HIGHLIGHTS

SINGAPORE

3-8 / july / 2023

Con el patrocinio de:

ucb

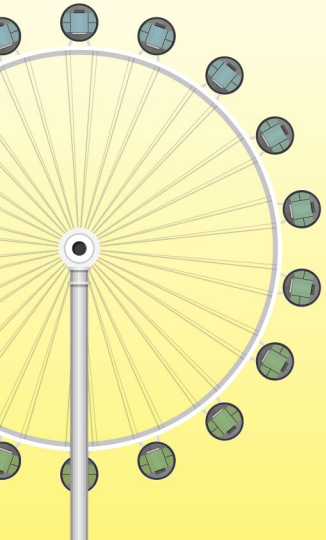
Iniciativa científica de:

AEDV 1909

ACADEMIA ESPAÑOLA
DE DERMATOLOGÍA
Y VENEREOLOGÍA

PSORIASIS 2ª parte

Highlights Singapore



ROSA IZU BELLOSO

HOSPITAL UNIVERSITARIO BASURTO. BILBAO

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CONFLICTOS DE INTERÉS

UCB ha financiado mi participación en este congreso

PSORIASIS E INHIBIDORES JAK-KINASAS

Bruce Strober 11:55

JAK inhibitors for Psoriasis, Alopecia Areata and Vitiligo

Bruce E. Strober, MD, PhD

Clinical Professor of Dermatology
Yale University
Department of Dermatology
New Haven, CT USA
&
Central Connecticut Dermatology
Cromwell, CT USA

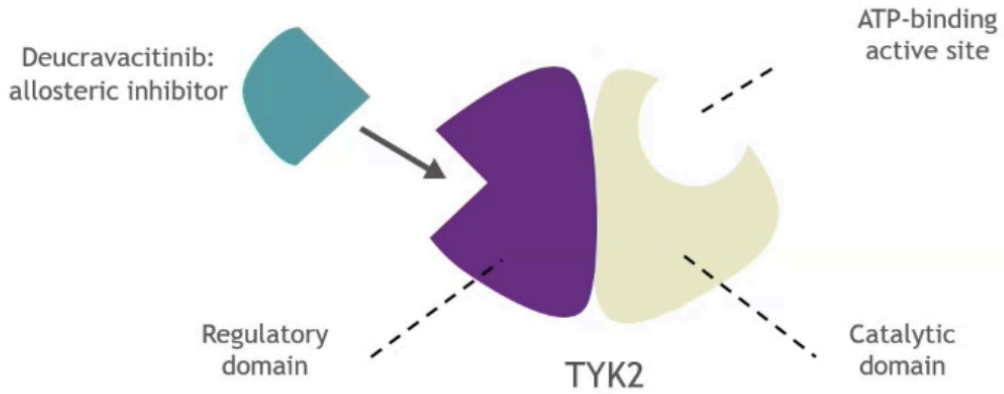
PSORIASIS E INHIBIDORES JAK-KINASAS

Bruce Strober 8:41

Deucravacitinib, an Oral, Selective Tyrosine Kinase 2 (TYK2) Inhibitor, Compared With Placebo and Apremilast

Deucravacitinib

- Binds to the TYK2 regulatory domain with high selectivity and inhibits TYK2 via an allosteric mechanism
  - ≥100-fold greater selectivity for TYK2 vs JAK1/3 and ≥2000-fold greater selectivity for TYK2 vs JAK2
  - Inhibits TYK2-mediated signaling by cytokines involved in psoriasis pathogenesis (eg, IL-23, IL-12, and Type 1 interferon)



Strober B, et al. J Am Acad Dermatol. 2022 doi: https://doi.org/10.1016/j.jaad.2022.08.061. Online ahead of print; Armstrong AWJ Am Acad Dermatol. 2022 Jul 9:S0190-9622(22)02256-3. doi: 10.1016/j.jaad.2022.07.002. Online ahead of print

PSORIASIS

Bruce Strober

Deucravac

Mean daily inhibition (%)

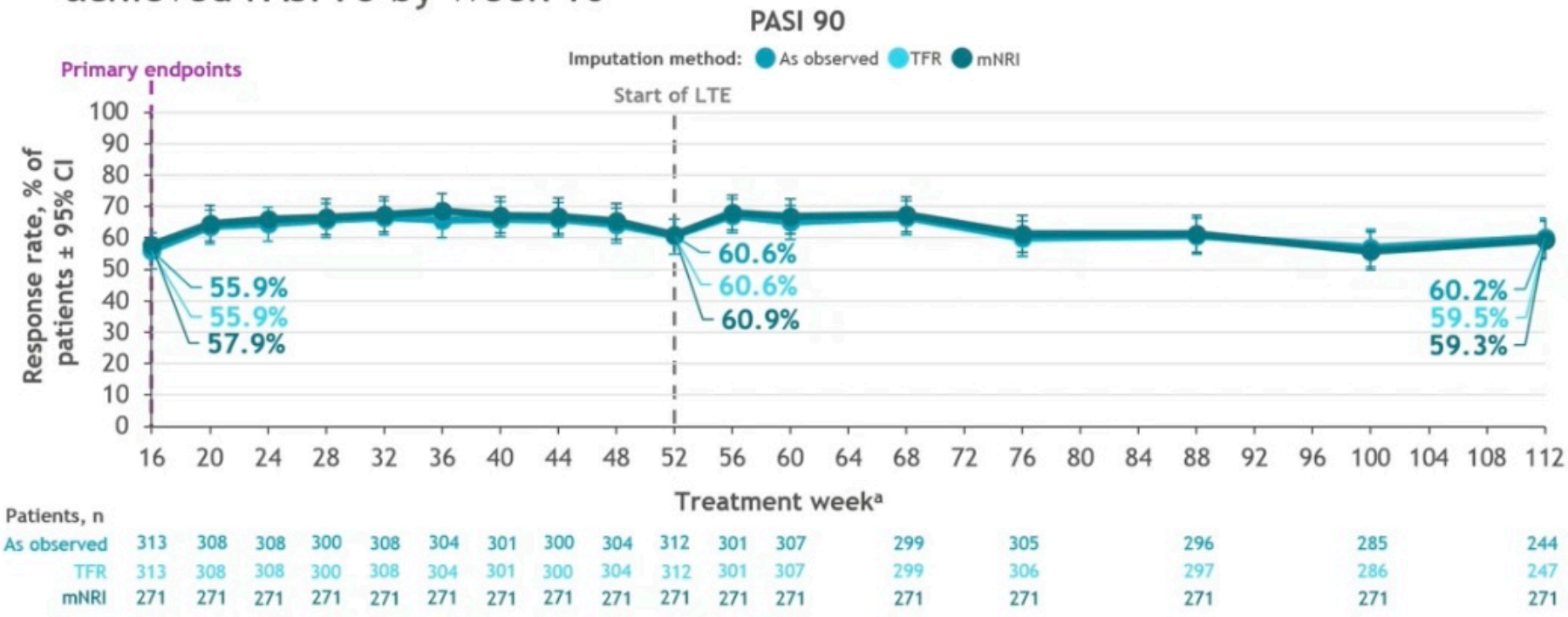
Mark G. Lebwohl

5:07

POETYK PSO-1, PSO-2, and LTE

Maintenance of PASI 90 in Week 16 PASI 75 responders with continuous deucravacitinib treatment for up to 112 weeks

- PASI 90 responses were maintained from Week 16 to Week 112 in patients who achieved PASI 75 by Week 16



Patients, n																			
As observed	313	308	308	300	308	304	301	300	304	312	301	307	299	305	296	285	244
TFR	313	308	308	300	308	304	301	300	304	312	301	307	299	306	297	286	247
mNRI	271	271	271	271	271	271	271	271	271	271	271	271	271	271	271	271	271

[a]Treatment week was calculated from Week 1 of POETYK PSO-1 and PSO-2.
CI, confidence interval; LTE, long-term extension; mNRI, modified nonresponder imputation; PASI 75/90, ≥75%/≥90% reduction from baseline in Psoriasis Area and Severity Index; TFR, treatment failure rules.

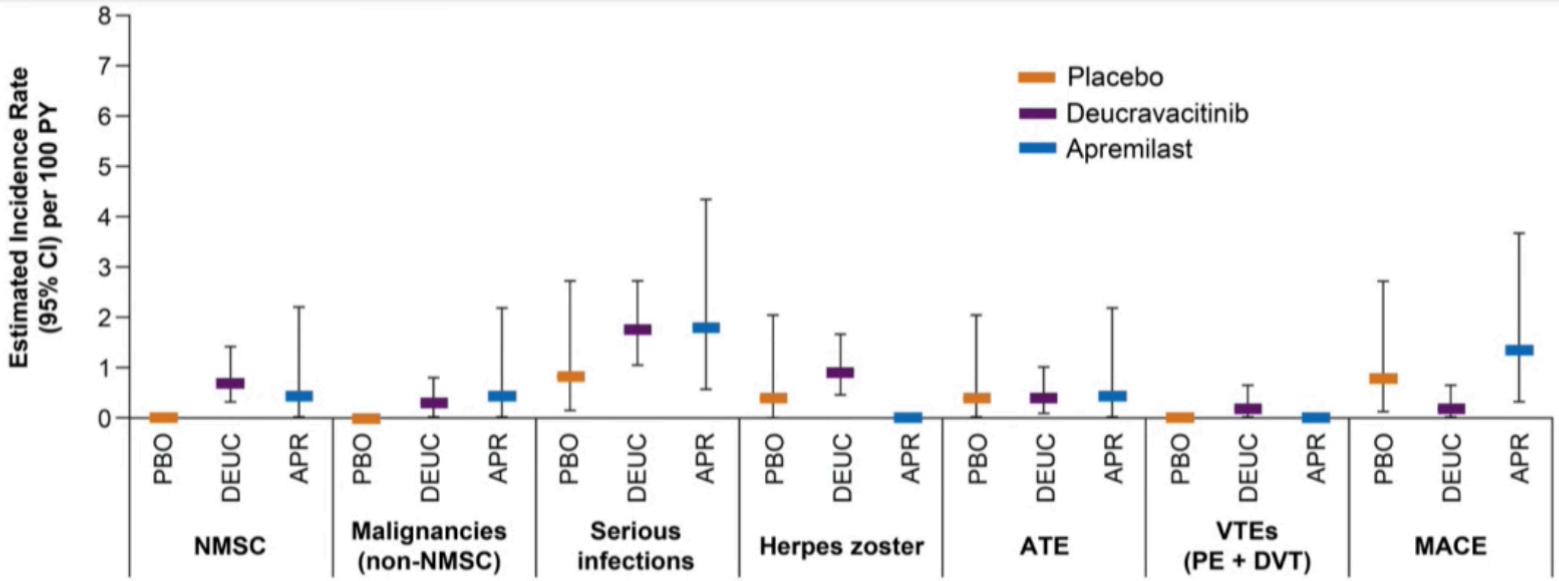
13

1. Chimalakonda A, et al. Dermatol Ther (Heidelb) 2021;11:1763–76; 2. Armstrong A, et al. J Am Acad Dermatol 2023;88:29–39

PSORIASIS E INHIBIDORES JAK-KINASAS

April Armstrong 1:27

Deucravacitinib AEs of Interest (Integrated): Weeks 0-52[1,2]



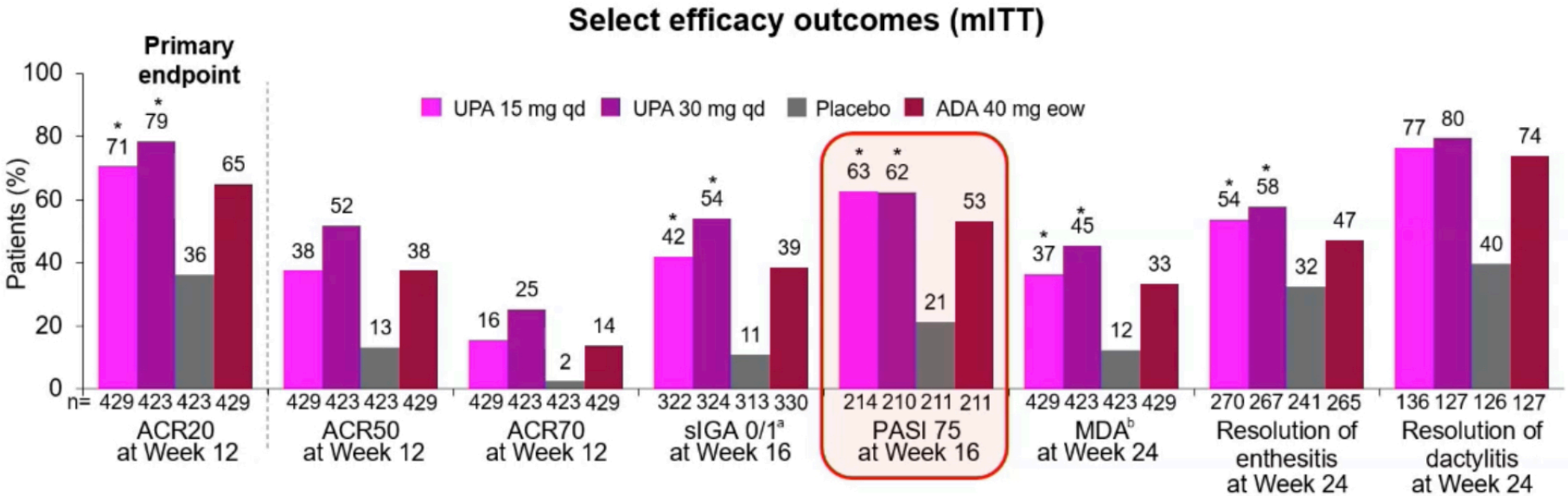
- **No boxed warnings**
- None of the serious infections with deucravacitinib led to discontinuation
- No cases of herpes zoster with deucravacitinib were serious or led to discontinuation
- No TB events and no opportunistic systemic infections were reported with deucravacitinib
- There were two cases of VTE in the deucravacitinib group; neither was attributed to the drug by investigator (EAIR: 0.21 per 100 PY)

1. Armstrong A et al. AAD VMX 2021. Oral presentation. 2. Warren R et al. San Diego Dermatology Symposium 2022.

PSORIASIS E INHIBIDORES JAK-KINASAS

Bruce Strober 5 12

SELECT-PsA 1: Key outcomes after treatment with upadacitinib versus placebo and adalimumab among adults with psoriatic arthritis

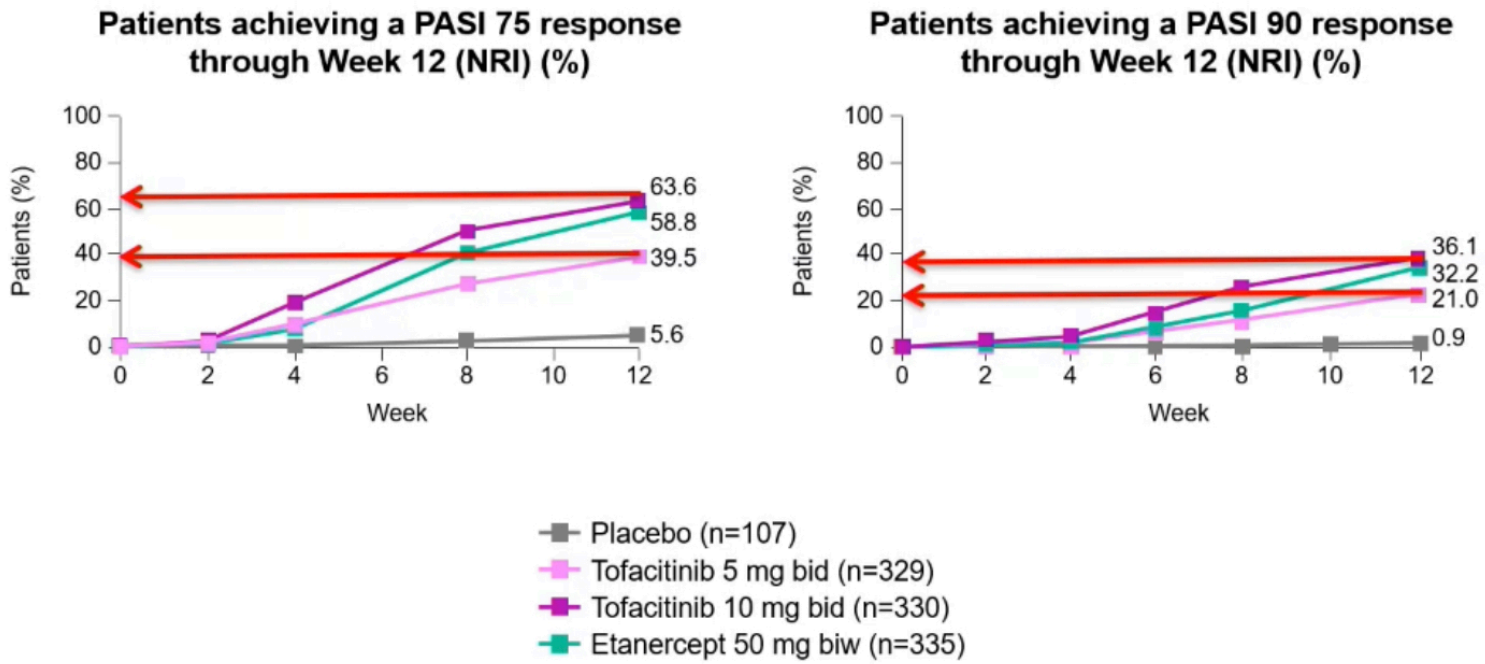


*P<0.001 vs placebo (controlled for multiplicity)
For binary endpoints, NRI was used to handle missing data
[a]Plus ≥2-point decrease from baseline; [b]MDA determined as fulfilment of 5 of 7 criteria: Tender joint count ≤1, swollen joint count ≤1, PASI score ≤1 or ≤3% BSA involvement, patient pain NRS ≤1.5, PtGA-disease activity NRS ≤2.0, HAQ-DI score ≤0.5, Leeds Enthesitis Index ≤1

McInnes IB, et al. N Engl J Med 2021;384:1227–39.

PSORIASIS E INHIBIDORES JAK-KINASAS

Tofacitinib vs etanercept or placebo in moderate to severe chronic plaque psoriasis: Responder rates

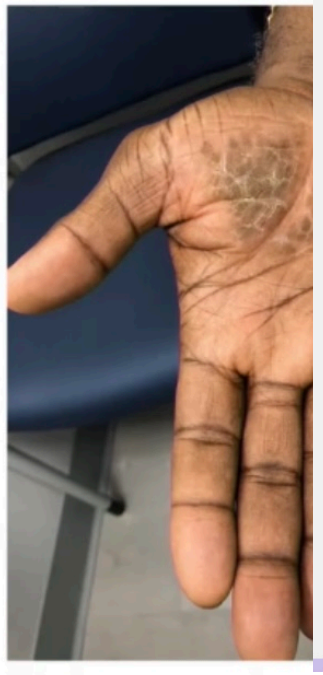


Bachelez H, et al. Lancet 2015;386:522–61

PSORIASIS

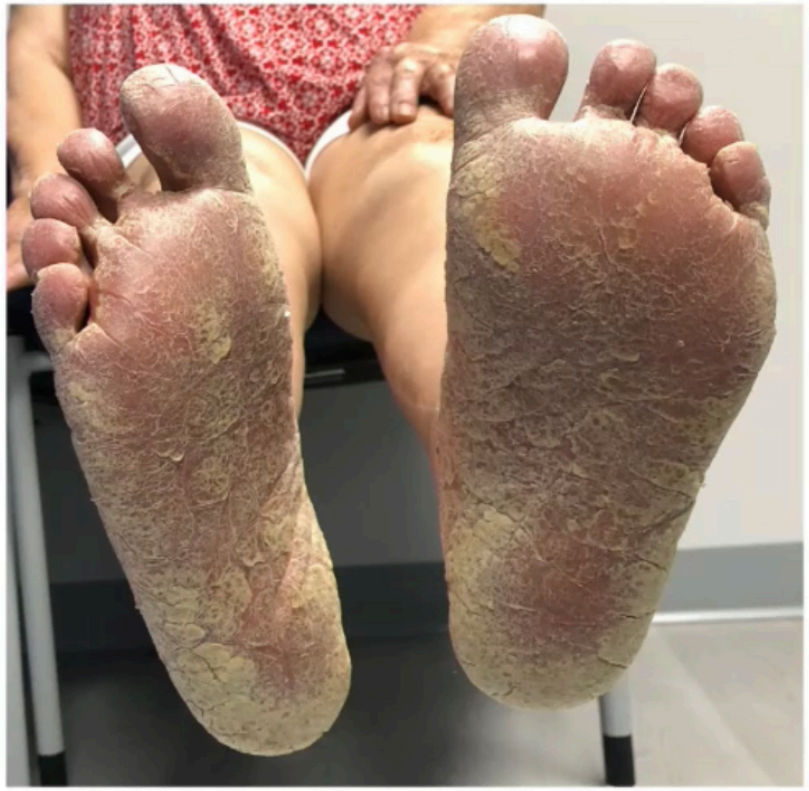
Bruce Strober

Tofacitinib 11

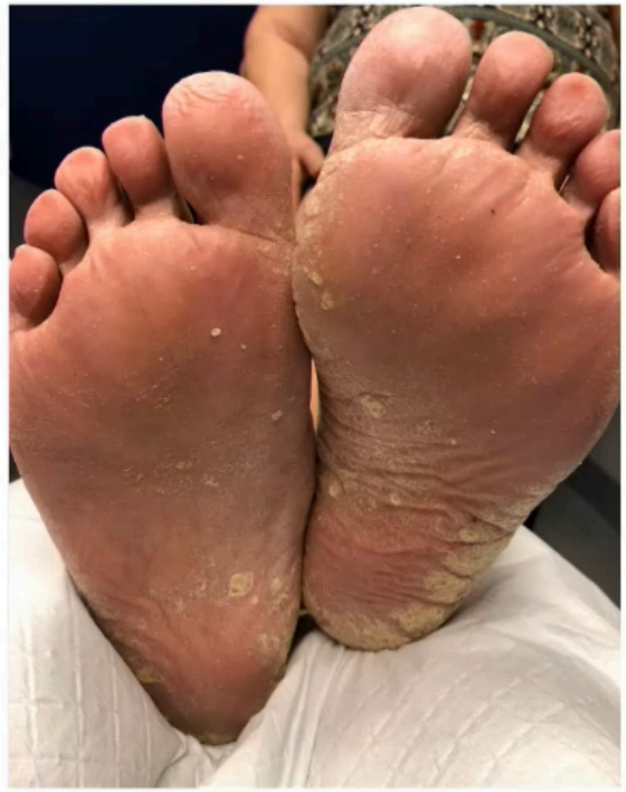


Baseline

Tofacitinib 11 mg once daily



Baseline



2 months

Muzumdar, S., Leonardi, C., and Strober, B. (2021). Journal of Psoriasis and Psoriatic Arthritis. 2021;6(2):93-98

Baseline 1 month 2 months

Muzumdar, S., Leonardi, C., and Strober, B. (2021). Journal of Psoriasis and Psoriatic Arthritis. 2021;6(2):93-98

PSORIASIS E INHIBIDORES JAK-KINASAS

Mark G. Lebwohl

15:55

Why We Should Use JAK Inhibitors: Risk/Benefit Ratio

Mark Lebwohl, MD
Dean for Clinical Therapeutics
Icahn School of Medicine at Mount Sinai
Chairman Emeritus
Kimberly and Eric J. Waldman
Department of Dermatology

PSORIASIS E INHIBIDORES JAK-KINASAS

Mark G. Lebwohl

12 16

What are the incidence rates for serious adverse events? (Events

Drug	Malig (Ex-N
Upadacitinib (15mg)	0
Upadacitinib (30mg)	0
Abrocitinib (100mg)	0
Abrocitinib (200mg)	0
Methotrexate[a]	0
Cyclosporine	0
Systemic Steroids	4

JAK Inhibitor Safety Compared
Stefano G. Daniele, Christopher

Mark G. Lebwohl

8 38

Table 1. EAER of Malignancy, Adjudicated MACE, and VTE Through 3 Years[a]

Event, EAIR (95% CI), [n]	Continuous UPA 15 mg QD + MTX n=398; PY=994.1	Continuous Humira 40 mg EOW + MTX n=168; PY=373
Malignancy (excluding NMSC)	0.8 (0.3, 1.6) [8]	1.1 (0.3, 2.7) [4]
MACE (adjudicated)	0.1 (0, 0.6) [1]	0.5 (0.1, 1.9) [2]
VTE (adjudicated)	0.2 (0, 0.7) [2]	0.8 (0.2, 2.4) [3]

[a] EAIRs were the same as EAERs for these events
Source: Fleischman, 2022a.

PSORIASIS E INHIBIDORES JAK-KINASAS

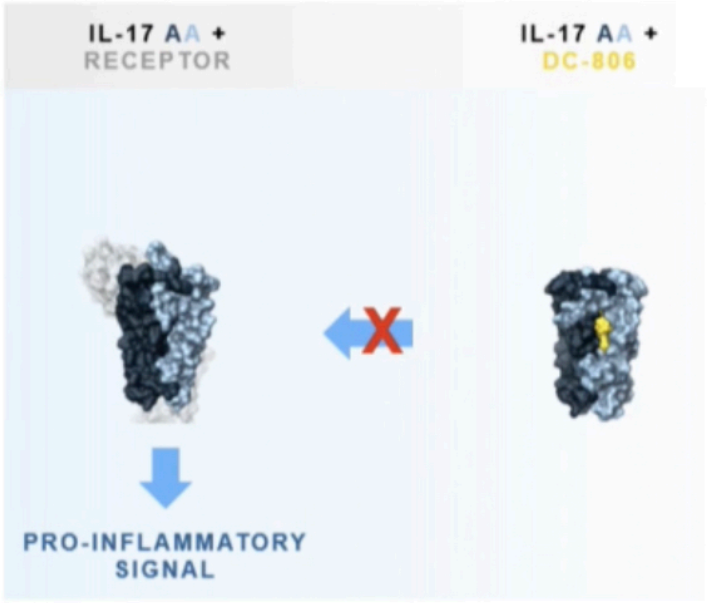
Nayera Hassan Moftah 5 16

Topical JAK inhibitors in Psoriasis

- **Tofacitinib 2%** *(JAK1/ 3i)* Phase IIb in adults with mild to moderate plaque psoriasis, showed greater efficacy than vehicle at Week 8, but not Week 12.
- **Ruxolitinib** (*JAK1, 2 i*) (0.5%., 1%, 1.5%) showed significant improvement in total lesion score compared with vehicle for 3 months.
- **Brepocitinib** (*JAK1/TYK2i)* is in phase IIb clinical trial in psoriasis.

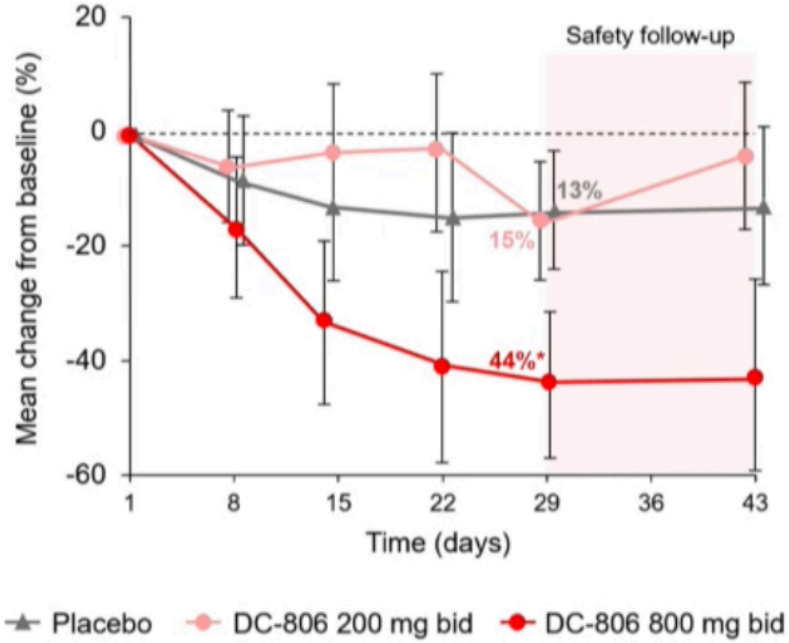
-Callis DK, et al. Novel mechanism for topical treatment of plaque psoriasis e results of a . randomized, double blind, concentration ranging, vehicle controlled 12 week study with JAK 1/2 inhibitor INCB018424 cream. The 70th SID meeting; Atlanta GA, USA. 2010. p. 261.J Invest Dermatol Abstract.
-Punwani N, Burn T, Scherle P, et al. Downmodulation of key inflammatory cell markers with a topical Janus kinase ½ inhibitor. Br J Dermatol. 2015;173(4):989-997.
-Krueger et al. Tyrosine kinase 2 and Janus kinase–signal transducer and activator of transcription signaling and inhibition in plaque psoriasis. J Am Acad Dermatol 2022;86:148-57.)

DC-806: ORAL INHIBITION OF IL17A



- **DC-806** is a small molecule that intercalates into the IL-17A homodimer and inhibits via allosteric binding event

Change in PASI scores over time



Warren RB, et al. AAD 2023, Late-breaking abstract.

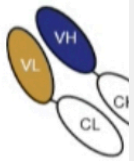
PSORI

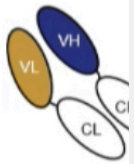
Kenneth Gordon

Phase 2
an IL-17

Ig

Ig





Fab

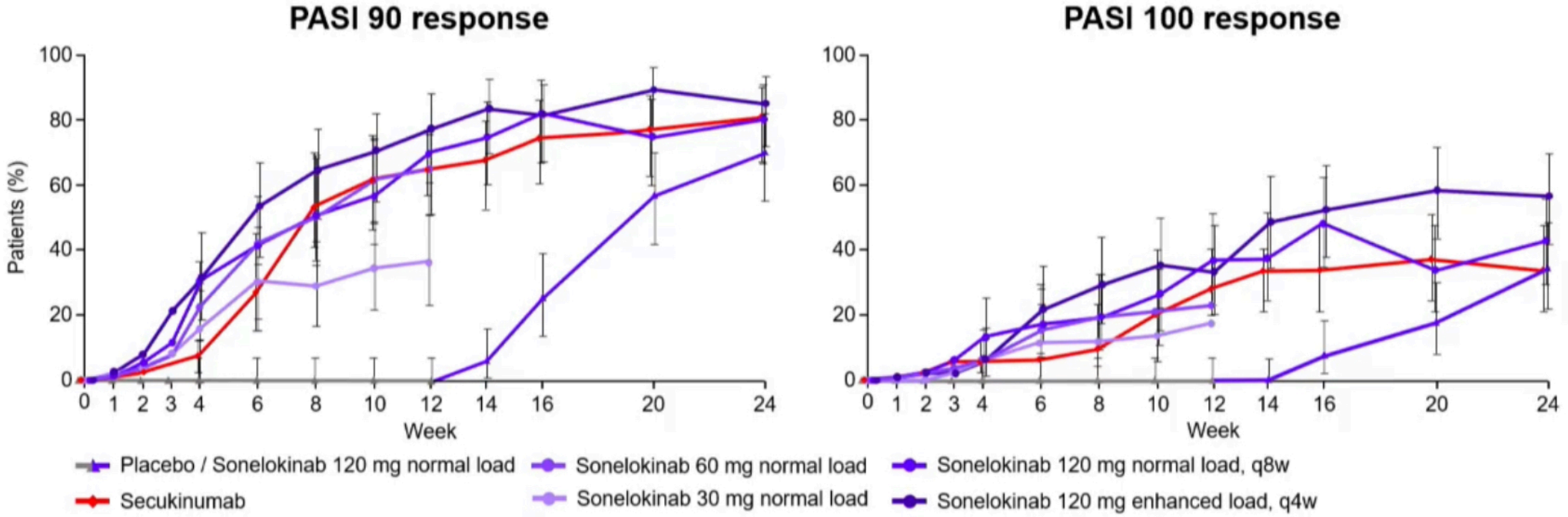
- The nan

Papp K, et al. EA

Kenneth Gordon

1:43

Phase 2b trial: PASI responses through Week 24 with sonelokinab (M1095) for patients with moderate to severe chronic psoriasis



Patient numbers and methodology for imputation of missing data not provided

Papp K, et al. EADV 2020, Late breaking news D1T03.3B

PSORIASIS- NUEVOS TOPICOS

HIGHLIGHTS SINGAPORE 3-8 / july / 2023

era Hassan Moftah 19 54

25th World Congress of Dermatology SINGAPORE 2023 DERMATOLOGY BEYOND BORDERS SCIENCE·CARE·COMMUNITIES ILDS

New topical anti-inflammatory drugs

Nayera Moftah, *MD, DTQM, DHPE*
Professor of Dermatology and Venereology, Al-Azhar University, Cairo, Egypt
Editor in Chief of Journal of the Egyptian Women's Dermatologic Society
www.jewd.eg.net

opical therap

Session Details: Topical therapies I.
Code: SY47A – 06 July 2023- Level3-Room 308+309. Time: 08:00-9:20
Symposium : Topical Therapies
09:00:00 - 09:20:00

www.wcd2023singapore.org

Nayera Hassan Moftah 18:13

What are the new topical antinfammatory targeted drugs groups?

I.Phosphodiesterase-4 inhibitors	II.Aryl hydrocarbons receptors Modulating agents	III.Janus kinase/signal transducer and activator of transcription (JAK/STAT) inhibitors

Other groups are still in the pipeline

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yera Hassan Moftah 17:03

Topical Inhibitors of PDE-4

Crisaborole

Crisaborole 2% ointment is FDA approved in December 2016 for the treatment of mild-to-moderate AD in children ≥ 2 years and in March 2020 for infants ≥ 3 months of age.

Roflumilast

Roflumilast 0.3% is FDA approved in plaque psoriasis ≥ 12 years old in July 2022.

Difamilast

In Japan, at the end of 2021, difamilast ointment was approved for the treatment of AD patients ≥ 2 years.
-Under trial for < 2 years.

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JAMA | Original Investigation

Effect of Roflumilast Cream vs Vehicle Cream on Chronic Plaque Psoriasis
The DERMIS-1 and DERMIS-2 Randomized Clinical Trials

Mark G. Lebwohl, MD; Leon H. Kircik, MD; Angela Y. Moore, MD; Linda Stein Gold, MD; Zoe D. Draelos, MD; Melinda J. Gooderham, MD; Kim A. Papp, MD, PhD; Jerry Bagel, MD; Neal Bhatia, MD; James Q. Del Rosso, DO; Laura K. Ferris, MD; Lawrence J. Green, MD; Adelaide A. Hebert, MD; Terry Jones, MD; Steven E. Kempers, MD; David M. Pariser, MD; Paul S. Yamauchi, MD, PhD; Matthew Zirwas, MD; Lorne Albrecht, MD; Alim R. Devani, MD; Mark

- At 8 6.1% the
- Rofl and
- **Rofl is di**

Stein Gold L et presented at: A

Clin

Topical

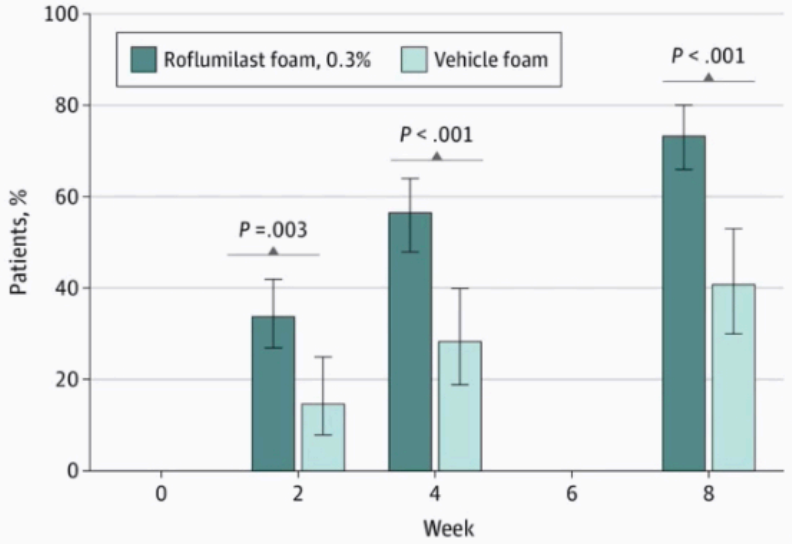
Topical Roflumilast Cream → PDE4i*

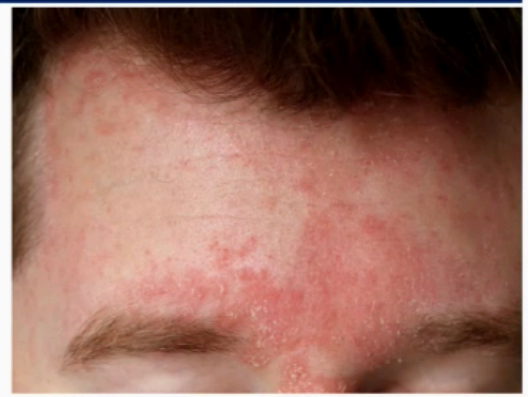
Topical Roflumilast Cream → PDE4i*

Topical Roflumilast Foam → PDE4i*

Safari

Roflumilast foam 0.3% in seborrheic dermatitis





Once-daily roflumilast foam, 0.3% was effective (erythema, scaling, and itch) and safe.

Zirwas MJ et al. Efficacy of Roflumilast Foam, 0.3%, in Patients With Seborrheic Dermatitis: A Double-blind, Vehicle-Controlled Phase 2a Randomized Clinical Trial. JAMA Dermatol. 2023 May 3:e230846. doi: 10.1001/jamadermatol.2023.0846

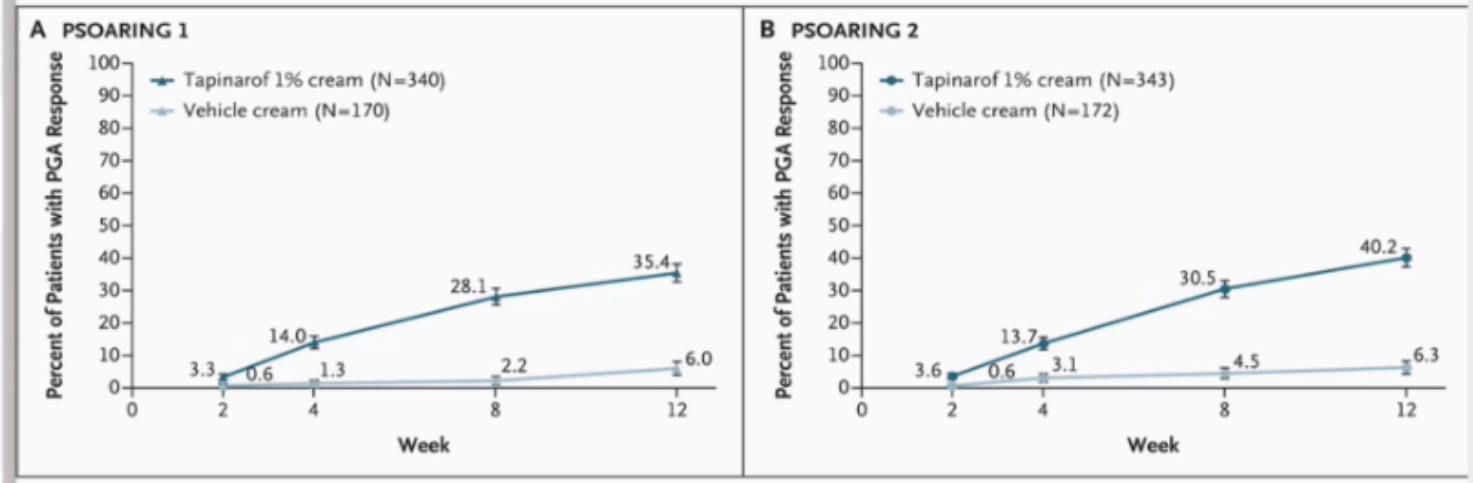
PSORIASIS- NUEVOS TOPICOS Tapinarof

Nayera Hassan Moftah

11:09

How long does Tapinarof take to work in psoriasis?

- Improvements in symptoms of psoriasis as early as 4 weeks after starting Tapinarof.
- It took 12 weeks to improve or clear up completely.



Phase 3 Trials of Tapinarof Cream for Plaque Psoriasis. *Lebwohl MG et al. DOI: 10.1056/NEJMoa2103629*

Biol

Drug cla

Anti-IL-1

Biologics

Drug class	Drug name	Effect on fertility and sexual function	Risk of teratogenicity
Anti-IL-12/23	Ustekinumab	• Limited human data • No impairment of fertility in animal studies • Weak recommendation in favor for use in males trying to conceive (*BETA-PSO*)	• Acceptable for use in men attempting conception (*AAD-NPF*) • Discontinuation at 15 weeks before trying to conceive can be considered in patients with well-controlled psoriasis and wish to avoid fetal exposure. (*APC*)
Anti-IL-23	Guselkumab	• Limited data. No effects on fertility in animal studies • No clear data suggesting increased risk. Weak recommendation in favor for use in males trying to conceive (*BETA-PSO*)	• No data found
	Risankizumab	• No impairment of male fertility in an animal study • No clear data suggesting increased risk. Weak recommendation in favor for use in males trying to conceive (*BETA-PSO*)	• No data found

Hui EX, Huang X, Oon HH. *Andrology*. 2022;10(7):1272-1285.
Lambert JLW, Segaert S, Ghislain PD, et al. *J Eur Acad Dermatol Venereol*. 2020;34(8):1654-1665.

Hui EX, Huang X, Oon HH. *Andrology*. 2022;10(7):1272-1285.
Lambert JLW, Segaert S, Ghislain PD, et al. *J Eur Acad Dermatol Venereol*. 2020;34(8):1654-1665.

APC= The Australasian Psoriasis Collaboration

PSORIASIS- OTROS

Christopher Bunick

9 54

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DERMATOLOGY BEYOND BORDERS
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ILDS

Enhancing precision medicine: the structure of IL-23 inhibitor epitopes correlates with short-term clinical efficacy in plaque psoriasis

Christopher G. Bunick, MD, PhD

Associate Professor of Dermatology & Program in Translational Biomedicine

Yale University

FC17 Psoriasis 2

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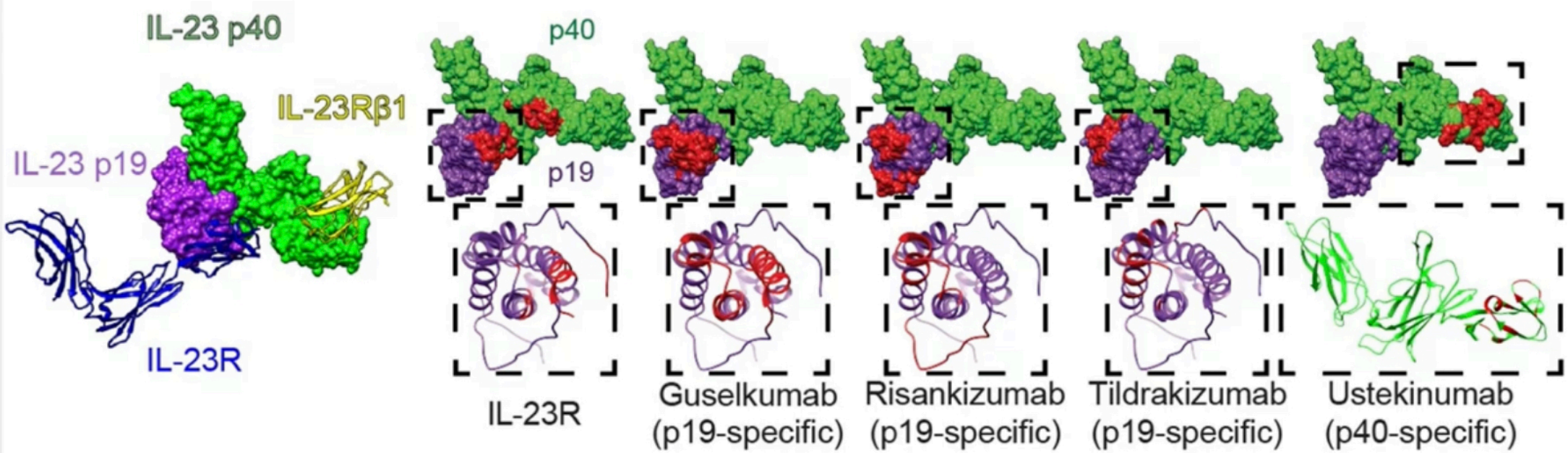
PSORIASIS- OTROS

Christopher Bunick 4:53

IL-23 Inhibitors Are NOT Created Equal: They Have Unique Epitopes



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Daniele SG, Eldirany SA, Ho M, Bunick CG. Structural basis for differential p19 targeting by IL-23 biologics. bioRxiv [Preprint]. 2023 Mar 9:2023.03.09.531913.

PSORIASIS- OTROS

Christopher Bunick 0 38

Molecular thinking impacts patient care

- Understanding molecular differentiation of dermatologic therapies improves dermatologist competency and patient treatment decisions.
- p19-specific IL-23 biologics are very different medicines.
- Epitope surface area is a fundamental driver of k_{off}, K_D, and biologic efficacy in the short- and long-term treatment of psoriasis patients.
- Atomic resolution structural mechanisms of dermatologic therapeutics provide key insights into what matters to patients: how a drug achieves efficacy and safety

Daniele SG, Eldirany SA, Ho M, Bunick CG. Structural basis for differential p19 targeting by IL-23 biologics. bioRxiv [Preprint]. 2023 Mar 9:2023.03.09.531913.

PSORIASIS- OTROS

Richard Langley 9:51

Systematic Targeted Review of Study Design and Analytic Methods in Long-term Biologic Studies for Moderate-to-severe Psoriasis

July 5th, 2023

DALHOUSIE UNIVERSITY
Inspiring Minds

Richard GB Langley MD
Professor of Dermatology
Director of Research
Division of Dermatology
Dalhousie University
Halifax, Nova Scotia
Canada

Clinical Trials: AbbVie, Amgen, Celgene, Centocor/Janssen, Eli-Lilly, Merck, Novartis, Pfizer

Peer Reviewed: Canadian Dermatology Foundation, DMRF, NSHRF

Richard Langley

4 26

Richard Langley

- 0:41

Conclusions

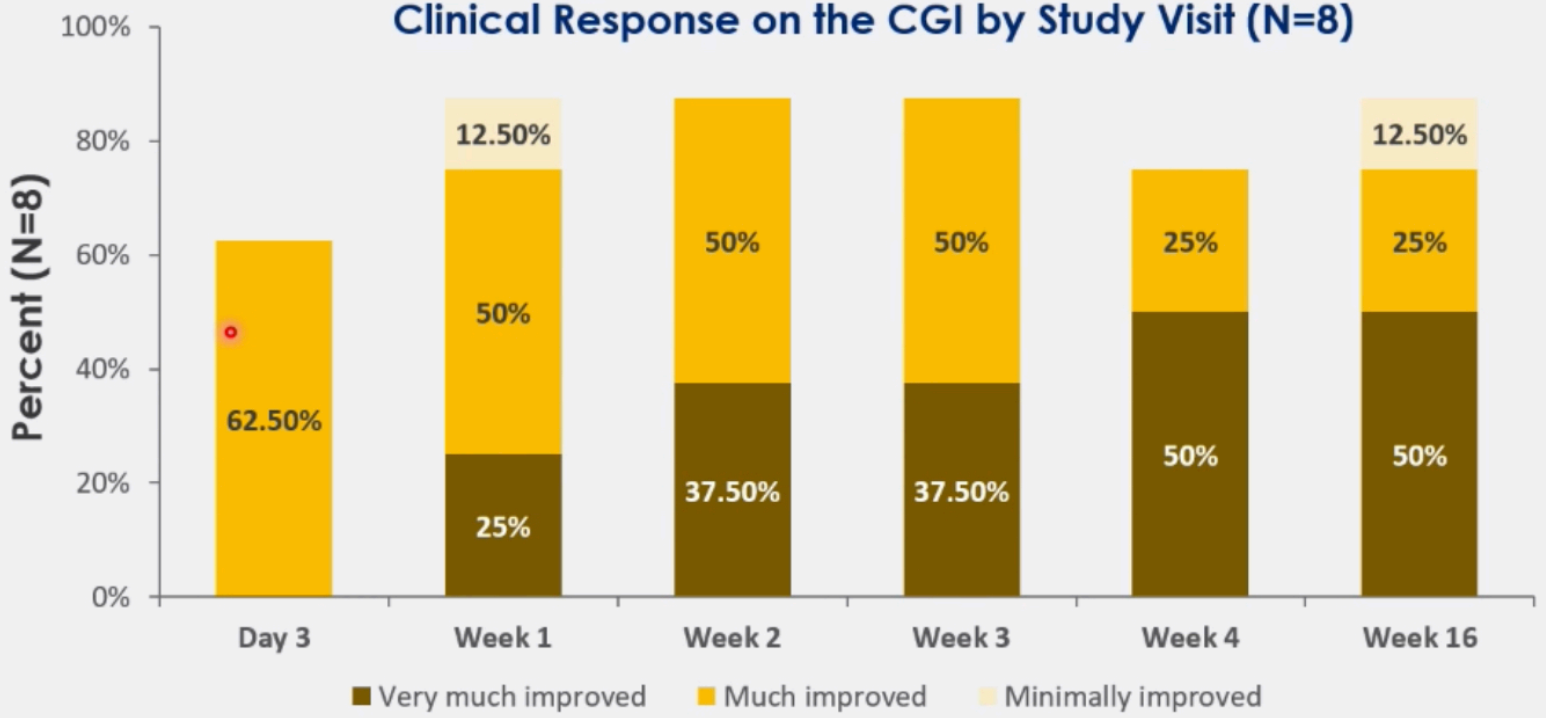
There will be no fair method of comparing data across long-term extension studies identified in the systematic targeted review due to variabilities in study design and in handling missing data.

Even randomized trials using the same imputation method will provide incomparable results (eg, 2 trials using mNRI with different definitions will still not be comparable).

Methodological standardization of trial design and approach to handling missing data is needed for future long-term extension studies of biologics in moderate-to-severe psoriasis.

GALLOP: Efficacy

Primary Efficacy Endpoint: Proportion of Patients Achieving Clinical Response on the CGI by Study Visit (N=8)



Imsidolimab is an investigational product and is not approved for any indication in any country.
CGI, Clinical Global Impression.
Warren RB, et al. *Br J Dermatol.* 2023;ljad083. doi: 10.1093/bjd/ljad083. Online ahead of print.

HIGHLIGHTS SINGAPORE

25th World Congress of Dermatology

3-8 / july / 2023

La Academia Española de Dermatología y Venereología expresa su agradecimiento al patrocinador UCB, por su especial apoyo y contribución con la actividad formativa Highlights 2023.

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Y VENEREOLOGÍA