Everything You Need to Know to Prescribe JAK Inhibitors

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Updated 4/6/24

JAK Inhibitors

- Boxed warnings: what are the real risks?
- For what conditions do they work?
- What are they?
- Role in atopic dermatitis
- Role in psoriasis
- Role in alopecia areata
- Role in vitiligo
- What could go wrong?
- Baseline monitoring, followup monitoring

U.S. FOOD & DRUG ADMINISTRATION

FDA requires warnings about increased risk of serious heart-related events, cancer, blood clots, and death for JAK inhibitors that treat certain chronic inflammatory conditions

Approved uses also being limited to certain patients

IBUPROFEN

BOXED WARNING
Cardiovascular Risk

NSAIDs may cause an increased risk of serious cardiovasculararthrombotic events, myocardial infarction, and stroke,which can be fatal. This risk may increase with duration ofuse. Patients with cardiovascular disease or risk factors forcardiovascular disease may be at greater risk (See WARNINGS).
IBU tablets are contraindicated for treatment of peri-operativepain in the setting of coronary artery bypass graft (CABG)surgery (See WARNINGS).
Gastrointestinal Risk

NSAIDS cause an increased risk of serious gastrointestinaladverse events including bleeding, ulceration, and perforationof the stomach or intestines, which can be fatal. These eventscan occur at any time during use and without warning symptoms.Elderly patients are at greater risk for serious gastrointestinalevents. (See WARNINGS).

Risk of acute myocardial infarction with NSAIDs in real world use: bayesian meta-analysis of individual patient data.
Bally M, et al
BMJ. 2017 May 9;357:j1909.

With use for one to seven days the probability of increased myocardial infarction risk

- 92% for celecoxib, 97% for ibuprofen, and 99% for diclofenac, naproxen, and rofecoxib.

- corresponding odds ratios for acute MIs(95% credible intervals) were 1.24 (0.91 to 1.82) for celecoxib, 1.48 (1.00 to 2.26) for ibuprofen, 1.50 (1.06 to 2.04) for diclofenac, 1.53 (1.07 to 2.33) for naproxen, and 1.58 (1.07 to 2.17) for rofecoxib.

- Treatment with the JAK inhibitor was associated with an increased risk for major adverse cardiac events (MACE), including MI, cardiovascular death, and stroke (HR 1.33, 95% CI 0.91-1.94)

FDA Slaps Restrictions on JAK Inhibitors Over Serious Safety ...https://www.medpagetoday.com › Rheumatology › Arthitis

What are the incidence rates for serious adverse events? (Events per 100 patient-years)					
Drug	Malignancy (Ex-NMSC)	NMSC	MACE	VTE	Ref
Upadacitinib (15mg)	0.2	0.4	0.1	0.1	(1)
Upadacitinib (30mg)	0.5	0.4	0.0	0.1	(1)
Abrocitinib (100mg)	0.2	0.6	0.6	0.0	(2)
Abrocitinib (200mg)	0.2	0.4	0.2	0.4	(2)
Methotrexate[a]	0.5	0.3	0.5	0.5	(3)
Cyclosporine	0.6[b]	0.5[b]		DNF	(4)
			2.8[c]		(5)
Systemic Steroids	4.3[d]	3.9[d]			(6)
			7.6[e]		(7)
				0.02[f]	(8)

JAK Inhibitor Safety Compared to Traditional Systemic Immunosuppressive Therapies
Stefano G. Daniele, Christopher G. Bunick Presented at Fallclinical22

EMA recommends measures to minimize risk of serious side effects with JAK inhibitors

- Serious side effects associated with JAK inhibitors include cardiovascular conditions, blood clots, cancer, and serious infections

Recommended use in the following patients
only if no suitable treatment alternatives are available:

- *Patients aged ≥65 years*
- *Patients increased risk of major cardiovascular problems (eg, heart attack or stroke)*
- *Current smokers (or those who have done so for a long time in the past)*
- *Patients at increased risk of cancer*

*Recommended use in the following patients **with caution:***

- *Patients with risk factors for blood clots in the lungs and in deep veins (VTE) other than those listed*

*The **doses should be reduced** in some patient groups who may be at risk of**:***

- *VTE*
- *Cancer*
- *Major cardiovascular problems*

EMA press release, October 28, 2022. Available at https://www.ema.europa.eu/en/news/ema-recommends-measures-minimise-risk-serious-side-effects-janus-kinase-inhibitors-chronic

Which drugs have boxed safety warnings?

Drug	Boxed Warning?	Specific Warning
Upadacitinib	Yes	MACE, malignancies, VTE, infection
Abrocitinib	Yes	MACE, malignancies, VTE, infection
Methotrexate	Yes	Fetal death, teratogenicity, malignancy, infection, liver toxicity, pulmonary toxicity, hemorrhagic enteritis, tumor lysis syndrome, severe adverse cutaneous reactions
Cyclosporine	Yes	Malignancy, infection, hypertension, renal toxicity
Systemic Steroids	No	N/A

JAK Inhibitor Safety Compared to Traditional Systemic Immunosuppressive Therapies
Stefano G. Daniele, Christopher G. Bunick Presented at Fallclinical22

SCHER RK. TRIAMCINOLONE ACETONIDE INTRAMUSCULARLY: EFFECTIVE LONG-ACTING STEROID THERAPY IN DERMATOLOGIC DISORDERS.
J Am Geriatr Soc. 1964 Apr;12:328-36.

Rowland K. Short-term use of oral corticosteroids was linked to increased risk for sepsis, VTE, and fractures.
Ann Intern Med. 2017;167:JC20.

- **median steroid use 6 days (327,452 users vs 1,221,493 nonusers)**
- **IRR over 5-30/31-90 days:**
  - **-sepsis: 5.30 / 2.91**
  - **-VTE: 3.33 / 1.44**
  - **-fractures: 1.87 / 2.07**

Oral Glucocorticoids and Incident Treatment of Diabetes Mellitus, Hypertension, and Venous Thromboembolism in Children

Horton, D. B., Xie, F., Chen, L., et. al.

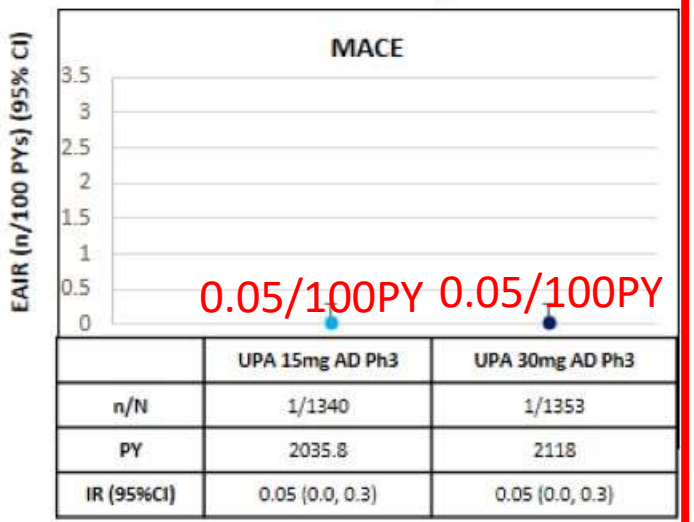
American Journal of Epidemiology, kwaa197, Sept. 2020

Advance online publication.

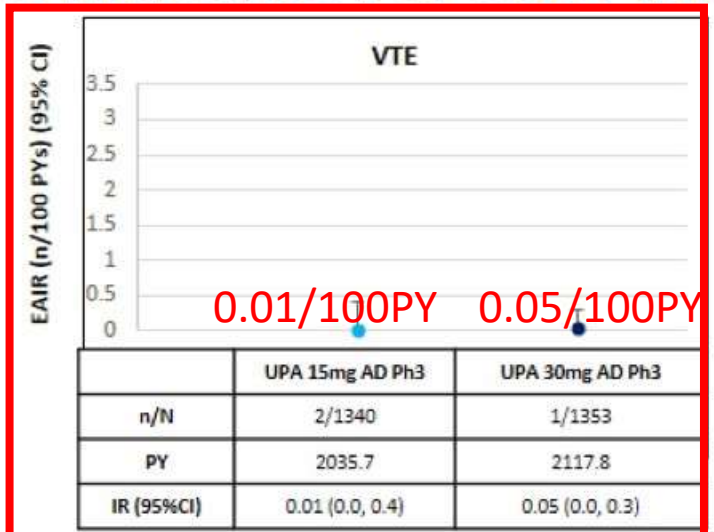
high-dose glucocorticoids:

- diabetes mellitus HR:5.93 (95%CI 3.94, 8.91]
- hypertension HR:19.13 [95% CI 15.43, 23.73]
- VTE HR:16.16 [95% CI 8.94, 29.22]).

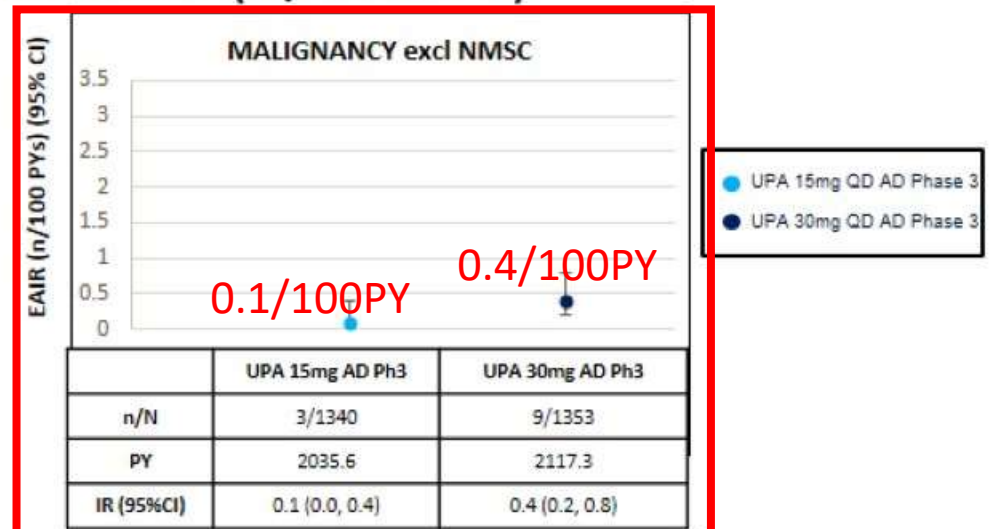
Phase 3 Long Term Treatment Emergent AE of Special Interest in AD Patients Treated with Upadacitinib: Incidence Per 100 Patient Years (n/100 PY)



	UPA 15mg AD Ph3	UPA 30mg AD Ph3
n/N	1/1340	1/1353
PY	2035.8	2118
IR (95%CI)	0.05 (0.0, 0.3)	0.05 (0.0, 0.3)



	UPA 15mg AD Ph3	UPA 30mg AD Ph3
n/N	2/1340	1/1353
PY	2035.7	2117.8
IR (95%CI)	0.01 (0.0, 0.4)	0.05 (0.0, 0.3)



	UPA 15mg AD Ph3	UPA 30mg AD Ph3
n/N	3/1340	9/1353
PY	2035.6	2117.3
IR (95%CI)	0.1 (0.0, 0.4)	0.4 (0.2, 0.8)

AbbVie DOF ABVRRTI74288

Real World Incidence Rate Estimates: MACE, VTE, and Malignancy excluding NMSC in AD & General Population

LIMITATIONS. Results should be interpreted with caution and cross-study comparison is not advised. Variability across data sources exists and observational data may potentially overestimate risk as the results may be influenced by confounding factors including, but not limited to: Outcomes as defined by diagnostic codes, may be subject to measurement error (limited sensitivity or specificity) vs RCT case adjudication; Patient heterogeneity (age/gender/geographical location); Variability in the distribution of risk factors (comorbidities and medication use)

Outcome	Study	Treatments/Patient Population	Incidence Rate per 100PY (95% CI)
MACE (Composite Endpoint: MI/Stroke/CV death)	Population based study – Danish nationwide registers (1997-2011)[1]	All Danish citizens aged 15 yrs or older with mod/sev AD[a] (N=2527)	0.63 (0.51-0.78)
VTE (PE, DVT, or other venous thrombosis)	US administrative claims database (IBM Watson MarketScan) (2012-2017)[2]	Adults (≥18 years old) with mod/sev AD[b] (N=113,927)	0.31 (0.29, 0.34
Malignancy excluding NMSC	Retrospective cohort study in The Health Improvement Network (THIN) Database.(UK 1992-2006)[3]	Patients of all ages with AD (mild-severe)[c] (N=66,258)	0.33 (0.30, 0.36)
	Surveillance, Epidemiology, and End Results (SEER) Program 5 Year-Age Adjusted to the 2000 US Std Population (2015-2019)[4]	General population	0.45 (0.45, 0.45)

a. Moderate/Severe AD was identified using systemic therapy for AD as a proxy measure including azathioprine, methotrexate, cyclosporine, and/or mycophenolate mofetil b. 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). c. Patients with AD were identified by the presence of at least two correlative codes of AD, or by the presence of AD codes entered by a specialist

1. Anderson, Y. et al. J Allergy Clin Immunol 2016; http://dx.doi.org/10.1016/j.jaci.2016.01.015 Letter to the Editor 2. Meyers, K, et al. Dermatol Ther (Heidelb) 2021; 11:1041-1052. 3. Arana, A et al. BJD 2010;163: 1036-1043.

SO WHY DID JAK INHIBITORS GET THESE BOXED WARNINGS?

ORAL SURVEILLANCE trial-Tofacitinib

- RA patients have more comorbidities
- RA patients are older
- RA patients are on concomitant meds (NSAIDs, MTX, steroids opioids)
- Included higher doses of Tofa (10 bid)
- Tofa is a pan-JAK inhibitor

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- Role in alopecia areata
- Role in vitiligo
- What could go wrong?

Tofacitinib for cutaneous and pulmonary sarcoidosis: A case series

Kerkemeyer KL, Meah N, Sinclair RD.
J Am Acad Dermatol. 2021 Feb;84(2):581-583.

Recalcitrant granuloma annulare induced by two different biologic agents resolved after Janus kinase inhibitor treatment

Ballová A, Kmečová Z, Péč J, Vorčáková K.
Dermatol Ther. 2022;35(8):e15641.

Successful treatment of ulcerative necrobiosis lipoidica with janus kinase inhibitor

Erfurt-Berge C, Sticherling M.
J Eur Acad Dermatol Venereol. 2020 Jul;34(7):e331-e333.

Phase 1 double-blind randomized safety trial of the Janus kinase inhibitor tofacitinib in systemic lupus erythematosus

Hasni SA, Gupta S, et al.

Nat Commun. 2021 Jun 7;12(1):3391.

Tofacitinib counteracts IL-6 overexpression induced by deficient autophagy: implications in Sjögren's syndrome.

Barrera MJ, et
Rheumatology (Oxford). 2021;60(4):1951-1962.

JAK-inhibitors for dermatomyositis: A concise literature review

Paudyal A, Zheng M, Lyu L, Thapa C, Gong S, Yang Y, Lyu X.
Dermatol Ther. 2021 May;34(3):e14939.

Janus kinase inhibitors for treatment of morphea and systemic sclerosis: A literature review

McGaugh Set al

Dermatol Ther. 2022;35(6):e15437.

Full histological and clinical regression of morphea with tofacitinib

Scheinberg M, Sabbagh C, Ferreira S, Michalany N.
Clin Rheumatol. 2020;39(9):2827-2828.

A systematic review of clinical and preclinical evidences for Janus kinase inhibitors in large vessel vasculitis

Rathore U, et al
Clin Rheumatol. 2022 Jan;41:33-44.

Tofacitinib for the treatment of refractory or glucocorticoid-dependent cutaneous leukocytoclastic vasculitis.

Ma J, et al
Dermatol Ther. 2022 Aug 21:e15780.

Efficacy of Oral Ruxolitinib in a Patient with Refractory Chronic Spontaneous Urticaria

Fukunaga A, Ito M, Nishigori C.

Acta Derm Venereol. 2018;98(9):904-905.

Real-World Safety and Clinical Response of Janus Kinase Inhibitor Upadacitinib in the Treatment of Hidradenitis Suppurativa: A Retrospective Cohort Study

•Emily Kozera, Akshay Flora, John W. Frew,

•JAAD 2022, in press

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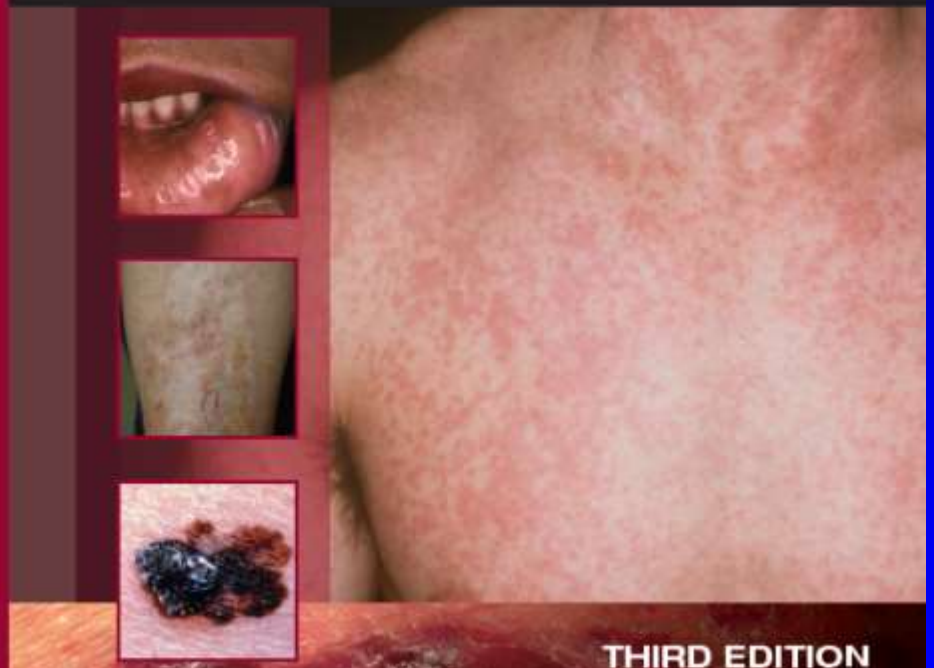
Treatment of Skin Disease

COMPREHENSIVE THERAPEUTIC STRATEGIES



THIRD EDITION

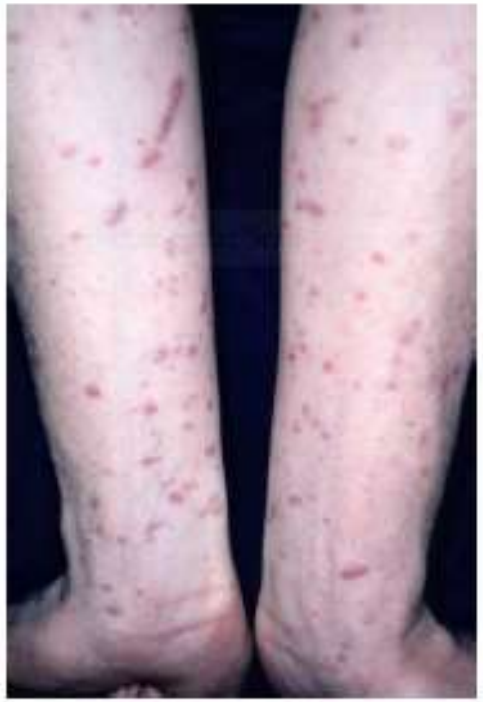
Edited by

Mark G Lebwohl • Warren R Heymann
John Berth-Jones • Ian Coulson

SAUNDERS
ELSEVIER

Lichen planus

Mark G Lebwohl



p0005 Lichen planus is a pruritic papulosquamous disease with characteristic histopathologic and clinical features. Oral erosive lichen planus, a painful erosive condition that can affect mucous membranes, is addressed in a separate chapter.

MANAGEMENT STRATEGY

p0015 Although lichen planus can resolve spontaneously, treatment is usually demanded by patients, who can be severely symptomatic. Underlying diseases such as hepatitis C or associated drugs should be sought.

p0020 In patients with localized disease, *superpotent corticosteroids* should be applied twice daily for 2–4 weeks. If the response is inadequate, *intralesional injection of corticosteroids* into localized lesions may be beneficial. Topical antipruritic agents containing *menthol, phenol, camphor, lidocaine, pramoxine* or *doxepin hydrochloride* can be useful. *Oral antihistamines* may offer limited benefit in severely pruritic patients. Sedating antihistamines are helpful at bedtime.

p0025 Traditionally, patients with extensive lichen planus have been treated with systemic corticosteroids. In recent years *oral metronidazole* has emerged as a safe and effective alternative to systemic corticosteroids: 500 mg twice daily for 20–60 days has proved effective in many patients. In patients who do not respond, *oral prednisone* 30–60 mg daily for 2–6 weeks, or its equivalent, tapered over the ensuing 2–6 weeks, is often effective. Unfortunately, even in patients who clear with systemic corticosteroids, relapses are frequent. If patients require more than two courses of high-dose systemic corticosteroids over the span of a few months, alternative treatments should be sought.

Isotretinoin in doses of 30 mg orally twice daily for 2 months has been reported to clear lichen planus in several patients, and *acitretin* 30 mg has also resulted in marked improvement or remission. In refractory cases, *psoralen and UVA (PUVA)* or narrowband UVB has demonstrated efficacy in the treatment of lichen planus. PUVA has been particularly beneficial in the lichen planus-like eruption associated with graft-versus-host disease. For severe and refractory lichen planus unresponsive to other therapies, immunosuppressive agents, including *cyclosporin, mycophenolate mofetil*, or *azathioprine*, are often effective.

SPECIFIC INVESTIGATIONS

- Serology for hepatitis B and C
- Liver function tests
- Drug history

Lichen planus and other cutaneous manifestations in chronic hepatitis C: pre- and post-interferon-based treatment prevalence vary in a cohort of patients from low hepatitis C virus endemic area. Matičić M, Poljak M, Lunder T, Rener-Sitar K, Stojanovic L. J Eur Acad Dermatol Venereol 2008; 22: 779–88.

Lichen planus was found in 2.3% of 171 hepatitis C virus-seropositive patients, compared to no cases in 171 age- and gender-matched controls.

The association between hepatitis C virus and lichen planus has been controversial, with an association reported in some studied populations but not others.

Lichen planus and chronic active hepatitis. A retrospective survey. Rebora A, Rongioletti F. Acta Dermatol Venereol 1984; 64: 52–6.

Six of 44 patients with lichen planus had abnormal liver function tests, and five of the six were found to have chronic active hepatitis on liver biopsy.

Drug-induced lichen planus. Thompson DF, Skaehill PA. Pharmacotherapy 1994; 14: 561–71.

β-Blockers, methyldopa, penicillamine, quinidine, quinine, and non-steroidal anti-inflammatory agents play a role in the development of lichen planus. There is insufficient evidence to implicate angiotensin-converting enzyme inhibitors, sulfonylurea agents, carbamazepine, gold, lithium, and other drugs.

Many drugs and chemicals have been associated with lichenoid drug eruptions, which can be difficult to distinguish from true lichen planus. In addition to those mentioned above, hepatitis B and influenza vaccinations, allopurinol, tetracyclines, furosemide, hydrochlorothiazide, isoniazid, phenytoin,, and etanercept are reported to cause lichenoid eruptions.

FIRST-LINE THERAPIES

▶ Topical corticosteroids	C
▶ Intralesional corticosteroids	D
▶ Antihistamines	C

SECOND-LINE THERAPIES

▶ Metronidazole	C
▶ Systemic corticosteroids	B
▶ Isotretinoin, acitretin	A
▶ Narrowband or broad band UVB	C
▶ PUVA	C

Ruxolitinib Cream in the Treatment of Cutaneous Lichen Planus: A Prospective, Open-Label Study. J Invest Dermatol. 2022;142:2109-2116.e4

Brumfiel CM, Patel MH, Severson KJ, Zhang N, Li X, Quillen JK, Zunich SM, Branch EL, Nelson SA, Pittelkow MR, Mangold AR.

- Total lesion count decreased by a median of 50 lesions
- *"Topical ruxolitinib was highly effective in the treatment of cutaneous LP."*

JAK inhibitors for Lichen Planus

Treatment of severe lichen planus with the JAK inhibitor tofacitinib.
J Allergy Clin Immunol. 2020; 145:1708-1710.e2.
Damsky W, Wang A, Olamiju B, Peterson D, Galan A, King B.

Treatment of Oral Erosive Lichen Planus With Upadacitinib

Balestri R, Bortolotti R, Rech G, Girardelli CR, Zorzi MG, Magnano M.

JAMA Dermatol. 2022;158:457-458.

Alleviation of erosive oral and esophageal lichen planus by the JAK1 inhibitor upadacitinib

Kooybaran NR, Petzold G, Ströbel P, Schön MP, Mössner R.

J Dtsch Dermatol Ges. 2021;19:1778-1780.

Effective treatment of oral lichen planus with the JAK inhibitor baricitinib.

Moussa A, Colla T, Morrison B, Sinclair R.

Australas J Dermatol. 2022 May;63(2):276-277

Tofacitinib for the treatment of lichen planopilaris:
A case series.
Yang CC, Khanna T, Sallee B, Christiano AM, Bordone LA.
Dermatol Ther. 2018 Nov;31(6):e12656

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Dermatol Ther. 2018 Nov;31(6):e12656

87 yo BF with adenocarcinoma of lung

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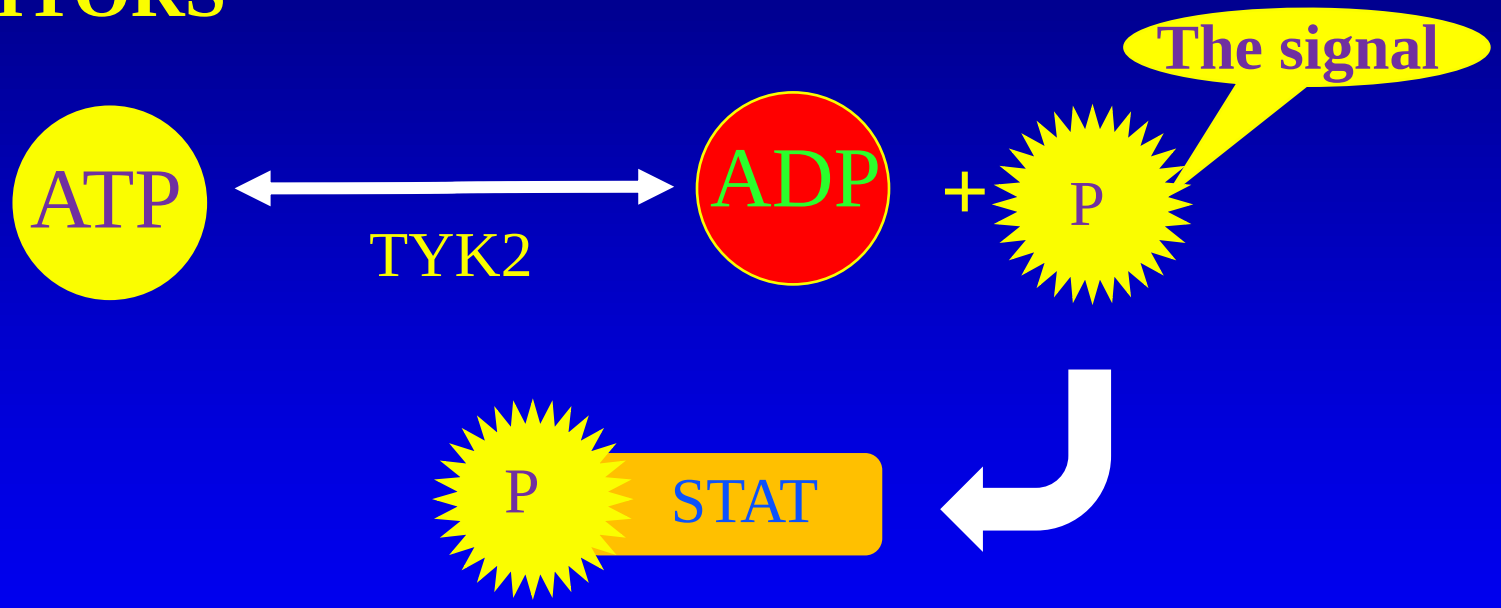
- Role in atopic dermatitis
- Role in psoriasis
- Role in alopecia areata
- Role in vitiligo
- What could go wrong?

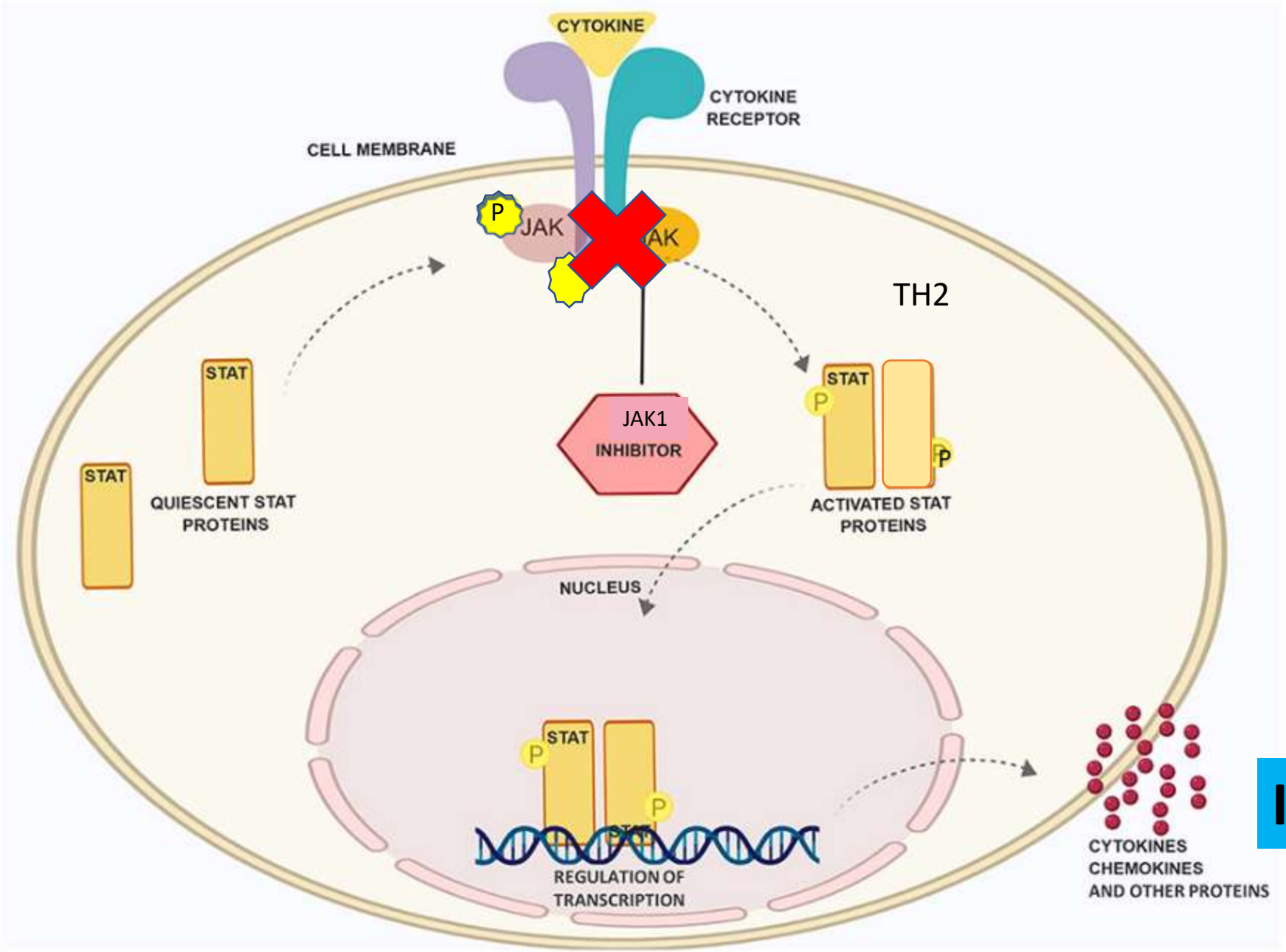
What are JAK's? What is signal transduction?

JANUS KINASE INHIBITORS

JAK1
JAK2
JAK3
TYK2



GENERATES CYTOKINES LIKE IL4, IL17, IL23 & OTHERS



Modified from Solimani F, et al. Emerging Topical and Systemic JAK Inhibitors in Dermatology. Front Immunol. 2019;10:2847.

The use of JAKs by different cytokines

BARICITINIB
RUXOLITINIB
TOFACITINIB
UPADACITINIB
ABROCITINIB

BARICITINIB
RUXOLITINIB
TOFACITINIB
UPADACITINIB
Abrocitinib

TOFACITINIB
UPADACITINIB
Abrocitinib

DEUCRAVACITINIB
TOFACITINIB
BARICITINIB
RUXOLITINIB
UPADACITINIB
Abrocitinib

JAK1

- **γc family**: IL-2, IL-4, IL-7, IL-9, IL-15
- **gp130 family**: IL-6, IL-11, OSM, LIF
- IFNα/β, IFNγ, IL-10

JAK2

- **gp130 family**: IL-6, IL-11, OSM, LIF
- **βc family**: IL-3, IL-5, GM-CSF
- EPO, TPO, IFNγ
- IL-12/IL-23

JAK3

- **γc family:** IL-2, IL-4, IL-7, IL-9, IL-15

TYK2

- **gp130 family**: IL-6, IL-11, OSM, LIF
- IFNα/β
- IL-12/IL-23

OSM, oncostatin M; LIF, leukemia inhibitory factor; GM-CSF, granulocyte macrophage colony-stimulating factor; EPO, erythropoietin; TPO, thrombopoietin

Adapted from John O'Shea, et al. Ann Rhem Dis 2013;72(Suppl 2):ii111-5

Tofacitinib
Upadacitinib

Deucravacitinib

Abrocitinib
Upadacitinib
Ruxolitinib cream

Baricitinib
Ritlecitinib
Deuruxolitinib

Topical ruxolitinib
1.5% cream

JAK Inhibitors

- Boxed warnings: what are the real risks?
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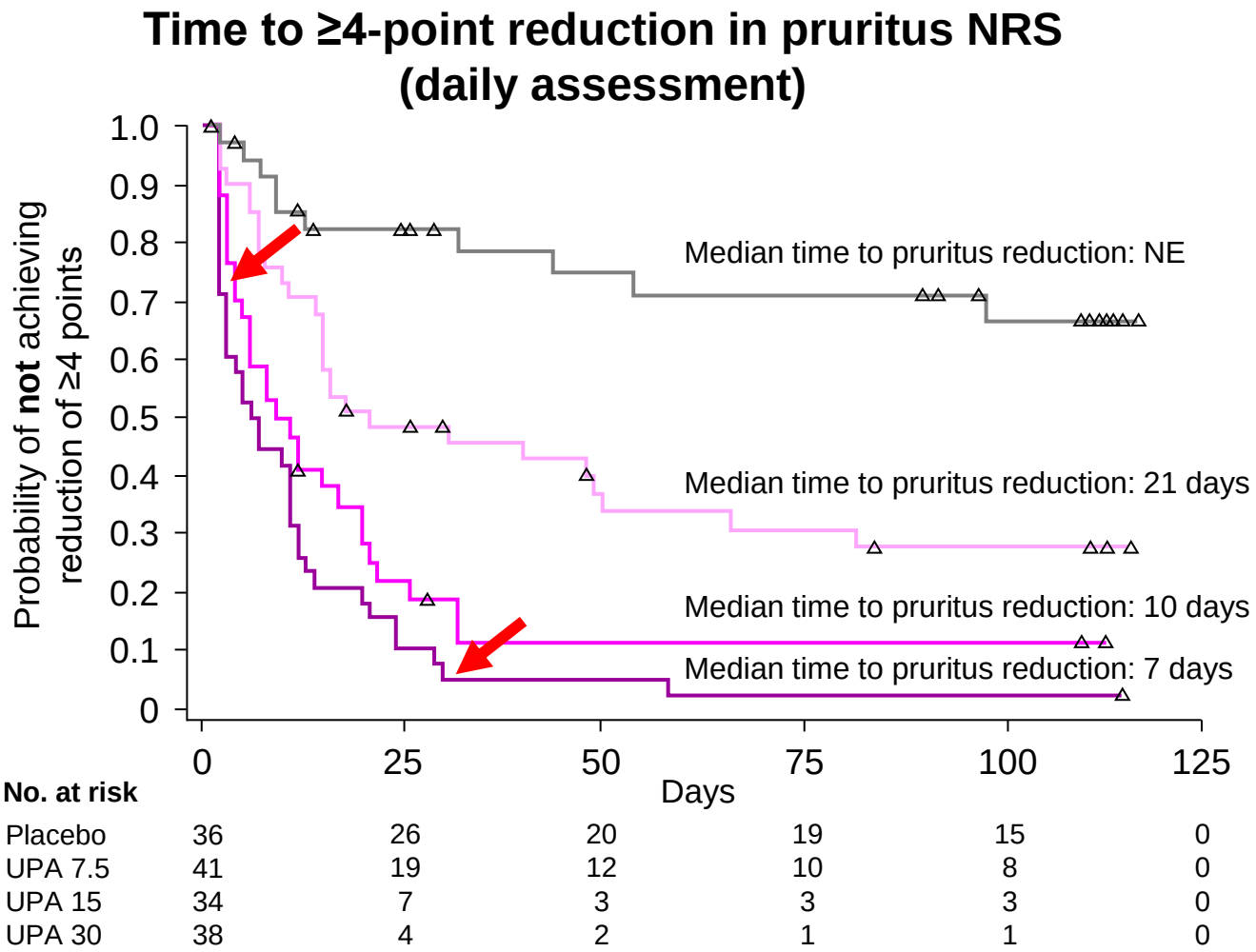
- Role in atopic dermatitis
- Ps
- Aa
- vitiligo
- What could go wrong?

Phase 2b trial: Time to achieve ≥4-point reduction in pruritus NRS with upadacitinib for patients with moderate to severe AD



No. at risk

Placebo	36	26	20	19	15	0
UPA 7.5	41	19	12	10	8	0
UPA 15	34	7	3	3	3	0
UPA 30	38	4	2	1	1	0

- JAK inhibitors are known for rapid itch reduction
- This sets a new bar – rapid holistic improvement

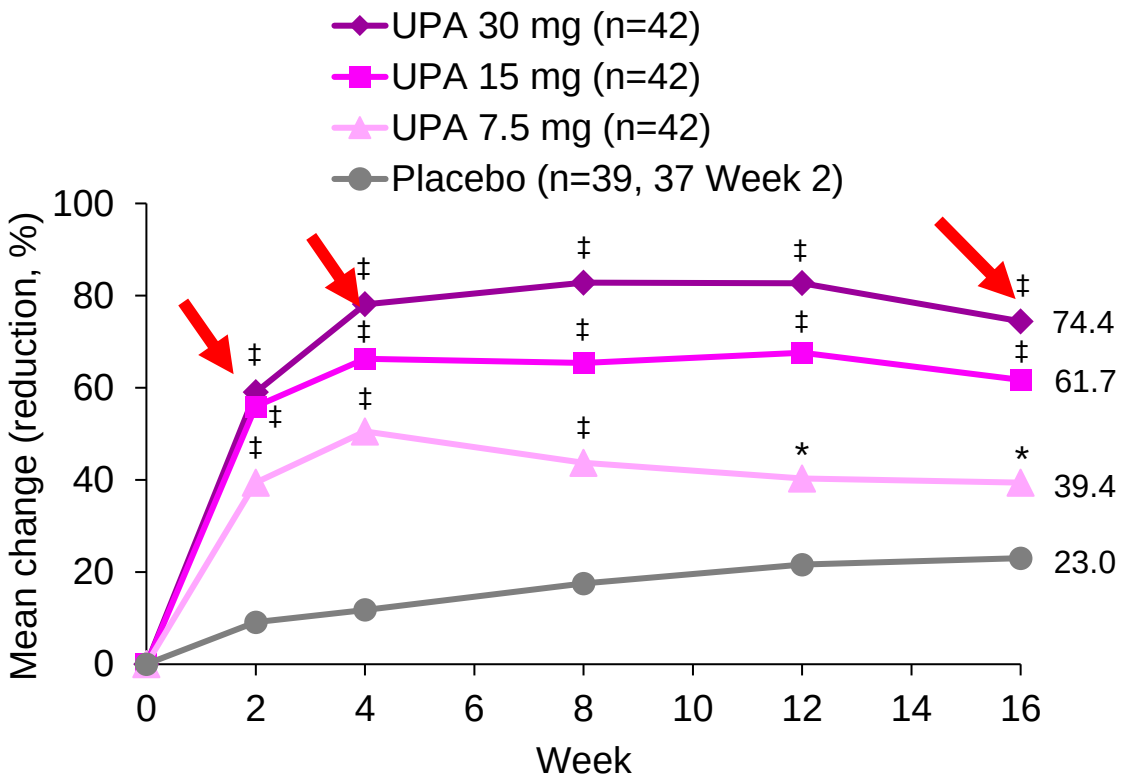
NE, not estimable

Reich K, et al. EADV 2019, FC07.06 Sponsored by AbbVie Inc.

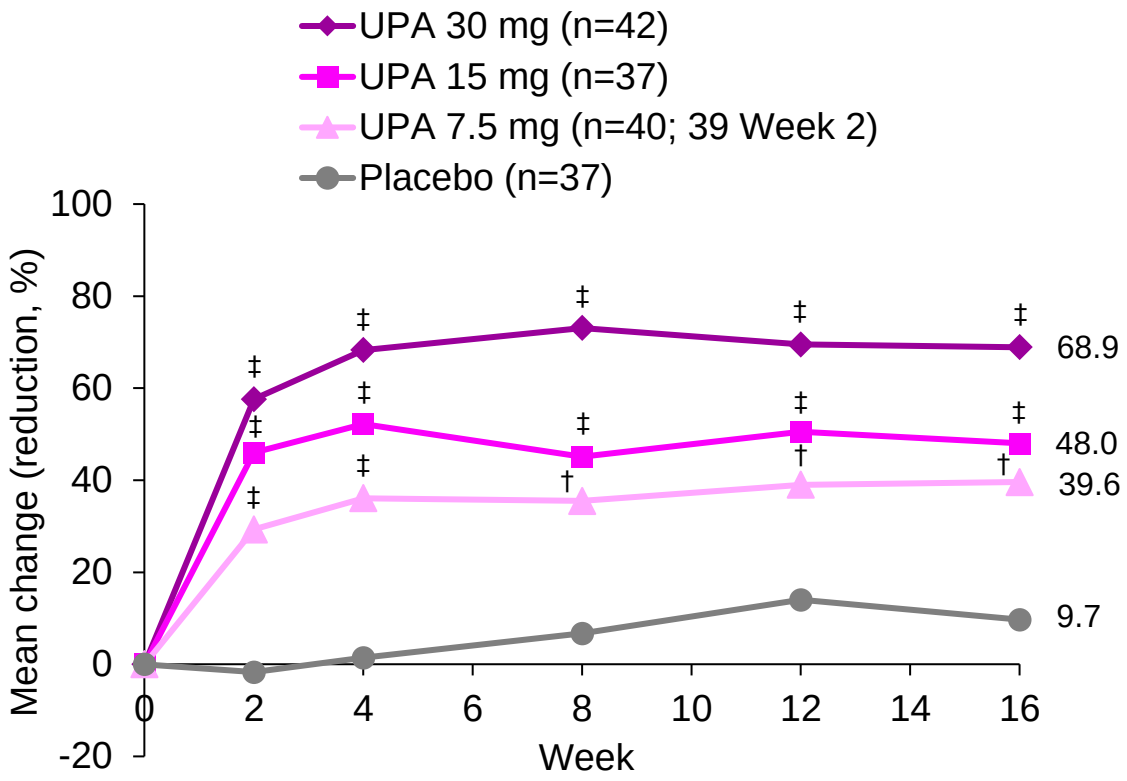
Phase 2 study upadacitinib FOR AD

- **Objective:** Analyze serum protein biomarkers of AD over 16 weeks of upadacitinib treatment
- Dose response observed in Phase 2 trial:

Change from baseline in EASI score (LOCF)[1]



Change from baseline in pruritus NRS (LOCF)[1]

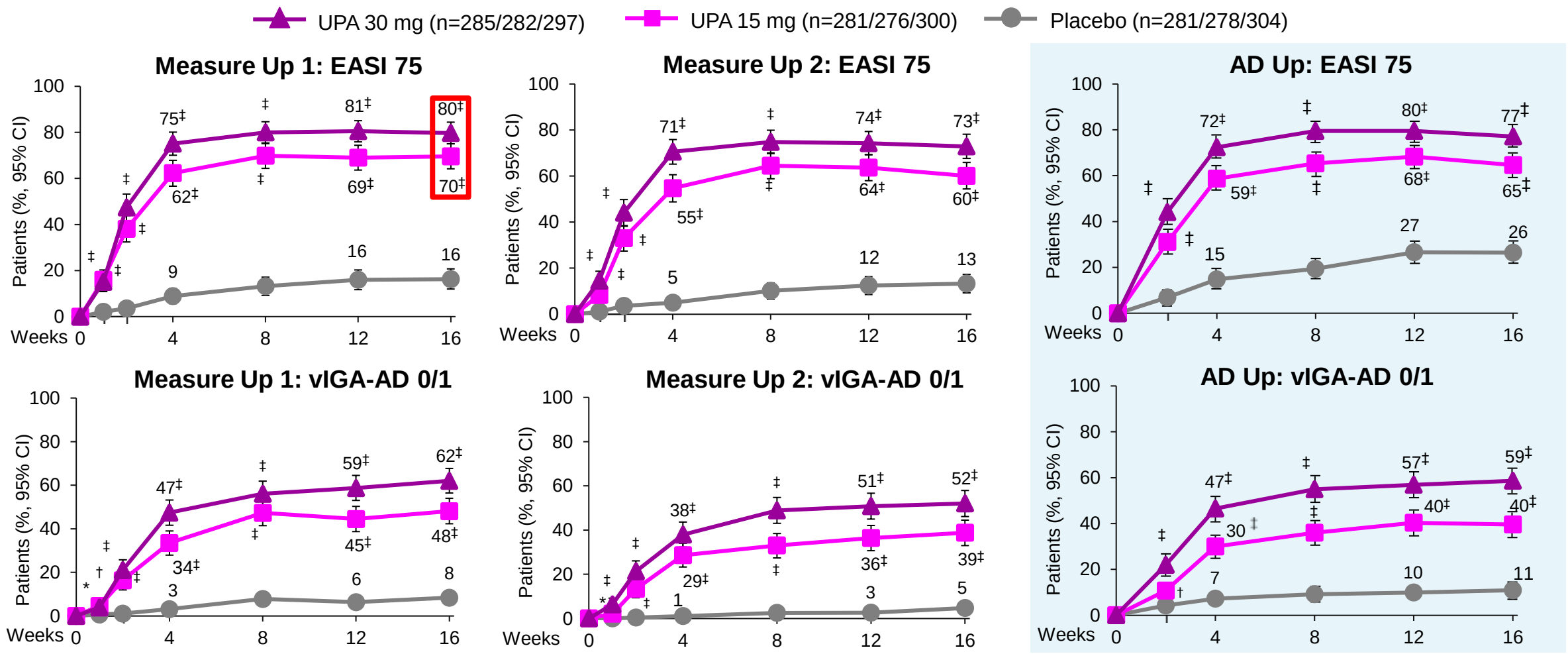


*P<0.05; †P<0.01; ‡P<0.001 UPA vs placebo

1. Guttman-Yassky E, et al. AAD 2018, Late-breaking Research: Clinical Trials

Guttman E, et al. EADV 2019, P0272 Sponsored by AbbVie Inc.

Measure Up 1, 2, and AD Up: Coprimary endpoint results (NRI-C)

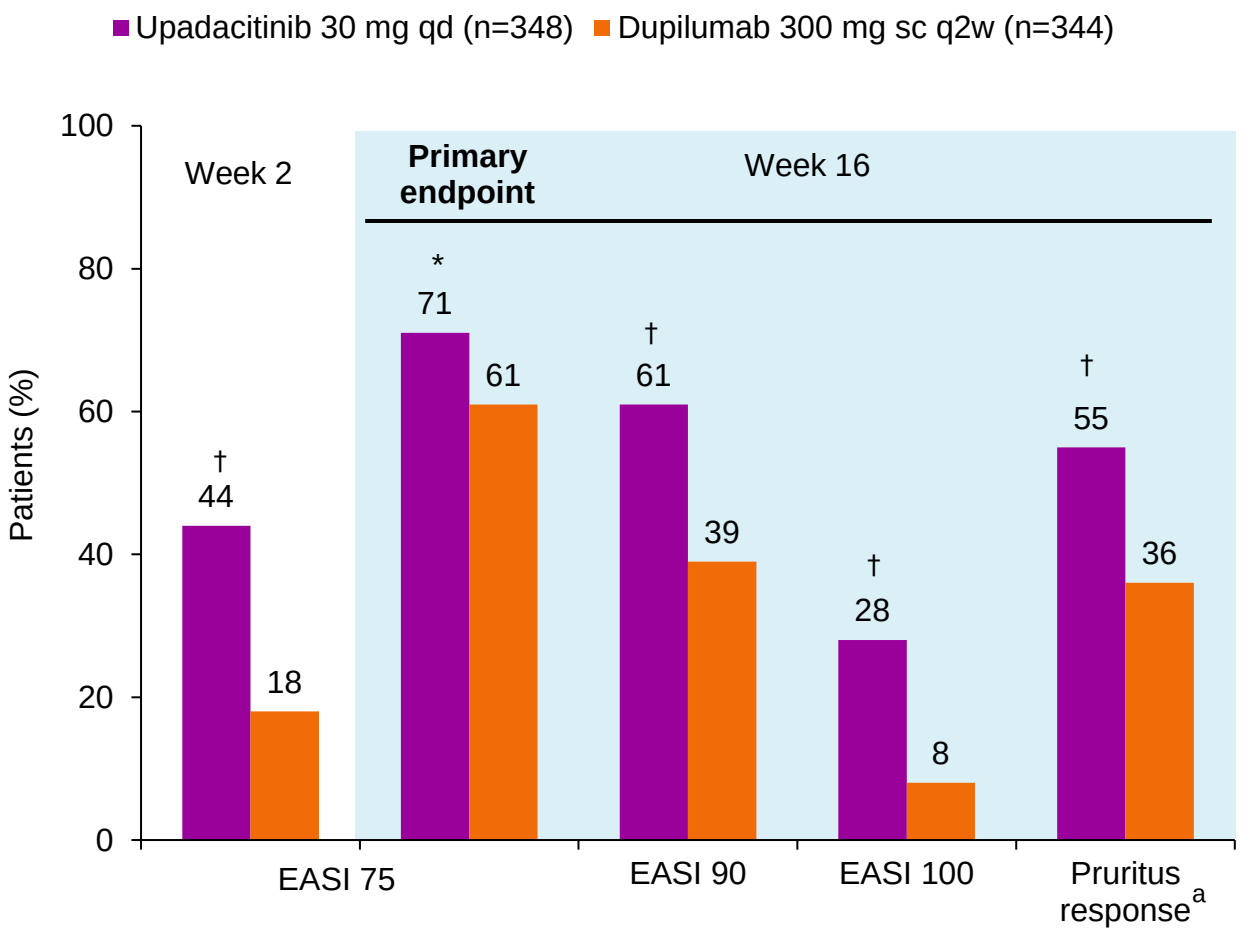


*P≤0.05; †P≤0.01; ‡P≤0.001 UPA vs placebo ±TCS (P values multiplicity controlled at Weeks 2, 4 (AD Up) and 16 for EASI 75 and at Week 16 only for vIGA-AD 0/1. P values for all other time points are nominal); NRI-C, nonresponder imputation, though multiple imputation used to handle missing data due to COVID-19

Simpson E, et al. AAD VMX 2021, P27915; Guttman-Yassky E, et al. EADV 2020, D3T03.4B late-breaking news;
Reich K, et al. RAD 2020, P321. All posters sponsored by AbbVie Inc.

Heads Up: Key efficacy outcomes among adults with moderate to severe AD treated with upadacitinib versus dupilumab for 16 weeks

Patients achieving EASI and pruritus responses at Week 16



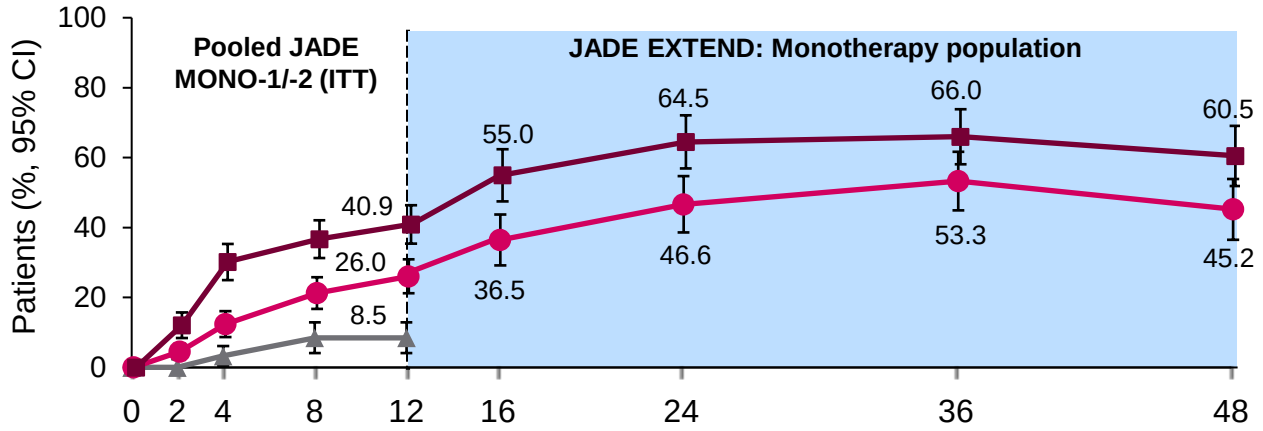
- Early differentiation may have been down to monotherapy use in the trial: Patients typically need to use TCS in addition to dupilumab to achieve an early response, which is not the case for upadacitinib (as shown by the minimal additive efficacy TCS provided at the early timepoints of AD Up)
- Withholding TCS from dupilumab patients limits the ability to reach responses early: As responses are achieved more slowly, the efficacy difference narrows by Week 16
- If upadacitinib has already reached most of its EASI 75 response at Week 16, the difference between the therapies may reduce further at later timepoints
  - If this is the case, will some patients need the 30 mg dose long term? From the perspective of risk mitigation, it will be difficult to justify longer term use of the 30 mg dose if, beyond 16 weeks, the efficacy benefit versus dupilumab is diminished

*P=0.006, †P<0.001 vs dupilumab; [a]≥4-point improvement in worst pruritus NRS. For pruritus, upadacitinib 30 mg qd: n=340, dupilumab 300 mg sc q2w: n=336
Details of statistical analyses, including imputation methods, not provided in press release

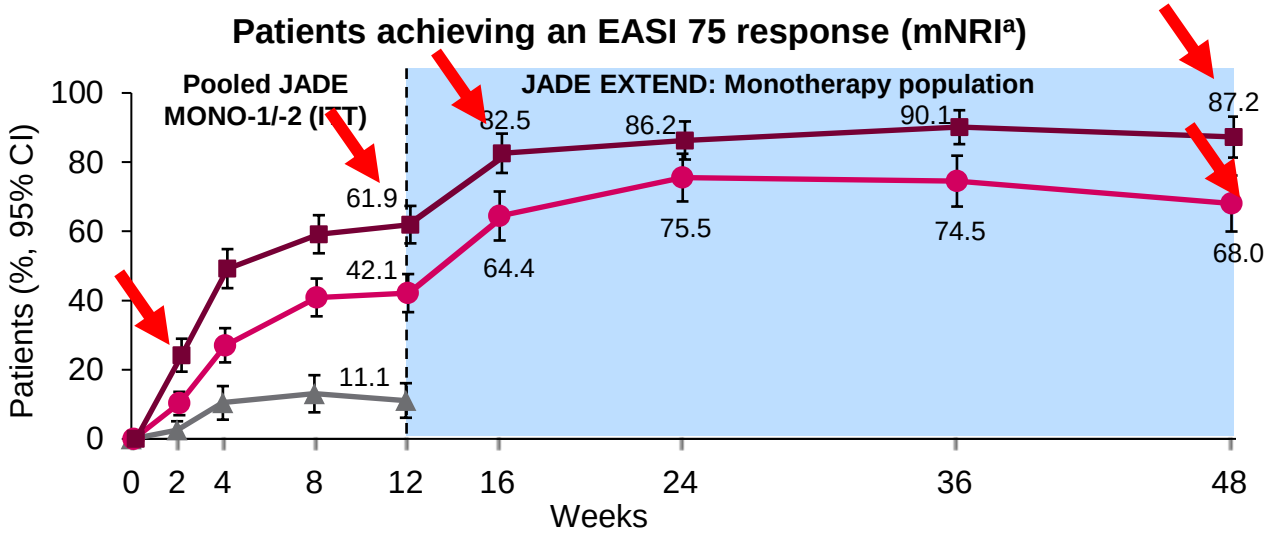
AbbVie press release (December 10, 2020), available at: https://news.abbvie.com/news/press-releases; ClinicalTrials.gov: NCT03738397

JADE EXTEND LTE: IGA and EASI 75 response through 48 weeks among patients with AD who maintained abrocitinib monotherapy

Patients achieving IGA 0/1 and ≥2-point reduction from baseline (mNRI[a])



Patients achieving an EASI 75 response (mNRI[a])



ABR 200 mg	n = 309	309	309	309	171 (2)	152 (19)	141 (36)	124 (45)
ABR 100 mg	n = 314	314	314	314	170 (2)	148 (25)	135 (39)	126 (45)
PBO	n = 153	153	153	153				

- Baseline characteristics were comparable with those reported for JADE MONO-1/-2

From Week 12 to 16:

- EASI 90 response increased by 49% for the 200 mg dose and 57% for the 100 mg dose of abrocitinib
- EASI 100 response increased by 138% (200 mg) and 78% (100 mg)
- PP NRS ≥4-point reduction response increased by 32% (200 mg) and 19% (100 mg)

- The unexpected increase in performance on all measures between Week 12 and 16, which does not endure, is likely related to the difference in patient population reported for Weeks 0–12 and 12–48 (ie, ITT vs monotherapy population) – data for the same patients should have been reported for all time points
- Retrospectively selecting only those patients who maintained monotherapy introduces a bias because these patients were likely achieving high levels of response at Week 12
- It's advisable to first present data for all patients before looking at subpopulations

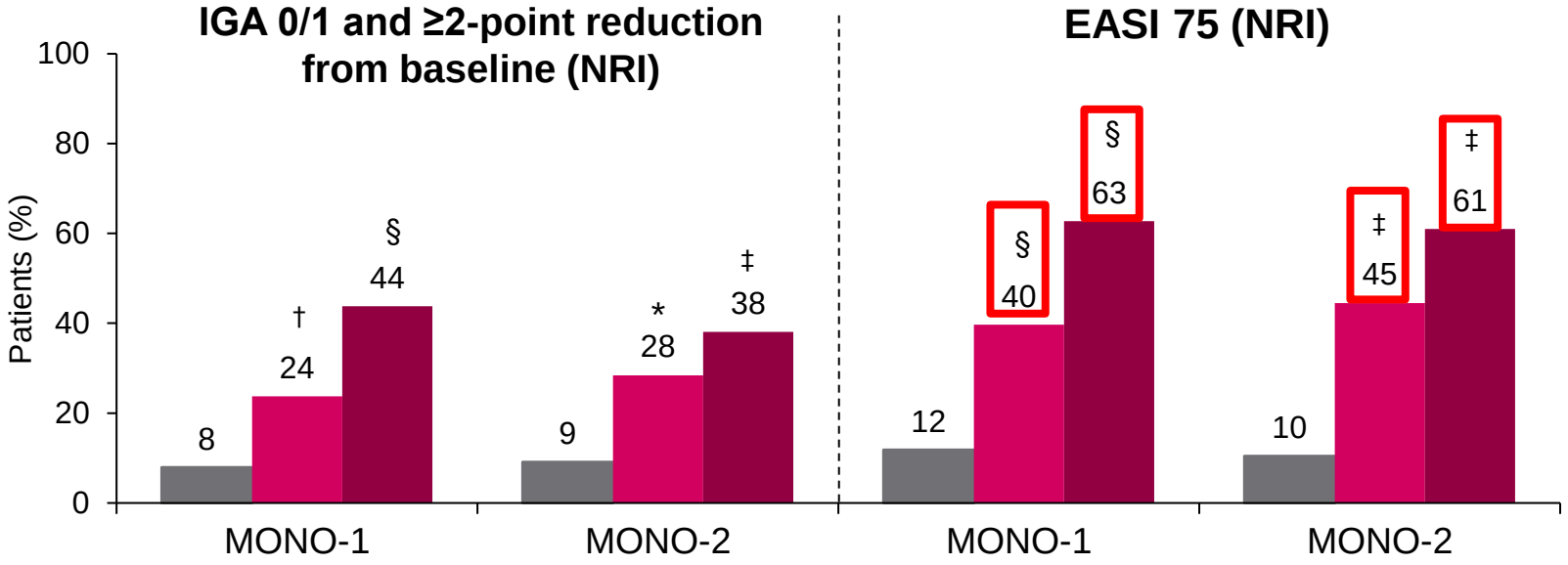
[a]mNRI: Data for patients who permanently discontinued are imputed as nonresponse and all other missing data are as observed
Dropouts shown in parentheses for Weeks 16–48

Reich K, et al. EADV 2020, D3T03.4C late-breaking news Sponsored by Pfizer Inc

JADE MONO-1 and -2: Key baseline characteristics and coprimary endpoints with 12 weeks abrocitinib monotherapy among patients with AD

Key baseline characteristics	MONO-1[1]			MONO-2[2,3]		
	Placebo (n=77)	ABR 100 mg (n=156)	ABR 200 mg (n=154)	Placebo (n=78)	ABR 100 mg (n=158)	ABR 200 mg (n=155)
Age, years <18 years	31.5 ±14.4 17 (22)	32.6 ±15.4 34 (22)	33.0 ±17.4 33 (21)	33.4 ±13.8 8 (10)	37.4 ±15.8 17 (11)	33.5 ±14.7 15 (10)
Prior systemic therapy[a]	41 (53)	78 (50)	68 (44)	32 (41)	70 (44)	60 (39)
EASI score	28.7 ±12.5	31.3 ±13.6	30.6 ±14.1	28.0 ±10.2	28.4 ±11.2	29.0 ±12.4
Peak pruritus NRS	7.0 ±1.8	6.9 ±2.0	7.1 ±1.9	6.7 ±1.9	7.1 ±1.6	7.0 ±1.6

Data are mean ±SD or n (%)



Pooled SOLO 1 and 2: Efficacy outcomes at Week 16 (NRI excluding TCS rescue)

	Placebo (n=460)	DUP q2w (n=457)	DUP qw (n=462)
IGA 0/1 and ≥2-point reduction, %	9.3	37.0[§]	36.8[§]
EASI 75, %	13.3	47.7[§]	50.2[§]

Data included for illustrative purposes only (not based on head-to-head trials between ABR and DUP and thus cannot be directly compared)

Thaçi D, et al. J Dermatol Sci 2019;94:266–75

[a]Includes mycophenolate mofetil, methotrexate, azathioprine, corticosteroids, cyclosporine and dupilumab; *P<0.05, †P<0.01, ‡P≤0.001, §P<0.0001 vs placebo

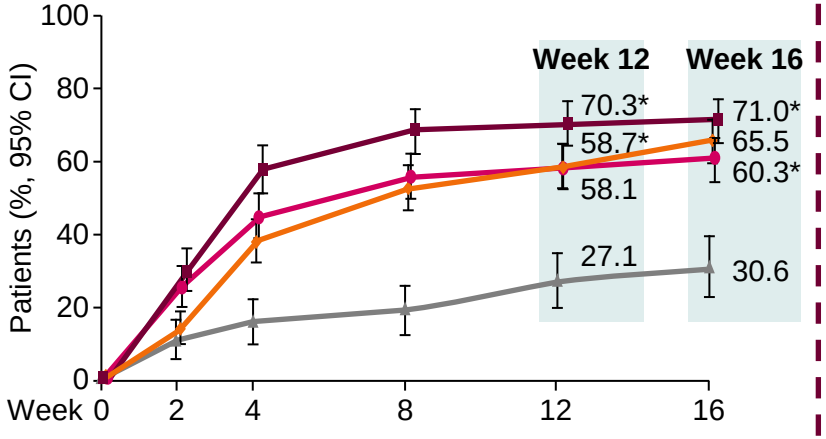
1. Simpson EL, et al. EADV 2019, D3T01.1I; 2. Silverberg JI, et al. JAMA Dermatol 2020; epub ahead of print;
3. Silverberg JI, et al. AAD 2020, Late-breaking research: Clinical trials. Sponsored by Pfizer Inc

JADE COMPARE: Effect of abrocitinib or dupilumab (with topical therapy) on patient-reported outcomes for patients with moderate to severe atopic dermatitis

Eligibility criteria:

- Adults ≥18 years old
- AD diagnosis for ≥1 year
- Current moderate to severe AD (≥10% BSA involvement, IGA ≥3, EASI ≥16, PP NRS ≥4)
- Inadequate response to topical therapy or need for systemic therapy

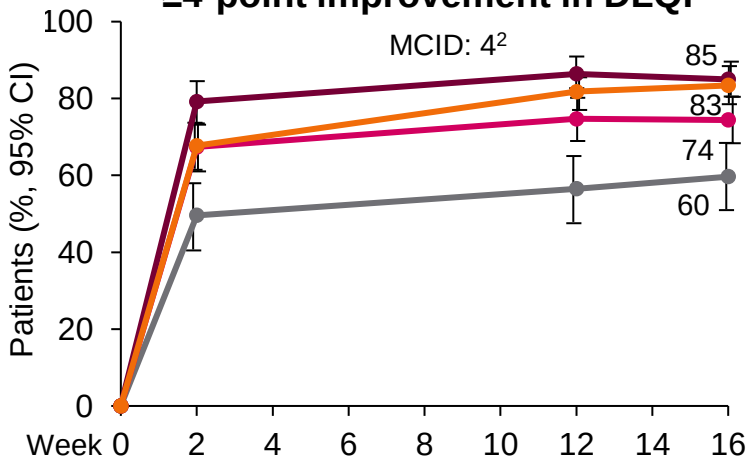
JADE COMPARE: EASI 75 response (NRI)[1]



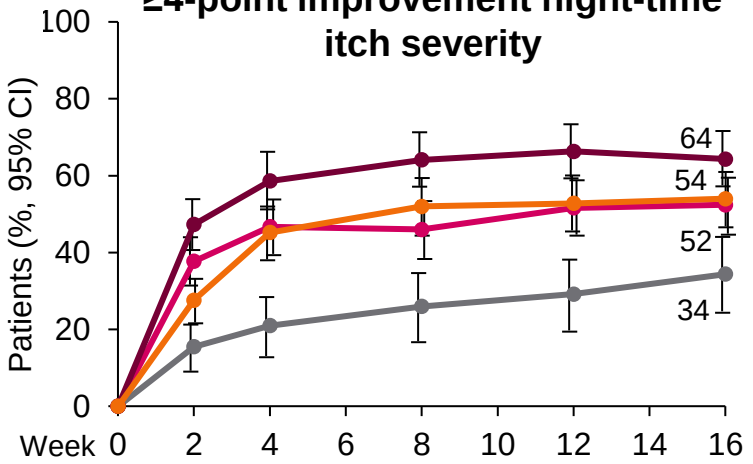
*P<0.0001 for abrocitinib vs placebo

Placebo (n=131) ABR 100 mg qd (n=238) ABR 200 mg qd (n=226) DUP 300 mg q2w (n=242)

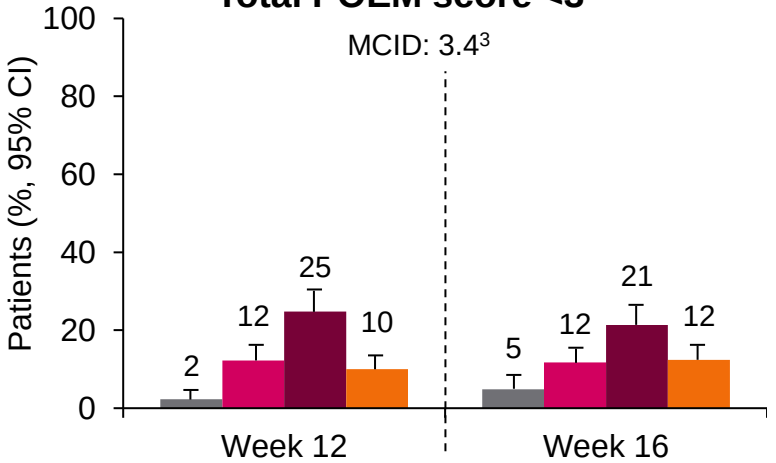
≥4-point improvement in DLQI



≥4-point improvement night-time itch severity



Total POEM score <3



- Appear to be ad hoc analyses, not prespecified
- Quality of life improvements mirror improvements in clinical responses
- Unclear whether the kinetics of the POEM response also follow the EASI/IGA data – what happened in the first 12 weeks?
- Patients itch all day and night: Knowing how much they itch just at night doesn't add much
- Pruritus NRS remains the best available tool for assessing itch improvement

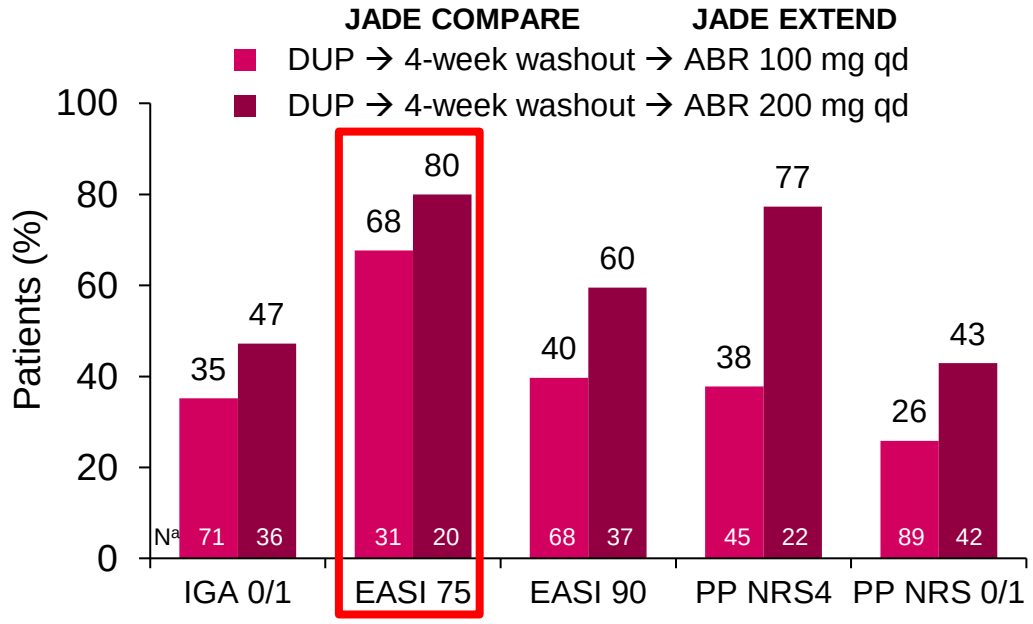
1. Bieber T, et al. N Engl J Med 2021;384:12; 2. Basra MKA, et al. Dermatology 2015;230:27–33; 3. Schram ME, et al. Allergy 2012;67:99–106

P values vs placebo reported in the poster for PROs are all nominal

Yosipovitch G, et al. AAD VMX 2021, P27237. Sponsored by Pfizer Inc.

JADE-EXTEND: Efficacy of 12 weeks' abrocitinib among patients not achieving responses to 16 weeks' dupilumab

Efficacy outcomes with abrocitinib at Week 12 of JADE EXTEND among nonresponders[a] to 16 weeks' dupilumab in JADE COMPARE



[a]**Nonresponders** = patients receiving dupilumab who did not achieve the responses displayed at Week 16 of JADE COMPARE

Statistical methodology, including imputation methods, not included in poster

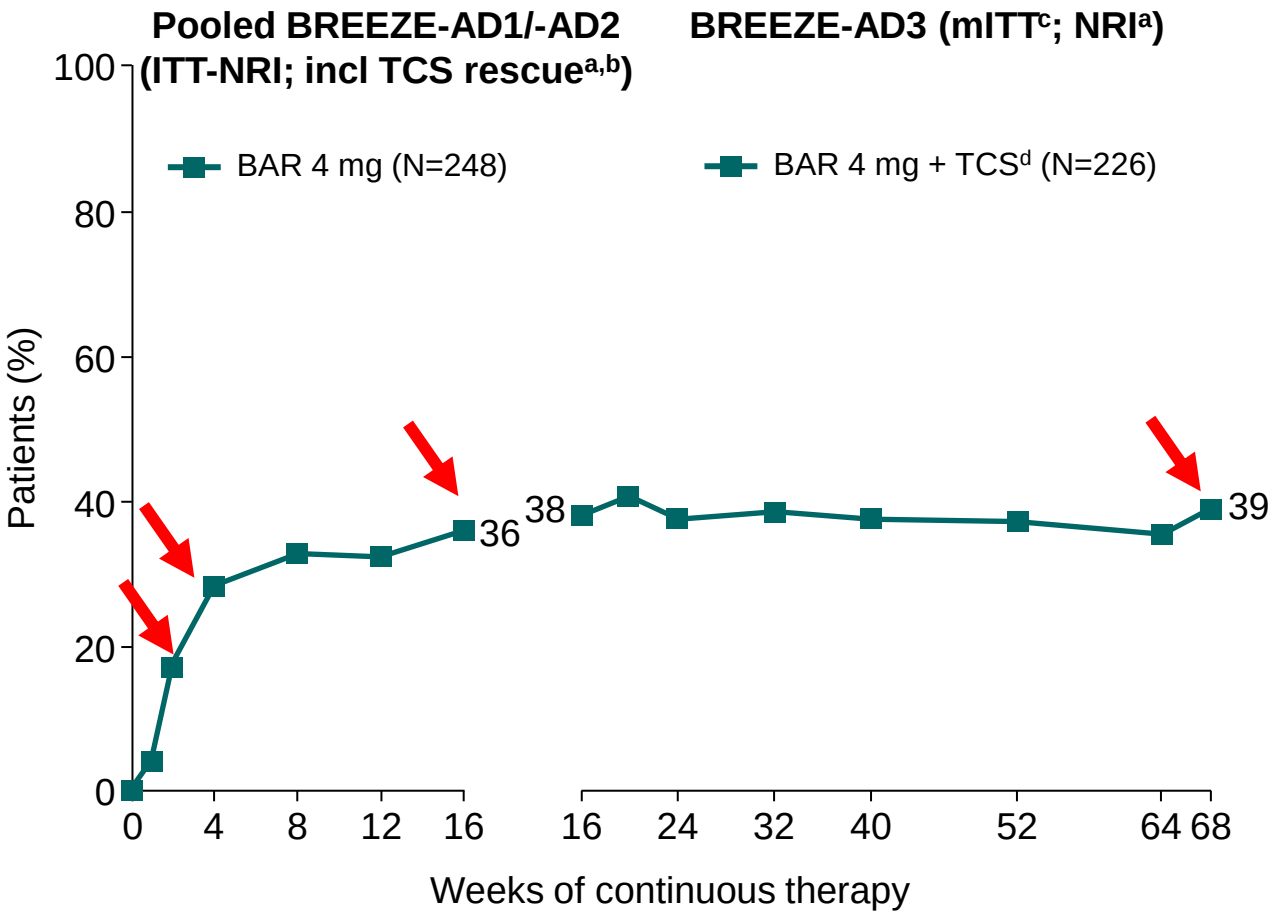
1. Bieber T, et al. N Engl J Med 2021;384:1101–12

Shi V, et al. AAD VMX 2021, P27590. Sponsored by Pfizer Inc.

- Dose dependent increases in nasopharyngitis, nausea, acne, headache after switching to abrocitinib

- Important data supporting abrocitinib use after dupilumab failure. The design, however, does not likely approximate the real-life clinical scenario of drug switch
- Unique safety population that is unlike other JADE studies, in that it contains patients primed with dupilumab first
  - However, there are no consequential differences from AEs previously reported
  - Conjunctivitis is not listed or called out: JADE COMPARE has only a ~2-3% difference between dupilumab and abrocitinib[1] at baseline but 6x lower at Week 16
- In a presumably more resistant patient population (dupilumab 'failures'), the higher abrocitinib dose demonstrates greater performance differences vs the lower dose (9% difference between doses for EASI 90 in JADE COMPARE,[1] compared to 20% in this group)
- The authors' conclusion that "…this analysis supports the role of abrocitinib as treatment for patients with moderate to severe AD, regardless of prior experience with dupilumab" is hyperbolic and not accurate

BREEZE-AD1–3: EASI 75 response with 68 weeks of baricitinib 4 mg (with or without TCS) among all patients

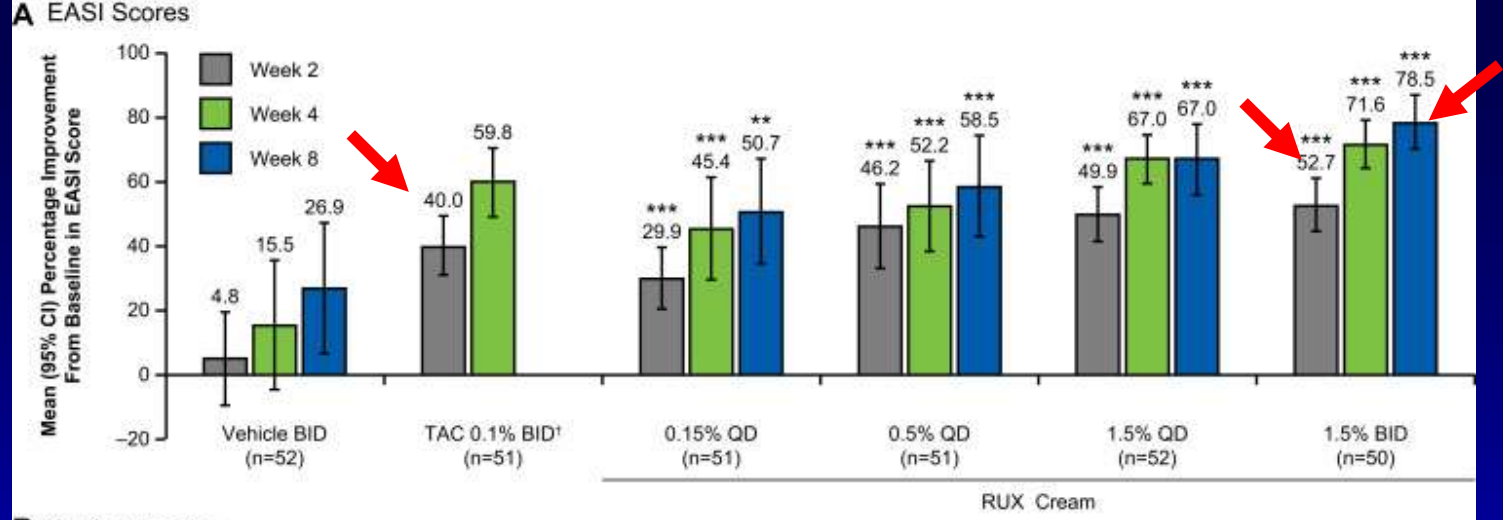


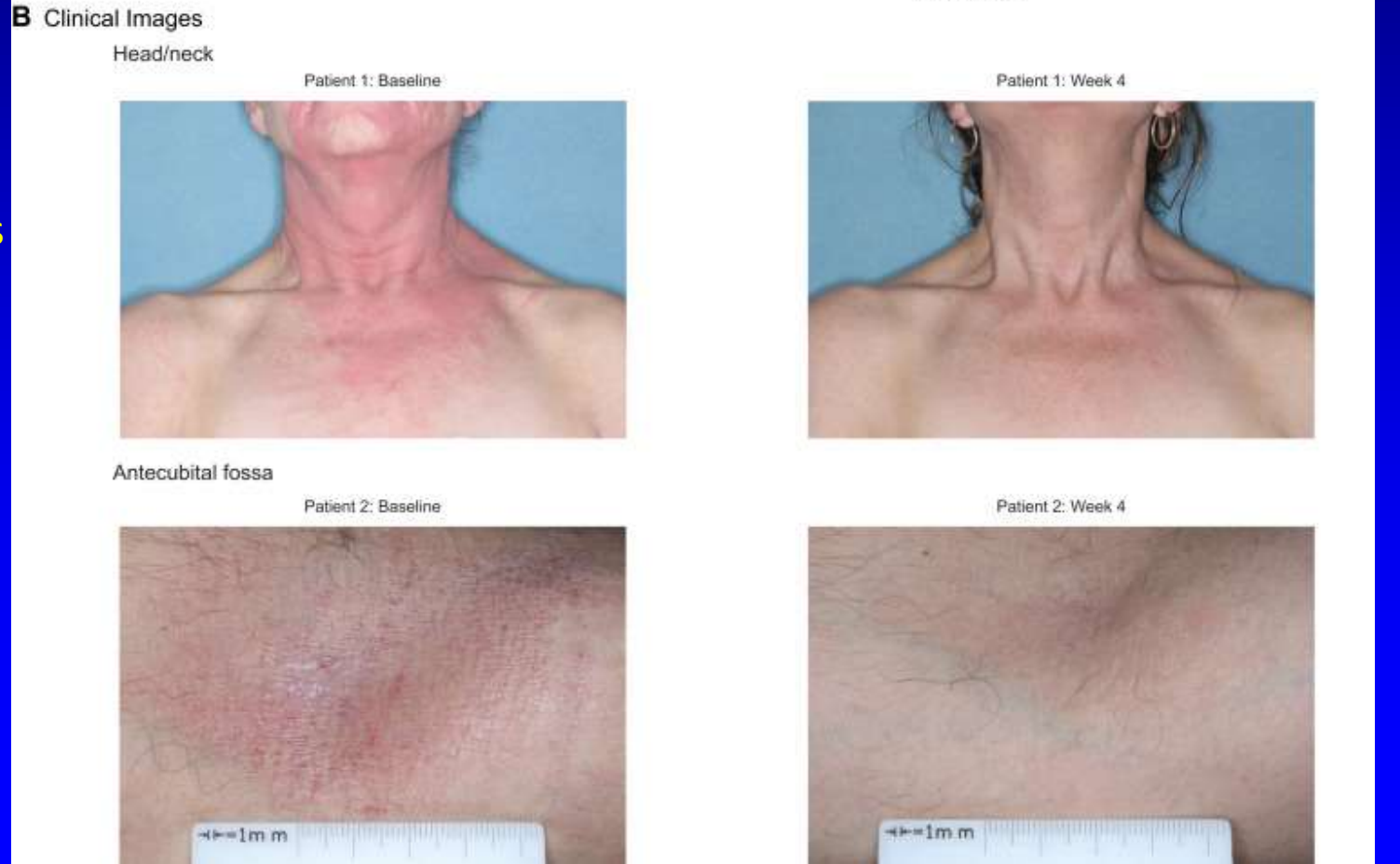
- It's good to see that EASI 75 response is maintained between Week 16 and 68 with baricitinib 4 mg and TCS in the overall patient population (ITT)
- These data provide a realistic view of the long-term efficacy of baricitinib in the real world
- Efficacy is more modest than that of other oral JAK inhibitors

[a]Only patients who discontinued baricitinib were imputed as nonresponders; [b]Data from patients who used TCS rescue during BREEZE-AD1/-AD2 included and not censored; [c]mITT includes all patients receiving ≥1 dose of baricitinib in BREEZE-AD3; [d]Background TCS used at investigator's discretion

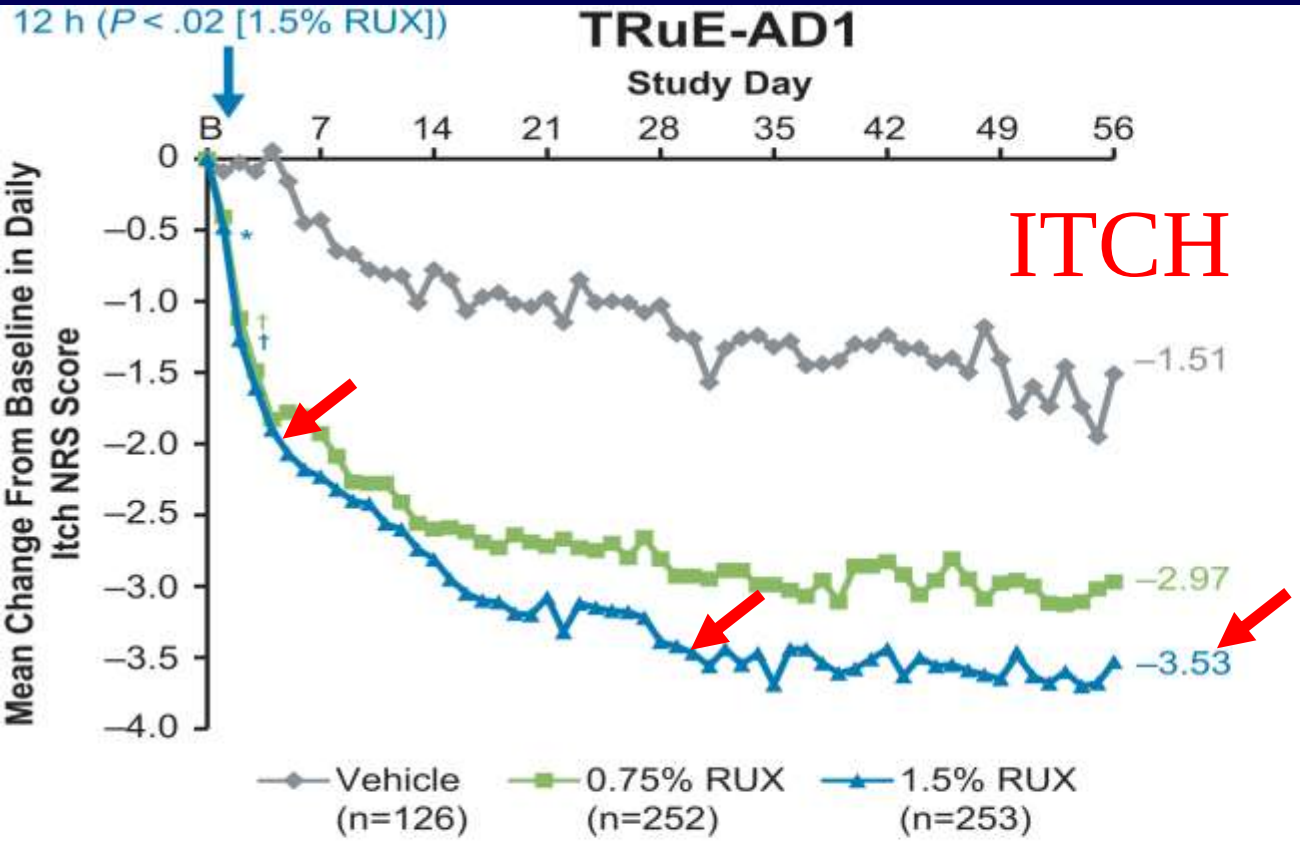
Silverberg JI, et al. D3T03.4A late-breaking news Sponsored by Eli Lilly and Company

RUXOLITINIB CREAM

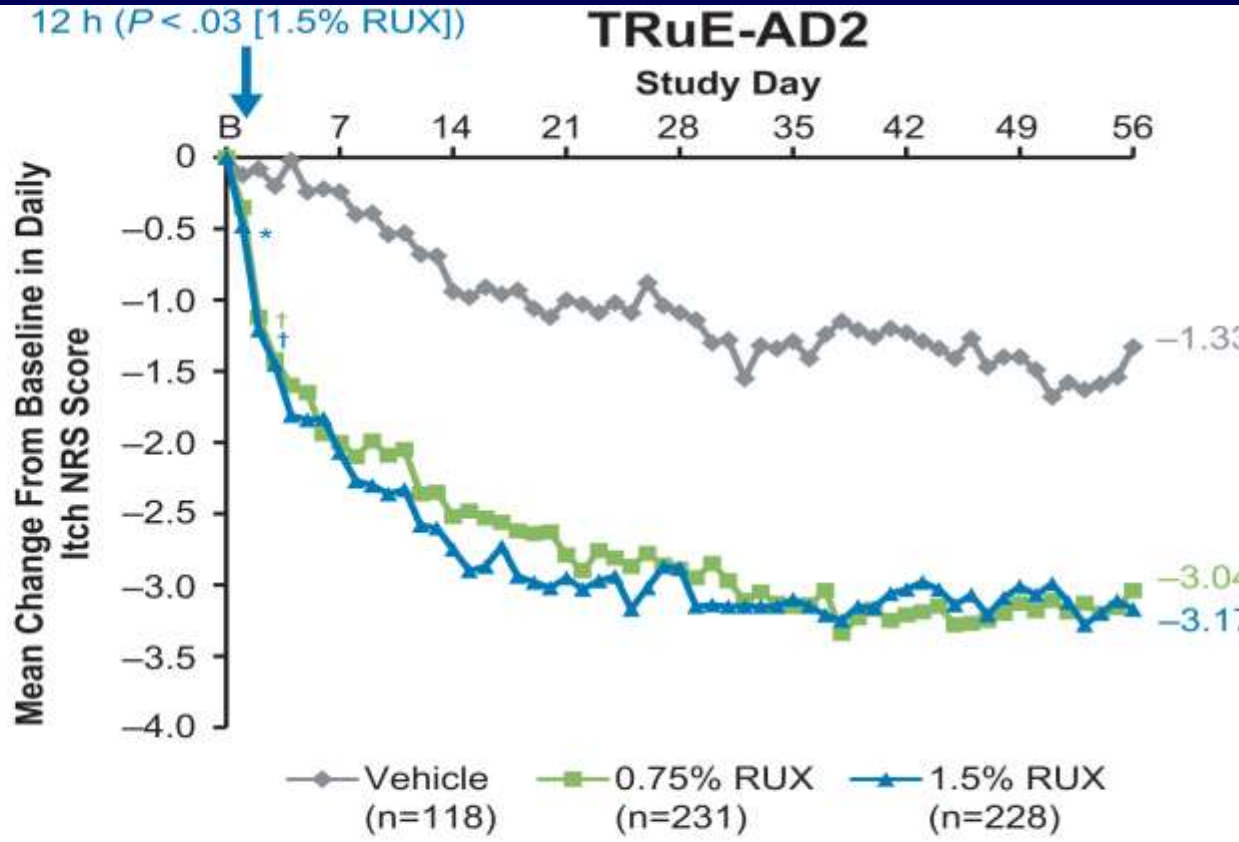




Treatment of atopic dermatitis with ruxolitinib cream (JAK1/JAK2 inhibitor) or triamcinolone cream.
Kim BS et al
J Allergy Clin Immunol. 2020 145:572-582.



Number of Patients	Day 14	Day 28	Day 56
Vehicle	105	94	59
0.75% RUX	208	199	146
1.5% RUX	218	220	158



Number of Patients	Day 14	Day 28	Day 56
Vehicle	99	96	64
0.75% RUX	190	86	129
1.5% RUX	190	184	149

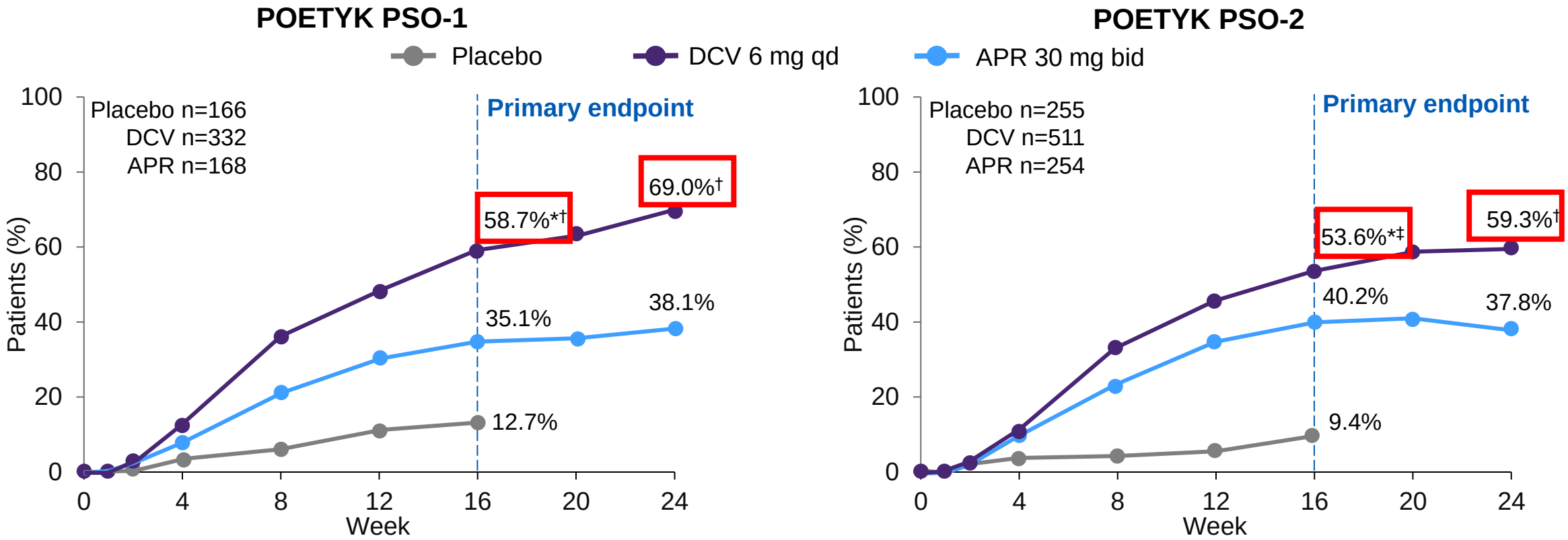
Efficacy and safety of ruxolitinib cream for the treatment of atopic dermatitis: Results from 2 phase 3, randomized, double-blind studies. Papp K, et al J Am Acad Dermatol. 2021 Oct;85(4):863-872

JAK Inhibitors

- Boxed warnings: what are the real risks?
- For what conditions do they work?
- What are they?
- Role in atopic dermatitis
- Role in psoriasis
- Role in alopecia areata
- Role in vitiligo
- What could go wrong?

DEUCRAVACITINIB: PASI 75 at Weeks 16 and 24

PASI 75 response at Week 16 (coprimary endpoint) and through Week 24 (NRI)



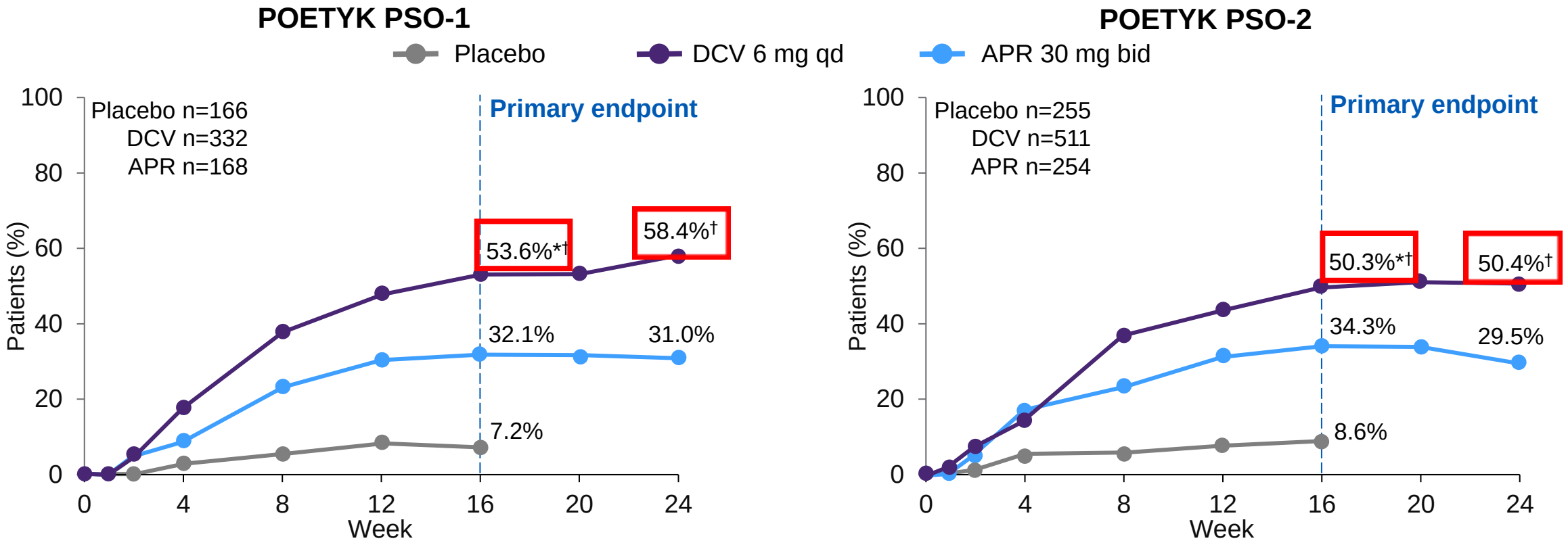
- 82.5% (PSO-1) and 81.4% (PSO-2) of deucravacitinib patients who achieved PASI 75 at Week 24, and continued treatment, maintained response at Week 52

*P<0.0001 vs placebo, †P<0.0001 vs apremilast, ‡P=0.0003 vs apremilast

Armstrong AW, et al. AAD VMX 2021, Late breaker. Sponsored by Bristol Myers Squibb

POETYK PSO-1 and PSO-2: sPGA at Weeks 16 and 24

sPGA 0/1 response at Week 16 (coprimary endpoint) and through Week 24 (NRI)



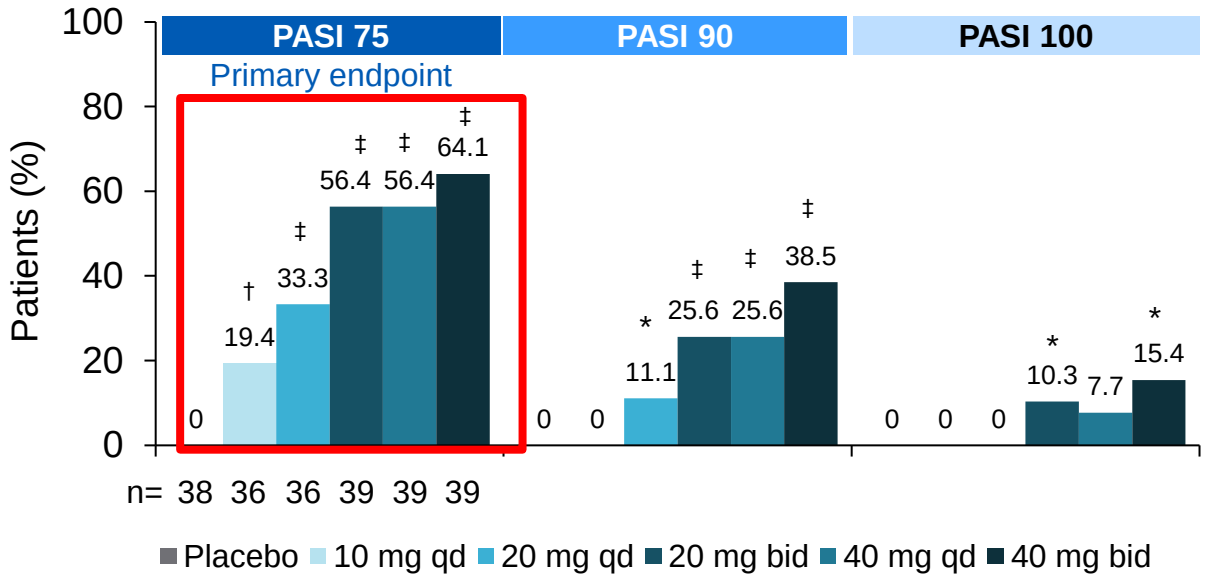
- All coprimary and secondary endpoints in the hierarchy were met, with the exception of the last one (PGA-F 0/1 [BL ≥3] at Week 16 vs placebo and PSSD Symptom Score 0 at Week 16 [BL ≥1] vs apremilast)

*P<0.0001 vs placebo, †P<0.0001 vs apremilast. Response defined as sPGA score of 0 or 1 with ≥2-point improvement from baseline

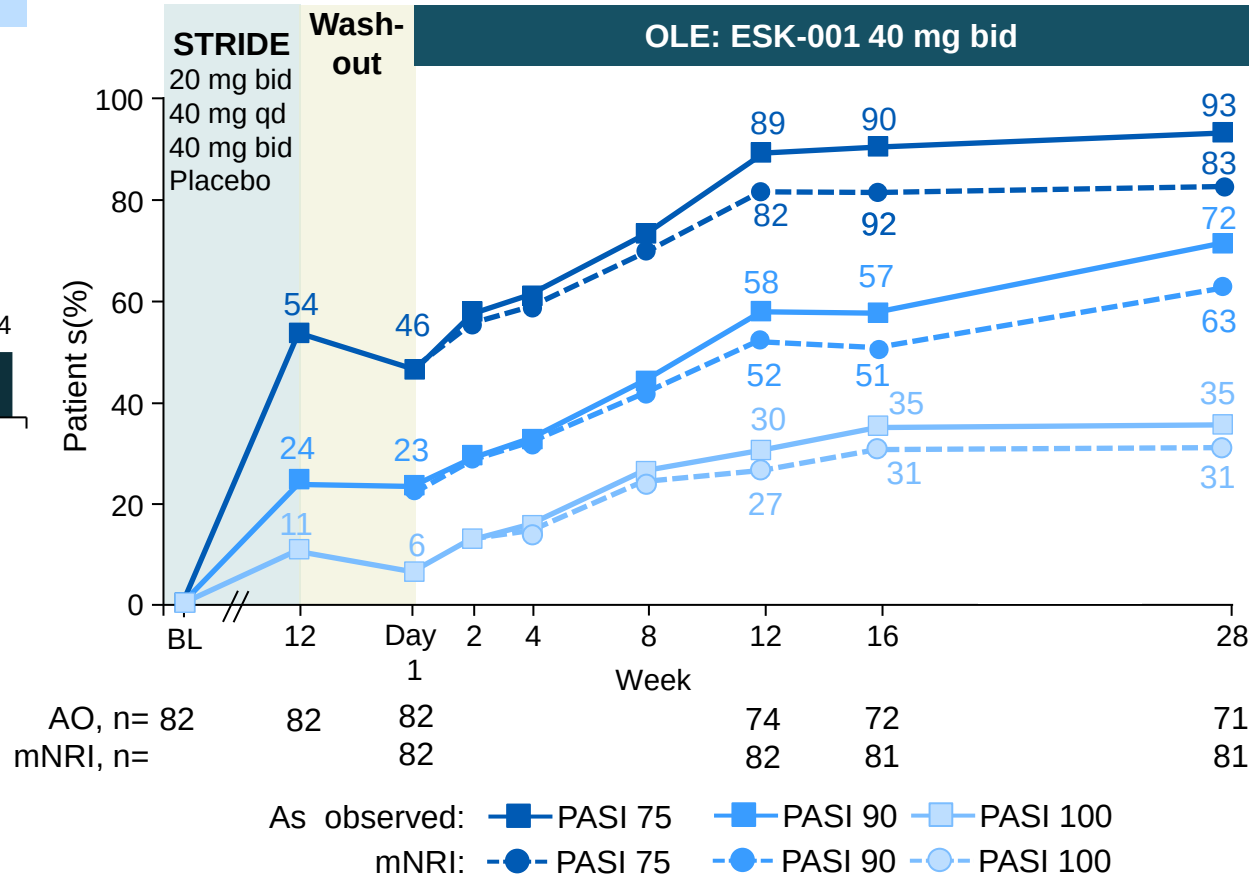
Armstrong AW, et al. AAD VMX 2021, Late breaker. Sponsored by Bristol Myers Squibb

STRIDE: Efficacy of oral TYK2 inhibitor ESK-001 at OLE Week 28

PASI responses at Week 12 (NRI)



PASI responses through Week 28 of OLE[a]



mNRI: if patient discontinued due to AE or inadequate response then imputed as non-responder; if discontinued for other reasons then imputed as LOCF

Steady-state time (hour)

	Dose	IC_{50}	IC_{90}
ESK-001	**40 mg qd**	19	7
	40 mg bid	>24	>24
Deucravacitinib	**6 mg qd**	9	0
Zasocitinib	**30 mg qd**	>24	5

*P<0.05; †P<0.005; ‡P<0.001 vs placebo; [a]Data as of March 1, 2024. mITT analysis set. Patients from all randomized groups who transitioned to 40 mg bid

Papp KA, et al. AAD 2024, Late-breaking abstract. Sponsored by Alumis Inc. Blauvelt A, et al. EADV 2024, D3T01.3D. Sponsored by Alumis Inc.

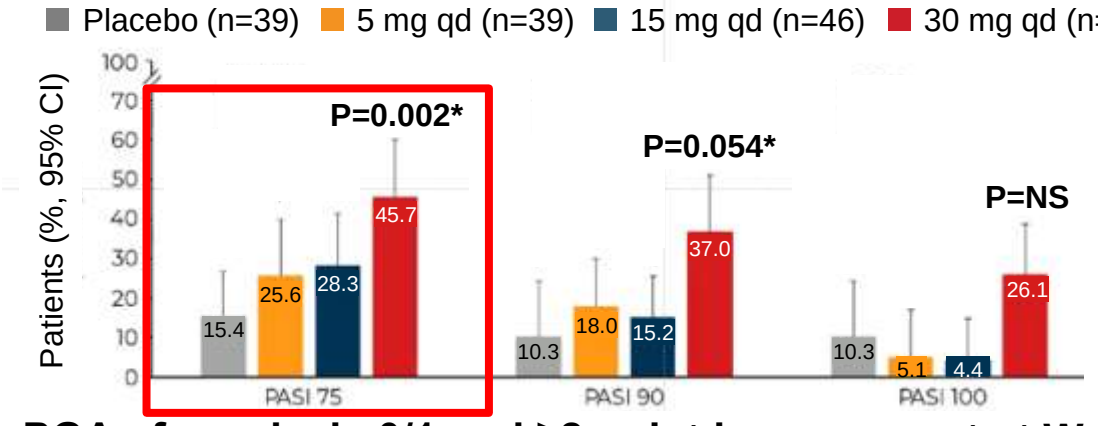
Efficacy of oral TYK2 inhibitor zasocitinib (TAK-279) in skin and joint disease: Phase 2b trial in patients with active PsA

- Multicentre, double-blind RCT
  - 1:1:1:1 to zasocitinib 5, 15 or 30 mg or PBO qd for 12 weeks[a]
- Eligibility
  - PsA symptoms ≥6 months before screening
  - Met CASPAR criteria
  - ≥3 TJC and ≥3 SJC despite prior therapy[b]
- **Primary endpoint**: ACR20 at Week 12
- Selected secondary endpoints
  - PASI 75 (in patients with ≥3% psoriasis BSA)
  - PGA of psoriasis 0/1 and ≥2-point improvement from BL in patients with psoriasis PGA ≥3% at BL
  - **Minimal disease activity (MDA)** – composite measure that captures PsA joint and skin manifestations and patient-reported outcomes

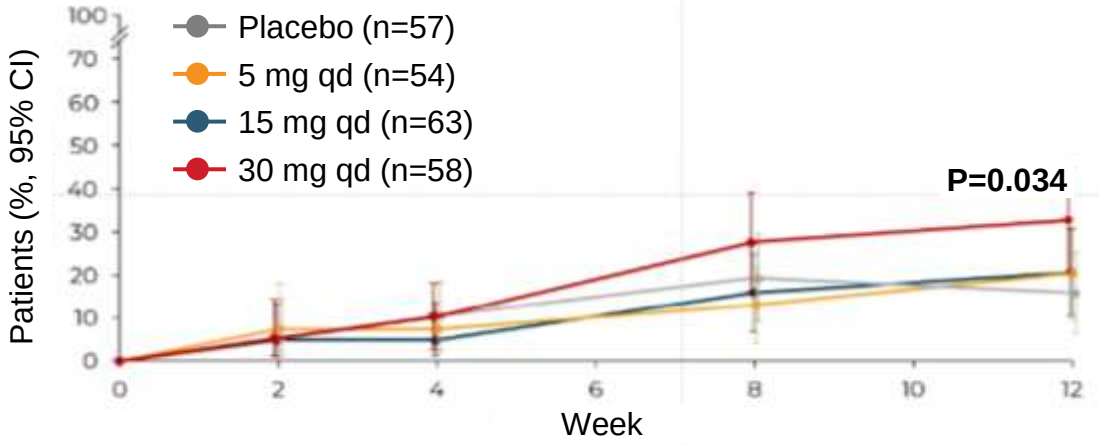
Patient achieves MDA when ≥5 of 7 criteria are met

1. TJC ≤1
2. SJC ≤1
3. PASI ≤1 or BSA ≤3%
4. Pain VAS ≤15
5. PtGA of PsA, VAS ≤20
6. HAQ-DI score ≤0.5
7. Tender entheseal points ≤1

PASI response at Week 12 in patients with ≥3% BSA at BL



PGA of psoriasis 0/1 and ≥2-point improvement at Week 12



[a]Safety follow-up for a further 4 weeks; [b]NSAID, csDMARD, biologics. *Nominal P-values vs PBO. Patients with missing data were classified nonresponders. PASI 75 and PGA were compared using 2-sided Mantel-Haenszel test stratified by randomization factors (prior b/tsDMARD; region) as covariates. PASI 90 and 100 were compared using 2-sided Chi-square test or Fisher's exact method if n<5. HAQ-DI, health assessment questionnaire-Disability Index; PGA, physician global assessment; PtGA, patient global assessment of PsA

Gottlieb AB, et al. EADV 2024, FC05.02. Sponsored by Takeda.

JAK Inhibitors

- Boxed warnings: what are the real risks?
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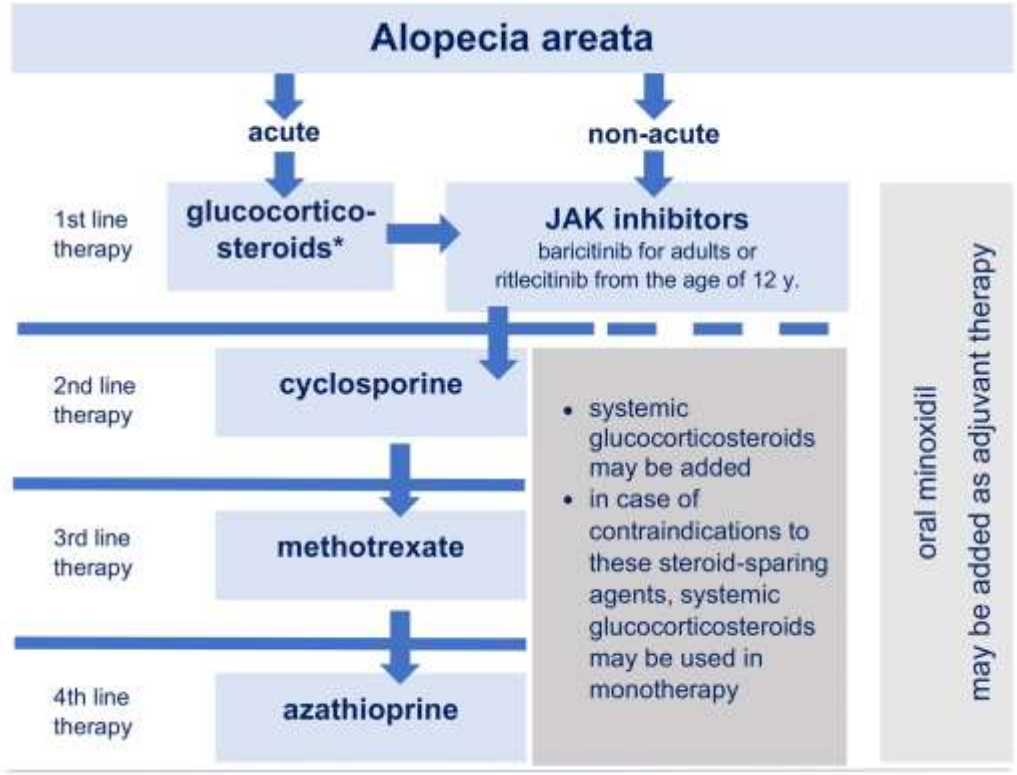
- Role in psoriasis
- Role in alopecia areata
- Role in vitiligo
- What could go wrong?

European expert consensus statement on the systemic treatment of alopecia areata



Acad Dermatol Venereol, Volume: 38, Issue: 4, Pages: 687-694, First published: 02 January 2024, DOI: (10.1111/jdv.19768)

- Baricitinib
- Ritlecitinib
- Deuroxolitinib

- How effective are they?
- Do they work for eye brows and eyelashes?
- How fast are they?
- Can you stop them after regrowth?

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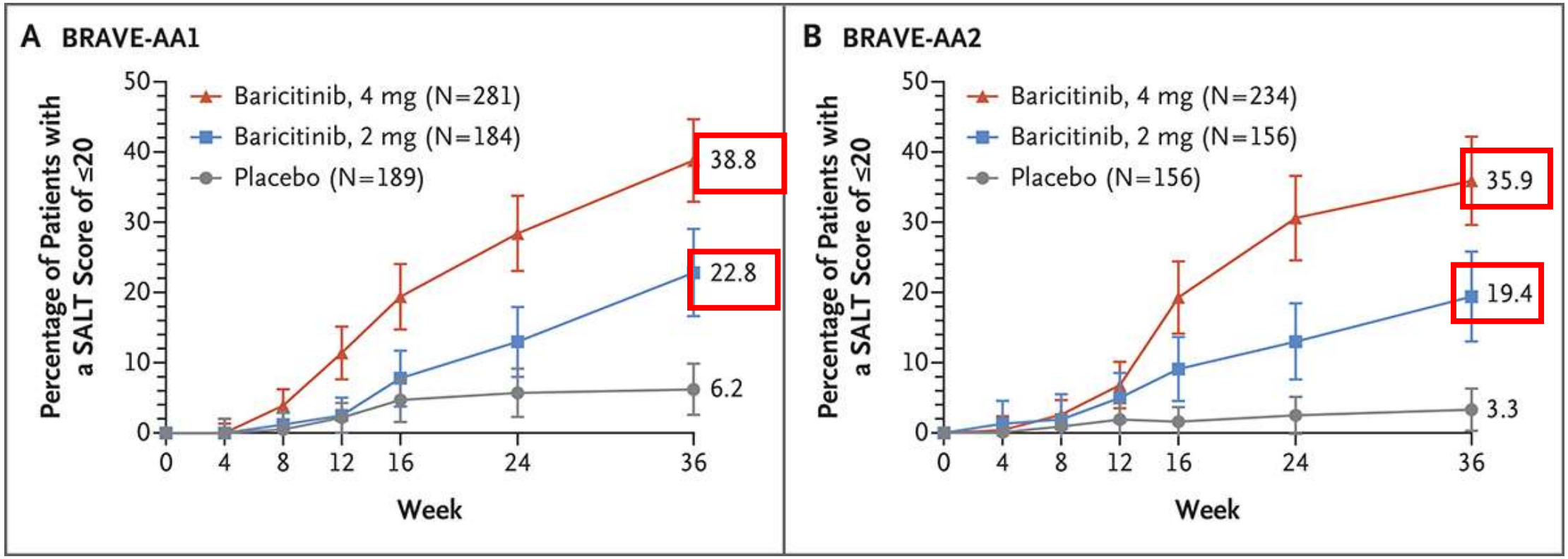
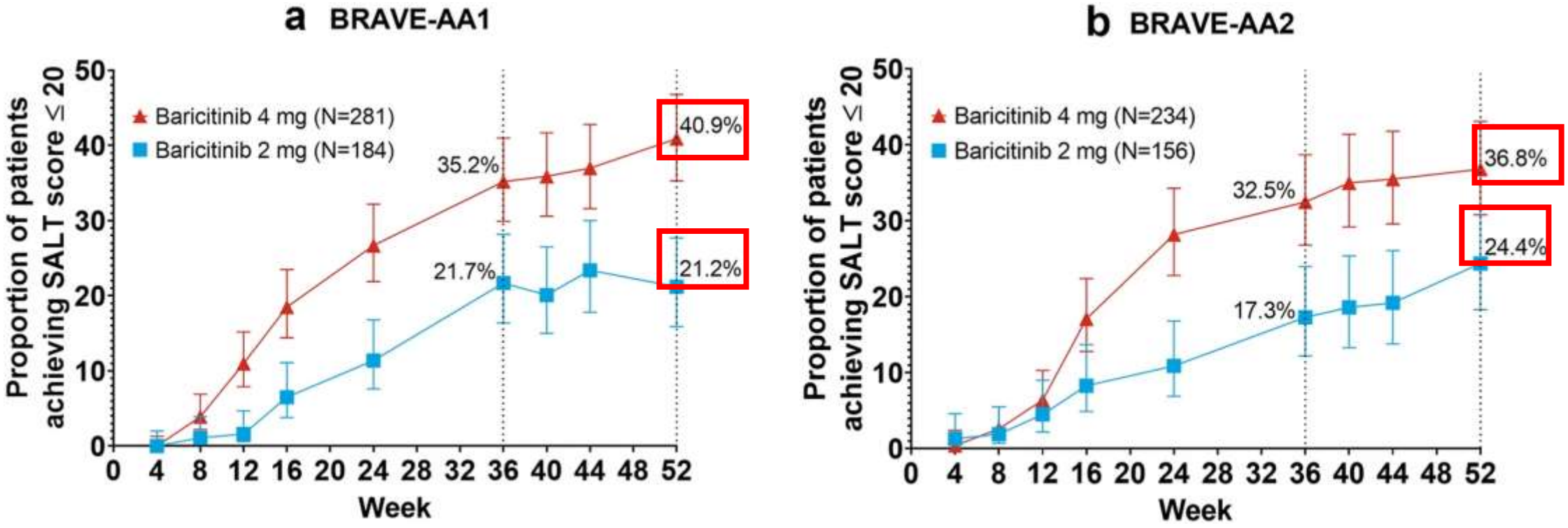
King B, Ohyama M, Kwon O, Zlotogorski A, Ko J, Mesinkovska NA, Hordinsky M, Dutronc Y, Wu WS, McCollam J, Chiasserini C, Yu G, Stanley S, Holzwarth K, DeLozier AM, Sinclair R; BRAVE-AA Investigators. Two Phase 3 Trials of Baricitinib for Alopecia Areata. N Engl J Med. 2022 May 5;386(18):1687-1699.

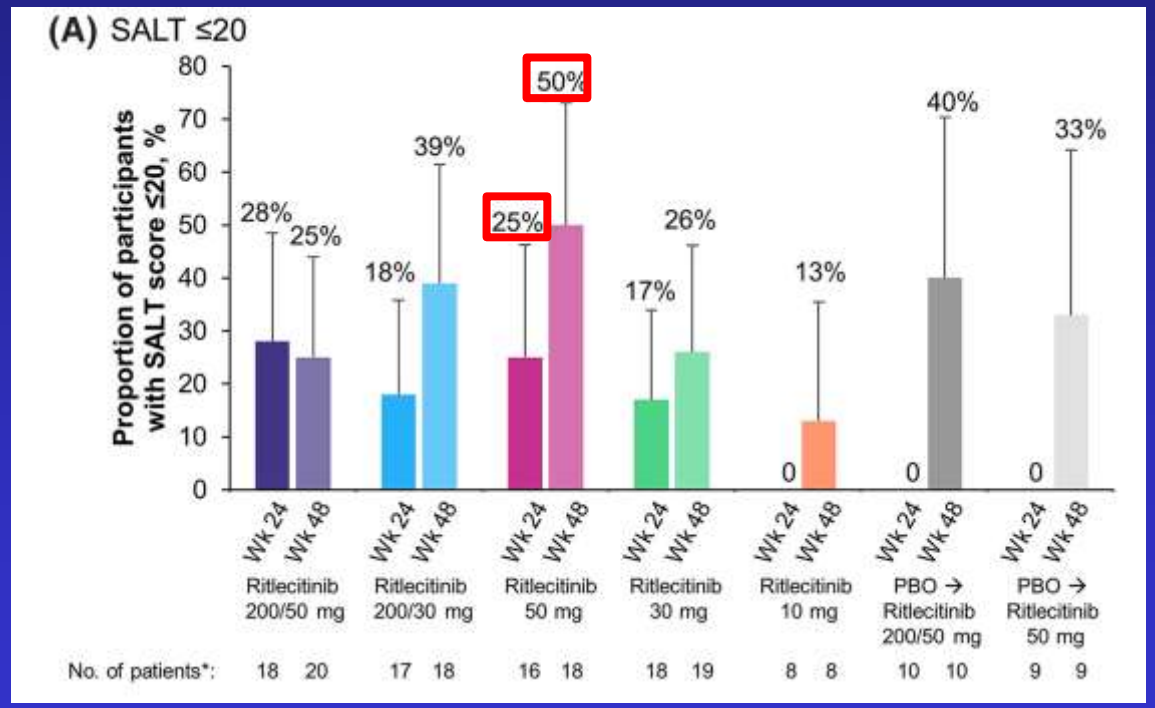
SALT≤20



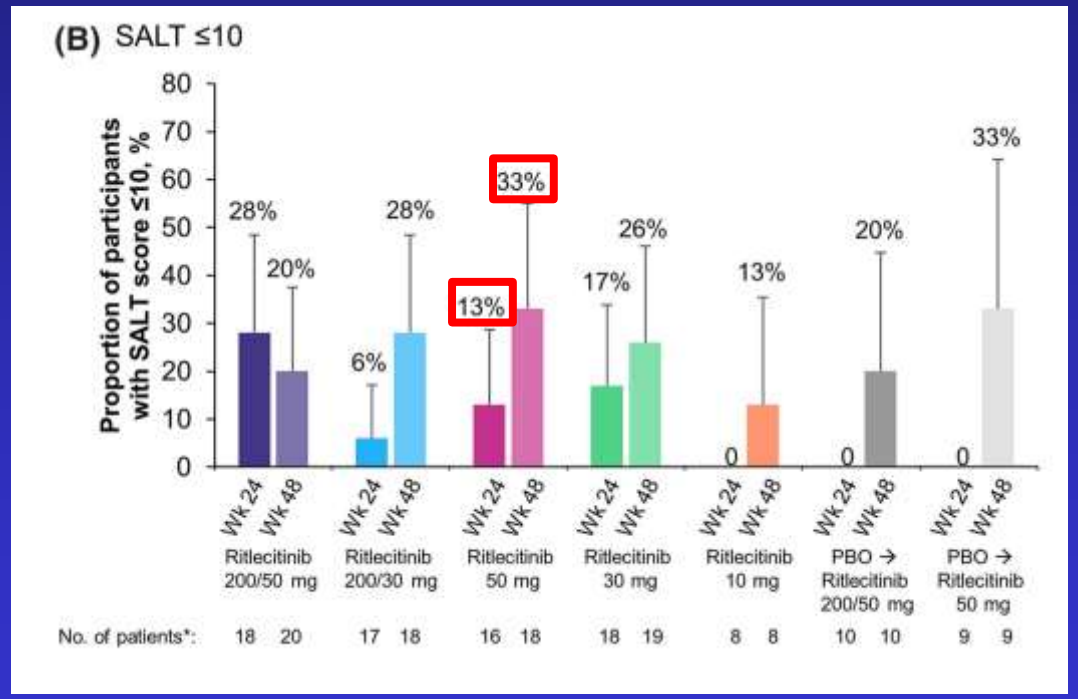
Kwon O, Senna MM, Sinclair R, Ito T, Dutronc Y, Lin CY, Yu G, Chiasserini C, McCollam J, Wu WS, King B. Efficacy and Safety of Baricitinib in Patients with Severe Alopecia Areata over 52 Weeks of Continuous Therapy in Two Phase III Trials (BRAVE-AA1 and BRAVE-AA2). Am J Clin Dermatol. 2023 May;24(3):443-451



Efficacy and safety of ritlecitinib in adolescents with alopecia areata: Results from the ALLEGRO phase 2b/3 randomized, double-blind, placebo-controlled trial.
Hordinsky M, Hebert AA, Gooderham M, Kwon O, Murashkin N, Fang H, Harada K, Law E, Wajsbrot D, Takiya L, Zwillich SH, Wolk R, Tran H.
Pediatr Dermatol.2023;40:1003-1009



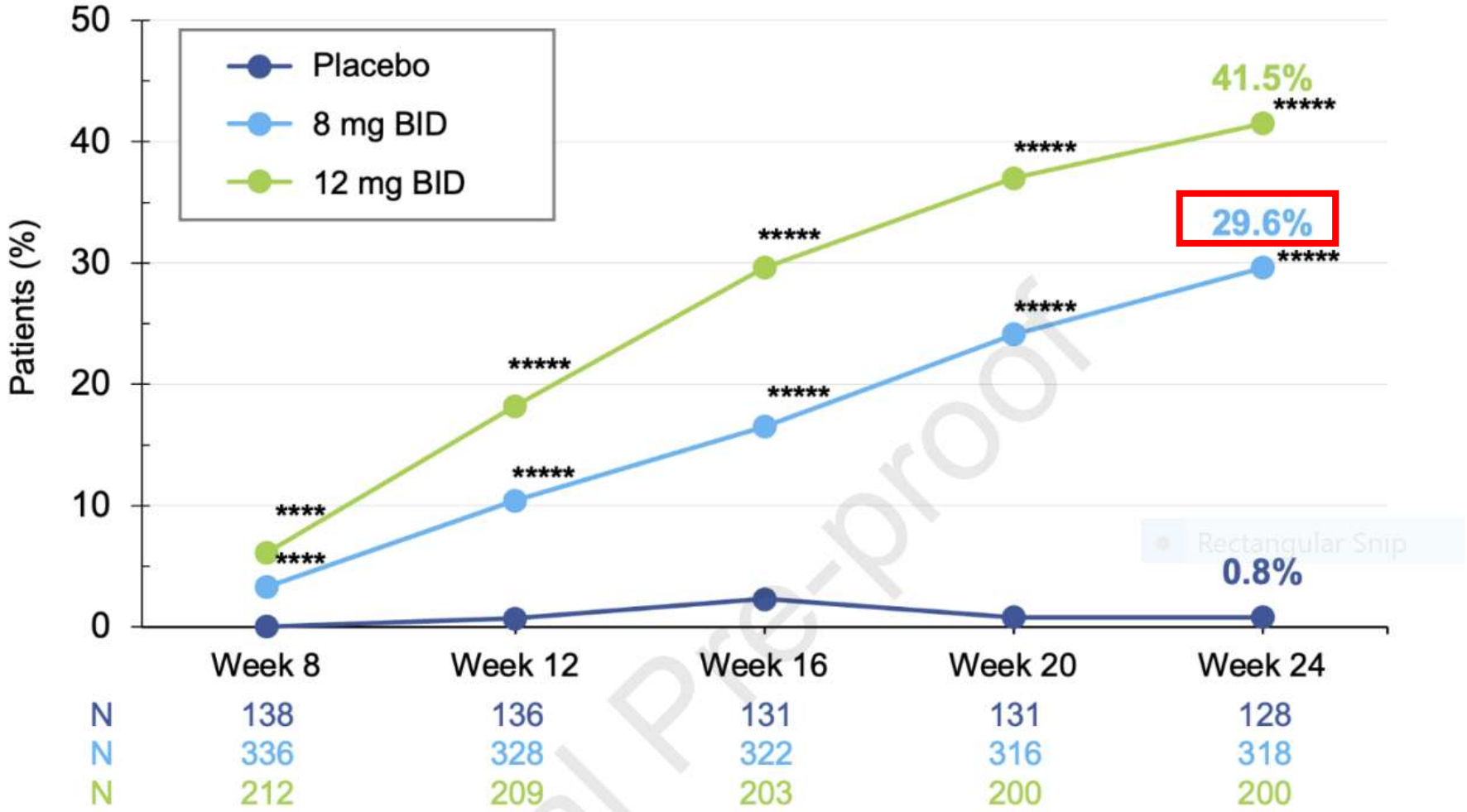
SALT≤20



SALT≤10

Figure 1: Percentage of patients with AA achieving a SALT score ≤20 throughout the treatment period

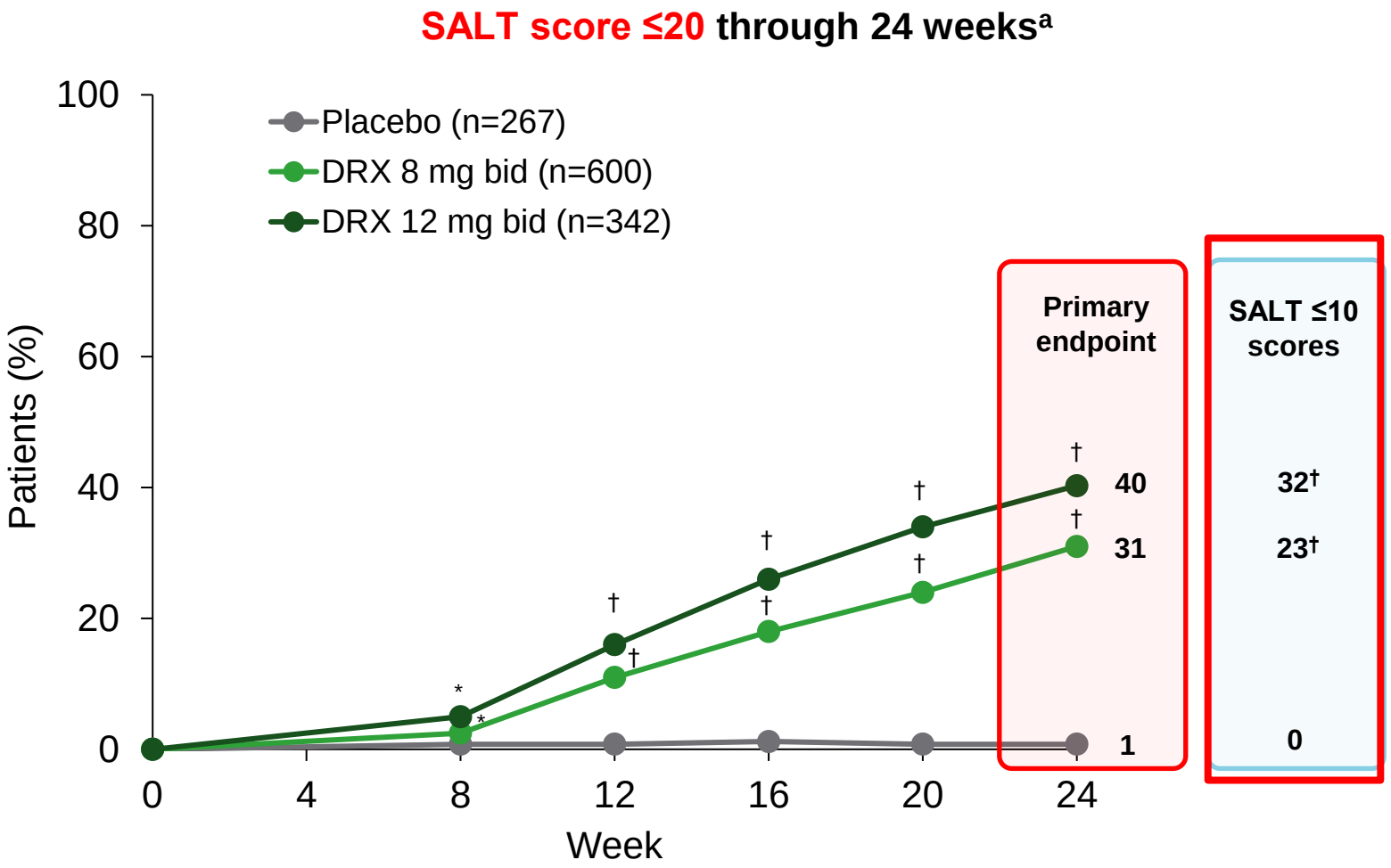
DEURUXOLITINIB



****p≤0.001 vs placebo; *****p≤0.0001 vs placebo.

mNRI

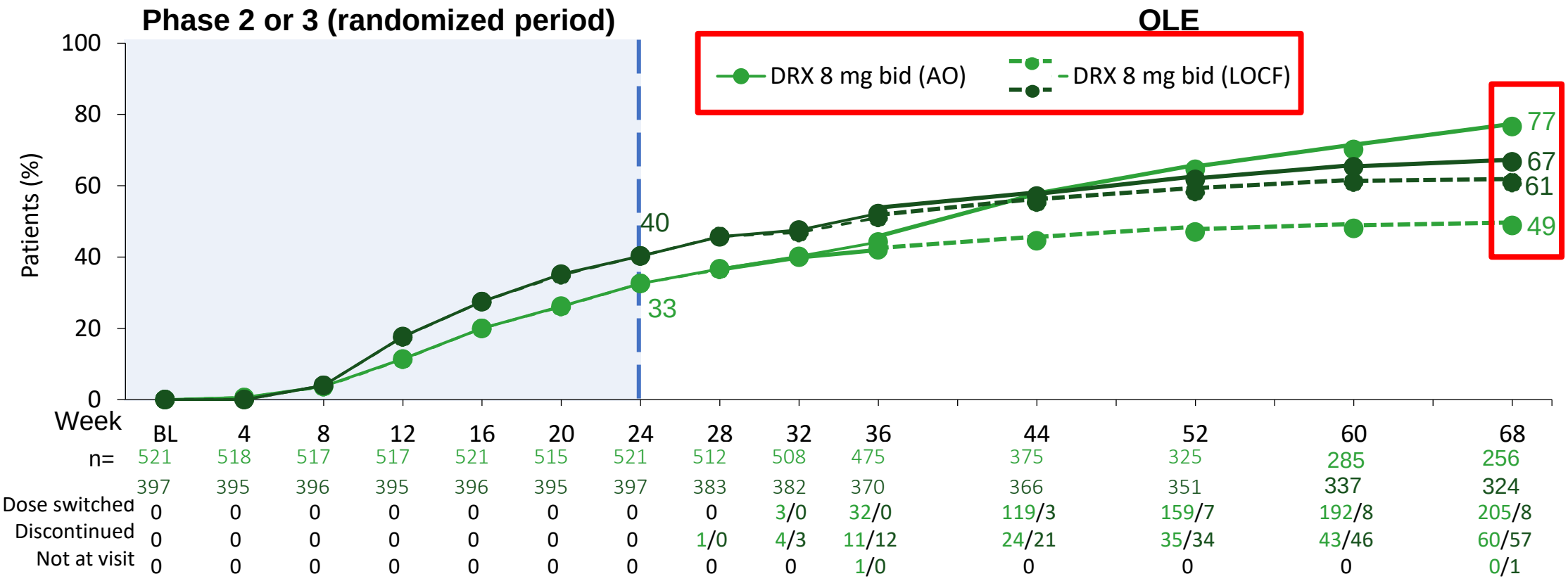
THRIVE-AA1/AA2 pooled analysis: Efficacy of deuruxolitinib (CTP-543) among patients with moderate to severe alopecia areata



*P=0.0005; †P<0.0001 vs placebo; [a]Imputation method not disclosed

Senna M, et al. AAD 2024, P51840. Sponsored by Concert Pharmaceuticals

THRIVE-AA1/AA2 pooled open-label extension trials: Achievement of SALT score ≤20 with deuruxolitinib through 68 weeks

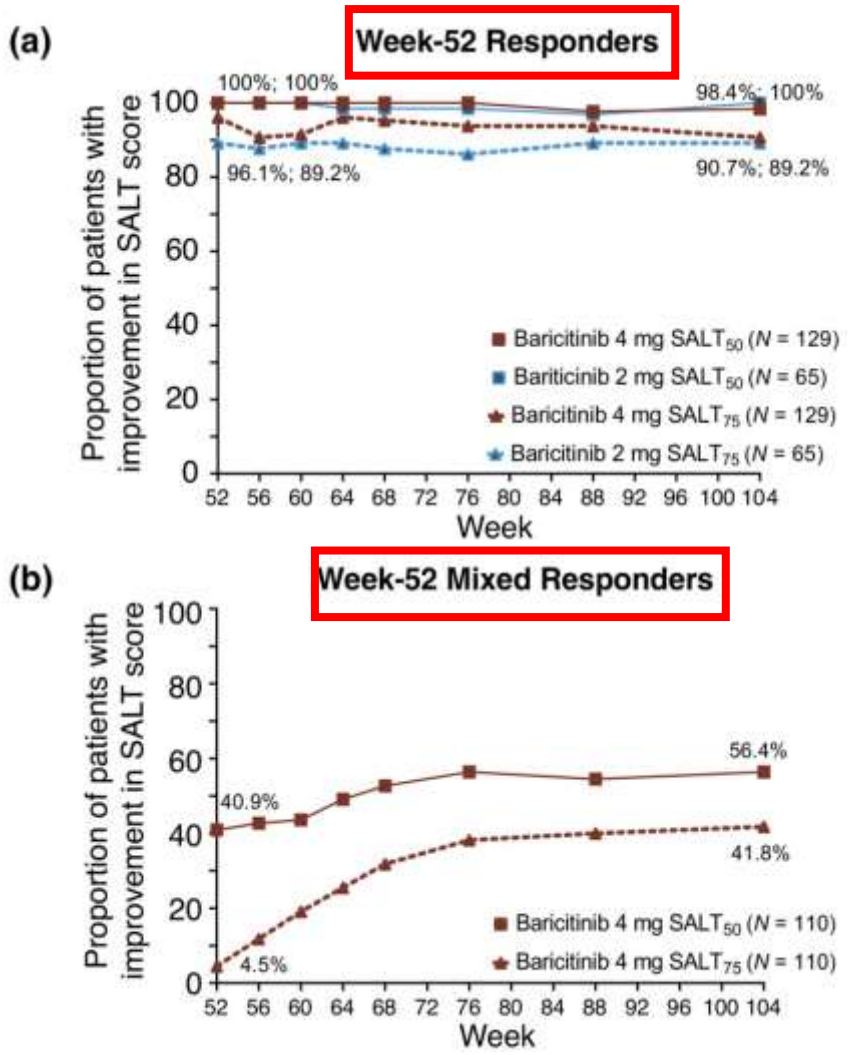


King B, et al. AAD 2024, Late-breaking abstract. Sponsored by Concert Pharmaceuticals

FIDE

Long-term efficacy and safety of baricitinib in patients with severe alopecia areata: 104-week results from BRAVE-AA1 and BRAVE-AA2

In responders, response Is maintained with continued therapy



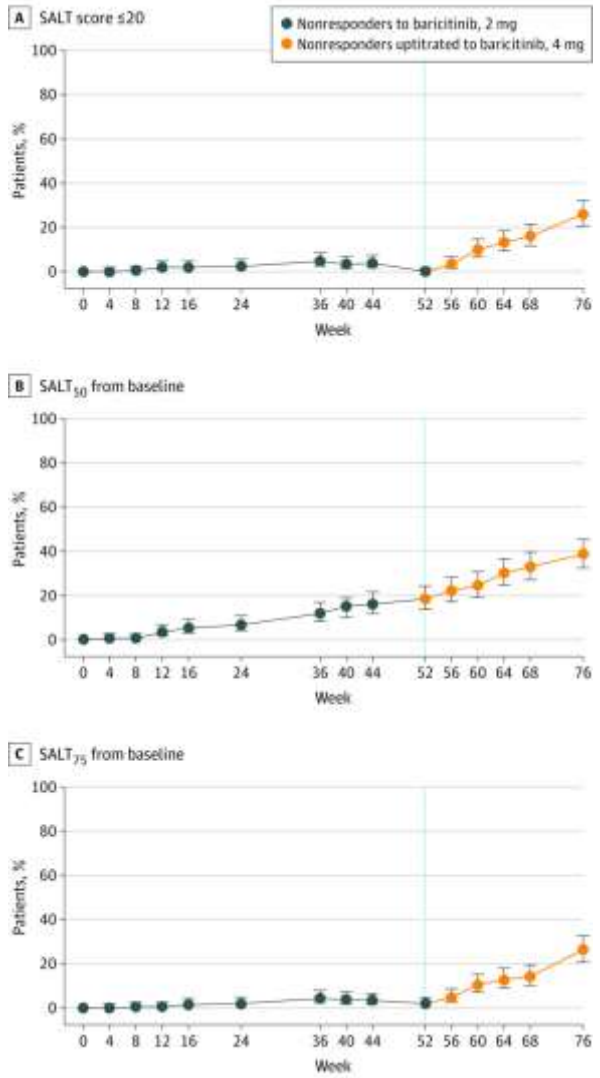
SALT

In mixed responders, response is increased with continued therapy

Acad Dermatol Venereol, Volume: 38, Issue: 3, Pages: 583-593, First published: 23 February 2024, DOI: (10.1111/jdv.19665)

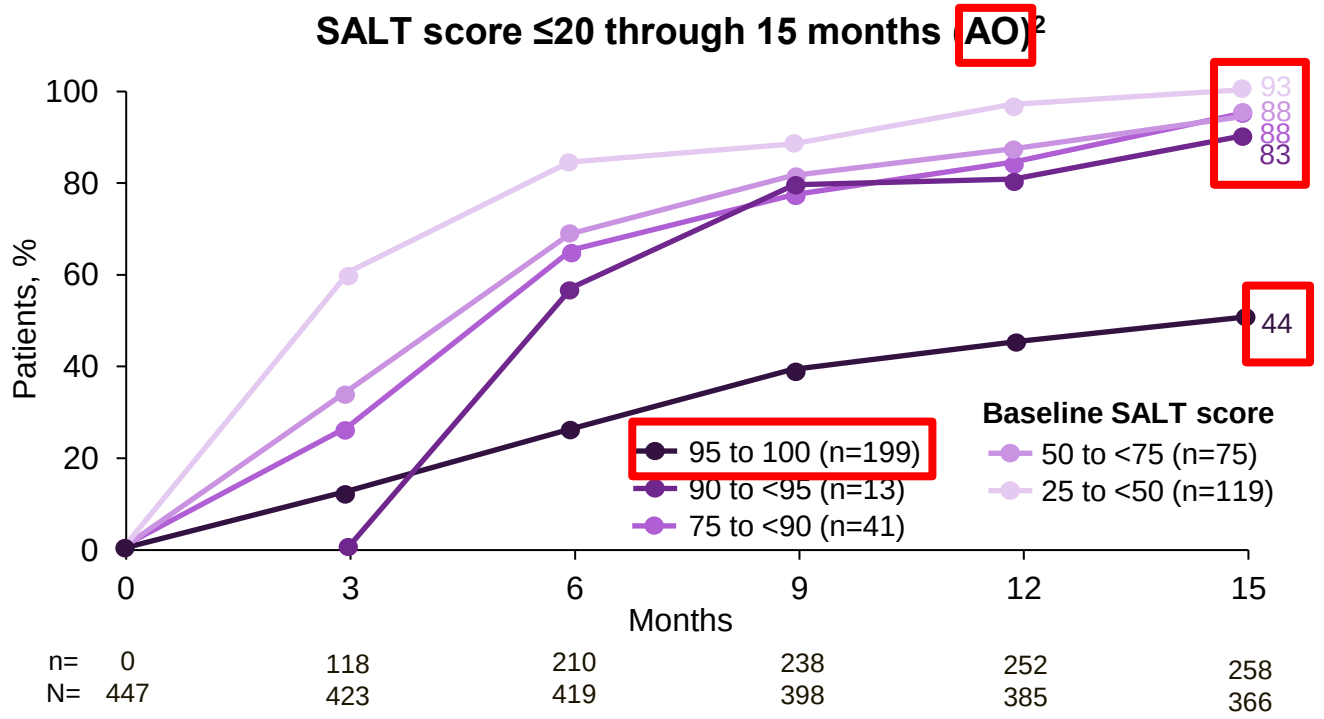
Ko JM, Mayo TT, Bergfeld WF, Dutronc Y, Yu G, Ball SG, Somani N, Craiglow BG. Clinical Outcomes for Uptitration of Baricitinib Therapy in Patients With Severe Alopecia Areata: A Pooled Analysis of the BRAVE-AA1 and BRAVE-AA2 Trials. JAMA Dermatol. 2023 Sep 1;159(9):970-976.

Higher doses
are more effective



ALLEGRO-LT post hoc analysis: Achievement of SALT score ≤20 in patients with alopecia areata by extent of hair loss at baseline

RITLECITINIB

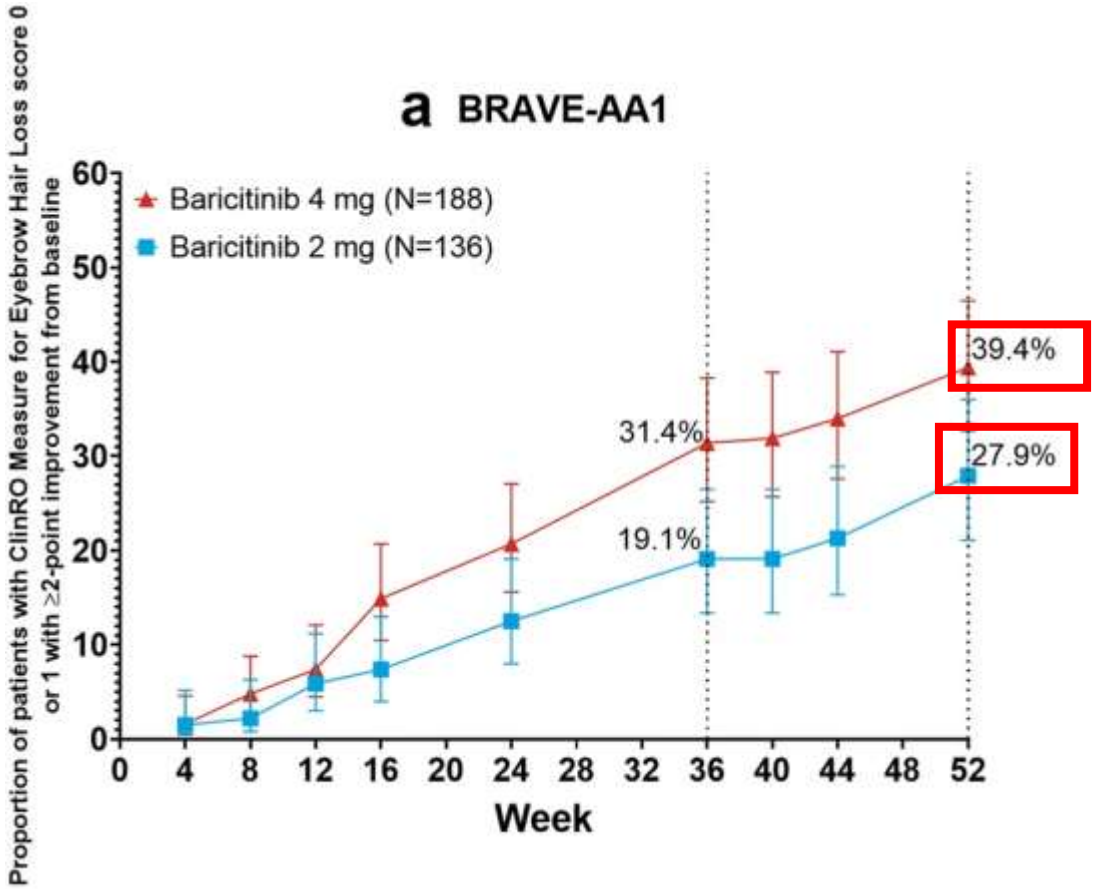


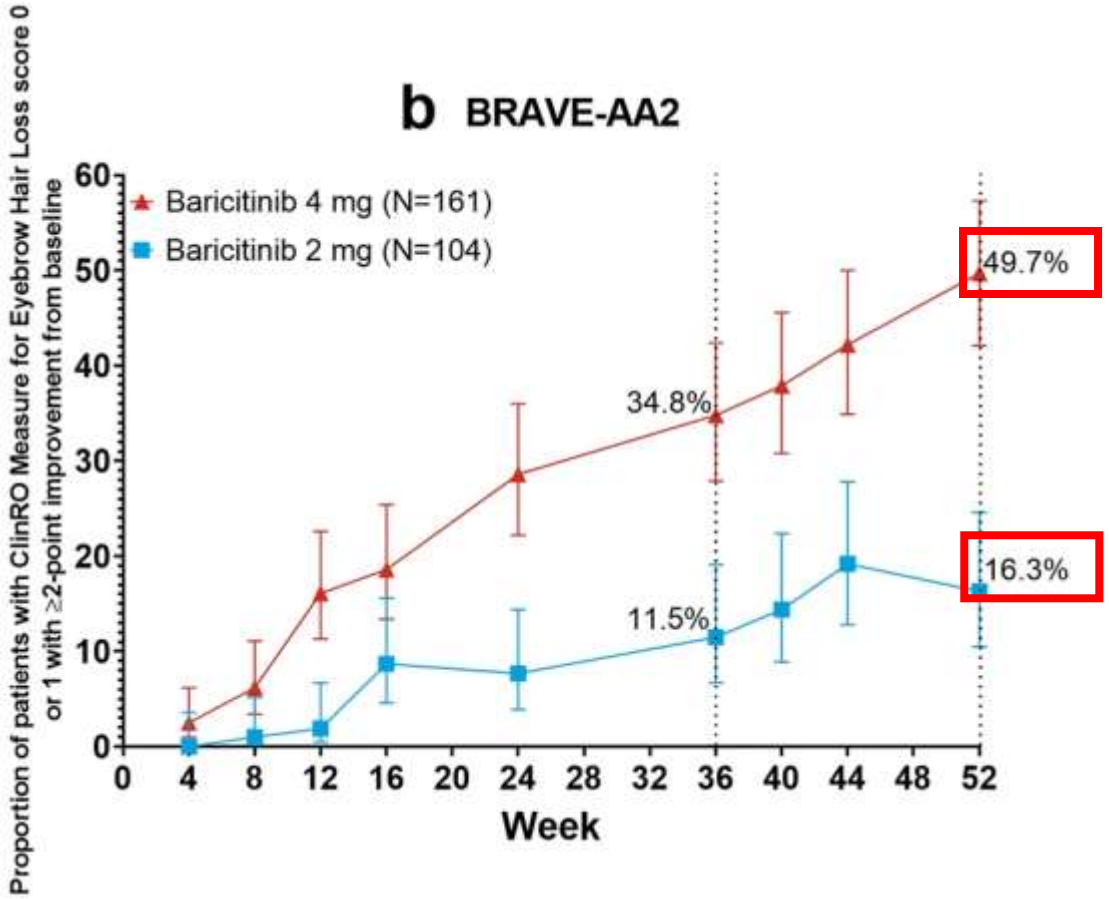
n=total number of patients with SALT score ≤20 response at each visit; N=total number of patients with data available at each visit

1. Soung J, et al. EADV 2023, D1T01.1F; 2. Tsianakas A, et al. EADV 2023, FC01.1. Sponsored by Pfizer Inc

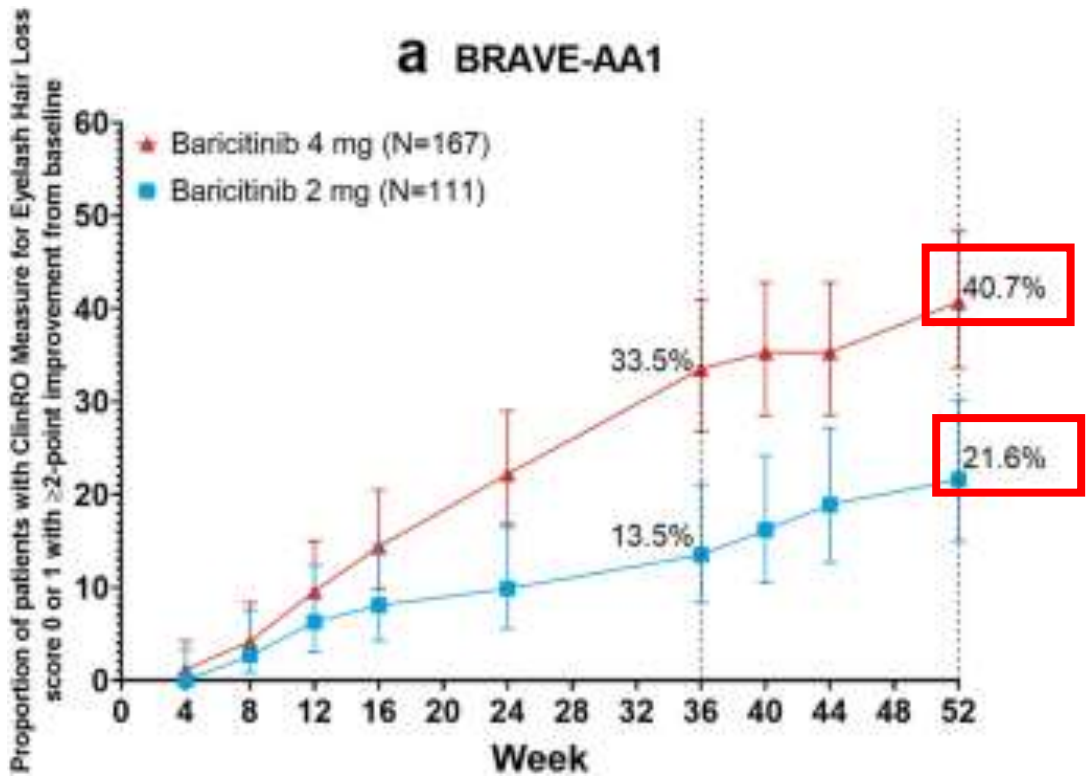
- How effective are they?
- Do they work for eye brows and eyelashes?
- How fast are they?
- Can you stop them after regrowth?

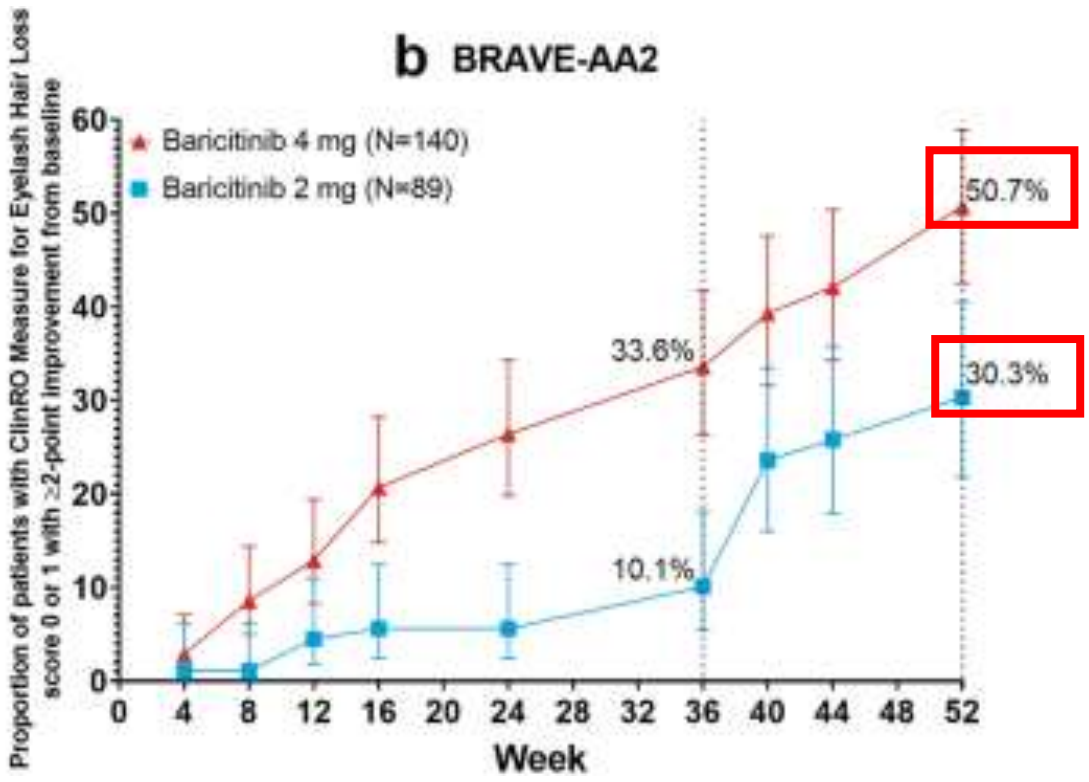
Baricitinib –eyebrow hairloss 0 or 1 with≥2 point improvement



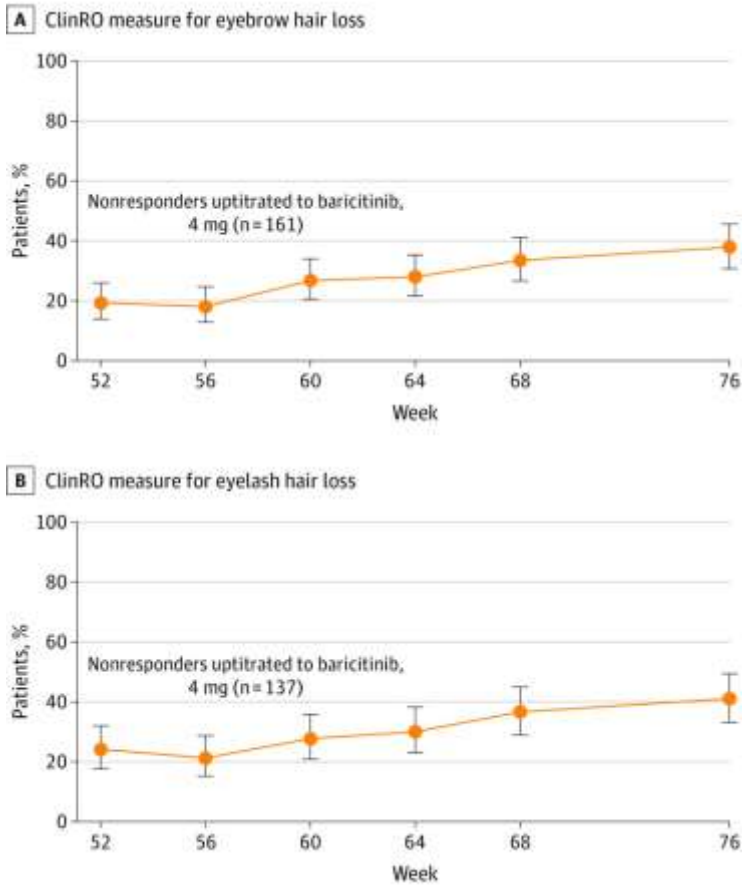


Baricitinib –eyelash hairloss 0 or 1 with≥2 point improvement

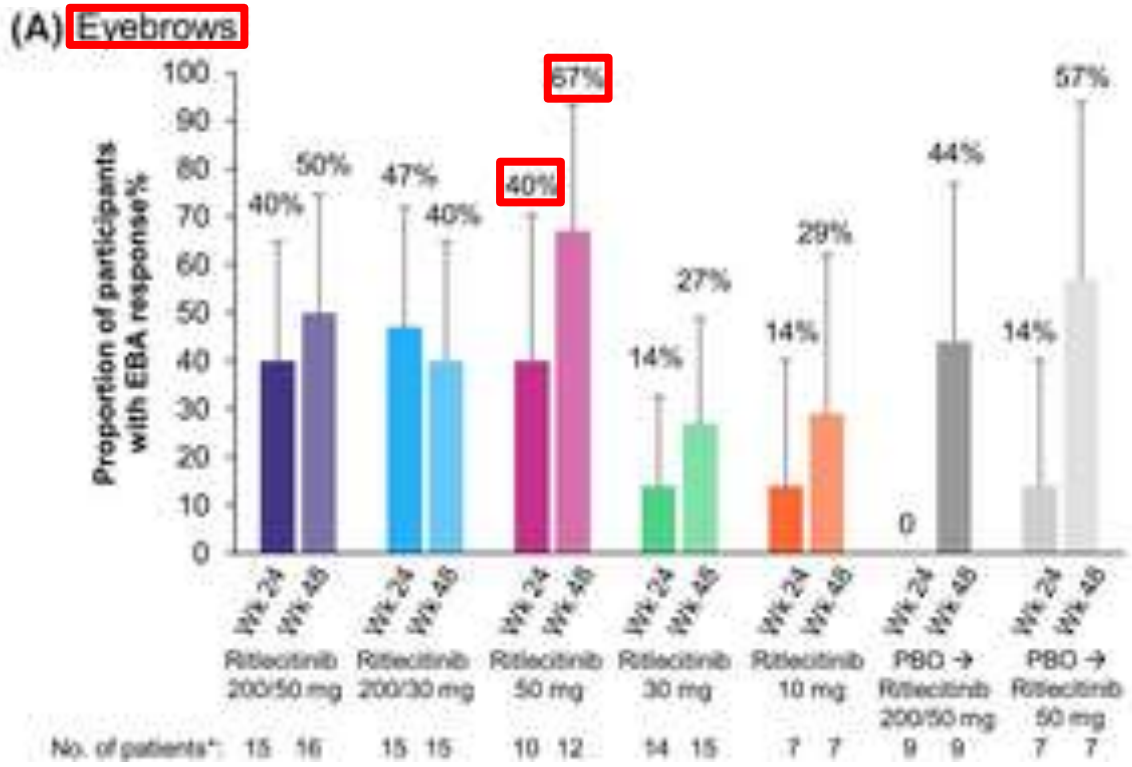


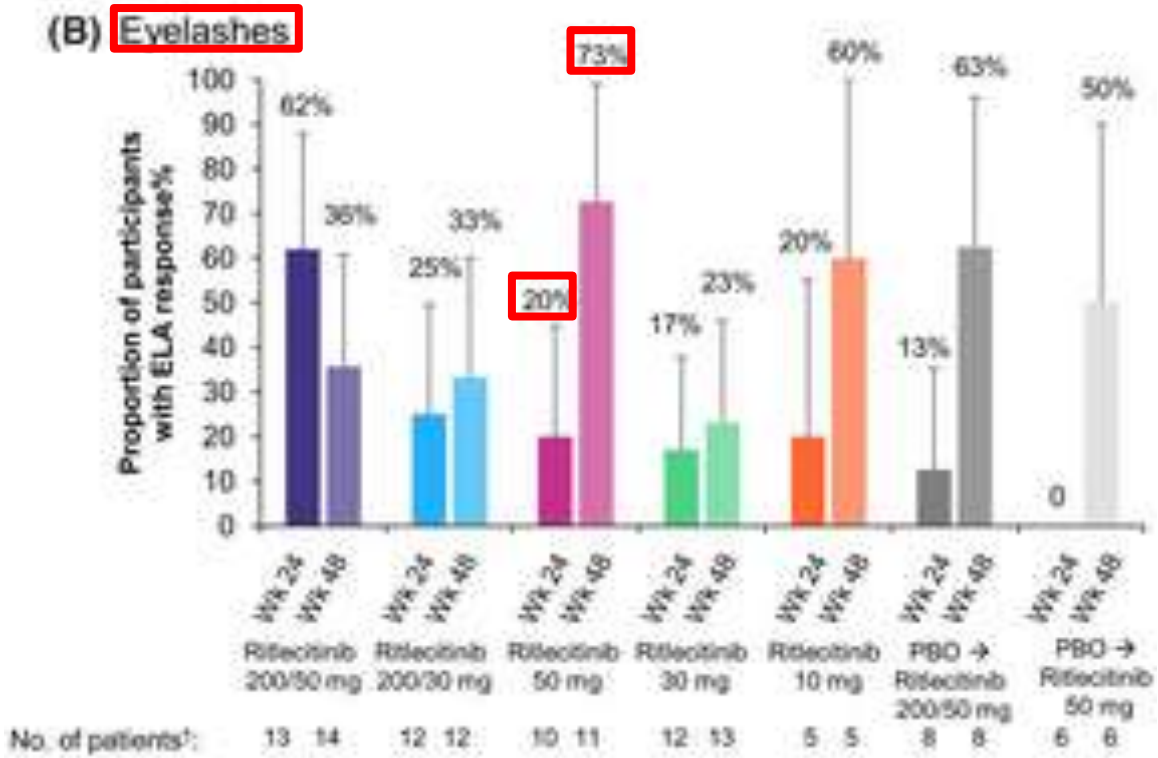


Uptitration of baricitinib for eyebrow and eyelash nonresponders



Efficacy and safety of ritlecitinib in adolescents with alopecia areata: Results from the ALLEGRO phase 2b/3 randomized, double-blind, placebo-controlled trial.
Hordinsky M, Hebert AA, Gooderham M, Kwon O, Murashkin N, Fang H, Harada K, Law E, Wajsbrot D, Takiya L, Zwillich SH, Wolk R, Tran H.
Pediatr Dermatol. 2023;40:1003-1009





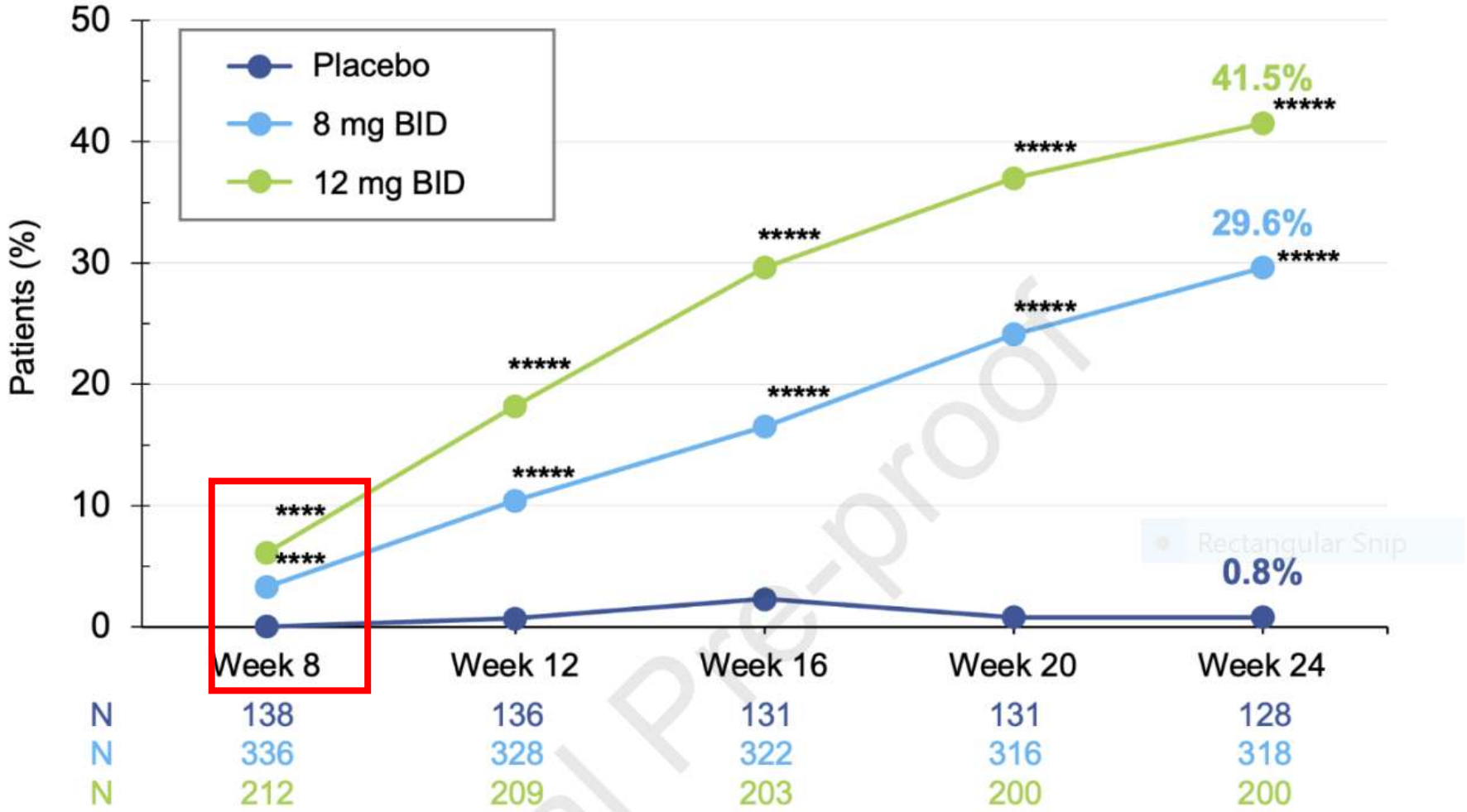
Efficacy and safety of ritlecitinib in adolescents with alopecia areata: Results from the ALLEGRO phase 2b/3 randomized, double-blind, placebo-controlled trial

Pediatric Dermatology, Volume: 40, Issue: 6, Pages: 1003-1009, First published: 17 July 2023, DOI: (10.1111/pde.15378)

- How effective are they?
- Do they work for eye brows and eyelashes?
- How fast are they?
- Can you stop them after regrowth?

Figure 1: Percentage of patients with AA achieving a SALT score ≤20 throughout the treatment period

DEURUXOLITINIB



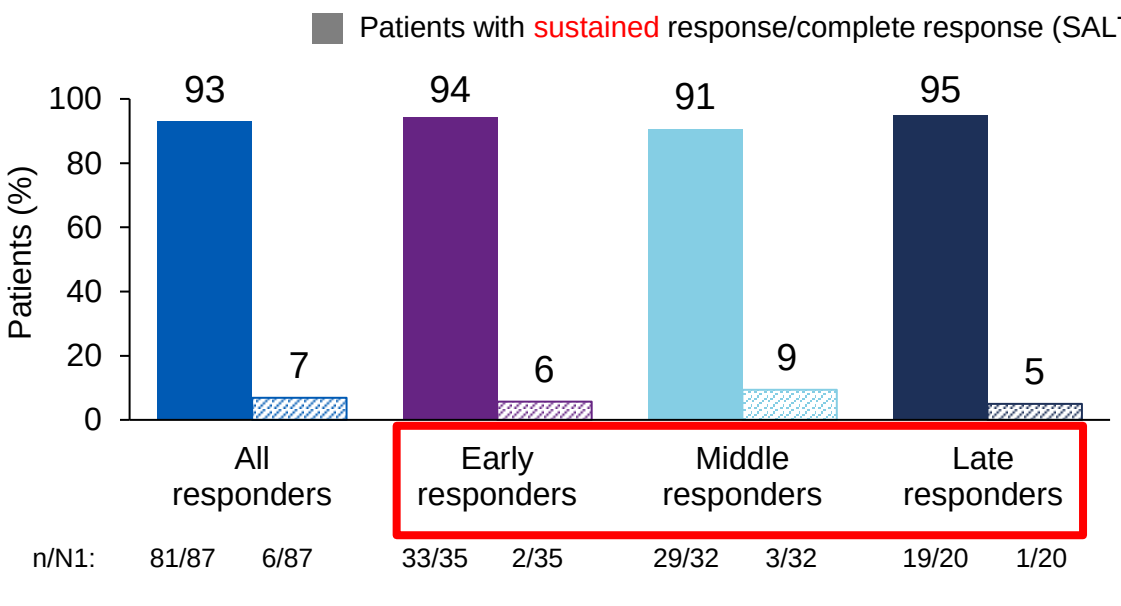
****p≤0.001 vs placebo; *****p≤0.0001 vs placebo.

mNRI

ALLEGRO and ALLEGRO-LT post hoc analysis: Sustained and complete responses among SALT score ≤20 responders through 24 months

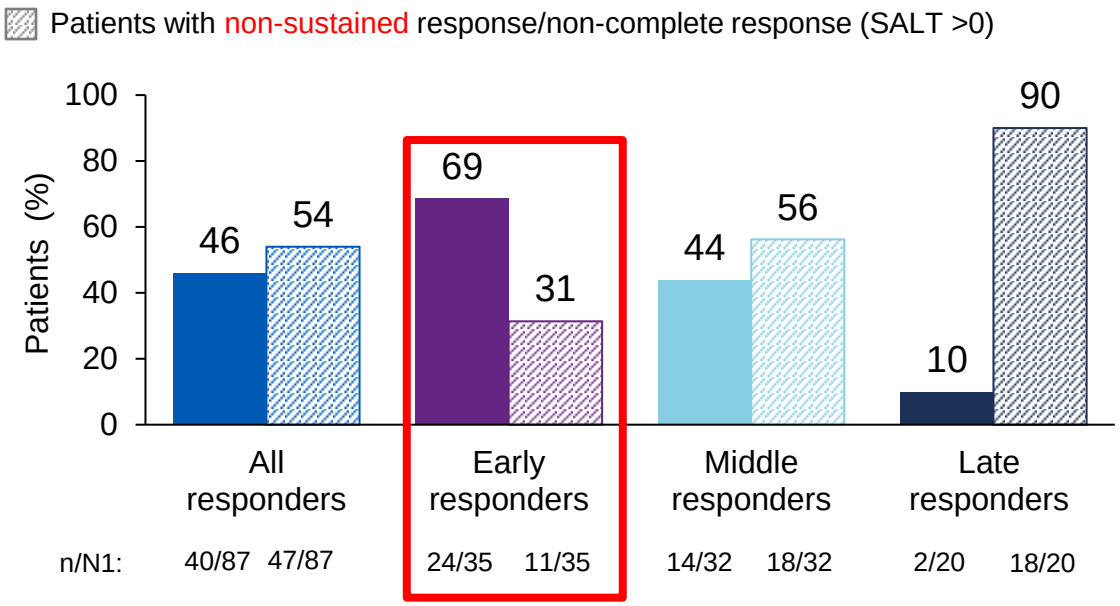
Sustained responses occur regardless of speed of response

Sustained responses[a] (AO)



Complete responses are most common in early responders

Complete responses[b] (AO)



RITLECITINIB

[a]Patients with sustained response achieved SALT score ≤20 at any timepoint and then maintained SALT score ≤20 at all subsequent timepoints. All available timepoints that a patient had between baseline and Week 96, where "available" means that the SALT value is non-missing. Patients who never achieved SALT score ≤20 and patients who achieved SALT score ≤20 but recorded SALT score >20 at subsequent timepoints, were excluded; [b]SALT score 0

King B, et al. EADV 2023, FC01.3. Sponsored by Pfizer Inc.

FIDE

King B, Shapiro J, Ohyama M, Egeberg A, Piraccini BM, Craiglow B, Sinclair R, Chen YF, Wu WS, Ding Y, Somani N, Dutronc Y. When to expect scalp hair regrowth during treatment of severe alopecia areata with baricitinib: insights from trajectories analyses of patients enrolled in two phase III trials. Br J Dermatol. 2023 Nov 16;189(6):666-673.

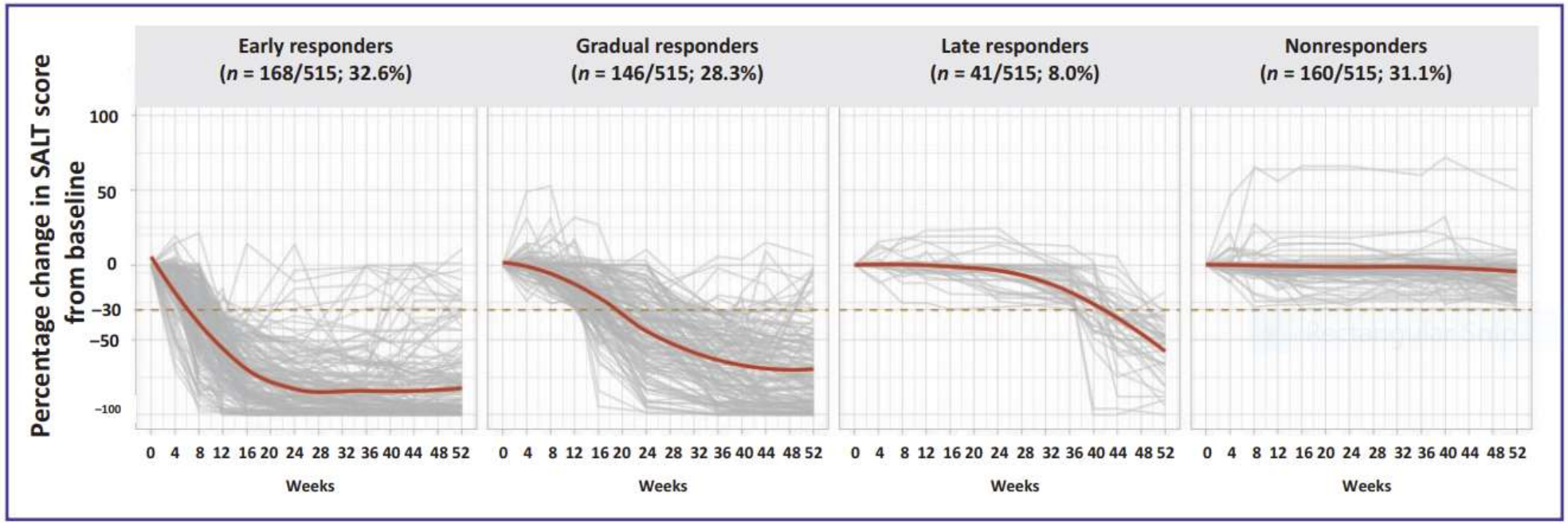


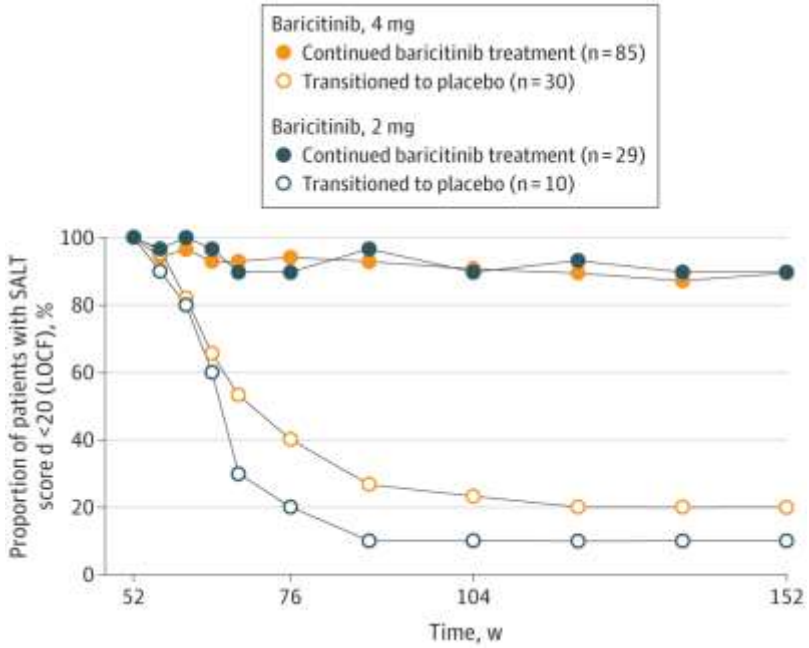
Figure 2 Percentage change in Severity of Alopecia Tool (SALT) score from baseline through to week 52 for $SALT_{30}$ (≥ 30% improvement from baseline in SALT score) early, gradual, late and nonresponders treated with baricitinib 4 mg. The grey lines indicate individual patients, the thick red lines are the smoothing lines using local polynomial regression fitting and the red dotted line indicates $SALT_{30}$. Data were censored after permanent study drug discontinuation or data collected via remote visits due to the COVID-19 pandemic. Missing data were imputed using a modified last observation carried forward method.

- How effective are they?
- Do they work for eye brows and eyelashes?
- How fast are they?
- Can you stop them after regrowth?

JAMA Network™

From: **Baricitinib Withdrawal and Retreatment in Patients With Severe Alopecia Areata: The BRAVE-AA1 Randomized Clinical Trial**

JAMA Dermatol. Published online August 14, 2024. doi:10.1001/jamadermatol.2024.2734



LOSS OF BENEFIT

Proportion of Patients With a Severity of Alopecia Tool (SALT) Score of 20 or Less From Weeks 52 to 152 for Patients Who Remained Taking Treatment and Who Were Withdrawn to PlaceboLOCF indicates last observation carried forward.

JAK Inhibitors

- Boxed warnings: what are the real risks?
- For what conditions do they work?
- What are they?
- Role in atopic dermatitis
- Role in psoriasis
- Role in alopecia areata
- Role in vitiligo
- What could go wrong?

Rapid repigmentation of vitiligo using tofacitinib plus low-dose, narrowband UV-B phototherapy.

Kim SR, et al.

JAMA Dermatol. 2018;154(3):370-1.

Treatment of vitiligo with the topical Janus kinase inhibitor ruxolitinib.

Rothstein B, et al.

J Am Acad Dermatol. 2017; 76(6):1054-60.

- 4/11 → ↑ 76% facial VASI w. 20
  (95% CI 53-99%; P = .001)
- all patients → 23%↑VASI w.20 (95% CI 4-43%; P = .02).
- 3/8 patients responded on body surfaces
- 1/8 patients responded on acral surfaces.

Treatment of vitiligo with the topical Janus kinase inhibitor ruxolitinib: A 32-week open-label extension study with optional narrow-band ultraviolet B.

Joshipura D, et al.

J Am Acad Dermatol. 2018; 78(6):1205-7.

- 37.6% ↑ VASI
- 5/8 >0.5% on face → ↑facial VASI 92% at w.52
- 3/6 → 12.6% ↑ VASI nonacral UE's
- 2/3 (both had UVB) → 16.7% ↑ VASI trunk
- One → sl. Acral repigmentation

Presented at the 24th World Congress of Dermatology
June 10−15, 2019; Milan, Italy

Efficacy and Safety of Ruxolitinib Cream for the Treatment of Vitiligo: Results of a 24-Week, Randomized, Double-Blind, Dose-Ranging, Vehicle-Controlled Study

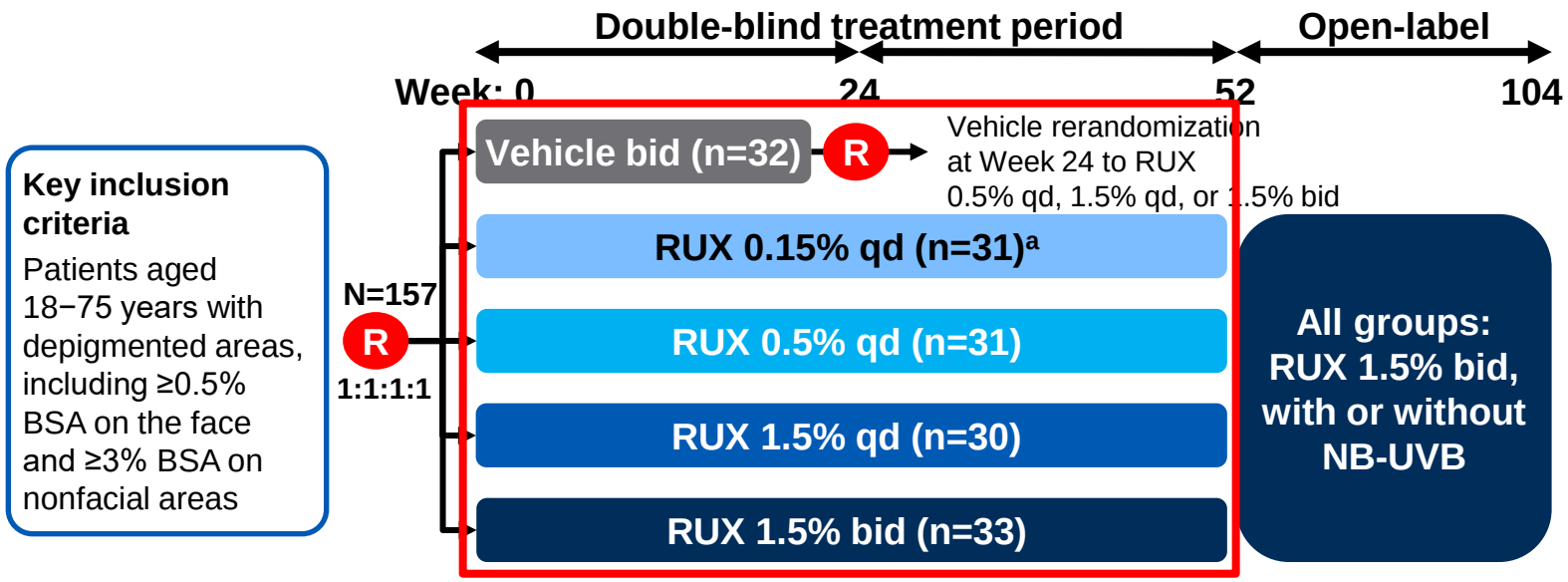
David Rosmarin, MD,[1] Amit G. Pandya, MD,[2] Mark Lebwohl, MD,[3] Pearl Grimes, MD,[4] Iltefat Hamzavi, MD,[5] Alice B. Gottlieb, MD, PhD,[6] Kathleen Butler, MD,[7] Fiona Kuo, PhD,[7] Michael D. Howell, PhD,[7] Kang Sun, PhD,[7] John E. Harris, MD, PhD[8]

[1]Tufts Medical Center, Boston, MA, USA; [2]University of Southwestern Medical Center, Dallas, TX, USA; [3]Mount Sinai Hospital, New York, NY, USA; [4]The Vitiligo & Pigmentation Institute of Southern California, Los Angeles, CA, USA; [5]Henry Ford Medical Center, Detroit, MI, USA; [6]Icahn School of Medicine at Mount Sinai, New York, NY, USA; [7]Incyte Corporation, Wilmington, DE, USA; [8]University of Massachusetts Medical School, Worcester, MA, USA

Phase 2, randomized, double-blind, vehicle-controlled trial of topical ruxolitinib cream, a JAK1/JAK2 inhibitor, for adult patients with vitiligo

Previously presented slide

- Oral ruxolitinib is FDA approved for polycythemia vera, myelofibrosis, and acute graft versus host disease
  - Topical RUX is not yet approved by the FDA



Baseline demographics and clinical characteristics were similar across treatment groups

F-VASI 75 responders during double-blind treatment[1]

F-VASI 75, % of patients	Vehicle (n=32)	RUX 0.15% qd (n=31)	RUX 0.5% qd (n=31)	RUX 1.5% qd (n=30)	RUX 1.5% bid (n=33)
Week 24	0	10	16	17	30
Week 52	N/A	N/A	29	30	52

Efficacy endpoints: ≥50% improvement from baseline in T-VASI score (T-VASI 50) and ≥75% improvement from baseline in T-VASI score (T-VASI 75), both at Week 24 and Week 52

Subgroup analysis: Patients initially randomized to ruxolitinib 1.5% qd and 1.5% bid and patients with ≤20% of total BSA

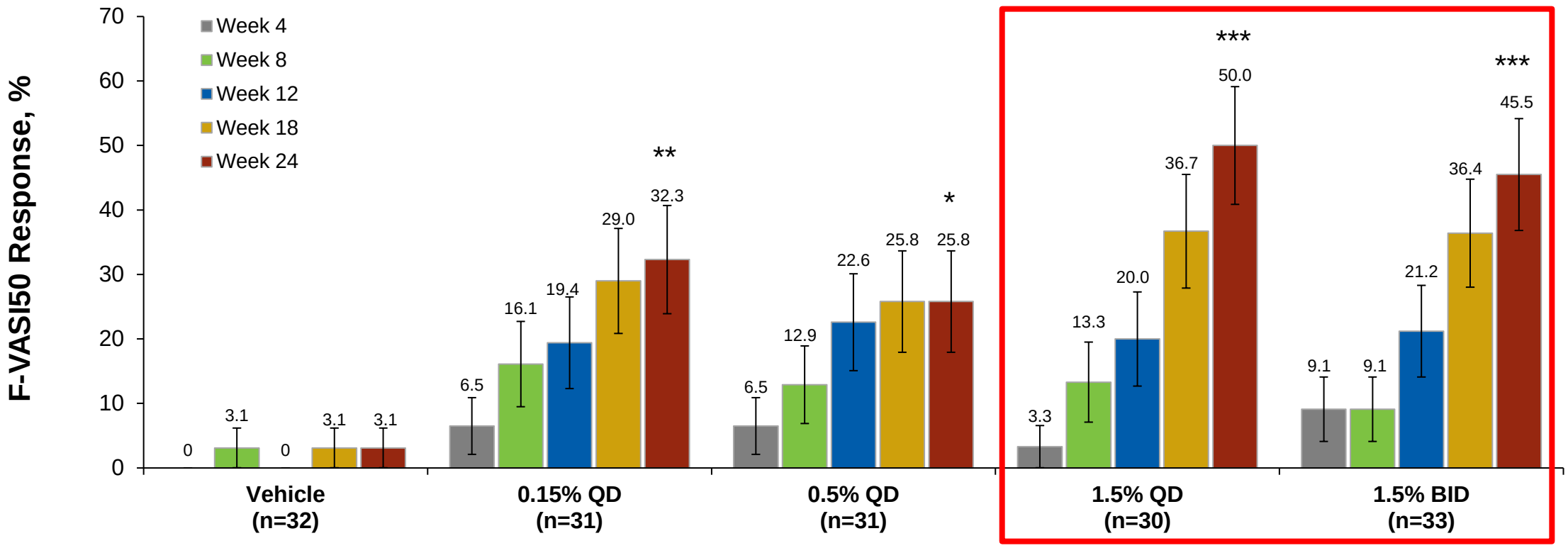
[a]Rerandomization at Week 24 to RUX 0.5% qd, 1.5% qd, or 1.5% bid if <25% improvement in F-VASI; [b]Percentage of total BSA
F-VASI, facial Vitiligo Area Scoring Index; T-VASI, total Vitiligo Area Scoring Index; F-PGVA, facial Physician's Global Vitiligo Assessment

1. Rosmarin D, et al. Lancet 2020;396:110–20 (supplementary material)

Grimes P, et al. AAD 2020, P17752 Sponsored by Incyte Corporation

F-VASI50

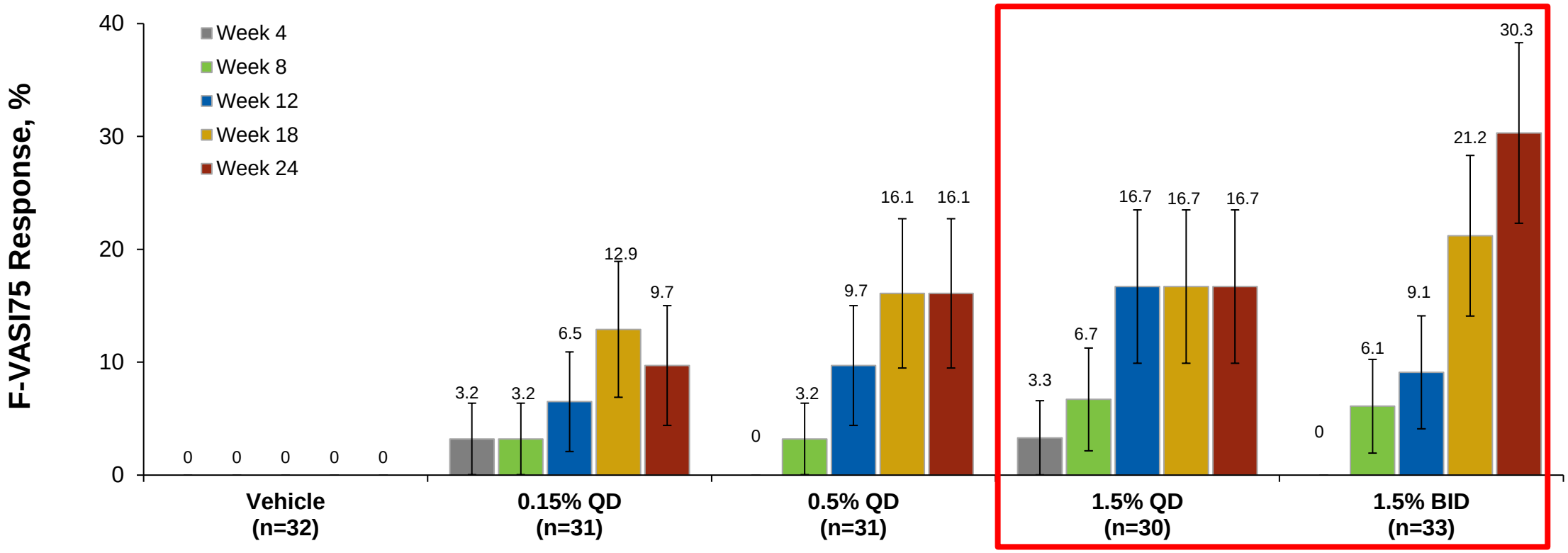
- At Week 24, the highest F-VASI50 response was achieved with the ruxolitinib cream 1.5% QD and BID regimens



Error bars indicate standard error.
*** *P*<0.001 vs vehicle at Week 24; ** *P*<0.01 vs vehicle at Week 24; * *P*<0.05 vs vehicle at Week 24.

F-VASI75

- At Week 24, the highest F-VASI75 response was achieved with the ruxolitinib cream 1.5% BID regimen

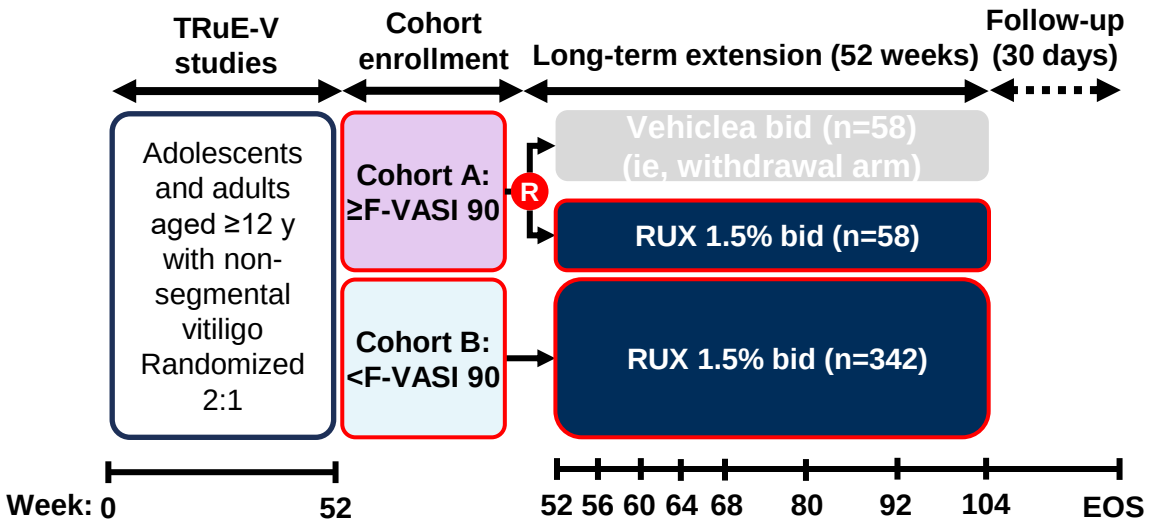


Error bars indicate standard error.

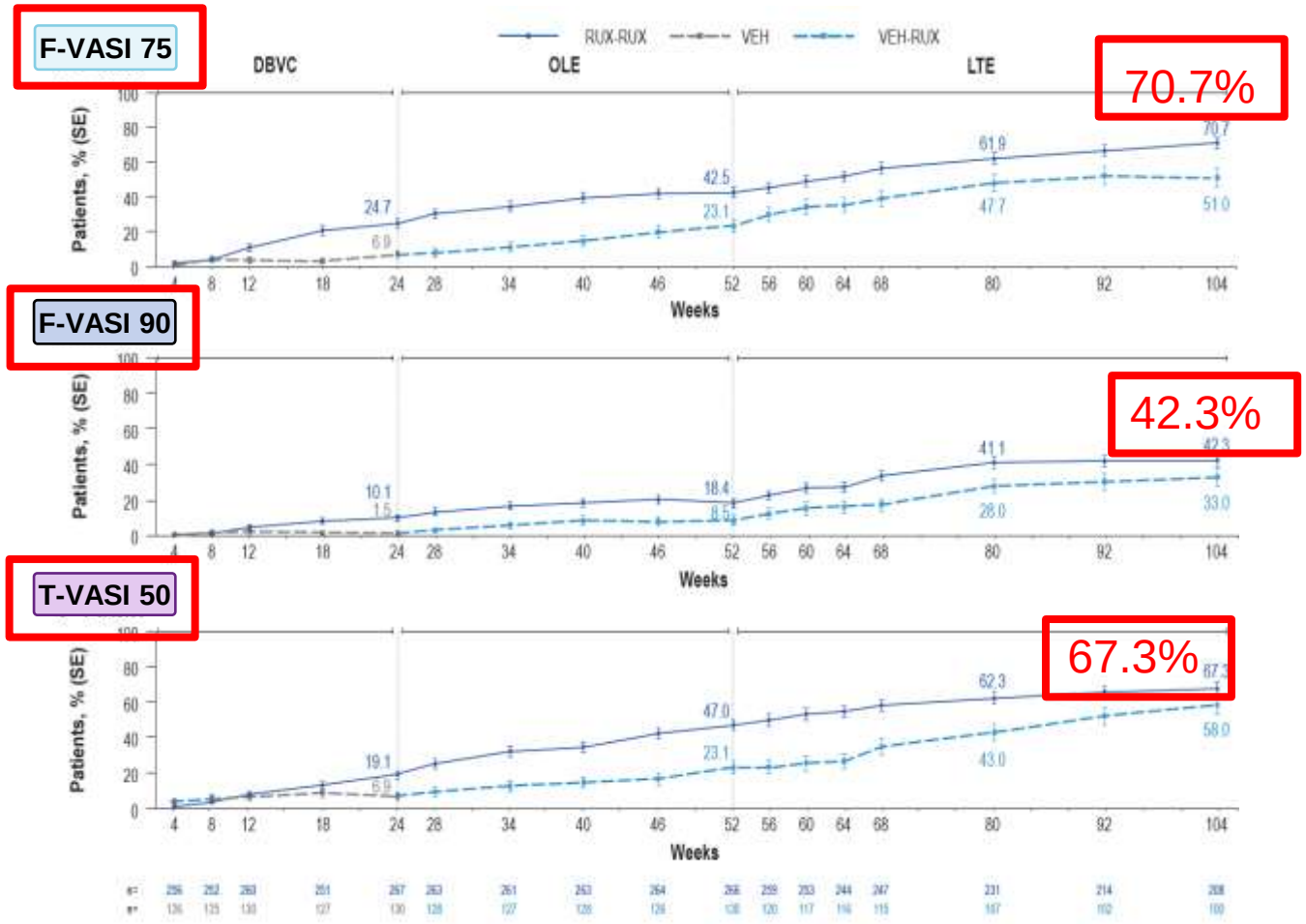
Pearl #1: Results at 6 months are noticeable but not enough to impact QOL in many

Pearl #2: With continued Rx, patients continue to improve; long term treatment essential

TRuE-V1/TRuE-V2 and TRuE-V LTE: Efficacy of topical ruxolitinib through Week 104 for the treatment of vitiligo



F-VASI and T-VASI response rates through Week 104 (ITT)[b]

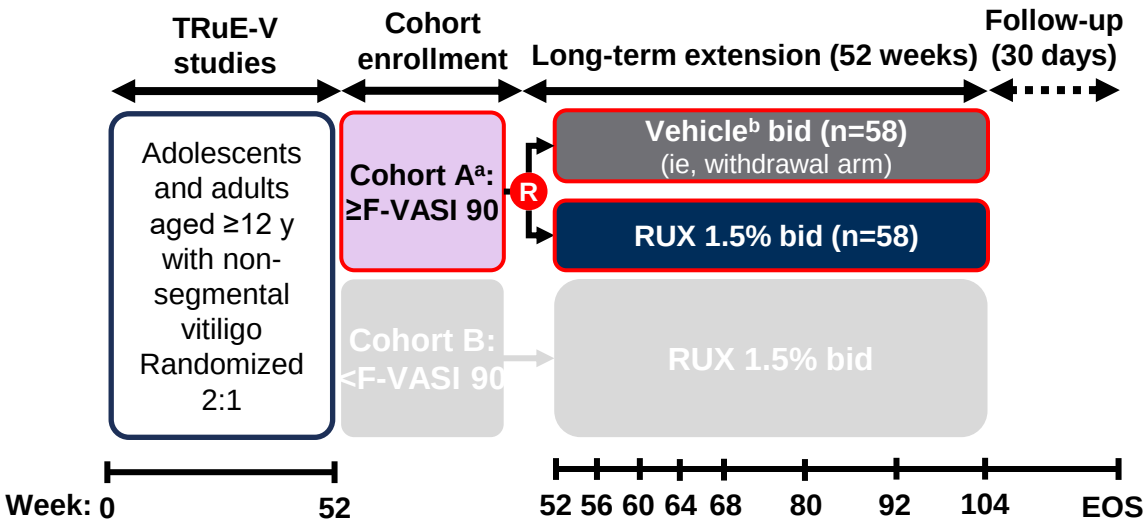


[a]Patients randomized to vehicle who relapsed (ie, <F-VASI 75) could apply ruxolitinib 1.5% bid rescue treatment for the remainder of the LTE period;
[b]Imputation method not diclosed in poster
López Estebaranz JL, et al. EADV 2024, P2983. Sponsored by Incyte Corporation

Pearl #3: Rux cream effective for hands and feet
- but slow

Pearl #4: Some patients lose benefit on discontinuation of Rux

Withdrawal study w.52-w.104

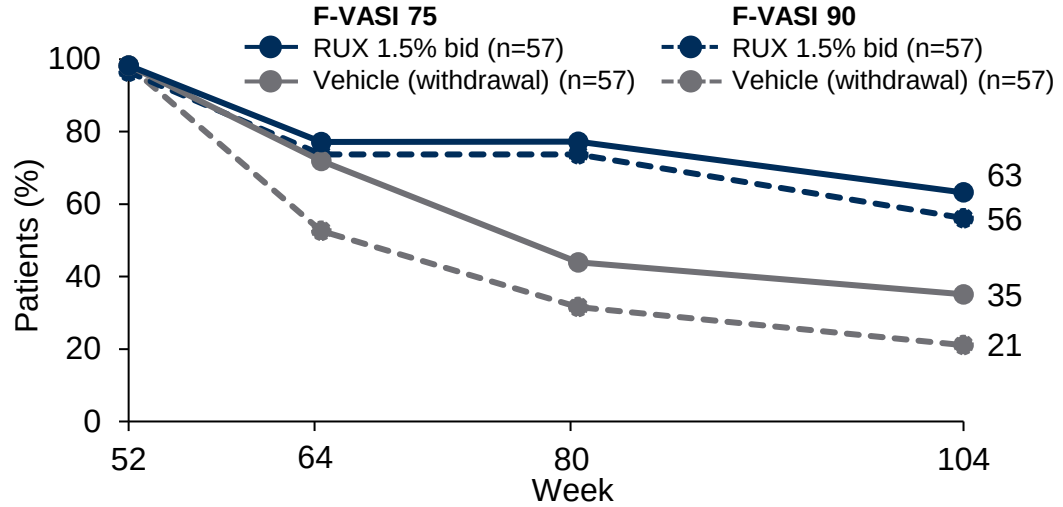


[a]Patients randomized to vehicle who relapsed (ie, <F-VASI 75) could apply ruxolitinib 1.5% bid rescue treatment for the remainder of the LTE period; [b]Five patients were incorrectly assigned to Cohort A (ie, had <F-VASI 90 at Week 52) and are included in analyses (n=2 RUX arm; n=1 vehicle arm

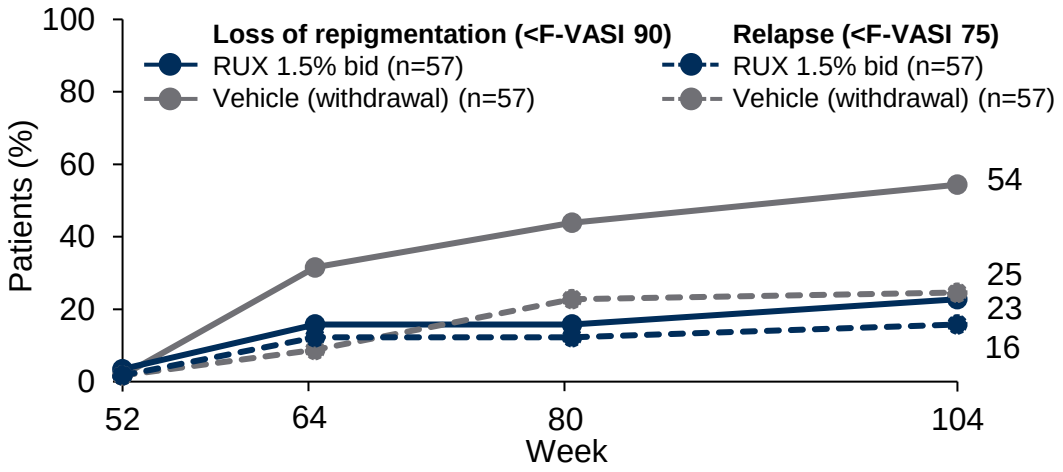
- At Week 104 in the withdrawal arm, a larger percentage of patients who maintained repigmentation (F-VASI 90/F-VASI 75) were **female, White, from Europe, and had Fitzpatrick skin types I–III**

While majority maintain repigmentation, switching to placebo leads to relapse→restart rux bid

Maintenance of F-VASI 75 and F-VASI 90 through Week 104 (AO)[a]



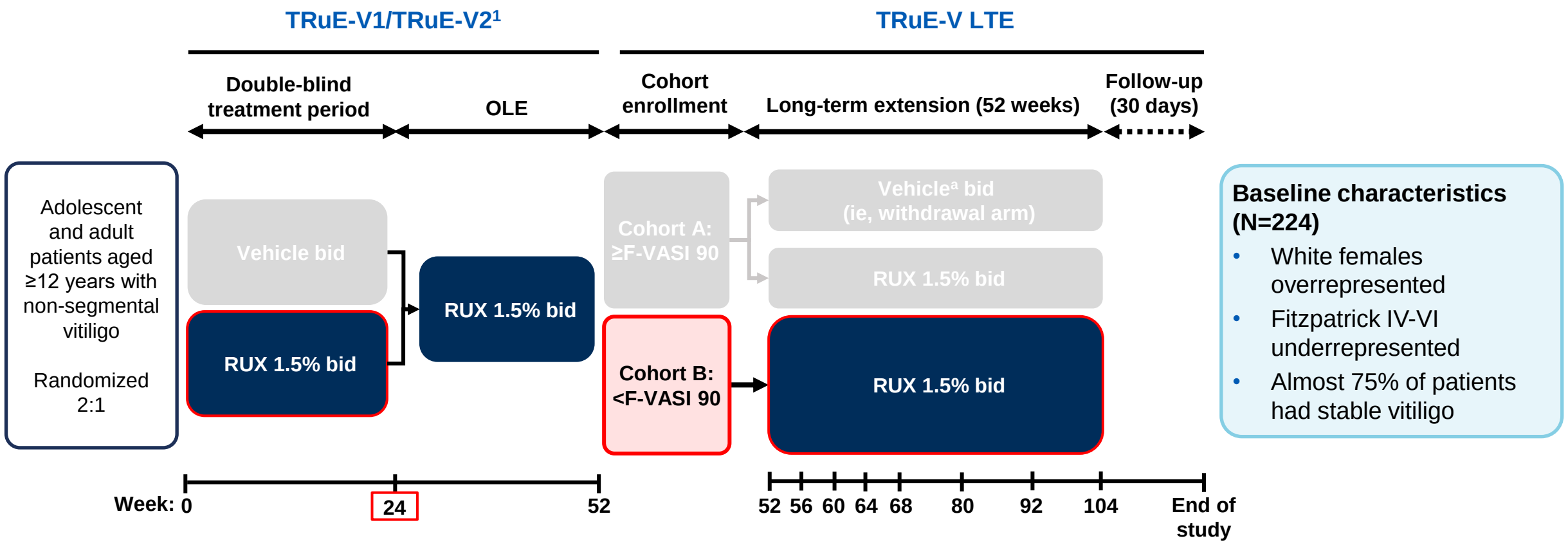
Loss of repigmentation (<F-VASI 90) or relapse (<F-VASI 75) through Week 104 (AO)



Rosmarin D, et al. EADV 2024, P2984. Sponsored by Incyte Corporation

Pearl #5: In poor responders at w. 24 and w. 52, continued Rx leads to more repigmentation

Efficacy of prolonged ruxolitinib cream for vitiligo among patients with limited or no initial response at 6 months



Baseline characteristics (N=224)

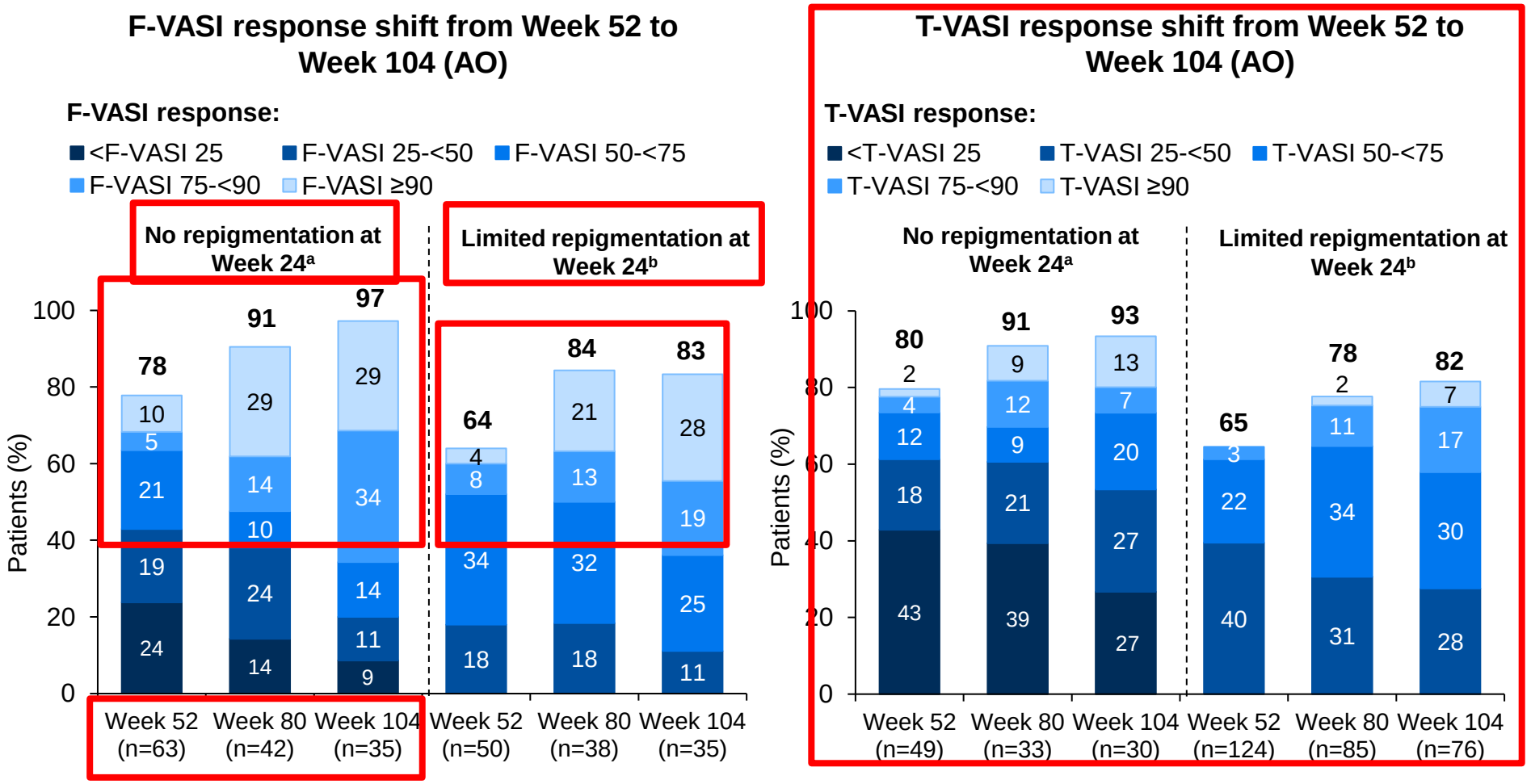
- White females overrepresented
- Fitzpatrick IV-VI underrepresented
- Almost 75% of patients had stable vitiligo

[a]Patients randomized to vehicle who relapsed (ie, <F-VASI 75) could apply ruxolitinib 1.5% bid rescue treatment for the remainder of the LTE period;

1. Rosmarin D, et al. N Engl J Med 2022;387:1445–1455.

Wolkerstorfer A, et al. EADV 2023, D1T01.1I. Sponsored by Incyte Corporation

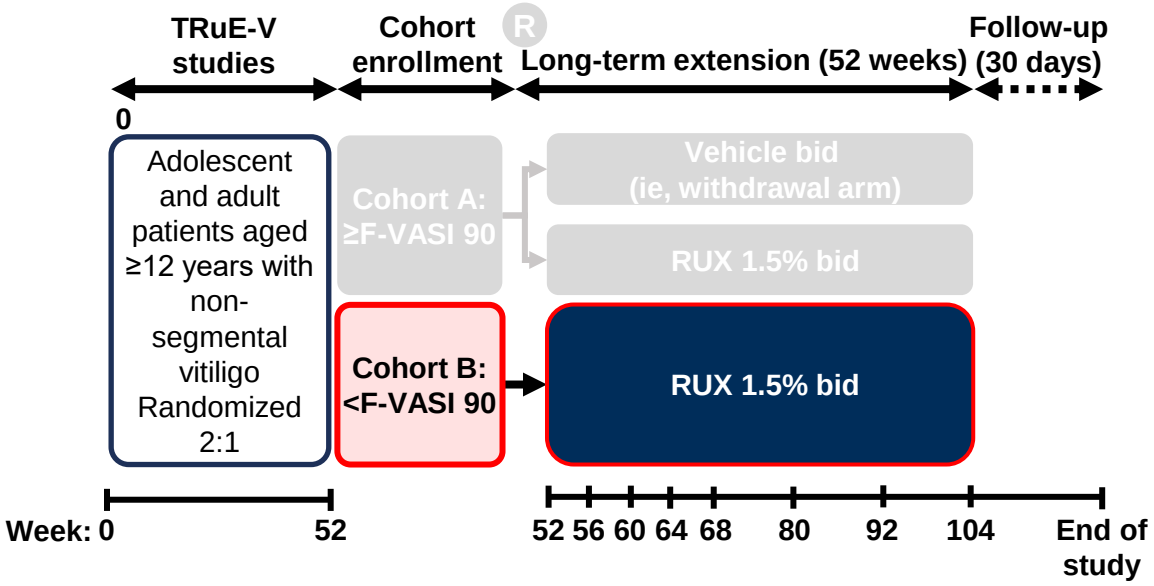
TRuE-V1/TRuE-V2 and TRuE-V LTE: F-VASI and T-VASI response shift with ruxolitinib cream among patients with no or limited initial response at 6 months



[a]Patients with worsening or no improvement in F-VASI/T-VASI (ie, ≤0%) at Week 24 and nonmissing F-VASI/T-VASI at Weeks 52, 80, or 104;
[b]Patients with >0% to <25% improvement in F-VASI/T-VASI at Week 24 and nonmissing F-VASI/T-VASI values at Week 52, 80, or 104. Data at Weeks 80 and 104 are from Cohort B

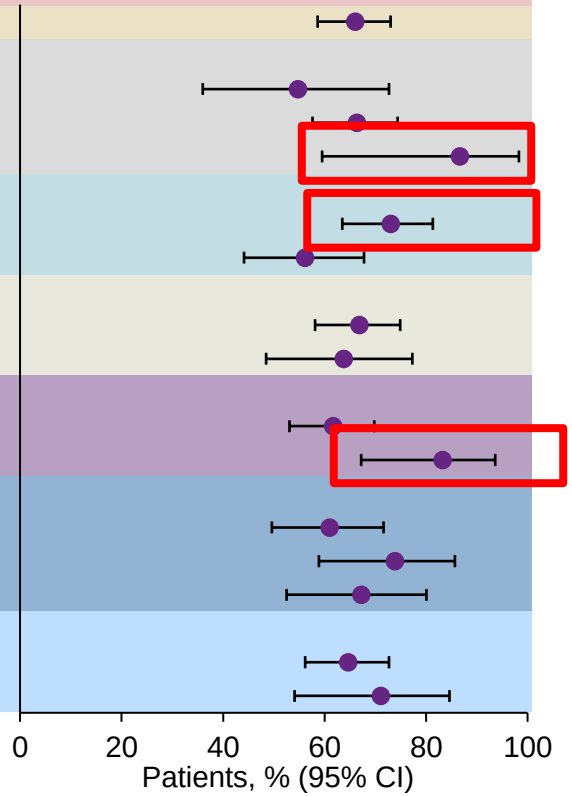
Wolkerstorfer A, et al. EADV 2023, D1T01.1I. Sponsored by Incyte Corporation

TRuE-V-LT: Efficacy and safety of ruxolitinib cream through week 104 for the treatment of vitiligo by patient demographics and baseline clinical characteristics



F-VASI 75 response rate at Week 104 by baseline demographics and clinical characteristics among patients who only applied RUX

Subgroups	n	F-VASI 75 response rate, % (95% CI)
All patients	177	66 (59, 73)
Age		
12–17	31	55 (36, 73)
18 – 64	131	66 (58, 74)
≥65	15	87 (60, 98)
Sex		
Female	104	73 (64, 81)
Male	73	56 (44, 68)
Fitzpatrick skin type		
I–III	130	67 (58, 75)
IV–VI	47	64 (49, 77)
F-BSA		
<1.5%	141	62 (53, 70)
≥1.5%	36	83 (67, 94)
Disease duration, years		
<10	82	61 (50, 72)
10–20	46	74 (59, 86)
>20	49	67 (53, 80)
Disease stability		
Stable	139	65 (56, 73)
Progressive	38	71 (54, 85)

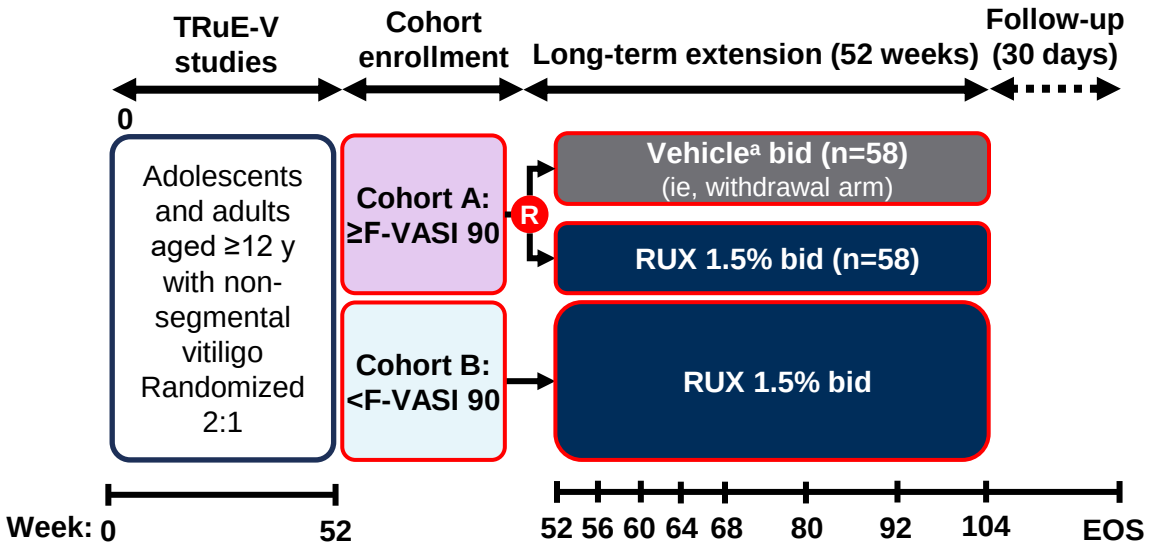


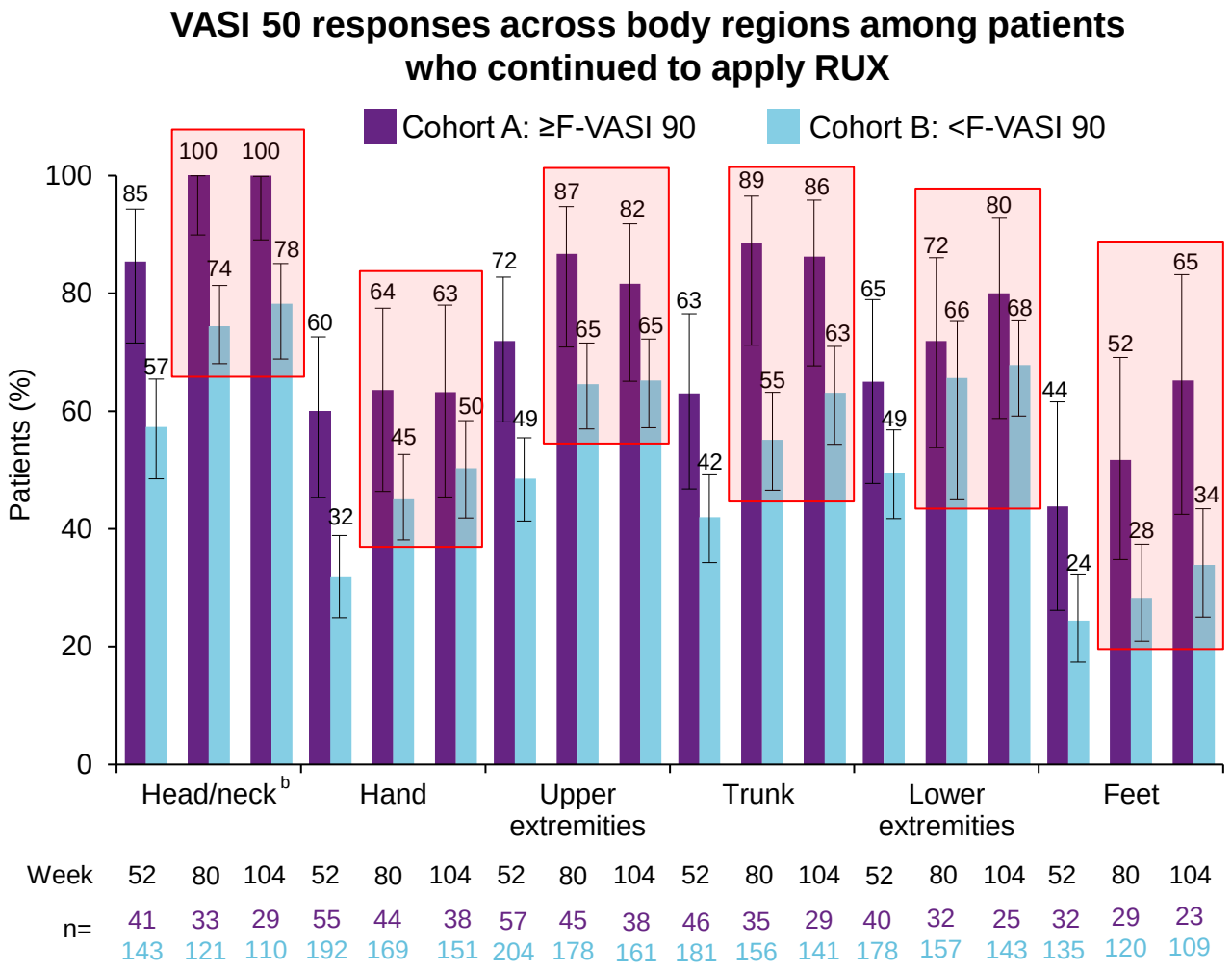
Safety of interest

- Treatment-related AEs occurred in 6% of patients, all of which were mild or moderate, with generally similar rates across demographic subgroups

Seneschal J, et al. EADV 2023, P2229. Sponsored by Incyte Corporation

TRuE-V-LT: Effect of ruxolitinib cream on VASI 50 achievement by body region through Week 104 in patients with vitiligo





[a]Patients randomized to vehicle who relapsed (ie, <F-VASI 75) could apply ruxolitinib 1.5% bid rescue treatment for the remainder of the LTE period;
[b]Excluding face

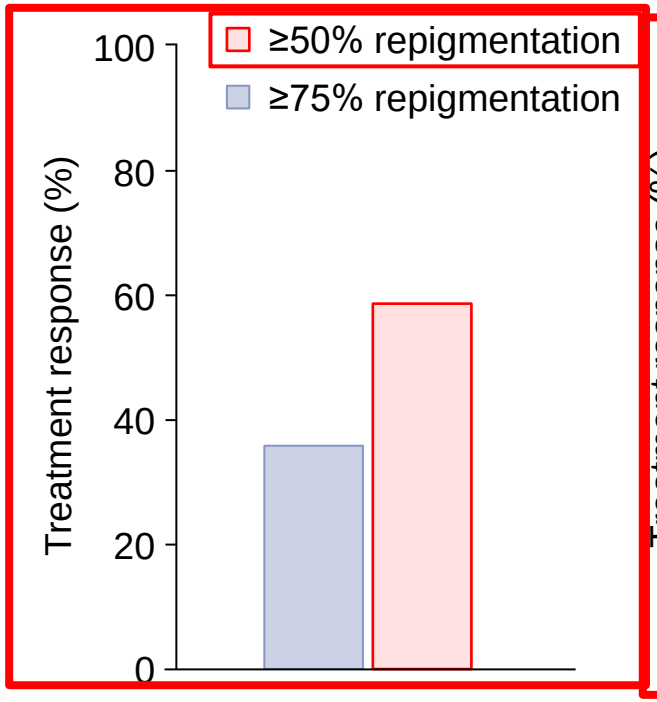
Passeron T, et al. EADV 2023, P2228. Sponsored by Incyte Corporation

Comparison of topical ruxolitinib 1.5% bid with topical calcineurin inhibitors for facial vitiligo

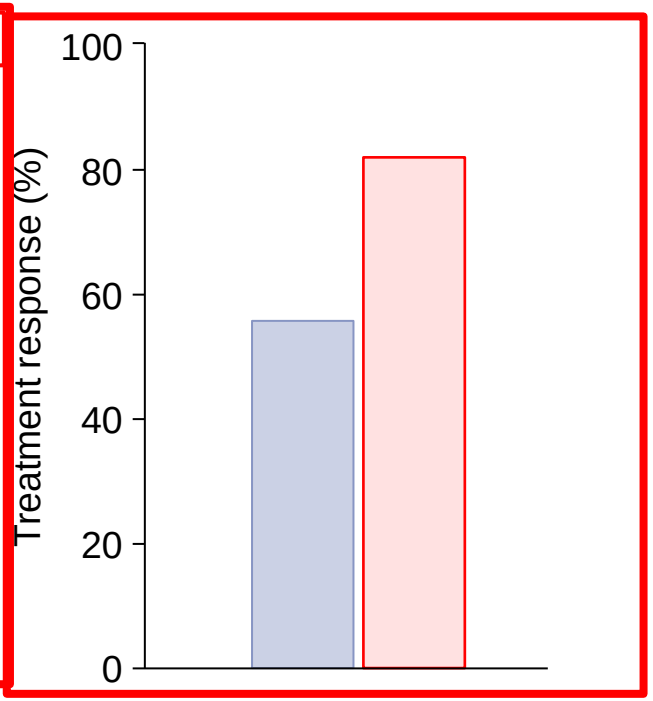
EADV 2019 FINAL 31Oct19

Efficacy outcome[1]	RUX 1.5% bid (n=33)	
	Week 24	Week 52
F-VASI 50 response, %	45	58
F-VASI 75 response, %	30	52

TCI monotherapy
Face and neck[2]



TCI plus phototherapy:
Face and neck[2]



*P<0.05 vs vehicle, †P<0.01 vs vehicle, ‡P<0.001
F-VASI, facial Vitiligo Area Severity Index

1. Harris JE, et al. EADV 2019, D3T01.L Sponsored by Incyte
2. Lee JH, et al. JAMA Dermatol 2019; Epub ahead of print

What you should know from the package insert

WARNING: SERIOUS INFECTIONS, MORTALITY, MALIGNANCY, MAJOR ADVERSE CARDIOVASCULAR EVENTS (MACE), AND THROMBOSIS

See full prescribing information for complete boxed warning. • Serious infections leading to hospitalization or death, including tuberculosis and bacterial, invasive fungal, viral, and other opportunistic infections, have occurred in patients receiving Janus kinase inhibitors for inflammatory conditions. (5.1) • Higher rate of all-cause mortality, including sudden cardiovascular death have been observed in patients treated with Janus kinase inhibitors for inflammatory conditions. (5.2) • Lymphoma and other malignancies have been observed in patients treated with Janus kinase inhibitors for inflammatory conditions. (5.3) • Higher rate of MACE (including cardiovascular death, myocardial infarction, and stroke) has been observed in patients treated with Janus kinase inhibitors for inflammatory conditions. (5.4) • Thrombosis, including deep venous thrombosis, pulmonary embolism, and arterial thrombosis, some fatal, have occurred in patients

Table 1: Adverse Reactions Occurring in ≥ 1% of Subjects Treated with OPZELURA for Atopic Dermatitis through Week 8 in TRuE-AD1 and TRuE-AD2

Adverse Reaction	OPZELURA (N = 499) n (%)	Vehicle (N = 250) n (%)
*Subjects with any TEAE**	*132 (27)*	*83 (33)*
Nasopharyngitis	13 (3)	2 (1)
Bronchitis	4 (1)	0 (0)
Ear infection	4 (1)	0 (0)
Eosinophil count increased	4 (1)	0 (0)
Urticaria	4 (1)	0 (0)
Diarrhea	3 (1)	1 (< 1)
Folliculitis	3 (1)	0 (0)
Tonsillitis	3 (1)	0 (0)
Rhinorrhea	3 (1)	1 (< 1)

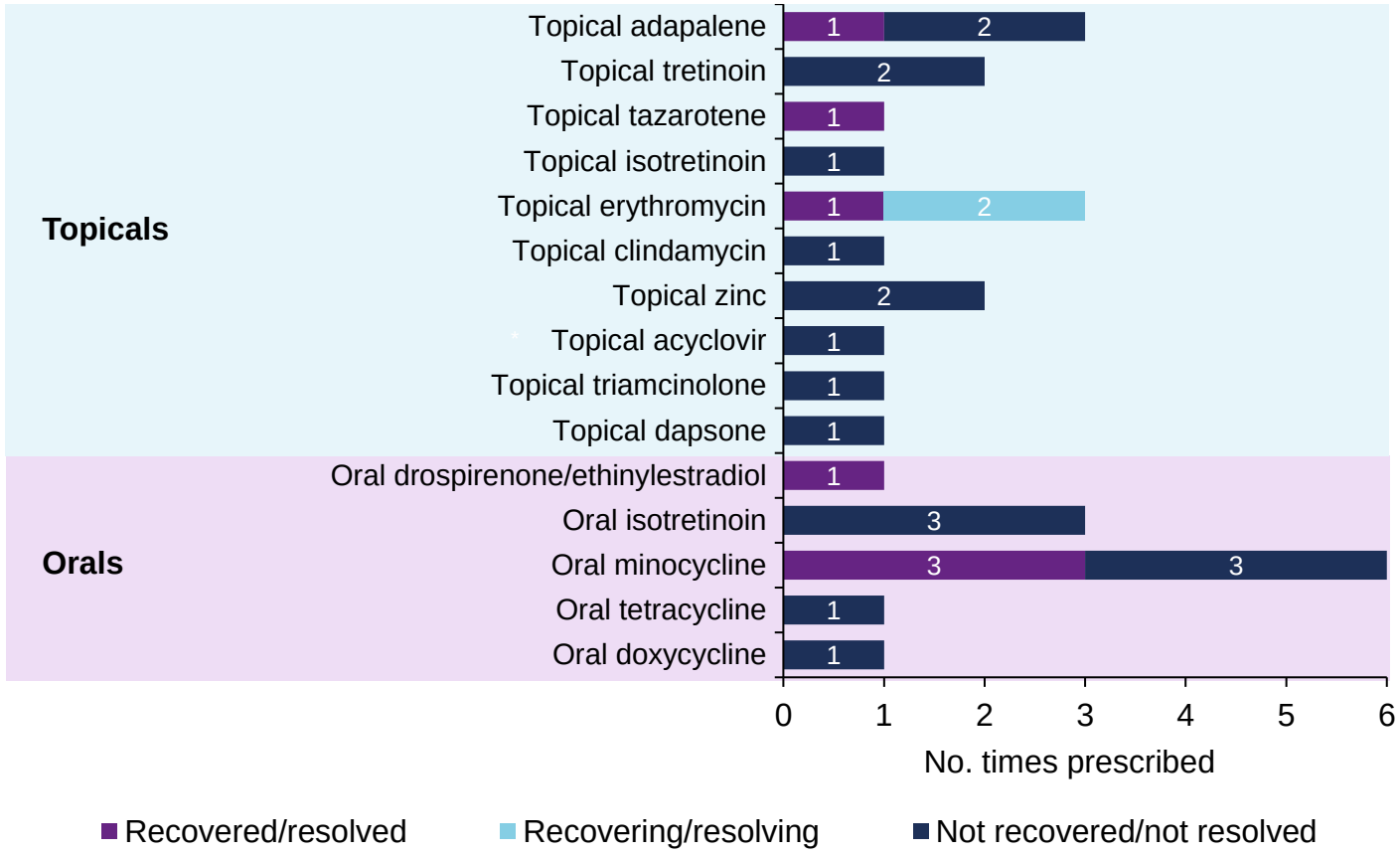
*TEAE – treatment emergent adverse events

Table 2: Adverse Reactions Occurring in ≥ 1% of Subjects Treated with OPZELURA for Nonsegmental Vitiligo through Week 24 in TRuE-V1 and TRuE-V2

Adverse Reaction	OPZELURA (N = 449) n (%)	Vehicle (N = 224) n (%)
*Subjects with any TEAE**	*214 (48)*	*79 (35)*
Application site acne	26 (6)	2 (1)
Application site pruritus	23 (5)	6 (3)
Nasopharyngitis	19 (4)	5 (2)
Headache	17 (4)	6 (3)
Urinary tract infection	7 (2)	1 (< 1)
Application site erythema	7 (2)	1 (< 1)
Pyrexia	6 (1)	0

*TEAE – treatment emergent adverse events

Acne treatments prescribed for patients with acne events[a] (n=46)



- All acne and application site acne events were mild or moderate (Grade 1, n=37 [72.5%]; Grade 2, n=14 [27.5%]), and none were considered serious

[a]Patients could receive ≥1 treatment or receive the same treatment for ≥1 treatment episode. One treatment (topical tazarotene) was prescribed to a patient who experienced acne while applying vehicle cream. All other treatments were prescribed to patients applying ruxolitinib cream

Rosmarin D, et al. EADV 2023, P2246. Sponsored by Incyte Corporation

WARNINGS AND PRECAUTIONS

• Serious Infections: Serious bacterial, mycobacterial, fungal and viral infections have occurred. Regularly monitor patients for infection and manage it promptly.

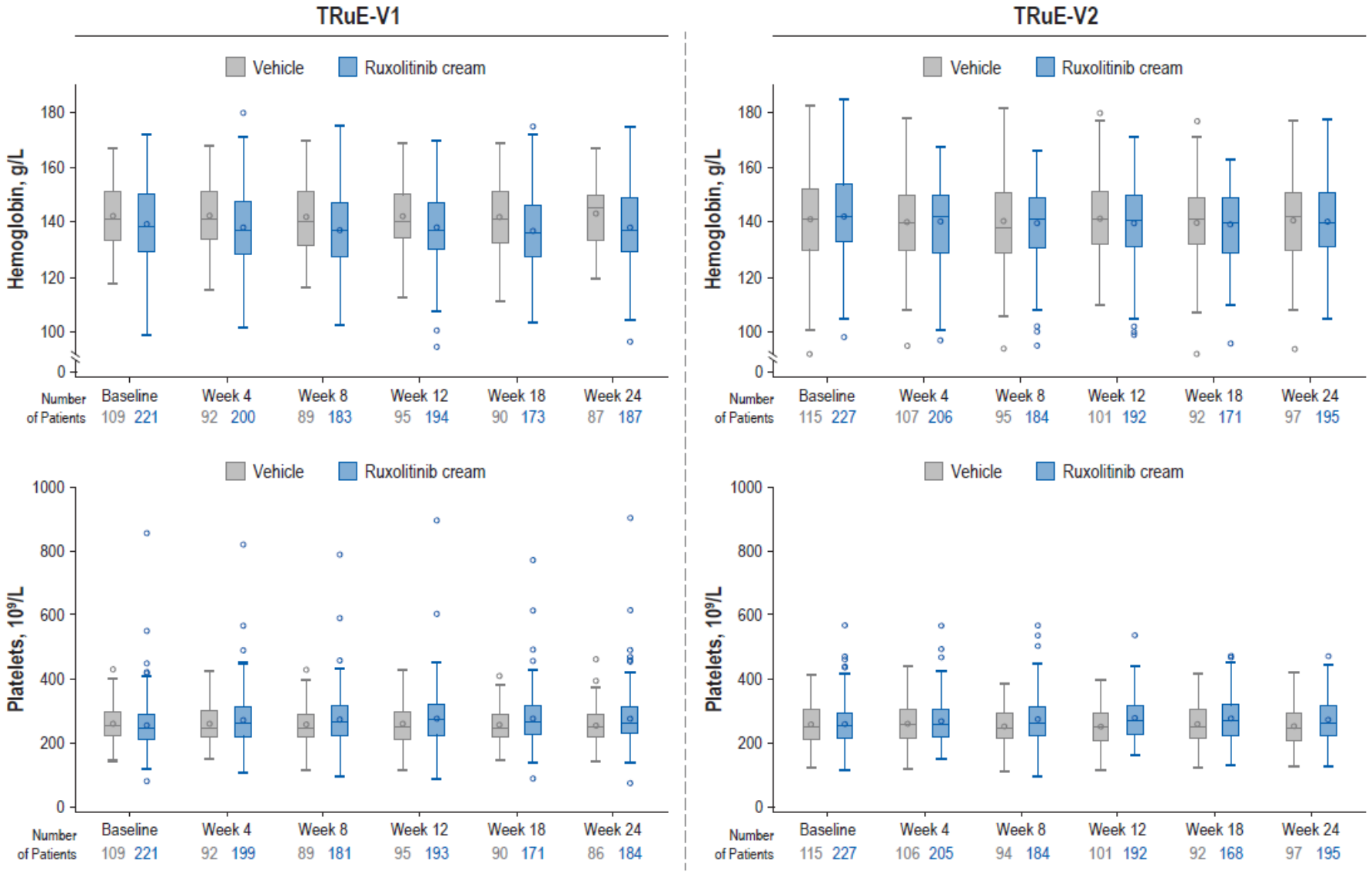
• Non-melanoma Skin Cancers. Basal cell and squamous cell carcinoma have occurred. Perform periodic skin examinations during treatment and following treatment as appropriate.

• Thrombosis. Thromboembolic events have occurred.

• Thrombocytopenia, Anemia, and Neutropenia: Thrombocytopenia, anemia, and neutropenia have occurred. Perform CBC monitoring as clinically indicated.

Hemoglobin and Platelet Values During Treatment

- There were no clinically significant changes in hemoglobin or platelet levels



Data per interim analyses at Week 24 are reported.

What you have to know from the package insert

- Do not use more than one 60 gram tube per week or one 100 gram tube per 2 weeks.
- For atopic dermatitis:Apply thin layer of ruxolitinib cream twice daily to affected areas of up to 20% body surface area.
- For vitiligo:Apply thin layer of ruxolitinib cream twice daily to affected areas of up to 10% body surface area.
- Advise women not to breastfeed during treatment with OPZELURA and for approximately four weeks after the last dose

Pregnancy

Pregnancy Exposure Registry There is a pregnancy registry that monitors pregnancy outcomes in pregnant persons exposed to OPZELURA during pregnancy. Pregnant persons exposed to OPZELURA and healthcare providers should report OPZELURA exposure by calling 1-855-463-3463.

Available data from pregnancies reported in clinical trials with OPZELURA are not sufficient to evaluate a drug-associated risk for major birth defects, miscarriage, or other adverse maternal or fetal outcomes. In animal reproduction studies, oral administration of ruxolitinib to pregnant rats and rabbits during the period of organogenesis resulted in adverse developmental outcomes at doses associated with maternal toxicity

Ruxolitinib was administered orally to pregnant rats or rabbits during the period of organogenesis, at doses of 15, 30, or 60 mg/kg/day in rats and 10, 30, or 60 mg/kg/day in rabbits. There were no treatment-related malformations at any dose. A decrease in fetal weight of approximately 9% was noted in rats at the highest and maternally toxic dose of 60 mg/kg/day. This dose resulted in systemic exposure approximately 22 times the clinical systemic exposure at the maximum recommended human dose (MRHD; the clinical systemic exposure from ruxolitinib cream, 1.5% applied twice daily to 25-40% atopic dermatitis-affected body surface area is used for calculation of multiples of human exposure). In rabbits, lower fetal weights of approximately 8% and increased late resorptions were noted at the highest and maternally toxic dose of 60 mg/kg/day. This dose resulted in systemic exposure approximately 70% the MRHD clinical systemic exposure.

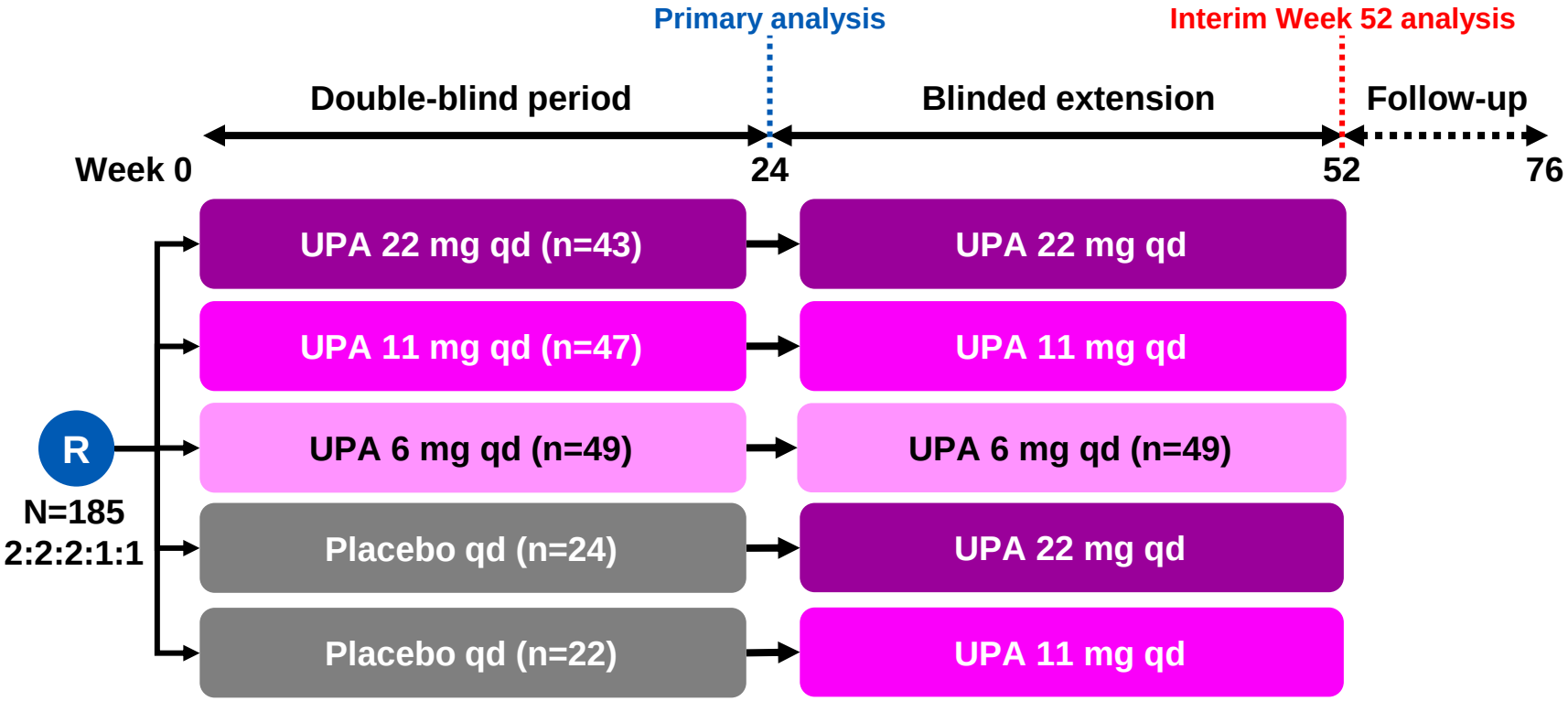
Phase 2 randomized, double-blind, dose-ranging study of upadacitinib for adults with extensive non-segmental vitiligo

Key inclusion criteria

- Patients aged 18−65 years with a clinical diagnosis of NSV
- Baseline F-VASI ≥0.5 and T-VASI ≥5
- No prior topical or systemic JAK inhibitor use

Baseline characteristics

- White patients overrepresented
- Black and Asian patients grossly under-represented
- Not all Fitzpatrick skin type captured
- Around 2/3 of patients had active vitiligo



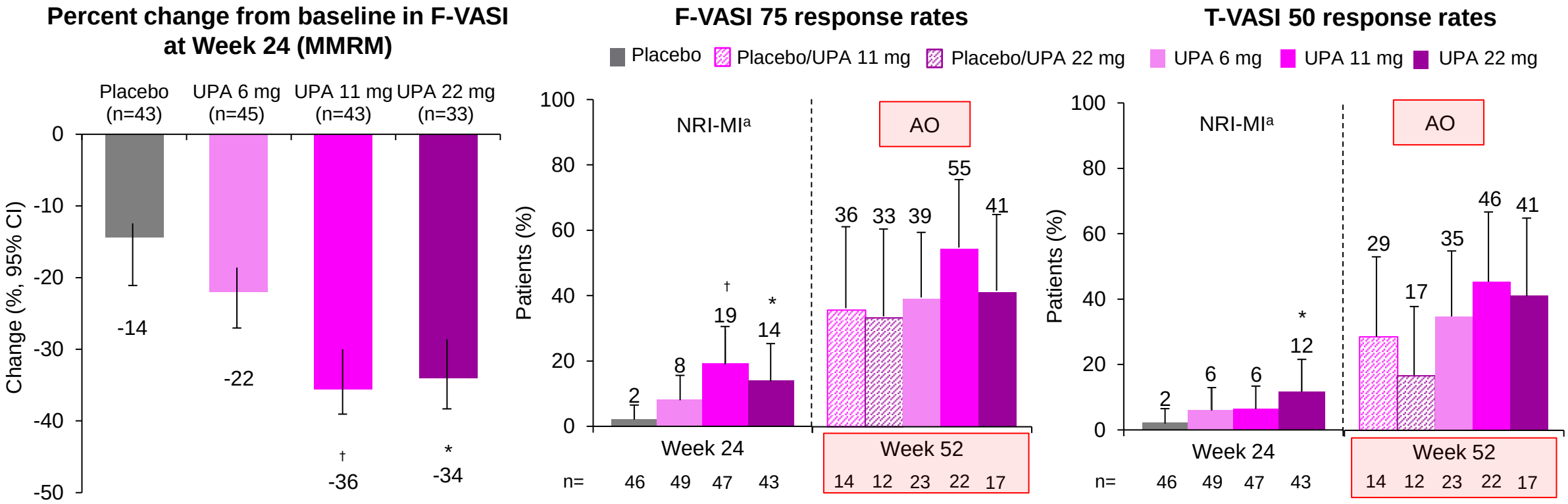
Data cutoff date: 13 January 2023
(58% of patients had an opportunity to reach Week 52)

Primary endpoint: Percent change from baseline in F-VASI at Week 24

Key secondary endpoints: Percentage of patients who achieved F-VASI 75 and T-VASI 50 at Week 24

Passeron T, et al. EADV 2023, FC02.08. Sponsored by AbbVie Inc.

Phase 2 trial: Efficacy of upadacitinib among adults with extensive non-segmental vitiligo



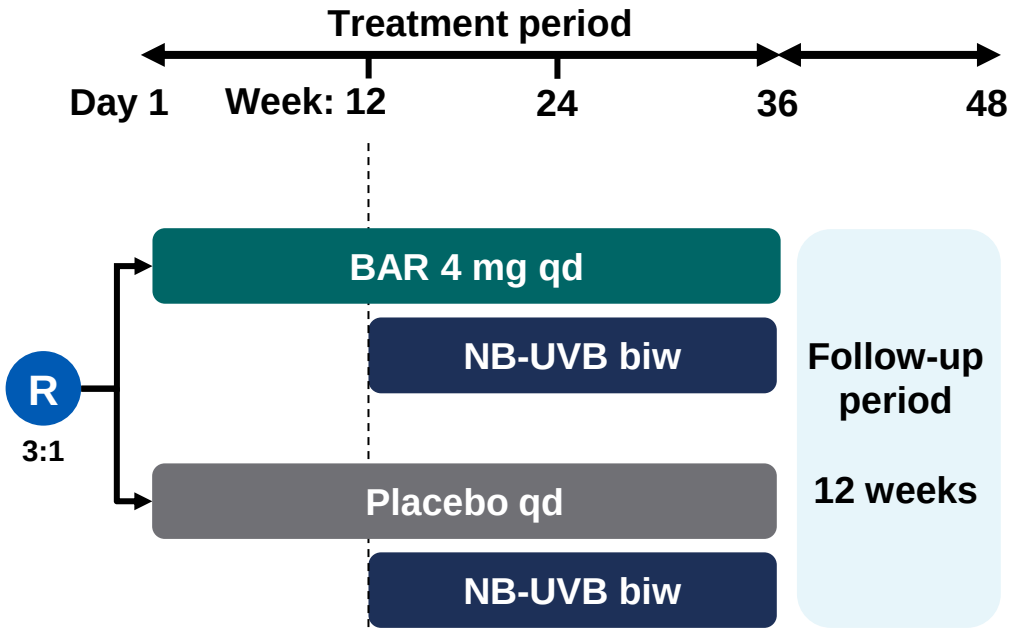
*P<0.05; †P<0.01 vs placebo; [a]NRI while incorporating MI to handle missing data due to COVID-19 or any other missing data that can be reasonably assumed to be missing at random

Passeron T, et al. EADV 2023, FC02.08. Sponsored by AbbVie Inc.

BARVIT: Phase 2 randomized, double-blind, proof of concept study of baricitinib in combination with NB-UVB for adult patients with active vitiligo

Inclusion criteria

- Patients aged 18−75 years
- Active NSV
- Total BSA involvement >5% (excluding hands and feet)



	Placebo + NB-UVB (n=12)	BAR 4 mg + NB-UVB (n=37)
Age, years	45.4 ±11.3	50.5 ±14.4
Female	7 (58)	28 (76)
Fitzpatrick skin type I-III IV-VI	 10 (83) 2 (17)	 33 (89) 4 (11)
Duration of vitiligo, years	17.6 ±16.3	18.4 ±12.1
VSAS	4.7 ±2.7	6.2 ±4.0

Data are mean ±SD or n (%)

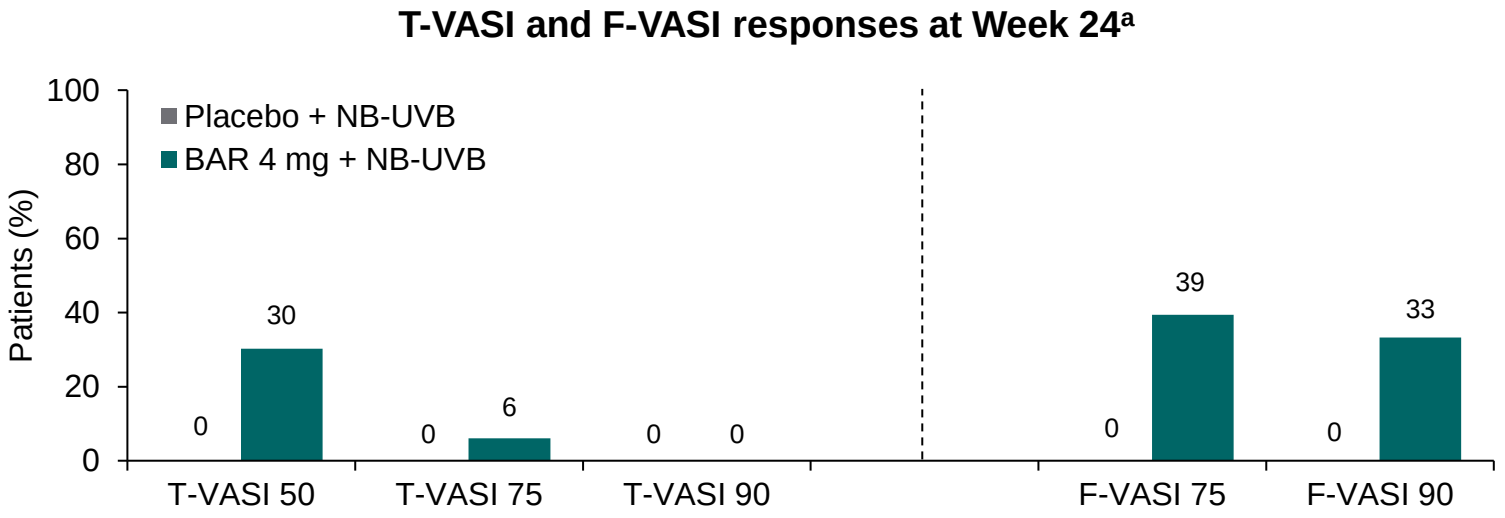
Efficacy endpoints:

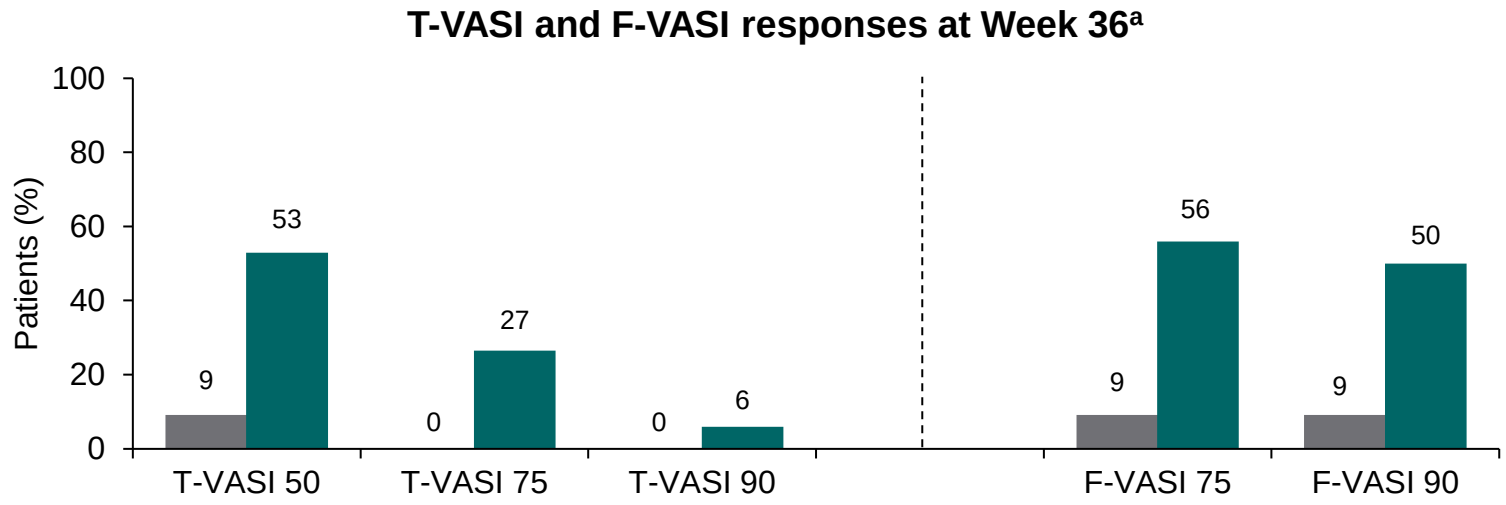
- Percent change from baseline in T-VASI and F-VASI
- Percent of patients achieving T-VASI 50/75/90 and F-VASI 75/90
- Percent change from baseline in DLQI, SkinDex29, VIPs

Safety endpoint: Incidence of AEs

Seneschal J, et al. EADV 2023, D3T01.3D.

BARVIT: Efficacy of baricitinib in combination with NB-UVB for adult patients with active vitiligo

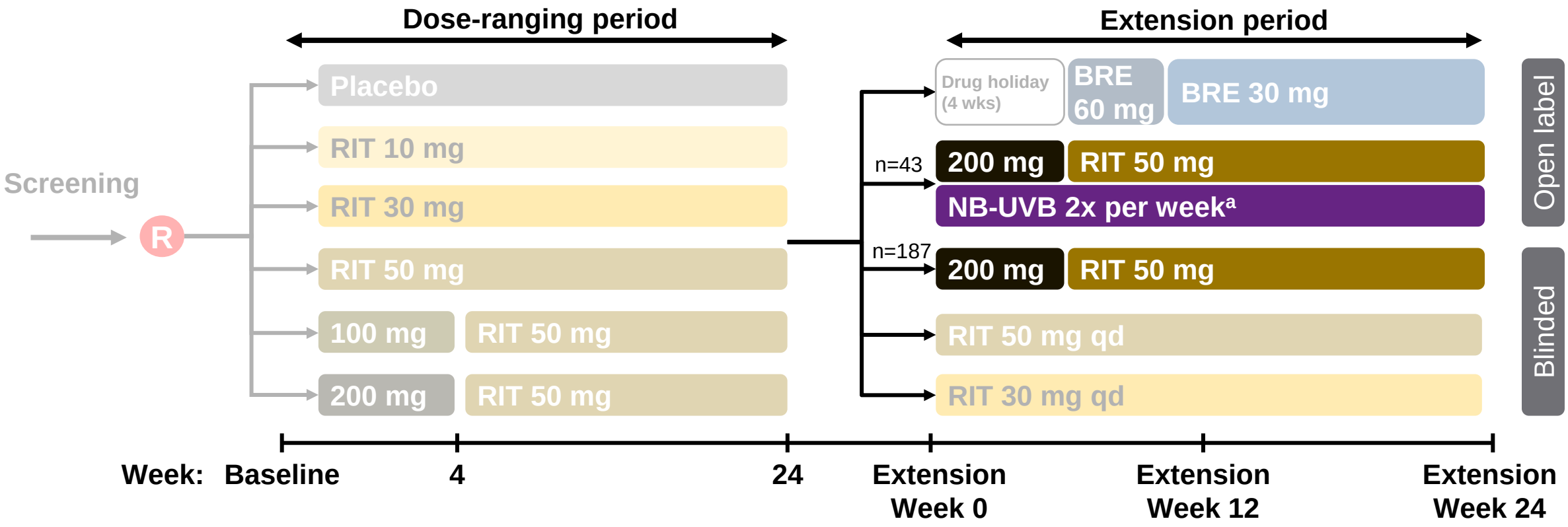




[a]Imputation method not disclosed in presentation

Seneschal J, et al. EADV 2023, D3T01.3D.

Phase 2b, randomized, dose-ranging trial of oral ritlecitinib (PF-06651600) with or without NB-UVB for adult patients with active nonsegmental vitiligo



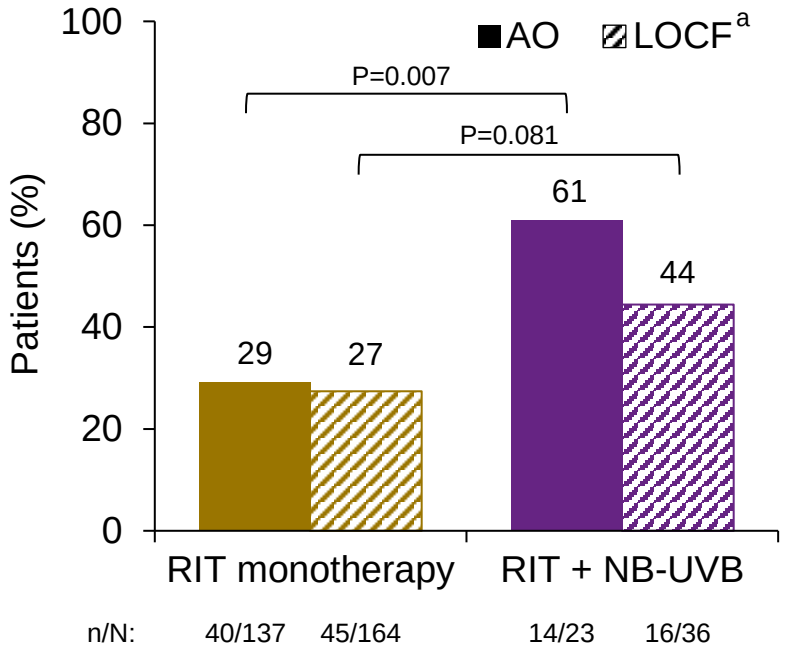
Discontinuation criterion: Patients in the RIT + NB-UVB group only who had <10% improvement in T-VASI at extension Week 12 from extension Week 0 (after the 24-week dose-ranging period)[b]

[a]NB-UVB phototherapy administration followed the Vitiligo Working Group (VWG) recommendations; [b]Discontinuation criterion was FDA recommended to consider patients' inconvenience and by the guidance at San Gallicano Dermatological Institute (Rome, Italy) shown in VWG Recommendations

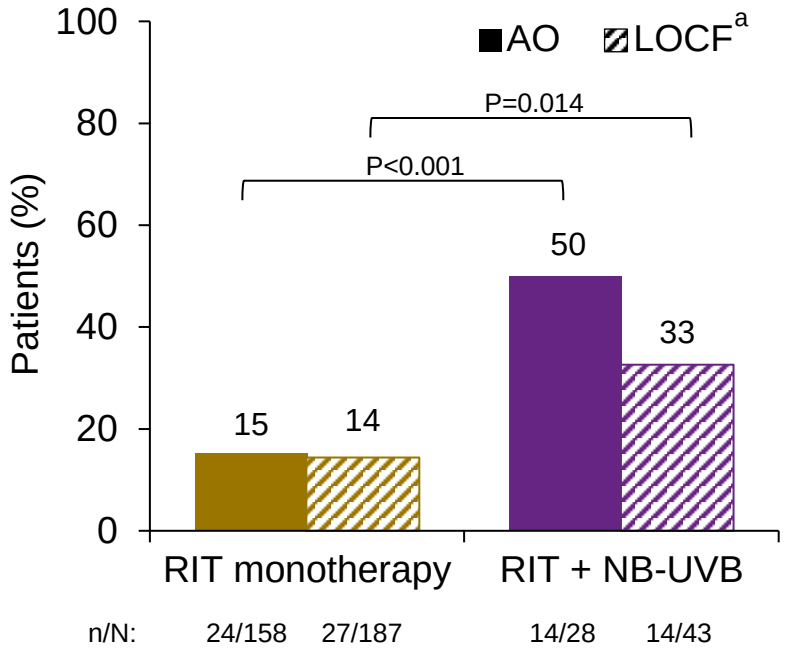
Yamaguchi Y, et al. AAD 2024, Late-breaking abstract. Sponsored by Pfizer Inc.

Phase 2b trial: Efficacy of oral ritlecitinib (PF-06651600) with or without NB-UVB among adult patients with active nonsegmental vitiligo

F-VASI 75 response at Extension Week 24

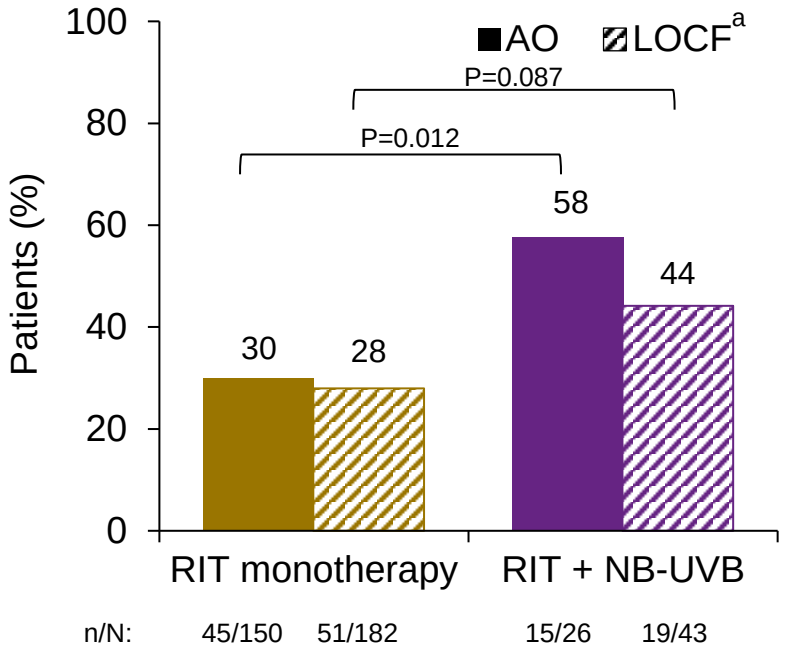


T-VASI 50 response at Extension Week 24



PGIC-V response at Extension Week 24[b]

"much improved" or "very much improved"



AO, as observed; LOCF, last observation carried forward

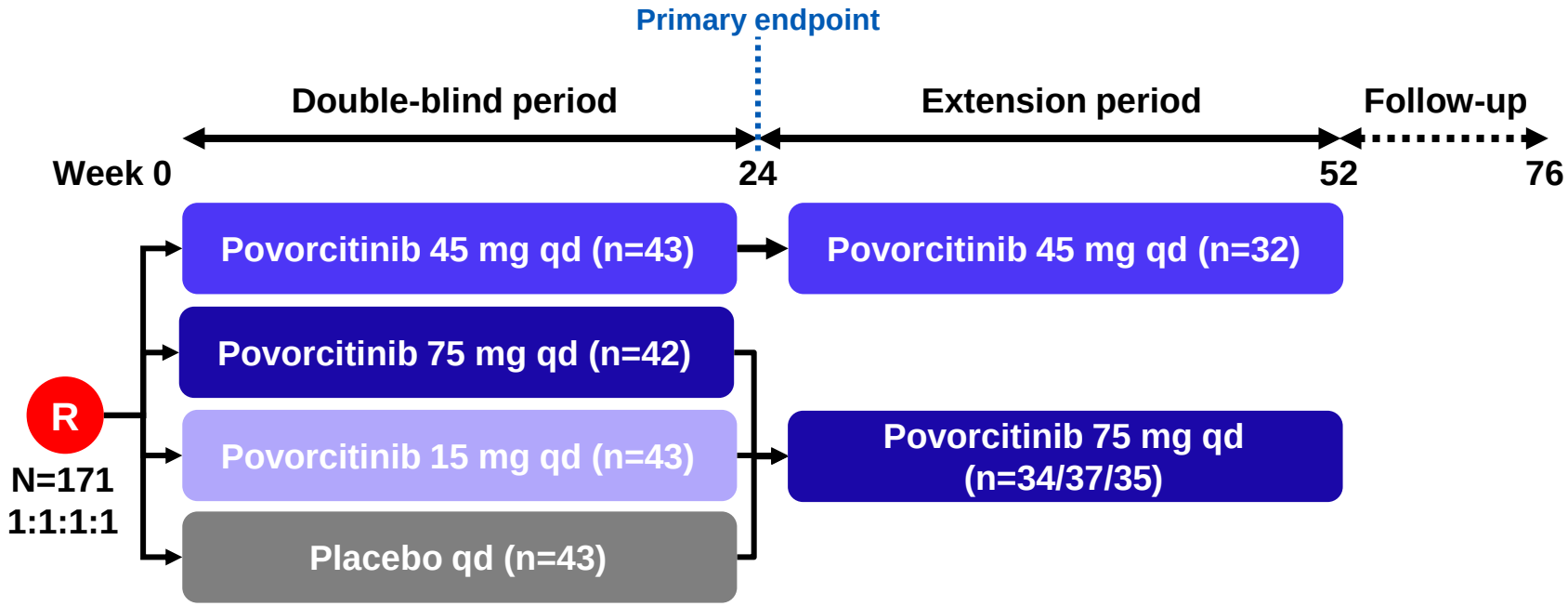
[a]Due to protocol-required lack-of-efficacy-dropout at Extension Week 12 for the NB-UVB group, supportive analyses using LOCF were included that adjust the dropout effect on the efficacy of add-on NB-UVB against monotherapy; [b]From baseline (dose-ranging Day 1)

Yamaguchi Y, et al. AAD 2024, Late-breaking abstract. Sponsored by Pfizer Inc.

Phase 2b trial of oral povorcitinib, a selective JAK1 inhibitor, for adult patients with extensive nonsegmental vitiligo

Key inclusion criteria

- 18−75 years old
- Total body BSA ≥8%
- Face BSA ≥0.5%
- T-VASI score ≥8
- F-VASI score ≥0.5



Primary endpoint: Percent change from baseline in T-VASI at Week 24

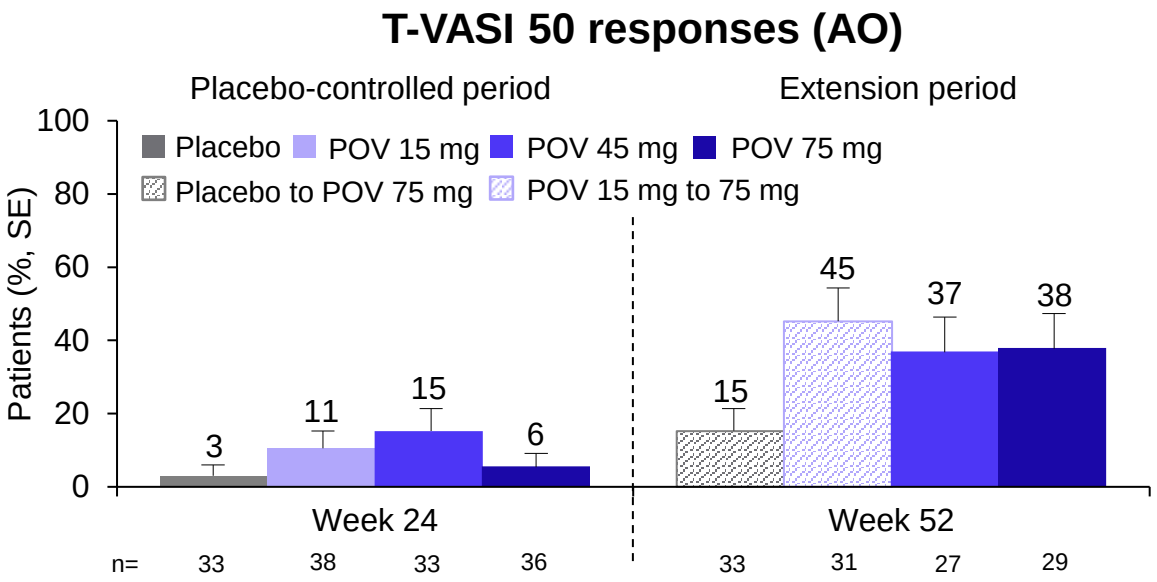
Other efficacy endpoints: T-VASI 50, F-VASI 50, and F-VASI 75

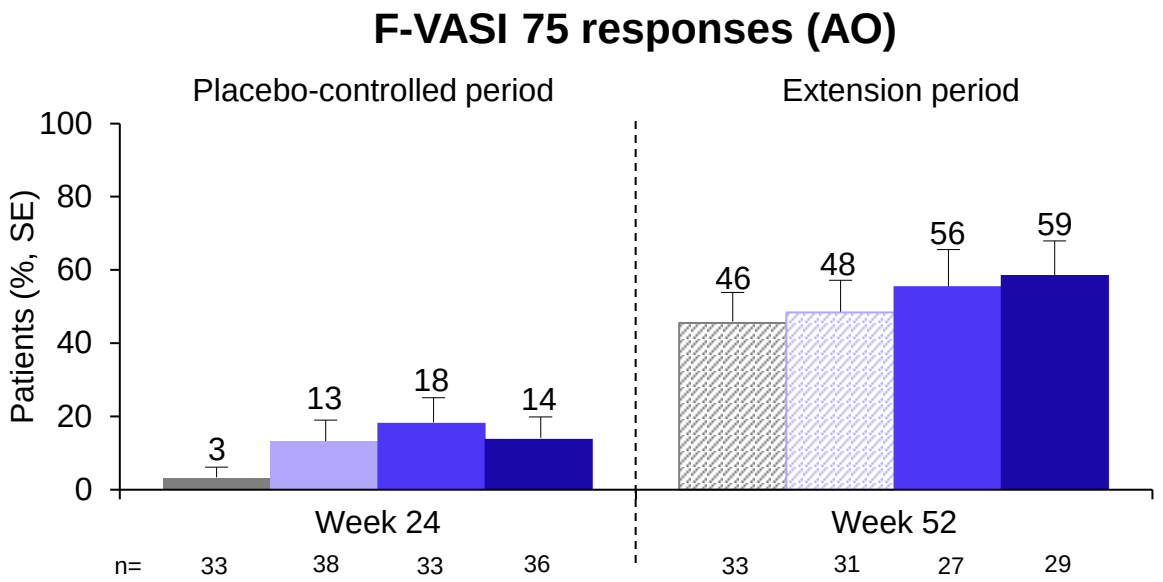
Baseline characteristics

- Overall, treatment arms were relatively well balanced, aside from:
  - White patients were overrepresented; Fitzpatrick skin type IV-VI underrepresented

Pandya LB, et al. AAD 2023, late-breaking abstract; Ezzedine K, et al. EADV 2023, D1T01.1A. Both Sponsored by Incyte Corporation

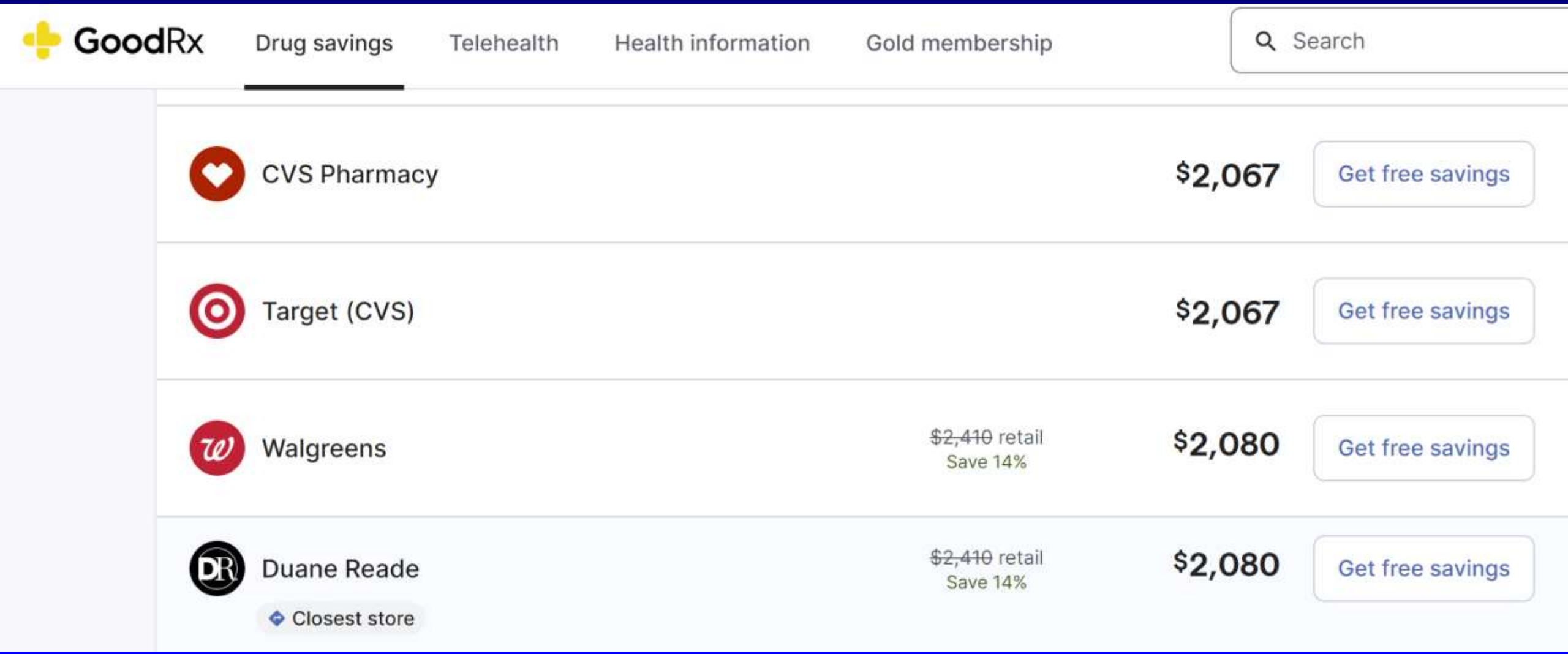
Phase 2b trial: T-VASI and F-VASI responses of oral povorcitinib among adult patients with extensive nonsegmental vitiligo





Ezzedine K, et al. EADV 2023, D1T01.1A. Sponsored by Incyte Corporation

RUXOLITINIB CREAM



- CVS price for Ruxolitinib cream $2067.00

- Walgreens price for Ruxolitinib cream $2067.00

NOT ON GOODRX.COM

- Apotheco Ruxolitinib cream $0-35
- Apotheco Ruxolitinib cream medicare $0-1900
- Pillcloudrx Ruxolitinib cream $0-35
- Pillcloudrx Ruxolitinib cream $0-1900

Prices on 10/18/24

- Apothecopharmacy.com
- Pillcloudrx.com

JAK Inhibitors

- Boxed warnings: what are the real risks?
- For what conditions do they work?
- What are they?
- Role in atopic dermatitis
- Role in psoriasis
- Role in alopecia areata
- Role in vitiligo
- What could go wrong?

Risk of tuberculosis reactivation with tofacitinib (CP-690550)

Maiga M, Lun S, Guo H, Winglee K, Ammerman NC, Bishai WR.
J Infect Dis. 2012 Jun;205(11):1705-8.

Tuberculosis reactivation related with ruxolitinib in a patient with primary myelofibrosis

Pepeler MS, Özkurt ZN, Güzel ÖT, Akyürek N.
J Infect Dev Ctries. 2018 Oct 31;12(10):926-928.

WARNING: SERIOUS INFECTIONS AND MALIGNANCY

See full prescribing information for complete boxed warning.

- **Serious infections leading to hospitalization or death, including tuberculosis and bacterial, invasive fungal, viral, and other opportunistic infections, have occurred in patients receiving XELJANZ. (5.1)**
- **If a serious infection develops, interrupt XELJANZ/XELJANZ XR until the infection is controlled. (5.1)**
- **Prior to starting XELJANZ/XELJANZ XR, perform a test for latent tuberculosis; if it is positive, start treatment for tuberculosis prior to starting XELJANZ/XELJANZ XR. (5.1)**
- **Monitor all patients for active tuberculosis during treatment, even if the initial latent tuberculosis test is negative. (5.1)**
- **Lymphoma and other malignancies have been observed in patients treated with XELJANZ. Epstein Barr Virus-associated post-transplant lymphoproliferative disorder has been observed at an increased rate in renal transplant patients treated with XELJANZ and concomitant immunosuppressive medications. (5.2)**

Mind the lipids: hyperlipidaemia resultant from JAK inhibitor use in inflammatory bowel disease

Ng A.

Eur J Gastroenterol Hepatol. 2021 Dec 1;33(1S Suppl 1):e1090.

Lipid profile and effect of statin treatment in pooled phase II and phase III baricitinib studies

WL, Schlichting DE, Rooney TP, de Bono S, McInnes IB.

Ann Rheum Dis. 2018 Jul;77(7):988-995.

Lipid Profiles in Patients With Ulcerative Colitis Receiving Tofacitinib-Implications for Cardiovascular Risk and Patient Management

Sands BE, Colombel JF, Ha C, Farnier M, Armuzzi A, Quirk D, Friedman GS, Kwok K, Salese L, Su C, Taub PR.

Inflamm Bowel Dis. 2021 May 17;27(6):797-808.

Effect of Upadacitinib on the Pharmacokinetics of Rosuvastatin or Atorvastatin in Healthy Subjects

Mohamed MF, Coppola S, Feng T, Camp HS, Kim E, Othman AA.
Clin Pharmacol Drug Dev. 2021 Nov;10(11):1335-1344.

- Statins didn’t affect upadacitinib levels
- Upadacitinib didn’t affect statin levels

Table 1: Dose Adjustments for Lymphopenia

Low Lymphocyte Count *[see Warnings and Precautions (5.4)]*	
Lab Value (cells/mm^3)	**Recommendation**
Lymphocyte count greater than or equal to 500	Maintain dose
Lymphocyte count less than 500 (Confirmed by repeat testing)	Discontinue XELJANZ/XELJANZ XR

Table 2: Dose Adjustments for Neutropenia

Low ANC *[see Warnings and Precautions (5.4)]*	
Lab Value (cells/mm^3)	**Recommendation**
ANC greater than 1000	Maintain dose
ANC 500–1000	For persistent decreases in this range, interrupt dosing until ANC is greater than 1000 • When ANC is greater than 1000, resume XELJANZ 5 mg twice daily/XELJANZ XR 11 mg once daily
ANC less than 500 (Confirmed by repeat testing)	Discontinue XELJANZ/XELJANZ XR

Table 3: Dose Adjustments for Anemia

Low Hemoglobin Value *[see Warnings and Precautions (5.4)]*	
Lab Value (g/dL)	**Recommendation**
Less than or equal to 2 g/dL decrease and greater than or equal to 9.0 g/dL	Maintain dose
Greater than 2 g/dL decrease or less than 8.0 g/dL (Confirmed by repeat testing)	Interrupt the administration of XELJANZ/XELJANZ XR until hemoglobin values have normalized

Liver Enzyme Elevations

Treatment with XELJANZ was associated with an increased incidence of liver enzyme elevation compared to placebo. Most of these abnormalities occurred in studies with background DMARD (primarily methotrexate) therapy.

Routine monitoring of liver tests and prompt investigation of the causes of liver enzyme elevations is recommended to identify potential cases of drug-induced liver injury. If drug-induced liver injury is suspected, the administration of XELJANZ/XELJANZ XR should be interrupted until this diagnosis has been excluded.

Lipid Elevations

Treatment with XELJANZ was associated with increases in lipid parameters including total cholesterol, low-density lipoprotein (LDL) cholesterol, and high-density lipoprotein (HDL) cholesterol. Maximum effects were generally observed within 6 weeks. The effect of these lipid parameter elevations on cardiovascular morbidity and mortality has not been determined.

Assessment of lipid parameters should be performed approximately 4–8 weeks following initiation of XELJANZ/XELJANZ XR therapy.

Monitoring Recommendations for Tofacitinib
(from package insert)

- Tb test baseline and “per applicable guidelines” (annually)
- CBC +plts baseline; after 4-8 weeks; q3mos
- LFT’s “routine monitoring” – baseline and q3-6mos
- Lipids – baseline and at 4-8 weeks

LET'S MAKE THIS SIMPLE

Dose	**Abrocitinib** 100mg qd	**Upadacitinib** 15mg qd	**Baricitinib** 2mg qd	**Deucravacitinib** 6mg qd	**Tofacitinib** 5mg bid/ 11mgXR qd
Indication	Atopic Dermatitis	Atopic Dermatitis PsA	Alopecia areata	Psoriasis PsA	PsA
BASELINE MONITORING	**TB, CBC, CMP, Lipids,Viral Hepatitis Screening Preg*, HIV*,vaccinations**				
FOLLOWUP MONITORING	**TB ANNUALLY; CBC, CMP & Lipids AT 4-12W.; REPEAT ANNUALLY**			**Lipids (routine)**	**TB annually CBC 4-8 weeks;then Q3mos; LFTs q3-6mos; Lipids 4-8w then annually**
Dose adjustment	200mg/d	30mg/d (AD)	4mg/d	6mg/d	5mg bid/ 11mgXR qd

‘The most common cause of death is myocardial infacrction. There is a specific boxed warning on Jak inhibitor package inserts regarding myocardial infarction.

What do I say to a family (or their lawyer) when my patient dies of a Myocardial infarction and blames the JAK inhibitor?”

Answer: *Did he ever take an Advil?*