AAD **ANNUAL** MEETING **2025**

AEDV 7 - 11 MARZO ORLANDO

highlights

Dermatitis atópica e Inmunoalergia Cutánea

Maria Sin Soler

Parc Taulí Hospital Universitari

Una iniciativa de:

ACADEMIA ESPAÑOLA DE DERMATOLOGÍA Y VENEREOLOGÍA

FUNDACIÓN AEDV PIEL SANA

ACADEMIA ESPAÑOLA DE DERMATOLOGÍA Y VENEREOLOGÍA

Con el patrocinio de:

ucb

AAD **ANNUAL** MEETING **2025**

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highlights

NO TENGO CONFLICTOS DE INTERÉS

AAD **ANNUAL** MEETING **2025**

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highlights

Atopic Dermatitis

Una iniciativa de:

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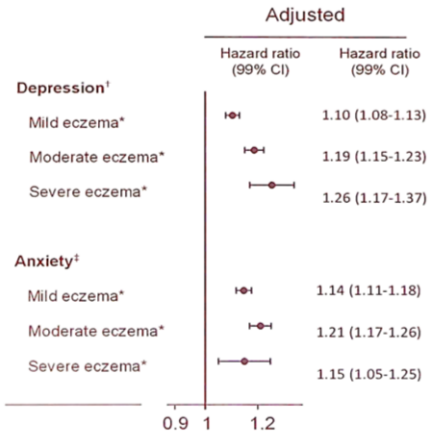
Con el patrocinio de:

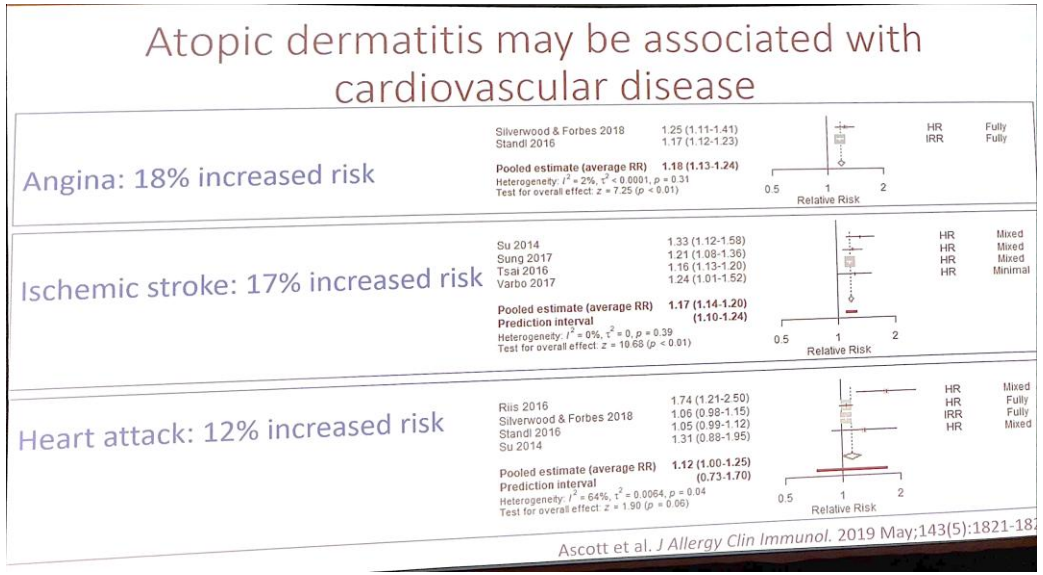
ucb

Comorbilidades en la dermatitis atópica

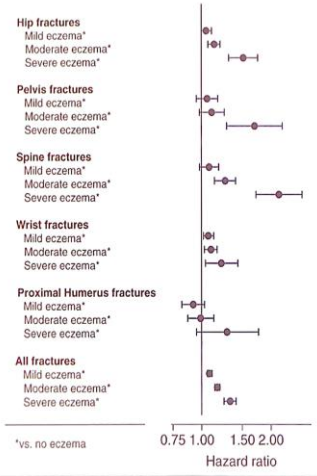
Atopic dermatitis is associated with depression and anxiety



Atopic dermatitis may be associated with cardiovascular disease

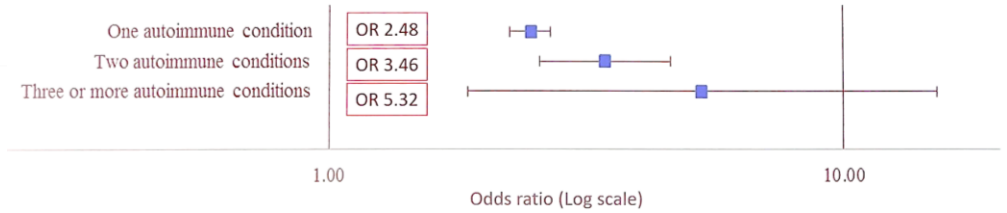


Atopic dermatitis is associated with bone fractures



Lowe et al. *J Allergy Clin Immunol.* 2020;145:563-571.

Atopic dermatitis is associated with autoimmune/inflammatory diseases

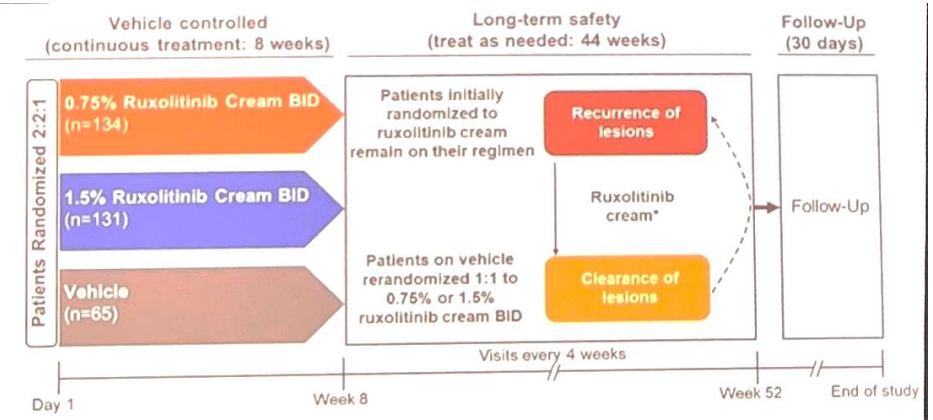


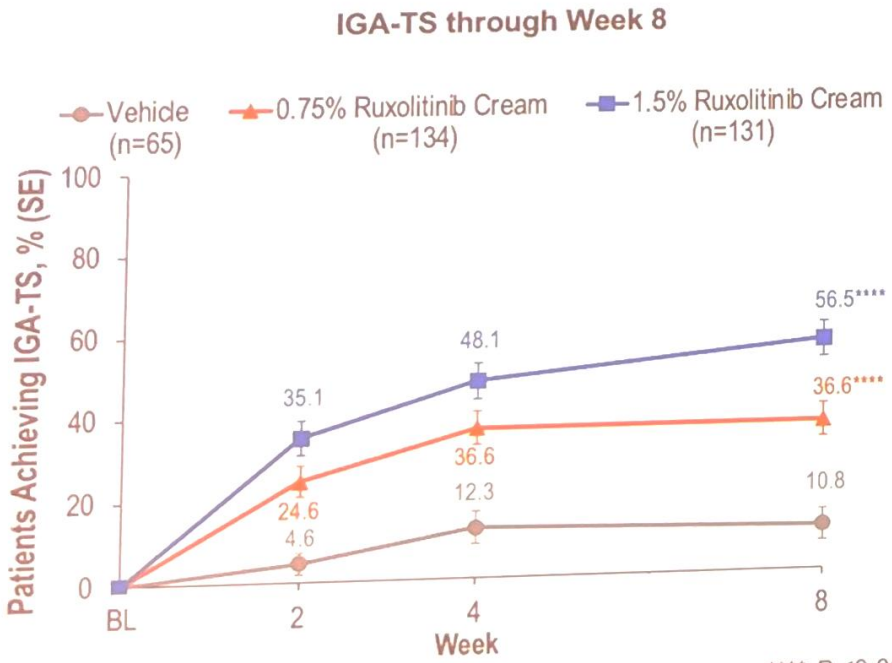
Andersen et al. *J Am Acad Dermatol.* 2017 Feb;76(2):274-280.

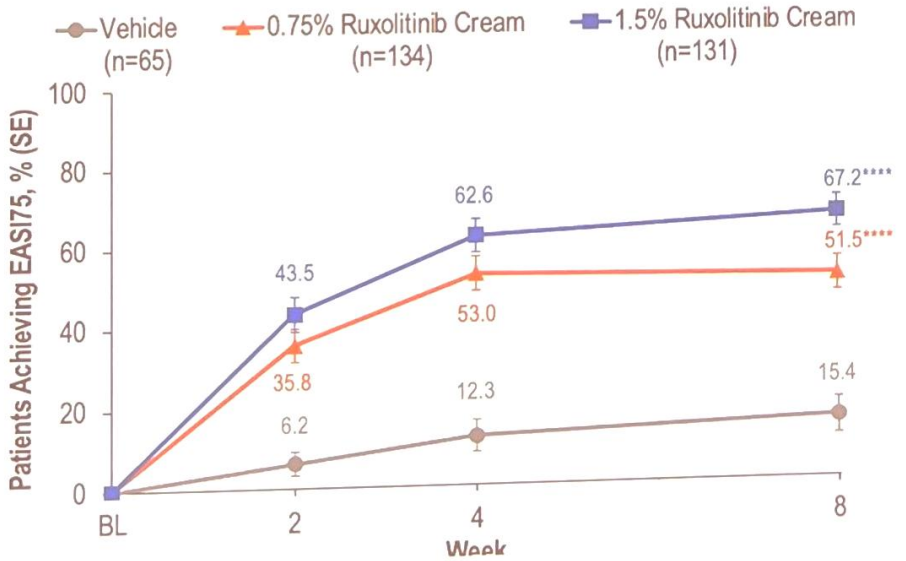
Tratamientos tópicos en dermatitis atópica

Topical Ruxolitinib 1.5%: 2 to 12 yr Atopic dermatitis

- Efficacy and safety very similar to adult data
- No SAE's; Low rates of discontinuation



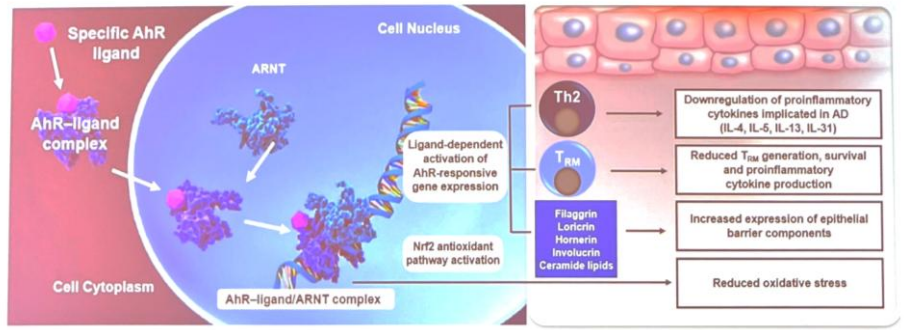




**** $P \leq 0.0001$ vs vehicle

Eichenfield L, et al. EADV 2023, D3T01.3L. Sponsored by Incyte Corporation.

Tapinarof: modulator of AhR- Proposed MOA



Tapinarof cream 1% once daily: Significant efficacy in the treatment of moderate to severe atopic dermatitis in adults and children down to 2 years of age in the pivotal phase 3 ADORING trials

Jonathan I. Silverberg, MD, PhD, MPH,[a] Lawrence F. Eichenfield, MD,[b] Adelaide A. Hebert, MD,[c] Eric L. Simpson, MD, MCR,[d] Linda Stein Gold, MD,[e] Robert Bissonnette, MD,[f] Kim A. Papp, MD, PhD,[g,h] John Browning, MD,[i] Pearl Kwong, MD, PhD,[j] Neil J. Korman, MD, PhD,[k] Philip M. Brown, MD, JD,[l] David S. Rubenstein, MD, PhD,[l] Stephen C. Piscitelli, PharmD,[l] Matthew C. Somerville, MS,[l] Anna M. Tallman, PharmD,[l] and Leon Kircik, MD[m,n]

Background: Tapinarof cream 1% once daily (QD), a topical aryl hydrocarbon receptor agonist, downregulates pro-inflammatory Th2 cytokines, upregulates skin-barrier components, and reduces oxidative stress.

Objective: To assess tapinarof efficacy and safety in adults and children down to 2 years of age with atopic dermatitis (AD).

Methods: Eight hundred and thirteen patients were randomized to tapinarof or vehicle QD in two 8-week phase 3 trials.

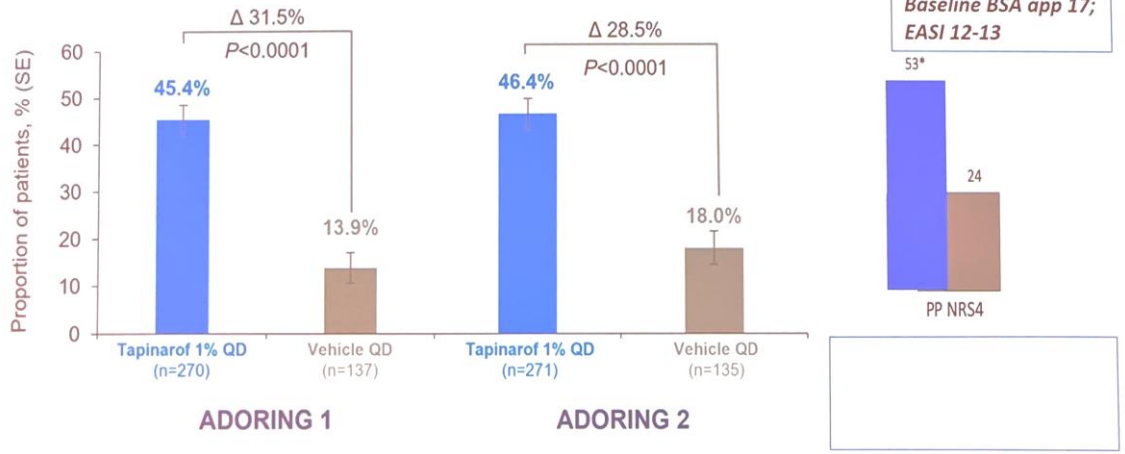
Results: The primary efficacy endpoint, Validated Investigator Global Assessment for Atopic Dermatitis score of 0 or 1 and ≥2-grade improvement from baseline at Week 8, was met with statistical significance in both trials: 45.4% versus 13.9% and 46.4% versus 18.0% (tapinarof vs vehicle; both $P < .0001$). Significantly superior Eczema Area and Severity Index 75 (EASI75) responses were also observed with tapinarof versus vehicle at Week 8: 55.8% versus 22.9% and 59.1% versus 21.2% (both $P < .0001$). Rapid improvements in patient-reported pruritus were also significant with tapinarof versus vehicle. Common adverse events (≥5%) of folliculitis, headache, and nasopharyngitis were mostly mild or moderate, with lower discontinuations due to adverse events in the tapinarof groups than with vehicle.

Silverberg JI, Eichenfield LF et al. J Am Acad Dermatol. 2024 Sep;91(3):457-465. doi: 10.1016/j.jaad.2024.05.023.

Tapinarof Week 8 responses: V-IGA and Itch
Qday application- Moderate to severe AD

- Aged ≥2 years
- vIGA-AD™ ≥3†
- EASI score ≥6
- BSA 5–35%

Baseline BSA app 17; EASI 12-13

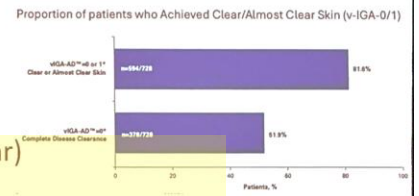


Silverberg JI, Eichenfield LF et al. J Am Acad Dermatol. 2024 Sep;91(3):457-465
Simpson EL et al. Dermatol Ther 2025 Jan:15:111-124

Tapinarof Cream 1%: >8 weeks
48 week extension study

Open-label extension: ADORING 3 ((from ADORING 1 and 2 and MUPK +76
Direct enroll (2-17 yrs)

- Diverse population (47% non-white); 2 to 81 years
- CLEAR (v-IGA=0): ***51.9%***



- 81.6%: (vIGA-AD™) scale score of 0 (clear) or 1 (almost clear)
- 80.7% (574/711): at EASI-75% or greater improvement
- 92.3% (656/711): achieved at least a 1-grade improvement in vIGA-AD score
- No new safety signals with good toleration data

Bissonnette R et al. AAD 2024 Poster
Bissonette R, Stein-Gold L et al. Skin J of Cut Med. 2024;Nov 8:6

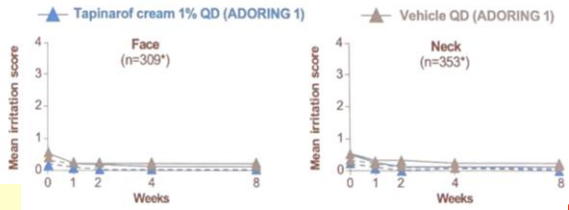
Tapinarof Cream 1% for AD: Tolerability? Safety?

Assessed in Core Phase 3 ADORING 1 and 2 trials

- At Week 8, mean local tolerability scores for tapinarof cream versus vehicle
  - 0.2–0.4 vs 0.7–0.8 for burning/stinging; 0.6–0.8 vs 1.1–1.1 for itching

- Trial discontinuation rates due to TEAEs: lower with tapinarof versus vehicle (ADORING 1: 1.9% vs 3.6%; ADORING 2: 1.5% vs 3.0%)

Contact dermatitis: 1.1% tapinarof vs 1.5% vehicle
Follicular event: 8.9% tapinarof vs 1.5% vehicle
Headache: 1.5% tapinarof vs 0% vehicle



No to minimal irritation in sensitive skin areas;
Improvement vs baseline scores

Silverberg JI, Eichenfield LF et al. J Am Acad Dermatol. 2024 Sep;91(3):457-465.
Simpson EL et al. Poster; AAD Mar 8-12, 2024

ROFLUMILAST CREAM: Novel PDE-4 inhibitor

Psoriasis: Initially approved 0.3% cream; Now6+ years
Seborrheic Dermatitis: 0.3% Foam: Approved: 9+ yrs

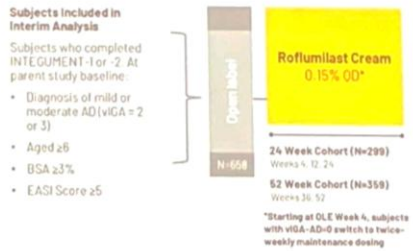
Atopic Dermatitis: 0.15% cream: Approved 6 years+

ROFLUMILAST 0.15% cream

Ages 6+: 0.15% Cream: 4 week, QD application

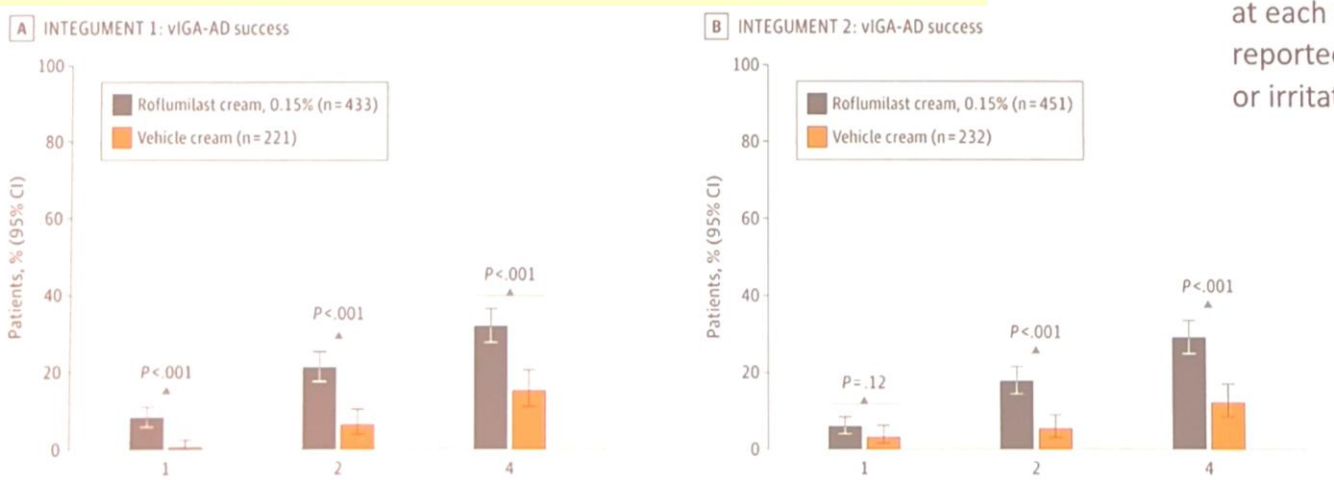
Met primary end points in AD patients

- 1337 patients; Mean BSA=13.6%
- App 30% Clear/almost +2 step vs. 12-15% vehicle
- App 42-43% EASI 75 response vs. 20-22% vehicle



Low TEAEs

- >95% of patients at each time point reported ***no signs*** or irritation



Simpson EL, Eichenfield LF et al. Roflumilast Cream, 0.15%, for Atopic Dermatitis in Adults and Children: INTEGUMENT-1 and INTEGUMENT-2 Randomized Clinical Trials. JAMA Dermatol. 2024 Nov 1;160(11):1161-1170

Dermatitis®
Vol 0 Iss 0, January 10, 2025

https://doi.org/10.1089/derm.2024.0418

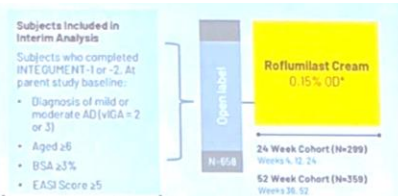
Mary Ann Liebert, Inc. publishers

Long-Term Safety and Efficacy with Roflumilast Cream 0.15% in Patients Aged ≥6 Years with Atopic Dermatitis: A Phase 3 Open-Label Extension Trial

Eric L. Simpson[a], Lawrence F. Eichenfield[b], Kim A. Papp[c,d], Seth B. Forman[e], Adelaide A. Hebert[f], Mercedes E. Gonzalez[g], Melinda J. Gooderham[h], H. Chih-ho Hong[i], Vimal H. Prajapati[j], Emma Guttman-Yassky[k], Jonathan I. Silverberg[l], Melissa S. Seal[m], David Krupa[m], Erin Almaraz[m], Diane Hanna[m], Patrick Burnett[m], Scott Snyder[m], David H. Chu[m], Robert C. Higham[m], and David R. Berk[m]

ROFLUMILAST 0.15% Cream for AD 6 +years

Extension study



- Open-label trial Daily application for up to 56 weeks (as part of study ages 2+)
- Two cohorts: 24 wks or 52 weeks: Subjects had to complete prior 4 wk trial with TEAE or SAE that precluded further treatment

Novel method: If clear, went to 2x/week (BIW) proactive application to areas most commonly and/or recently affected by AD

- If worsened on BIW, called center and did QD application

RESULTS:

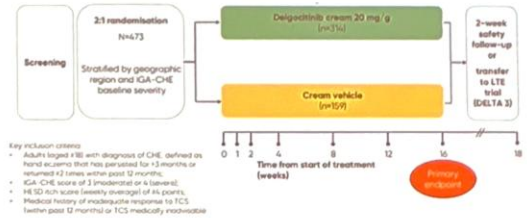
- **2/3** of these participants remained on twice weekly schedule **for > 50%** of the study time;
- Maintained clear/almost clear for a median of 281 days)

Simpson EL, Eichenfield LF et al. Dermatitis;2025 Jan 10. doi: 10.1089/derm.2024.0418

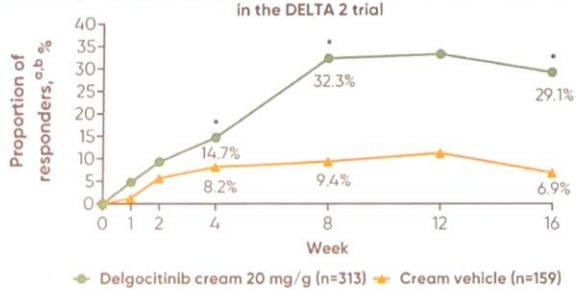
Delogocitinib: Development update: Chronic Hand Eczema

- Delgocitinib: novel topical pan-JAK inhibitor (20 mg/g) cream
- Delta 1 and 2 pivotal Phase 3 trials: Showed improvement in primary and all key secondary efficacy endpoints
- Extension trial (2 wk safety; 36 week on label)

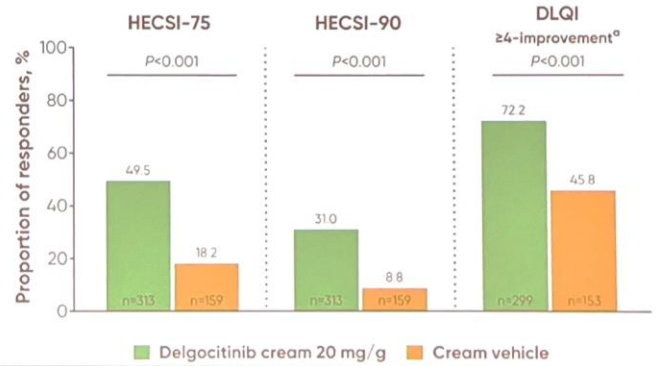
Tough primary endpoint: IGA-CHE treatment success defined as of 0/1 [clear/almost clear:, no/barely perceptible erythema and no other signs]

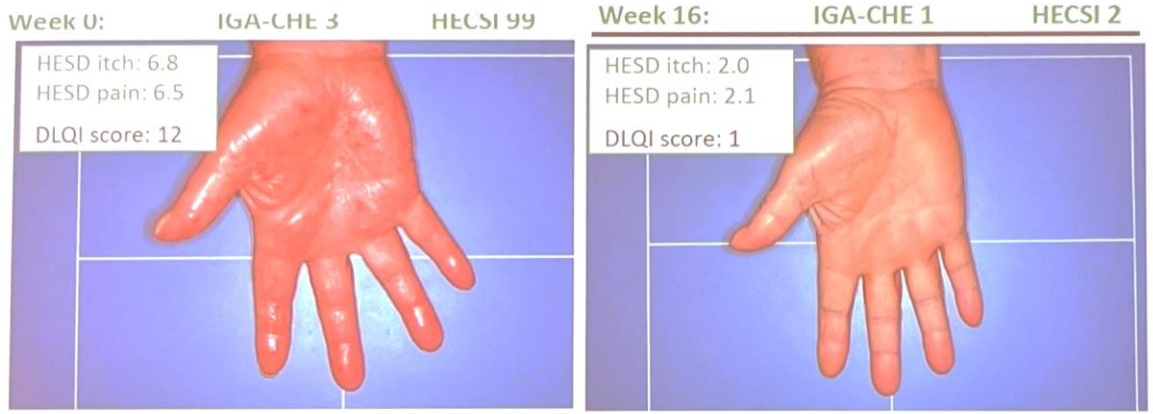


Proportion of patients achieving IGA-CHE treatment success from baseline to Week 16 in the DELTA 2 trial



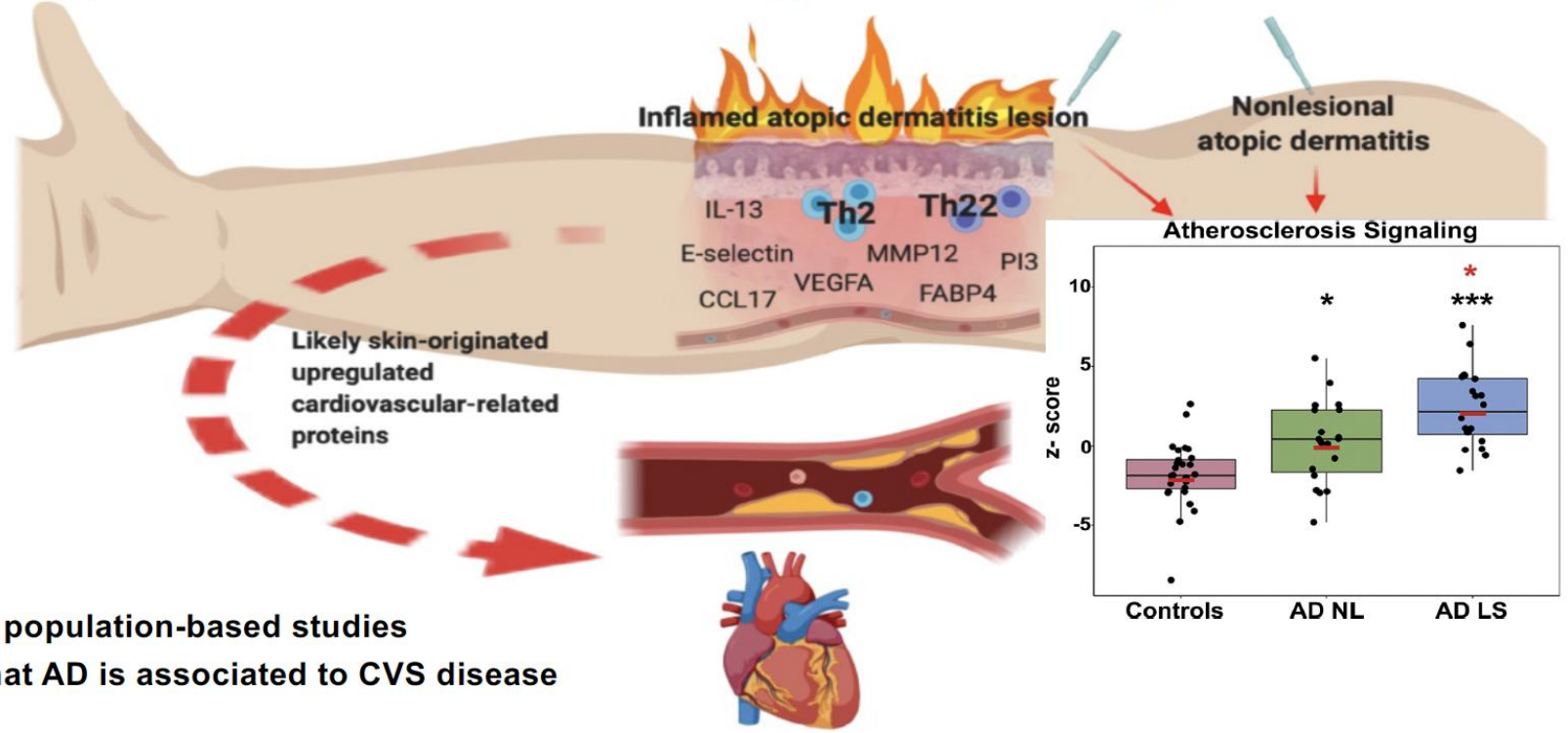
Proportion of patients achieving HECSI-75, HECSI-90, and ≥4-point DLQI improvement from baseline at Week 16 in the DELTA 2 trial





Tratamientos sistémicos en adultos

Inflammation is More than Skin Deep: Atopic Dermatitis Emerges As a Systemic Disease

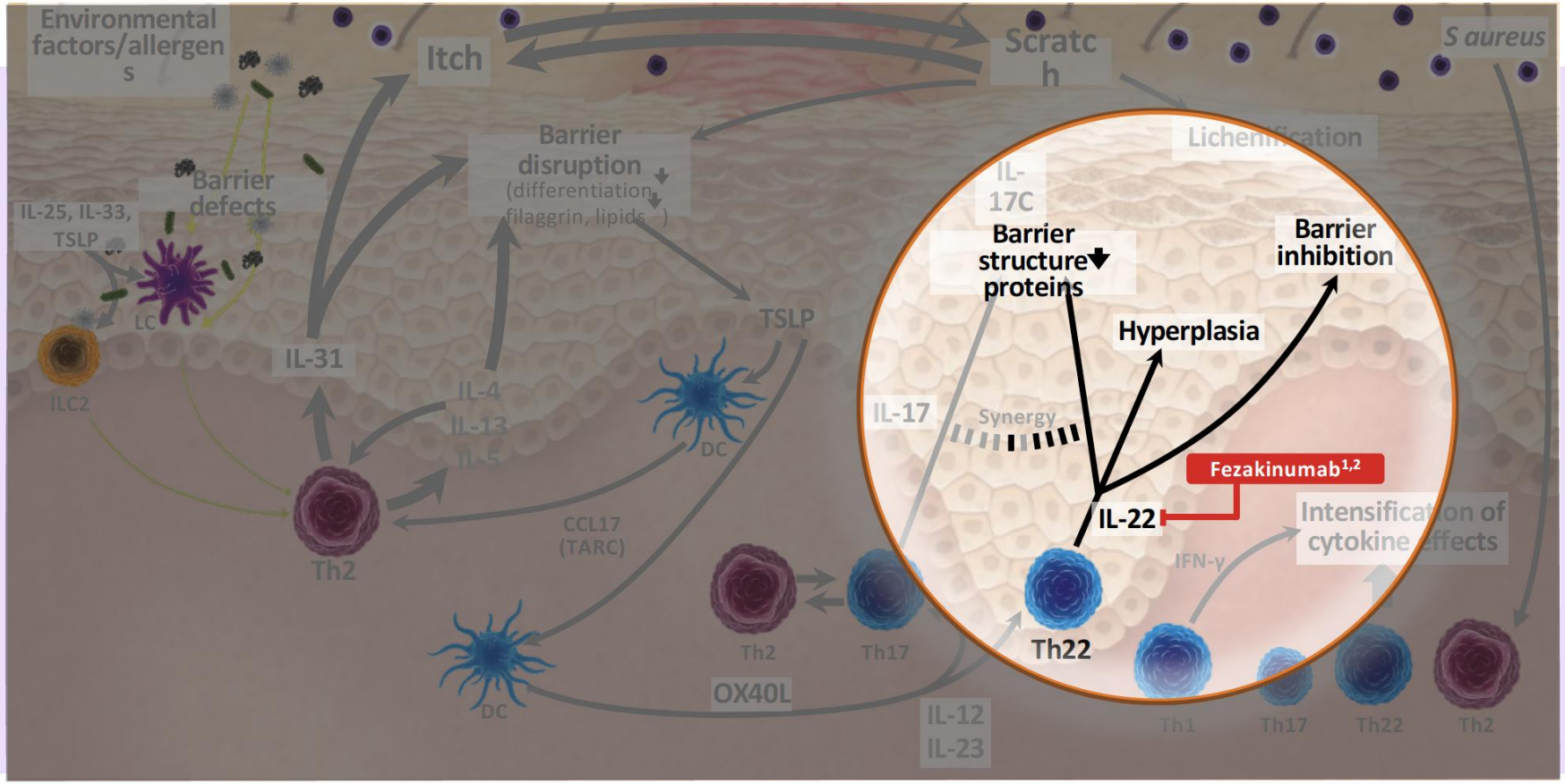


- **Several population-based studies showed that AD is associated to CVS disease**

Implications for systemic treatment in patients with AD involving ≥10% BSA

Pavel AB…and Guttman-Yassky E. J Am Acad Dermatol. 2020; Czarnowicki T….and Guttman-Yassky E..: J Allergy Clin Immunol. 2015 Jul;136(1):208-11; Ungar B….and Guttman-Yassky E et al.: J Invest Dermatol 2016; Brunner PM…Guttman-Yassky E. Sci Reports 2017. Silverberg JI Allergy 2015 70: 1300–1308

FEZAKINUMAB TARGETS IL-22[1,2]



- Note: fezakinumab is not licensed.
- 1. Nygaard U, et al. *Dermatology*. 2017;233(5):344-357. 2. ClinicalTrials.gov. Randomized placebo controlled study to determine safety, pharmacodynamics, and efficacy of ILV-094 in atopic dermatitis. https://clinicaltrials.gov/ct2/show/NCT01941537. Accessed March 20, 2018.

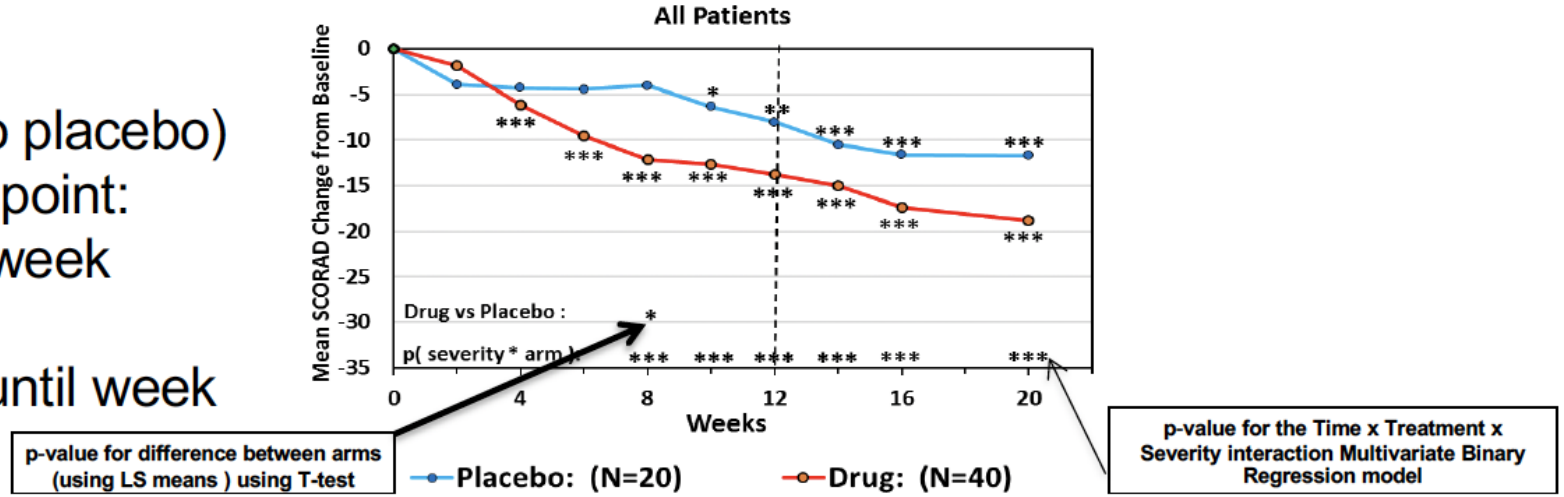
A monotherapy study with ILV-094/anti-IL-22 in AD

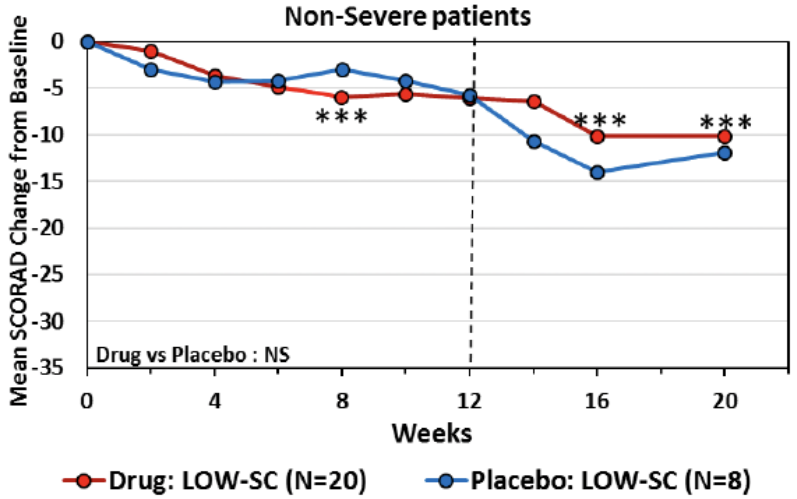
Methods:

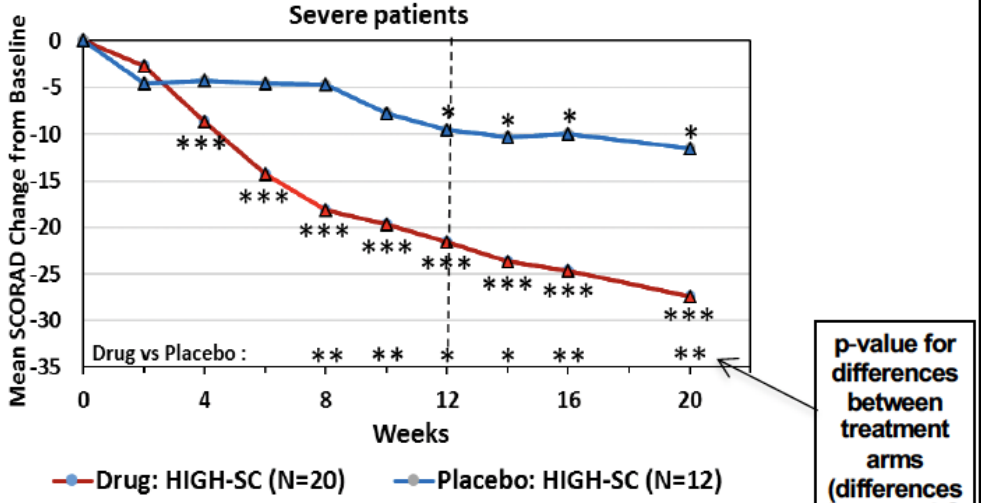
N=60 (2:1 to placebo)

Primary endpoint: week 12, 8 week follow up

6 IV doses until week 10







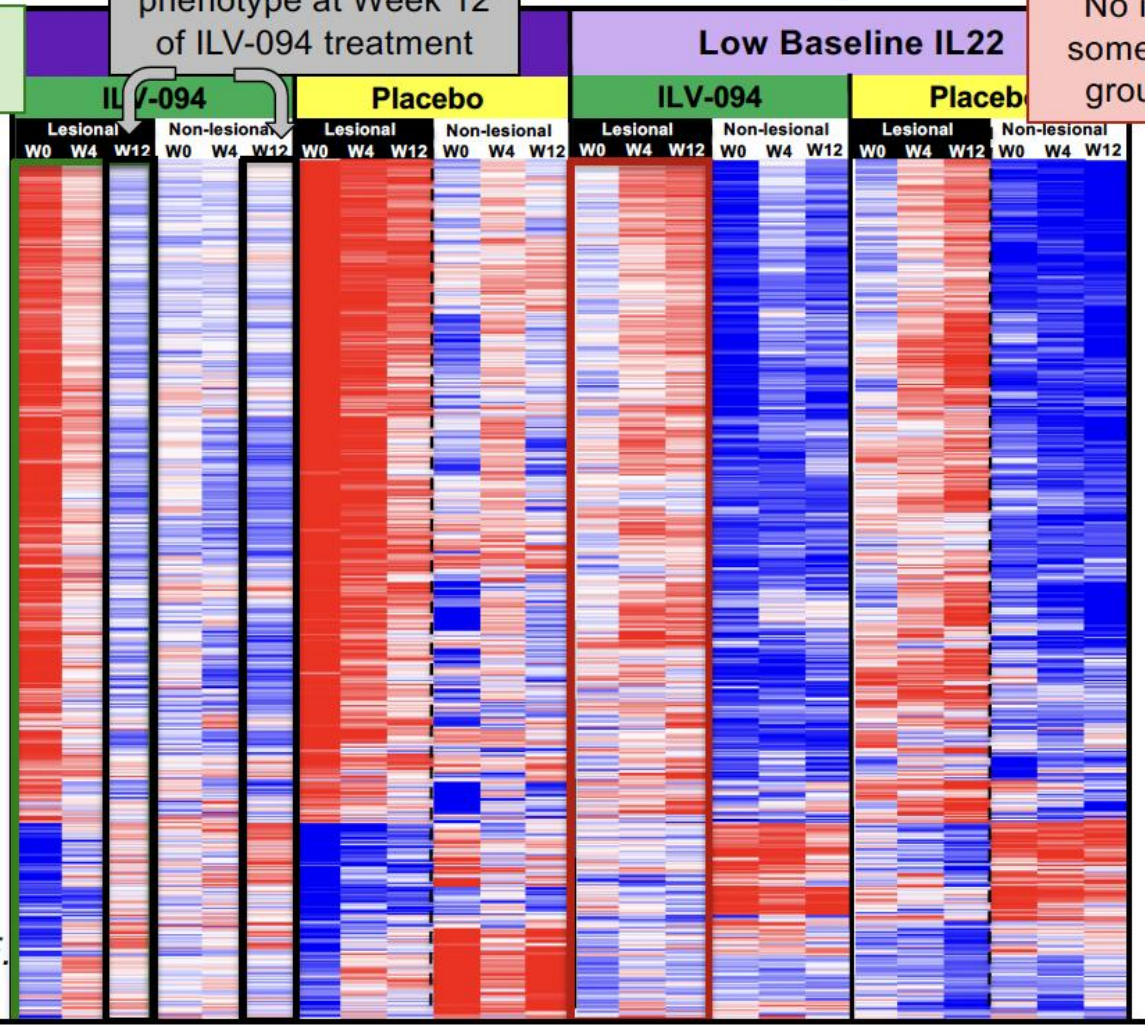
Guttman-Yassky E el. JAAD January 2018

Higher M… …ponse in Patients with Increa… …e IL22 Expression

Larger improvement in the high IL-22 group

The LS phenotype of the high IL-22 group approaches the NL phenotype at Week 12 of ILV-094 treatment

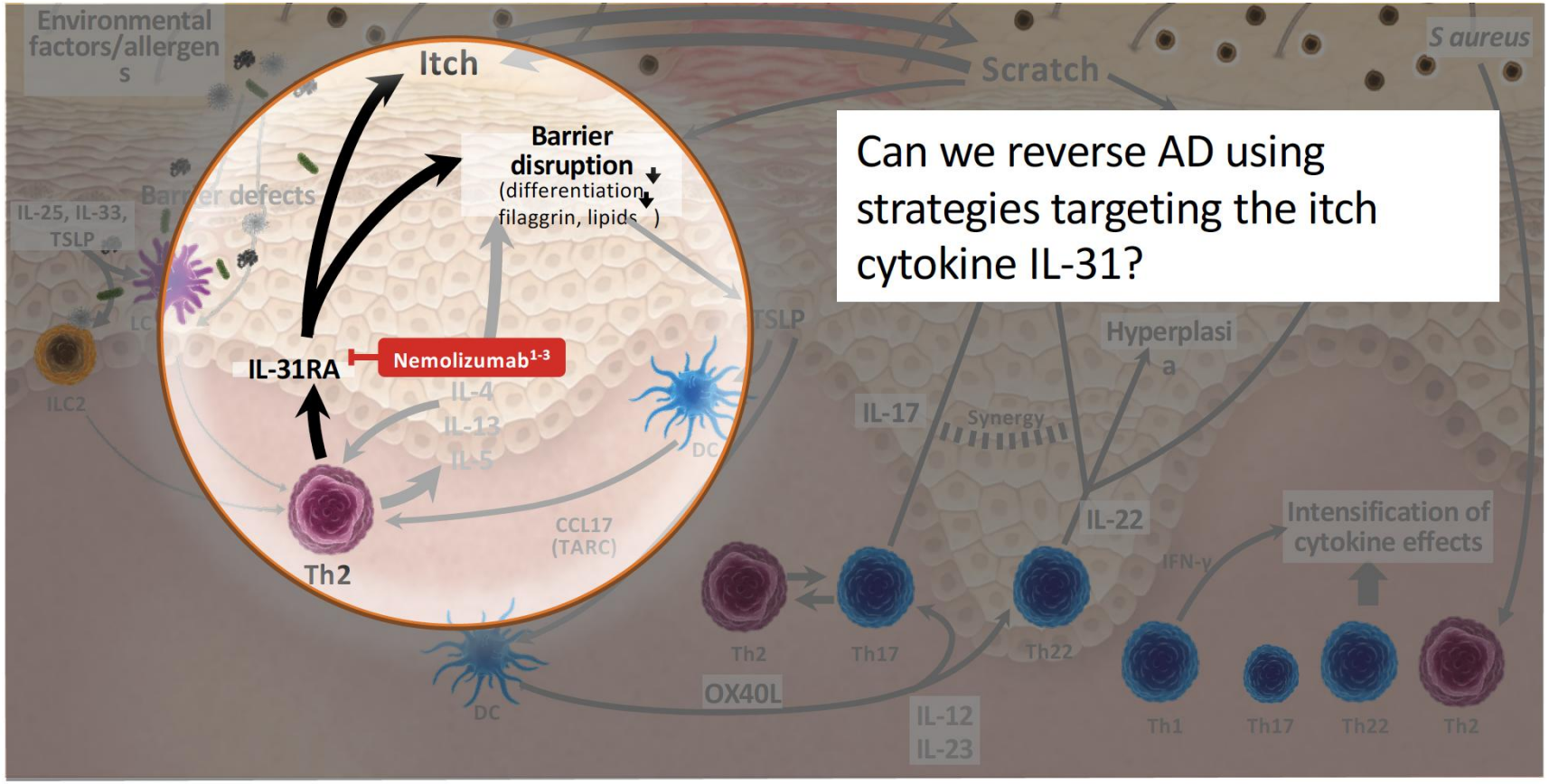
No improvement and even some worsening in low IL-22 group treated with ILV-094



FDR<0.05, |FCH|>2

Brunner P….Guttman-Yassky E. JACI August 2018

NEMOLIZUMAB TARGETS IL-31

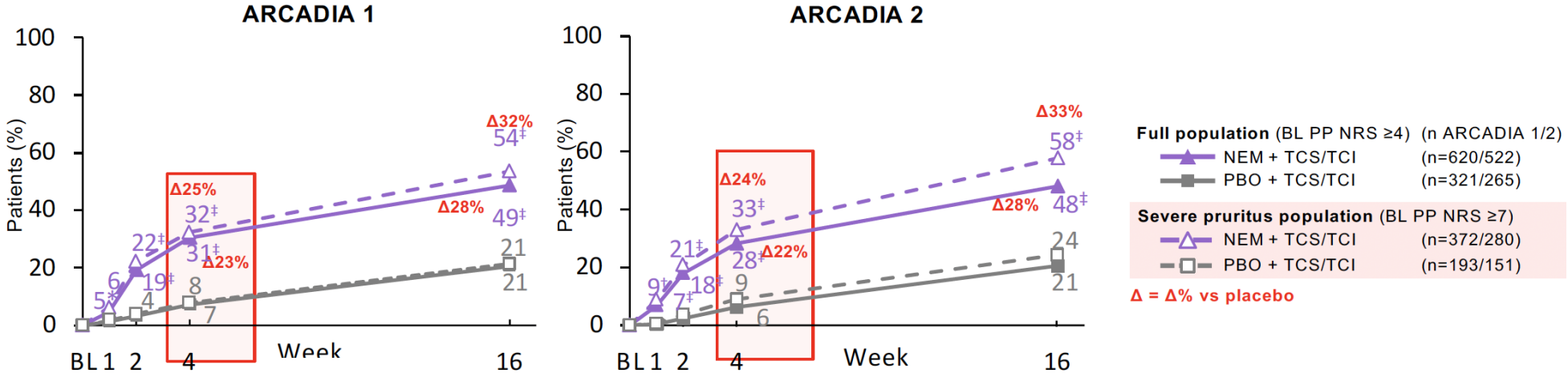


Can we reverse AD using strategies targeting the itch cytokine IL-31?

1. Paller AS, et al. *J Allergy Clin Immunol*. 2017;140(3):633-643. 2. ClinicalTrials.gov. Dose-ranging study of nemolizumab in atopic dermatitis. https://clinicaltrials.gov/ct2/show/NCT
Accessed March 20, 2018. 3. Adis Insight. Nemolizumab – Chugai Pharmaceutical. https://adisinsight.springer.com/drugs/800036524. Accessed July 2018.

ARCADIA 1 and 2: Effect of nemolizumab with concomitant TCS/TCI on pruritus among adults and adolescents with moderate to severe AD

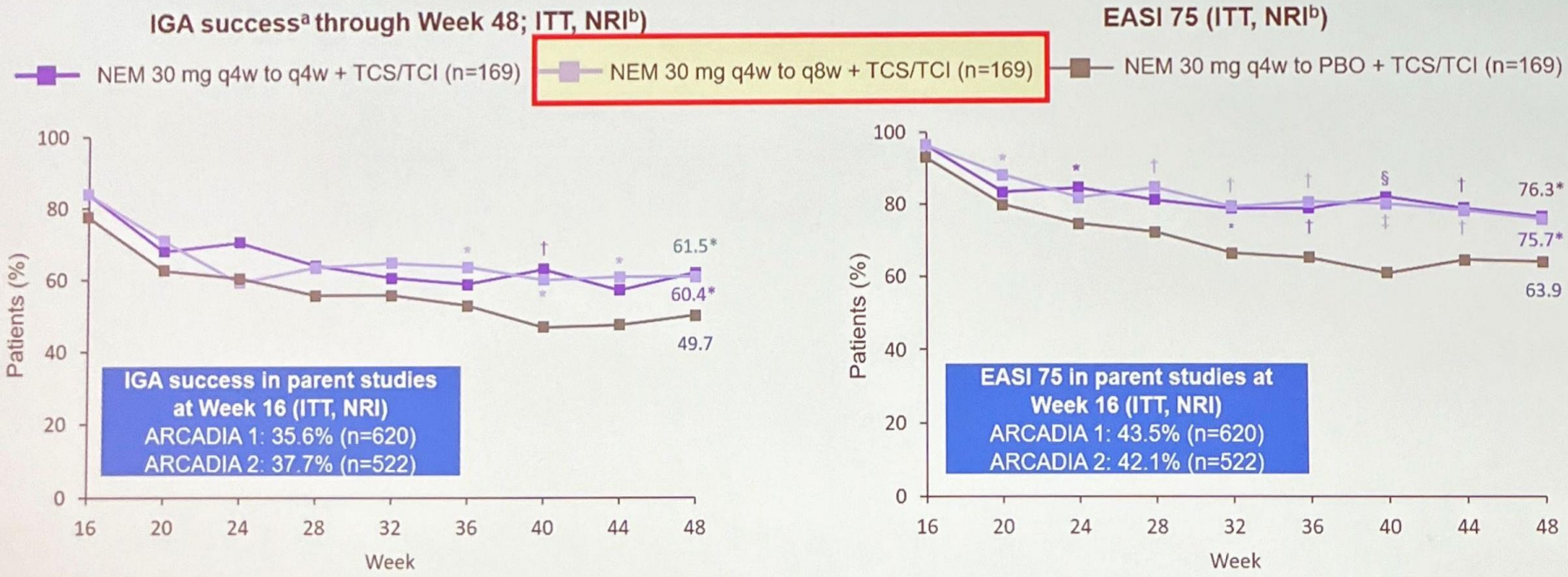
Key secondary endpoint: ≥4-point improvement in PP NRS score[a] (ITT, MI MAR[b])



- Highly statistically significant endpoints with nemolizumab
- Slightly more effective for itch in the severe pruritus at baseline population
- Good clinical improvement in lesional severity
- Nemolizumab appears to be more effective in these two Phase 3 studies than in the Japanese Phase 3 studies

- *P≤0.01; †P≤0.001; ‡P≤0.0001 vs respective placebo + TCS/TCI; MAR, missing at random; [a]Weekly PP NRS calculated using data of 7 consecutive days and set to missing if data for <4 days available; [b]Patients receiving rescue therapy were considered treatment failures; Strata adjusted P-values are presented derived from a CMH test adjusting for randomized stratification variables (full population: IGA and PP NRS [≥7/<7]. Baseline PP NRS ≥7 population: IGA only)
- Silverberg JI, et al. EADV 2023, D1T01.1C. Sponsored by Galderma

ARCADIA 1 and 2: Maintenance of IGA success and EASI 75 to Week 48

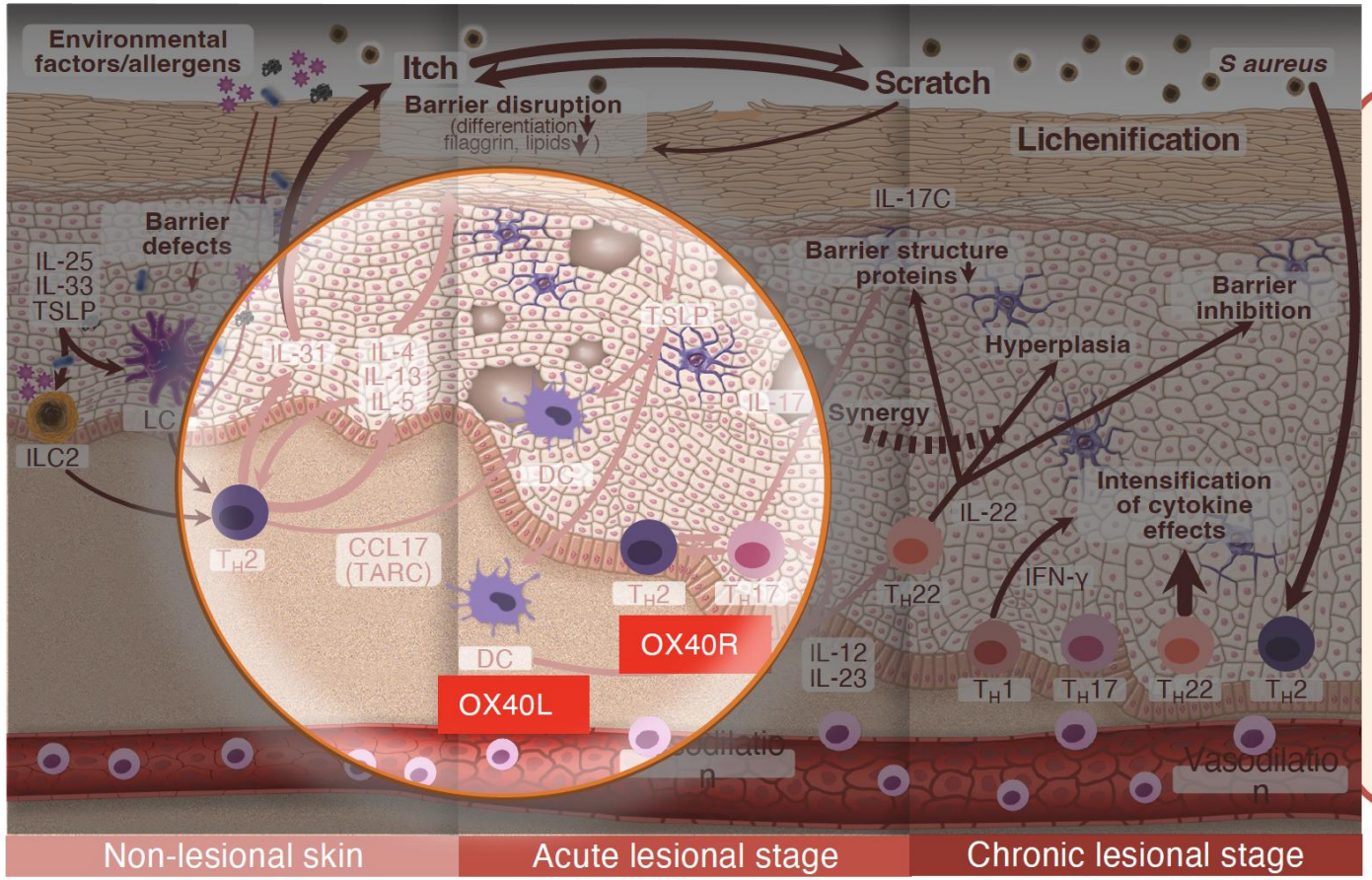


Silverberg JI, et al. AAD 2024, Late-breaking abstract.

Safety: Overall summary of treatment-emergent adverse events

	ARCADIA 1		ARCADIA 2	
	Nemolizumab§ + TCS/TCI *N*=616	Placebo + TCS/TCI *N*=321	Nemolizumab§ + TCS/TCI *N*=519	Placebo + TCS/TCI *N*=263
AEs or SAEs, *n* (%)				
Any TEAE	306 (49.7)	146 (45.5)	215 (41.4)	117 (44.5)
Any serious TEAE	6 (1.0)	4 (1.2)	13 (2.5)	3 (1.1)
Any serious TEAE related to study drug	0	0	5 (1.0)	0
Any TEAE leading to study discontinuation, *n* (%)	9 (1.5)	3 (0.9)	15 (2.9)	3 (1.1)
Any TEAE leading to death, *n* (%)	0	0	0	0
Any severe TEAE, *n* (%)	18 (2.9)	8 (2.5)	21 (4.0)	7 (2.7)
AESI, *n* (%)	56 (9.1)	20 (6.2)	47 (9.1)	21 (8.0)
Elevated ALT or AST (>3xULN) in combination with elevated bilirubin (>2xULN)	0	0	0	0
Infections	20 (3.2)	10 (3.1)	20 (3.9)	12 (4.6)
Injection-related reactions	1 (0.2)	0	0	0
Peripheral edema: limbs, bilateral; facial edema	7 (1.1)	1 (0.3)	12 (2.3)	1 (0.4)
Worsening of asthma (post-adjudication by IAC)	32 (5.2)	13 (4.0)	7 (1.3)	6 (2.3)
TEAEs ≥5% (MedDRA Preferred Term), *n* (%)				
Asthma	33 (5.4)	13 (4.0)	11 (2.1)	7 (2.7)
Dermatitis atopic	75 (12.2)	34 (10.6)	37 (7.1)	15 (5.7)

OX40R/OX40L: A new pathway to explore in AD



- The OX40 receptor is primarily expressed by activated T cells and binds OX40L on APCs
- Rocatinlimab is a fully human, anti-OX40 monoclonal antibody
- Amlitelimab targets OX40L on dendritic cells and other cells

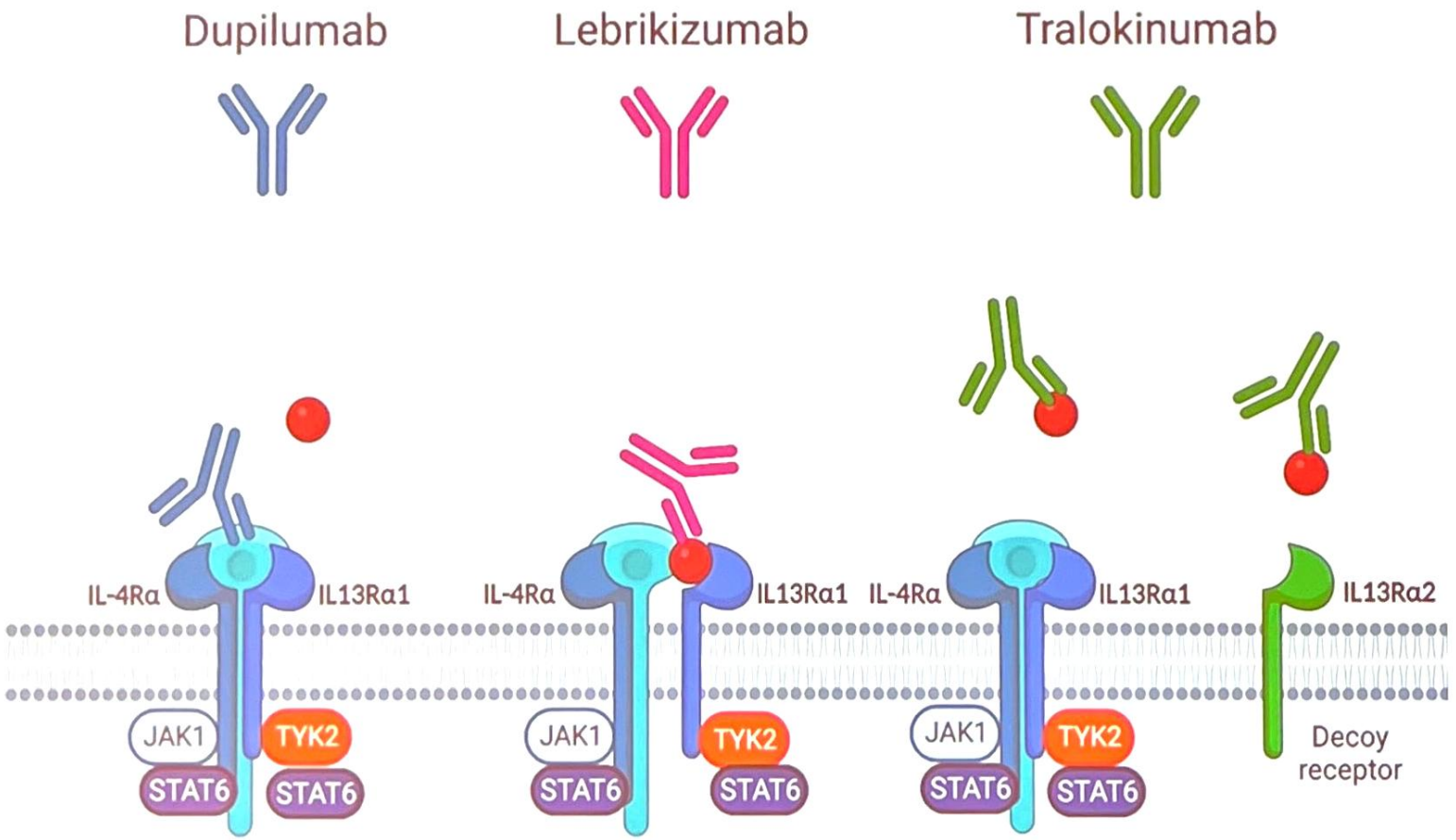
1. Guttman-Yassky E, et al. Lancet 2023;401:204–214; 2. Guttman-Yassky E, et al. J Allergy Clin Immunol 2019;144:482–493; 3. Nakagawa H, et al. J Dermatol Sci 2020;99:82–89; 4. Furue M, et al. J Clin Med 2021;10:2578.

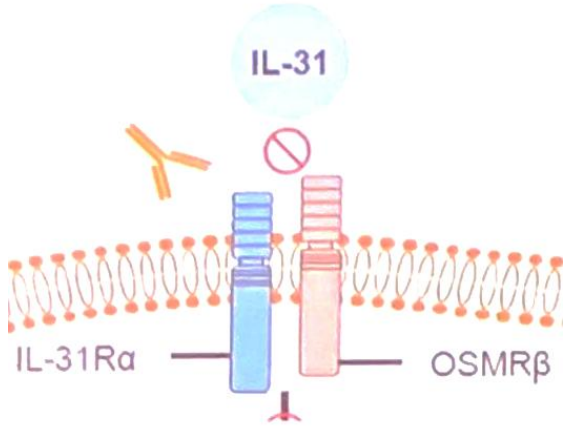
Tratamientos sistémicos en edad pediátrica

6 meses	12 años	12 años	12 años

Nemolizumab

* Japón 6a





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Prurigo Nodularis

Director: Shawn Kwatra, MD, FAAD

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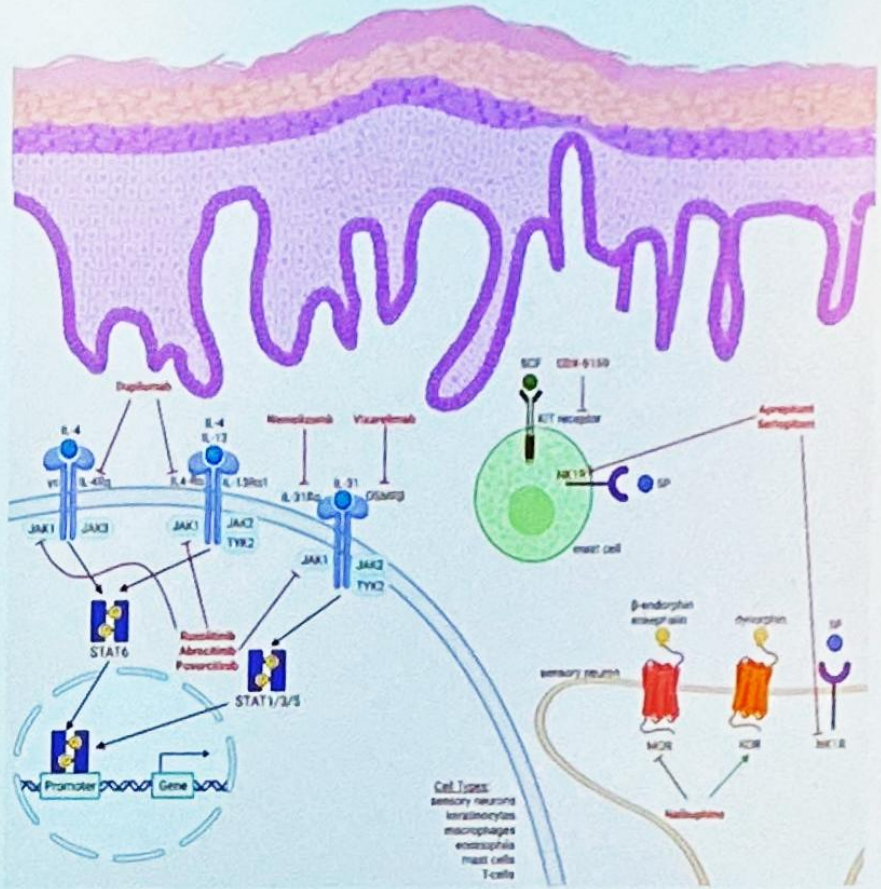
Emerging Therapies in PN

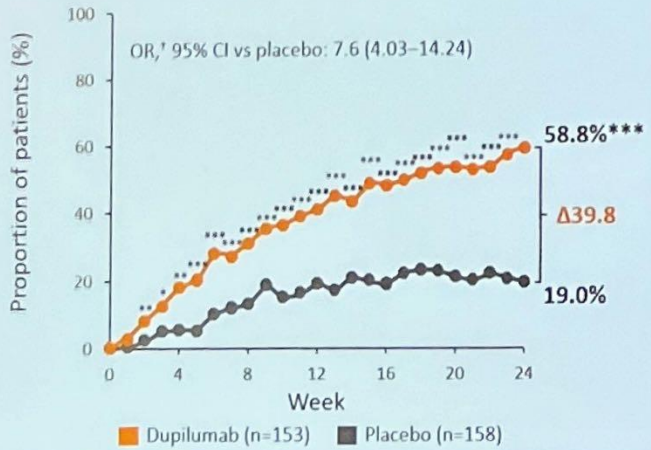
	Candidate	Pre-clinical	Phase 1	Phase 2	Phase 3	Approved
Biologic Drugs	Dupilumab					✓
	Nemolizumab					✓
	Vixarelimab					
	Barzolvolimab					
JAK Inhibitors	Ruxolitinib					
	Abrocitinib					
	Povorcitinib					
Opioid Receptor Antagonist	Nalbuphine					
NK1R Antagonists	Aprepitant				✗	
	Serlopitant					✗



Comparison Between Dupilumab and Nemolizumab for PN

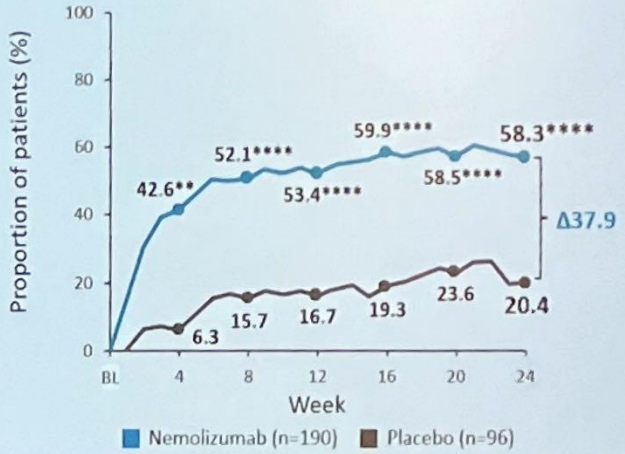
PRIME/PRIME2[1] (pooled data)

≥4-point improvement in WI-NRS



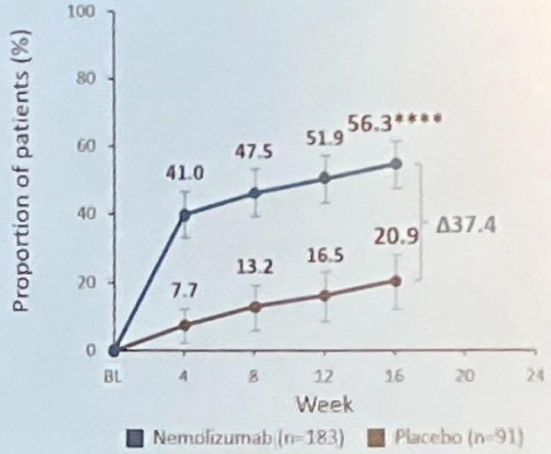
OLYMPIA1[2]

≥4-point improvement in PP-NRS



OLYMPIA2[3]

≥4-point improvement in PP-NRS

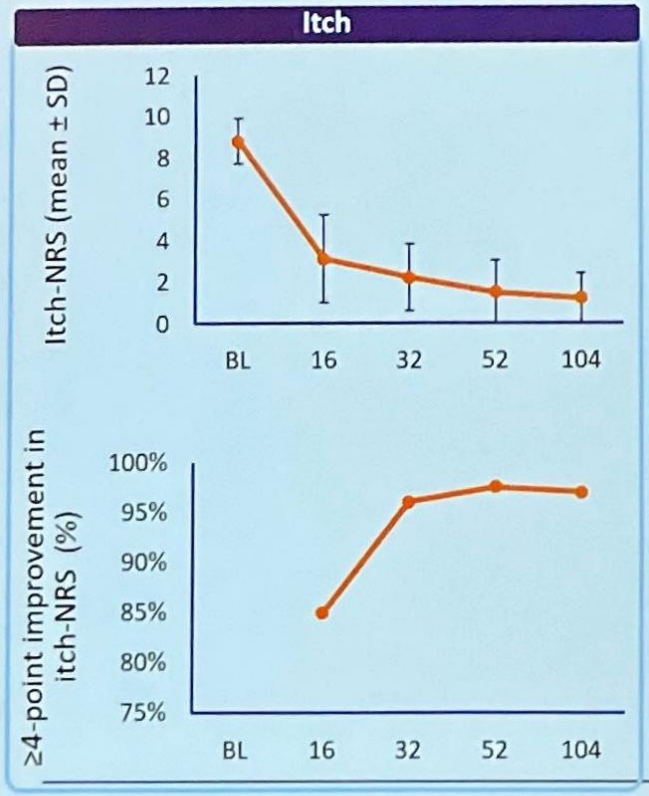


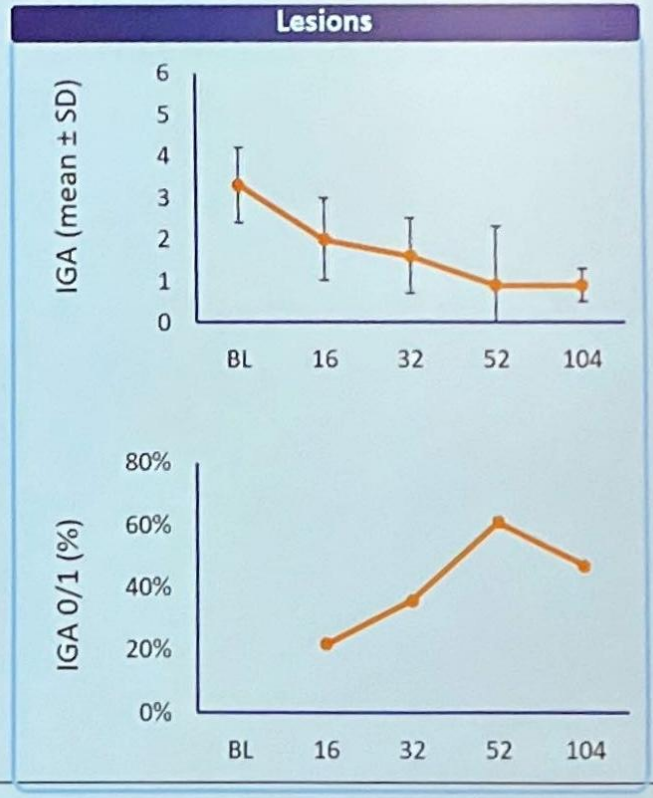
Direct comparison between dupilumab and nemolizumab (and their respective trials) is not possible due to differences in study design, study populations, and study endpoints

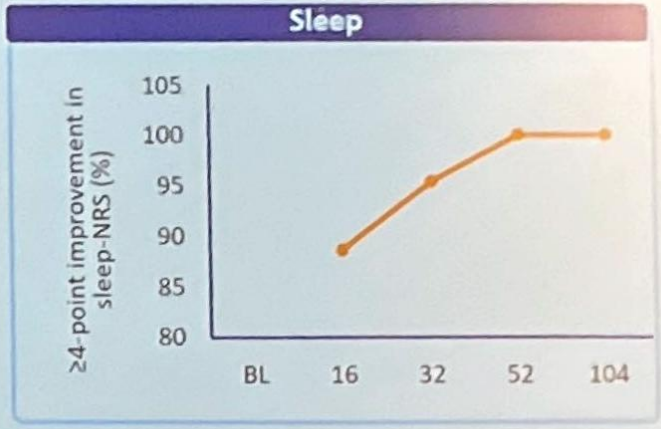
Yosipovitch et al. . Nat Med. 2023;29(5):1180-1190. Kwatra et al. N Engl J Med. 2023 Oct 26;389:1579-1589

Dupilumab Provided Sustained Improvement in Itch, Lesions, and Sleep up to Week 104

Iricozzi et al JEADV 2024 (N=64)







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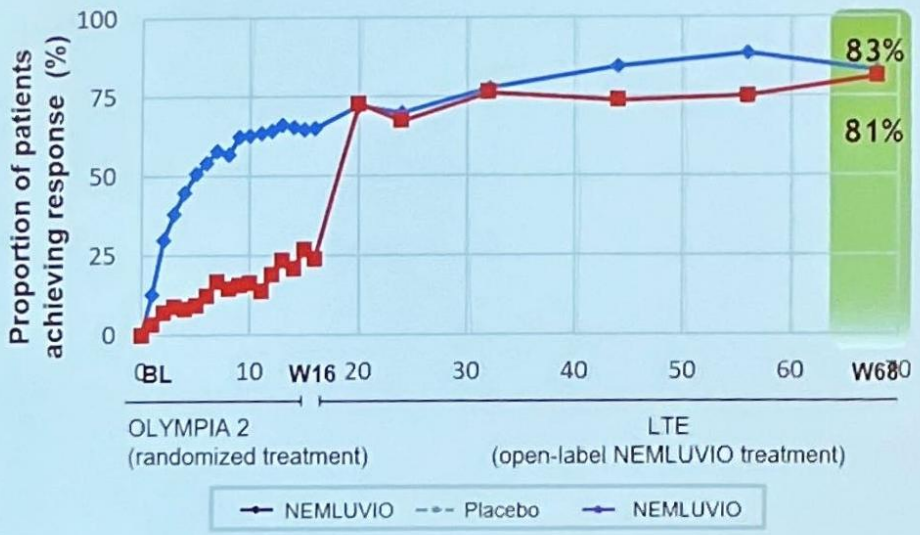
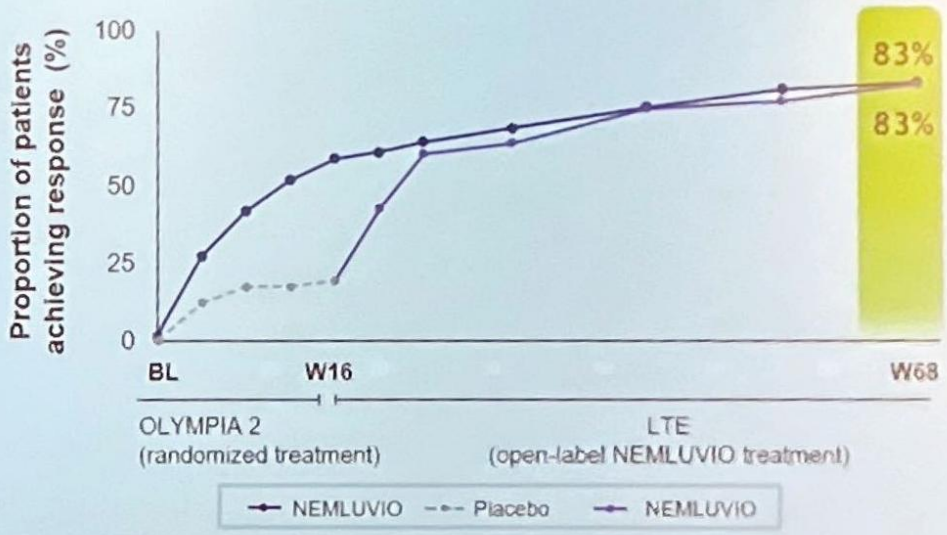
Long Term Effect of Nemolizumab

Data from observed cases in OLYMPIA 2 treat-through population, interim analysis (52 weeks) of the OLYMPIA LTE

≥4-point improvement in weekly average Peak Pruritus NRS



PAS item 5b (76% to 100% healed prurigo lesions)



8 out of 10 patients with PN maintained itch relief and healed lesions with Nemo

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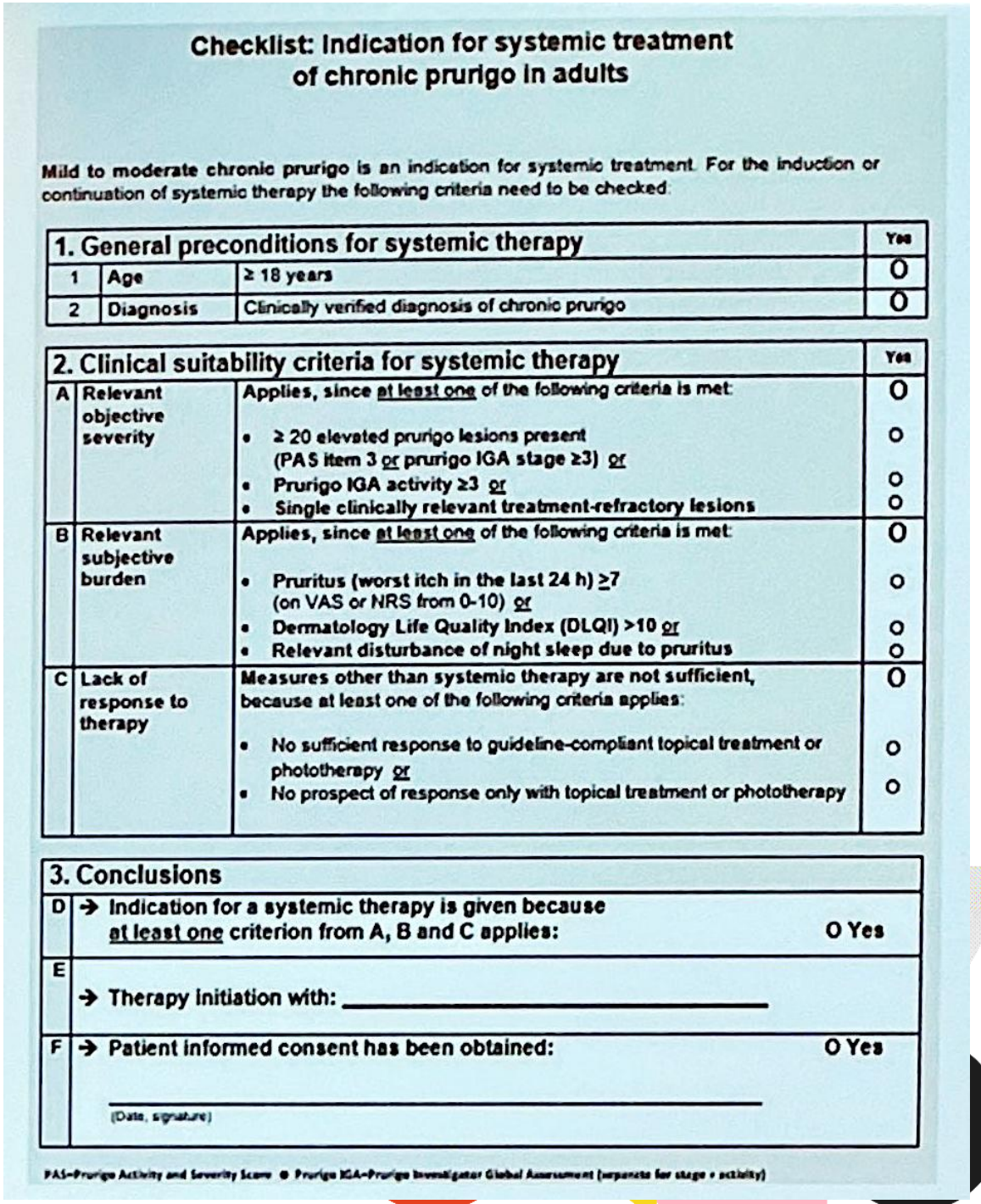
Other Emerging Therapies for PN in Late-Stage Clinical Development[1]

Agent	MOA	Trial	Phase
Rocatinlimab	OX-40 inhibitor	A Phase 3, Placebo-controlled, Double-blind Study Assessing Rocatinlimab in Prurigo Nodularis	3
Abrocitinib	JAK1 inhibitor	Efficacy of Abrocitinib for Reducing Pruritus in Adults With PN and Chronic Pruritus of Unknown Origin (NCT05038982)	2
Povorcitinib	JAK1 inhibitor	A Study to Evaluate the Efficacy and Safety of INCB054707 in Participants With PN (NCT05061693)	2
Ruxolitinib cream	JAK 1/2 inhibitor	A Study to Evaluate the Safety and Efficacy of Ruxolitinib Cream in Participants With Prurigo Nodularis (PN) (TRuE-PN1) A Study to Evaluate the Efficacy and Safety of Ruxolitinib Cream in Participants With Prurigo Nodularis (PN) (TRuE-PN2)	3
Vixarelimab	OSMRβ inhibitor	Study to Assess the Efficacy, Safety, and Tolerability of Vixarelimab in Reducing Pruritus in PN (NCT03816891)	2
Barzolvolimab (CDX-0159)	KIT (CD117)	A Study of Barzolvolimab in Patients with Prurigo Nodularis	2

Indicación para tratamiento sistémico

- Grado de severidad objetiva
- Carga subjetiva
- Falta de respuesta al tratamiento



Checklist: Indication for systemic treatment of chronic prurigo in adults

Mild to moderate chronic prurigo is an indication for systemic treatment. For the induction or continuation of systemic therapy the following criteria need to be checked:

1. General preconditions for systemic therapy			Yes
1	Age	≥ 18 years	O
2	Diagnosis	Clinically verified diagnosis of chronic prurigo	O

2. Clinical suitability criteria for systemic therapy			Yes
A	Relevant objective severity	Applies, since at least one of the following criteria is met:	O
		• ≥ 20 elevated prurigo lesions present (PAS item 3 or prurigo IGA stage ≥3) or	O
		• Prurigo IGA activity ≥3 or	O
		• Single clinically relevant treatment-refractory lesions	O
B	Relevant subjective burden	Applies, since at least one of the following criteria is met:	O
		• Pruritus (worst itch in the last 24 h) ≥7 (on VAS or NRS from 0-10) or	O
		• Dermatology Life Quality Index (DLQI) >10 or	O
		• Relevant disturbance of night sleep due to pruritus	O
C	Lack of response to therapy	Measures other than systemic therapy are not sufficient, because at least one of the following criteria applies:	O
		• No sufficient response to guideline-compliant topical treatment or phototherapy or	O
		• No prospect of response only with topical treatment or phototherapy	O

3. Conclusions		
D	→ Indication for a systemic therapy is given because at least one criterion from A, B and C applies:	O Yes
E	→ Therapy initiation with: _____	
F	→ Patient informed consent has been obtained:	O Yes
	_____ (Date, signature)	

PAS=Prurigo Activity and Severity Score ● Prurigo IGA=Prurigo Investigator Global Assessment (separate for stage + activity)

English/German online: Augustin M et al. J Dtsch Dermatol Ges. 2023 Sep 18. doi: 10.1111/ddg.15152. www.arzneimittelleitfaden.de

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Inmunoalergia Cutánea

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DRESS/DIHS

Una iniciativa de:

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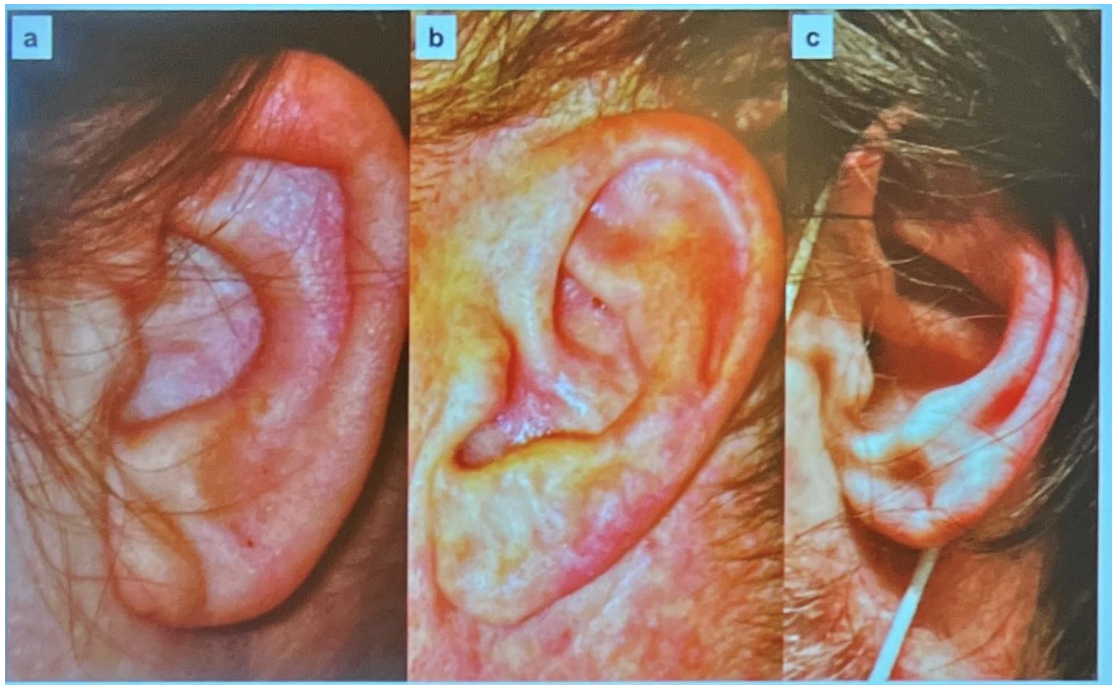
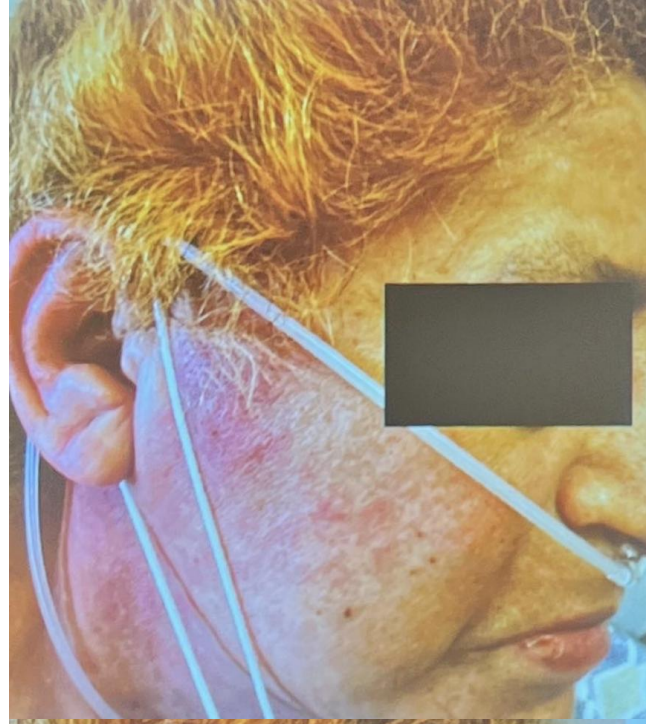
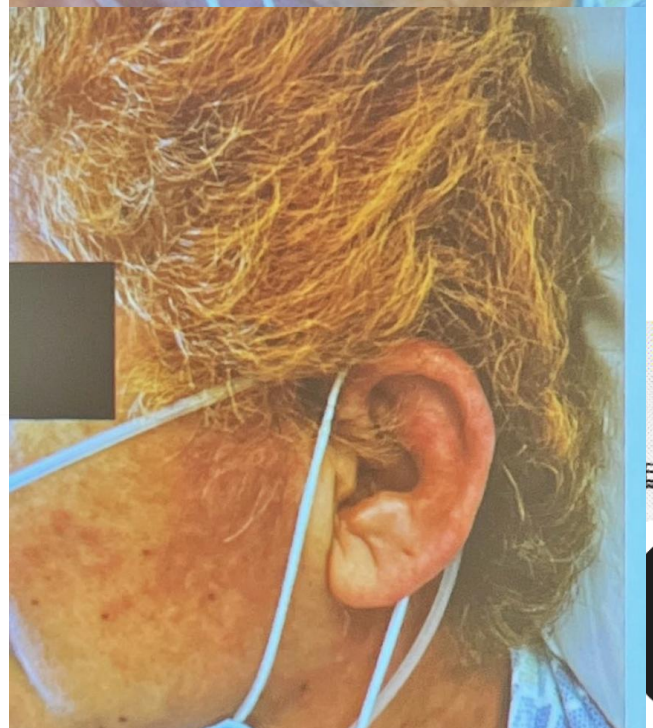
Oblique earlobe crease in DRESS/DIHS

- Sensibilidad 81%
- Especificidad 71%

- VVP 68%







Tratamiento DRESS/DIHS

JAMA Dermatol. 2024 Jan 1;160(1):37-44. doi: 10.1001/jamadermatol.2023.4450.

Management of Adult Patients With Drug Reaction With Eosinophilia and Systemic Symptoms: A Delphi–Based International Consensus

Table. DRESS Acute Phase Management and Follow-Up Care

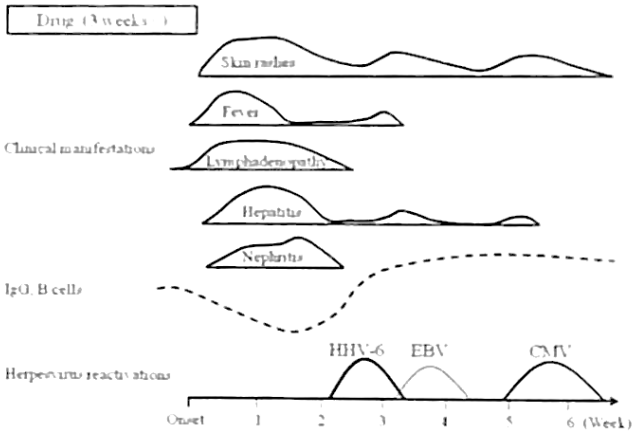
Consensus on DRESS treatment[a]	
General recommendations	• Treatment should be based on disease severity assessment • Corticosteroids should be initiated in all patients with confirmed DRESS
Mild DRESS[b]	• Topical very high potency steroids should be initiated • Steroids should be tapered over 6 wk to 3 mo
Moderate DRESS[b]	• Topical very high potency steroids can be considered • Systemic glucocorticoids can be considered in patients with moderate disease • Steroids should be tapered over 6 wk to 3 mo
Severe DRESS[b]	• Systemic glucocorticoids should be initiated in all patients • Systemic glucocorticoids should be tapered over 3 to 6 mo

Brüggen et al. JAMA Derm. 2024.

Stanford MEDICINE

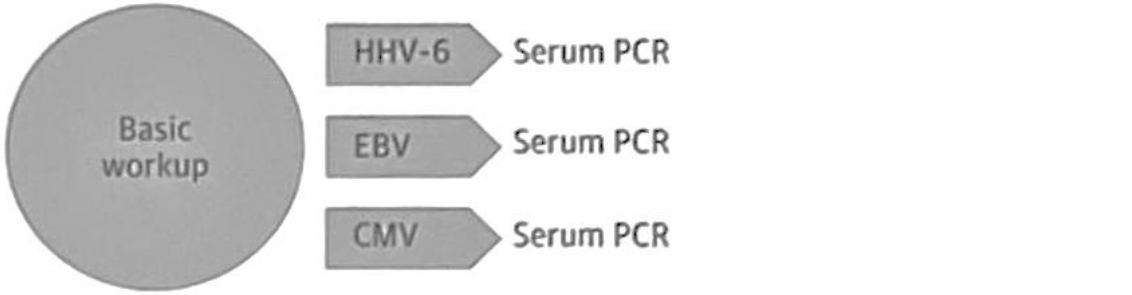
Viral Reactivation and DRESS

- Viral reactivation typically occurs 2–4 wks after symptoms
  - Rates of HHV-6 reactivation: 36-80%
  - Associated w/ longer disease, flares, & more severe outcomes
- Routine use of antiviral tx is not indicated due to spontaneous resolution of viral reactivation and SE of therapy
- We treat: viral induced organ damage or viral reactivation is suspected to be a contributory factor to severe disease



B Workup investigating HHV reactivations

All patients with suspected DRESS



DRESS with high serum CMV viral load

- Antiviral treatment (ganciclovir/valganciclovir) can be considered

Complicaciones a largo plazo de DRESS/DIHS

- Long-term complications ~11.5%
  - Both immune and non-immune
- Autoimmune sequelae:
  - Most common: Autoimmune thyroid disease and fulminant type 1 diabetes
    - Onset 2–4 months post-DRESS/DIHS
  - Can occur after all acute symptoms are quiescent, following weaning off steroids, and may occur 5+ years later

Hama et al. J Allergy Clin Immunol Pract. 2022.
Stirton et al. Biomedicines. 2022.
Brüggen et al. JAMA Derm. 2024.

Short-term sequelae (within weeks following acute DIHS/DRESS onset)

Fulminant type 1 diabetes mellitus [21, 22]

Fulminant hepatic failure [23, 24]

Autoimmune hemolytic anemia [25]

Renal failure [75]

Disseminated intravascular coagulation [76]

Table 3. Composite Scores for Predicting the Development of Autoimmune Diseases in Patients with DiHS/DRESS

Parameters	Grade/Extent	Score
Acute phase		
Number of lymphocytes (/μl)	>2,400	1
Liver dysfunction (ALT) (IU/l)	80–300/>300	1/2
Serum IL-2 (≤ 0.3 pg/ml) and IL-4 (≤ 2.8 pg/ml)	Yes	2
Subacute phase		
Pulse prednisone[1]	Yes	1
IVIg infusion	Yes	2
Increase in liver enzyme (ALT) (IU/l)[2]	100–400/>400	1/2
Increase in globulin[3]	>0.7	2
EBV and/or HHV-6 reactivation for >3 months[4]	EBV or HHV-6/ both	1/2

Low: ≤ 1 point

Intermediate: 2-3 points

High: ≥ 4 points

Mizukawa Y, Aoyama Y, Takahashi H, Takahashi R, Shiohara T. Risk of Progression to Autoimmune Disease in Severe Drug Eruption: Risk Factors and the Factor-Guided Stratification. J Invest Dermatol. 2022;142(3) Pt B:960-968.e9. doi:10.1016/j.jid.2021.11.008

Complicaciones a largo plazo de DRESS/DIHS

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    - Onset 2–4 months post-DRESS/DIHS
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Short-term sequelae (within weeks following acute DIHS/DRESS onset)

Fulminant type 1 diabetes mellitus

Fulminant hepatic failure

Autoimmune hemolytic anemia

Renal failure

Disseminated intravascular coagulation

Myocarditis

Pneumonitis

Hemophagocytic lymphohistiocytosis (HLH)

Autoimmune thyroiditis

Long-term sequelae (persistent and/or months to years following acute DIHS/DRESS onset)

Arthralgia (rheumatoid arthritis)

Autoimmune thyroiditis

Vitiligo

Alopecia areata

Myocarditis

Hama et
Stirton e
Brüggen

Consensus on follow-up care[a]	
Timing of follow-up	• Regular follow-up consultations beginning in the first month after discharge • Regular follow-up consultations during the first 6 mo after onset and thereafter according the patients' needs
Content of follow-up consultations	• Blood tests according to the initial organ involvement • Screening for autoantibodies in the convalescence phase • Screening for thyroid dysfunction in the convalescence phase • Screening for steroid adverse effects in patients receiving prolonged systemic steroids • Active offering of psychological support

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Paradoxal Reactions

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Reacciones paradójicas

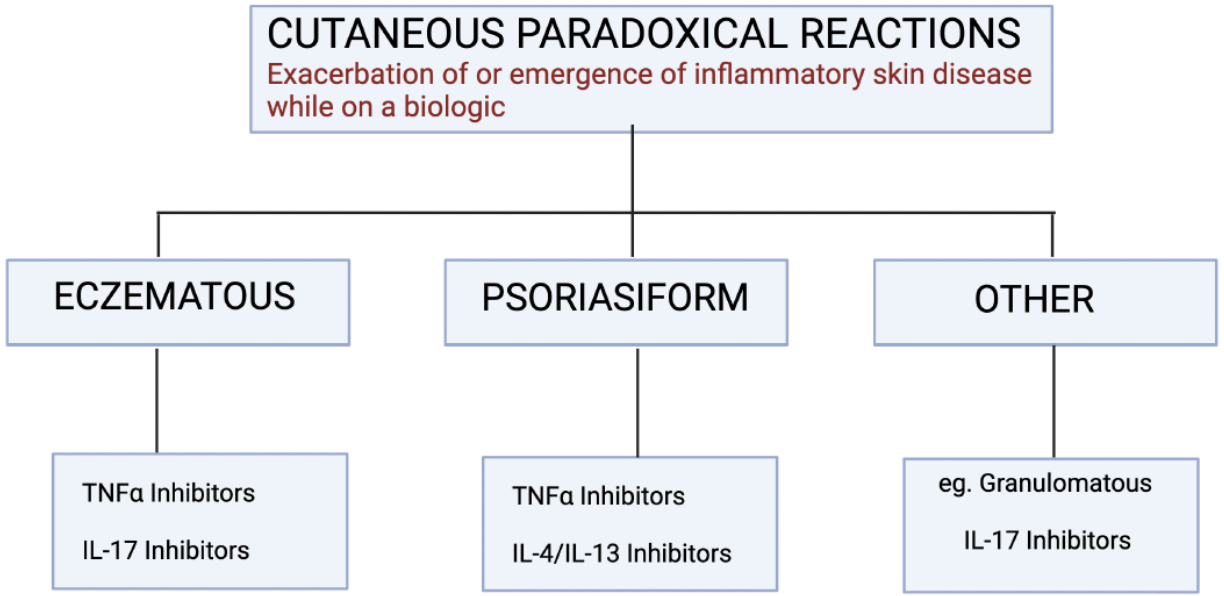
Biologics are targeted, but unintended effects still occur

Paradoxical Reactions (PRs)

Development of New
OR
Exacerbation of Existing
Immune mediated disorder in setting of biologic therapy

Important to be able to recognize and manage PRs

PRs provide insight into Immunology of disease and therapy



	TNFα Inhibitors	IL-23 / IL-12/23 Inhibitors	IL-17 Inhibitors	IL-4/IL-13 Inhibitors
Most Common PRs	Paradoxical Psoriasis Paradoxical Eczematous Eruption	Paradoxical Eczematous Eruption	Paradoxical Eczematous Eruption	Paradoxical Psoriasiform Eruption
Management Pearls	Start with topicals, often need to switch biologic class, other systemic medications or phototherapy may be needed	Start with topicals, can sometimes treat through, other systemic medications or phototherapy may be needed	Start with topicals, can sometimes treat through, other systemic medications or phototherapy may be needed	Start with topicals, can sometimes treat through, other systemic medications or phototherapy may be needed

THE JOURNAL OF MEDICINE
J Am Acad Dermatol. 2022 May;86(5):1080-1091.

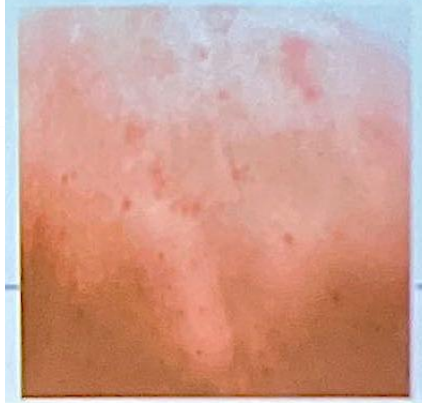
Management Pearls:
- Start with topicals
- Can often treat through (with the exception of TNFa PRs--generally need to switch)
- Phototherapy or oral medications can be effective
- Sometiems an additional biologic or JAK inhibitor may be needed
- Think critically to make sure nothing important is missed (such as CTCL in setting of dupilumab)

IL-4/IL-13 Inhibitors: Beware of CTCL

There have been reports of CTCL emerging in patients treated with dupilumab

Whether this represents emergence of CTCL or pre-existing CTCL that declares itself on dupilumab remains unknown (likely both scenarios exist)

If patient flares on dupilumab or displays any concerning signs for CTCL, skin biopsy and additional workup needed



J Am Acad Dermatol. 2022 Dec;87(6):e241-e242.
J Am Acad Dermatol. 2025 Feb 1:S0190-9622(25)00188-4.
J Am Acad Dermatol. 2024 Dec 15:S0190-9622(24)03371-1.
Int J Dermatol. 2023 Jul;62(7):862-876.
Dermatopathology (Basel). 2022 Nov 30;9(4):385-391.

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Efectos adversos cutáneos de los inhibidores de puntos de control inmunitario

Jennifer N. Choi, MD

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National Comprehensive Cancer Network®

NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®)

Management of Immunotherapy-Related Toxicities

Version 1.2025 — December 20, 2024

NCCN.org

NCCN recognizes the importance of clinical trials and encourages participation when applicable and available. Trials should be designed to maximize inclusiveness and broad representative enrollment.

Continue

NCCN Guidelines for Patients® available at www.nccn.org/patients

https://www.nccn.org/professionals/physician_gls/pdf/immunotherapy.pdf

Use of steroids with immunotherapy for cancer treatment

- High-dose steroids do not appear to interfere with antitumor responses.
- However, data from several studies suggest that administration of steroids (prednisone ≥ 10 mg daily) within a few weeks of starting treatment might result in inferior outcomes.
- Prednisone >10 mg/day for > 2 weeks associated with poorer survival outcomes.

Clinical Pearl

- For Grade ≥ 2 exanthems, if possible, try to avoid systemic steroids if within first few weeks of immunotherapy.
- If using, try to avoid prolonged courses (i.e. taper within 4 weeks).
- If persistent, consider switching to steroid alternative therapy.

Impact of antibiotics on immunotherapy outcome

- Gut microbiota implicated in numerous physiological and pathological processes in humans
- Closely related to optimum functioning of immune system
- The use of antibiotics as an independent risk factor for the development of cancer
  - Petrelli F et al (2019) Use of antibiotics and risk of cancer: a systematic review and meta-analysis of observational studies. Cancers 11:1174

- Exposure to broad-spectrum antibiotic -> negatively influences the results of treatment with ICIs by modulation of gut microbiota
- ? Timing
- Cumulative or prolonged use of abx -> decreased PFS or OS
  - Tinsley N et al. (2020) Oncologist 25:55–63
- Negative correlation for all outcomes in the case of abx administration *before* the beginning of treatment with ICIs but not concurrent administration of abx and IT
  - Huemer F et al (2018) Oncotarget 9:16512–16520

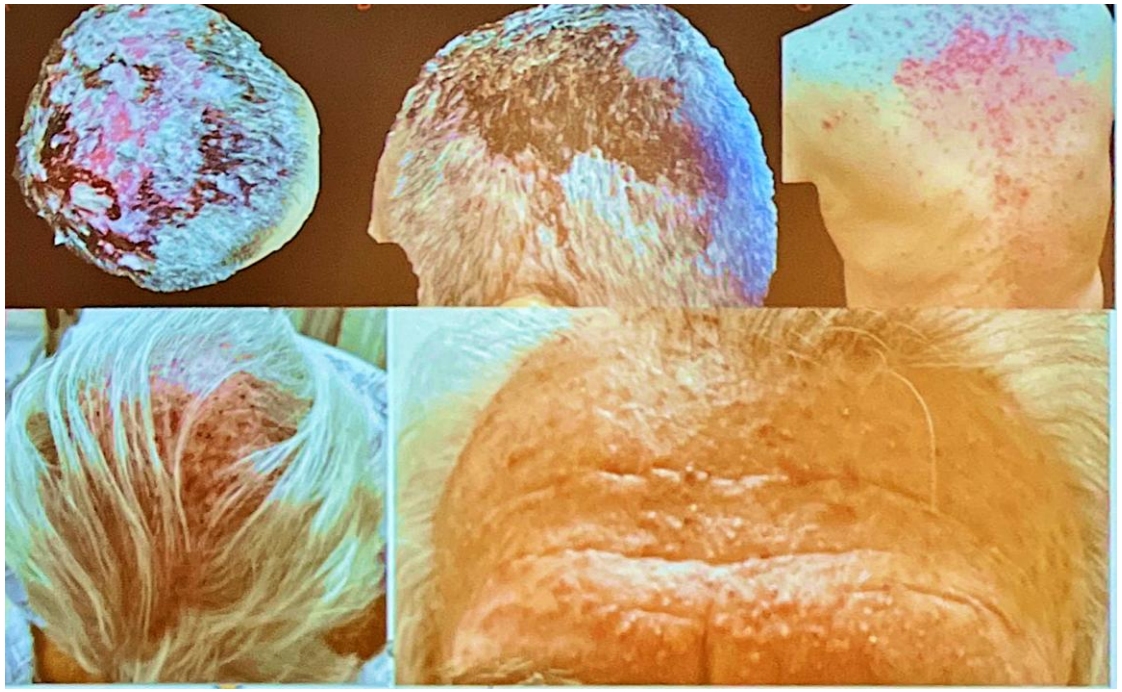
- Systematic review and large meta-analyses of 766 observational studies on abx and ICIs
  - Eighteen studies and 826 pts
  - OS was 3.4 times longer in pts who did not receive any abx in the 42 days prior to immunotherapy
  - PFS was also longer in pts who did not receive abx
- Exposure to abx before 60 days starting or during immunotherapy seems *not* to influence the clinical outcomes

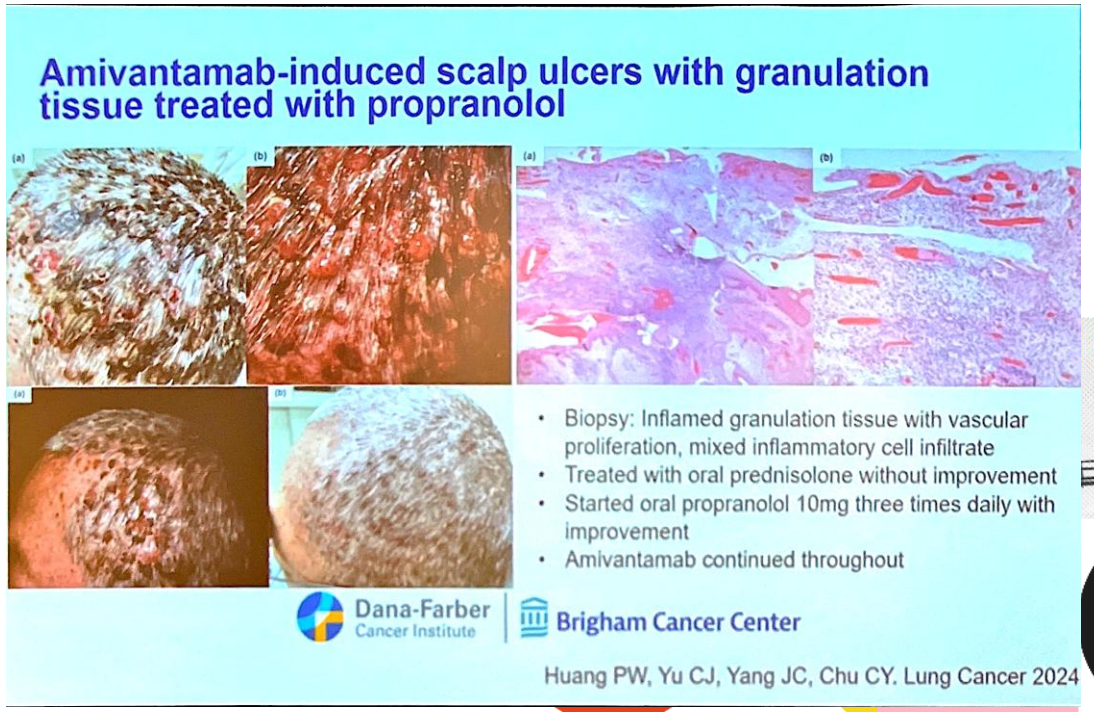
Wilson B et al (2020) Cancer Immunolimmunother 69:343–354

- * Try to avoid antibiotic use unless absolutely needed, particularly within 60 days prior to or within first few weeks of starting, and in patients responding to or stable on immunotherapy
- *Would not recommend using for anti-inflammatory purposes

Novel EGFR inhibitors and cutaneous side effect profiles

- Amivantamab: Bispecific monoclonal antibody to EGFR and mesenchymal epithelial transition factor (MET)
- FDA approved in 2021 for non-small cell lung cancer
- High prevalence of cutaneous toxicities:
  - 68.5% with acneiform rash, 30% with paronychia
  - **Scalp toxicities appear to be enriched in amivantamab-treated patients, affecting over 20% of patients**
    - Erosive Pustular Dermatosis and Scalp Folliculitis/Acneiform Eruption





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"Cada vez más cerca de una medicina personalizada."

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¡Muchas gracias!

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