AAD ANNUAL MEETING 2025

AEDV 7 - 11 MARZO ORLANDO

highlights

Psoriasis y otras enfermedades inflamatorias

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Una iniciativa de:

ACADEMIA ESPAÑOLA DE DERMATOLOGÍA Y VENEREOLOGÍA

FUNDACIÓN AEDV PIEL SANA

ACADEMIA ESPAÑOLA DE DERMATOLOGÍA Y VENEREOLOGÍA

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ucb

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CONFLICTOS DE INTERÉS

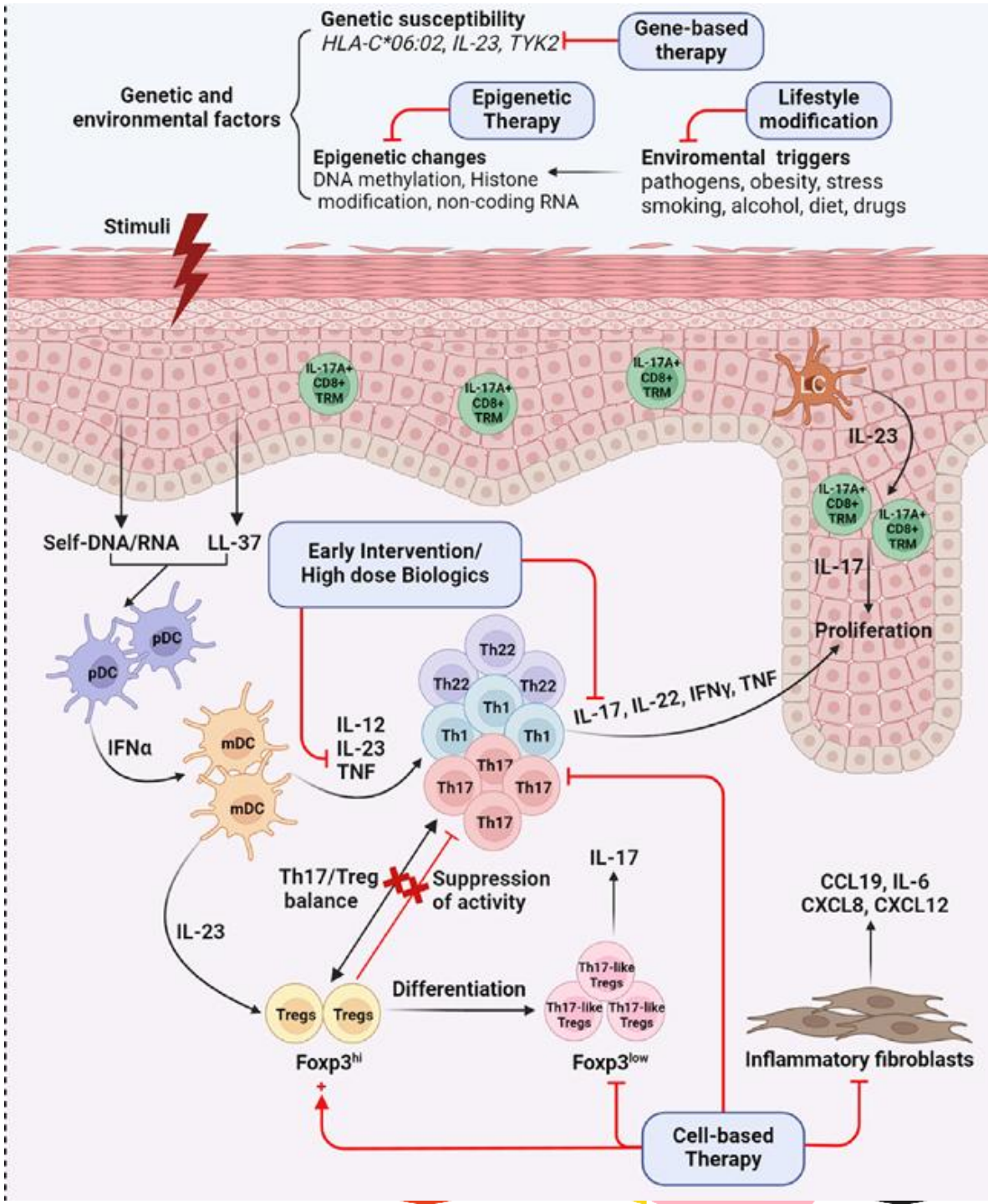
Amgen, Leo Pharma

Parte 1: Psoriasis- Tratamiento

Parte 2: Psoriasis-Comorbilidades
Otras enfermedades inflamatorias

Curing Psoriasis?
Andrew Blauvelt

- Intervención temprana/ dosis altas biológicos
- TPHP
- Células mesenquimales estromales
- Tregs
- CART
- BiTe
- Terapia génica
- MicroRNA editing



Curing Psoriasis?
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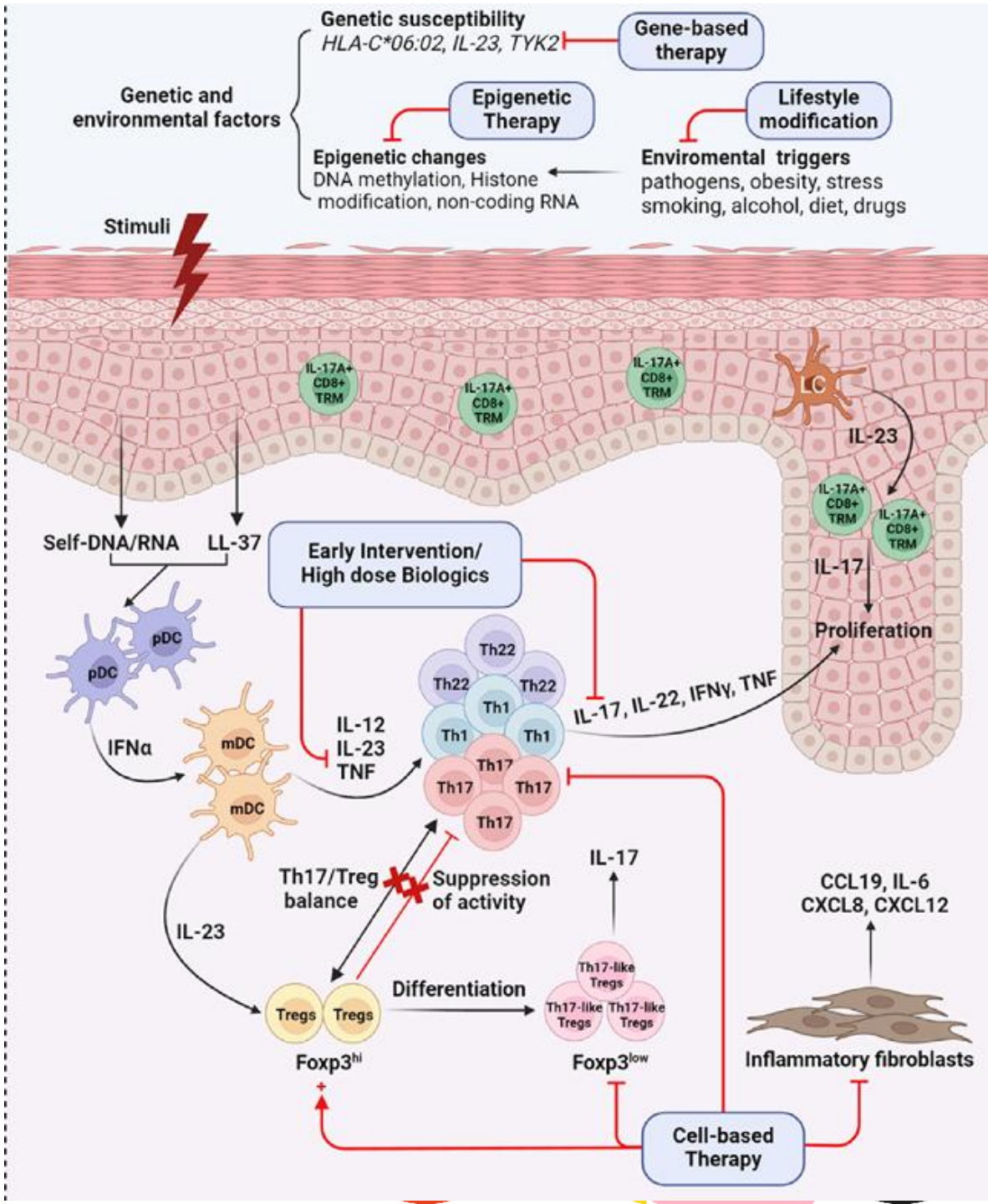


Curing Psoriasis?
Andrew Blauvelt

ELSEVIER

Journal of Investigative Dermatology

Volume 144, Issue 12, December 2024, Pages 2645-2649

Perspective

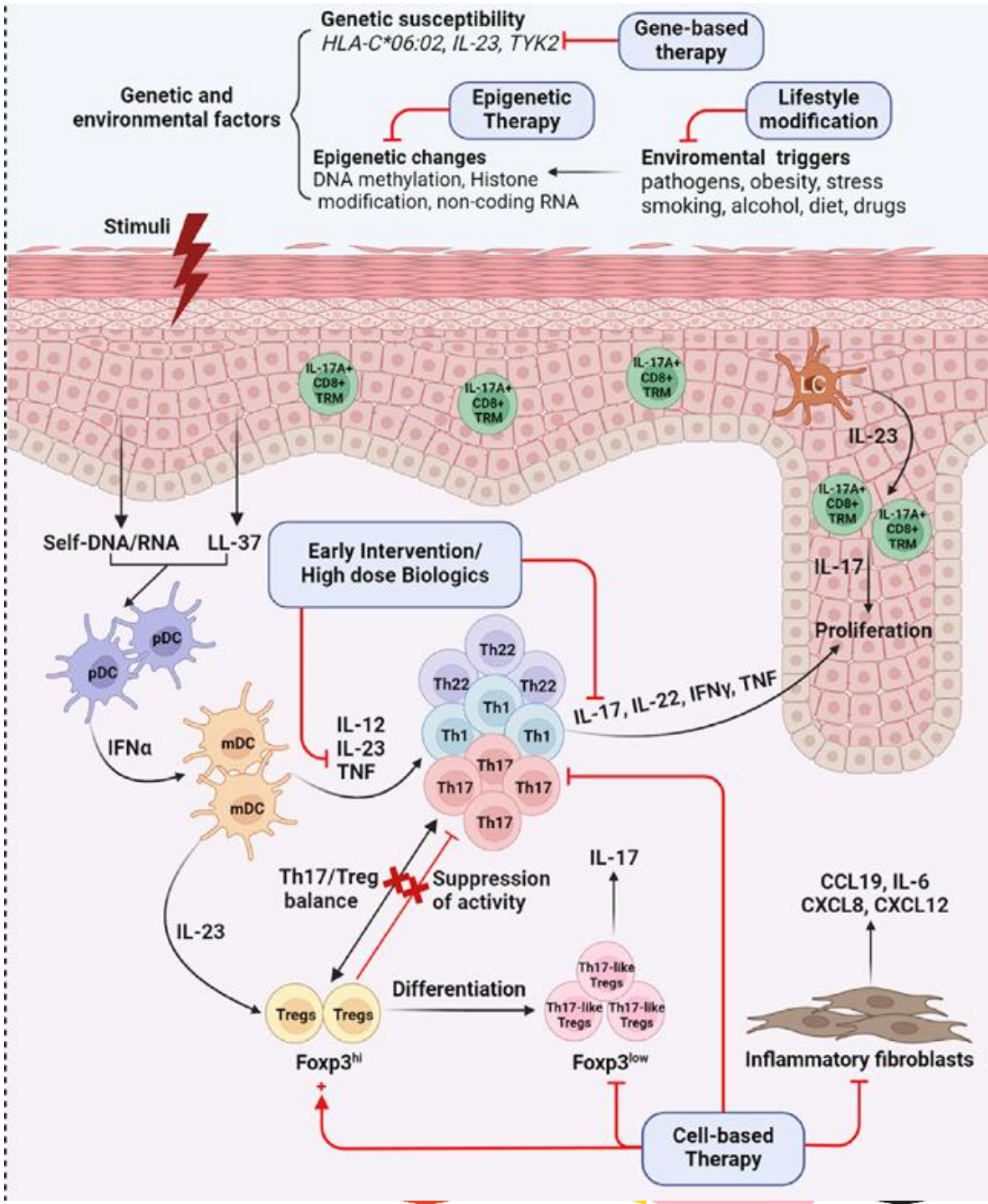
Curing Psoriasis

Su M. Lwin [1 2 7], Shir Azrielant [2 3 7], Juan He [2 4], Christopher E.M. Griffiths [2 5 6]

EARLY INTERVENTION WITH SYSTEMIC THERAPY

A key challenge in psoriasis management is recurrence upon withdrawal of therapy, which is dependent on accumulation and persistence of IL-23–dependent CD8+ tissue-resident memory T cells (TRMs) in the epidermis of resolved psoriasis skin (Matos et al, 2017) (Figure 1). Furthermore, there is a

targeting TRMs early in the disease course, preferably within the first year of onset, whatever the severity, particularly with anti–IL-23p19 biologics, could provide a potential cure. Indeed, it is known that the anti–IL-23p19 biologic guselkumab is more likely to produce clearance of psoriasis in patients with short (≤2 years) rather than long disease duration (Schäkel et al, 2023). Similarly, patients receiving the anti–IL-17A



JEADV
JOURNAL OF THE EUROPEAN ACADEMY OF DERMATOLOGY & VENEREOLOGY

Original Article | Open Access

Secukinumab treatment in new-onset psoriasis: aiming to understand the potential for disease modification – rationale and design of the randomized, multicenter STEPIn study

L. Iversen, L. Eidsmo, J. Austad, M. de Rie, A. Osmancevic, L. Skov, T. Talme, I. Bachmann, P. van de Kerkhof, M. Stahle, R. Banerjee, J. Oliver, A.E.R. Fasth, J. Frueh

First published: 06 April 2018 | https://doi.org/10.1111/jdv.14979 | Citations: 48

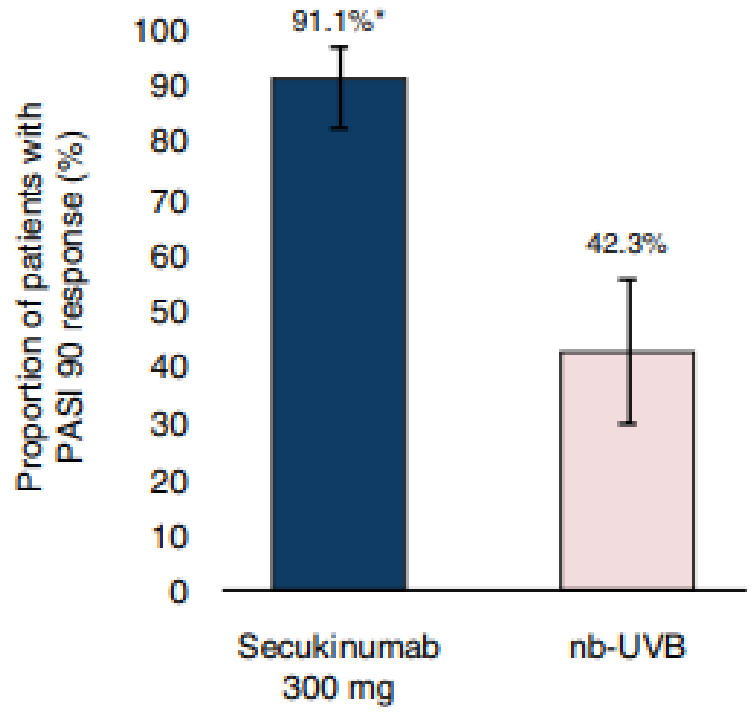
Received: 16 August 2022 | Accepted: 13 December 2022

DOI: 10.1111/jdv.18846

ORIGINAL ARTICLE

JEADV

Secukinumab demonstrates superiority over narrow-band ultraviolet B phototherapy in new-onset moderate to severe plaque psoriasis patients: Week 52 results from the STEPIn study



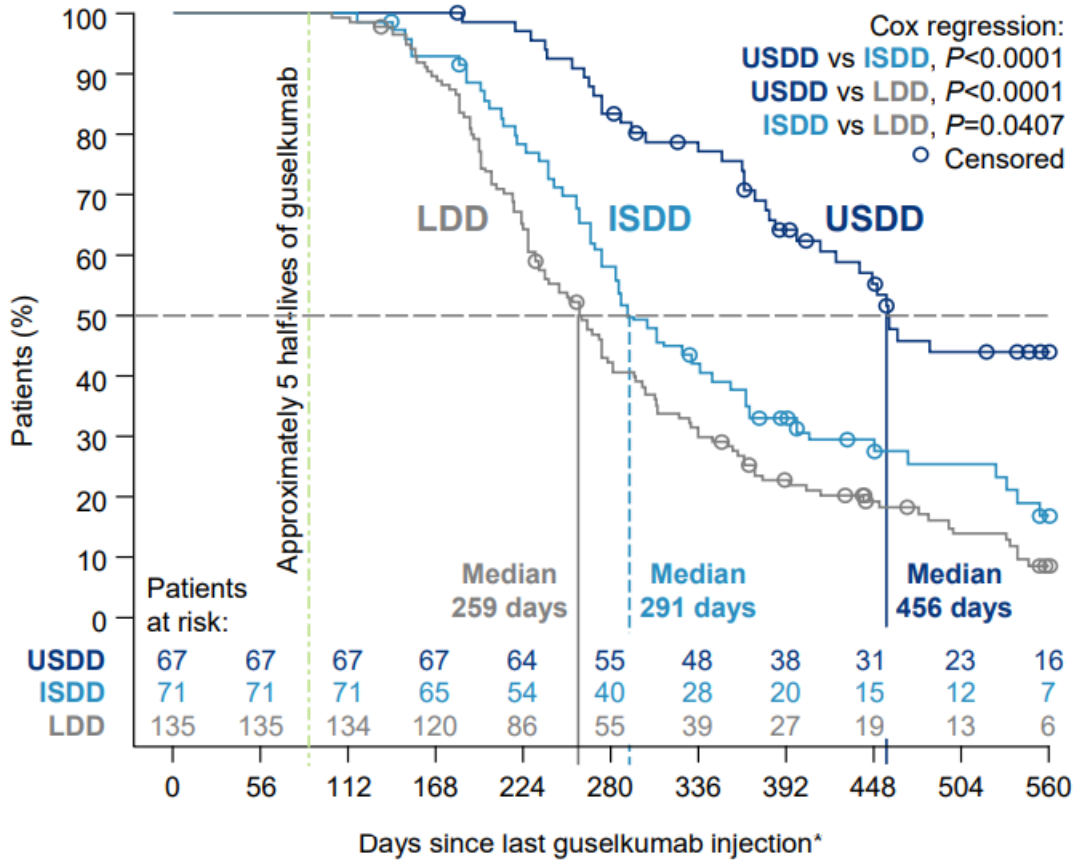
GUIDE trial results after withdrawal in part 3: long-term remission in patients with psoriasis treated with guselkumab within 15 months from onset of symptoms

AAD 2024
50236

K. Schäkel,[1] K. Asadullah,[2,3] A. Pinter,[4] P. Weisenseel,[5] R. Sabat,[2] M. Hoffmann,[6] C. Paul,[7] F. Taut,[8] N. Spindler,[9] S. Tabori,[9] K. Eyerich[10]

Patients with disease duration <15 months (USDD) remained treatment free significantly longer than those with disease duration >15 months (ISDD and LDD)

Figure 3. Treatment-free period (**N=273**)



Disease duration	Months since symptom onset
Long disease duration (LDD)	>24
Intermediate-short disease duration (ISDD)	≥15–≤24
Ultra-short disease duration (USDD)	<15

Median treatment-free period

- USDD patients: **456** days
- ISDD patients: **291** days
- LDD patients: **259** days

USDD vs **ISDD**: ↑ **165 days (57%)**
HR = 0.41, 95% CI 0.27–0.62
P<0.0001

USDD vs **LDD**: ↑ **197 days (76%)**
HR = 0.30, 95% CI 0.21–0.44
P<0.0001

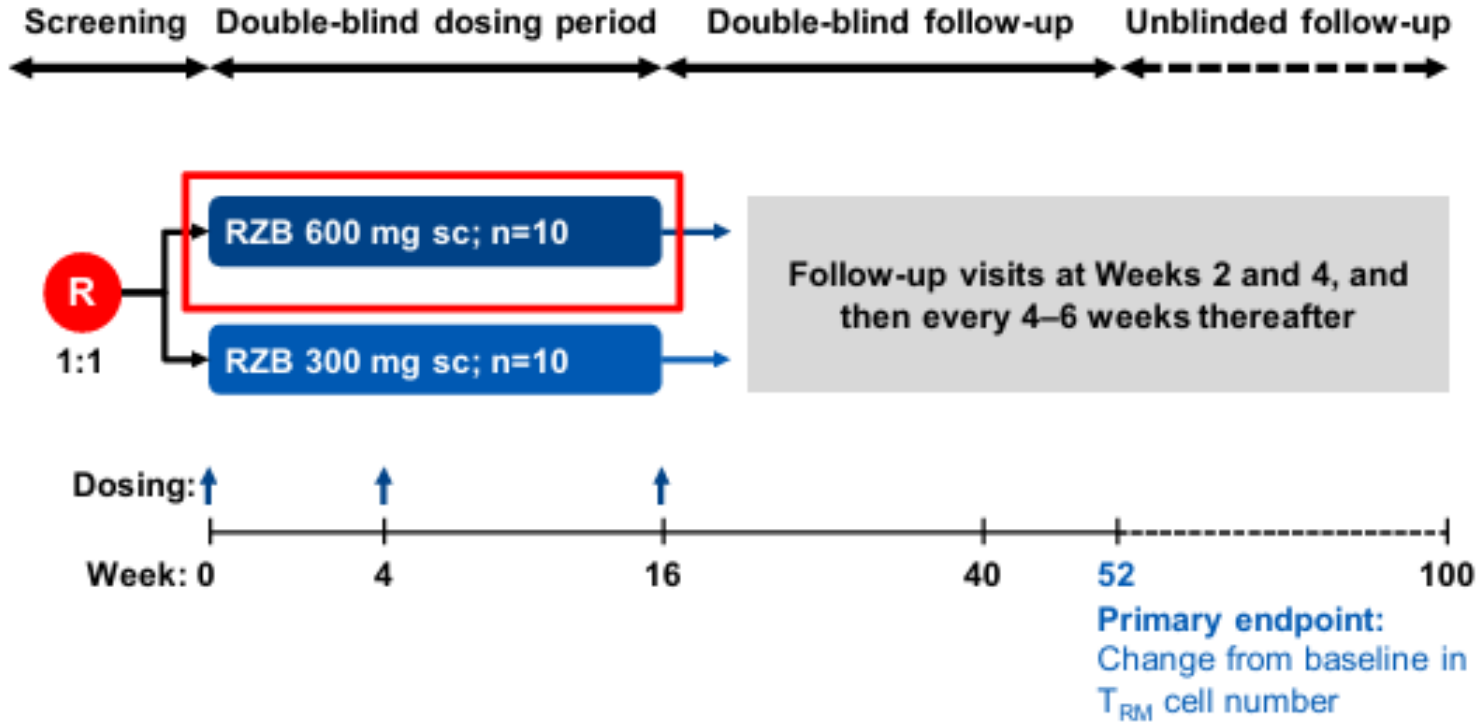
The treatment-free observation period is ongoing (to W220)

Loss of maintenance of response was defined as PASI >5, at which point treatment was re-initiated. Time to end of the treatment-free period was calculated from time of last guselkumab injection in study part 2 to the date of the first re-treatment visit (irrespective of PASI assessments). If no re-treatment was started, time was censored to the date of the W116 visit or the date of study termination, whichever came first

KNOCKOUT: Phase 2 trial of high induction dosing of risankizumab for moderate to severe psoriasis—52-week results

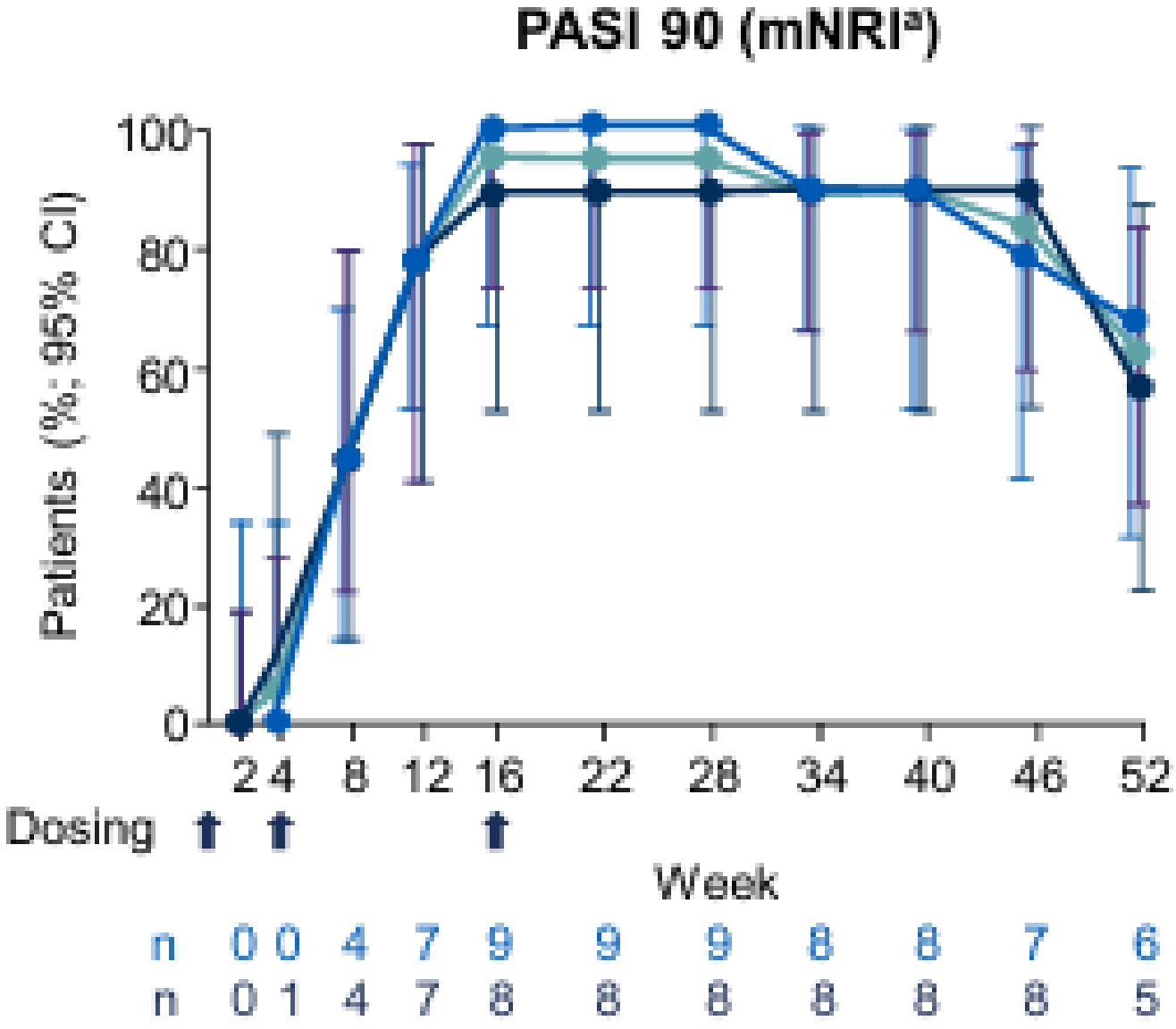
- T_{RM} cells are responsible for psoriasis recurrences and are dependent on IL-23 for their survival
- High-dose IL-23 inhibition early in the treatment course may be an effective strategy for inducing long-term remission by decreasing T_{RM} cell numbers in psoriasis skin lesions

Key eligibility criteria
- Age ≥18 years
- PASI score ≥12; BSA ≥10%
- Psoriasis diagnosis for ≥6 months
- No prior RZB use



T_{RM}, resident memory T cells

Blauvelt A, et al. AAD 2024, Late-breaking abstract; Blauvelt A, et al. WCD 2023, Late-breaking oral. Sponsored by AbbVie.


PASI 90 (mNRI[a])
Patients (%; 95% CI)
100
80
60
40
20
0
2 4 8 12 16 22 28 34 40 46 52
Dosing
Week
n 0 0 4 7 9 9 9 8 8 7 6
n 0 1 4 7 8 8 8 8 8 8 5

nature > nature communications > articles > article

Article | Open access | Published: 25 October 2024

The regulatory T cell-selective interleukin-2 receptor agonist rezpegaldesleukin in the treatment of inflammatory skin diseases: two randomized, double-blind, placebo-controlled phase 1b trials

The IL23R R381Q Gene Variant Protects against Immune-Mediated Diseases by Impairing IL-23-Induced Th17 Effector Response in Humans

Paola Di Meglio, Antonella Di Cesare, Ute Laggner, Chung-Ching Chu, Luca Napolitano, Federica Villanova, Isabella Tosi, Francesca Capon, Richard C. Trembath, Ketty Peris, Frank O. Nestle

Published: February 22, 2011 • https://doi.org/10.1371/journal.pone.0017160

- Terapia génica CRISPR

Novedades- Pipeline

Sonelokimab: IL17A/F nanobody. Fase 2b

ORKA-001: Anticuerpo monoclonal IL23p19

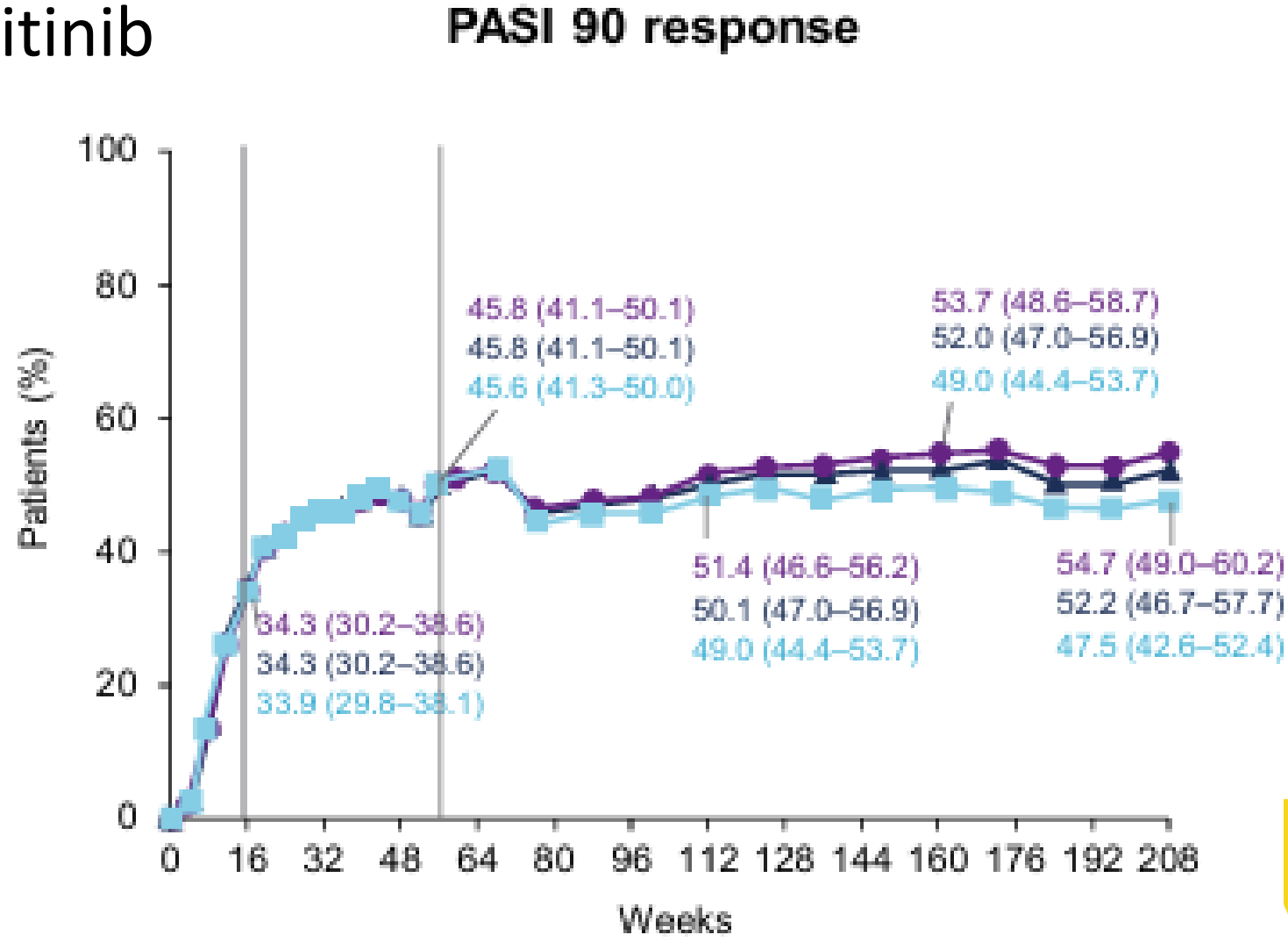
- En estudios en primates no humanos: semivida x3 risankizumab

Orales:

- Icotrokinra: IL 23 oral. Fase 3 adolescentes y adultos
- Zasocitinib TYK 2. Fase 2b
- LY4100511: IL 17 oral
- SAR441566: TNFR1 oral

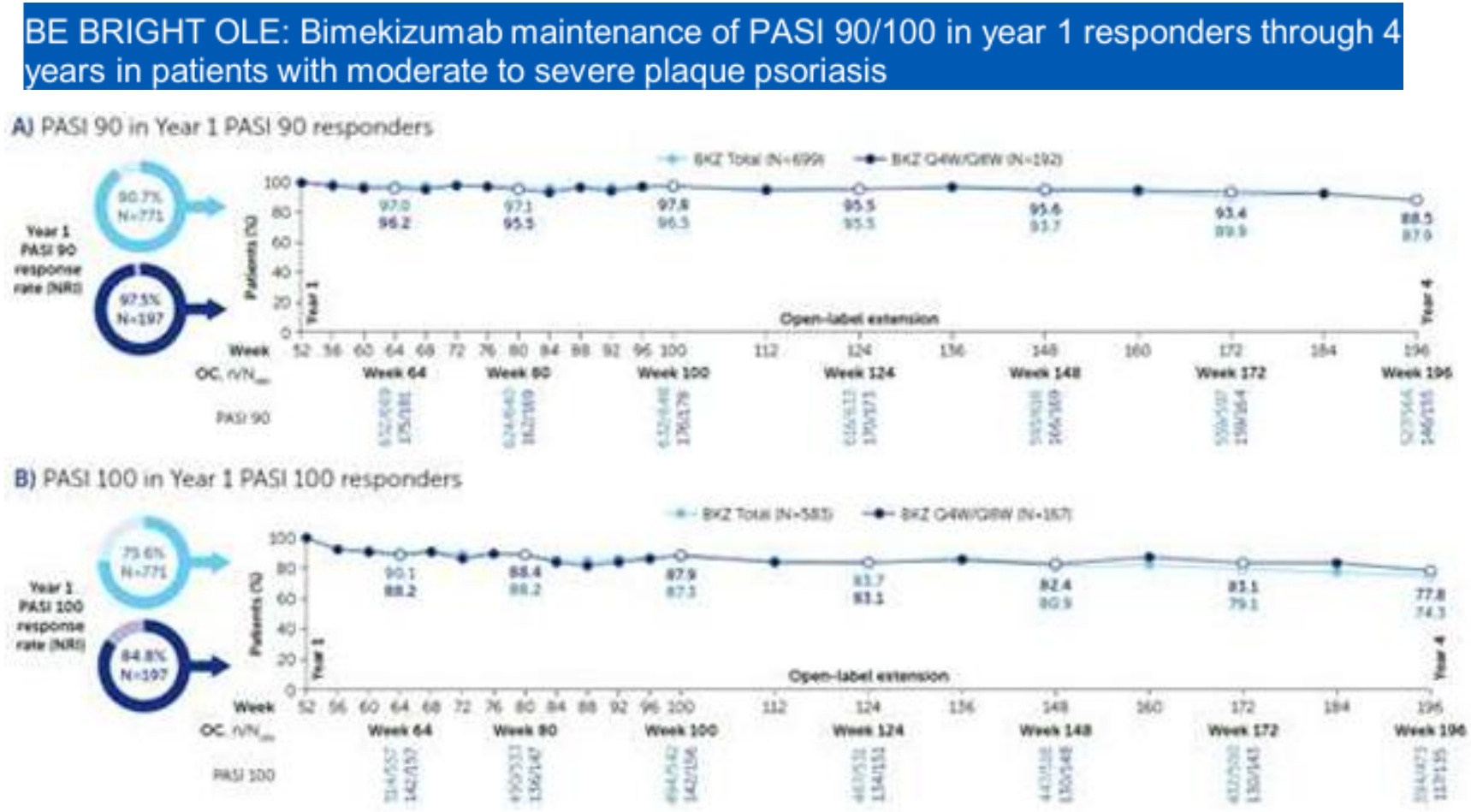
Novedades- Resultados a largo plazo

- Deucravacitinib



Novedades- Resultados a largo plazo

- Bimekizumab



Gordon B, et al. AAD 2024, P3805. Sponsored by UCB Pharma.

Summary of Newer Immunomodulatory Systemic Agents for Hard-to-Treat Psoriasis

	TNFα Inhibitors	IL-12/23 Inhibitor	IL-23 Inhibitors	IL-17 Inhibitors	Oral PDE-4 Inhibitor	Oral TYK2 Inhibitor	JAK Inhibitors	IL-36R Inhibitors
Inverse	++	++	+++	+++	++	++	?	---
Genital	++	++	+++	+++	++	++	?	---
Nail	++	+	++	+++	+	++	++	---
Generalized Pustular	+	+	++	++	---	---	---	+++

*Often Combination Therapy Required

Much of this is JMC opinion and reflects JMC practice.

Jeffrey M. Cohen, MD
Yale Dermatology

March 8, 2025

Nail psoriasis *Boni E. Elewski*

- Consider topical treatment or ILK for three or less affected psoriatic nails; more than 3 nails may require systemic therapy even without joint or skin involvement
- When using topical treatment for nail psoriasis- determine if disease is in nail bed or nail matrix

ROTATIONAL THERAPY

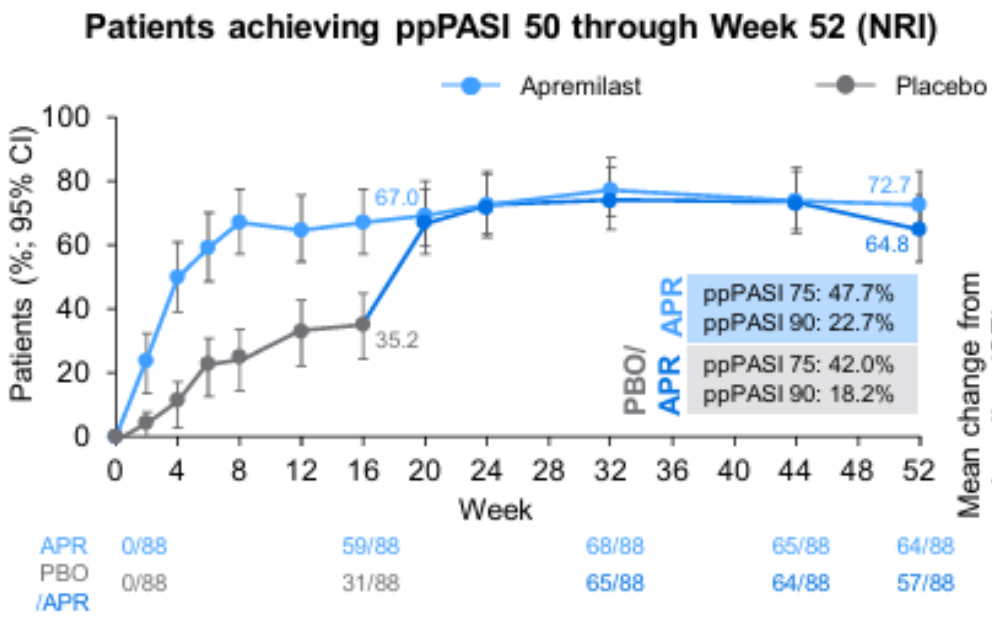
- 62 PATIENTS with 142 abnormal fingernails
- Vit D ointment weekdays and clobetasol gel or ointment on weekends each once daily
- 72% reduction in the hyperkeratosis at 6 months and 81% at 12 months
- No significant adverse events

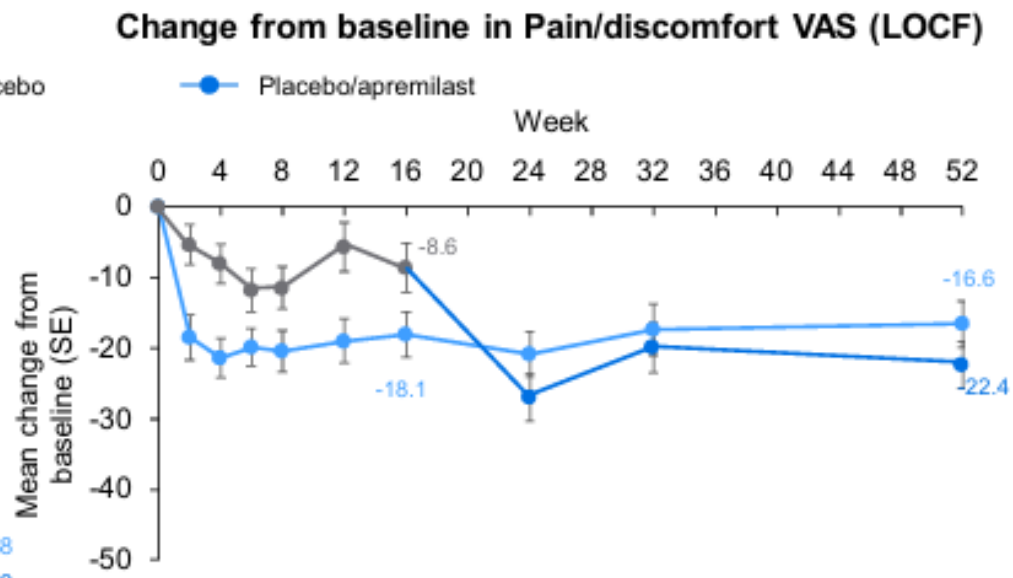
- Biologics and systemic agents that are used for PSA may be most effective in nail psoriasis and ixekizumab was the best treatment found in FOUR meta analysis for 100% improvement in nail disease

Pustulosis palmoplantar

Efficacy and Safety of Apremilast for the Treatment of Japanese Patients with Palmoplantar Pustulosis: Results from a Phase 2, Randomized, Placebo-Controlled Study

Phase 3 trial: Efficacy of apremilast for the treatment of Japanese patients with palmoplantar pustulosis through 52 weeks





Pustulosis palmoplantar

Clinical efficacy and safety of upadacitinib in the treatment of palmoplantar pustulosis: A single-center retrospective study

Yunhong Zheng[*], Xiaoxu Zhang[*], Huiping Wang, Runping Yang[1], Suju Luo

Front Med (Lausanne). 2024 Nov 6;11:1476793. doi: 10.3389/fmed.2024.1476793

Successful treatment of refractory palmoplantar pustulosis by upadacitinib: report of 28 patients

Na Du [1], Jingyi Yang [1,†], Yiwen Zhang [1], Xinyan Lv [1], Lei Cao [2,3,4,*,‡], Wei Min [1,*,‡]

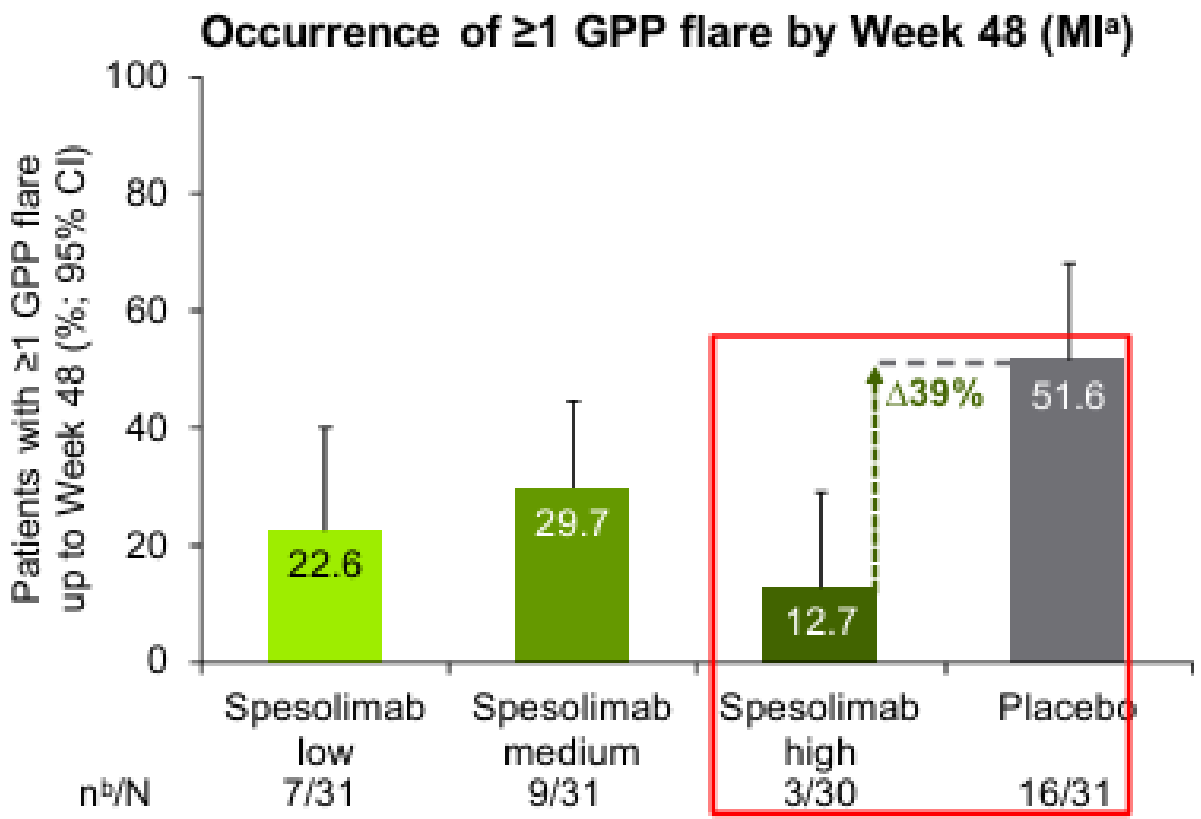
Infect Drug Resist. 2023 Aug 9;16:5165–5172. doi: 10.2147/IDR.S421299

Refractory Palmoplantar Pustulosis Successfully Treated with JAK Inhibitor Tofacitinib: A Case Series

Qingqing Xu [1], Xiaochen Wang [2], Anbo Yang [3,✉], Guo Wei [1]

Psoriasis pustulosa generalizada

Effisayil 2: Phase 2, randomized, dose-ranging trial of the IL-36 receptor antagonist spesolimab for preventing flares in patients with a history of GPP



High-dosage spesolimab was superior to placebo with a 39% delta in flare occurrence (95% CI −0.62, −0.16; P=0.0013)[c]

- Infection rates were similar across treatment arms; there were no deaths and no hypersensitivity reactions leading to discontinuation

Combining Systemic Therapies- Erin E. Boh

- ¿Cuándo? Siempre mejor monoterapia
  - Para tratar brotes, antes que cambiar tratamiento
  - Para tratar comorbilidades
  - Falta de respuesta en pacientes con fallo a múltiples tratamientos
- ¿Cómo?
  - Ninguna combinación aprobada
  - Diferentes mecanismos de acción y perfil de seguridad
  - Vida media larga + vida media corta
  - Reducir el riesgo de inmunogenicidad (MTX)

Combining Systemic Therapies- Erin E. Boh

- IL12/23 e IL23 +
  - Apremilast
  - MTX
  - Acitretino
  - JAKi
  - TYK2?
- IL17
  - Apremilast
  - MTX
  - Acitretino
  - JAKi (candidiasis)
  - TYK2?
- Anti TNF
  - Apremilast
  - MTX
  - Acitretino
  - TYK2?

* Ciclosporina <6 meses (brotes o puente previo a conseguir cambio de tratamiento)

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