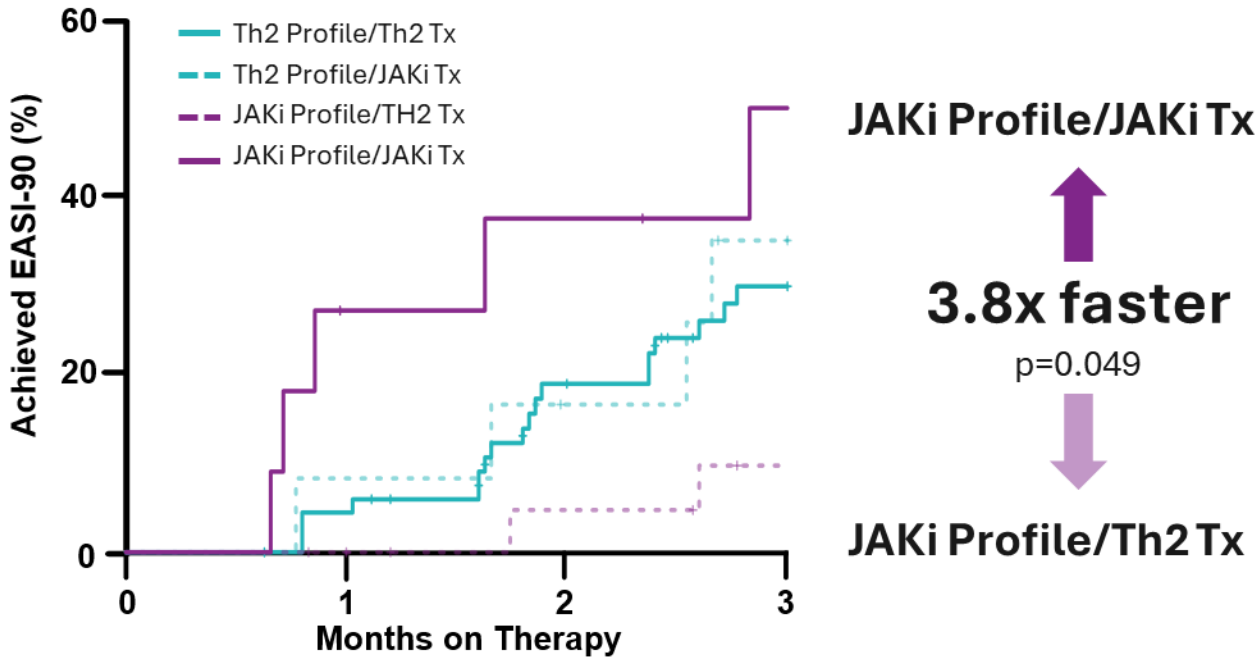
487-GEP MEASURES KEY PATHWAYS DRIVING ATOPIC DERMATITIS



Adapted from Silverberg J, et al. Fall Clinical Dermatology Conference, 2025. Data on file.

WHY IT MATTERS

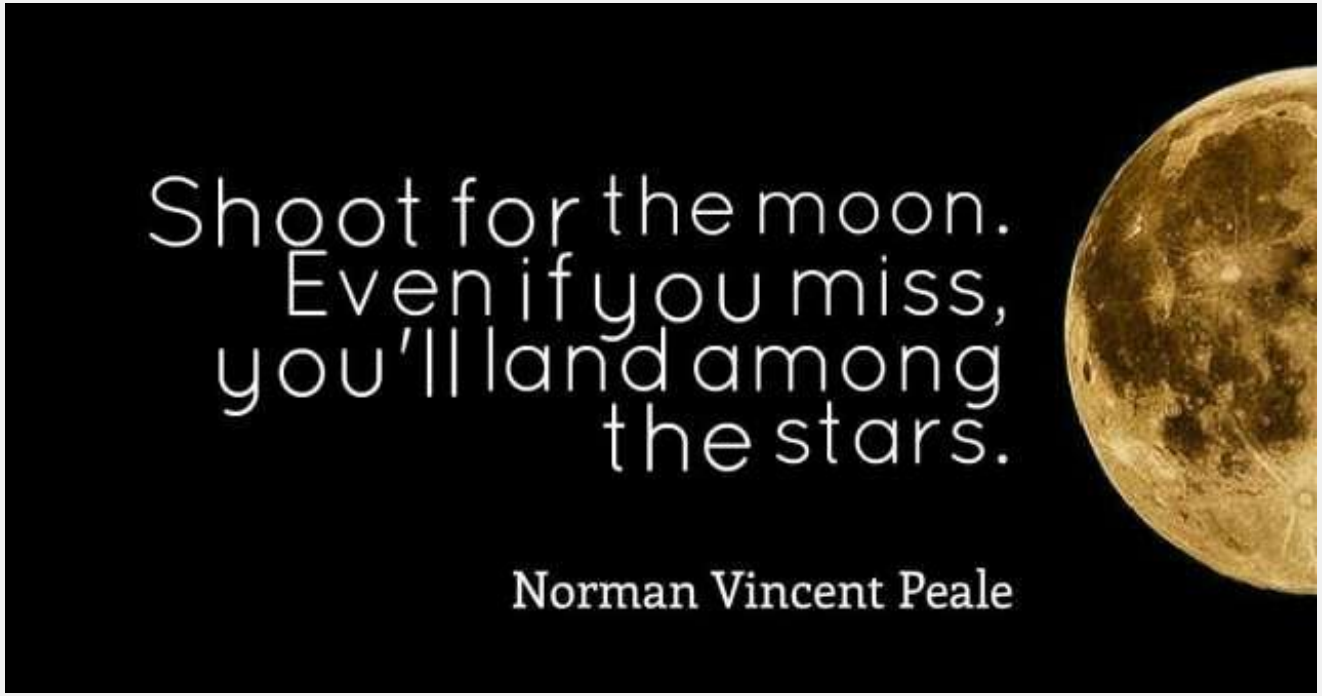


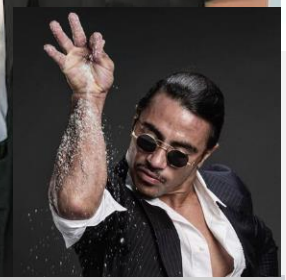


Adapted from Silverberg J, et al. Fall Clinical Dermatology Conference, 2025. Data on file.

SUMMARY

- Aim High
- Overcome therapeutic inertia
- Embrace advanced therapeutics and molecular tools





LAS VEGAS DERMATOLOGY
for a healthier & more beautiful life

Gentlemen
of Dermatology Society

The DermBros

THANK YOU FOR YOUR ATTENTION!

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