Horizonte en DA: nuevas moléculas

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Badalona

Germans Trias i Pujol Hospital

IV EDICIÓN
INMUNOTERAPIA EN DERMATOLOGÍA

30 de marzo de 2023

Recinte Modernista de Sant Pau, Barcelona

Conflicto de intereses

He participado como IP/SI y/o ponente invitado y/o advisor para Sanofi, Pfizer, Leo-Pharma, Abbvie, Galderma, Lilly, UCB.

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Recruiting
A Study of MG-K10 in Subjects With Atopic Dermatitis
Atopic Dermatitis
Drug: MG-K10
Drug: Placebo
2
Recruiting
An Efficacy and Safety Study of RPT193 in Adults With Atopic Dermatitis
Atopic Dermatitis
Drug: RPT193
Other: Placebo
2749 artículos en 2022; 619 en enero-febrero


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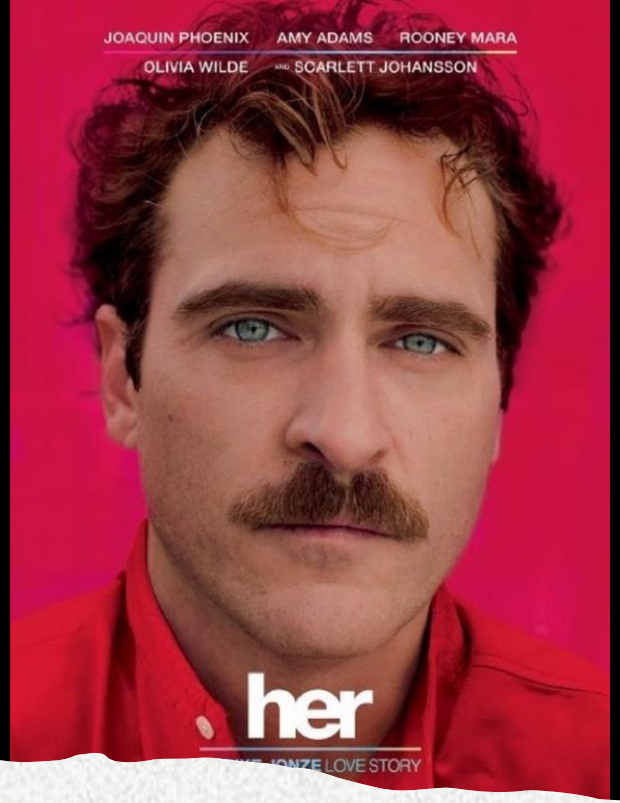
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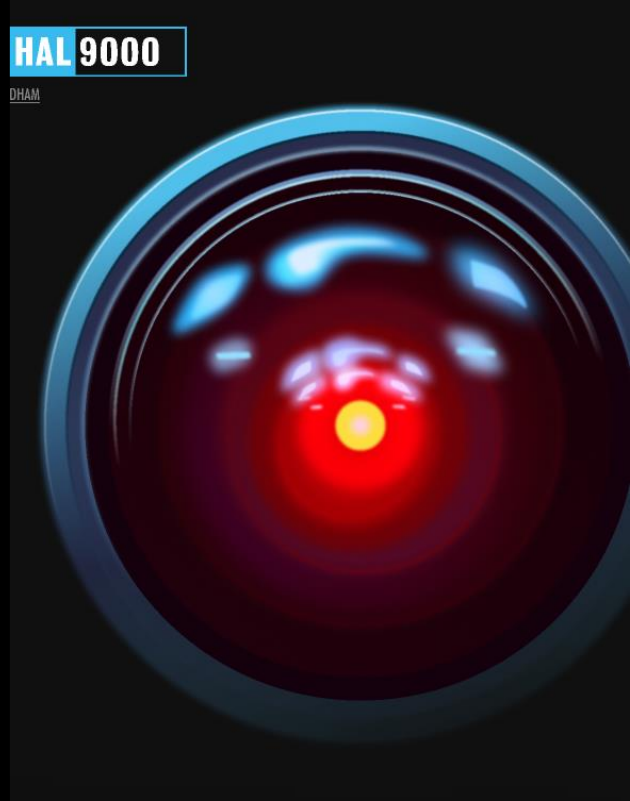
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We need an AI.....


pidermal barrier
dysfunction
Allergens
Irritants
Dehydration
FLG gene
Scratching
Inhibit keratinocyte terminal differentiation
Epidermal hyperplasia
Cutaneous sensory neuron
Th2 cell
TSLP
IL-31
IL-4
IL-13
IL-5
IL-13
IL-4
IL-13
IL-31
IL-22
Th22 cell
The "itch-scratch cycle"
IgE
Histamine
Itch
Mast cell
B cell
↓ Lipid synthesis/ AMPs
Eosinophil proliferation
Dermis

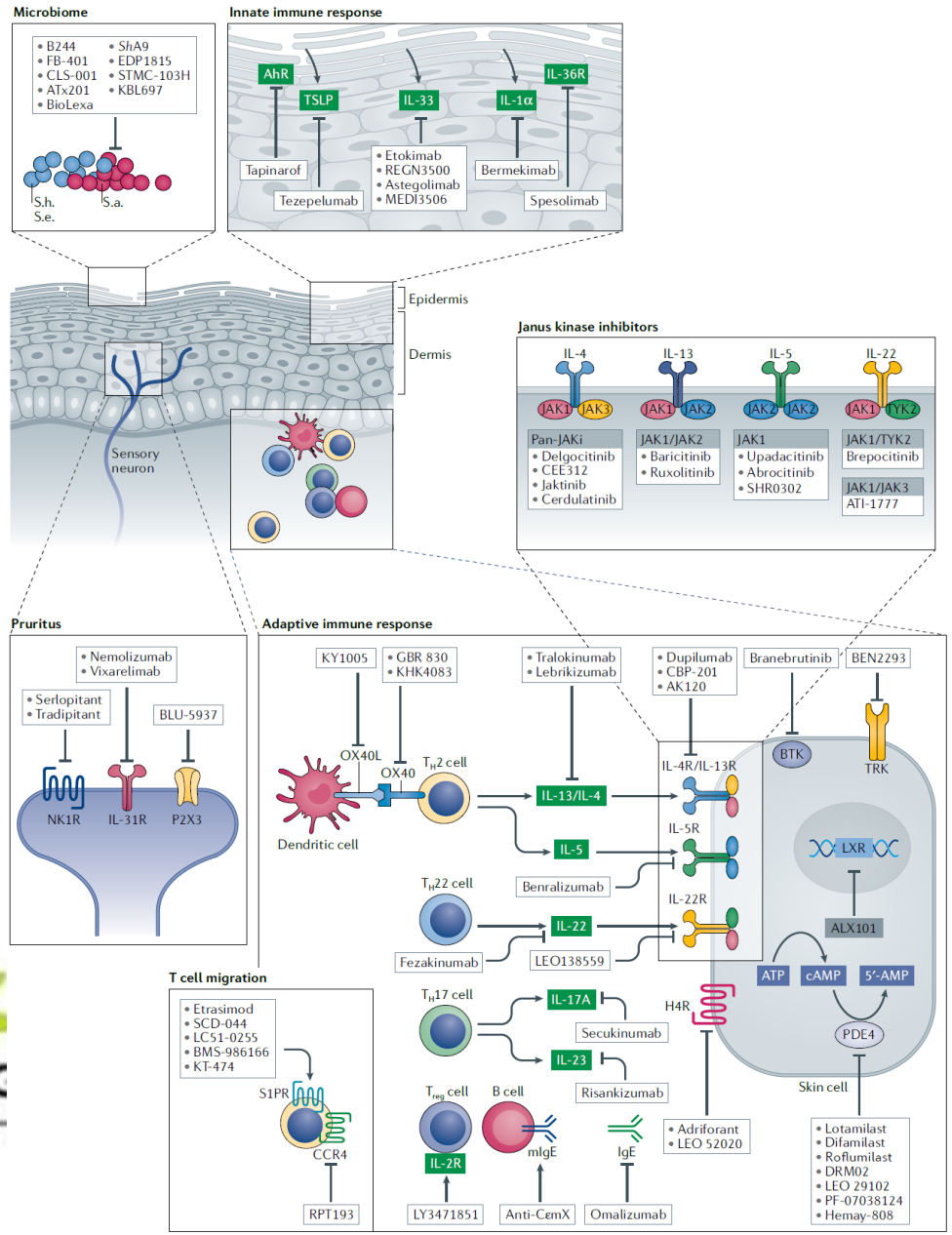


Table 1 | **Current therapeutic pipeline for atopic dermatitis**

Strategy	Drug type and mode of application	Agent/company	Mode of action/target	Clinical development phase in atopic dermatitis	Clinical trial ID
Modulating the microbiome	Bacterial strains — topical	B244 (AOBiome)	Nitric oxide donor	IIb	NCT04490109
		ShA9 (NIAID)	Targeted microbiome transplant	I/IIa	NCT03151148
		FB-401 (Forte Biosciences)	Bacterial replacement, anti-inflammation via TLR5 and TNFR activation	IIb	NCT04504279
	Small molecule — topical	CLS-001/omiganan (Cutaneous Life Sciences)	Cell membrane enhancer	II	NCT02456480
		ATx201/niclosamide (Union Therapeutics)	Protonophore activity	II	NCT04339985
	Bacterial strains — oral	EDP1815 (Evelo)	Modulation of systemic inflammation	Ib	NCT03733353
		STMC-103H (Siolta therapeutics)	Immunomodulation via microbiome manipulation	Ib	NCT03819881
Targeting the innate immune response	Small molecule — topical	Tapinarof/benvitimod (Dermavant)	AhR agonist	IIb	NA
	Biologic — injection	Tezepelumab (Amgen/AstraZeneca)	TSLP	IIa	NCT02525094
		Etokimab (AnaptysBio)	IL-33	IIa	NCT03533751
		REGN3500 (Regeneron)	IL-33	IIa	NCT03738423
		Astegolimab (Genentech)	IL-33	IIa	NCT03747575
		MEDI3506 (MedImmune)	IL-33	IIa	NCT04212169
		Bermekimab (Janssen)	IL-1α	IIa	NCT03496974
		Spesolimab (Böhringer Ingelheim)	IL-36R	IIa	NCT03822832
Targeting the adaptive immune response	Biologic — injection	GBR 830/ISB 830 (Glenmark/Ichnos)	OX40	IIb	NCT03568162
		KHK4083 (Kyrin)	OX40	IIb	NCT03703102
		KY1005 (Kymab/Sanofi)	OX40L	IIa	NCT03754309
		Dupilumab (Regeneron/Sanofi)	IL-4Rα	Approved globally, staggered paediatric programme ongoing	NCT03346434
		CBP-201 (Connect Biopharma)	IL-4Rα	IIb	NCT04444752
		AK120 (Akesobio)	IL-4Rα	Ib	NCT04256174
		ASLAN004 (ASLAN)	IL-13Rα1	Ib	NCT04090229
		Tralokinumab (LEO Pharma)	IL-13	Approved in EU, staggered paediatric programme ongoing	NCT03526861
		Lebrikizumab (Allmiral/Lilly)	IL-13	III, staggered paediatric programme ongoing	NCT04250350
		Benralizumab (AstraZeneca)	IL-5Rα	II	NCT04605094
		Omalizumab (Novartis)	IgE	II	NCT02300701
		FB825/anti-CεmX (LEO Pharma/Oneness Biotech)	mIgE	IIa	NCT04413942
		Fezakinumab (ill)	IL-22	IIa	NCT01941537
		LEO 138559 (LEO Pharma)	IL-22R1	Ib	NCT03514511
		Secukinumab (Novartis)	IL-17A	IIa	NCT02594098, NCT03568136
		Risankizumab (AbbVie)	IL-23	IIa	NCT03706040
		LY3471851 (Lilly)	rhIL-2 to T_{reg} cells	Ib	NCT04081350

Table 1 (cont.) | **Current therapeutic pipeline for atopic dermatitis**

Strategy	Drug type and mode of application	Agent/company	Mode of action/target	Clinical development phase in atopic dermatitis	Clinical trial ID
Targeting the adaptive immune response (cont.)	Small molecule — oral	Adriforant (Novartis)	H4R	IIb	NCT03517566
		LEO 152020/JW1601 (LEO Pharma)	H4R	I	NCT04203836
		RPT193 (RAPT Therapeutics)	CCR4	IIa	NCT04271514
		Etrasimod (Arena Pharma)	S1PR1, S1PR4, S1PR5	IIb	NCT04162769
		SCD-044 (Sun Pharma)	S1PR1	IIa	NCT04684485
		LC51-0255 (LG Chem)	S1PR1	I	NA
		BMS-986166 (Bristol Myers Squibb)	S1PR1	IIa	NCT03038711
		KT-474 (Kymera)	S1PR1	Ib	NCT04772885
	Small molecule — topical	AKP-19 (Akaal Pharma)	S1PR1	II	NA
		Lotamilast (RVT-501 /E6005) (Dermavant)	PDE4	II	NCT03394677, NCT02950922
		Difamilast (OPA-15406/MM36) (Otsuka)	PDE4	II	NCT02945657
		DRM02 (Dermira)	PDE4	II	NCT01993420
		LEO 29102 (LEO Pharma)	PDE4	II	NCT01037881
		Roflumilast (AstraZeneca)	PDE4	II; pharmacokinetics and efficacy in paediatrics	NCT04156191
		Hemay-808 (Tianjin Hemay Pharmaceutical)	PDE4	II	NCT04352595
		PF-07038124 (Pfizer)	PDE4	II	NCT04664153
		BEN2293 (BenevolentAI)	TRK	I/II	NCT04737304
		HY209 (Shaperon)	GPCR19	IIa	NCT04530643
		VTP-38543 (Vitae Pharma)	Liver X receptor-β	I/II	NCT02655679
		ALX 101 (Ralexar)	Liver X receptor	II	NCT03859986
Targeting itching	Biologic — injection	Nemolizumab (Galderma)	IL-31	III	NCT03989349, NCT03985943
		Vixarelimab (Kiniksa Pharma)	OSMRβ	IIa/b	NCT03816891
	Small molecule — oral	Serlopitant (Menlo)	NK1R	II	NCT02975206
		Tradipitant (Vanda)	NK1R	II	NCT03568331
		BLU-5937 (Bellus)	P2X3	II	NCT04693195
Inhibiting Janus kinases	Small molecule — topical	Delgocitinib (Japan Tobacco/LEO)	Pan-JAK	IIb in EU, approved in Japan	NCT03725722
		Ruxolitinib (Incyte)	JAK1/JAK2	III	NCT03745638, NCT03745651
		Cerdulatinib (RVT/DMVT502) (Dermavant)	Pan-JAK/SYK	Ib	NA
		Brepocitinib (Pfizer)	JAK1/TYK2	IIb	NCT03903822
		ATI-1777 (Aclaris)	JAK1/JAK3	II	NCT04588269
		CEE321 (Novartis)	Pan-JAK	I	NCT04612062
		Jaktinib (Suzhou Zeigen Biopharma)	Pan-JAK	IIa	NCT04539639
		SHR0302 (Reistone Biopharma)	JAK1	II	NCT04717310
	Small molecule — oral	Baricitinib (Lilly)	JAK1/JAK2	Approved in EU for adults, staggered paediatric programme ongoing	NCT03952559
		Upadacitinib (AbbVie)	JAK1	III, staggered paediatric programme ongoing	NCT03646604
		Abrocitinib (Pfizer)	JAK1	III, staggered paediatric programme ongoing	NCT03627767
		SHR0302 (Reistone Biopharma)	JAK1	II	NCT04162899

AhR, aryl-hydrocarbon receptor; BTK, Bruton tyrosine kinase; CCR4, C-C chemokine receptor 4; GPCR19, G protein-coupled receptor 19; H4R, type 4 histamine receptor; IL-4Rα, α-chain of the IL-4 receptor; IL-5Rα, α-chain of the IL-5 receptor; IL-13Rα1, α1 chain of the IL-13 receptor; IL-22R1, IL-22 receptor 1; JAK, Janus kinase; NK1R, neurokinin 1 receptor; NA, not applicable; OSMRβ, oncostatin M receptor β; OX40L, OX40 ligand; PDE4, phosphodiesterase 4; P2X3, purinoreceptor 3; rhIL-2, recombinant human IL-2; S1PR1, sphingosine 1-phosphate receptor 1; T_{reg} cell, regulatory T cell; TRK, tropomyosin receptor kinase; TSLP, thymic stromal

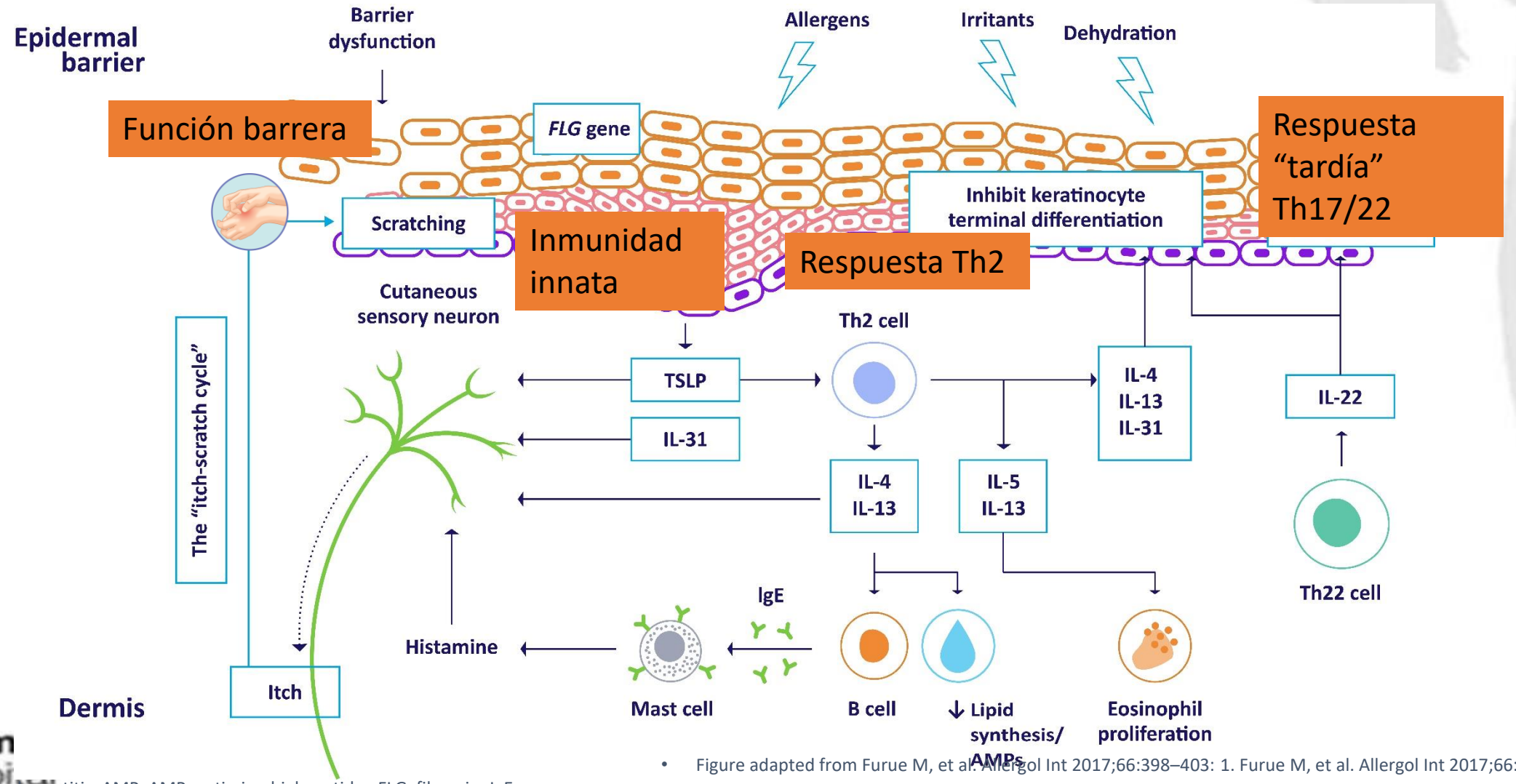
REVIEWS

Check for updates

Atopic dermatitis: an expanding therapeutic pipeline for a complex disease

https://doi.org/10.1038/s41573-021-00266-6

Fisiopatogenia de la Dermatitis atópica en 1 minuto



- AD, atopic dermatitis; AMP, AMP, antimicrobial peptide ; FLG, filaggrin; IgE, immunoglobulin E; IL, interleukin; Th, T helper; TSLP, thymic stromal lymphopoietin

- Figure adapted from Furue M, et al. Allergol Int 2017;66:398–403: 1. Furue M, et al. Allergol Int 2017;66:398–403;
- 2. Bao L, et al. JAK-STAT 2013;2:e24137

Modulación de la microbiota

Rebalancing the skin microbiota can lead to a **reduction in the SA load**

- **A spray product containing *Nitrosomonas eutropha*** an ammonia-oxidizing bacterium able to produce nitric oxide, is a mediator with anti-inflammatory and metabolic properties.
- Application of **a topical ointment of 2% niclosamide (ATx201)** has also been shown to be effective in reducing SA

Colonization

- **Oral integration with preparations of bacterial strains** with therapeutic potential capable of altering the intestinal microbiome

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Biomedicines **2022**, *10*, 2700. https://doi.org/10.3390/biomedicines10112700

Table 1. Clinical trials targeting skin microbiome molecules in AD.

Target Molecule	Clin Trial Gov	Type of Study	Status
Microbiome			
Topical bacterial strains			
Targeted Microbiome Transplant Lotion (TMT)	NCT03151148	Phase I/II for AD	Completed
Autologous Microbial Transplant	NCT03158012	Phase I for AD	Completed
Autologous Microbial Transplant	NCT01959113	Phase I for AD	Completed
Three strains of Roseomonas mucosa FB-401	NCT04504279	Phase II for AD	Completed
Three strains of Roseomonas mucosa FB-401	NCT04936113	Phase II for AD	Terminated (Failure of the Phase II study (protocol FB401-01) to meet its endpoint))
Lyophilized strain of Staphylococcus hominis A9 (ShA9) (ADRN-UCSD-001)	NCT05177328	Phase I for AD	Recruiting
Nitrosomonas eutropha spray (B244)	NCT04490109	Phase II for AD	Completed
Topical small molecule			
Topical niclosamide 2% (ATx201)	NCT04339985	Phase II for AD	Completed
Topical niclosamide 2% (ATx201)	NCT03304470	Phase II for AD	Completed

biomedicines MDPI

Systematic Review

A Systematic Review of Atopic Dermatitis: The Intriguing Journey Starting from Physiopathology to Treatment, from Laboratory Bench to Bedside

Giulia Radi †, Anna Campanti †, Federico Diotallevi *, Emanuela Martina, Andrea Marani and Annamaria Offidani

Omiganan:….going down….

Results

In all omiganan treatment groups, dysbiosis was recovered by reducing *Staphylococcus* species abundance and increasing diversity. A reduction of cultured *S aureus* was observed in all omiganan treatment groups, with a significant reduction for omiganan 2.5% compared to vehicle (-93.5%; 95% CI, -99.2 to -28.5%; *P* = .02). No significant clinical improvement was observed.

Niemeyer-van der Kolk T et alJ Am Acad Dermatol. 2022 Apr;86(4):854-862. doi: 10.1016/j.jaad.2020.08.132. Epub 2020 Oct 1. PMID: 33010325.

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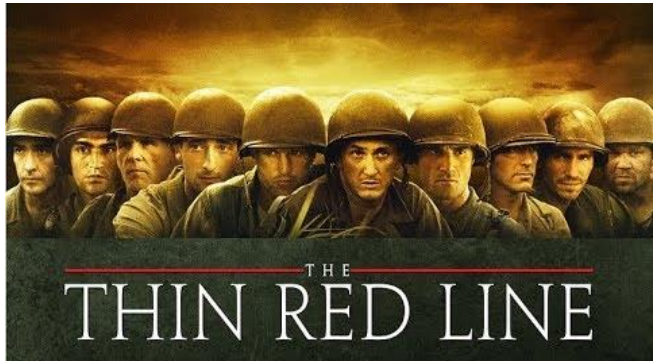
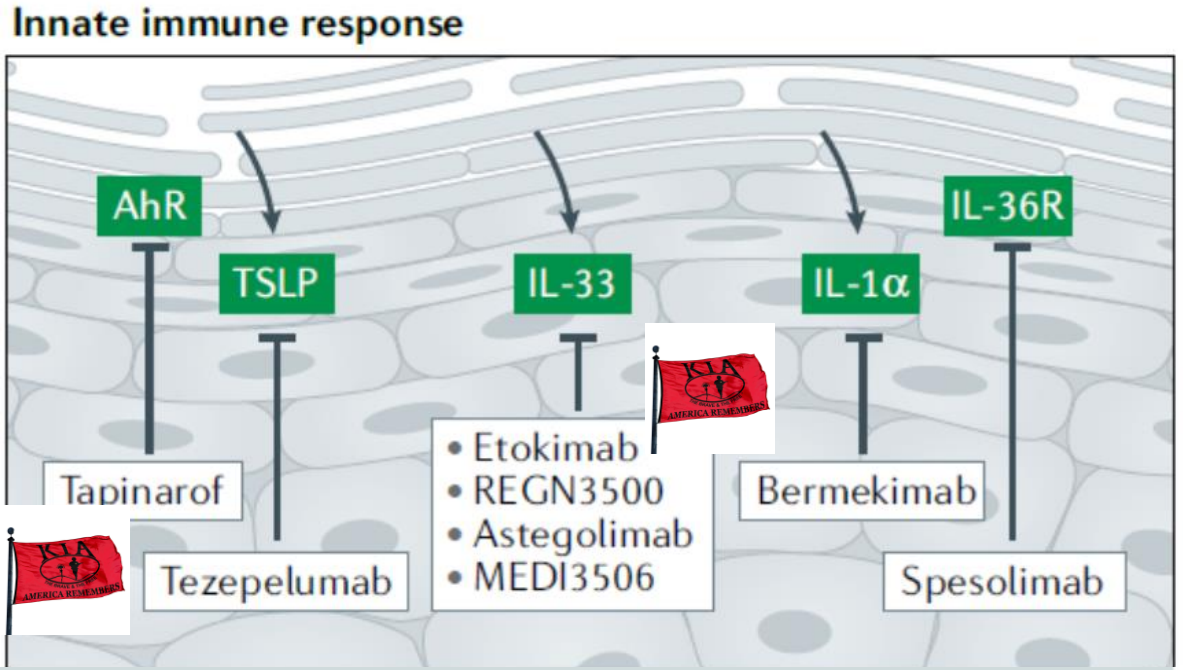
Respuesta innata: algunas decepciones....y nuevas esperanzas

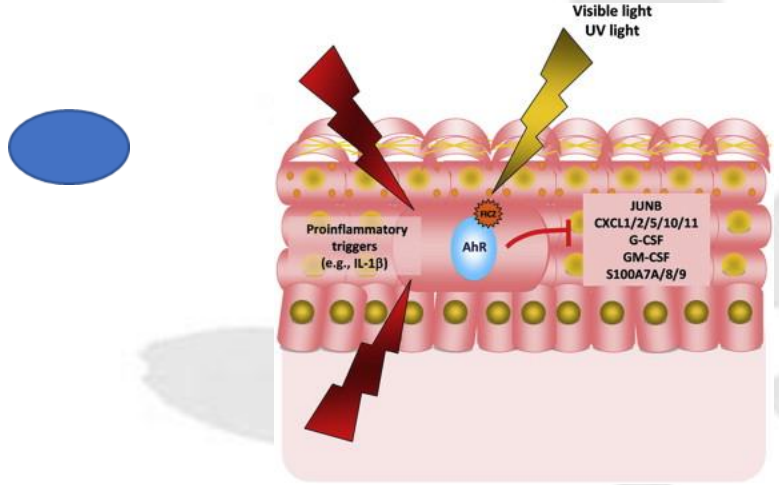




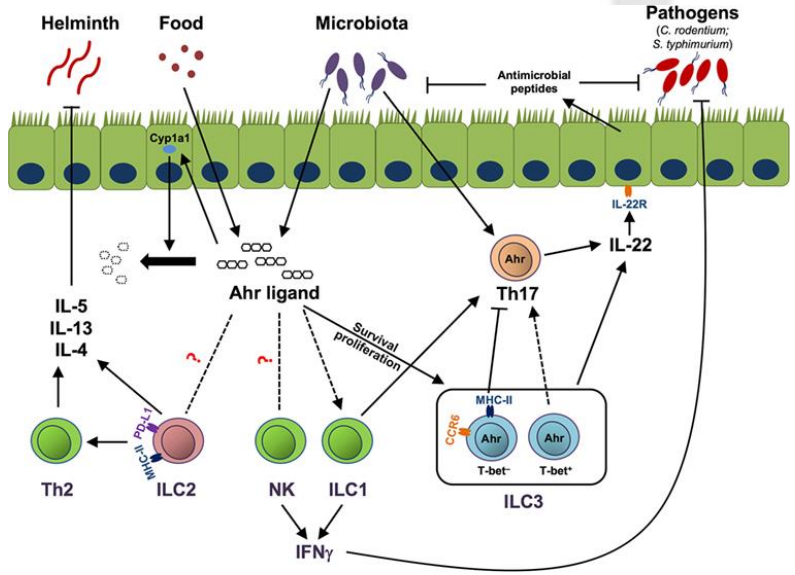
Targeting the innate immune response	Small molecule — topical	Tapinarof/benvitimod (Dermavant)	AhR agonist	IIb	NA
	Biologic — injection	Tezepelumab (Amgen/AstraZeneca)	TSLP	IIa	NCT02525094
		Etokimab (AnaptysBio)	IL-33	IIa	NCT03533751
		REGN3500 (Regeneron)	IL-33	IIa	NCT03738423
		Astegolimab (Genentech)	IL-33	IIa	NCT03747575
		MEDI3506 (MedImmune)	IL-33	IIa	NCT04212169
		Bermekimab (Janssen)	IL-1α	IIa	NCT03496974
		Spesolimab (Böhringer Ingelheim)	IL-36R	IIa	NCT03822832

https://doi.org/10.1038/s41573-021-00266-6

Tapinarof (GSK2894512 cream) for the treatment of atopic dermatitis



- Nonsteroidal topical agent known as therapeutic aryl hydrocarbon receptor (AhR) modulating agents.
- Binding the AhR and activating the AhR pathway in multiple cells and tissue-based systems
- **Controls the expression of IL-21 and IL-22 and plays an important role in the differentiation of T-helper 17 cells in vivo and in vitro**
- Antioxidant by inhibiting reactive oxygen species
- Inhibition pro-inflammatory vs immunosuppressive ??



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Am Acad Dermatol 2019;80:714-21.

A phase 2, randomized dose-finding study of tapinarof (GSK2894512 cream) for the treatment of atopic dermatitis

Johnny Peppers, PhD,[a] Amy S. Paller, MD,[b] Tomoko Maeda-Chubachi, MD, PhD,[c] Sterling Wu, PhD,[d] Kevin Robbins, BSc, LLM,[d] Kelly Gallagher, MS,[d] and John E. Kraus, MD, PhD[e]
Raleigh, Morrisville, and Research Triangle Park, North Carolina; Chicago, Illinois; and Collegeville, Pennsylvania

Tapinarof (GSK2894512 cream) for the treatment of atopic dermatitis

- Week 12 IGA responses were higher in the tapinarof groups versus the vehicle group, reaching statistical significance with tapinarof 1% twice daily
- 75%/90% improvement in EASI from baseline were significantly higher in the tapinarof groups (except 0.5% once daily and 0.5% twice daily),

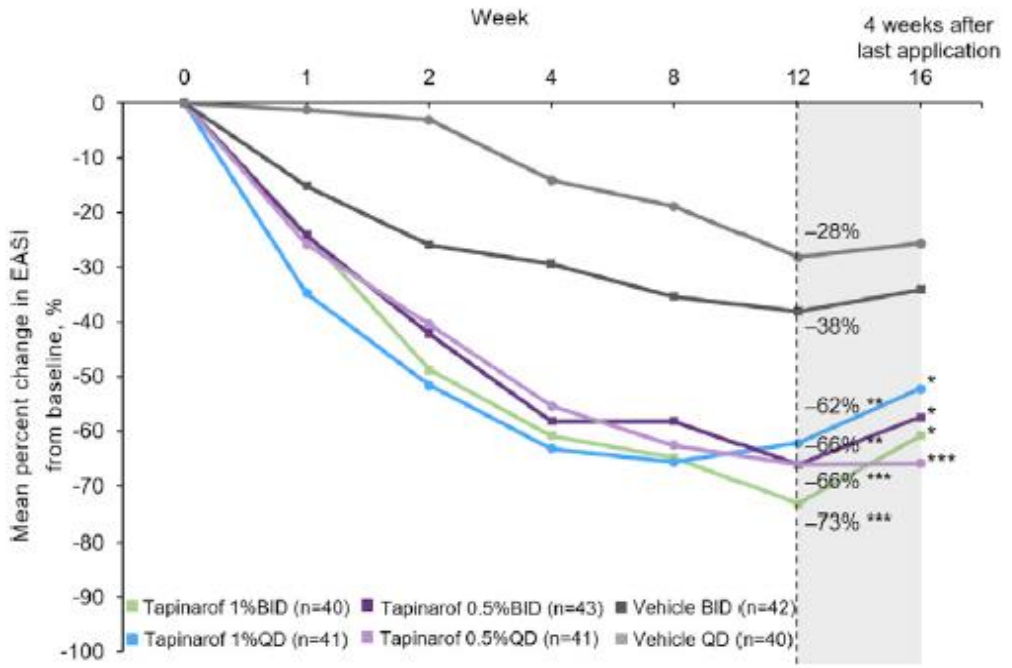

Fig 1. Mean percent change in EASI scores from baseline

FDA approved for psoriasis !!!!

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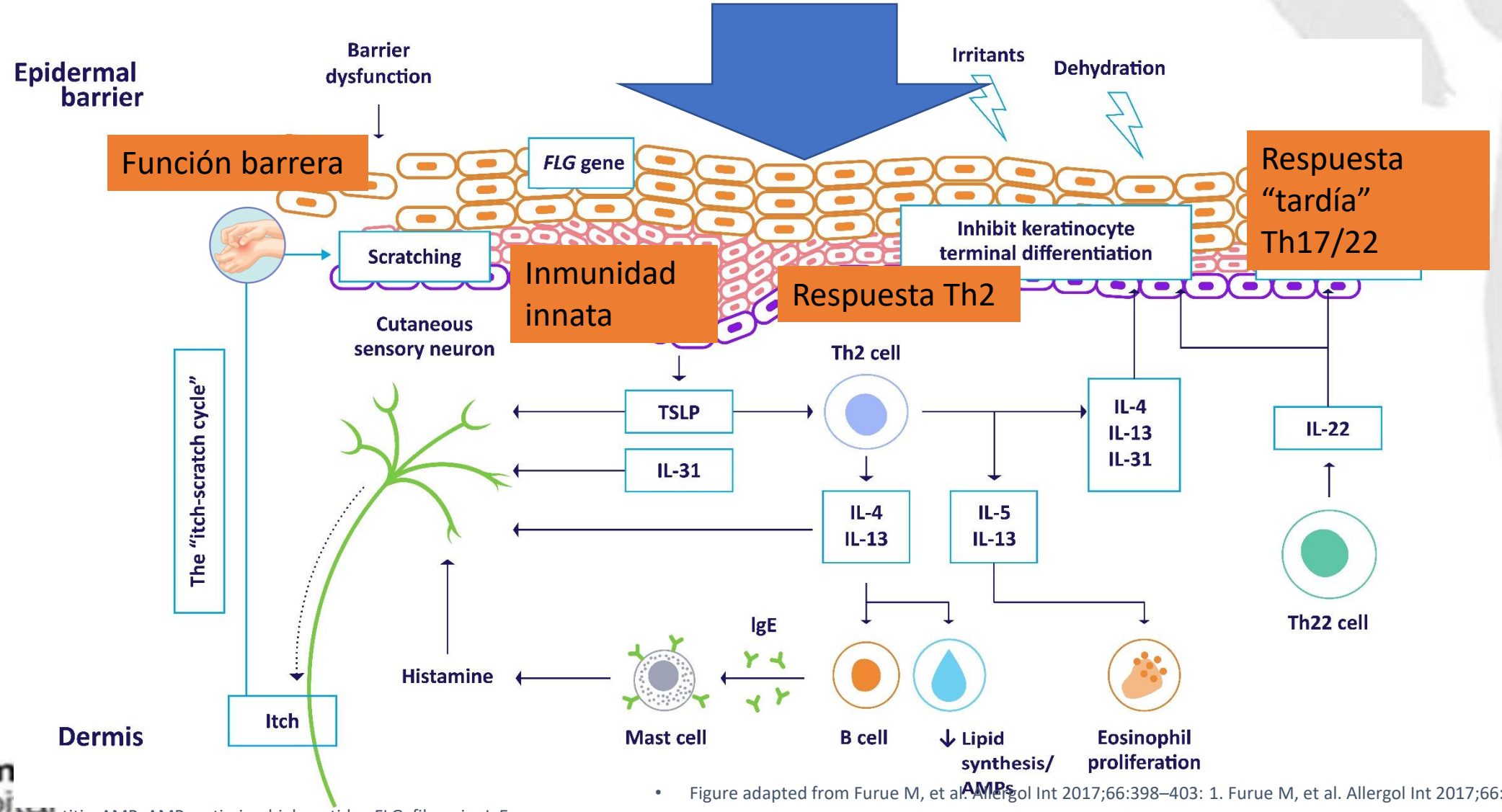
J Am Acad Dermatol 2021;84:632-8.)

Efficacy and patient-reported outcomes from a phase 2b, randomized clinical trial of tapinarof cream for the treatment of adolescents and adults with atopic dermatitis

Amy S. Paller, MD,[a] Linda Stein Gold, MD,[b] Jennifer Soung, MD,[c] Anna M. Tallman, PharmD,[d] David S. Rubenstein, MD, PhD,[e] and Melinda Gooderham, MD, FRCPC[f]
Chicago, Illinois; Detroit, Michigan; Long Beach, California; Durham, North Carolina; and Peterborough, Ontario, Canada

Fisiopatogenia de la Dermatitis atópica en 1 minuto



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		LY3471851 (Lilly)	rhIL-2 to T_{reg} cells	Ib	NCT04081350

Inmunidad innata/ adaptativa Th2

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https://doi.org/10.1038/s41573-021-00266-6

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		Etrasimod (Arena Pharma)	S1PR1, S1PR4, S1PR5	IIb	NCT04162769
		SCD-044 (Sun Pharma)	S1PR1	IIa	NCT04684485
		LC51-0255 (LG Chem)	S1PR1	I	NA
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		KT-474 (Kymera)	S1PR1	Ib	NCT04772885
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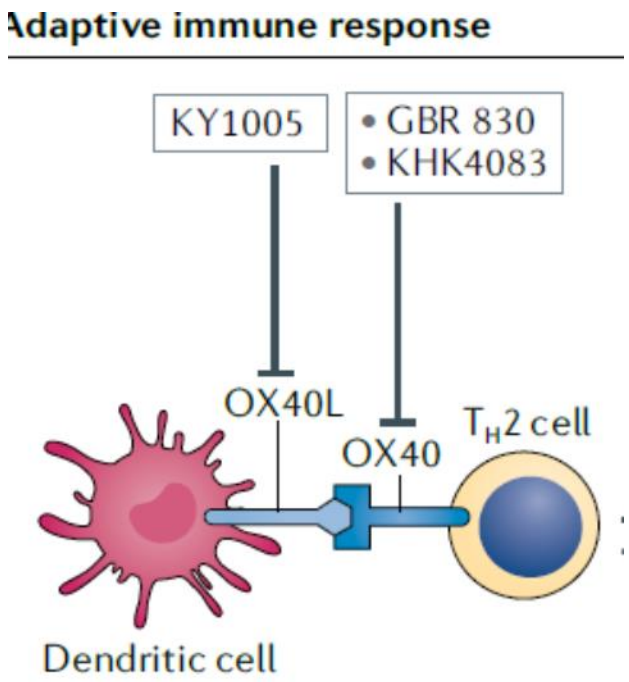
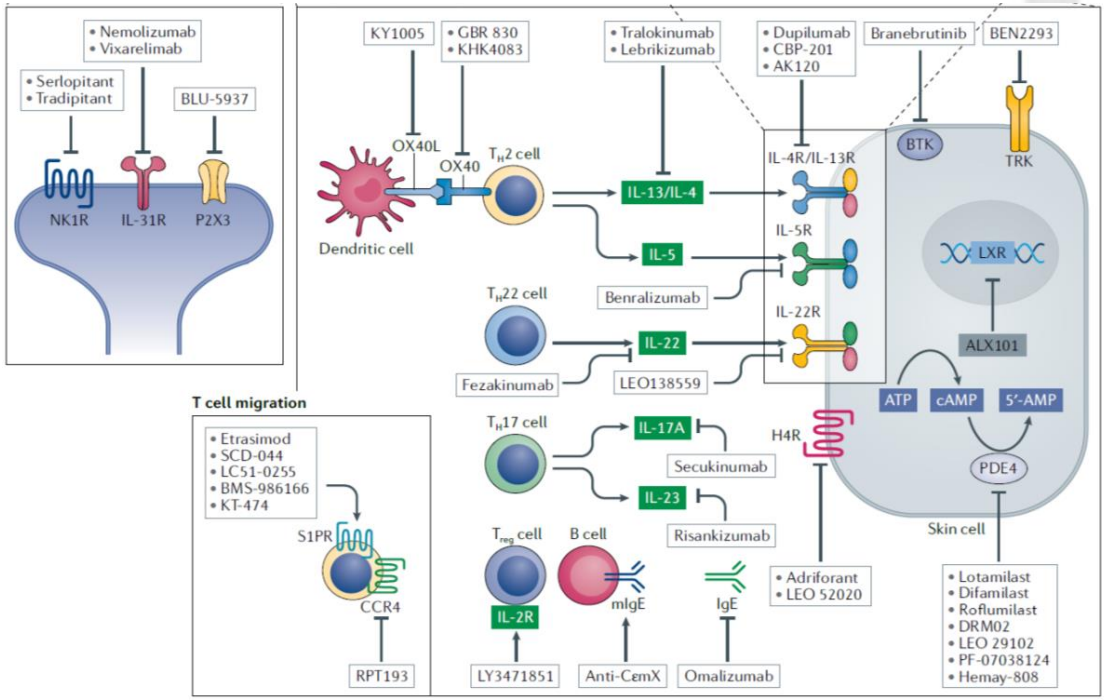
		HY209 (Shaperon)	GPCR19	IIa	NCT04530643
		VTP-38543 (Vitae Pharma)	Liver X receptor-β	I/II	NCT02655679
		ALX 101 (Ralexar)	Liver X receptor	II	NCT03859986

OX-OX40 pathway….¿la tercera via ?





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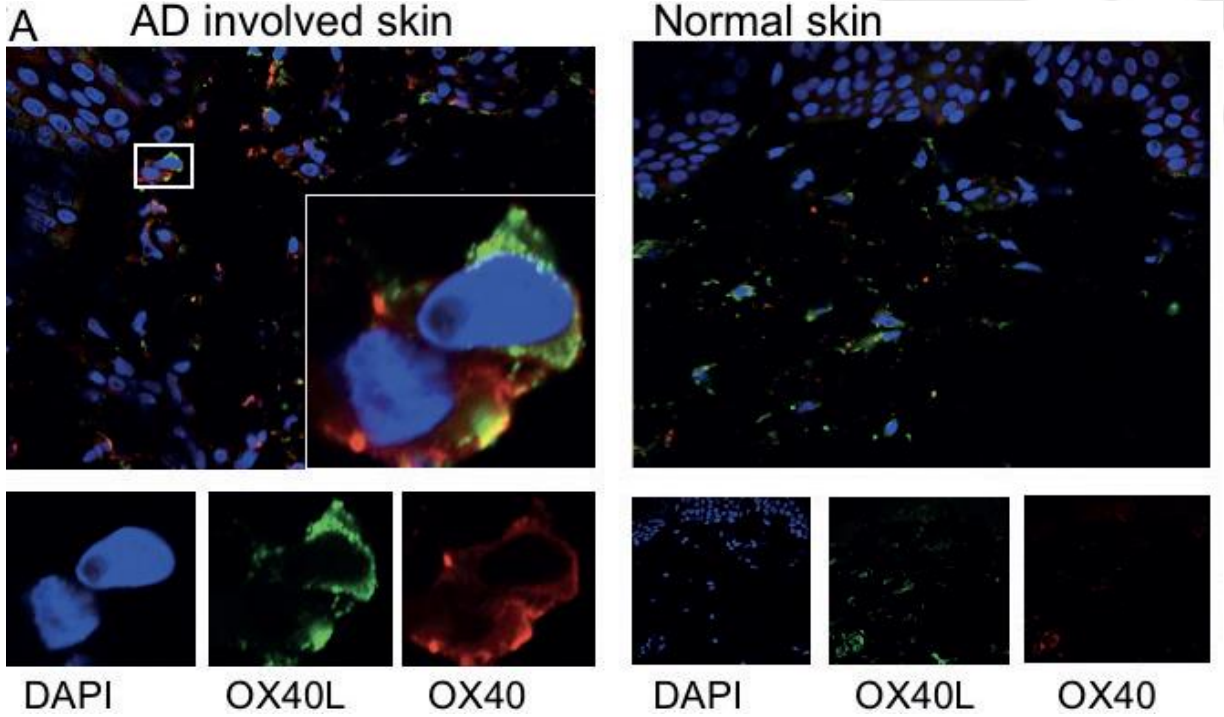
OX40/OX40L en DA

- OX40 expression is increased on skin homing T cells
- OX40 and OX40L are co-localized in the skin T-cell expression of OX40 and antigen-presenting cells
- *The signal through OX40 enhances T-cell clonal expansion and, especially, survival of TH2 cells*



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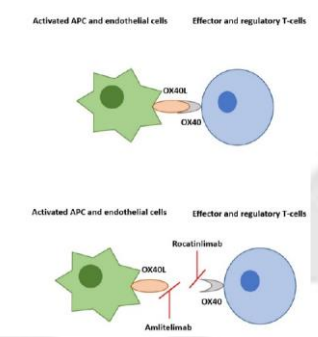
doi: 10.2340/00015555-3452
Acta Derm Venereol 2020; 100: adv00099

The OX40 Axis is Associated with Both Systemic and Local Involvement in Atopic Dermatitis

Julie Sophie Hohwü ELSNER[1,2], Michael CARLSSON[3], Julie Kristine STOUGAARD[2], Uffe NYGAARD[1], Matthias BUCHNER[4], Regina FÖLSTER-HOLST[4], Malene HVID[2,5], Christian VESTERGAARD[1], Mette DELEURAN[1] and Bent DELEURAN[2,6]
Departments of [1]Dermato-Venereology and [6]Rheumatology, Aarhus University Hospital, Departments of [2]Biomedicine and [5]Clinical Medicine, Aarhus University, Aarhus, [3]Agilent Technologies Denmark ApS, Glostrup, Denmark, and [4]Department of Dermatology, Allergology and Venereology, Kiel University Hospital, Kiel, Germany

Rocantilimab(anti OX 40) en AD



Rocatinlimab NCT03703102	2b	Multi-center, double-blind, placebo-controlled 274 subjects with moderate-to-severe AD Randomized 1:1:1:1:1 to: • rocatinlimab 150 mg SC Q4W • rocatinlimab 600 mg SC Q4W • rocatinlimab 300 mg SC Q2W • rocatinlimab 600 mg SC Q2W • placebo 18 weeks of treatment + 20 weeks of follow-up	% EASI change from baseline at week 16	% EASI change from baseline at week 16 (−48.3% to −61.1%) vs. placebo (−15.0%; all $p < 0.001$). ≥4-point improvement from baseline in pruritus NRS score (36.5% to 55.8%) vs. placebo (19.3%) A *post hoc* analysis reported EASI score improvements up to 20 weeks after treatment has ceased At week 18, most treatment-emergent adverse events were pyrexia and chills after the first administration of rocatinlimab, nasopharyngitis, and atopic dermatitis

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Review

OX40-OX40L Inhibition for the Treatment of Atopic Dermatitis—Focus on Rocatinlimab and Amlitelimab

Ana Maria Lé [1] and Tiago Torres [1,2,*]

Telazorlimab(ISB 80) – anti OX 40-

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Phase 2b Study to Evaluate the Efficacy and Safety of ISB 830 in Adults With Moderate to Severe Atopic Dermatitis

The safety and scientific validity of this study is the responsibility of the study sponsor and investigators. Listing a study does not mean it has been evaluated by the U.S. Federal Government. Read our disclaimer for details.

ClinicalTrials.gov Identifier: NCT03568162

Recruitment Status : Completed
First Posted : June 26, 2018
Results First Posted : June 28, 2022
Last Update Posted : August 23, 2022

View this study on Beta.ClinicalTrials.gov

Sponsor:

Ichnos Sciences SA

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Amlitelimab (anti OX 40L) en AD

Amlitelimab NCT03754309	2a	Multi-center, parallel group, double-blind, randomized, placebo controlled 89 moderate-to-severe AD patients Randomized 1:1:1 to: - amlitelimab 200 mg loading dose + 100 mg Q4W - amlitelimab 500 mg loading dose + 250 mg Q4W - placebo 12 weeks of treatment + 24 weeks of follow-up	% EASI change from baseline to day 113 Incidence of treatment-emergent adverse events	Mean percentage change from baseline in EASI ate week 16: amlitelimab low-dose (−80.1%) and high-dose (−69.9%) vs. placebo (−49.4%; $p = 0.009$ and $p = 0.072$, respectively). % EASI-75: 59.3% in amlitelimab low-dose group, 51.9% in amlitelimab high-dose group and 25.0% in placebo group. Pruritus NRS ≥ 4-point improvement at week 16: 57.9% in amlitelimab low-dose, 62.5% in amlitelimab high-dose, and 38.1% in placebo group. No hypersensitivity or tolerability events were reported.

AD—atopic dermatitis; EASI—Eczema Area and Severity Index; NRS—numerical rating scale; Q2W—every 2 weeks;

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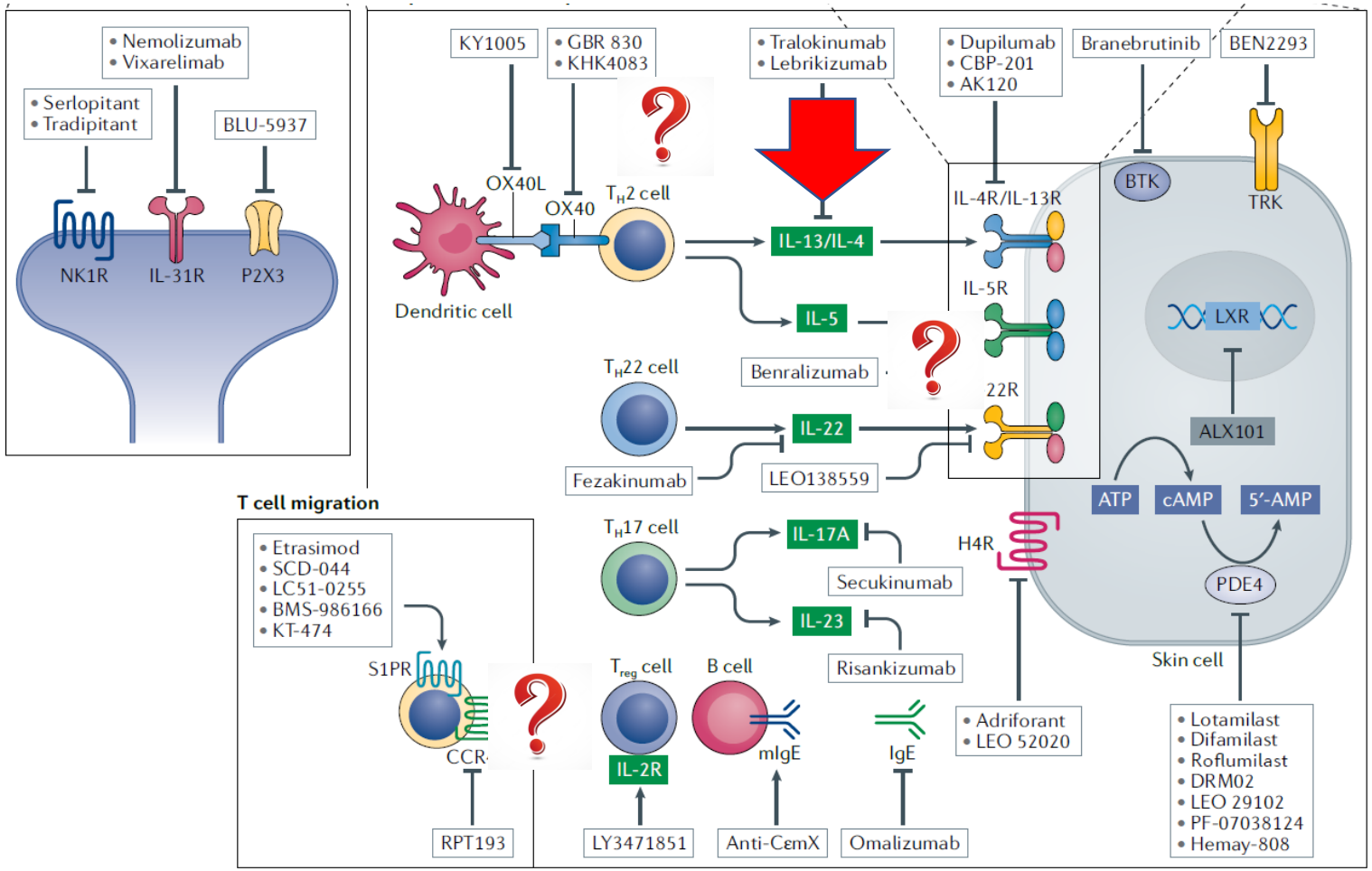
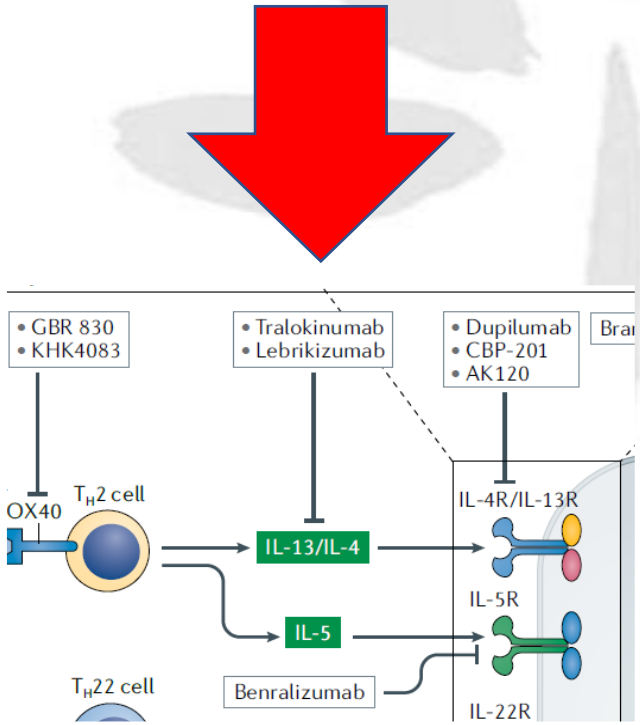
Review

OX40-OX40L Inhibition for the Treatment of Atopic Dermatitis—Focus on Rocatinlimab and Amlitelimab

Ana Maria Lé [1] and Tiago Torres [1,2,*]

Vía IL4/13


• Nemolizumab
• Vixarelimab
• Serlopitant
• Tradipitant
BLU-5937
NK1R
IL-31R
P2X3
KY1005
• GBR 830
• KHK4083
• Tralokinumab
• Lebrikizumab
• Dupilumab
• CBP-201
• AK120
Branebrutinib
BEN2293
OX40L
OX40
TH2 cell
Dendritic cell
IL-13/IL-4
IL-4R/IL-13R
BTK
TRK
IL-5
IL-5R
LXR
Benralizumab
TH22 cell
IL-22
22R
ALX101
Fezakinumab
LEO138559
ATP
cAMP
5′-AMP
T cell migration
TH17 cell
IL-17A
H4R
PDE4
• Etrasimod
• SCD-044
• LC51-0255
• BMS-986166
• KT-474
Secukinumab
IL-23
S1PR
Treg cell
B cell
Risankizumab
Skin cell
CCR
IL-2R
mIgE
IgE
• Adriforant
• LEO 52020
• Lotamilast
• Difamilast
• Roflumilast
• DRM02
• LEO 29102
• PF-07038124
• Hemay-808
RPT193
LY3471851
Anti-CεmX
Omalizumab


• GBR 830
• KHK4083
• Tralokinumab
• Lebrikizumab
• Dupilumab
• CBP-201
• AK120
OX40
TH2 cell
IL-13/IL-4
IL-4R/IL-13R
IL-5
IL-5R
Benralizumab
TH22 cell
IL-22R

Vía IL4/13

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V18 IL4/13

Nuevos anti IL 4/13

Table 14. Clinical trials targeting IL-4 e IL-13 in AD.

Target Molecule	Clin Trial Gov	Type of Study	Status
	IL-4Rα		
Anti-IL-4α monoclonal antibody Dupilumab		FDA approval for AD March 2017	
Anti-IL-4α monoclonal antibody CBP-201	NCT04444752	Phase II for AD	Completed
Anti-IL-4α monoclonal antibody CBP-201	NCT05017480	Phase II for AD	Recruiting
Anti-IL-4α monoclonal antibody AK120 (Akesobio)	NCT04256174	Phase Ib for AD	Completed
Anti-IL-4α monoclonal antibody AK120 (Akesobio)	NCT05048056	Phase II for AD	Recruiting

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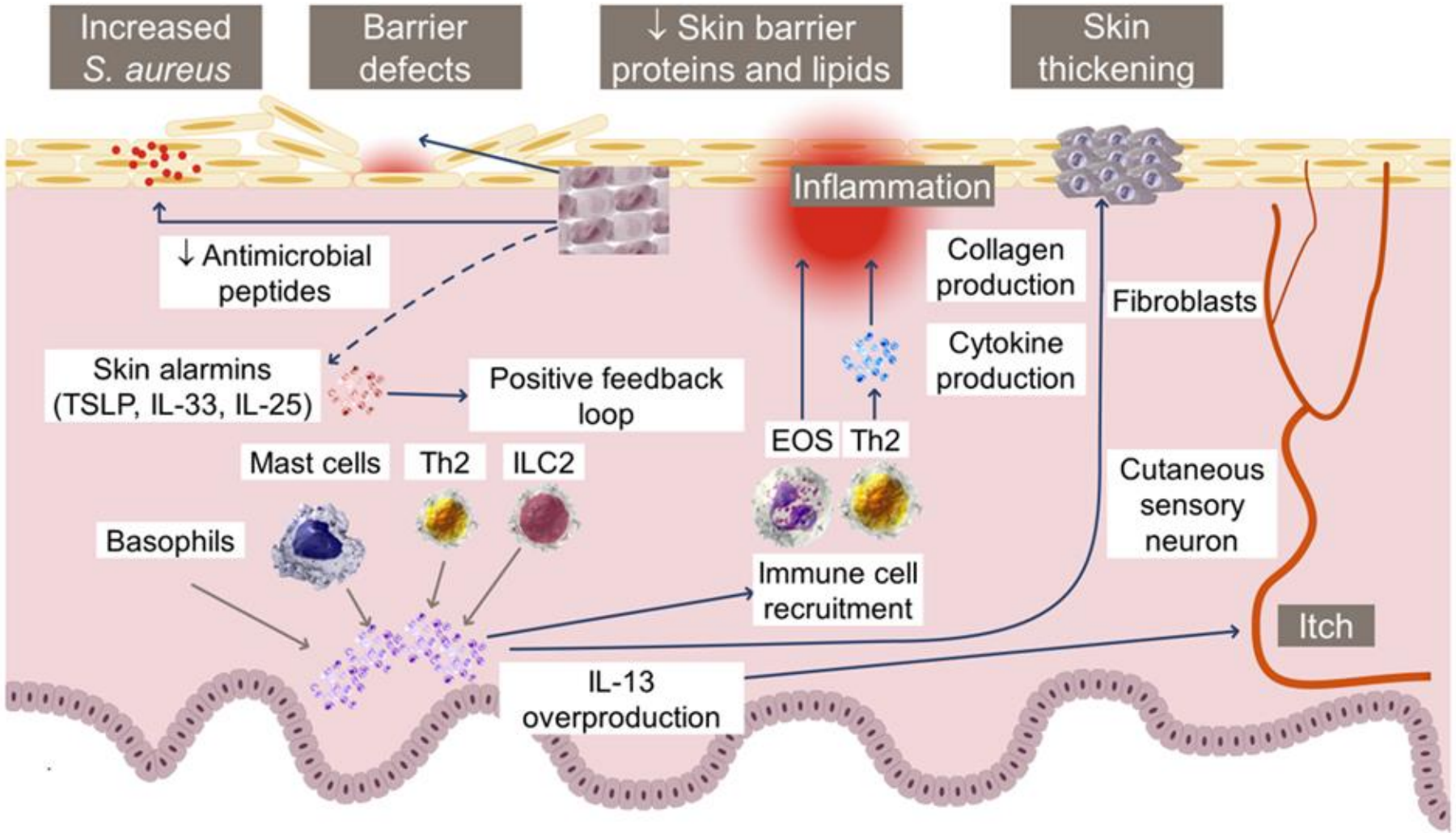
Review

Novel Therapeutic Strategies in the Topical Treatment of Atopic Dermatitis

Lorenzo Maria Pinto [1,2], Andrea Chiricozzi [1,2,*], Laura Calabrese [1,2], Maria Mannino [1,2] and Ketty Peris [1,2]

Pharmaceutics **2022**, *14*, 2767. https://doi.org/10.3390/pharmaceutics14122767

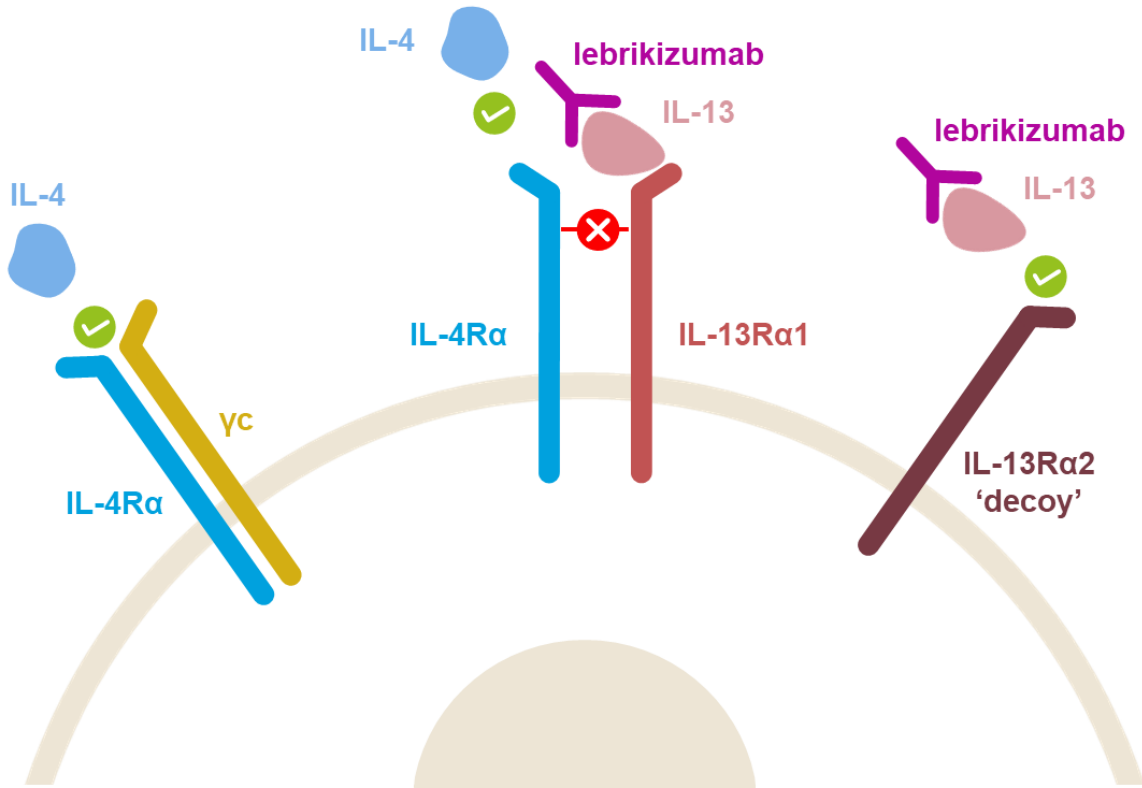
IL-13 en dermatitis atópica



IL-13 is overexpressed by different cell types in the skin of AD. This Th2 cytokine has a wide impact, including the decrease of the barrier function, inducing itch, and affecting the microbiome, particularly *S. aureus*. Adapted from Bieber T. *Allergy*. 2020;75:54-62.

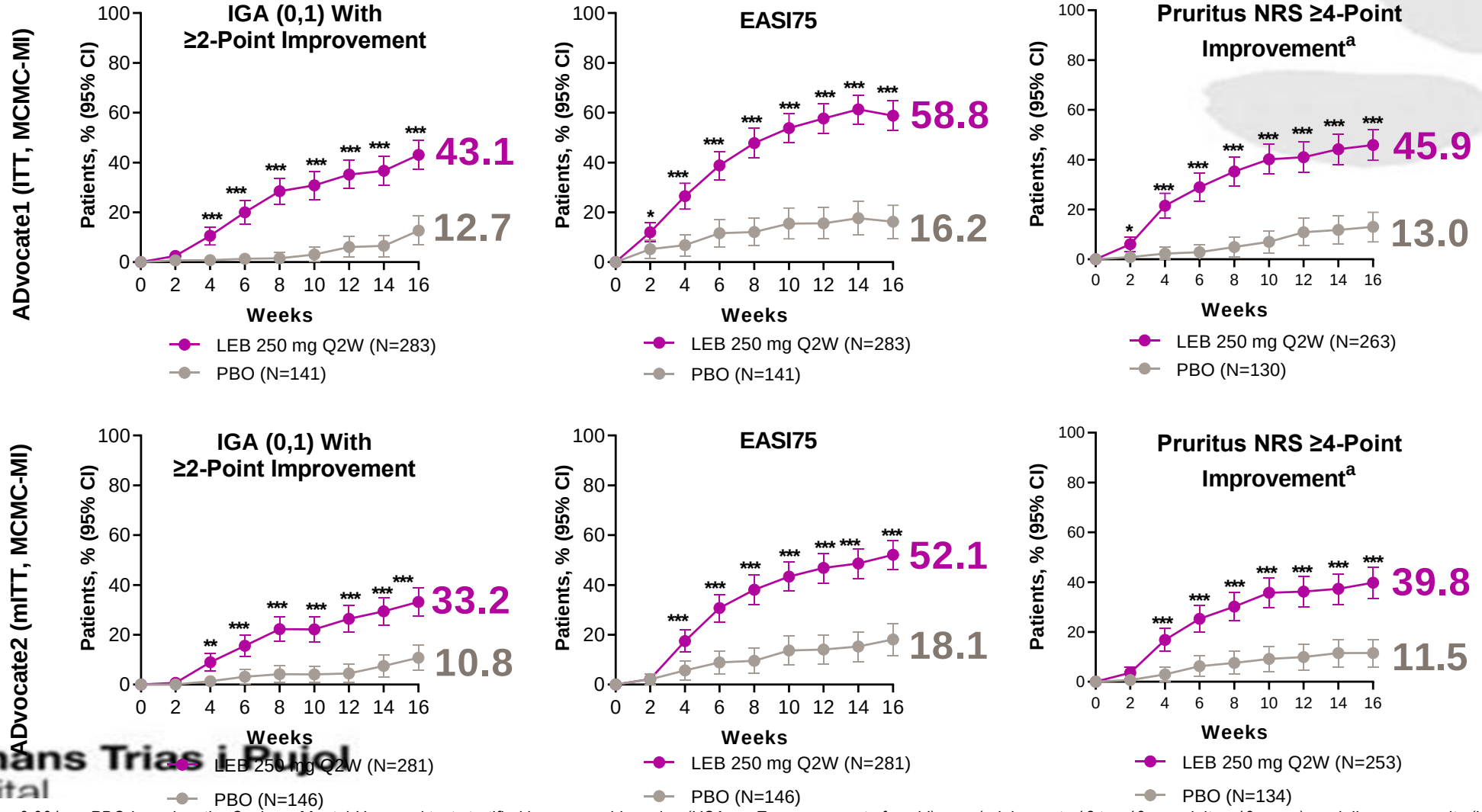
Lebrikizumab. MoAb anti Il13

- Lebrikizumab is a novel, high-affinity immunoglobulin G4 monoclonal antibody targeting interleukin (IL)-13
- Lebrikizumab selectively prevents formation of the IL-13Rα1/IL-4Rα heterodimer receptor signaling complex, thus blocking IL-13 signaling[1,2]
- Lebrikizumab does not prevent the binding of IL-13 to the IL-13Rα2 (decoy) receptor, which allows the internalization of IL-13 into the cell[3]



1. Simpson EL, et al. *J Am Acad Dermatol*. 2018;78:863-871.e11.
2. Gonçalves F, et al. *Drugs Context*. 2021;10:2021-1-7.
3. Wulur I, et al. Presented at 4th Inflammatory Skin Disease Summit. 2021.
IL=interleukin

Week 16 Efficacy Endpoints



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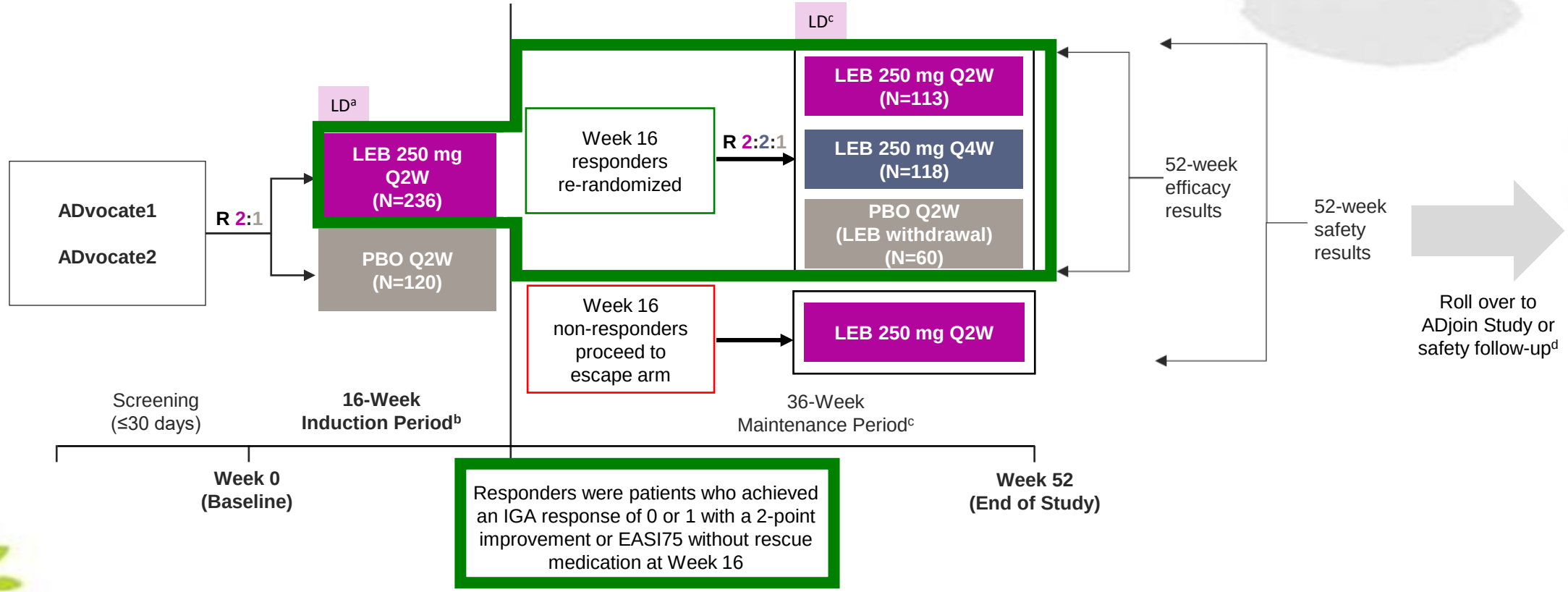
* p<0.05; ** p<0.01; *** p<0.001 vs. PBO based on the Cochran-Mantel-Haenszel test stratified by geographic region (USA vs. Europe vs. rest of world), age (adolescents 12 to <18 vs. adults ≥18 years), and disease severity (baseline IGA score of 3 vs. 4). Data after rescue medication or treatment discontinuation due to lack of efficacy were set to baseline values; missing data due to other reasons were imputed with MCMC-MI within treatment arms. [a] For patients with Pruritus NRS ≥4 at baseline

CI=confidence interval; EASI75=75% improvement from baseline in Eczema Area and Severity Index score; IGA=Investigator's Global Assessment; ITT=Intent-to-Treat; LEB=lebrikizumab; MCMC-MI=Markov Chain Monte Carlo multiple imputation; mITT=modified ITT; NRS=Numeric Rating Scale; PBO=placebo; Q2W=every 2 weeks

Study Design

ADvocate1 and ADvocate2



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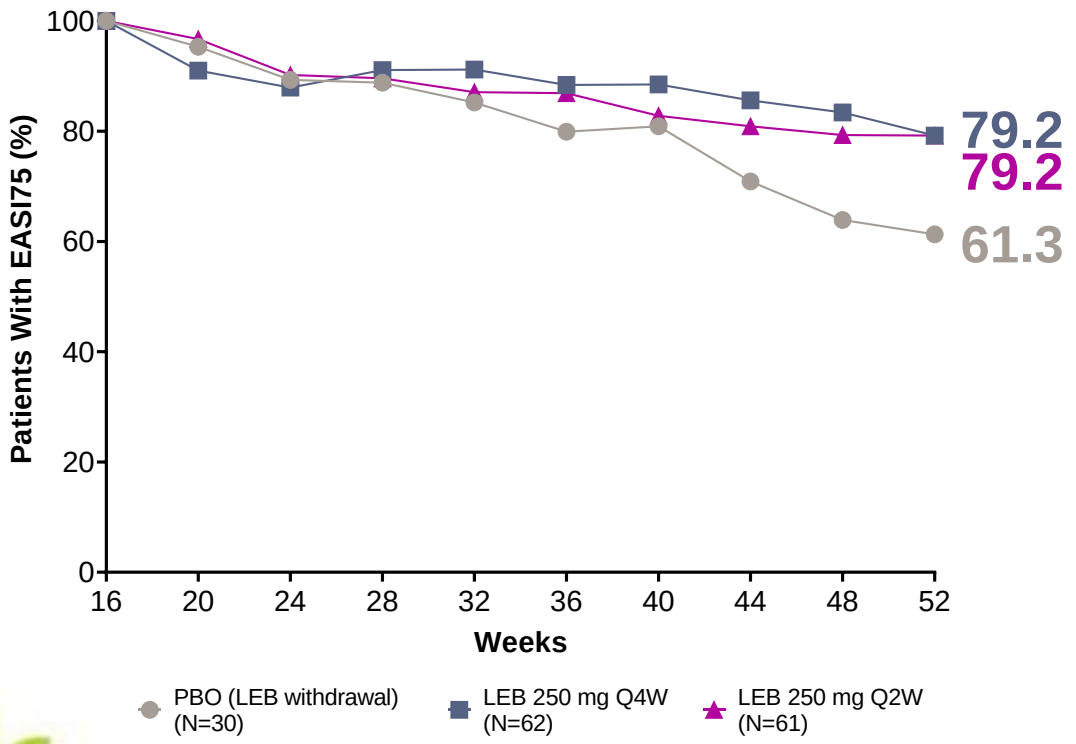
[a] LEB-treated patients received a 500-mg LD at Weeks 0 and 2; [b] Patients who used rescue therapy (including topical) during the Induction Period were considered to be non-responders; [c] Responders who received PBO and were re-randomized to LEB received an LD of LEB 500 mg at Week 16 or at Weeks 16 and 18, based on the active treatment group assigned in the Maintenance Period; [d] Patients who completed the study were offered treatment in ADjoin; otherwise, patients participated in a safety follow-up 12 weeks after their last dose

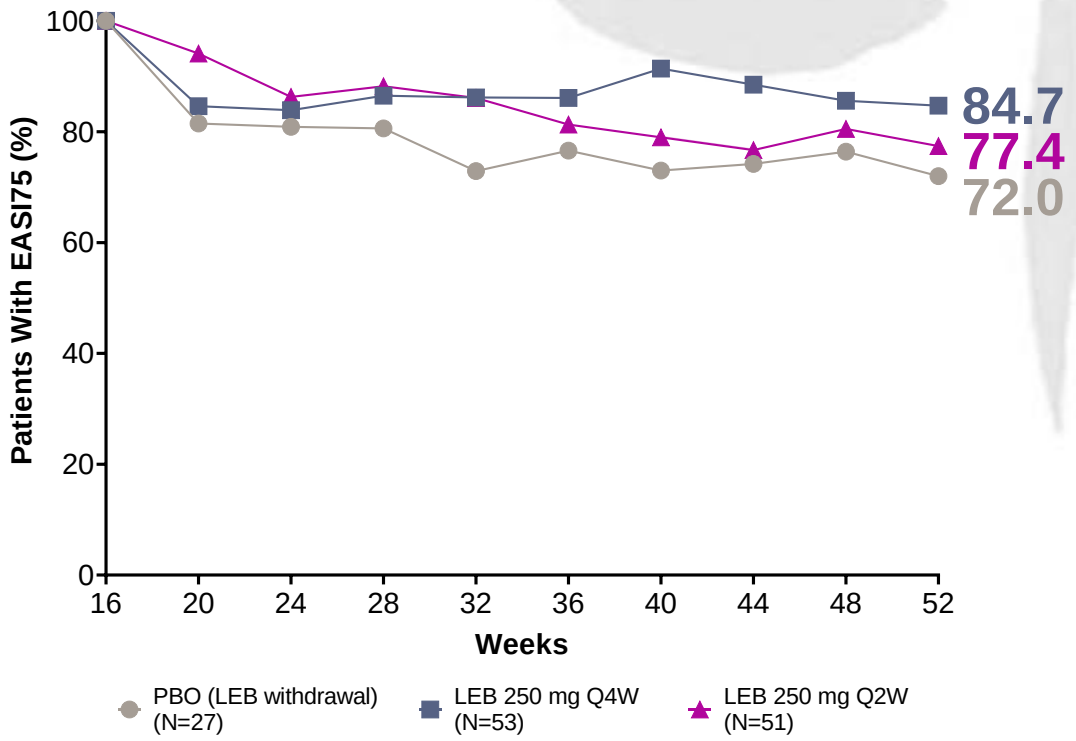
EASI75=75% improvement from baseline in Eczema Area and Severity Index score; IGA=Investigator's Global Assessment; LD=loading dose; LEB=lebrikizumab; PBO=placebo; Q2W=every 2 weeks; Q4W=every 4 weeks; R=randomization

Maintenance of EASI75 Over 52 Weeks

ADvocate1 (MPP,[a] MCMC-MI)



ADvocate2 (mMPP,[a] MCMC-MI)



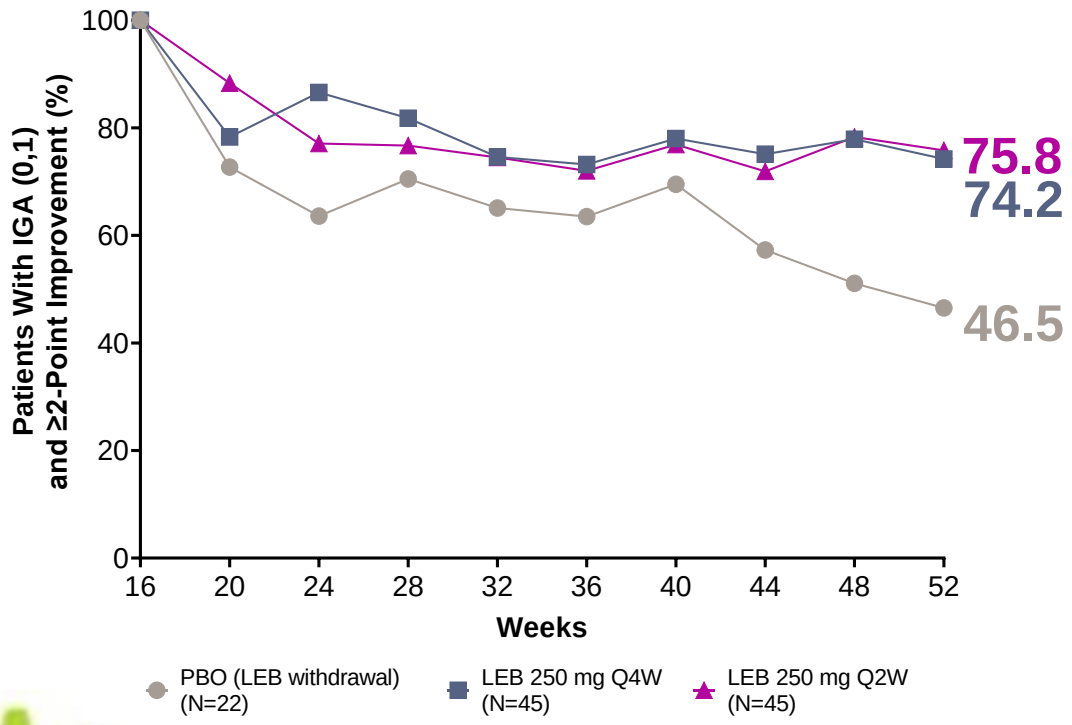
Note: Patients who received systemic rescue medication, discontinued treatment due to lack of efficacy, or transferred to the escape arm had values set to their baseline value subsequent to this time through Week 52; patients who received topical rescue medication or discontinued treatment due to other reasons had values set to missing subsequent to this time through Week 52; all the missing data were imputed with MCMC-MI

[a] Patients who achieved EASI75 at Week 16

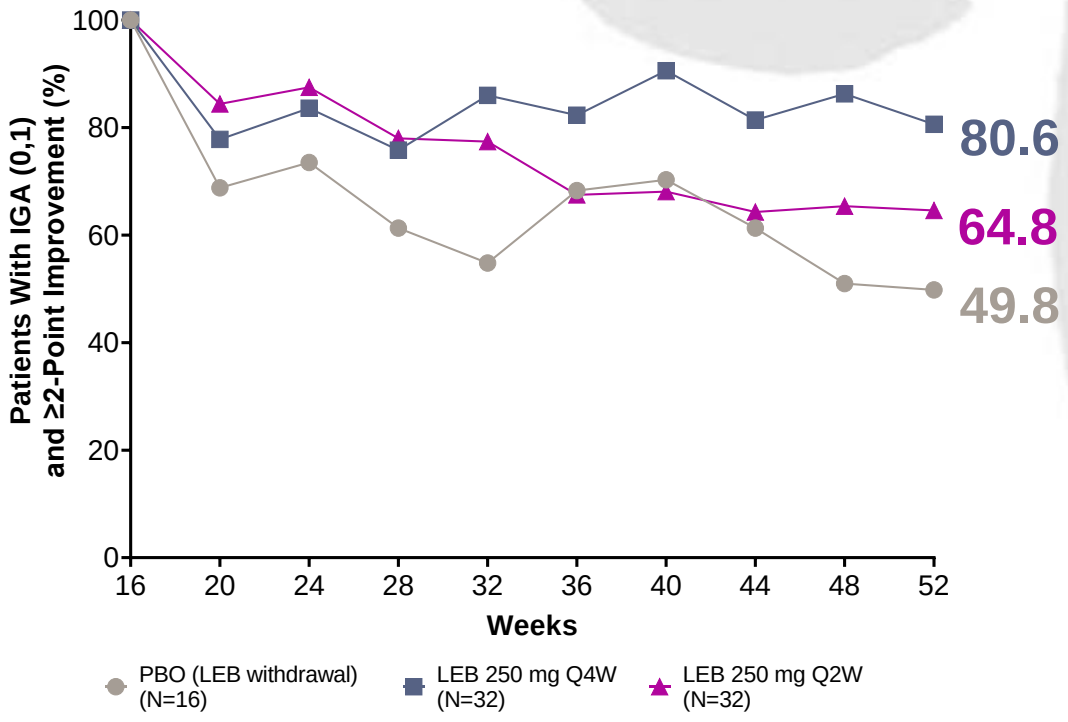
EASI75=75% improvement from baseline in Eczema Area and Severity Index score; LEB=lebrikizumab; MCMC-MI=Markov Chain Monte Carlo multiple imputation; mMPP=modified MPP; MPP=Maintenance Primary Population; PBO=placebo; Q2W=every 2 weeks; Q4W=every 4 weeks

Maintenance of IGA (0,1) and ≥2-Point Improvement Over 52 Weeks

ADvocate1 (MPP,[a] MCMC-MI)



ADvocate2 (mMPP,[a] MCMC-MI)



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Note: Patients who received systemic rescue medication, discontinued treatment due to lack of efficacy, or transferred to the escape arm had values set to their baseline value subsequent to this time through Week 52; patients who received topical rescue medication or discontinued treatment due to other reasons had values set to missing subsequent to this time through Week 52; all the missing data were imputed with MCMC-MI

[a] Patients who achieved IGA (0,1) at Week 16

IGA=Investigator's Global Assessment; LEB=lebrikizumab; MCMC-MI=Markov Chain Monte Carlo multiple imputation; mMPP=modified MPP; MPP=Maintenance Primary Population; PBO=placebo; Q2W=every 2 weeks; Q4W=every 4 weeks

Efficacy of Lebrikizumab in Patients Who Did Not Achieve Protocol-Defined Criteria for Response After Initial 16 Weeks of Therapy

42152

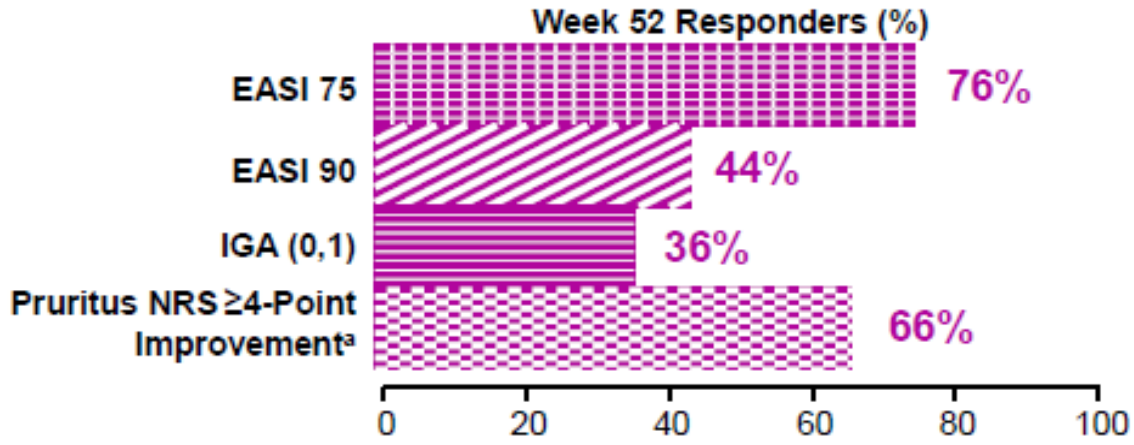
Emma Guttman-Yassky,[1] David Rosmarin,[2] Jacob P. Thyssen,[3] Stephan Weidinger,[4] Thomas Bieber,[5] Hany Elmaraghy,[6] Amber Reck Atwater,[6] Evangeline Pierce,[6] Chenjia Xu,[6] Helena Agell,[7] Eric Simpson[8]

[1]Icahn School of Medicine at Mount Sinai, New York, USA; [2]Indiana University School of Medicine, Indianapolis, USA; [3]Bispebjerg Hospital, University of Copenhagen, Copenhagen, Denmark; [4]University Hospital Schleswig-Holstein, Kiel, Germany; [5]University Hospital of Bonn, Bonn, Germany; [6]Eli Lilly and Company, Indianapolis, USA; [7]Almirall, S.A., Barcelona, Spain; [8]Oregon Health & Science University, Portland, USA

SUMMARY OF KEY FINDINGS

Pooled ADvocate1&2 MEP: LEB Q2W Weeks 16-52

Patients with AD who were considered per-protocol non-responders at Week 16 improved over the long term with **lebrikizumab** treatment



[a] In patients who had Pruritus NRS ≥4 points at baseline

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AAD 2023

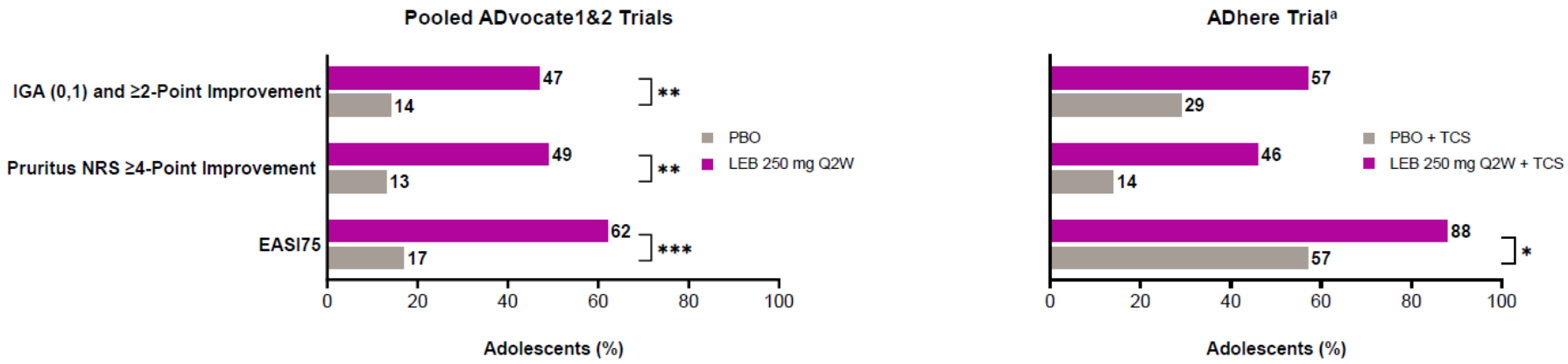
Efficacy of Lebrikizumab in Adolescent Patients With Moderate-to-Severe Atopic Dermatitis: 16-Week Results From Three Randomized Phase 3 Clinical Trials

43072

Adelaide Hebert,[1] Carsten Flohr,[2] H. Chih-ho Hong,[3] Alan Irvine,[4] Evangeline Pierce,[5] Hany Elmaraghy,[5] Wen Xu,[5] Sreekumar Pillai,[5] Zach Dawson,[5] Elaine Siegfried,[6] Stephan Weidinger[7]
[1]UTHealth McGovern Medical School, Houston, USA; [2]St John's Institute of Dermatology, King's College London, London, UK; [3]University of British Columbia, and Probity Medical Research, British Columbia, Canada; [4]Children's Health Ireland, Dublin, Ireland; [5]Eli Lilly and Company, Indianapolis, USA; [6]Saint Louis University, St. Louis, USA; [7]University Hospital Schleswig-Holstein, Kiel, Germany

SUMMARY OF KEY FINDINGS

Lebrikizumab, with or without TCS, demonstrated clinical efficacy at 16 weeks in adolescents with moderate-to-severe AD



* p<0.05; ** p<0.01; *** p<0.001 vs. PBO
[a] ADhere included TCS for both the LEB and PBO groups

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AAD 2023

Eblasakimab

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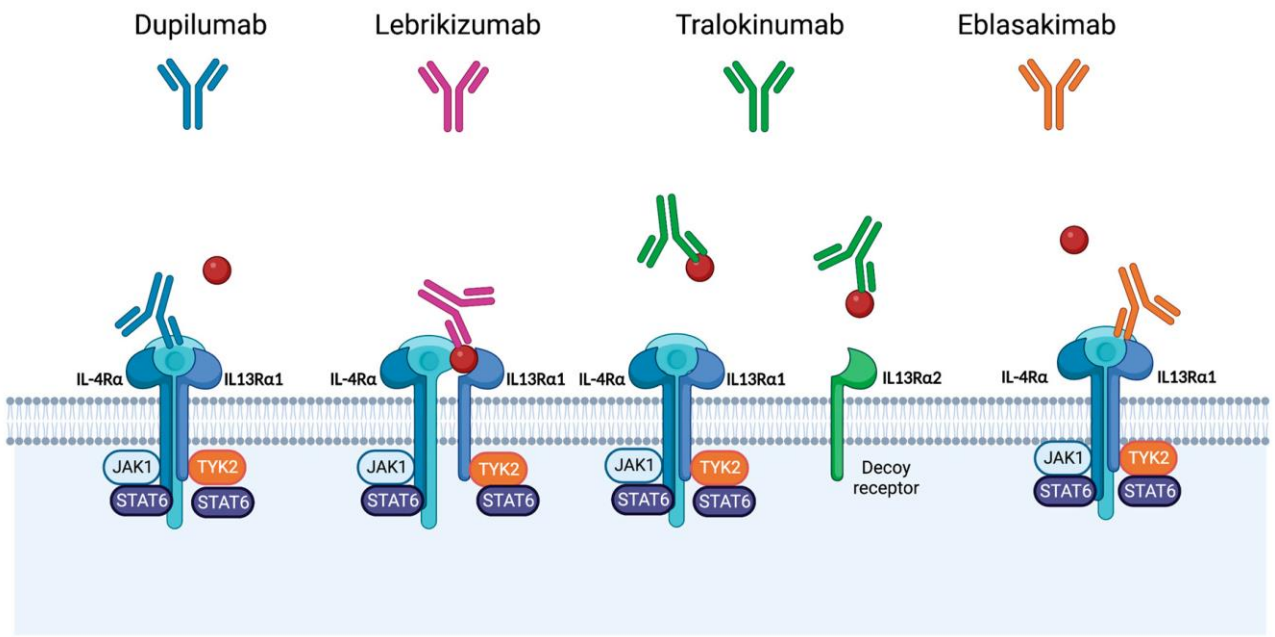
- Hotbed/Location (693,737)
- Career Advice (3,784)

ASLAN Pharmaceuticals Announces Completion of Recruitment in Phase 2b TREK-AD Study of Eblasakimab in Atopic Dermatitis Patients

Published: Feb 24, 2023

Eblasakimab
is a monoclonal antibody that targets the IL-13R1, a subunit of the type 2 receptor , interfering with the signaling of IL-13 and IL-4

EASI 75 was achieved in 50% of patients in the 200 mg group, 57% in the 400 mg group, and 50% in the 600 mg group, as opposed to 13% in the placebo group (p = 0.018



Pharmaceutics **2023**, *15*, 568. https://doi.org/10.3390/pharmaceutics15020568

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pharmaceutics MDPI

Review

Targeting Interleukin 13 for the Treatment of Atopic Dermatitis

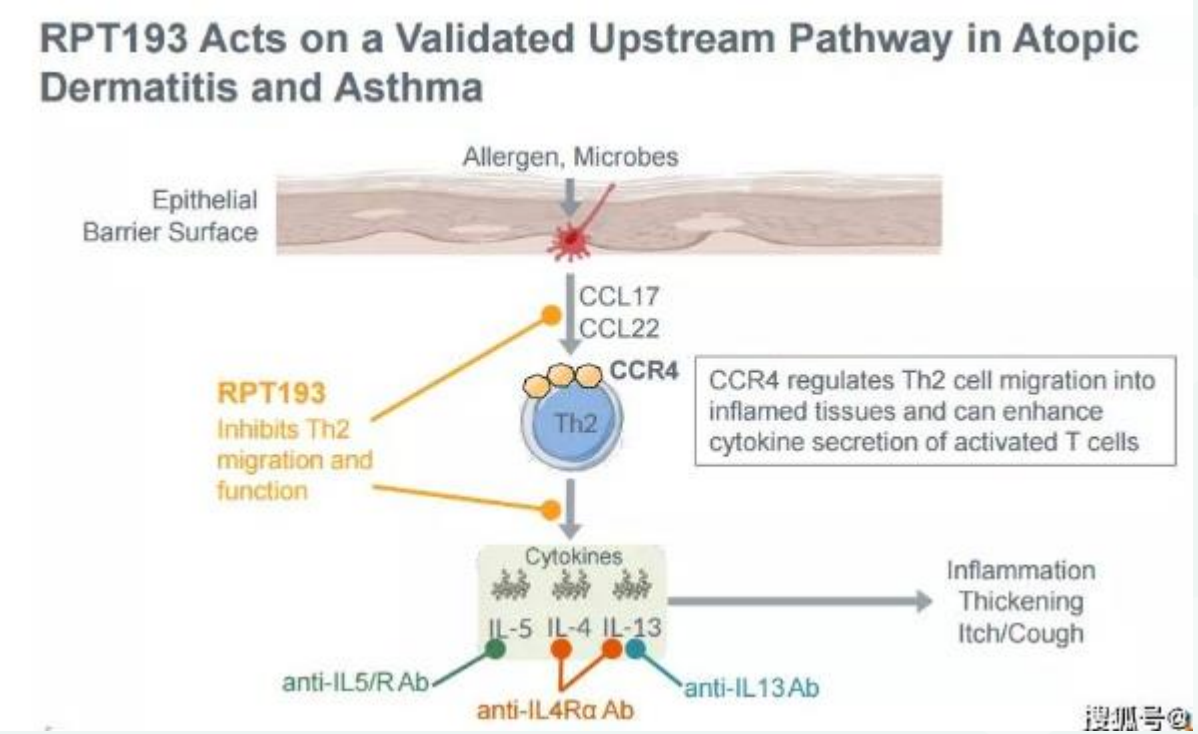
Yuliya Lytvyn [1] and Melinda Gooderham [2,3,4,*]

https://www.biospace.com/article/releases/aslan-pharmaceuticals-announces-completion-of-recruitment-in-phase-2b-trek-ad-study-of-eblasakimab-in-atopic-dermatitis-patients/

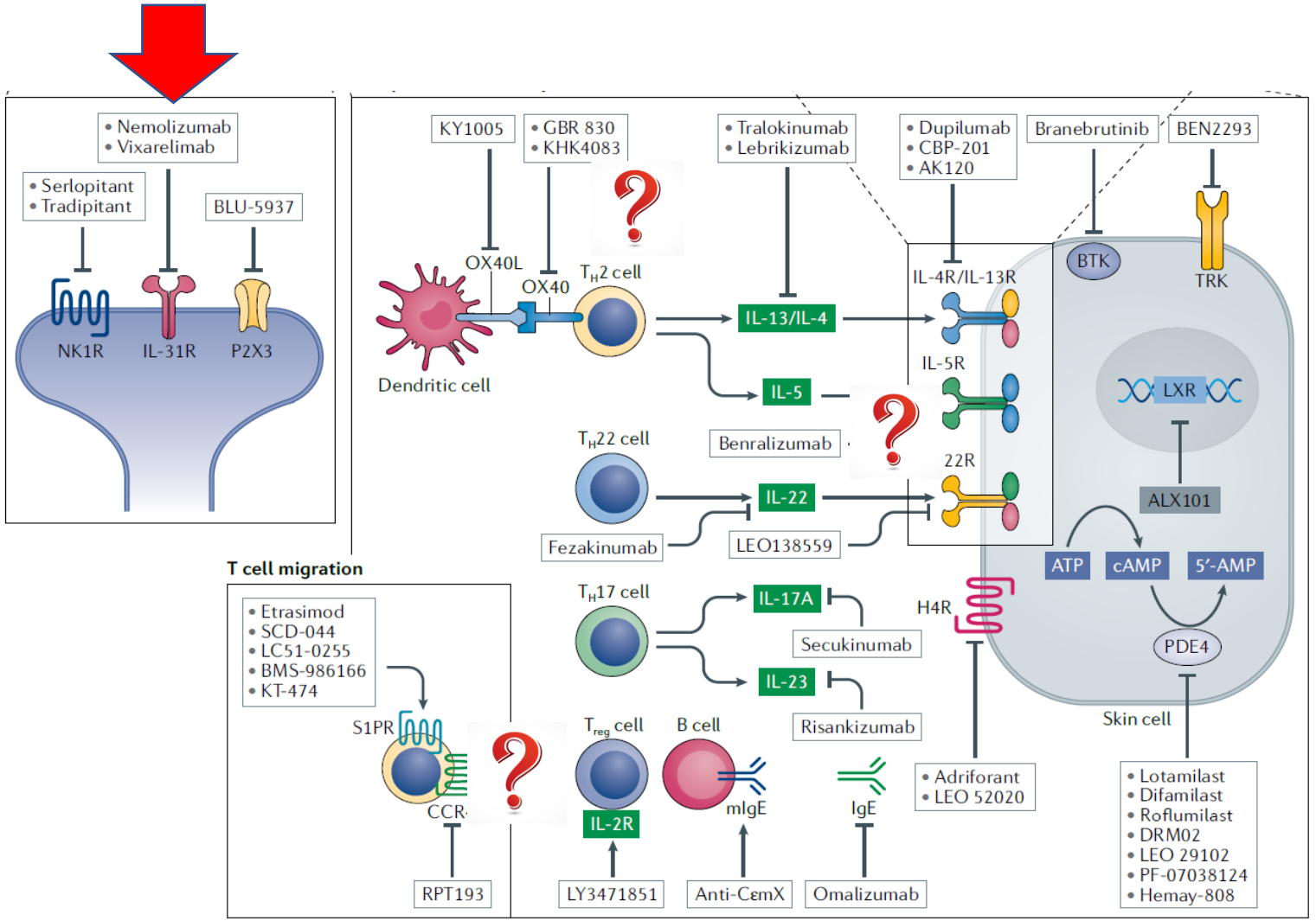
RPT193

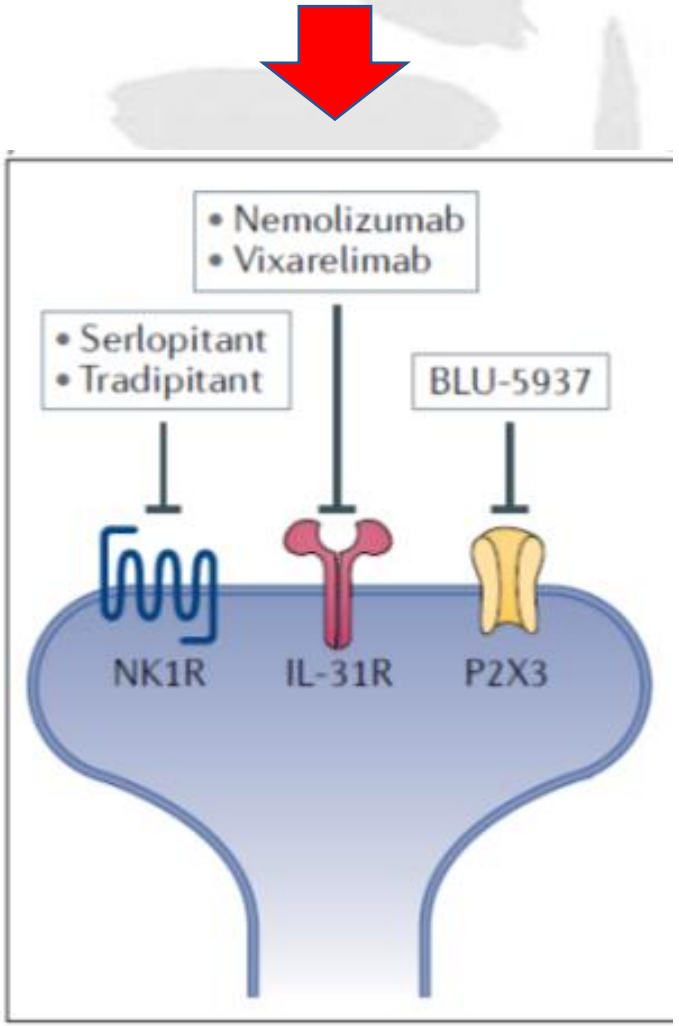
RPT193 is an orally active inhibitor of CCR4, blocks the recruitment of Th2 inflammatory immune cells into inflamed tissues. RPT193 can be used for allergic inflammation in atopic dermatitis, asthma, and other diseases research.

Phase 2 development
Administered oral
Indications seeking:
Adults With Atopic Dermatitis

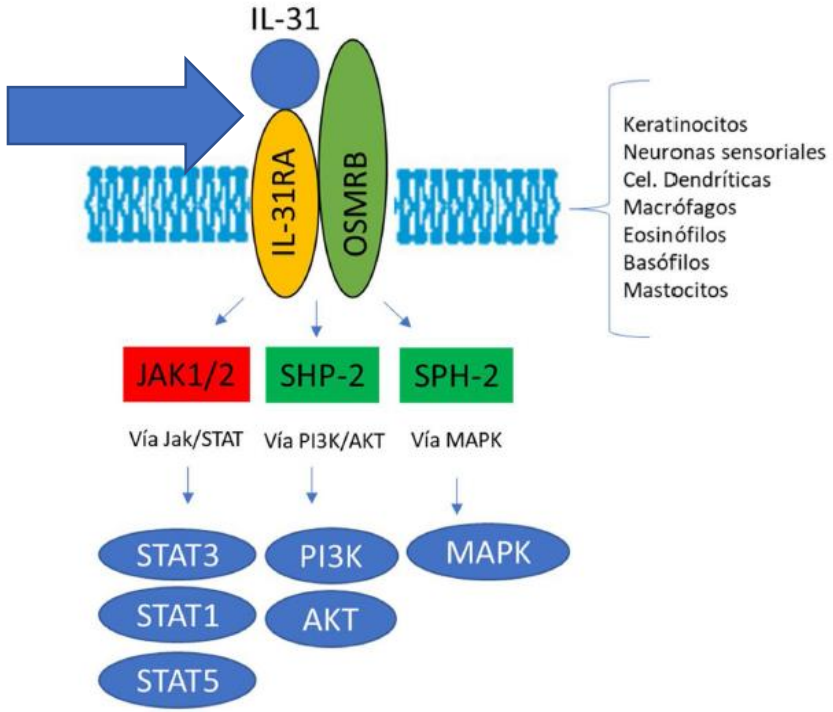


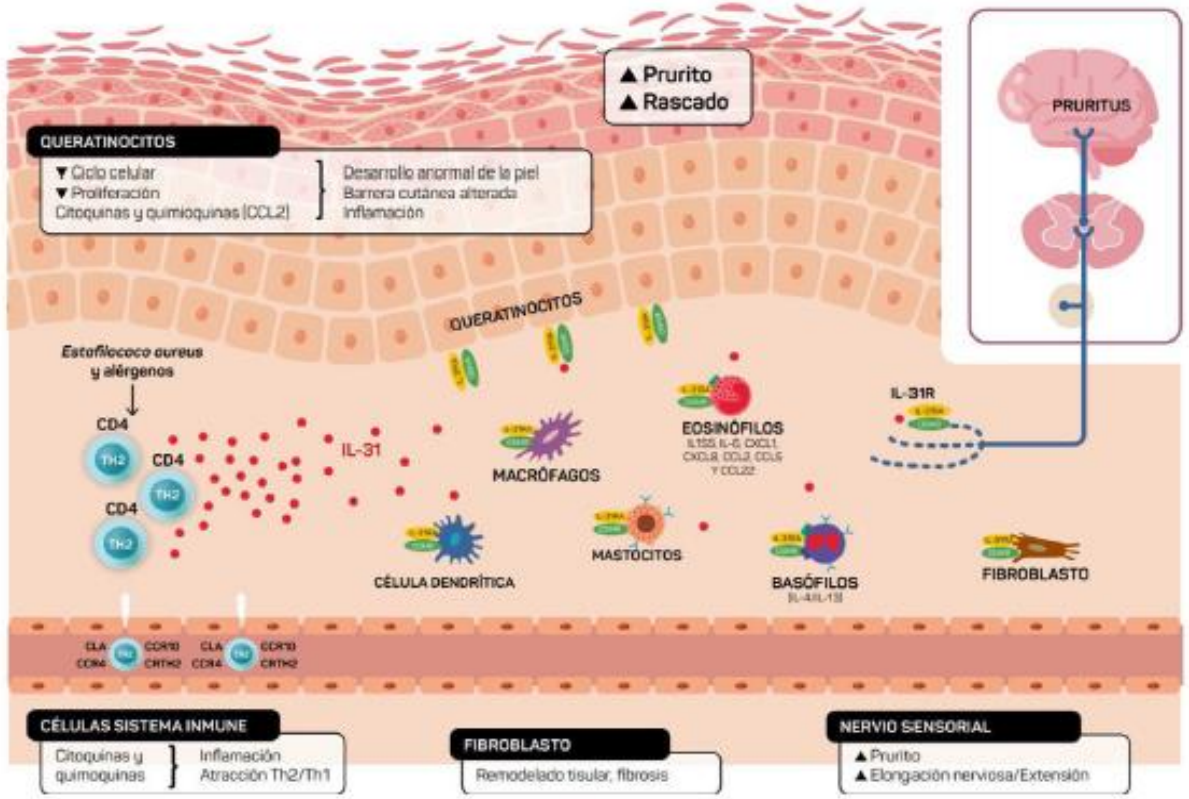
IL-31 La vía del prurito





Nemolizumab





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ACTAS Dermo-Sifiliográficas 113 (2022) 674–684

ACTAS Dermo-Sifiliográficas
Full English text available at www.actasdermo.org

REVISIÓN

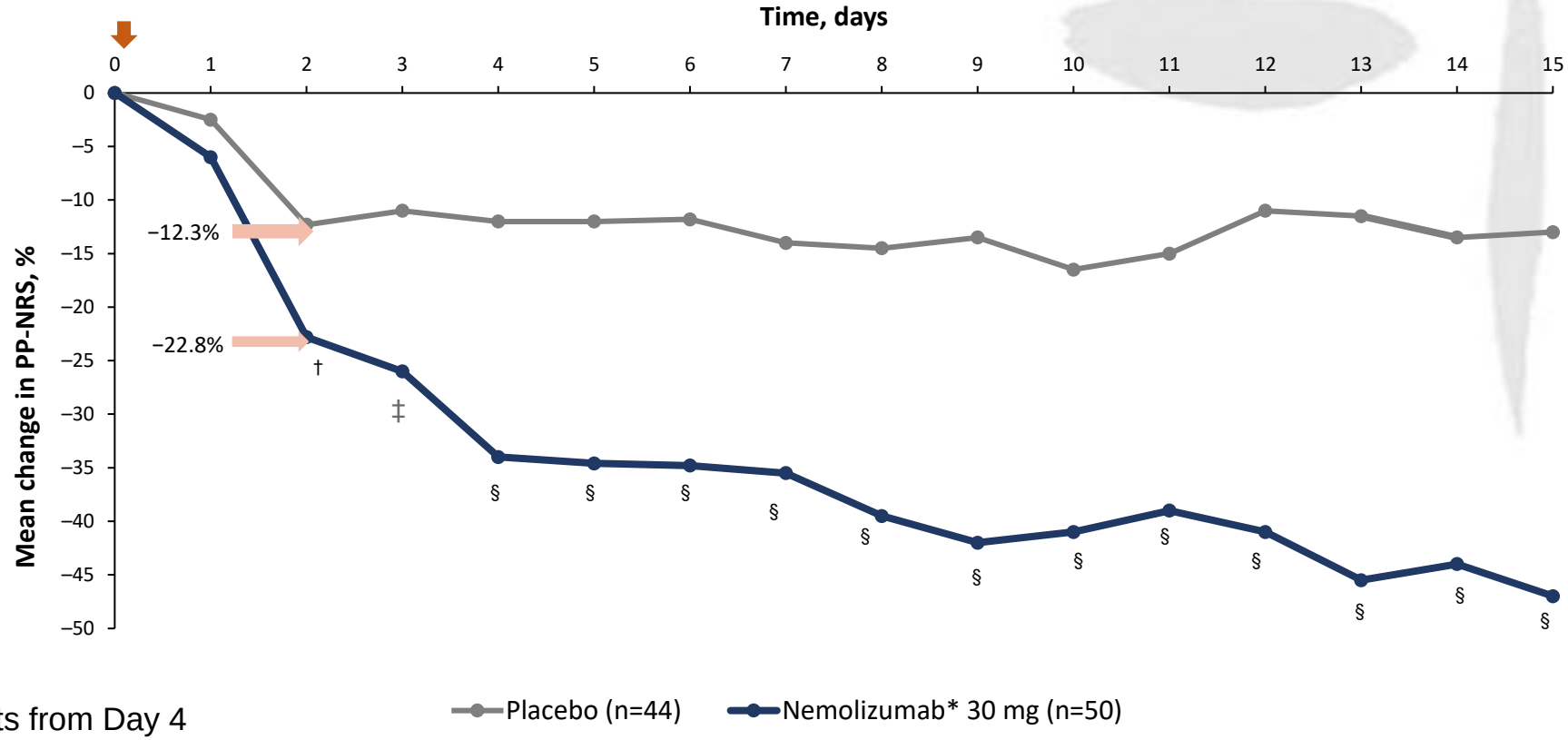
Nemolizumab: un innovador tratamiento biológico para el control de la interleuquina 31 (IL-31) clave en la dermatitis atópica y el prurigo nodular

E. Serra-Baldrich[a,*], L.F. Santamaría-Babí[b] y J. Francisco Silvestre[c]

There was a greater itch relief, apparent by Day 2, with nemolizumab* 30 mg vs placebo (*post-hoc* EASI ≥16)

Daily LS-mean percentage change from baseline in PP NRS from Day 1 to Day 15

A rapid improvement of itch and significant differences between the groups were observed from Day 2 for reductions in PP NRS (22.8% vs 12.3%, p=0.005)



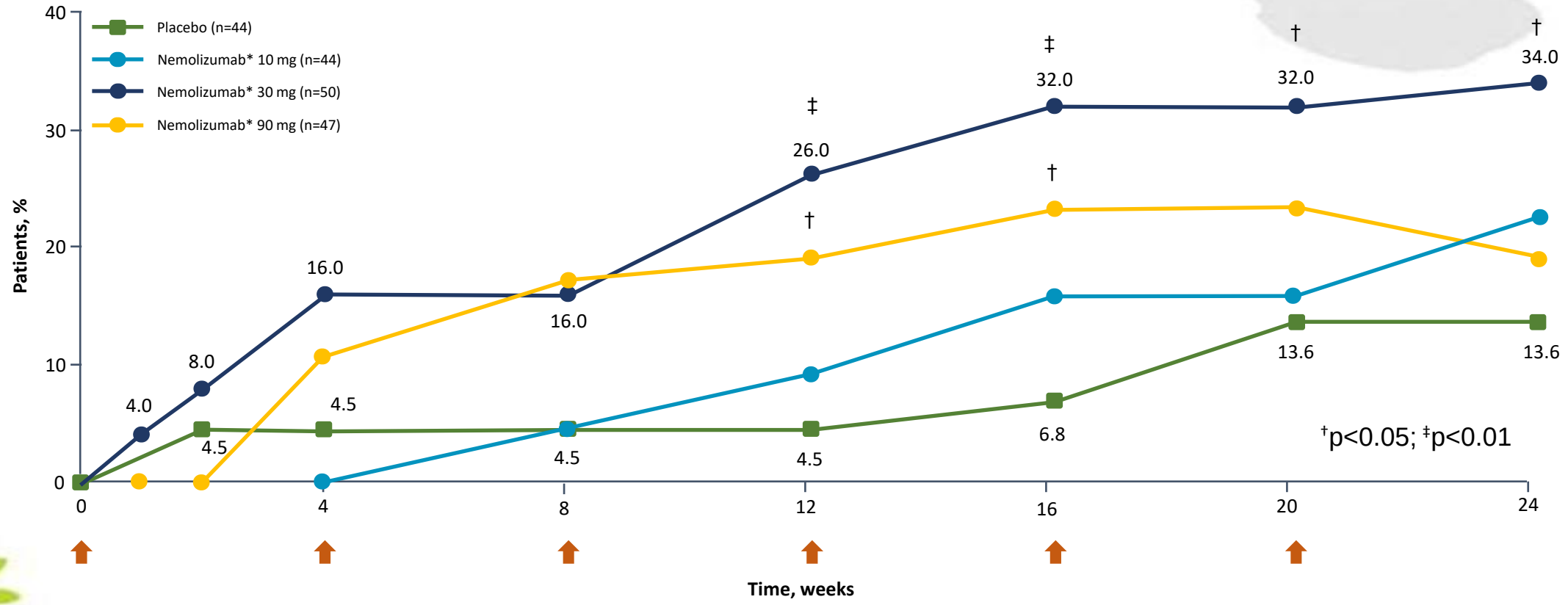
†p<0.05; ‡p<0.005; §p<0.001 for all visits from Day 4

*Nemolizumab is an investigational product not approved in any jurisdiction for any indication.
EASI, Eczema Area and Severity Index; LS, least squares; PP NRS, Peak Pruritus Numerical Rating Scale.
Silverberg JI, *et al. J Eur Acad Dermatol Venereol* 2021; 35: 1562–1568. Nemolizumab is associated with a rapid improvement in atopic dermatitis signs and symptoms: subpopulation (EASI ≥ 16) analysis of randomized phase 2B study, Silverberg JI et al.

Nemolizumab* administration

Nemolizumab* *post-hoc* analysis (EASI ≥16): IGA success rates

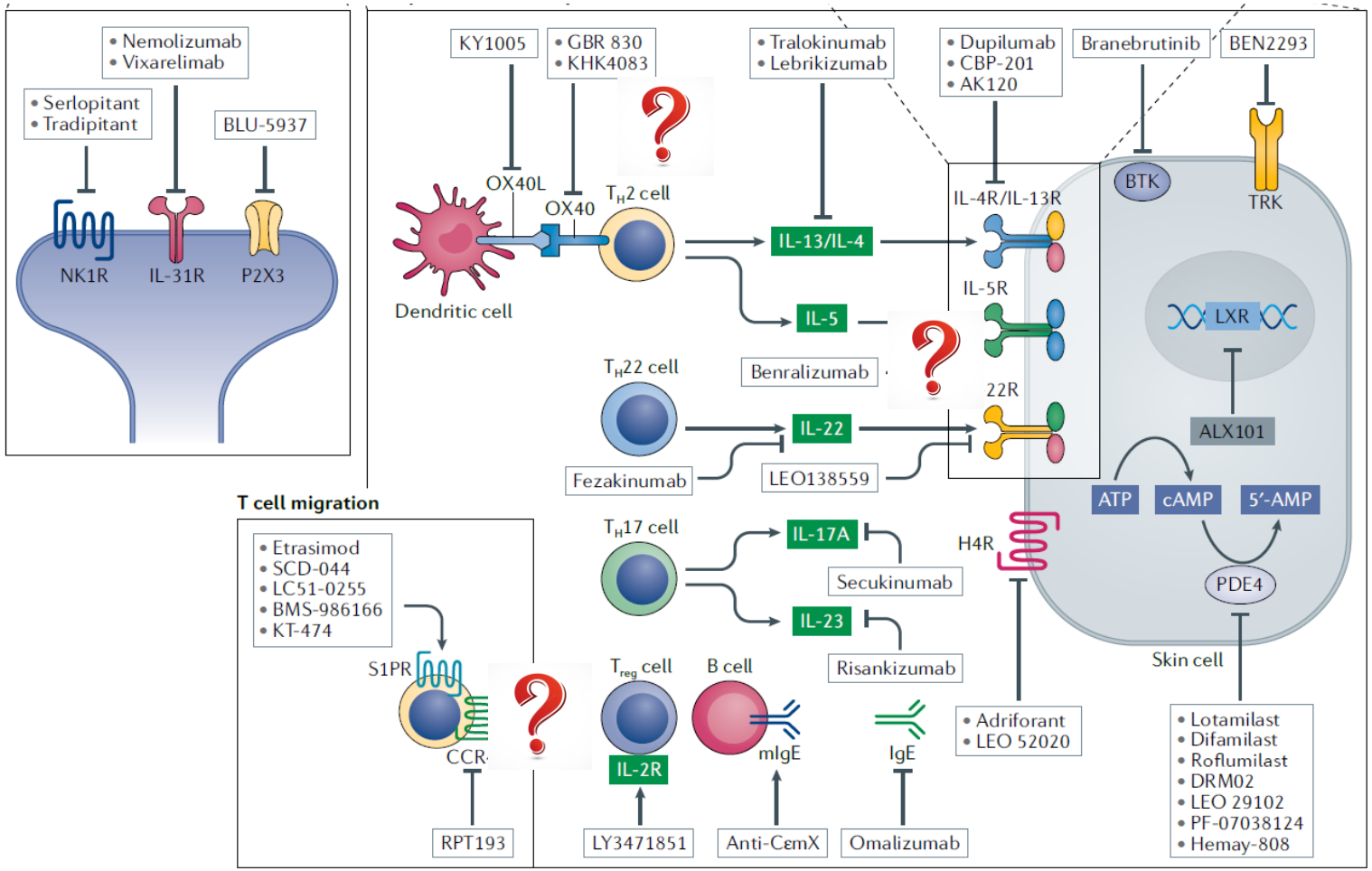
A significantly greater proportion of patients reached IGA 0/1 with nemolizumab* 30 mg vs placebo from Week 12 onwards[1,2]

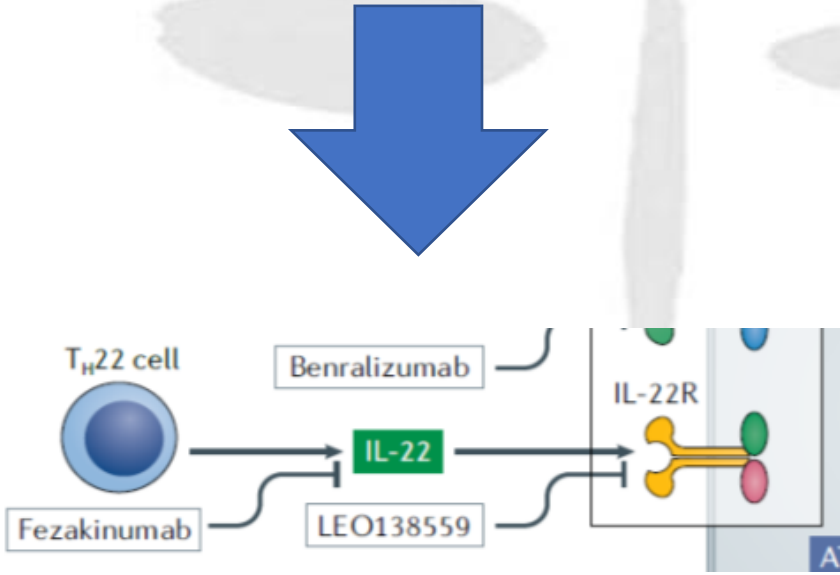


*Galderma is investigating the use of nemolizumab and has not received approval in any jurisdiction for any indication.
EASI, Eczema Area and Severity Index; IGA, Investigator Global Assessment.
1. Silverberg JI, *et al. J Eur Acad Dermatol Venereol* 2021; 35: 1562–1568. Nemolizumab is associated with a rapid improvement in atopic dermatitis signs and symptoms: subpopulation (EASI ≥ 16) analysis of randomized phase 2B study, Silverberg JI et al. Copyright © 2021 Journal of The European Academy of Dermatology and Venereology; 2. Galderma. Data on file. Nemolizumab in AD Phase 2b trial efficacy data (EASI ≥16 subpopulation). 2019.

Nemolizumab* administration

Inmunidad adaptativa: Vía IL22





IL-22 R1 en DA

Table 7. Clinical trials targeting IL-22 in AD.

Target Molecule	Clin Trial Gov	Type of Study	Status
IL-22			
Anti-IL-22 antibody Fezakinumab (ILV-094)	NCT01941537	Phase II	Completed
IL-22R1			
Anti-IL-22R1 antibody LEO 138559	NCT04922021	Phase II for AD	Active, not recruiting
Anti-IL-22R1 antibody LEO 138559	NCT03514511	Phase I	Completed
Anti-IL-22R1 antibody LEO 138559	NCT05099133	Phase I	Completed
Anti-IL-22R1 antibody LEO 138559	NCT05470114	Phase II	Recruiting

Good Clinical Practice NETWORK

REGULATIONS CRO LIST CLINICAL

ICH GCP > US Clinical Trials Registry > Clinical Trial NCT05470114

A Multi-omics Disease Signature Trial in Adult Patients With Moderate to Severe AD

July 21, 2022 updated by: LEO Pharma

A Randomized, Double-blinded, Active Comparator-controlled, 16-week, Single-site, Exploratory, Mechanistic Trial to Assess the Effect of LEO 138559 on the Molecular Signature and Safety in Adults With Moderate to Severe Atopic Dermatitis.

This clinical trial will investigate the effectiveness and safety of a new active ingredient (LEO 138559) in the treatment of moderate to severe atopic dermatitis (AD). It is given by subcutaneous injection. Some people in the trial will instead receive Dupixent® which is an approved treatment for moderate to severe AD. Dupixent® is also given by subcutaneous injection.

The main aim of this clinical trial is to investigate which changes in biomarkers in the skin are caused by LEO 138559 and Dupixent®.

The trial includes a screening phase of up to 4 weeks, followed by a treatment period of 16 weeks, and a safety follow-up period of 16 weeks.

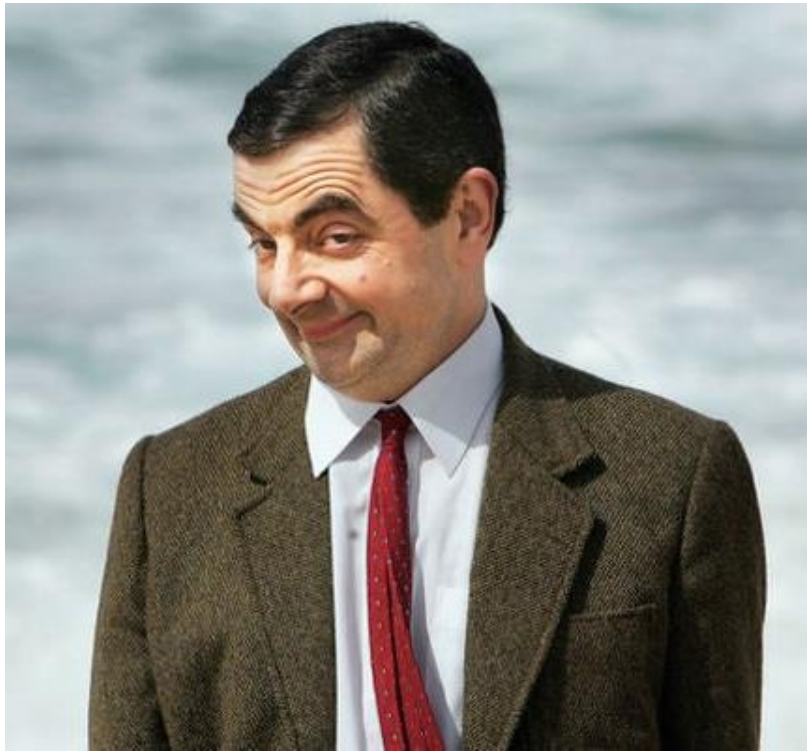
Study Overview

STATUS	CONDITIONS	INTERVENTION / TREATMENT
Recruiting	Atopic Dermatitis	Drug: LEO 138559 Drug: Dupixent®

Germans Trias i Pujol Hospital

Biomedicines **2022**, *10*, 2700. https://doi.org/10.3390/biomedicines10112700

¿ Queréis oir el nombre definitivo……?



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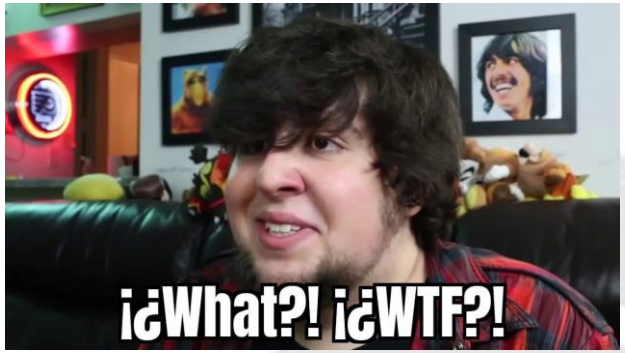
Rezpegaldesleukin !



- The IL-2 conjugate Treg stimulator, LY3471851, had a safety profile at the doses studied that supports further clinical development of LY3471851 in patients with AD
- A trend toward dose-dependent improvement was observed in EASI and vIGA-AD scores and EASI75, vIGA-AD (0,1), and Itch NRS ≥4-point improvement responder rates with LY3471851 vs. placebo through 12 weeks of treatment
- Improvements with LY3471851 24 µg/kg were sustained during follow-up to 48 weeks, up to 36 weeks following end of treatment
- Total Tregs and CD25^{bright} Tregs increased with LY3471851 vs. placebo up to Week 12

Nektar Therapeutics Presents Data for Rezpegaldesleukin (LY3471851) in Patients with Atopic Dermatitis and Psoriasis from Two Separate Clinical Studies at 2022 European Academy of Dermatology (EADV) Congress

PR Newswire Press Releases & Markets News

STOCKS INSIDE THE MARKET STOCK LEADERS STOCK MOVERS STOCK SCREENER DIVIDENDS & EARNINGS CALENDAR PRESS RELEASES

Nektar Therapeutics Presents Data for Rezpegaldesleukin (LY3471851) in Patients with Atopic Dermatitis and Psoriasis from Two Separate Clinical Studies at 2022 European Academy of Dermatology (EADV) Congress

PR Newswire - Wed Sep 7, 12:15AM CDT

SAN FRANCISCO, Sept. 7, 2022 /PRNewswire/ -- Nektar Therapeutics (Nasdaq: NKTR) today announced data presentations from two Phase 1b, proof-of-concept studies of rezpegaldesleukin (also known as LY3471851 or NKTR-358) in patients with atopic dermatitis (AD) and plaque psoriasis at the 2022 European Academy of Dermatology and Venereology (EADV) Congress.

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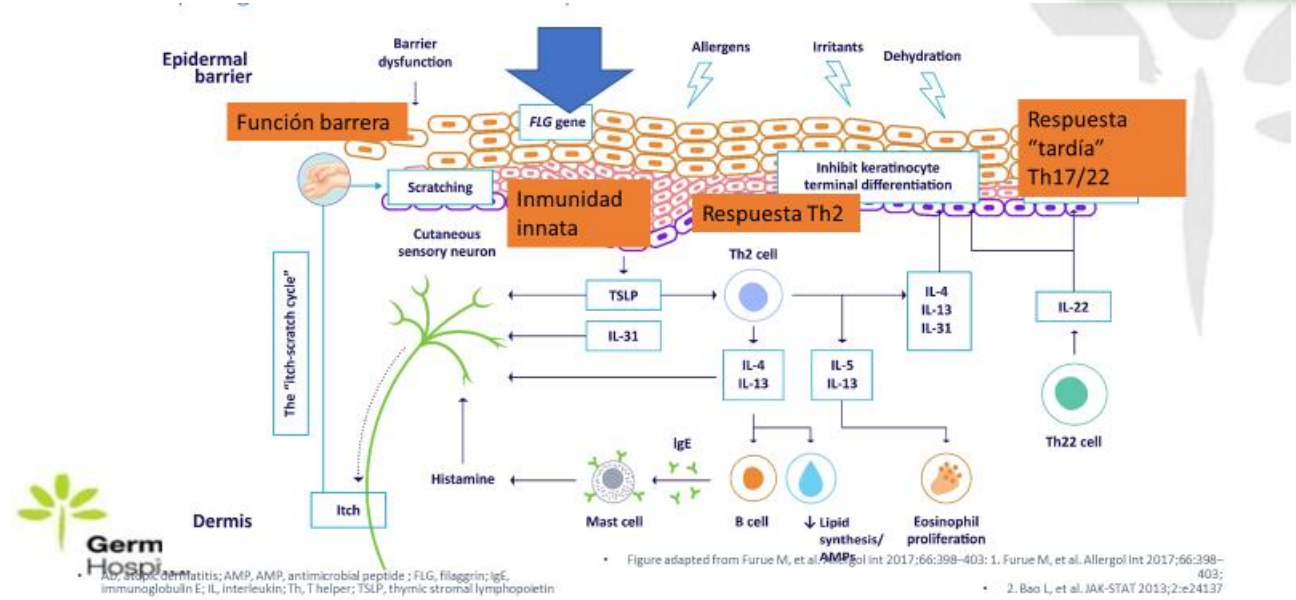
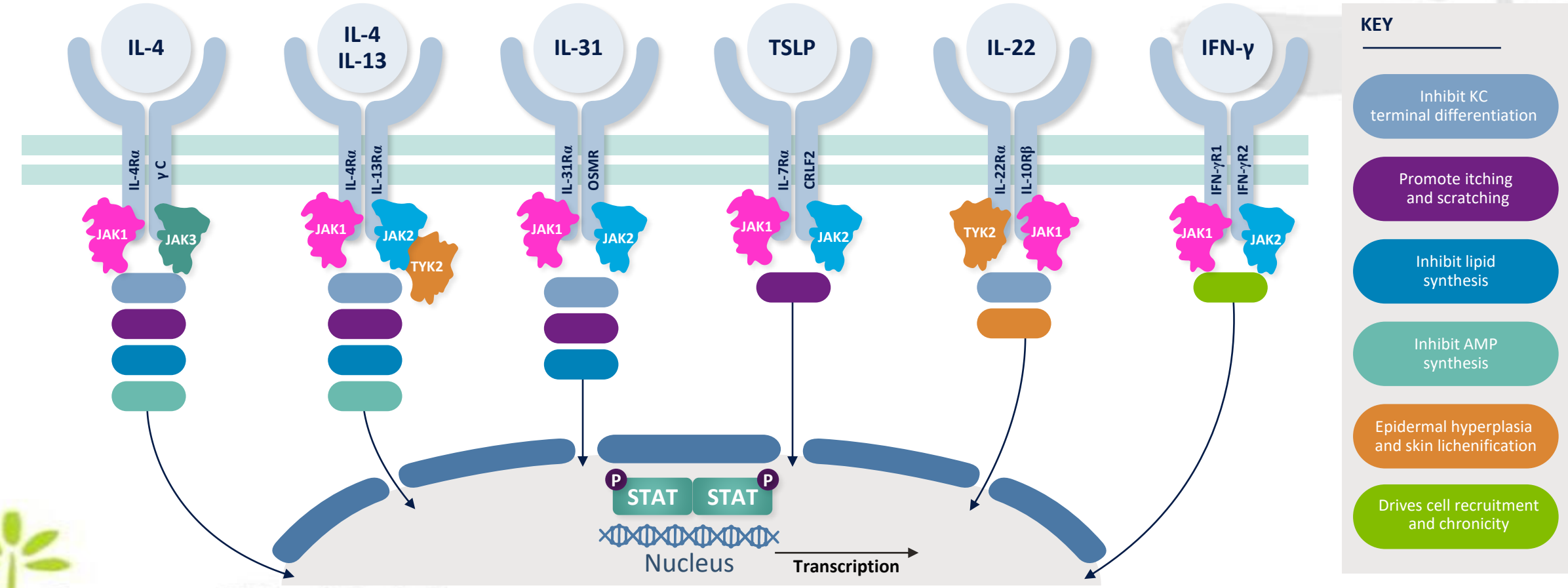
AD…too many targets?



AD, atopic dermatitis; AMP, AMP, antimicrobial peptide ; FLG, filaggrin; IgE, immunoglobulin E; IL, interleukin; Th, T helper; TSLP, thymic stromal lymphopoietin

- Figure adapted from Furue M, et al. Allergol Int 2017;66:398–403: 1. Furue M, et al. Allergol Int 2017;66:398–403;
- 2. Bao L, et al. JAK-STAT 2013;2:e24137

JAK inhib: la posibilidad de inhibición simultánea de diversas dianas moleculares en DA



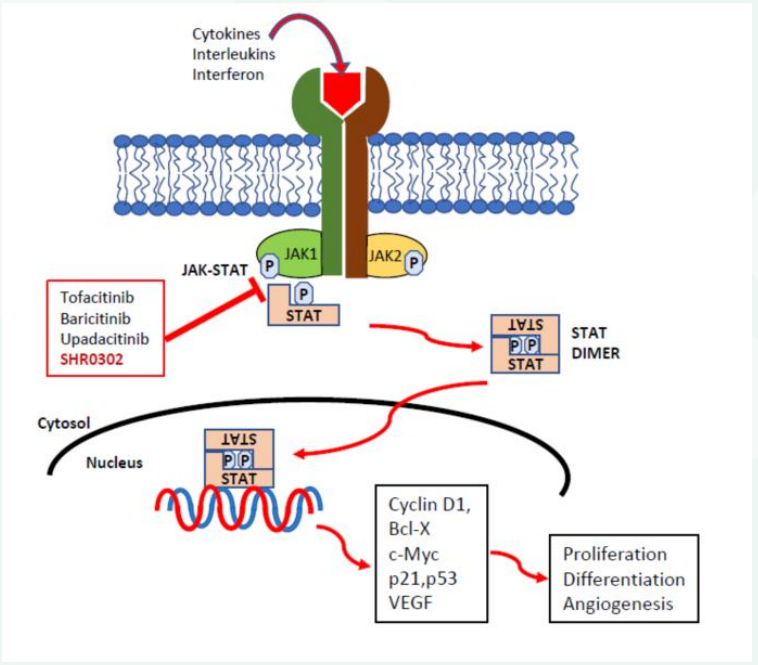
γ C, gamma chain; AD, atopic dermatitis; AMP, antimicrobial peptides; CRLF2, cytokine receptor-like factor 2; IFN, interferon; IL, interleukin; JAK, Janus kinase; KC, keratinocyte; OSMR, oncostatin M receptor; TSLP, thymic stromal lymphopoietin; TYK2, tyrosine kinase 2

Grewe M, et al, *Lancet* 1994;343(8888):25–6; Pastore S, et al. *J Aller Clin Immunol* 1998;101(4):538–44; Cornelissen C, et al. *Eur J Cell Bio* 2012;91:552–66; Clark JD, et al. *J Med Chem* 2014;57:5023–38; Winthrop KL, et al. *Nat Rev Rheumatol* 2017;13:234–43; Berdyshev E, et al. *JCI Insight* 2018;3:e98006; Castro F, et al. *Front Imm* 2018;9:847; Guttman-Yassky E, et al. *Exp Dermatol* 2018;27:409–17; Keegan AD, et al. *Front Imm* 2018:9:1037; Klonowska J, et al. *Int J Mol Sci* 2018;19:3086; Virtanen A, et al. *BioDrugs* 2019;33:15–32

Ivarmacitinib (SHR0302) (ARQ 252)

SHR0302 is a potent and orally active all members of the JAK family inhibitor, particularly JAK1. The selectivity of SHR0302 for JAK1 is >10-fold for JAK2, 77-fold for JAK3, 420-fold for Tyk2. SHR0302 inhibits JAK1-STAT3 phosphorylation and induces the apoptosis of hepatic stellate cells. SHR0302 has anti-proliferative and anti-inflammatory effects.

Phase 3 development
Administered oral
Indications seeking:
Adults With Atopic Dermatitis



Reistone Biopharma's oral Ivarmacitinib Meets Primary Endpoint in Phase III Study for Atopic Dermatitis

NEWS PROVIDED BY
Reistone Biopharma →
Nov 15, 2022, 08:00 ET

SHARE THIS ARTICLE

SHANGHAI, Nov. 15, 2022 /PRNewswire/ -- **Reistone Biopharma** (Reistone), a leading biotech company focused on development of innovative medicines for immune and inflammation diseases, today **announced positive results from a Phase III study – QUARTZ3 (NCT04875169) evaluating the efficacy and safety of once daily Ivarmacitinib as monotherapy in adults and adolescents with moderate-to-severe atopic dermatitis (AD)**. Two doses (8mg QD or 4mg QD) met the co-primary endpoints, demonstrating significantly improved IGA 0/1 response rate and EASI 75 response rate versus placebo at week 16 (P<0.001). Ivarmacitinib was well-tolerated at both doses without new safety findings.

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Frequent adverse events observed under treatment with JAK inhibitors

Infections
- Nasopharyngitis
- Upper respiratory tract infections
- Urinary tract infections

Herpes virus reactivation
- Herpes Zoster
- Lip/oral herpes simplex infections

Gastrointestinal disorders
- Nausea
- Diarrhea

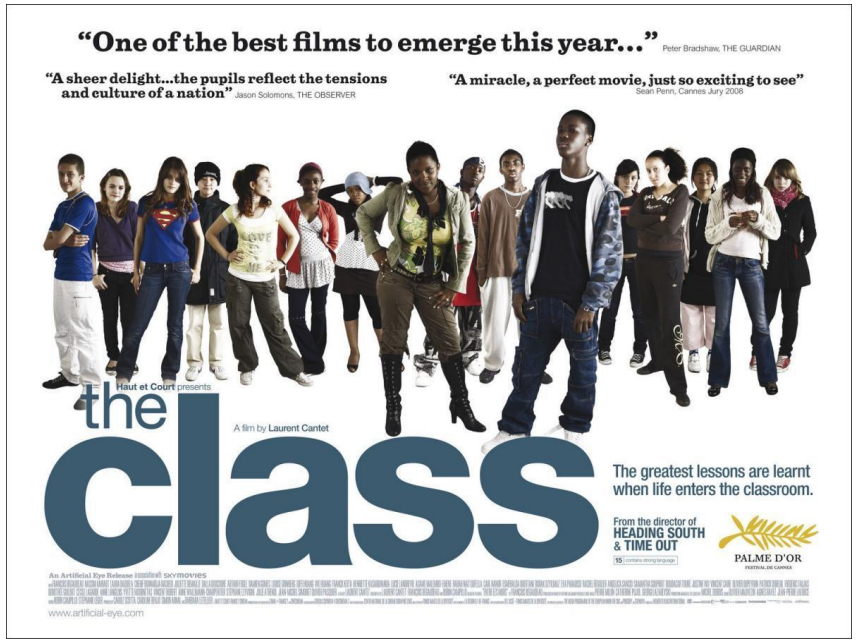
Blood/serum changes
- Elevation of liver enzymes [aspartate aminotransferase (AST). alanine aminotransferase (ALT)]
- Hyperlipidemia (increase in cholesterol, triglycerides)
- Increase in bilirubine
- Increase in creatine phosphokinase

Blood cell count alteration
- Decrease in hemoglobin level
- Decrease in white blood cell count
- Neutropenia

Rare adverse events reported under treatment with JAK inhibitors
- Thromboembolic events
- Non-melanoma skin cancers
- Solid cancers

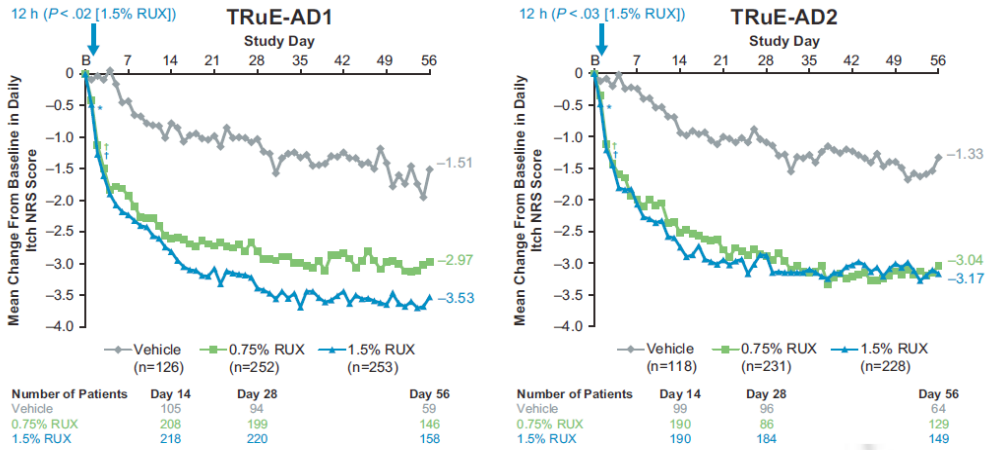
Efectos secundarios " de clase" de JAK- inhib

Van a variar en función de la dosis y la selectividad



Ruxolitinib (JAK 1 y 2) tópico

- IGA 2/3, and 3%-20% affected body surface area
- IGA 0/1 0.75% RUX cream (50.0%/39.0%) and 1.5% RUX cream (53.8%/51.3%) versus vehicle (15.1%/7.6%; P \.0001) at week 8
- Significant itch reductions versus vehicle were reported within 12 hours of first application of 1.5% RUX (P \.05).
- Application site reactions were infrequent (\1%) and lower with RUX versus vehicle; none were clinically significant



FDA approved !!!!

Germans Trias i Pujol Hospital

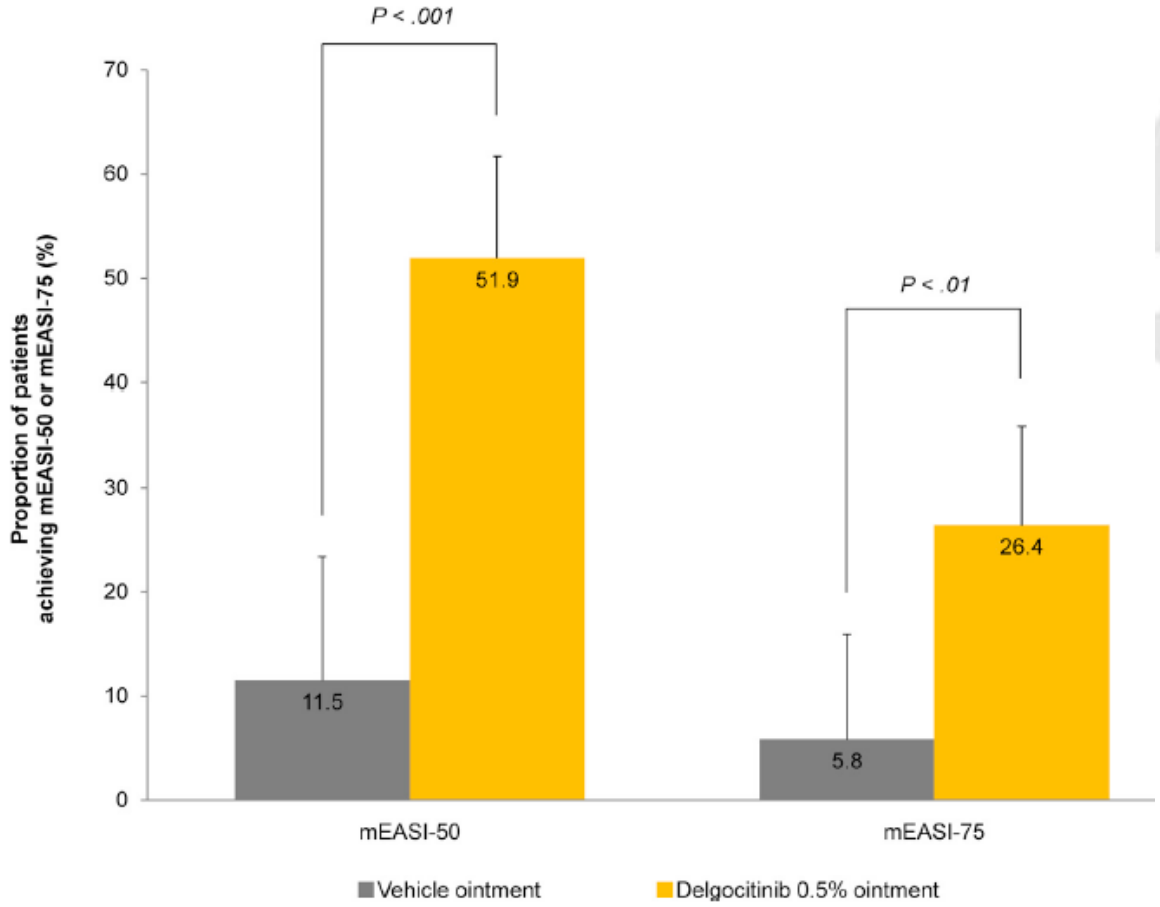
J Am Acad Dermatol 2021;85:863-72.

Efficacy and safety of ruxolitinib cream for the treatment of atopic dermatitis: Results from 2 phase 3, randomized, double-blind studies

Kim Papp, MD, PhD,[a] Jacek C. Szepietowski, MD, PhD,[b] Leon Kircik, MD,[c] Darryl Toth, MD,[d] Lawrence F. Eichenfield, MD,[e] Donald Y. M. Leung, MD, PhD,[f] Seth B. Forman, MD,[g] May E. Venturanza, MD,[h] Kang Sun, PhD,[h] Michael E. Kuligowski, MD, PhD, MBA,[h] and Eric L. Simpson, MD, MCR[i]
Waterloo and Windsor, Ontario, Canada; Wroclaw, Poland; New York, New York; San Diego, California; Denver, Colorado; Tampa, Florida; Wilmington, Delaware; and Portland, Oregon

Delgocitinib en DA

- Delgocitinib 0,5% pomada vs vehículo
- mEASI>10
- Estudio randomizado, doble ciego 4 semanas
- Buena tolerancia (no prurito, irritación)



Germans Trias i Pujol Hospital

Japan approved !!!!

J Am Acad Dermatol 2020;82:823-31

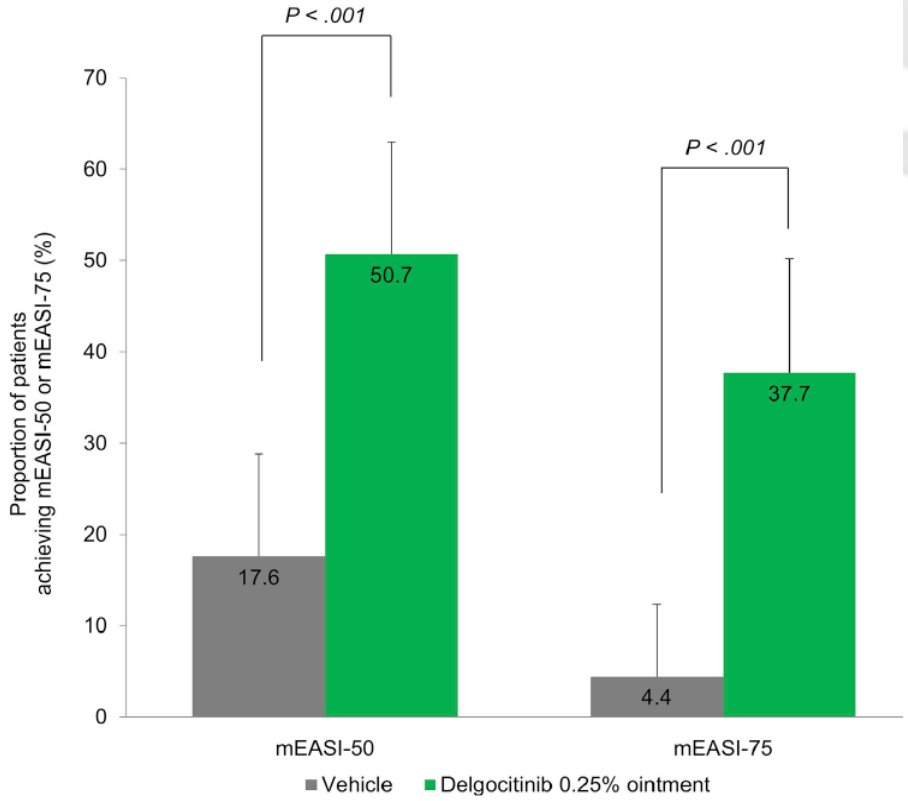
ORIGINAL ARTICLES

Delgocitinib ointment, a topical Janus kinase inhibitor, in adult patients with moderate to severe atopic dermatitis: A phase 3, randomized, double-blind, vehicle-controlled study and an open-label, long-term extension study

Hidemi Nakagawa, MD, PhD,[a] Osamu Nemoto, MD, PhD,[b] Atsuyuki Igarashi, MD, PhD,[c] Hidehisa Saeki, MD, PhD,[d] Hironobu Kaino, MS,[e] and Takeshi Nagata, MS[e]
Tokyo and Hokkaido, Japan

Delgocitinib en DA

- Pacientes pediátricos 2-15 años
- mEASI >5
- Delgocitinib durante 4 semanas vs placebo
- Algún caso de foliculitis y irritación leve
- Sin niveles plasmáticos



Japan approved !!!!

Germans Trias i Pujol Hospital

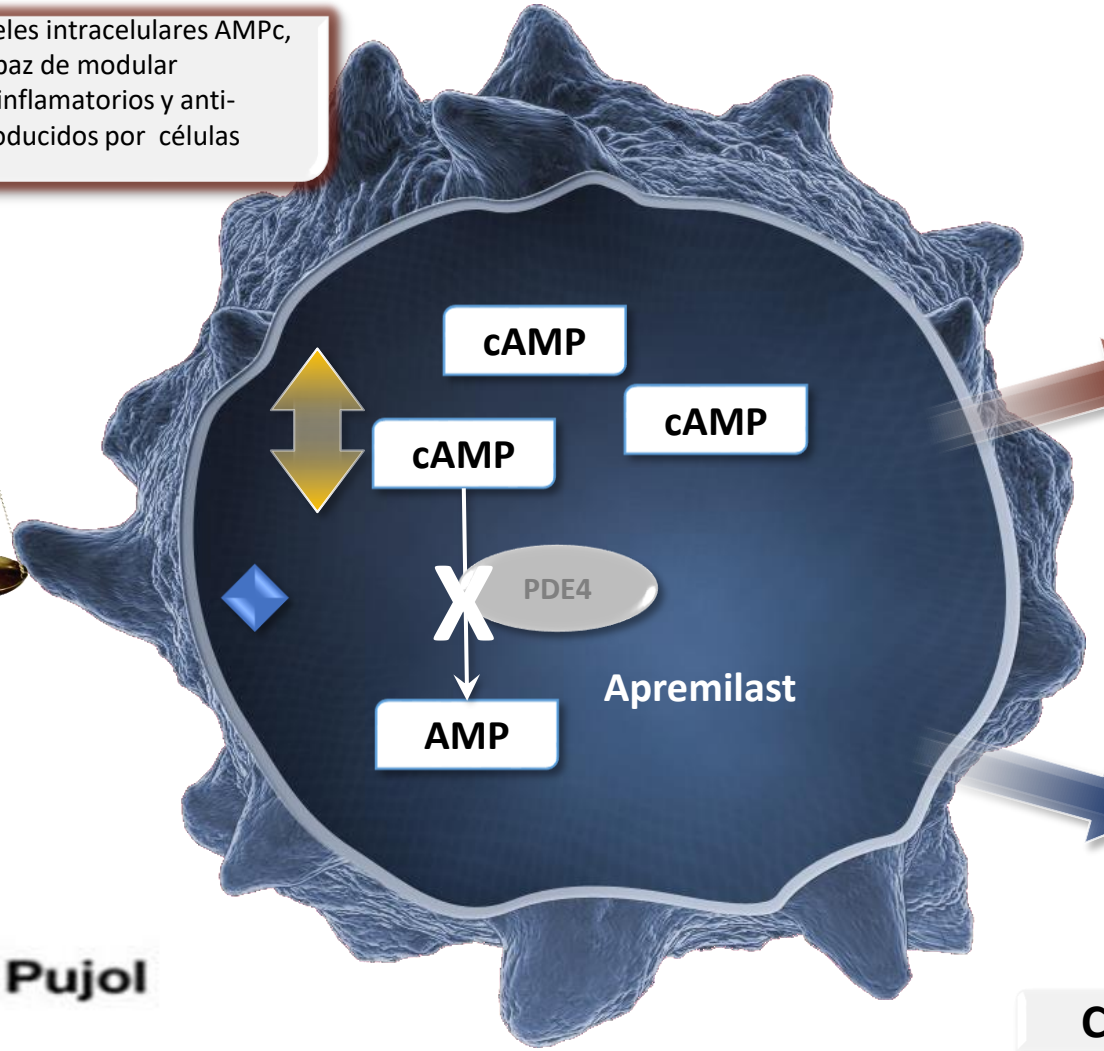
J Am Acad Dermatol 2021;85:854-62.

Delgocitinib ointment in pediatric patients with atopic dermatitis: A phase 3, randomized, double-blind, vehicle-controlled study and a subsequent open-label, long-term study

Hidemi Nakagawa, MD, PhD,[a] Osamu Nemoto, MD, PhD,[b] Atsuyuki Igarashi, MD, PhD,[c] Hidehisa Saeki, MD, PhD,[d] Kenji Kabashima, MD, PhD,[e] Manabu Oda, MS,[f] and Takeshi Nagata, BS[f]
Tokyo, Hokkaido, and Kyoto, Japan

Inhibición de la fosfodiesterasa 4

Elevando los niveles intracelulares AMPc, apremilast es capaz de modular mediadores pro inflamatorios y anti-inflamatorios producidos por células inmunitarias



Mediadores Pro-Inflamatorios (TNF-α, IL-17, IFN-γ)

Mediadores Anti-Inflamatorios (IL-10)

Cls Inmunitarias

Germans Trias i Pujol Hospital

Roflumilast en DA

Phase III on going

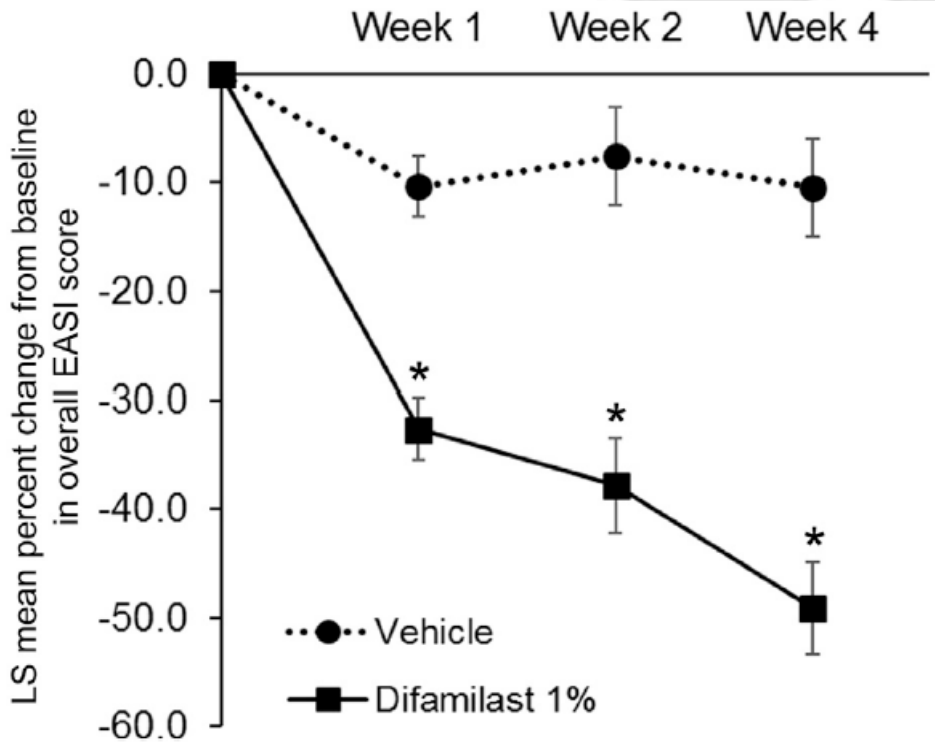
- Methods: In this phase 2, proof of concept trial, patients (N=136) aged ≥12 years with AD were randomized to once-daily roflumilast cream 0.15%, roflumilast cream 0.05%, or vehicle cream for 4 weeks
- At week 4, mean absolute changes in EASI were -6.4 (P=0.097 vs vehicle), -6.0 (P=0.356), and -4.8 with roflumilast 0.15%, roflumilast 0.05%, and vehicle, respectively.
- Treatment-related adverse events (AEs) occurred in 2 (2.2%) patients receiving roflumilast (mild rash and moderate application site pain).

Germans Trias i Pujol Hospital

Gooderham M et al. The Safety and Efficacy of Roflumilast Cream 0.15% and 0.05% in Patients With Atopic Dermatitis: Randomized, Double-Blind, Phase 2 Proof of Concept Study. J Drugs Dermatol. 2023 Feb 1;22(2):139-147. doi: 10.36849/JDD.7295. PMID: 36745371.

Difamilast (PDE-4 inh)

- Pacientes 15-70 años
- IGA 2-3 / BSA 5-40%
- Difamilast 1% (n:182) vs vehículo (n: 182)
- EASI-50 en EOT fue de 58,24% para 1% difamilast y 25,82% para vehículo (P < 0,0001); **EASI-75** fue de **42,86%** y **13,19%**, respectivamente (P < 0,0001); y EASI-90 fue de **24,73%** y **5,49%**, respectivamente (P < 0,0001)



Germans Trias i Pujol Hospital

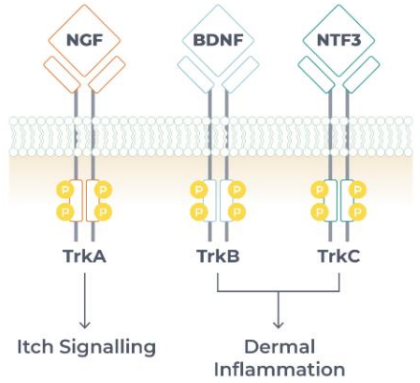
Japan approved !!!!

Difamilast ointment in adult patients with atopic dermatitis: A phase 3 randomized, double-blind, vehicle-controlled trial

Hidehisa Saeki, MD, PhD,[a] Kensuke Ito, MSc,[b] Daisuke Yokota, MS,[b] and Hidetsugu Tsubouchi, PhD[c]
Tokyo and Osaka, Japan

J Am Acad Dermatol 2022;86:607-14.

Nuevos tratamientos tópicos



Novel targeted therapies	*ShA9*	*Phase I*	*Moderate-to-severe AD*
	AMTX-100	*Phase I/II*	*Mild-to-moderate AD* *Target: nuclear transport modifier*
	BEN-2293	*Phase I/II*	*Mild-to-moderate AD* *Target: pan-TRK antagonist*
	PRN473	*Phase II*	*Mild-to-moderate AD* *Target: BTK inhibitor*

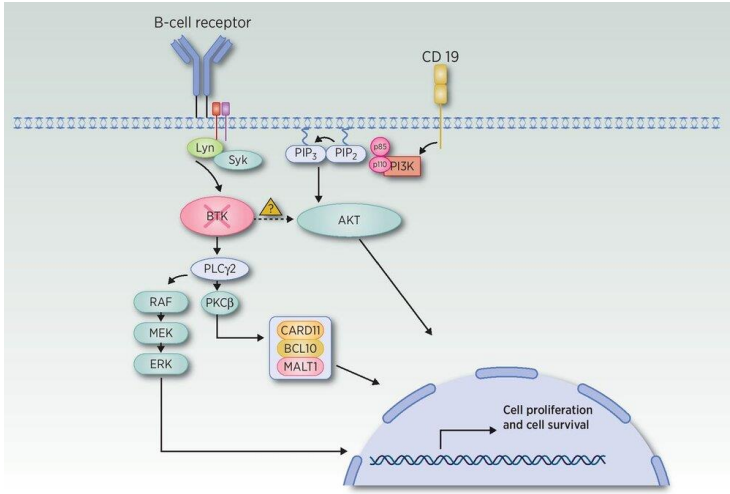
What's New in Topicals for Atopic Dermatitis?

Elana Kleinman[1,2,3] · Jennifer Laborada[1,2,4] · Lauren Metterle[1,2] · Lawrence F. Eichenfield[1,2]

Accepted: 4 July 2022 / Published online: 1 September 2022

Hospital

American Journal of Clinical Dermatology (2022) 23:595–603
https://doi.org/10.1007/s40257-022-00712-0

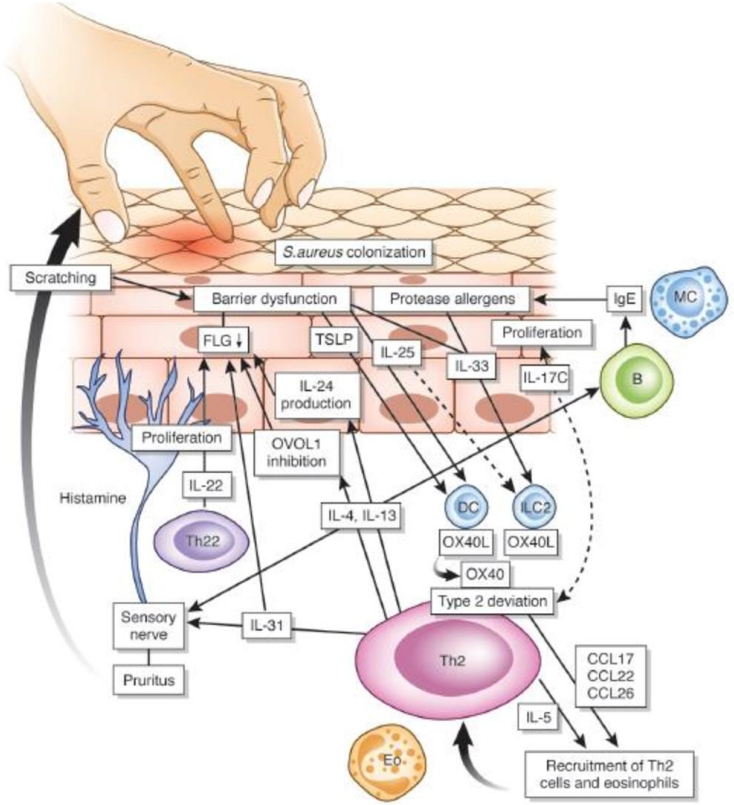


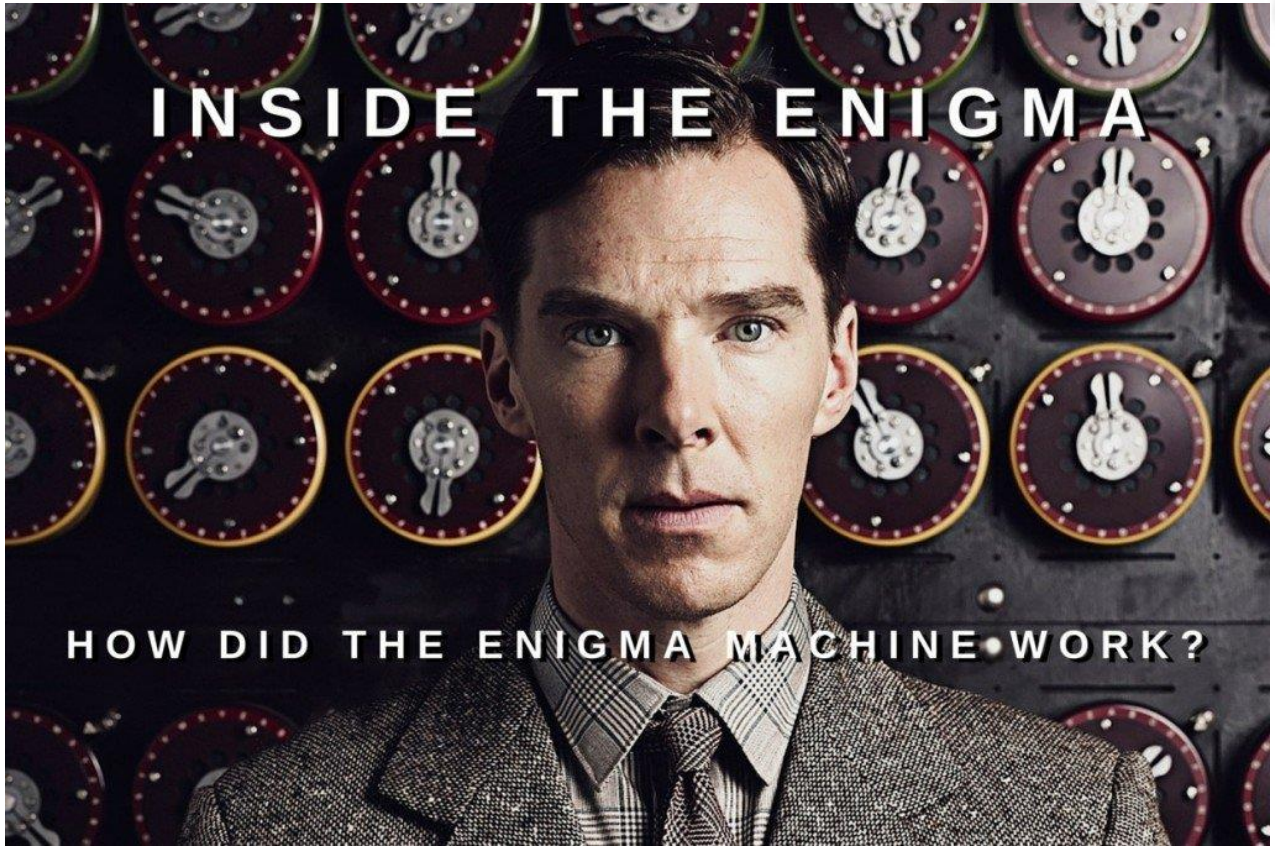
A FILM FROM DANIELS

EVERYTHING EVERYWHERE ALL AT ONCE

PÅ KINO 20. MAI

Ya queda menos para saber cómo funciona (y cómo controlar) la DA



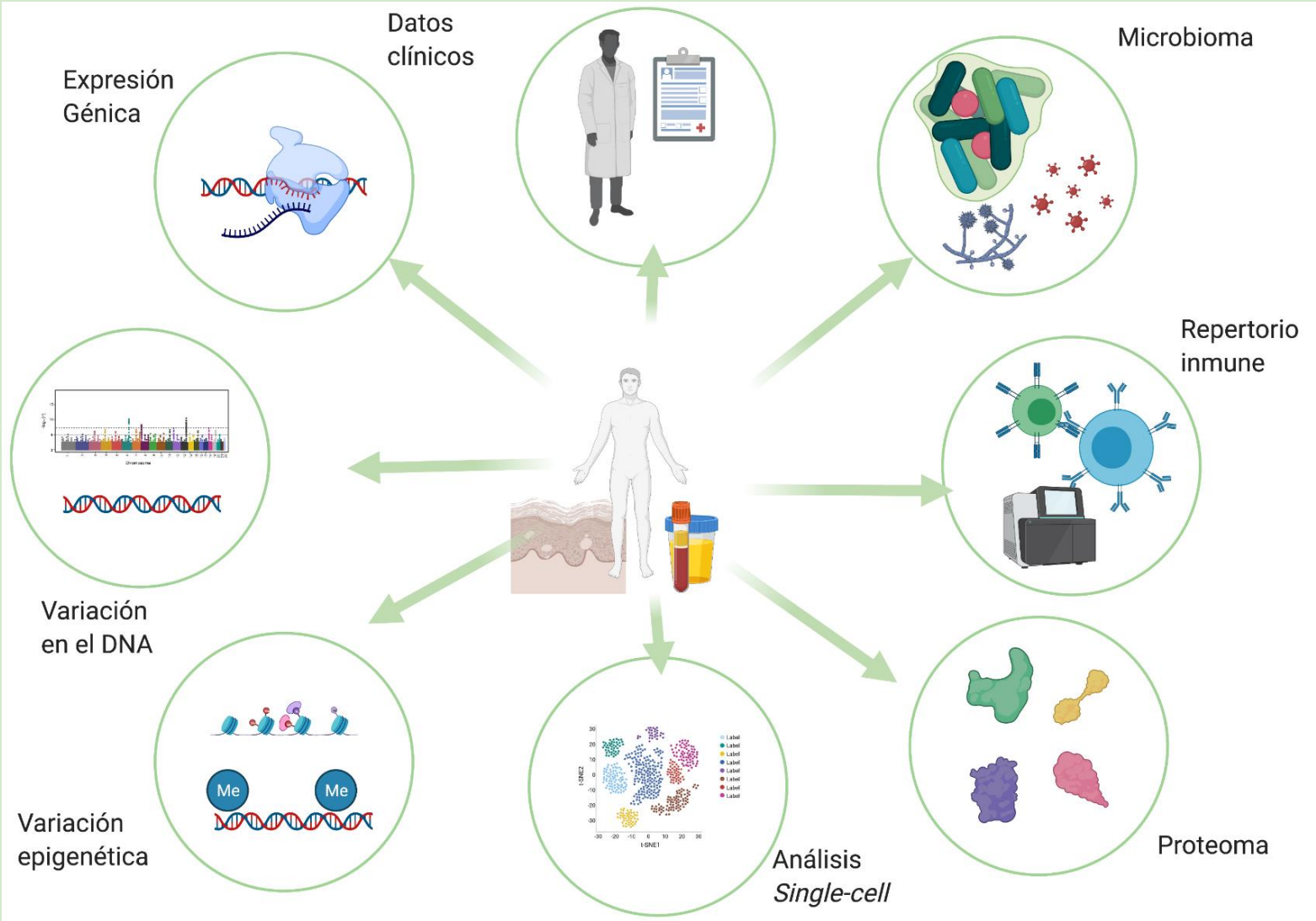


•DOI:10.22034/IJI.2019.80253
•Corpus ID: 184487929
Pathogenesis of Atopic Dermatitis: Current Paradigm.
•M. Furue, D. Ulzii, +3 authors T. Nakahara
•Published 1 June 2019
•Biology, Medicine
•Iranian journal of immunology : IJ

Proyecto SSAD: Medicina Personalizada en AD

Sólo desde la comprensión de las bases moleculares y celulares de heterogeneidad de la **dermatitis atópica** seremos capaces de identificar tratamientos efectivos para cada tipo de paciente

El uso combinado de **múltiples tecnologías** sobre una cohorte única marcará la diferencia



Pujol

Gracias por vuestra atención