ScienHub

Fundació FLI

Inmunoterapia en dermatología

V EDICIÓN

Dermatitis atópica: lo mejor de 2023 y *pipeline*

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Germans Trias i Pujol Hospital

Conflictos de interés

- Asistencia a cursos / congresos: Lilly, , Sanofi, Leo-Pharma, Almirall, Galderma, Abbvie
- Honorarios por asesoría científica, presentaciones u otras actividades relacionadas: Abbvie, Leo-Pharma, Janssen, Sanofi, Galderma
- Investigadora principal y Subinvestigadora en ensayos clínicos: Lilly, Leo-Pharma, Novartis, Janssen, Sanofi, Pfizer, Abbvie, Almirall, UCB y Galderma

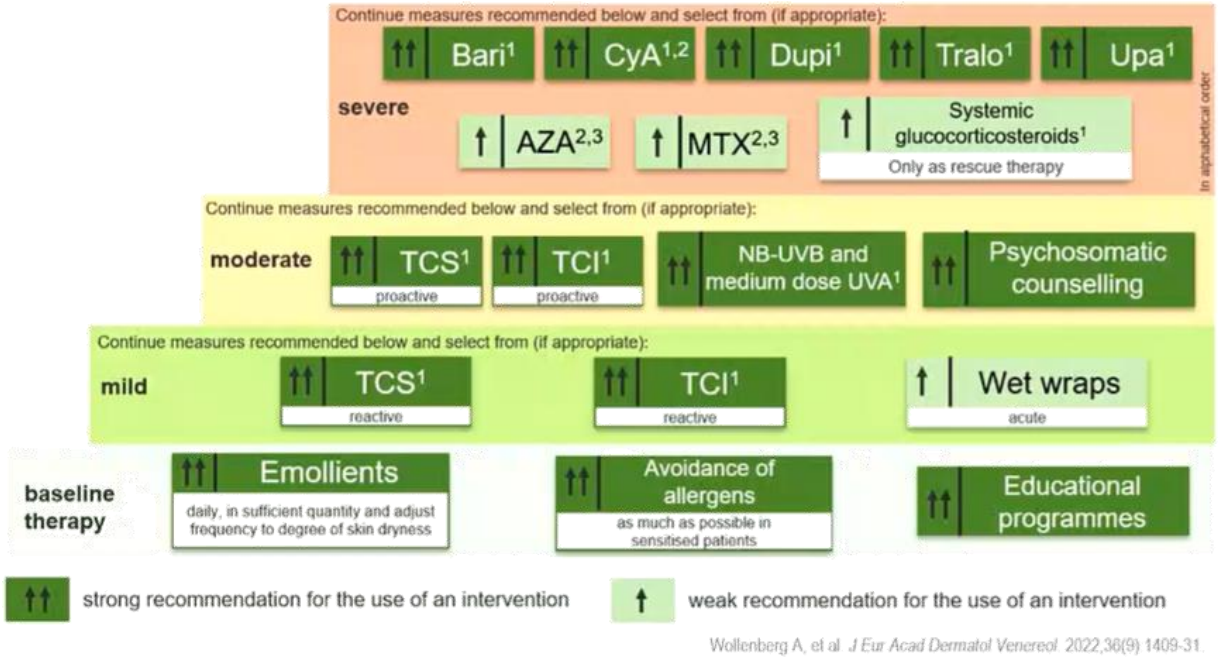
LO MEJOR DE 2023

DOI: 10.1111/jdv.18345 JEADV

GUIDELINE

European guideline (EuroGuiDerm) on atopic eczema: part I – systemic therapy

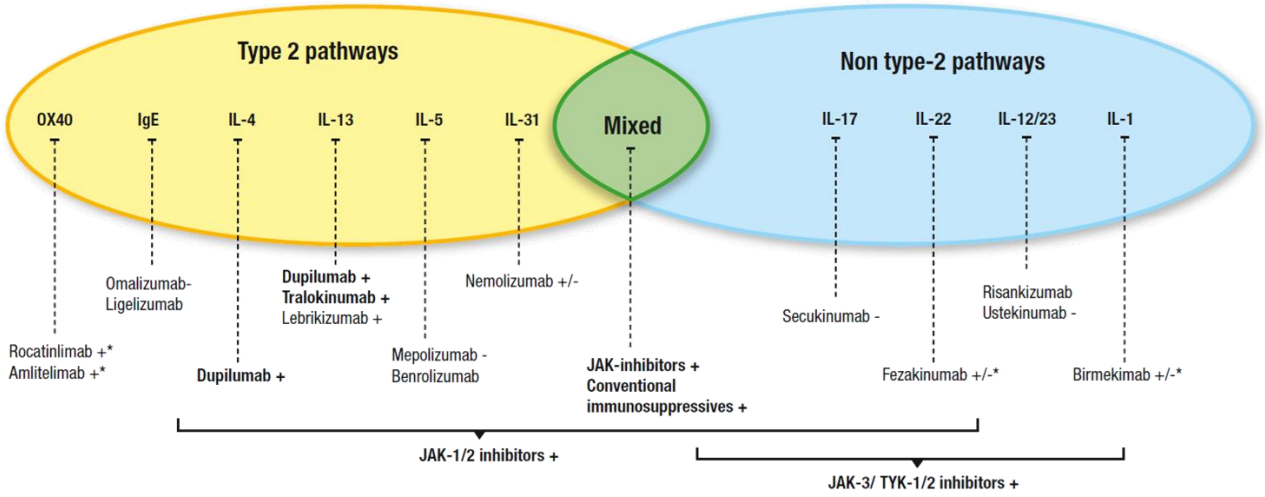
A. Wollenberg,[1,2,*] M. Kinberger,[3] B. Arents,[4] N. Aszodi,[1] G. Avila Valle,[3] S. Barbarot,[5] T. Bieber,[6] H.A. Brough,[7,8] P. Calzavara Pinton,[9] S. Christen-Zäch,[10] M. Deleuran,[11] M. Dittmann,[3] C. Dressler,[3] A.H. Fink-Wagner,[12] N. Fosse,[13] K. Gáspár,[14] L. Gerbens,[15] U. Gieler,[16] G. Girolomoni,[17] S. Gregoriou,[18] C.G. Mortz,[19] A. Nast,[3] U. Nygaard,[20] M. Redding,[21] E.M. Rehbinder,[22] J. Ring,[23] M. Rossi,[24] E. Serra-Baldrich,[25] D. Simon,[26] Z.Z. Szalai,[27] J.C. Szepietowski,[28] A. Torrelo,[29] T. Werfel,[30] C. Flohr[31,32,*]



Wollenberg A, et al. *J Eur Acad Dermatol Venereol.* 2022;36(9):1409-31.

Biomarkers in atopic dermatitis

Daphne Bakker, MD, PhD,[a] Marjolein de Bruin-Weller, MD, PhD,[a] Julia Drylewicz, PhD,[b] Femke van Wijk, MD, PhD,[b] and Judith Thijs, MD, PhD[a] *Utrecht, The Netherlands*



Dupilumab[1]	Tralokinumab[2]	Abrocitinib[3]	Upadacitinib[4]	Baricitinib[5]
Inhibidor IL-4/IL-13	Inhibidor IL-13	Inhibidor JAK1	Inhibidor JAK1	Inhibidor JAK1/2
300 mg[a]	300 mg	200 mg 100 mg 50 mg	30 mg 15 mg	4 mg 2 mg
s.c. Q2W		Oral QD		

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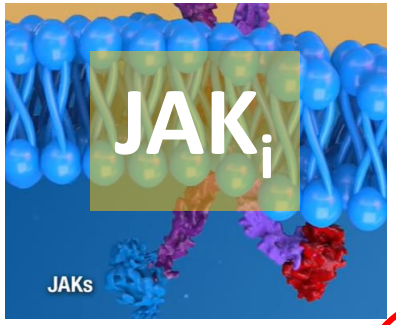
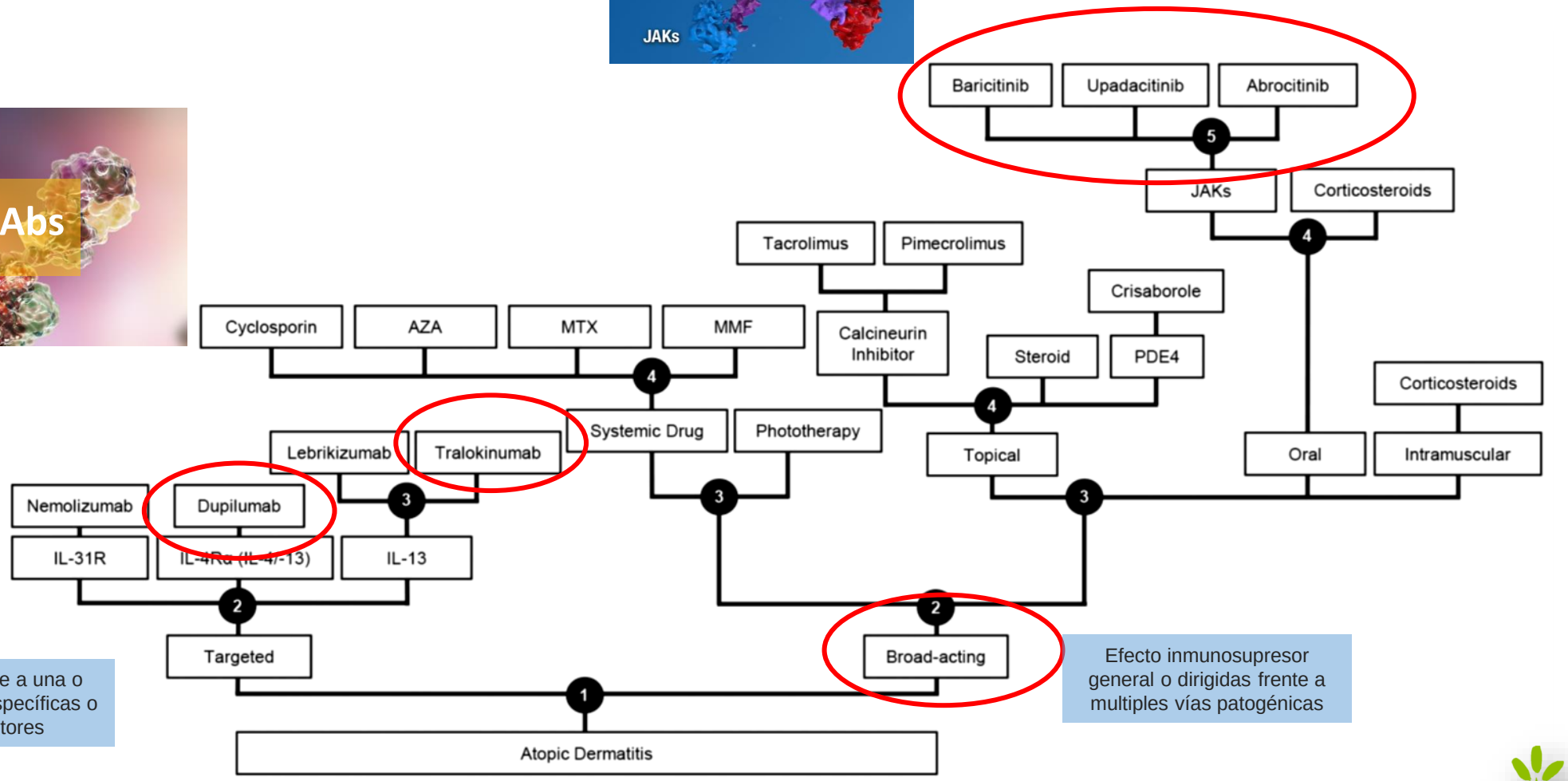
DOI: 10.1111/jdv.18225 JEADV
REVIEW ARTICLE

Atopic dermatitis: pathomechanisms and lessons learned from novel systemic therapeutic options

T. Bieber,[1,2,*] A.S. Paller,[3] K. Kabashima,[4] M. Feely,[5,6] M.J. Rueda,[5] J.A. Ross Terres,[5] A. Wollenberg[7,8]





Terapias frente a una o dos citocinas específicas o sus receptores

Efecto inmunosupresor general o dirigidas frente a multiples vías patogénicas

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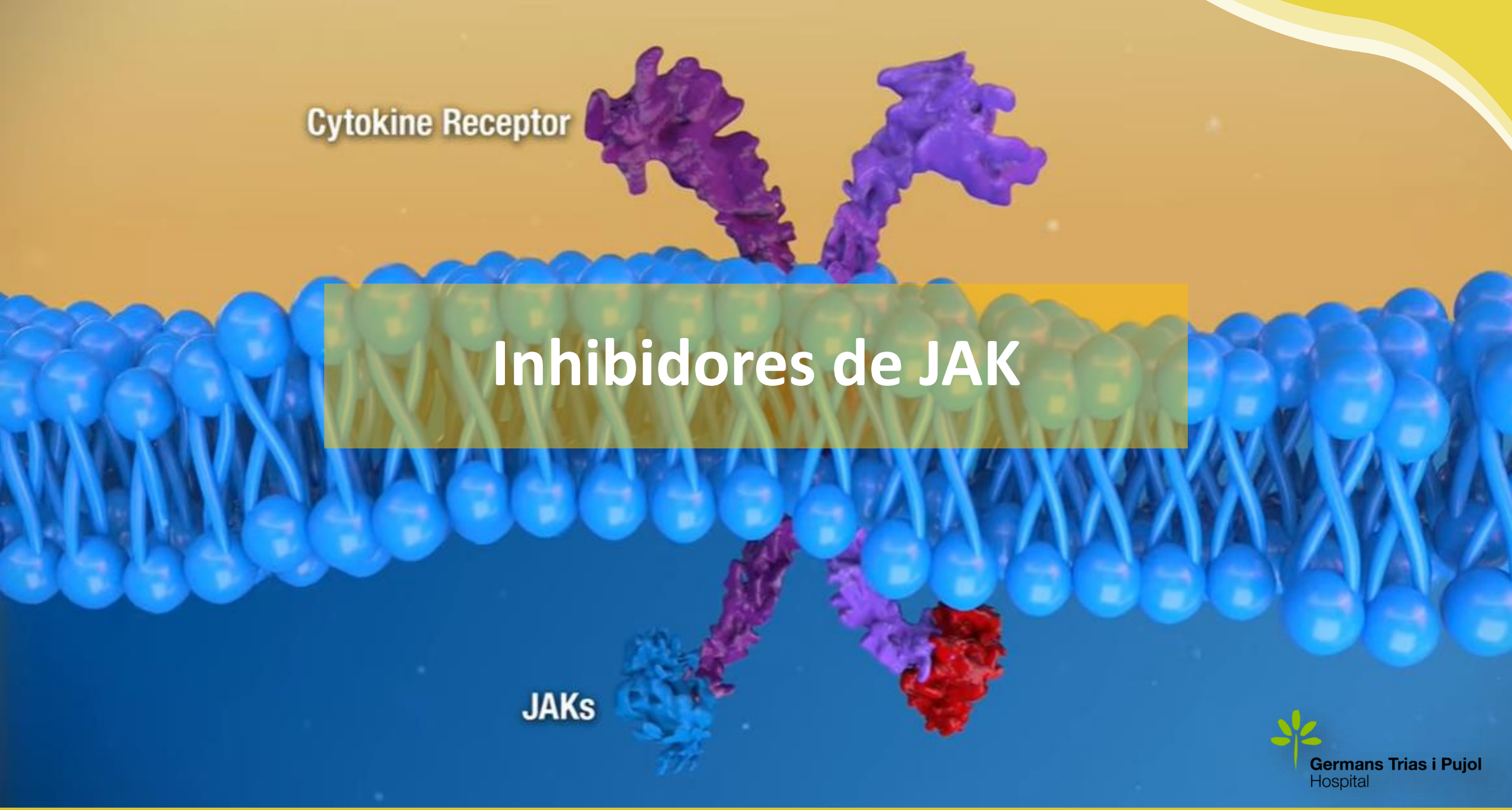

Inhibidores de JAK

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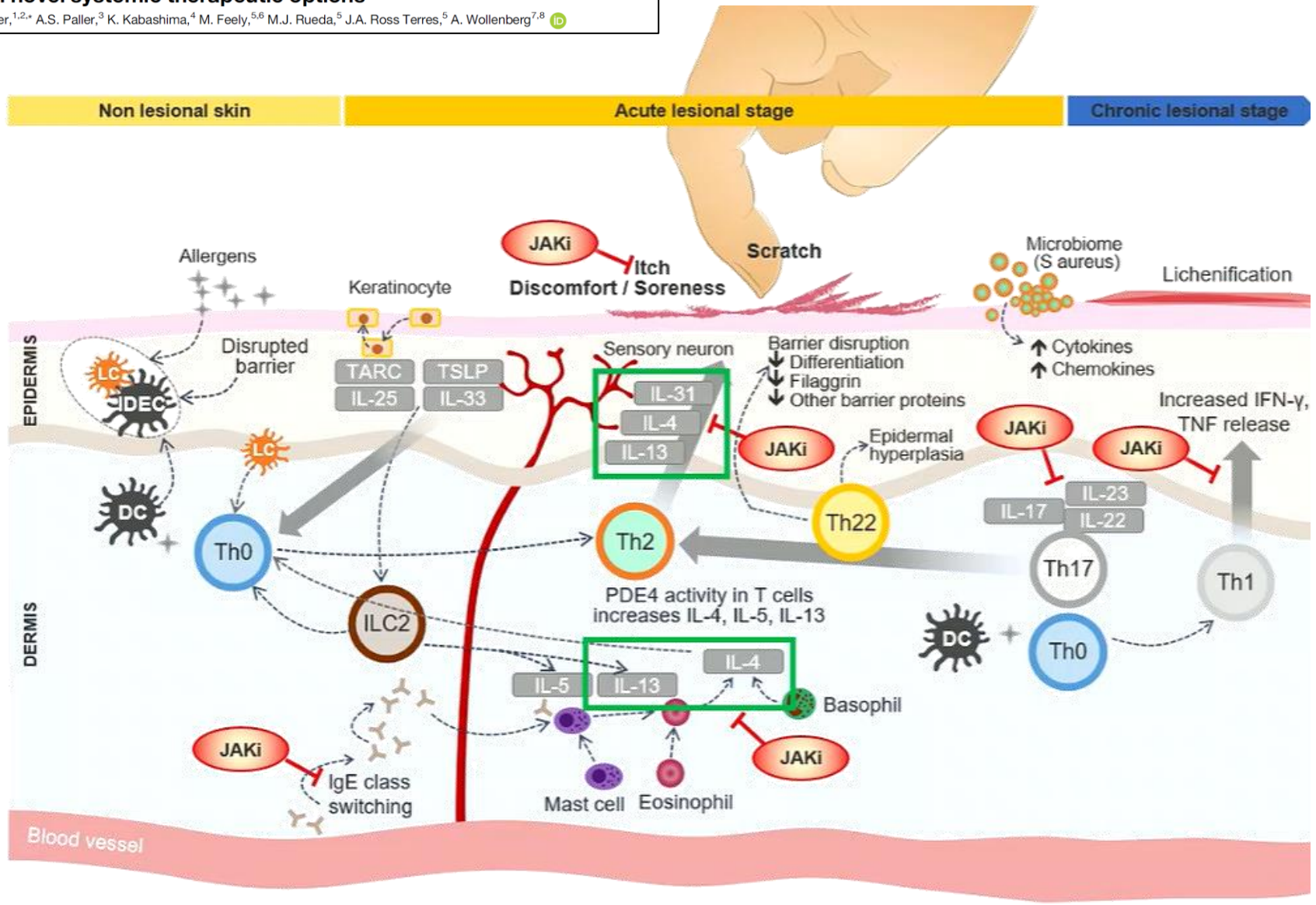
DOI: 10.1111/jdv.18225 JEADV
REVIEW ARTICLE

Atopic dermatitis: pathomechanisms and lessons learned from novel systemic therapeutic options

T. Bieber,[1,2,*] A.S. Paller,[3] K. Kabashima,[4] M. Feely,[5,6] M.J. Rueda,[5] J.A. Ross Terres,[5] A. Wollenberg[7,8]



- La DA está causada por una desregulación compleja de muchas vías inmunológicas
- La señalización de las citocinas clave en DA está mediada a través de receptores asociados a JAK

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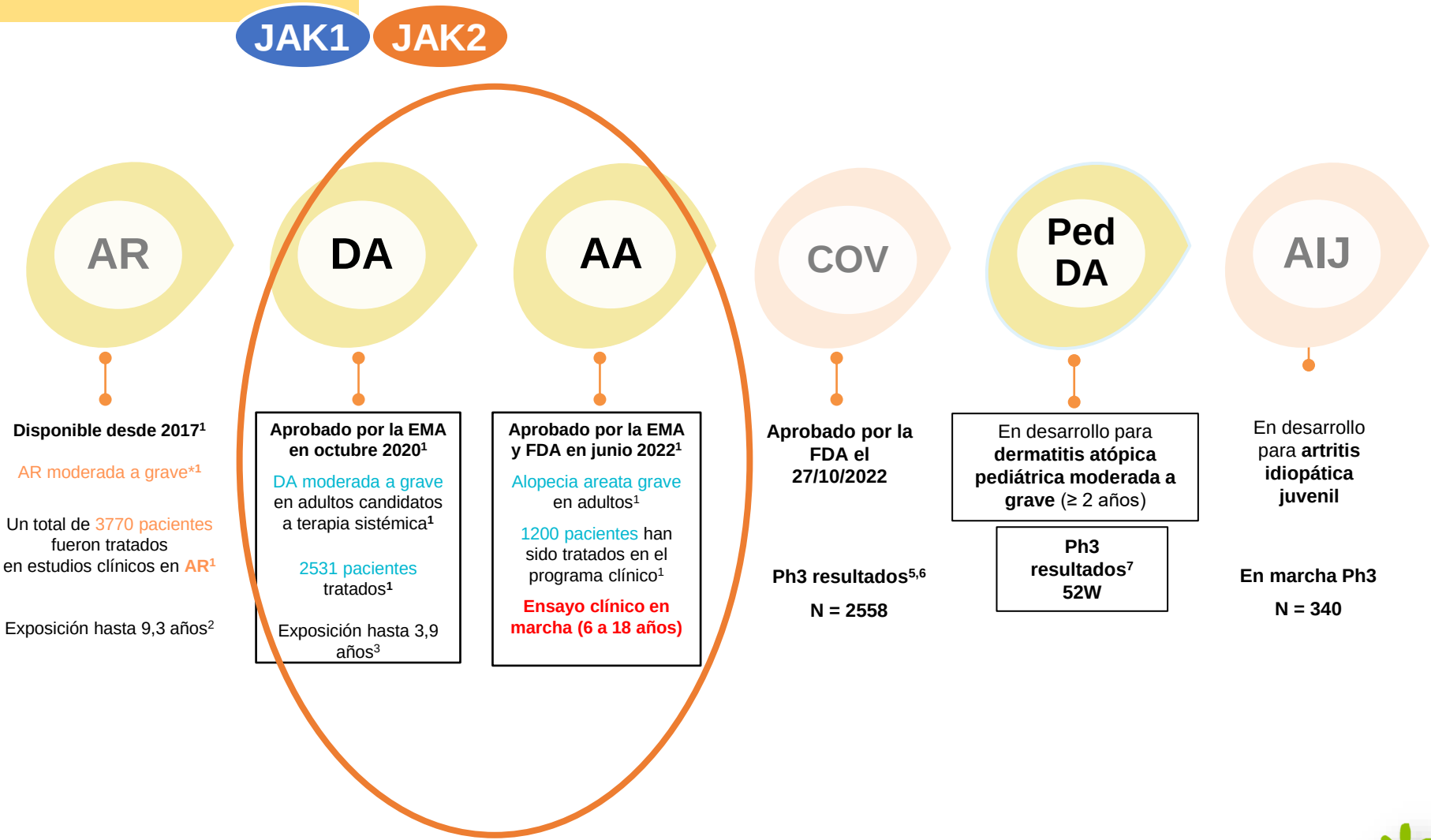
BARICITINIB: RCT



DA=Dermatitis atópica; EMA=European Medicines Agency; AR=artritis reumatoide COV= Covid-19. Ped DA= Dermatitis atópica pediátrica. AIJ= Artritis idiopática juvenil.1. Olumiant [Summary of Product Characteristics]. Eli Lilly Nederland B.V., the Netherlands; 2. Taylor, Peter C., et al. "Safety of baricitinib for the treatment of rheumatoid arthritis over a median of 4.6 and up to 9.3 years of treatment: final results from long-term extension study and integrated database." Annals of the Rheumatic Diseases (2021). 3. Bieber T., et al. EADV 2022. Safety of Baricitinib for the Treatment of Atopic Dermatitis Over a Median of 1.6 and Up to 3.9 Years Treatment: An Updated Integrated Analysis of 8 Clinical Trials 4. Kwon O, et al American Academy of Dermatology (AAD) 2022. Long-term Efficacy of Baricitinib in Patients With Severe Alopecia Areata: Week 52 Results From BRAVE-AA1 and BRAVE-AA2. 5. Marconi, Vincent C., et al. "Efficacy and safety of baricitinib for the treatment of hospitalised adults with COVID-19 (COV-BARRIER): a randomised, double-blind, parallel-group, placebo-controlled phase 3 trial." The Lancet Respiratory Medicine 9.12 (2021): 1407-1418. 6.Estudio fase 3 ACTT-2. NCT04401579 https://clinicaltrials.gov/ct2/show/NCT04401579. 7. Torrelo A, et al. EADV 2022. Efficacy and Safety of Baricitinib in a Phase 3, Randomized, Double-Blind, Placebo-Controlled Study in Pediatric Patients With Moderate-to-Severe Atopic Dermatitis

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BARICITINIB: RCT$_{ADULTOS}$

Research Article

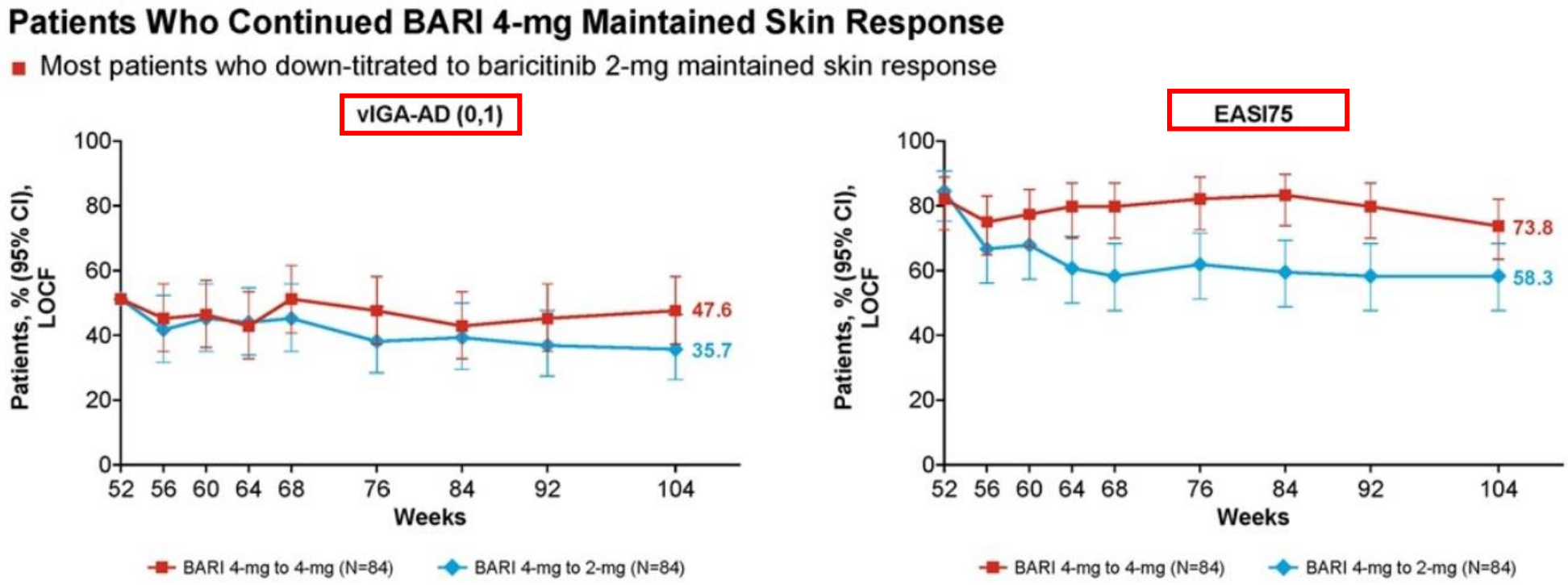
Maintained Improvement in Physician- and Patient-Reported Outcomes with Baricitinib in Adults with Moderate-to-Severe Atopic Dermatitis who were Treated for up to 104 Weeks in a Randomized Trial

Jacob P. Thyssen, Thomas Werfel, Sebastien Barbarot, Hamish J.A. Hunter, Evangeline Pierce, Luna Sun,

Received 13 Dec 2022, Accepted 09 Mar 2023, Accepted author version posted online: 13 Mar 2023

➢ **Eficacia a largo plazo (semana 104)**

(Respondedores de BREEZE-AD1/AD2/AD7 a 4mg/24h, re-aleatorizados a 4 o 2mg/24h)



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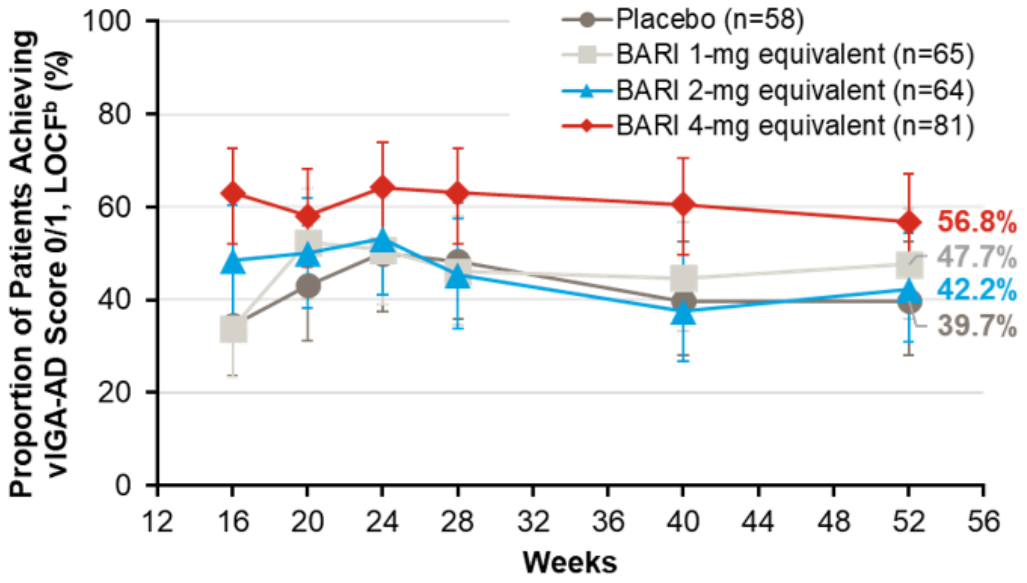
BARICITINIB: RCT PEDIATRÍA

NIÑOS Y ADOLESCENTES (2-17 años)

Proportion of Responders/Partial Responders[a] at Week 16 Achieving vIGA-AD Score 0/1 at Week 52

- Among Week 16 responders and partial responders who remained on double-blind study treatment, the proportion of patients achieving vIGA-AD score 0/1 at Week 52 was greater for patients receiving baricitinib 4-mg equivalent vs. all other treatment groups

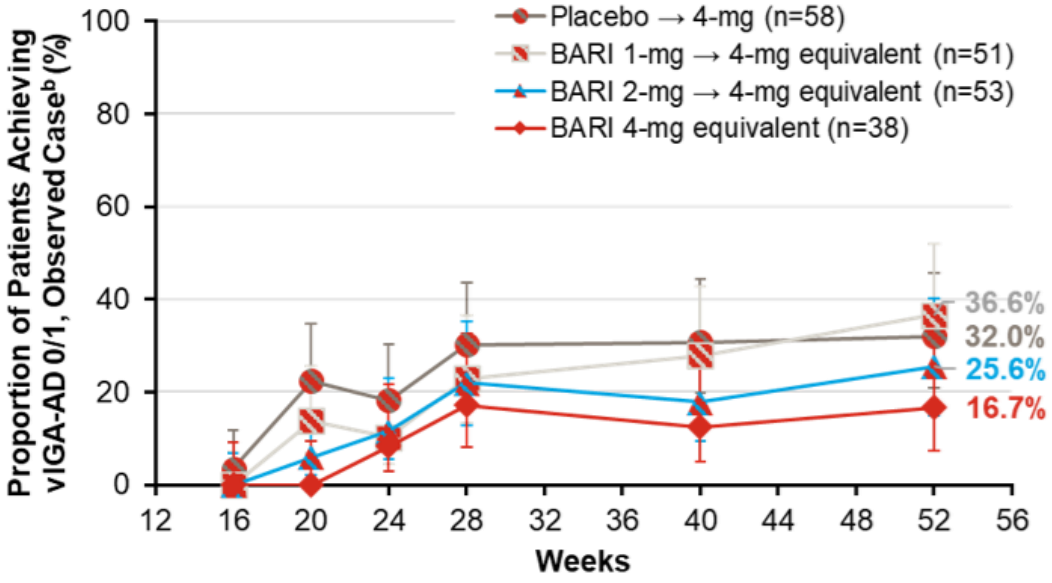


[a] Responders (vIGA-AD score 0/1) and partial responders (vIGA-AD score 2) at Week 16, who did not receive rescue therapy, remained on double-blind treatment at timepoints assessed; [b] Data were censored after permanent discontinuation of treatment or transition to open-label BARI 4-mg equivalent dose, and LOCF imputation was used

Note: Data cut-off date of 20 January 2023. Proportion of responders/partial responders at Week 16 achieving vIGA-AD score 0/1 at Week 52 was calculated as (number of patients in the specified category / number of patients with non-missing values) × 100. Bars represent 95% confidence intervals, constructed using Wilson method without continuity correction

Proportion of Nonresponders[a] at Week 16 Achieving vIGA-AD Score 0/1 at Week 52

- Among Week 16 non-responders who transitioned to open-label baricitinib 4-mg equivalent at Week 16, the proportion of patients achieving vIGA-AD score 0/1 at Week 52 was higher in all groups vs. that at Week 16



[a] Nonresponders (vIGA-AD score 3 or 4) at Week 16, or patients receiving rescue therapy, transitioned to open-label BARI high dose at Week 16; [b] Data were censored after permanent discontinuation of treatment

Note: Data cut-off date of 20 January 2023. Proportion of nonresponders at Week 16 achieving vIGA-AD score 0/1 at Week 52 was calculated as (number of patients in the specified category / number of patients with non-missing values) x 100. Bars represent 95% confidence intervals, constructed using Wilson method without continuity correction

P0499. Efficacy and Safety of Baricitinib Treatment in Pediatric Patients With Atopic Dermatitis Aged 2 to Less than 18 Years (Up to 3,6 Years of Exposure). Wollenberg. EADV Congress 2023

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UPADACITINIB: RCT

JAK1

Características principales

Inhibidor selectivo y reversible de JAK1

Indicado en adultos y adolescentes a partir de 12 años*

*Y peso corporal >30kg

Administración oral y rápida absorción

- Alcanza la concentración plasmática máxima en 1h
- Vida media corta (9-14h en DA)

Algunas interacciones farmacológicas

- Inhibidores de CYP3A4 → ↑[upadacitinib] (p.ej. itraconazol, claritromicina)
- Inductores del CYP3A4 → ↓[upadacitinib] (p.ej. rifampicina, fenitoína)

Eliminación renal (24%), heces (38%)

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UPADACITINIB: RCT

JAK1

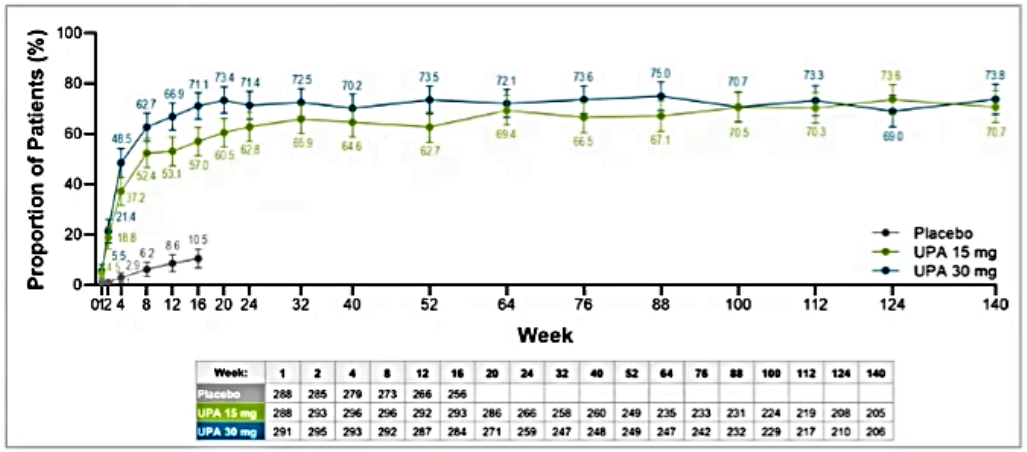
JOURNAL ARTICLE

502 - Efficacy and safety of upadacitinib through 140 weeks in adolescents and adults with moderate-to-severe atopic dermatitis: phase 3 randomized clinical trial results

Published: 07 February 2024

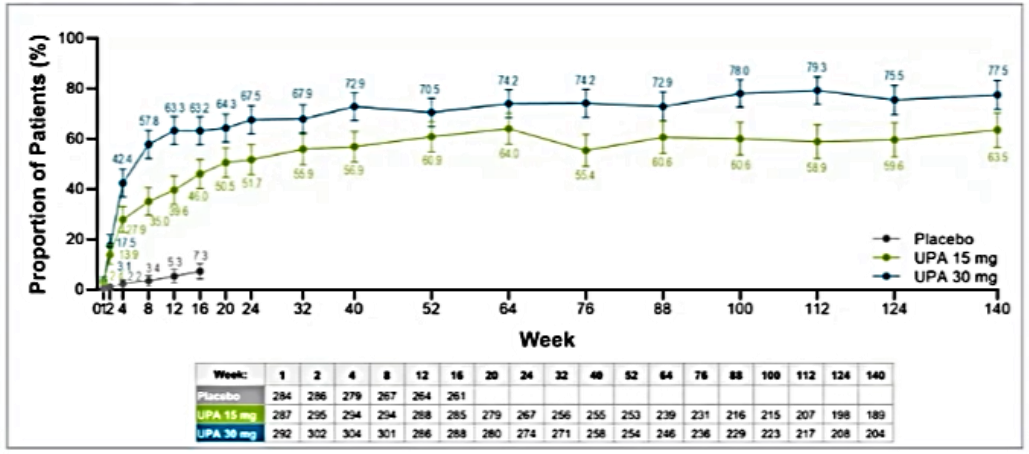
Figure 3. Proportion of patients achieving EASI 90 across 140 weeks in (a) Measure Up 1, (b) Measure Up 2, and (c) AD Up

(a) Measure Up 1: EASI 90



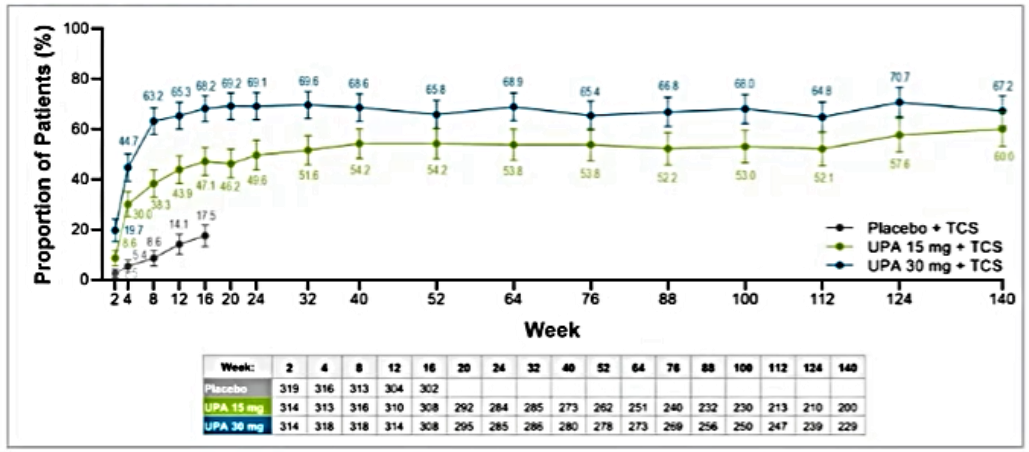
Week:	1	2	4	8	12	16	20	24	32	40	52	64	76	88	100	112	124	140
Placebo	288	285	279	273	266	256												
UPA 15 mg	288	293	296	296	292	293	286	266	258	260	249	235	233	231	224	219	208	205
UPA 30 mg	291	295	293	292	287	284	271	259	247	248	249	247	242	232	229	217	210	206

(b) Measure Up 2: EASI 90



Week:	1	2	4	8	12	16	20	24	32	40	52	64	76	88	100	112	124	140
Placebo	284	286	279	267	264	261												
UPA 15 mg	287	295	294	294	288	285	279	267	256	255	253	239	231	216	215	207	198	189
UPA 30 mg	292	302	304	301	286	288	280	274	271	258	254	246	236	229	223	217	208	204

(c) AD Up: EASI 90



Week:	2	4	8	12	16	20	24	32	40	52	64	76	88	100	112	124	140
Placebo	319	316	313	304	302												
UPA 15 mg	314	313	316	310	308	292	284	285	273	262	251	240	232	230	213	210	200
UPA 30 mg	314	318	318	314	308	295	285	286	280	278	273	269	256	250	247	239	229

- Patients in placebo groups that were re-randomized to UPA 15 mg or 30 mg after week 16 had response rates through week 140 that were similar to patients receiving UPA continuously (*data not shown*)

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ABROCITINIB: RCT

JAK1

Características principales

Inhibidor selectivo y reversible de JAK1

Administración oral y rápida absorción

- Alcanza la concentración plasmática máxima en 1h
- Vida media corta

Aclaramiento metabólico (<1% excreción inalterada en orina)

Algunas interacciones farmacológicas

- Inhibidores del CYP2C19/CYP2C9: ↑[abrocitinib] (p.ej. fluconazol).
- Inductores del CYP2C19/CYP2C9: ↓[abrocitinib] (p.ej. rifampicina)

pharmaceutics MDPI

Review

Efficacy and Safety of JAK1 Inhibitor Abrocitinib in Atopic Dermatitis

Helena Iznardo [1,2,3], Esther Roé [1,2,3], Esther Serra-Baldrich [1,2,3] and Lluís Puig [1,2,3,*]

>18-64 años:

- **200mg/24h**

Dosis de 100mg/24h:

- Adultos ≥65 años*
- FGe de >30-60ml/min (si >15-30ml: 50mg/24h)
- Considerar la dosis efectiva más baja para el mantenimiento

Considerar la suspensión del tratamiento en pacientes que no muestren evidencia de beneficio terapéutico después de 24 semanas de tratamiento

*Datos limitados en >75 años: utilizar con precaución

Cibinqo [Ficha técnica]: https://www.ema.europa.eu/en/documents/product-information/cibinqo-epar-product-information_es.pdf

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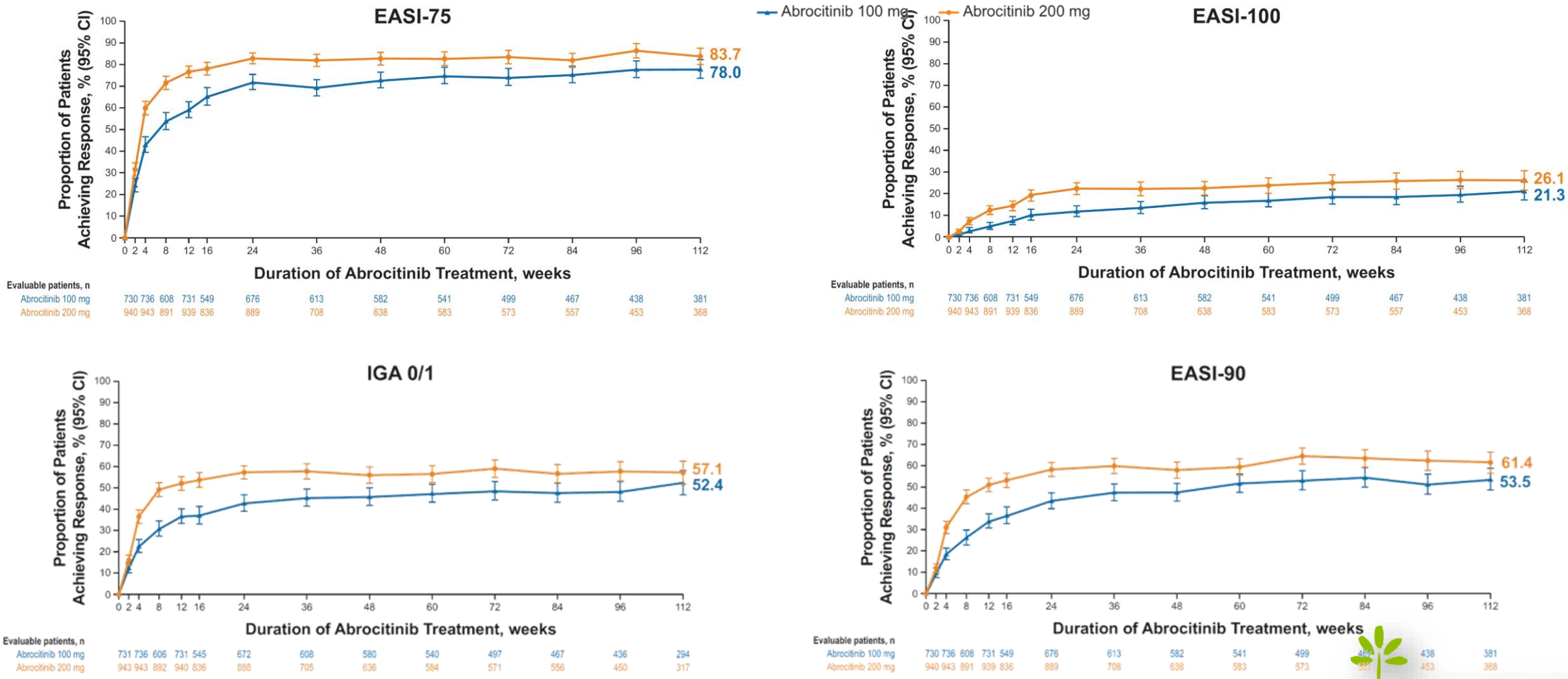
ABROCITINIB: RCT

Figure 1. Proportions of Patients Who Achieved Efficacy Responses Over 112 Weeks of Abrocitinib Treatment



Presented at the Annual European Academy of Dermatology and Venereology (EADV) Congress; October 11-14, 2023; Berlin, Germany

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ABROCITINIB: RCT

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

22 February 2024
EMA/CHMP/50/2024
Committee for Medicinal Products for Human Use (CHMP)

Summary of opinion[1] (post authorisation)

Cibinqo

abrocitinib

On 22 February 2024, the Committee for Medicinal Products for Human Use (CHMP) adopted a positive opinion recommending a change to the terms of the marketing authorisation for the medicinal product Cibinqo. The marketing authorisation holder for this medicinal product is Pfizer Europe MA EEIG.

The CHMP adopted an extension to the existing indication to include treatment of adolescents aged 12 years and older. For information, the full indication will therefore be as follows:[2]

> Cibinqo is indicated for the treatment of moderate-to-severe atopic dermatitis in adults **and adolescents 12 years and older** who are candidates for systemic therapy.

Detailed recommendations for the use of this product will be described in the updated summary of product characteristics (SmPC), which will be published in the revised European public assessment report (EPAR), and will be available in all official European Union languages after a decision on this change to the marketing authorisation has been granted by the European Commission.

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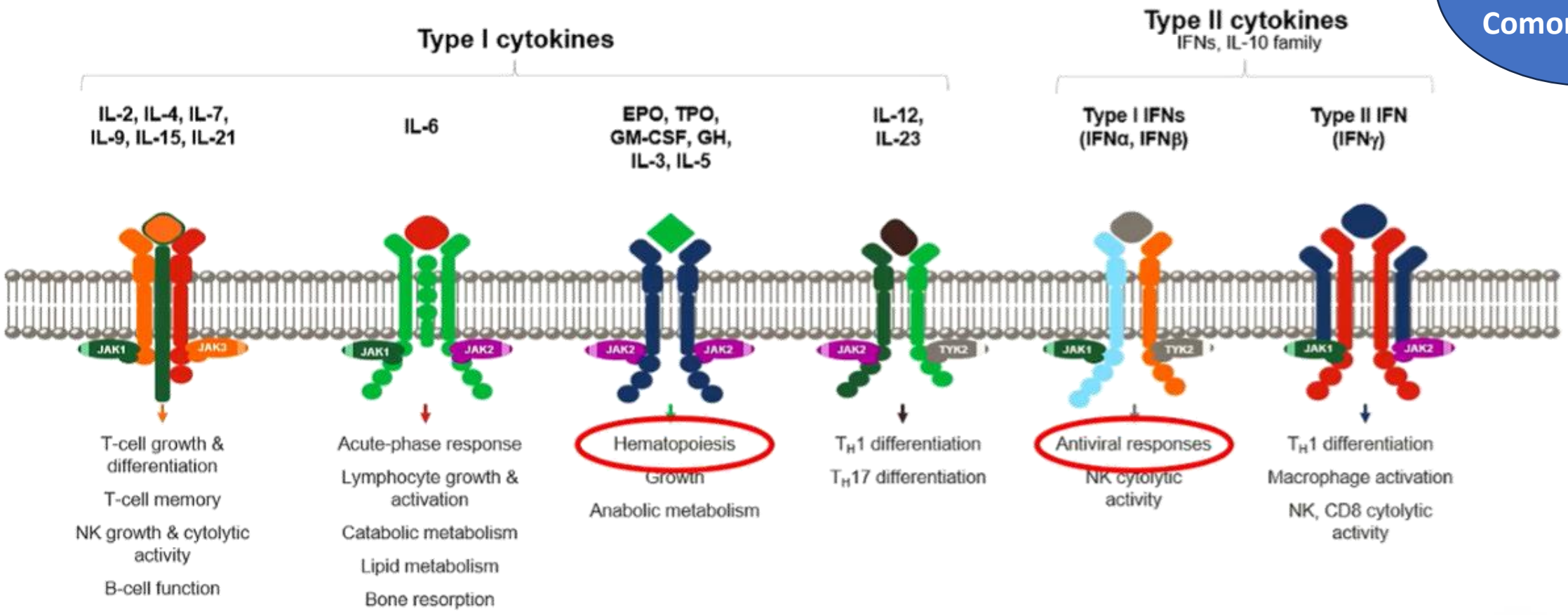
Physiological roles for Janus kinases

Janus kinases are essential for signaling by multiple cytokines involved in homeostasis

Dosis
Edad
Comorbilidades



CD=cluster of differentiation; EPO=erythropoietin; GH=growth hormone; GM-CSF=granulocyte-macrophage colony-stimulating factor; IFN=interferon; IL=interleukin; JAK=Janus kinase; NK=natural killer; STAT=signal transducer and activator of transcription ; T_H=T-helper cell; TPO=thrombopoietin; TYK=tyrosine kinase; Massimo Gadina M, et al. Rheumatology 2019;58:i4i16

	Abrocitinib[1*,a, b]	Baricitinib[2**, b]	Upadacitinib[3***, b]
Very common (≥ 1/10)	• Nausea	• Hypercholesterolemia • Upper respiratory tract infections	• Acne • Upper respiratory tract infections
Common (≥ 1/100 to < 1/10) for all 3 JAKi in alphabetical order	• Abdominal pain upper • CPK increased > 5 x ULN • Headache • Herpes simplex	• Abdominal pain • CPK increased > 5 x ULN • Headache • Herpes simplex	• Abdominal pain • Blood CPK increased • Headache • Herpes simplex
Common (≥ 1/100 to < 1/10) for 2 JAKi in alphabetical order	• Acne • Herpes zoster	• Acne • Herpes zoster • Rash • Urinary tract infection	• Herpes zoster • Rash • Urinary tract infection
Common (≥ 1/100 to < 1/10) for specific JAKi only in alphabetical order	• Dizziness • Vomiting	• Gastroenteritis • Pneumonia • Folliculitis • Thrombocytosis > 600 x 109 cells/L	• Anemia • Fatigue • Folliculitis • Bronchitis • ALT increased • AST increased • Influenza • Nausea • Neutropenia • Lymphopenia • NMSC • Hypercholesterolemia • Pyrexia • Urticaria • Weight increased • Hyperlipidemia

[b]The European Commission (after Art 20 referral) has updated the warnings and precautions (section 4.4) in the SmPC for Janus kinase (JAK) inhibitors to inform physicians that these medicines should be used in the following patients only if no suitable treatment alternatives are available: those aged 65 years or above, those at increased risk of major cardiovascular problems (such as heart attack or stroke), those who smoke or have done so for a long time in the past and those at increased risk of cancer . For more information, please see the final SmPCs[3,4,5]

*Frequencies observed in AD clinical studies. Adverse reactions indicated to be uncommon in AD are not listed here.

**Frequencies are based on integrated data from clinical trials and/or postmarketing settings across both rheumatoid arthritis, AD and alopecia areata indications; adverse reactions indicated to be uncommon in AD are not listed here.

***Frequencies are based on the higher of the rates for adverse reactions reported with Rinvoq in clinical trials of rheumatologic disease (15 mg), atopic dermatitis (15 mg and 30 mg) or ulcerative colitis (15 mg, 30 mg and 45 mg); adverse reactions indicated to be uncommon in AD are not listed here.

AD=atopic dermatitis; CPK=creatine phosphokinase; JAK=Janus kinase; NMSC: non-melanoma skin cancer; ULN=upper limit of normal.

1. Cibinqo (abrocitinib). Summary of product characteristics. Pfizer. 2023 2. Olumiant (baricitinib). Summary of product characteristics. Eli Lilly. 2023. 3. Rinvoq (upadacitinib). Summary of product characteristics. Abbvie. 2023.

※ Continued follow-up and further research, including long-term population-based studies, are on-going to fully understand the risk of outcomes, including malignancies, MACE and VTE, and the comparative real-world risk of baricitinib and therapies in RA(including TNFi). The JAK inhibitor class is being evaluated under the Art. 20 referral process.

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Received: 14 March 2023 | Accepted: 18 July 2023
DOI: 10.1111/jdv.19426

SYSTEMATIC REVIEW

The safety of systemic Janus kinase inhibitors in atopic dermatitis: A systematic review and meta-analysis of randomized controlled trials

Jak inhibitor type	Number of results (*n*)	No of subjects	Heterogeneity (%)[a]	Relative risk (95% confidence interval)[b]
Serious infection				
Baricitinib	3	1229	19	0.65 (0.16–2.74)
Abrocitinib	3	1229	0	0.94 (0.15–5.72)
Upadacitinib	5	3021	0	0.95 (0.36–2.54)
Herpes zoster				
Baricitinib	5	2591	0	1.77 (0.47–6.64)
Abrocitinib	5	1925	0	1.64 (0.42–6.39)
Upadacitinib	5	3021	0	2.23 (0.91–5.47)
Headache				
Baricitinib	5	2263	38	1.68 (0.96–2.94)
Abrocitinib	5	1925	0	1.47 (0.90–2.42)
Upadacitinib	4	2749	0	1.34 (0.93–1.92)
Nasopharyngitis				
Baricitinib	6	2591	38	1.05 (0.76–1.14)
Abrocitinib	4	1658	0	1.19 (0.81–1.74)
Upadacitinib	5	3021	0	1.25 (0.97–1.60)
Acne				
Baricitinib	1	328	Not applicable	2.45 (0.29–20.75)
Abrocitinib	4	1658	0	5.15 (1.43–18.57)
Upadacitinib	5	3021	0	5.08 (3.37–7.67)
Blood creatinine phosphokinase elevation				
Baricitinib	6	2578	0	1.69 (1.22–2.34)
Abrocitinib	3	1063	15	2.14 (0.54–8.51)
Upadacitinib	5	3021	0	2.10 (1.33–3.34)
Nausea				
Baricitinib	1	438	Not applicable	1.33 (0.36–4.95)
Abrocitinib	5	1925	0	5.35 (2.65–10.80)
Upadacitinib	1	166	Not applicable	2.22 (0.28–17.52)

Los estudios excluyen:
- Pacientes con AP de herpes zóster o herpes simple diseminado
- Pacientes con AP de herpes recurrente
- Pacientes con AP de eccema herpeticum

La incidencia de infección por VVZ podría ser superior en dichos pacientes

Se recomienda la vacunación con la vacuna recombinante del VVZ (Shingrix) en adultos (2 dosis separadas entre 2 a 6 meses)

Puede administrarse mientras el paciente ya ha iniciado tratamiento con iJAK, aunque no está claro su efecto sobre la eficacia de la vacuna

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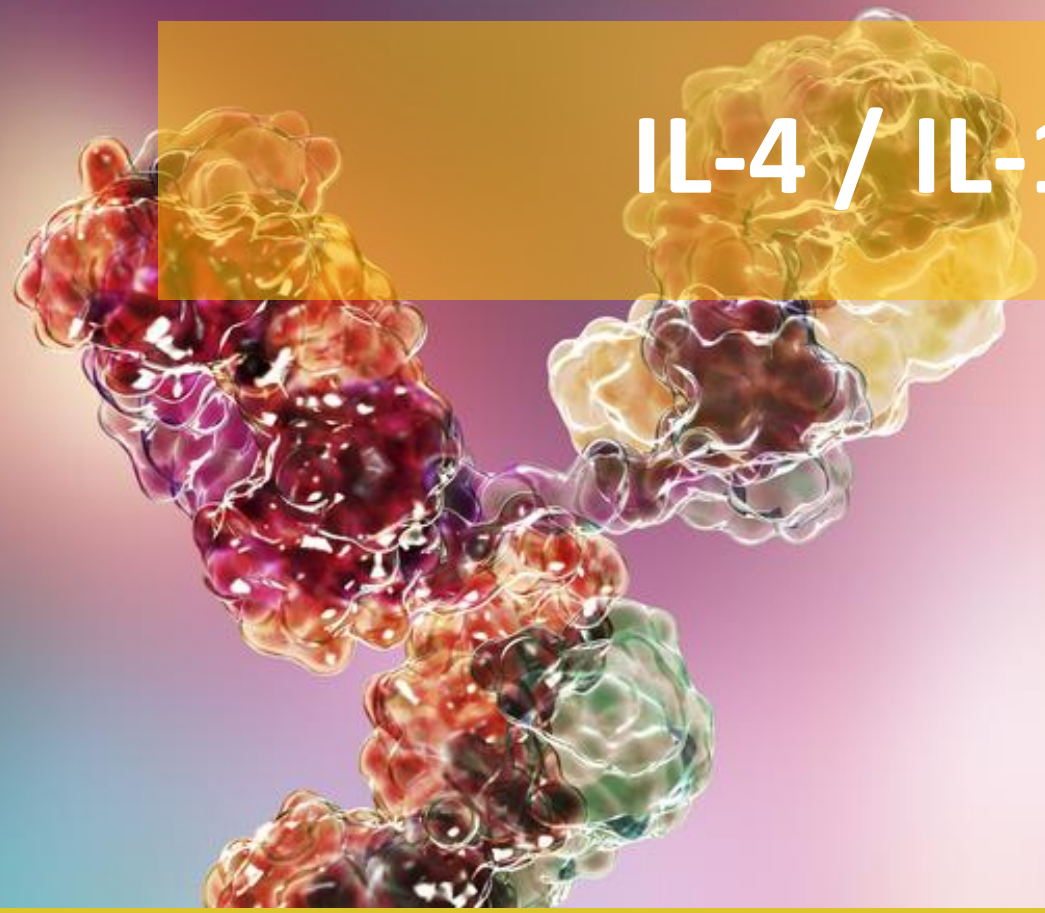
IL-4 / IL-13



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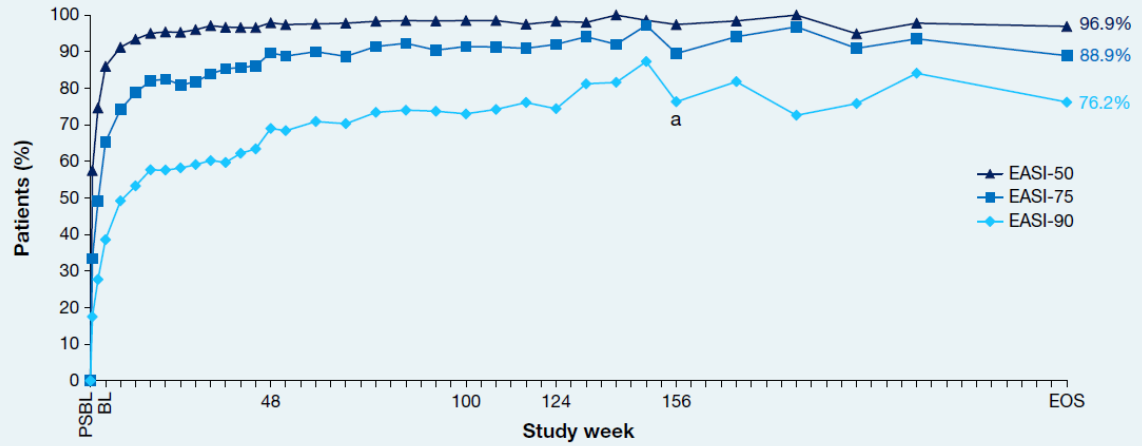
Hospital

DUPILUMAB: RCT

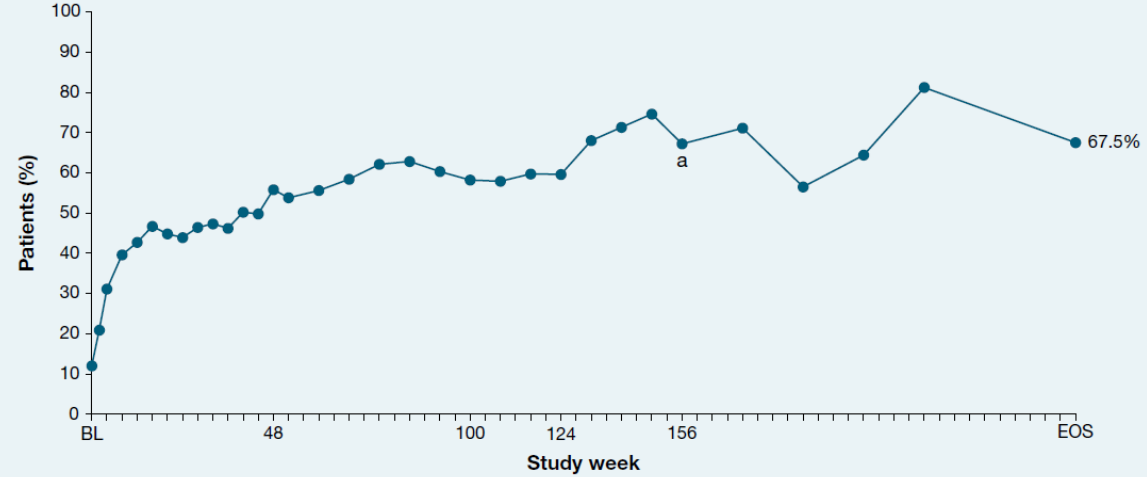


Number of patients

Total N = 2,677	2,647	2,310	999	473	114	324

[a]Following protocol amendments in June 2017 and January 2018, 114 and 272 patients, respectively, re-entered the trial, with 103 and 207 patients, respectively, having a treatment interruption of >8 weeks between study Weeks 148 and 164. BL, baseline; EASI-50/75/90, ≥50%/75%/90% improvement from PSBL in EASI; EOS, end of study: all study days ≥1,794 (Week ≥260) are included (study day is calculated relative to the date of first study drug injection); SE, standard error.

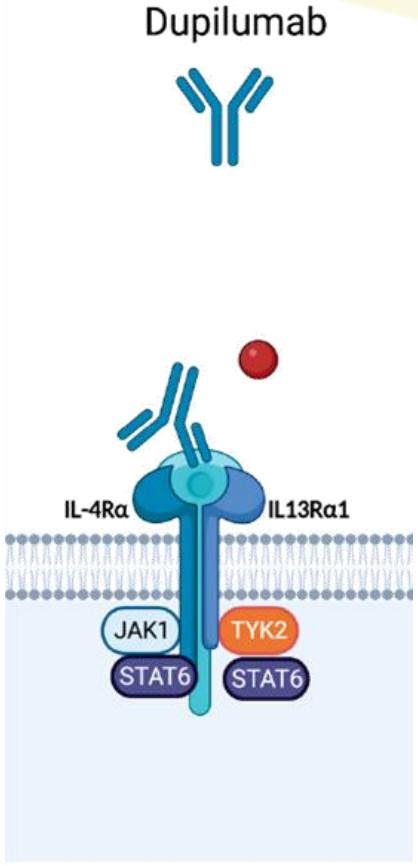
Figure 2. Proportion of patients achieving IGA score of 0 or 1 over time during the OLE study.



Number of patients

Total N = 2,677	2,677	2,341	1,019	478	116	326

[a]Following protocol amendments in June 2017 and January 2018, 114 and 272 patients, respectively, re-entered the trial, with 103 and 207 patients, respectively, having a treatment interruption of >8 weeks between study Weeks 148 and 164. IGA, Investigator's Global Assessment.



Long-Term Efficacy of Dupilumab for up to 5 Years in an Open-Label Extension Study of Adults With Moderate-to-Severe Atopic Dermatitis
Lisa A. Beck

Presented at the Annual Congress of the European Academy of Dermatology and Venereology (EADV); Berlin, Germany; October 11–14, 2023.

Germans Trias i Pujol Hospital

600mg, seguido de 300mg Q2W

W16 (monoterapia)	
IGA 0/1:	36-38%
EASI50:	65-69%
EASI75:	44-51%
EASI90:	30-36%

Peso ≥60kg: 600mg, seguido de 300mg Q2W
Peso 15-60kg: 400mg, seguido de 200mg Q2W

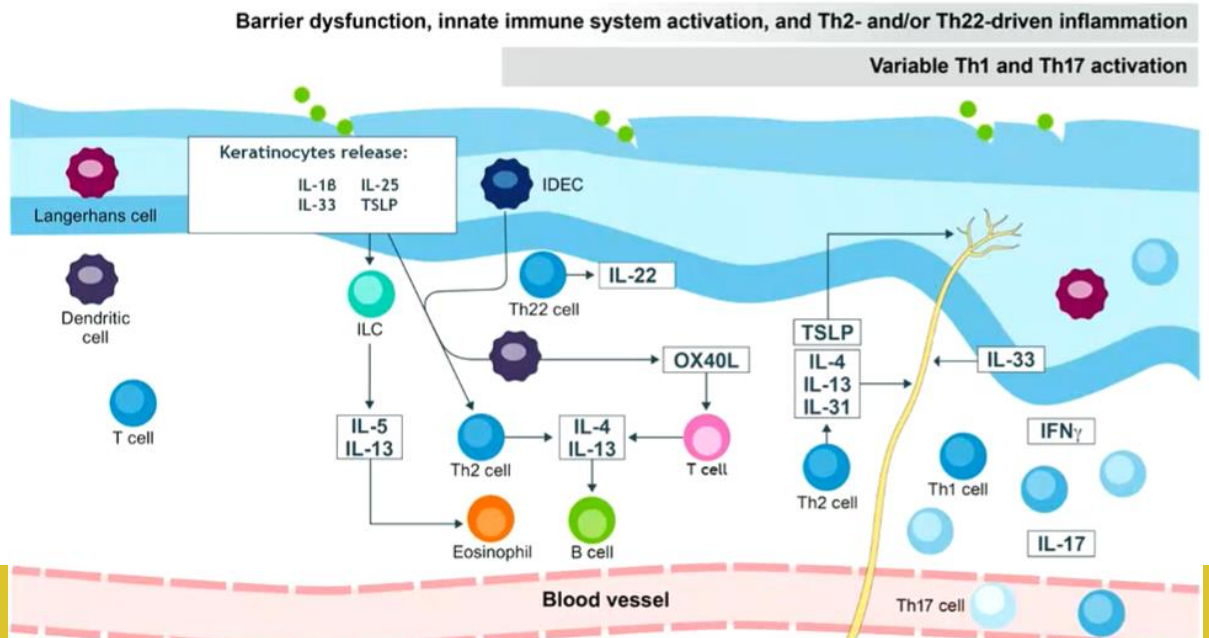
W16 (monoterapia)	
IGA 0/1:	24,%
EASI50:	61%
EASI75:	41,5%
EASI90:	23,3%

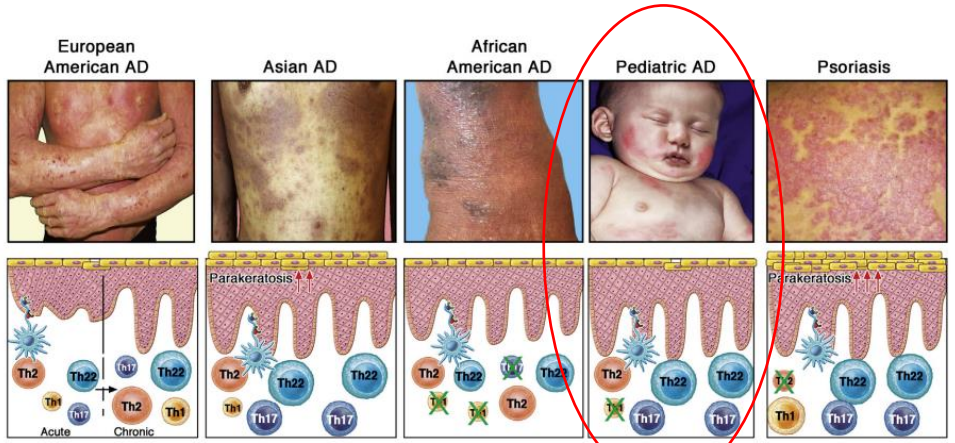
Peso ≥60kg: 600mg, seguido de 300mg Q2W
Peso 15-60kg*: *Puede realizarse dosis = adolescente
300mg día 1, 300mg día 15, después 300mg Q4W

W16 (+TCS)	
IGA 0/1:	32,8-39%
EASI50:	86,4-91%
EASI75:	69,7-74,4%
EASI90:	35,6-41,8%
NRSP4:	50,8-61,4%

Peso 15-30kg: 300mg Q4W (no dosis inicial)
Peso 5-<15kg: 200mg Q4W (no dosis inicial)

W16 (+TCS)	
IGA 0/1:	14,3-27,7%
EASI50:	60,3-68,7%
EASI75:	46-53%
EASI90:	15,9-25,3%
NRSP4:	42,3-48,1%





DOI: 10.1111/jdv.18225 JEADV
REVIEW ARTICLE
Atopic dermatitis: pathomechanisms and lessons learned from novel systemic therapeutic options
T. Bieber,[1,2,*] A.S. Paller,[3] K. Kabashima,[4] M. Feely,[5,6] M.J. Rueda,[5] J.A. Ross Terres,[5] A. Wollenberg[7,8]

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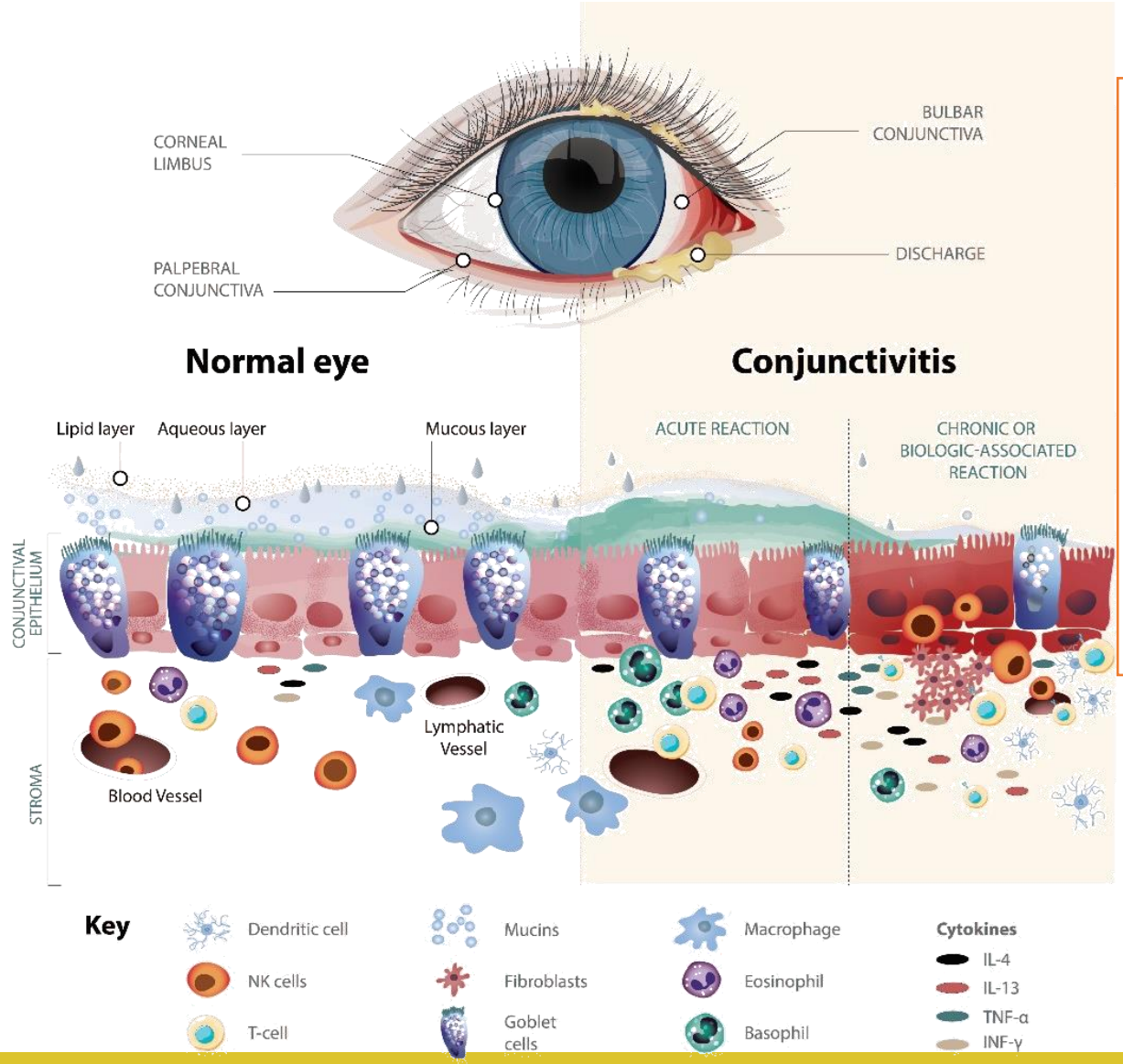
Enfermedad de la Superficie Ocular

Received: 20 October 2022 | Accepted: 16 January 2023
DOI: 10.1111/jdv.18922
JEADV
REVIEW ARTICLE

Expert consensus on the systemic treatment of atopic dermatitis in special populations

D. N. Adam[1,2,3] | M. J. Gooderham[3,4] | J. R. Beecker[3,5,6,7] | C. H. Hong[3,8,9] | C. S. Jack[10,11] | V. Jain[3,12] | P. Lansang[1,13,14] | C. W. Lynde[1,3,15] | K. A. Papp[3,16] | V. H. Prajapati[3,17,18,19,20,21] | I. Turchin[3,22,23] | J. Yeung[1,3,13,14]



- La DA se asocia a OSD (sobre todo conjuntivitis)
- **Su incidencia puede augmentar con biológicos que actúan sobre la vía Th2**
  - **De 3,6 a 31% en tratados con dupilumab**
  - **De 2 a 13,1% en tratados con tralokinumab**
  - *Lebrikizumab 2,7 a 9,6%
- Puede ser precoz (primeras 2W o tardío-52W)

PATOGÉNESIS

- La inhibición de IL-4/IL-13 conduce a una hipoplasia de las células caliciformes y de la producción de mucina
- Disminuye el grosor de la lágrima (capas lipídica, acuosa, y mucosa)
- Activación de linfocitos T, proliferación de fibroblastos
- Incremento IFN-γ

FACTORES DE RIESGO (DUPILUMAB)

- DA más grave
- Antecedentes de ojo seco
- Antecedentes de queratitis punteada superficial
- Eccema palpebral
- Historia de alergia alimentaria
- IgE total sérica >1000 kU/L

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De novo o exacerbación: head and neck dermatitis

- La mayoría de pacientes con afectación facial previa puede mejorar con dupilumab
- **En un 5 a 11% puede producirse un empeoramiento o aparición *de novo* de dermatitis facial**
- En algunos casos, asociado a retirada de TCS. Múltiples teorías propuestas
- En población pediátrica, podría ser más frecuent post-pubertad.

TEORÍAS PROPUESTAS	
Hypersensitivity reaction	• Some patients report nonfacial regional flaring
Site-specific failure	• Site-specific failure is known to occur in psoriasis patients receiving biologics
Seborrheic Dermatitis-like	• Occurs in seborrheic areas • Case within our series cleared with topical ketoconazole
Allergic contact dermatitis	• 3 patients who cleared after allergen identification and removal published • Paradoxical worsening of allergic contact dermatitis in patients receiving dupilumab could be accounted for by promotion of a TH1 response in otherwise TH2 predominant individuals via dupilumab-induced blockade of IL-4 and IL-13
Demodex associated rosacea like dermatosis	• Dupilumab inhibits T-helper cell 2 signaling, which may include immune responses against helminth infections. • In theory, the treatment of dupilumab could promote Demodex proliferation in follicles and increase IL-17-mediated inflammation involved in the pathophysiology of rosacea

ORIGINAL ARTICLE

Facial erythema in patients with atopic dermatitis treated with Dupilumab – a descriptive study of morphology and Aetiology

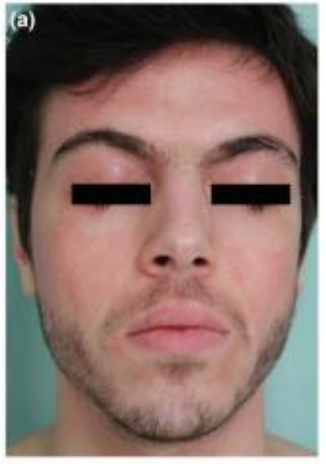
J. Ahn,[1,†] D.H. Lee,[1,†] C.H. Na,[2] D.H. Shim,[2] Y.S. Choi,[3] H.J. Jung,[1] E.L. Simpson[4,*]

Facial and neck erythema associated with dupilumab treatment: A systematic review

Christine E. Jo, BSc,[a] Alexandra Finstad, BScH, BAH,[a] Jorge R. Georgakopoulos, MD,[b] Vincent Piguet, MD, PhD, FRCP,[b,c] Jensen Yeung, MD, FRCPC,[b,c,d,e] and Aaron M. Drucker, MD, ScM, FRCPC[b,c]
Ottawa, Toronto, and Waterloo, Ontario, Canada

TRATAMIENTOS PROPUESTOS:

- TCS / TCI
- Metronidazol tópico
- Ivermectina oral (1 dosis de 12mg)
- Ketoconazol tópico
- Itraconazol oral (200mg dosis única, 200mg 1/24h por 2-4 semanas)



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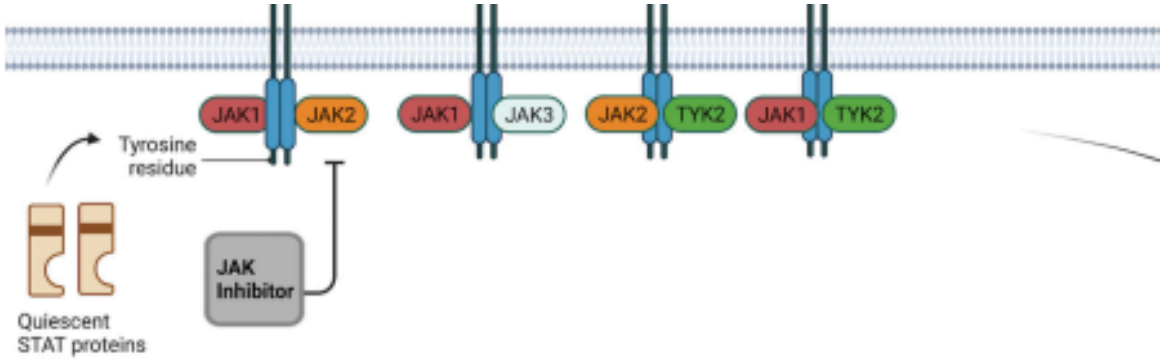
Erupción psoriasiforme

- Incidencia de hasta el 1,7%
- Mayor número de casos descritos en población adulta (pero también pediátrica)
- Discontinuación de dupilumab hasta en el 48% de los casos



Drug					FDA Approval
Barcitinib JAK1/JAK2 inhibitor	+	–	+	+	RA, AD, AA
Upadacitinib/ JAK1 inhibitor	+	+	–	+	AD, RA, PsoA, UC, AS
Abrocitinib/ JAK1 inhibitor	+	+	–	+	AD

T Helper 2 IL-4/IL-13 Dual Blockade with Dupilumab Is Linked to Some Emergent T Helper 17–Type Diseases, Including Seronegative Arthritis and Enthesitis/ Enthesopathy, but Not to Humoral Autoimmune Diseases

JID Open

Charlie Bridgewood[1], Miriam Wittmann[1,2,3], Tom Macleod[1], Abdulla Watad[1,4,5,6], Darren Newton[7], Kanchan Bhan[8], Howard Amital[4,5], Giovanni Damiani[9,10,11], Sami Giryes[1,12,13], Nicola Luigi Bragazzi[1,14] and Dennis McGonagle[1,2]

- 37.848 efectos adversos evaluados
- Mayor afectación: ocular, cutánea y musculoesquelética

<u>Asociaciones a dupilumab:</u>

- Artritis seonegativa (OR: 9,61)
- Psoriasis (OR: 1,48)
- Entesitis/entesopatía (OR: 12,65)
- Iridociclitis (OR: 3,77)

JOURNAL OF DERMATOLOGICAL TREATMENT
2023, VOL. 34, NO. 1, 2183729
https://doi.org/10.1080/09546634.2023.2183729

Taylor & Francis

BRIEF REPORT

OPEN ACCESS

Upadacitinib for the treatment of concomitant psoriasis and atopic dermatitis: a case series

Luigi Gargiulo[a,b], Luciano Ibba[a,b], Giulia Pavia[a,b], Jessica Avagliano[b], Andrea Cortese[a,b], Antonio Costanzo[a,b] and Alessandra Narcisi[b]

[a]Department of Biomedical Sciences, Humanitas University, Pieve Emanuele, MI, Italy; [b]Dermatology Unit, IRCCS Humanitas Research Hospital, Rozzano, MI, Italy

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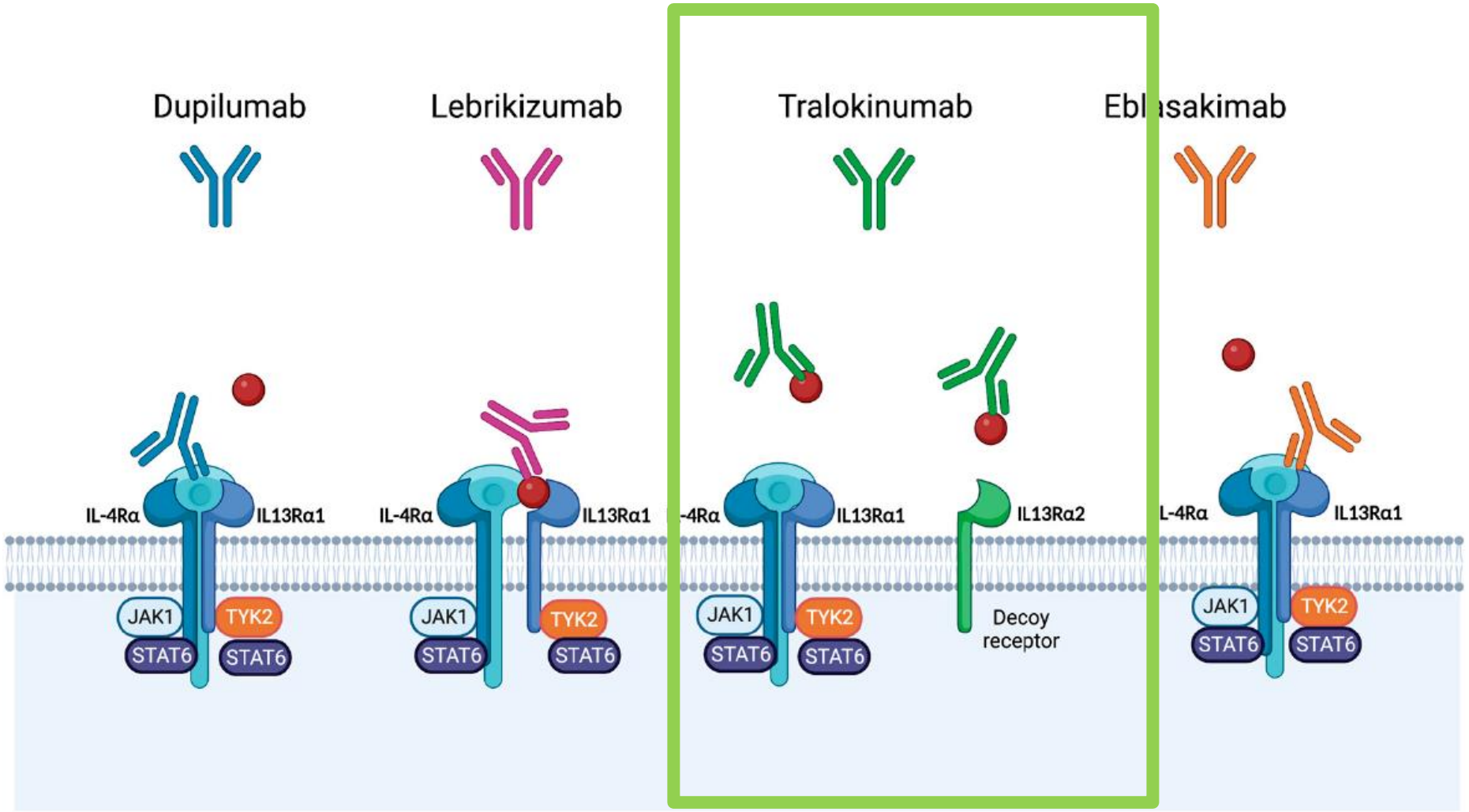
TRALOKINUMAB

pharmaceutics
MDPI
Review

Targeting Interleukin 13 for the Treatment of Atopic Dermatitis

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



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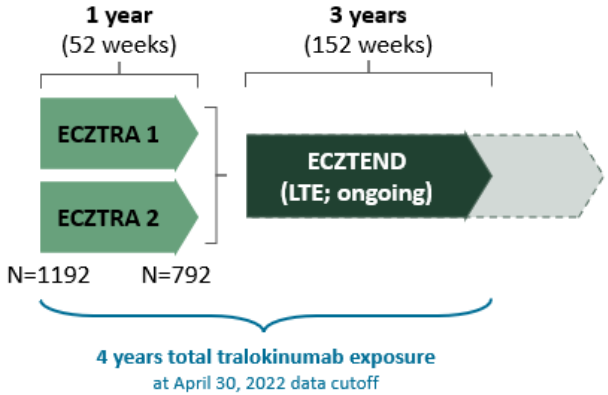
TRALOKINUMAB: RCT$_{\text{extensión a largo plazo (5a)}}$

JOURNAL ARTICLE

551 - Continuous tralokinumab treatment over 4 years in adults with moderate-to-severe atopic dermatitis provides long-term disease control

Published: 07 February 2024

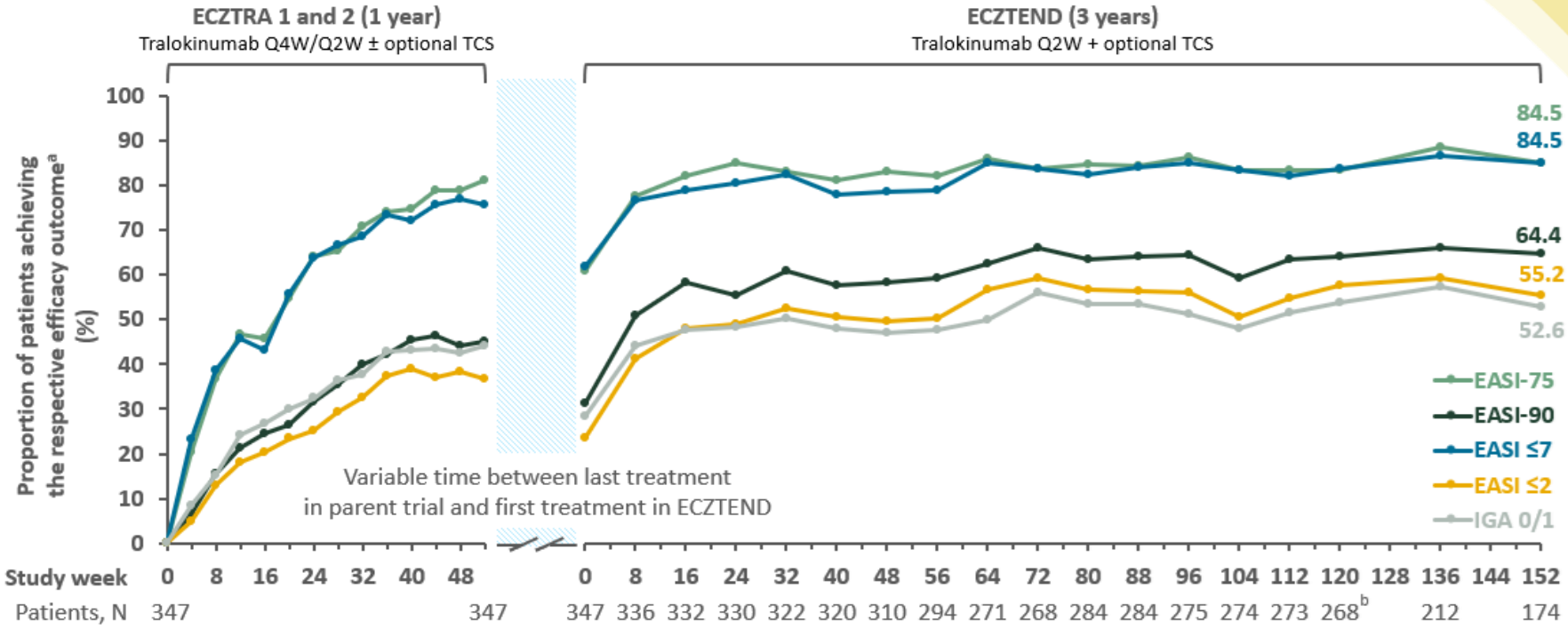
Ensayo ECZTEND: 4 años (Tralo 300mg Q2W)



Completed 52 weeks on tralokinumab in ECZTRA 1 and 2 in countries with ECZTEND
n=671

Entered ECZTEND
n=523

Enrolled in ECZTEND at least 3 years prior to data cutoff April 30, 2022
n=347



[a]As observed, includes patients from the parent trials ECZTRA 1 and 2 who had consistently received tralokinumab for a total of 4 years at data cutoff, April 30, 2022.

[b]83 subjects did not consent to continue in ECZTEND following a protocol amendment in May 2021 prolonging the trial from up to 3 to up to 5 years and changing the visit schedule from every 8 to every 16 weeks.

%, percentage of patients; EASI, Eczema Area and Severity Index; IGA, Investigator's Global Assessment; Max, maximum; Min, minimum; N, number of patients with recorded observation; NRI, non-responder imputation; Q, quartile; Q2W/Q4W, every 2/4 weeks; SD, standard deviation; TCS, topical corticosteroids.

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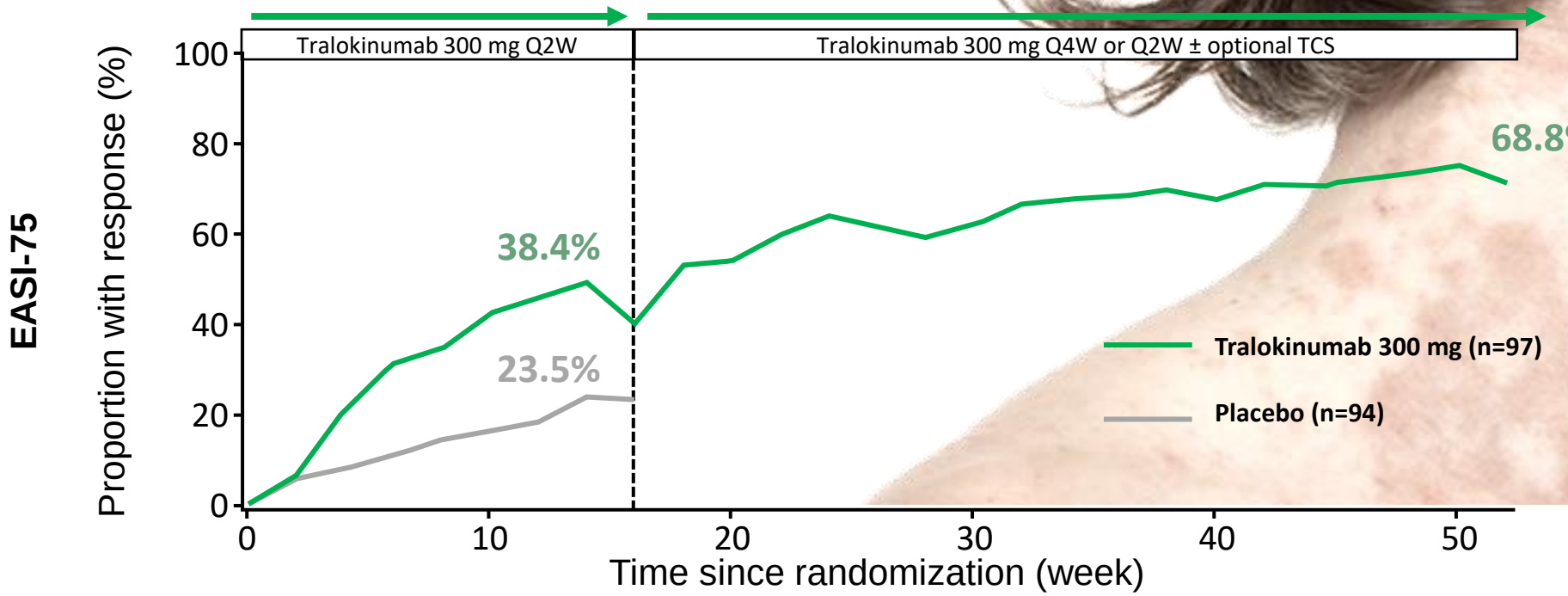
TRALOKINUMAB: RCT ADOLESCENTES

ECTRZA6 (tralokinumab ± TCS , 12-17 años, W16 y W52)



Treatments were reassigned at Week 16, and the placebo arm was only followed up to Week 16. The tralokinumab 300 mg arm was followed beyond Week 16 and the different dosing (Q2W vs. Q4W) was ignored. Treatment policy approach was adopted using observed data, regardless of rescue medication and treatment discontinuation. Missing data were imputed using multiple imputations and Rubin's rule was used to combine the results of the analyses of imputations. For binary endpoints the denominator was n=97 for tralokinumab and n=94 for placebo.
EASI, Eczema Area and Severity Index; Q2/4W, every 2/4 weeks; TCS, topical corticosteroids.

Wollenberg et. al, European Society for Pediatric Dermatology 21st Annual Meeting, 20-22 May 2022

Name and target	Approved age	Completed pediatric phase 3 clinical trials	Notable adverse events and disadvantages	Advantages
Tralokinumab; IL-13 inhibitor	≥18 y (FDA) ≥12 y (EMA)	1. NCT03526861: phase 3 (monotherapy), patients aged 12-17 y	1. Conjunctivitis 2. Injection site reactions 3. Likely lower efficacy than that of dupilumab and lebrikizumab, but no head-to-head trials	1. No laboratory monitoring required 2. Strong safety profile

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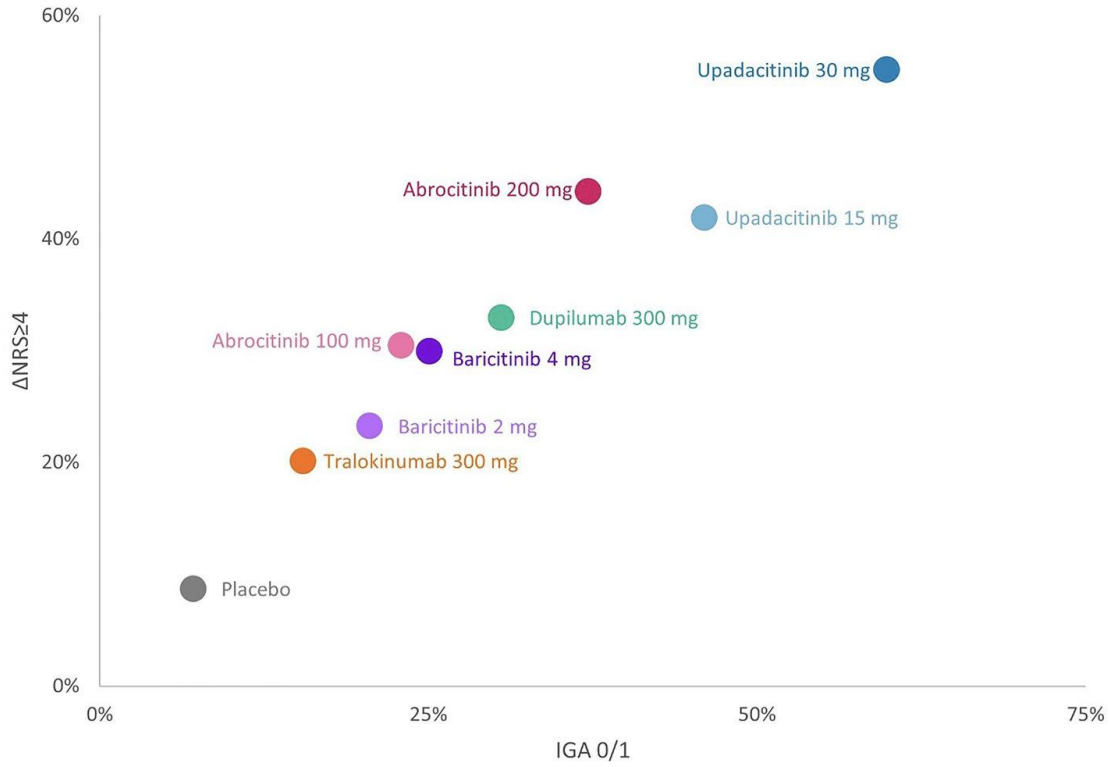


Article

Short-term effectiveness and safety of biologics and small molecule drugs for moderate to severe atopic dermatitis: a systematic review and network meta-analysis

José-Juan Pereyra-Rodriguez[1*], Sara Alcantara-Luna[2], Javier Domínguez-Cruz[3], Manuel Galán-Gutiérrez[4], Ricardo Ruiz-Villaverde[5], Samuel Vilar-Palomo[6] and José-Carlos Armario-Hita[7]

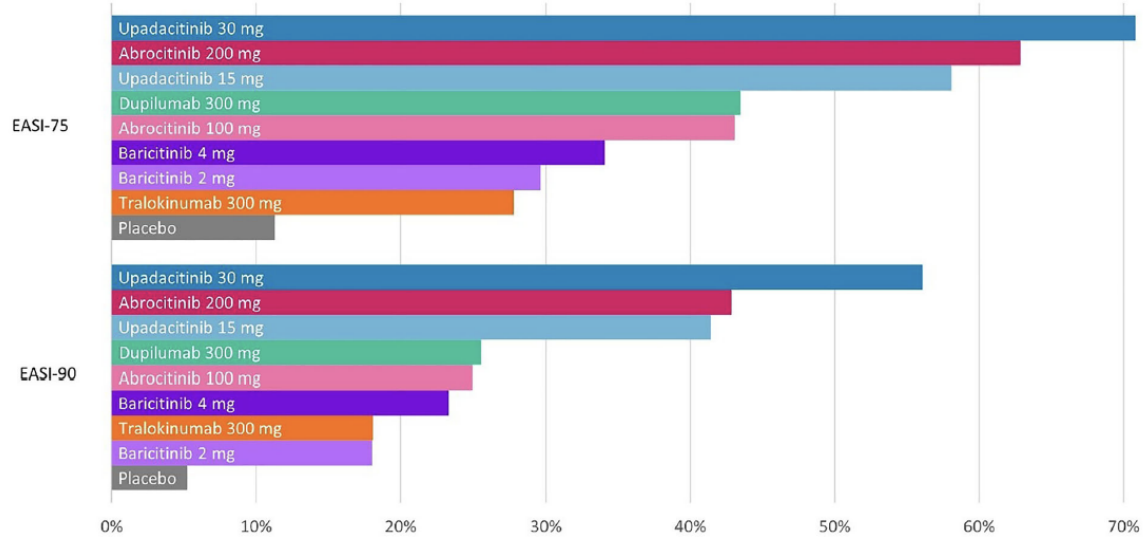


Fig. 3 EASI-75 and EASI-90 absolute response rate estimates for moderate to severe atopic dermatitis (primary endpoint timepoint). *EASI* Eczema Area and Severity Index

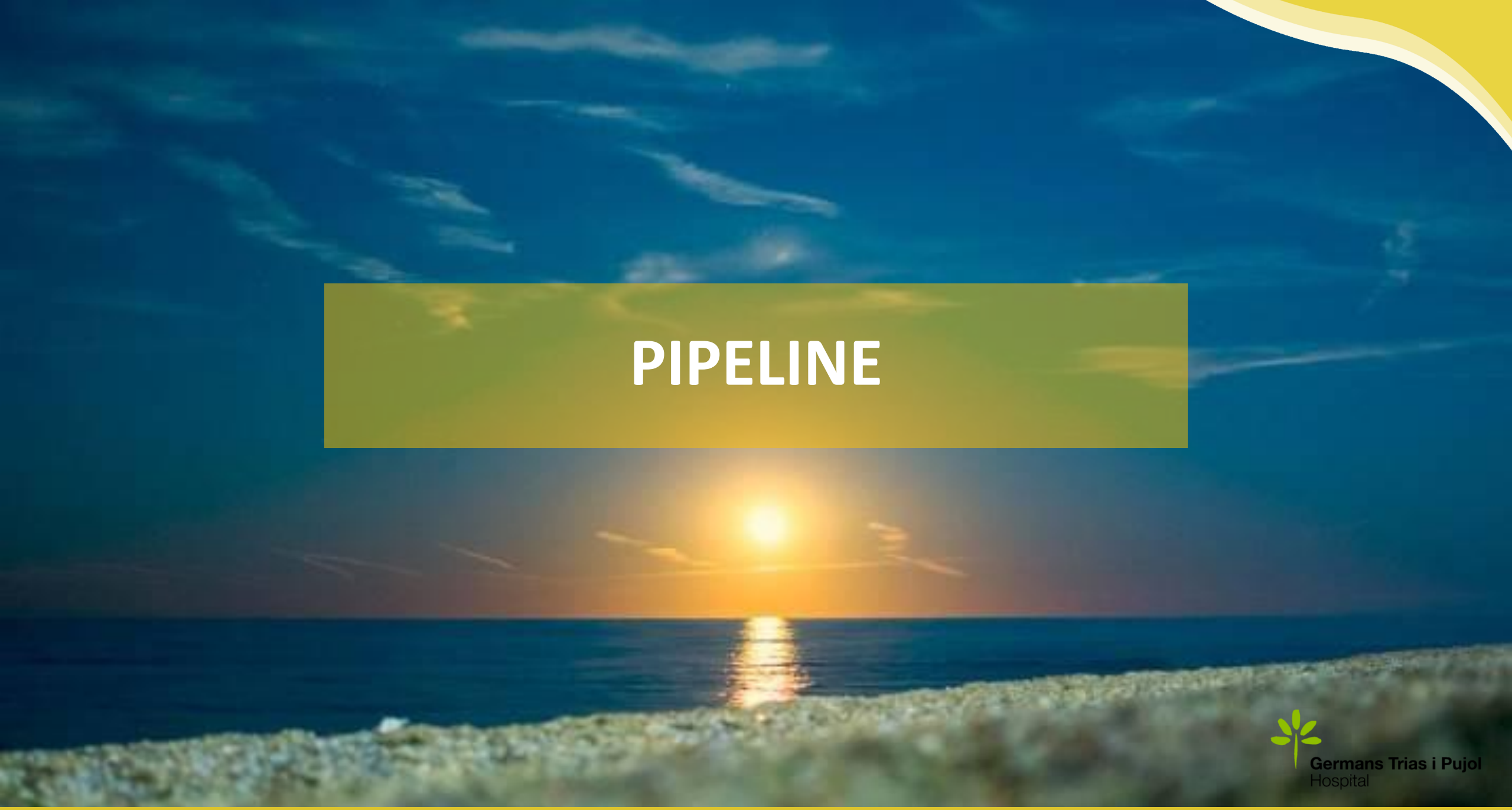
Dermatol Ther (Heidelb) (2022) 12:1181–1196
https://doi.org/10.1007/s13555-022-00721-1

ORIGINAL RESEARCH

Comparative Efficacy of Targeted Systemic Therapies for Moderate to Severe Atopic Dermatitis without Topical Corticosteroids: Systematic Review and Network Meta-analysis

Germans Trias i Pujol Hospital

PIPELINE



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Hospital

Target pathway	Drug name	Brand name (if available)/ manufacturer	Mechanism of action	Latest phase of clinical development for atopic dermatitis	Other investigated/approved clinical indications
Th2	Dupilumab	Dupixent/ Regeneron-Sanofi	IL-4 receptor α (IL4-Rα)	Approved	Prurigo nodularis, asthma, chronic rhinosinusitis with nasal polyps, eosinophilic esophagitis, chronic spontaneous uriticaria, bullous pemphigoid, chronic pruritis, allergic fungal rhinosinusitis, allergic bronchopulmonary aspergillosis
	CBP-201	Connect BioPharma		II	Asthma
	CM310	Keymed Biosciences		III	Chronic rhinosinusitis with nasal polyps, eosinophilic asthma, chronic pruritus, allergic rhinitis
	AK120	Akesobio		II	Asthma
	Tralokinumab	Adbry-Adtralza/LEO Pharma	IL-13	Approved	Asthma
	Lebrikizumab	Eli-Lilly		III	Chronic obstructive pulmonary disease, idiopathic pulmonary fibrosis, asthma
	Cendakimab	Bristol Meyers Squibb/ Celgene		II	Eosinophilic esophagitis, eosinophilic gastroenteritis,
	Eblasakimab (ASLAN004)	ASLAN Pharmaceuticals	IL-13 receptor α1 (IL-13Rα1)	II	Type 2 driven disease
	Nemolizumab	Galderma	IL-31 Receptor A (IL-31RA)	III	Prurigo nodularis, systemic sclerosis
	Vixarelimab	Kiniksa	Oncostatin M Receptor β (OSMβ)	I	Prurigo nodularis, chronic pruritic disease
	Mepolizumab	Nucala/GlaxoSmithKline	IL-5	II, Terminated	Chronic rhinosinusitis with nasal polyps, severe eosinophilic asthma, eosinophilic granulomatosis with polyangiitis, hypereosinophilic syndrome
	Benralizumab	Fasenra/Astrazeneca	IL-5 receptor α (IL-5Rα)	II	Severe eosinophilic asthma, bullous pemphigoid, chronic spontaneous urticaria, eosinophilic gastritis and eosinophilic gastritis/gastroenteritis, chronic prurigo
	Tozorakimab (MEDI3506)	Astrazeneca	IL-33	II	Symptomatic chronic obstructive pulmonary disease, asthma
	REGN3500	Regeneron		II, Terminated	Asthma, chronic obstructive pulmonary disease
	Etokimab	AnaptysBio		II, Terminated	Chronic rhinosinusitis with nasal polyps
	Torudokimab	Eli Lilly		II, Terminated	N/A
	PF-06817024	Pfizer		I	Chronic rhinosinusitis with nasal polyps
	CNTO7160	Janssen	IL-33 receptor (IL-33R/ST2)	I	Asthma
	Astegolimab (MSTT1041A)	Genentech		II	Chronic obstructive pulmonary disease, severe COVID-19 pneuomonia, asthma
	Omalizumab	Xolair/Genentech	IgE	IV	Allergic asthma, chronic spontaneous urticaria, chronic rhinosinusitis with nasal polyps, prurigo nodularis
	MEDI4212	Astrazeneca		I	Allergic rhinitis, allergic asthma
	FB825	OnenessBiotech/ LEOPharma	Membrane IgE (mIgE)	II	Allergic asthma
	Telazorlimab	Ichnos Sciences	OX40	II	N/A
	KHK4083	Amgen/Kyowa Kirin		II	Ulcerative colitis
	Amlitelimab (KY1005)	Kymab/Sanofi	OX40 ligand (OX40L)	II	Severe asthma
	Tezepelumab	Tezspire/Astrazeneca	TSLP	II, Terminated	Severe asthma
	CM326	Keymed Biosciences		I/II	Chronic rhinosinusitis with nasal polyps
	BSI-045B	Biosion		I	Severe asthma, chronic obstructive pulmonary disease

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David et al. Clin Exp Allergy 2023

Target pathway	Drug name	Brand name (if available)/ manufacturer	Mechanism of action	Latest phase of clinical development for atopic dermatitis	Other investigated/approved clinical indications
Th22	Fezakinumab	CreativeBio Labs	IL-22	II	Rheumatoid arthritis, psoriasis
	LEO 138559	LeoPharma	IL-22 receptor 1 (IL-22R1)	II	N/A
Innate Immunity	MOR106	MorphoSys-Galapagos	IL-17C	II, Terminated	Psoriasis
	Bermekimab	Janssen	IL-1α	II, Terminated	Hidradenitis suppurativa, systemic sclerosis, advanced cancers, colorectal cancer
	Spesolimab	Spevigo/Boehringer Ingelheim	IL-36 receptor (IL-36R)	II, Terminated	Generalized pustular psoriasis
	GSK1070806	GlaxoSmith Kline	IL-18	I	Severe crohn's, behcet's disease, type 2 diabetes, delayed graft rejection
	CMK389	Novartis		II	Pulmonary sarcoidosis
Th17/IL-23	Ustekinumab	Stelara/Janssen	IL-12/23p40	II	Psoriasis, juvenile psoriatic arthritis, crohn's, primary sjogren's, takayasu arteritis, ulcerative Colitis, polymyositis, dermatomyositis
	Risankizumab	Skyrizi/Abbvie	IL-23p19	II	Plaque psoriasis, psoriatic arthritis, Crohn's disease
	Secukinumab	Cosentyx/Novartis	IL-17A	II	Psoriasis, crohn's, juvenile psoriatic arthritis

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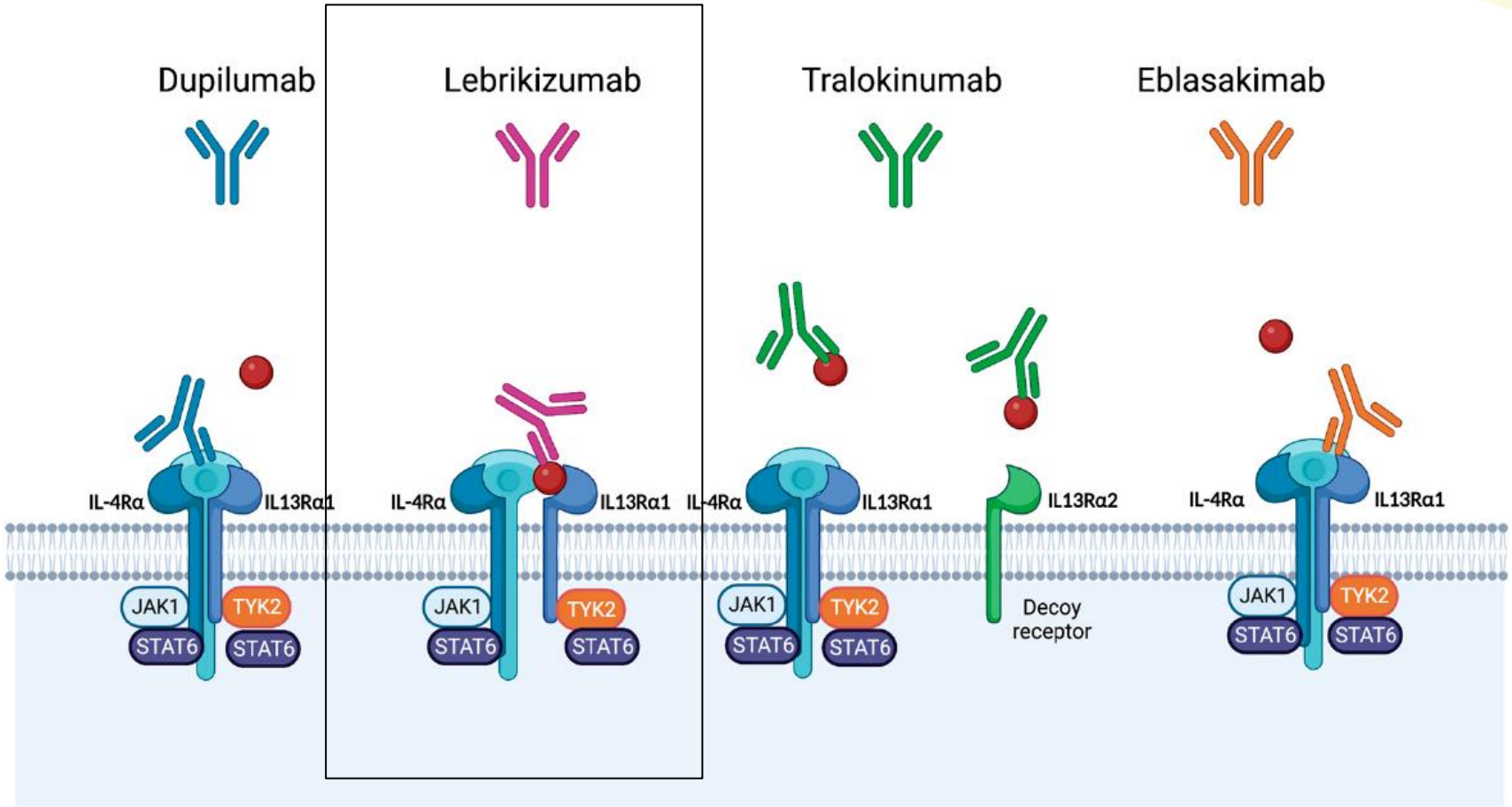
David et al. Clin Exp Allergy 2023

IL-4 / IL-13



pharmaceutics
MDPI

Review

Targeting Interleukin 13 for the Treatment of Atopic Dermatitis

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

Germans Trias i Pujol Hospital

ANTI-IL13

LEBRIKIZUMAB

Lebrikizumab binds IL-13 at an epitope that overlaps the binding site of IL-4Rα subunit, preventing heterodimerization of IL-13Rα1/IL-4Rα and blocking IL-13 signaling. IL-13 can still bind to the IL-13Rα2 'decoy' receptor.

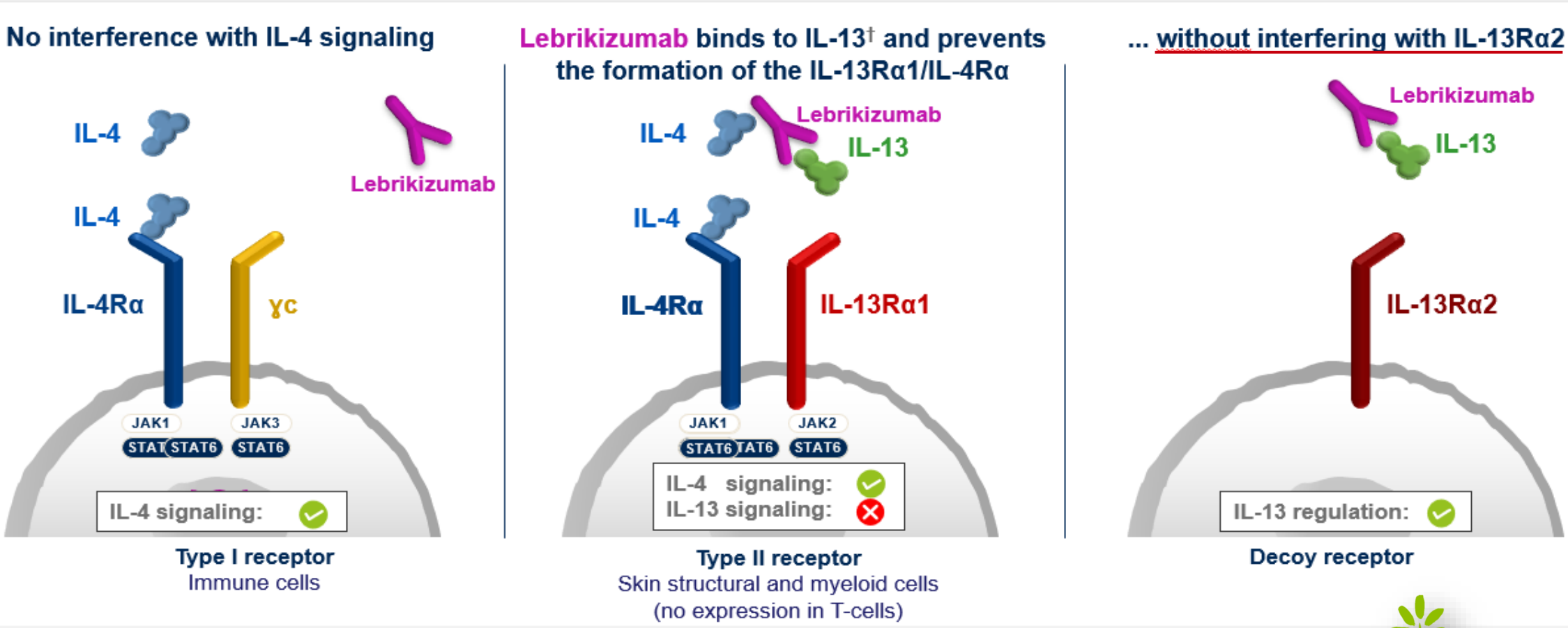


Figure adapted from Moyle M, *et al.* 2019[1] and Bieber T, 2020.[3]

Germans Trias i Pujol Hospital

ANTI-IL13

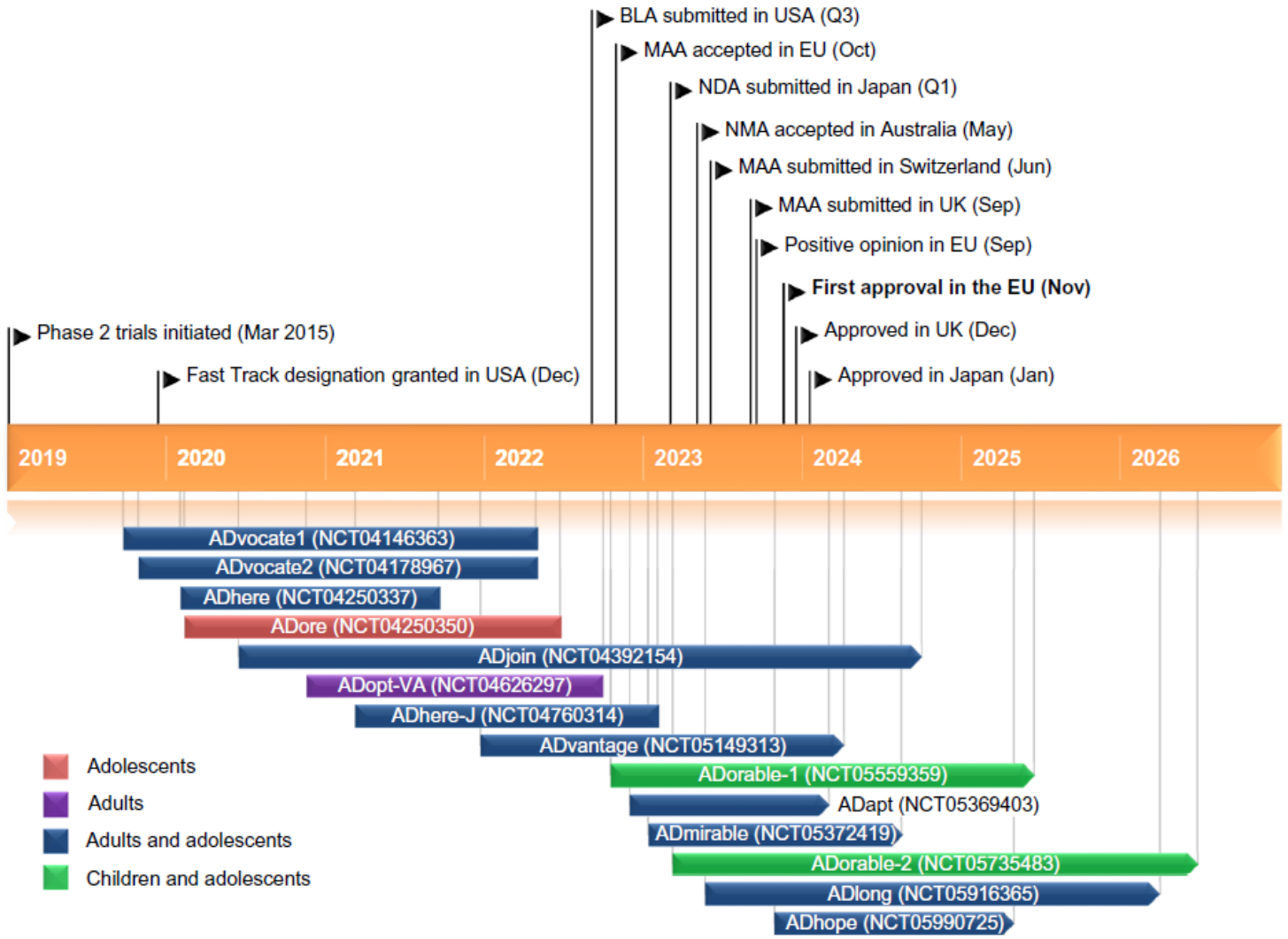
LEBRIKIZUMAB

Drugs
https://doi.org/10.1007/s40265-024-02000-z

ADISINSIGHT REPORT

Lebrikizumab: First Approval

Susan J. Keam[1]



- El 17 de noviembre de 2023, lebrikizumab recibió la aprobación por parte de la Comisión Europea (CE) para el **tratamiento de la dermatitis atópica de moderada a grave en adultos y adolescentes a partir de 12 años**, con un peso corporal de, al menos, 40 kg que sean candidatos a una terapia sistémica.

- **El 21 diciembre de 2023 la AEMPS lo ha autorizado en España**

Germans Trias i Pujol Hospital

ANTI-IL13

LEBRIKIZUMAB

	ADvocate 1[1,2]	ADvocate 2[1,2]	ADhere[3]	ADore[1,4]	ADopt-VA[1,5]	ADjoin LTE[1,6]	ADhere-J[1,7]	ADvantage[8]	ADapt[1,9]	ADmirable[1,10]	ADorable-1[11]
Regions	Global	**Global**	**Global**	**Global**	US	**Global**	Japan	EU	US	US	**Global**
N	424	427	211	206	254	~1000	286	331	~120	~80	~300
Background	Monotherapy	Monotherapy	+ TCS	TCS/TCI/ PDE4i optional	TCS/TCI optional	TCS/TCI/ PDE4i optional	+ TCS	+ TCS	DUPI-IR	SoC	+ TCS
Study population(s)	Adults and adolescents (≥40 kg)	Adults and adolescents (≥40 kg)	Adults and adolescents (≥40 kg)	Adolescents (≥40 kg)	Adults (≥18 yrs to ≤55 yrs)	Adults and adolescents (≥40 kg)	Adults and adolescents (≥40 kg)	Adults and adolescents (≥40 kg)	Adults and adolescents (≥40 kg)	Adults and adolescents (≥40 kg)	Peds+ adolescents (≥6 mo to <18 yrs)
Dosing arms	PBO LEBRI 250 mg Q2W LEBRI 250 mg Q4W	PBO LEBRI 250 mg Q2W LEBRI 250 mg Q4W	PBO LEBRI 250 mg Q2W	LEBRI 250 mg Q2W	PBO LEBRI 250 mg Q2W	LEBRI 250 mg Q2W LEBRI 250 mg Q4W	PBO LEBRI 250 mg Q2W LEBRI 250 mg Q4W	PBO LEBRI 250 mg Q2W	LEBRI 250 mg Q2W	LEBRI 250 mg Q2W LEBRI 250 mg Q4W	PBO LEBRI dose based on WT
Primary outcome (week)	16	**16**	**16**	**52**	**16**	100	**16**	**16**	**16**	**16**	**16**
Treatment duration (week)	52	52	16	52	16	100	68	52	24	24	16

Eligible patients can continue in the long-term extension study

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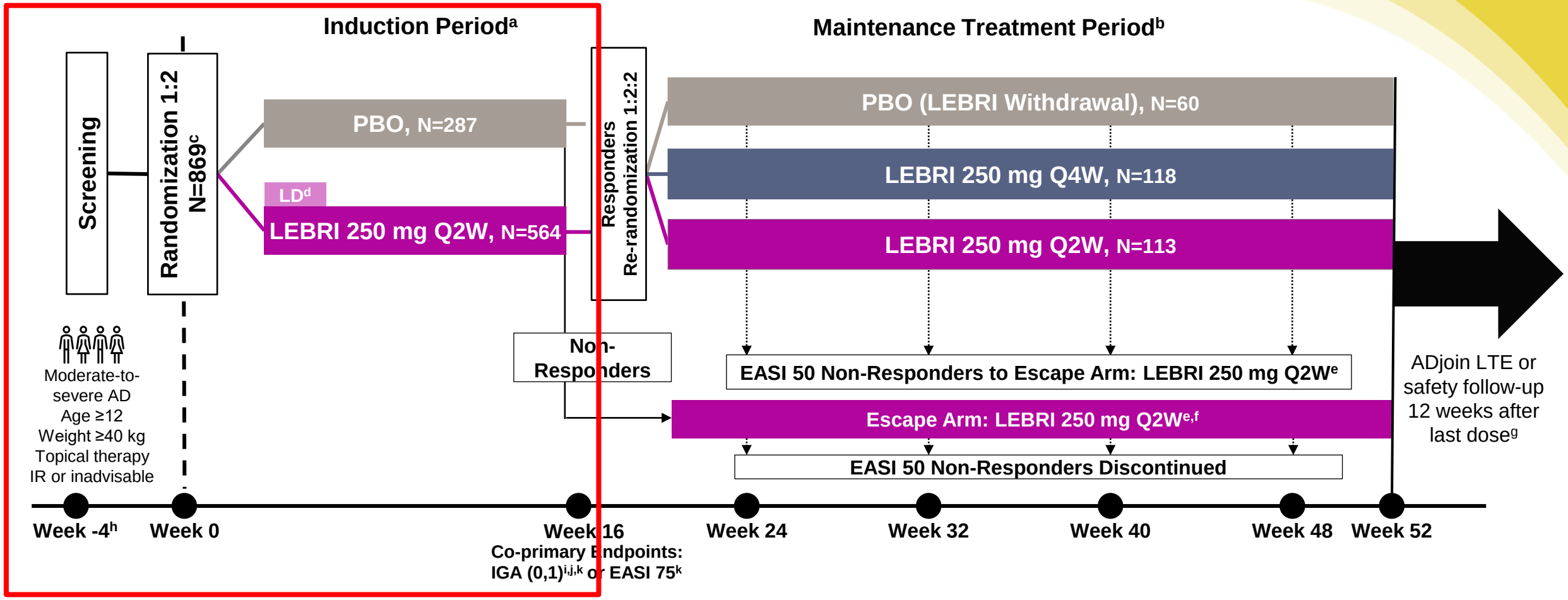

[a]Use of topical/systemic treatments for AD prohibited. [b]Use of intermittent topical rescue medications for AD permitted. Responders who received PBO during induction and who are re-randomized to LEBRI will receive a LD of either 500 mg given at W16 or 500 mg given at W16 and W18. [c]424 patients (ADvocate 1) and 445 patients (ADvocate 2) with moderate-to-severe AD. [d]500 mg LD at W0 and W2. [e]Maintenance of response assessed by EASI 50 at W24, W32, W40, and W48, respectively. Patients receiving systemic rescue medication will be required to washout for 5 half-lives prior to initiating treatment in the Escape Arm. [f]Participants who are eligible for the Escape Arm at W16 will receive blinded LD at W16 and W18, based on their prior treatment assignment. [g]Patients completing ADvocate 1/2 will be offered open-label treatment in ADjoin, otherwise patients will participate in a safety follow-up 12 weeks after their last dose. [h]≤30-day screening period. [i]IGA (0,1) with ≥2-point improvement from baseline. [j]FDA primary endpoint. [k]EMA co-primary endpoint. See speaker notes for abbreviations and references.

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ANTI-IL13

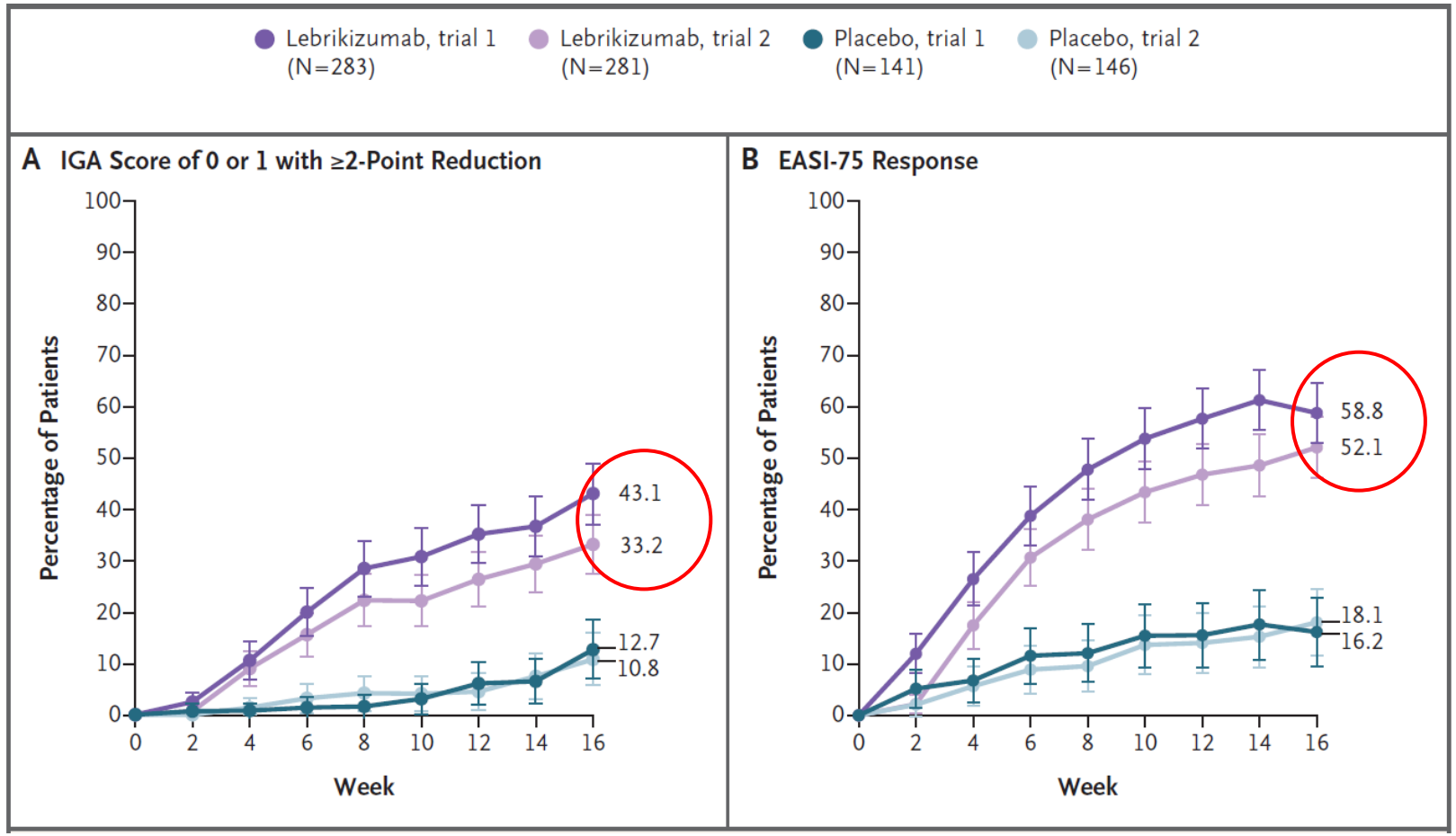
LEBRIKIZUMAB

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Two Phase 3 Trials of Lebrikizumab for Moderate-to-Severe Atopic Dermatitis

Jonathan I. Silverberg, M.D., Ph.D., M.P.H, Emma Guttman-Yassky, M.D., Ph.D., Diamant Thaçi, M.D., Alan D. Irvine, M.D., Linda Stein Gold, M.D., Andrew Blauvelt, M.D., Eric L. Simpson, M.D., Chia-Yu Chu, M.D., Ph.D., Zhuqing Liu, Ph.D., Renata Gontijo Lima, M.D., Sreekumar G. Pillai, Ph.D., and Julien Seneschal, M.D., Ph.D., for the ADvocate1 and ADvocate2 Investigators*



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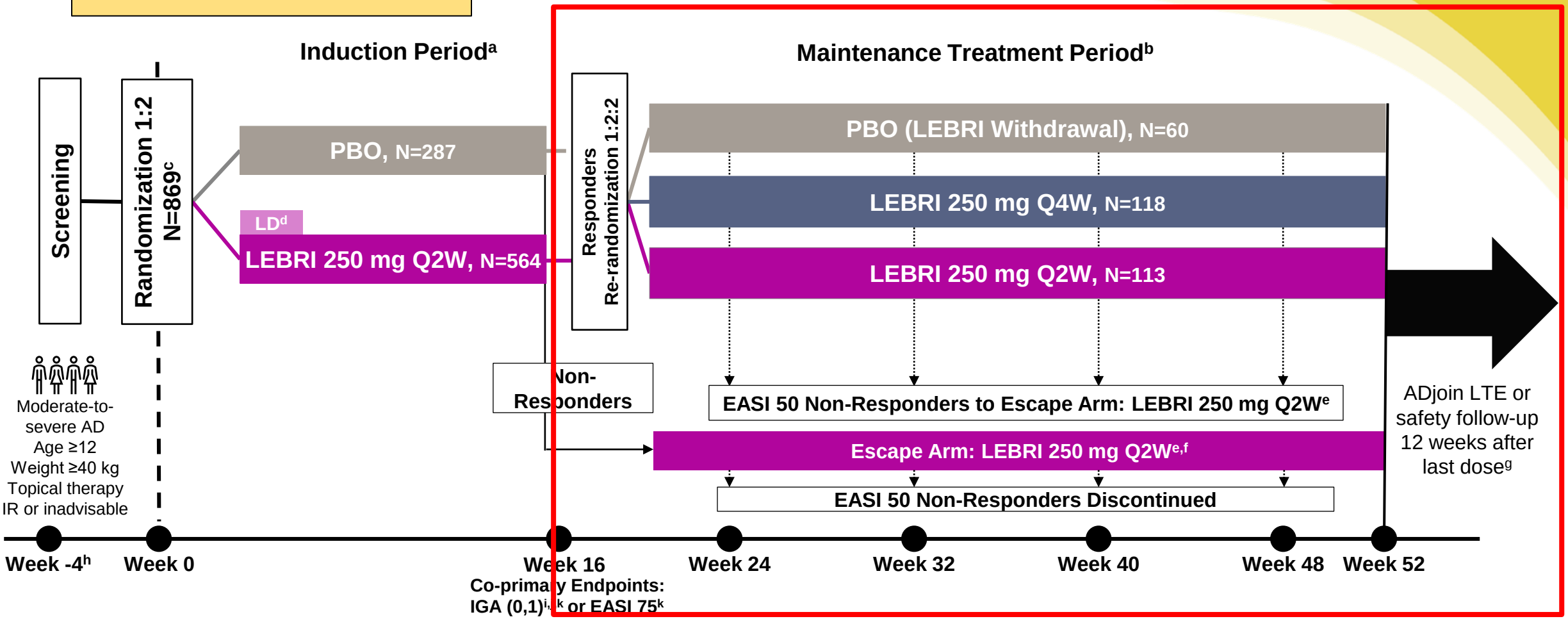

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LEBRIKIZUMAB

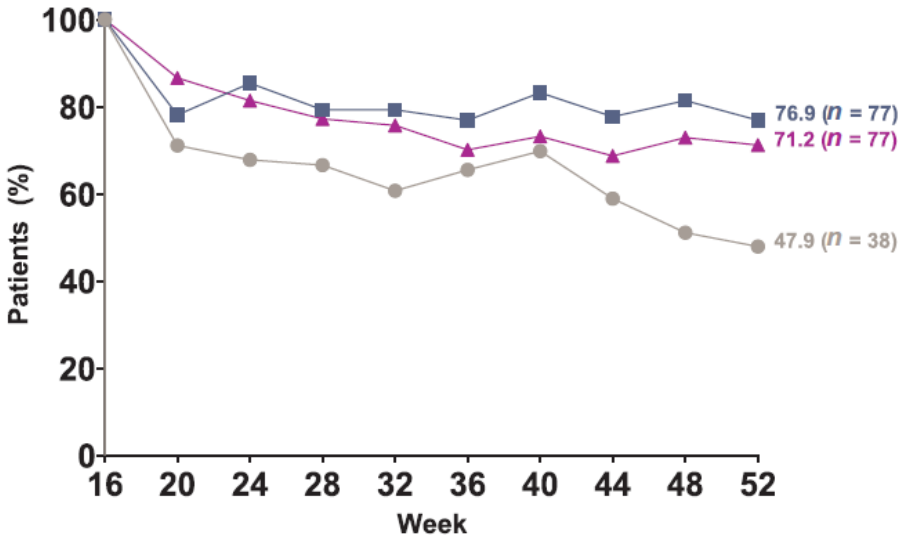
Br J Dermatol 2023; **00**:1–9
https://doi.org/10.1093/bjd/ljad022
Advance access publication date: 30 March 2023

BJD
British Journal of Dermatology
Clinical Trial

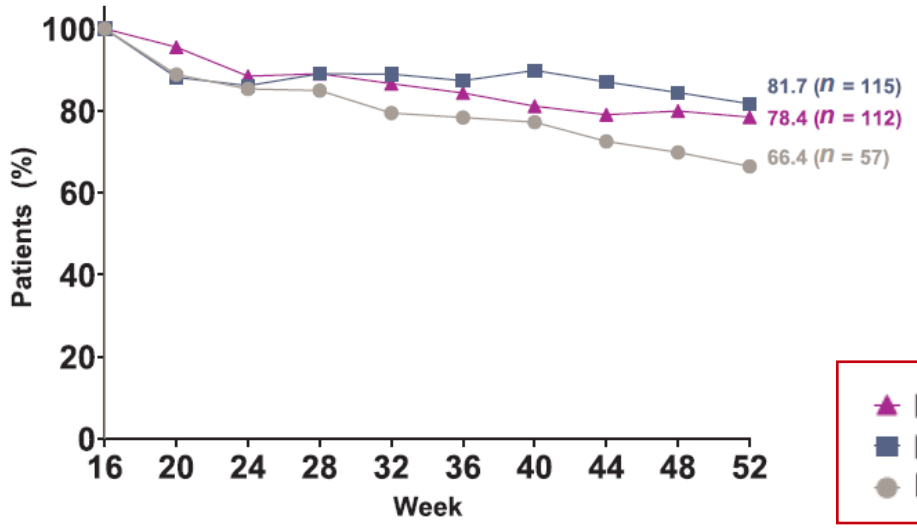
Efficacy and safety of lebrikizumab in moderate-to-severe atopic dermatitis: 52-week results of two randomized double-blinded placebo-controlled phase III trials

Andrew Blauvelt,[1] Jacob P. Thyssen,[2] Emma Guttman-Yassky,[3] Thomas Bieber,[4,5] Esther Serra-Baldrich,[6] Eric Simpson,[7] David Rosmarin,[8] Hany Elmaraghy,[9] Eric Meskimen,[9] Chitra R. Natalie,[9] Zhuqing Liu,[9] Chenjia Xu,[9] Evangeline Pierce,[9] MaryAnn Morgan-Cox,[9] Esther Garcia Gil[10] and Jonathan I. Silverberg[11]

(a) IGA (0,1) and ≥2-point Improvement

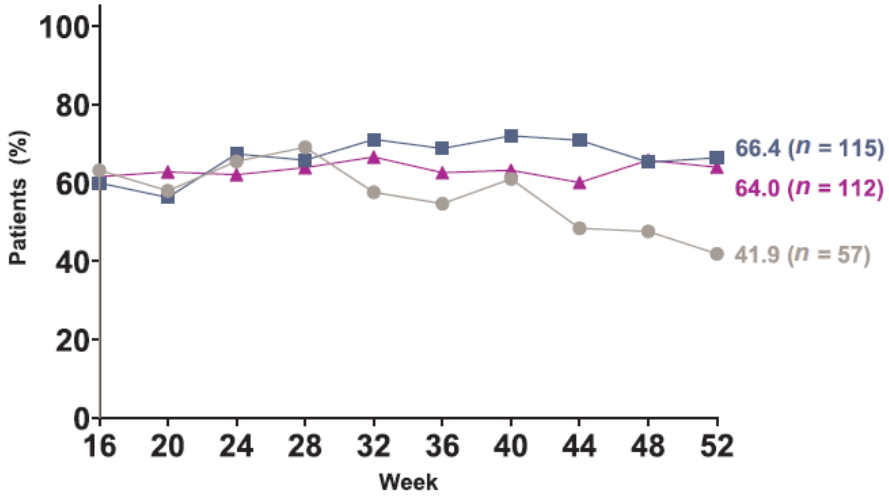


(b) EASI 75

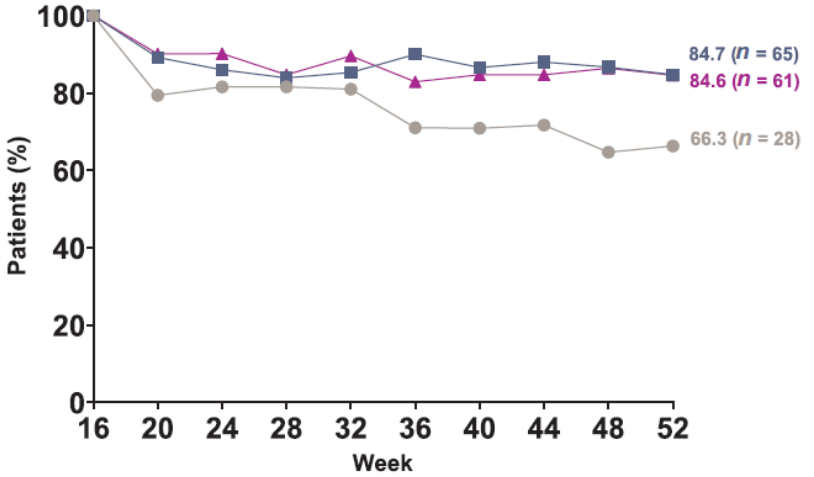


LEB 250 mg Q2W
LEB 250 mg Q4W
PBO (LEB withdrawal)

(e) EASI 90



(c) Pruritus NRS ≥4-point Improvement



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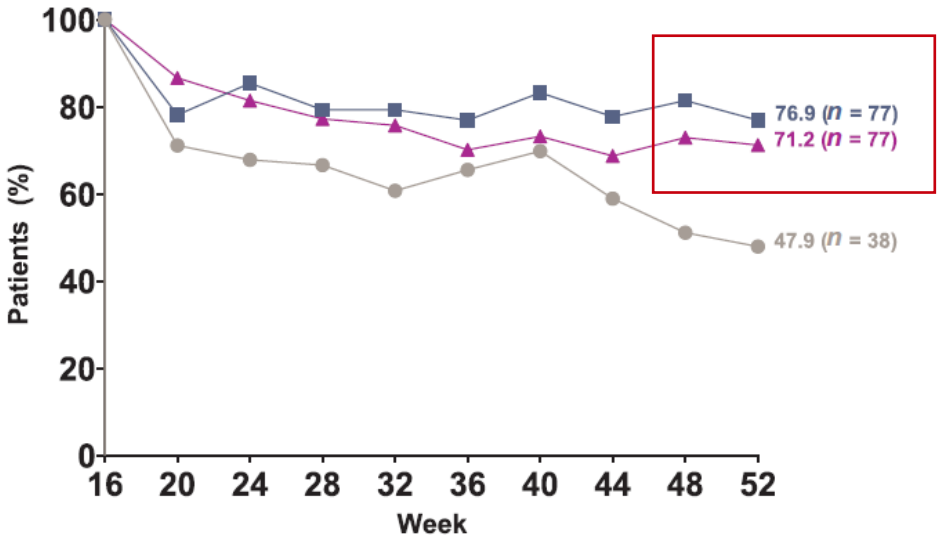
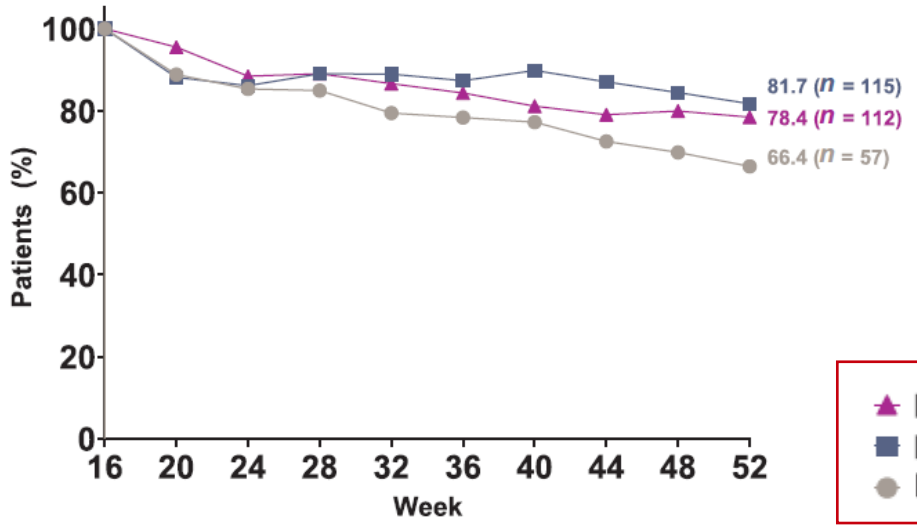
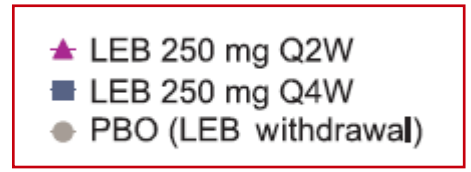
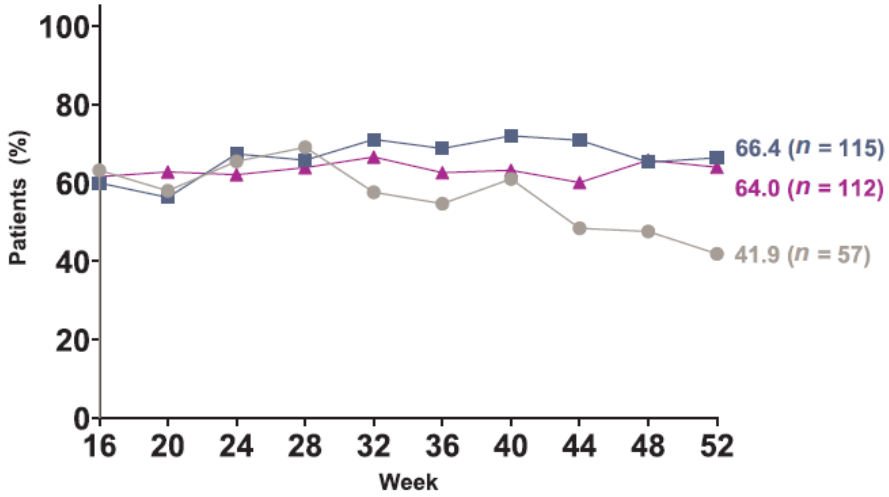


(b) EASI 75





(e) EASI 90



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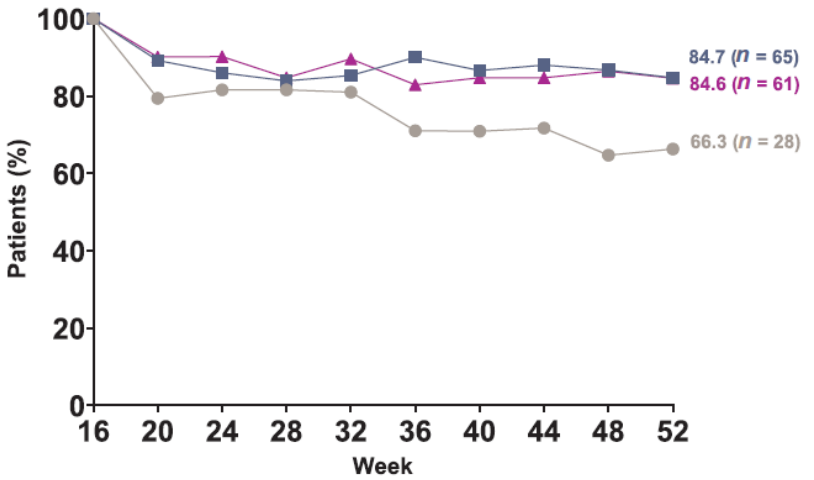

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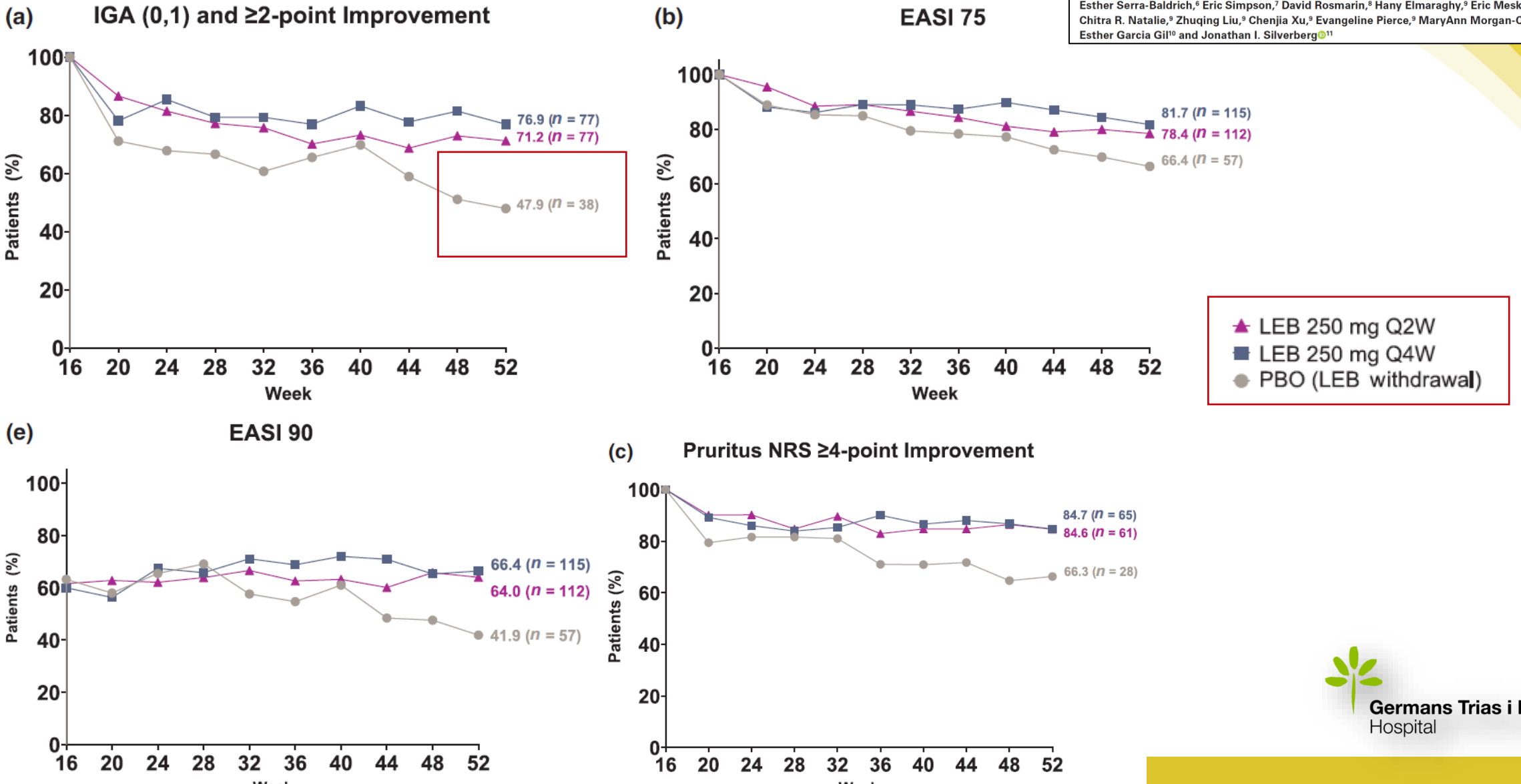

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LEBRIKIZUMAB

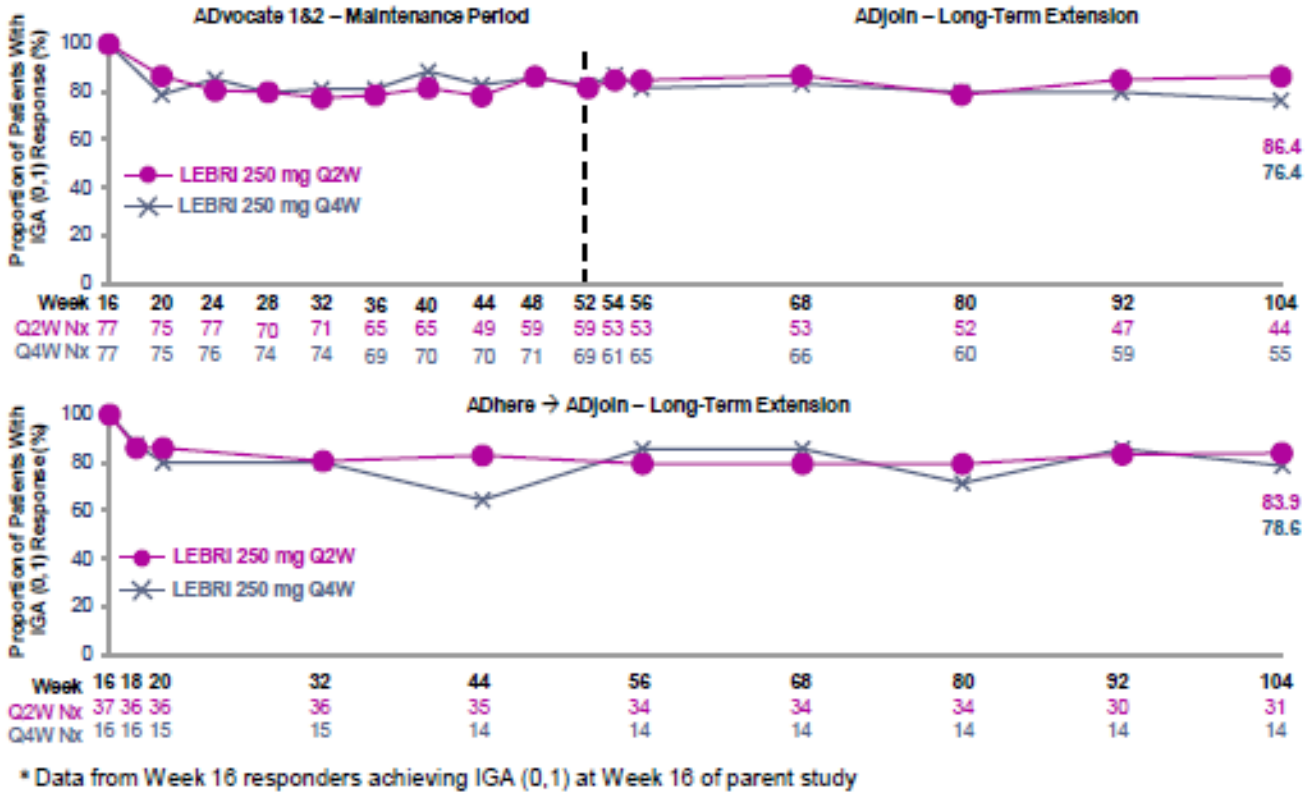
Eficacia y seguridad de lebrikizumab a 3 años en el LTE Adjoin en respondedores de los ensayos ADVOCATE 1 y 2 y Adhere (+ TCS). Adultos y adolescentes (≥12 años y ≥40kg)

Article

494 - Efficacy and safety of lebrikizumab is maintained to two years in patients with moderate-to-severe atopic dermatitis

February 2024 · British Journal of Dermatology 190(Supplement_2):ii3-ii4
DOI:10.1093/bjd/ljad498.005

IGA (0,1) Response Rates[a] Were Maintained in Patients Receiving Lebrikizumab Q2W or Q4W Through 104 Weeks



* Data from Week 16 responders achieving IGA (0,1) at Week 16 of parent study

Uso de TCS/TCI opcional

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LEBRIKIZUMAB

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SUMMARY OF KEY FINDINGS

Efficacy Outcomes Were Maintained Through 2 Years of Treatment With Lebrikizumab

Outcome, %	ADvocate 1&2 → ADjoin	ADhere → ADjoin
	LEBRI 250 mg Q4W (N=99)	LEBRI 250 mg Q4W (N=29)
IGA (0,1)	76.4	78.6
EASI 75	96.3	96.0
EASI 90	82.5	72.0
Pruritus NRS ≥4-point improvement	89.7	90.0[a]

[a] All outcomes shown through 104 weeks apart from Pruritus NRS ≥4-point improvement for ADhere → ADjoin study (68 weeks)

EASI=Eczema Area and Severity Index; EASI 75=at least 75% improvement from baseline in EASI; EASI 90=at least 90% improvement from baseline in EASI; IGA=Investigator's Global Assessment; IGA (0,1)=IGA response of clear or almost clear; LEBRI=lebrikizumab; NRS=numeric rating scale; Q2W=every 2 weeks; Q4W=every 4 weeks

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ANTI-IL13

LEBRIKIZUMAB

Article

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	ADvocate1&2 → ADjoin		ADhere → ADjoin	
	LEBRI 250 mg Q4W (N=99)	LEBRI 250 mg Q2W (N=82)	LEBRI 250 mg Q4W (N=29)	LEBRI 250 mg Q2W (N=57)
Patients with ≥1 TEAE	58 (58.6)	56 (68.3)	17 (58.6)	35 (61.4)
Mild	26 (26.3)	31 (37.8)	12 (41.4)	15 (26.3)
Moderate	27 (27.3)	22 (26.8)	4 (13.8)	19 (33.3)
Severe	5 (5.1)	3 (3.7)	1 (3.4)	1 (1.8)
Serious AE	3 (3.0)	2 (2.4)	2 (6.9)	3 (5.3)
Death	0	0	0	1 (1.8)[a]
Discontinuation from study treatment due to AE	2 (2.0)	2 (2.4)	0	2 (3.5)
Conjunctivitis cluster[b]	4 (4.0)	2 (2.4)	3 (10.3)	7 (12.3)
Keratitis cluster[c]	0	0	0	0
Infections Potential opportunistic infections[d] Herpes infections Parasitic infections	38 (38.4) 1 (1.0) 3 (3.0) 0	34 (41.5) 2 (2.4) 5 (6.1) 0	11 (37.9) 1 (3.4) 1 (3.4) 1 (3.4)	24 (42.1) 0 2 (3.5) 0
Injection-site reactions	0	1 (1.2)	1 (3.4)	1 (1.8)
Malignancies[e]	0	0	0	0
Anaphylactic reactions	0	0	0	0
Eosinophilia[f]	0	1 (1.2)	0	0

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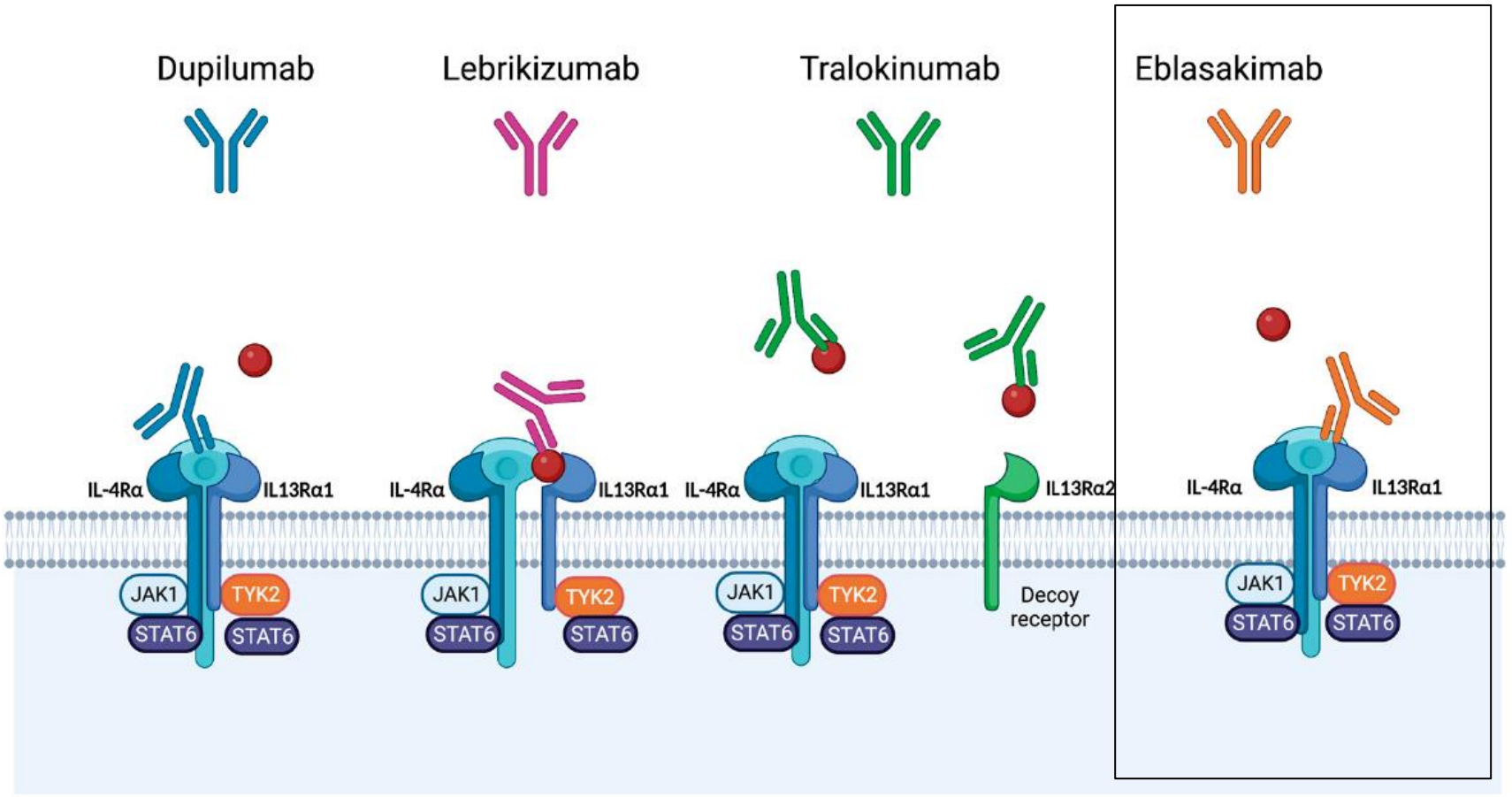
IL-4 / IL-13



pharmaceutics
MDPI

Review

Targeting Interleukin 13 for the Treatment of Atopic Dermatitis

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

Germans Trias i Pujol Hospital

ANTI-IL13Rα1

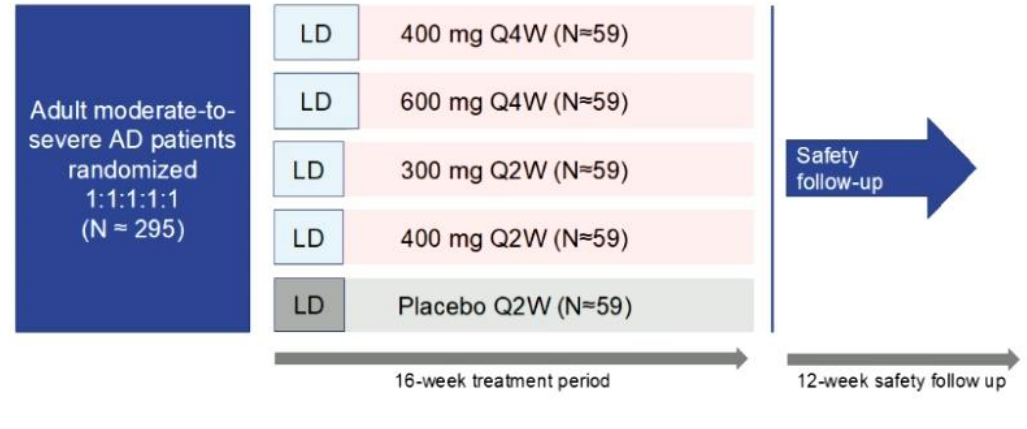
EBLASAKIMAB (ASLAN004)

Key inclusion criteria:

- Chronic AD present for ≥1 year prior to screening visit
- Disease scores at screening and baseline:
  - EASI ≥16
  - vIGA score ≥3 (scale of 0 to 4)
  - ≥10% body surface area (BSA) of AD involvement

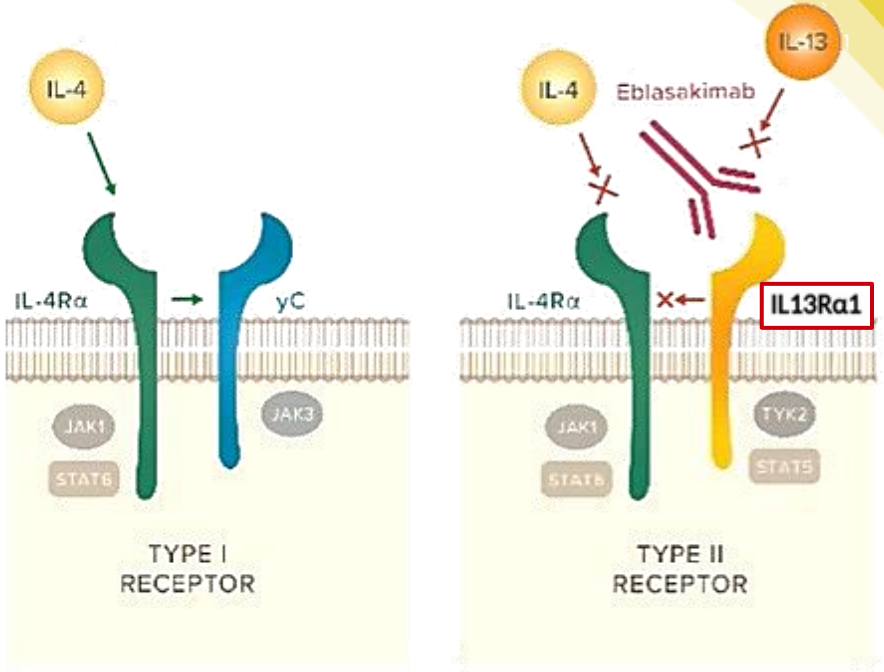
Endpoints:

- Primary efficacy – EASI percent change from baseline to week 16
- Secondary efficacy – EASI 75, EASI 90, vIGA 0/1



- Loading dose of 600mg for the Q2W dose groups at week 0 and week 1
- Loading dose of 600mg for the Q4W dose groups at week 0, week 1 and week 2

Eblasakimab



*Dupilumab

*Actualmente sólo ensayos en adultos ≥18 años

Ensayo fase 2b. TREK-AD (TRials with EblasaKimab in Atopic Dermatitis)
https://ir.aslanpharma.com

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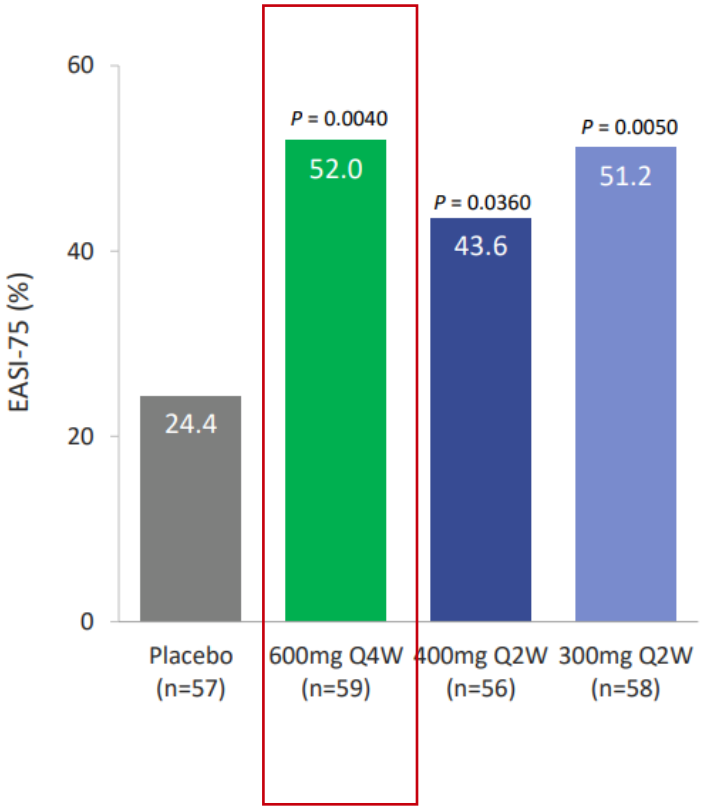
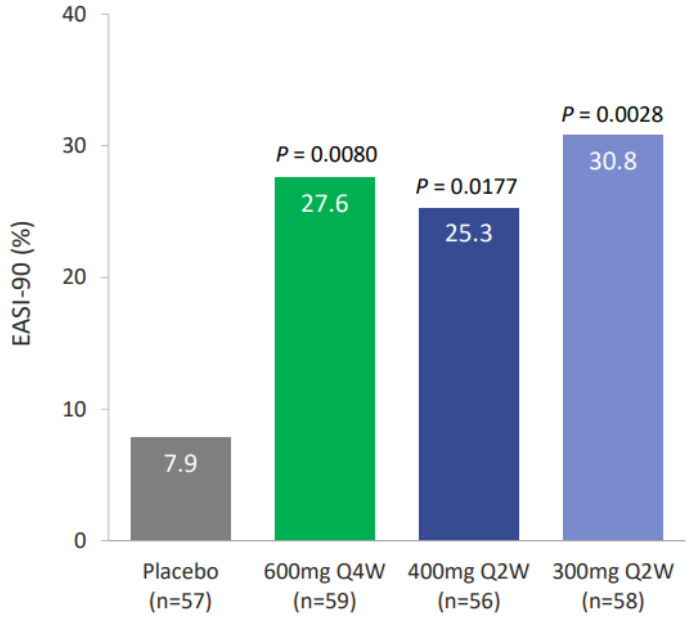
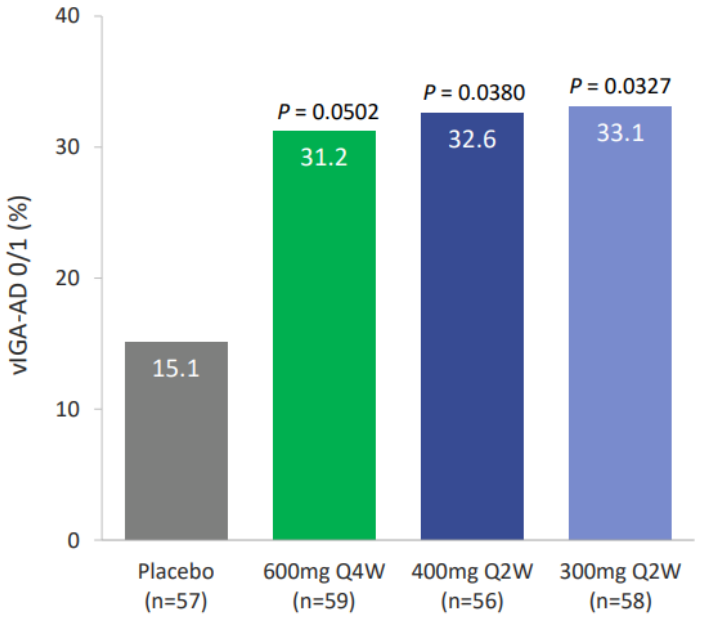
ANTI-IL13Rα1

EBLASAKIMAB (ASLAN004)







*La dosis de 400mg cada 4W no alcanzó respuestas estadísticamente significativas

Ensayo fase 2b. TREK-AD (TRials with EblasaKimab in Atopic Dermatitis). Resultados a semana 16
https://ir.aslanpharma.com

Germans Trias i Pujol Hospital

ANTI-IL13Rα1

EBLASAKIMAB

Treatment Emergent Adverse Event (TEAE)[1] by category - n (%)	Placebo (n=57)	All Ebla (n=232)	600mg Q4W (n=59)	400mg Q2W (n=56)	300mg Q2W (n=58)	400mg Q4W (n=59)
Any	33 (57.9)	164 (70.7)	41 (69.5)	43 (76.8)	32 (55.2)	48 (81.4)
Serious Adverse Event (SAE)[2]	1 (1.8)	3 (1.3)	0	1 (1.8)	1 (1.7)	1 (1.7)
AEs with frequency of 5% or more across treatment arms[3]:						
• Nasopharyngitis	5 (8.8)	31 (13.4)	8 (13.6)	8 (14.3)	5 (8.6)	10 (16.9)
• Dermatitis atopic	4 (7.0)	20 (8.6)	3 (5.1)	5 (8.9)	4 (6.9)	8 (13.6)
• Headache	4 (7.0)	16 (6.9)	8 (13.6)	1 (1.8)	1 (1.7)	6 (10.2)
• Upper respiratory tract infection	3 (5.3)	15 (6.5)	3 (5.1)	2 (3.6)	6 (10.3)	4 (6.8)
AEs of interest:						
• Injection site reactions	1 (1.8)	11 (4.7)	4 (6.8)	3 (5.4)	0	4 (6.8)
• Conjunctivitis[4]	1 (1.8)	12 (5.2)	4 (6.8)	5 (8.9)	1 (1.7)	2 (3.4)
• Herpes infections	2 (3.5)	7 (3.0)	3 (5.1)	0	1 (1.7)	3 (5.1)
- Herpes simplex infection[5]	2 (3.5)	6 (2.6)	3 (5.1)	0	0	3 (5.1)
- Herpes zoster infection	0	1 (0.4)	0	0	1 (1.7)	0

1 This includes all adverse events recorded through to week 16 or last dose for completed patients
2 None were deemed as being drug related, all three across active arms were worsening of AD
3 Applies to AEs that map to the Medical Dictionary for Regulatory Activities dictionary term
4 Includes conjunctivitis, noninfectious conjunctivitis and conjunctivitis allergic
5 Includes oral herpes, herpes simplex infection, herpes virus infection, nasal herpes and herpes ophthalmic

Ensayo fase 2b. TREK-AD (TRials with EblasaKimab in Atopic Dermatitis)
https://ir.aslanpharma.com

ANTI-IL13Rα1

EBLASAKIMAB

COMING SOON

Upcoming expected milestones:

1Q 2023	2Q 2023	3Q 2023	4Q 2023	1Q 2024
$20 million financing led by BVF	*Farudodstat* Phase 2a PoC study in AA initiation	*Eblasakimab* licensing deal for Japan signed	*Eblasakimab* Phase 2b TREK-AD topline data readout	*Eblasakimab* TREK-AD additional data: PROs, biomarkers[1]	*Eblasakimab* Phase 2 TREK-DX topline readout
Eblasakimab TREK-AD completion of enrollment					*Farudodstat* Phase 2a interim topline readout

Preparation for Phase 3

RECRUITING

NCT05694884

Study of Eblasakimab in Male or Female Moderate-to-Severe Atopic Dermatitis Patients Previously Treated With Dupilumab

Conditions

Atopic Dermatitis

Locations

Birmingham, Alabama, United States
Encino, California, United States
Fountain Valley, California, United States
Long Beach, California, United States

Show 27 more locations

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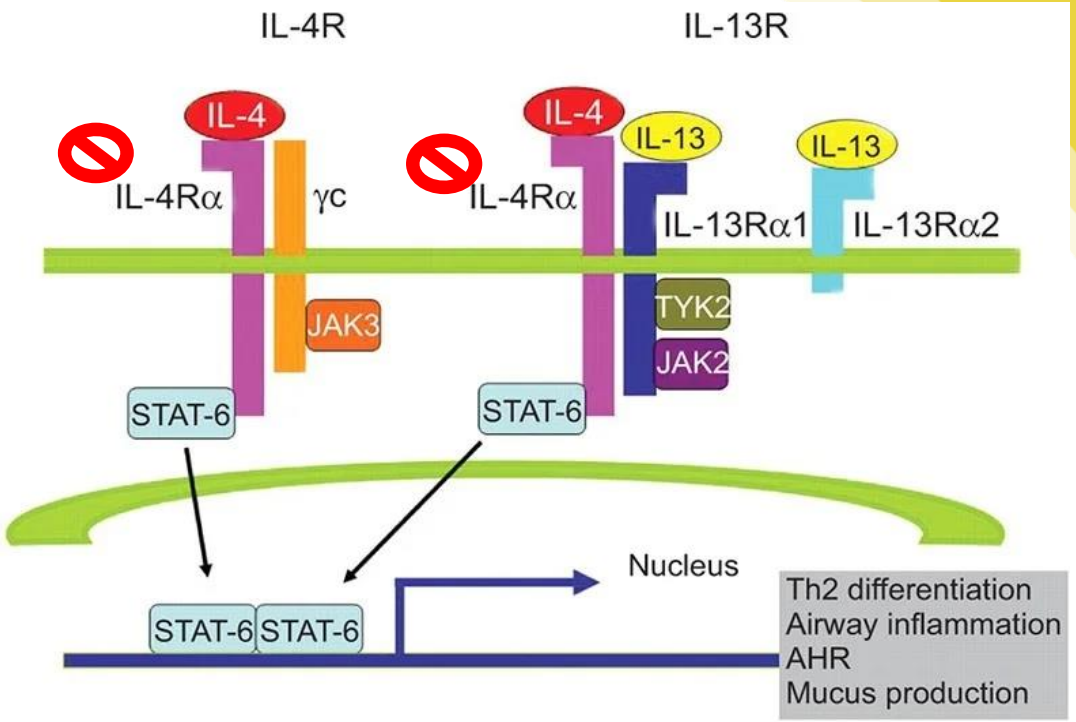
ANTI-IL4α

Drug Name	Highest Stage	Company	Indications
Dupilumab	Launched (2017)	Sanofi/Regeneron	Eosinophilic Esophagitis; Atopic Dermatitis; Sinusitis; Nasal Polyps; Asthma
CM-310	Phase III	Keymed Biosciences CSPC Pharmaceutical	Sinusitis; Nasal Polyps; Atopic Dermatitis; Pruritus; Solid Tumors; Asthma; Nasal Disorders; Allergic Rhinitis
Recombinant anti-IL-4Rα humanized monoclonal antibody	Phase II	Sunshine Guojian	Atopic Dermatitis
MG-K10	Phase II	MABGEEK Dragon Boat Pharmaceutical	Atopic Dermatitis; Asthma
Manfidokimab	Phase II	Akeso Pharmaceuticals	Atopic Dermatitis; Asthma
QX-005N	Phase II	Qyuns Therapeutics	Atopic Dermatitis; Prurigo; Asthma; Chronic Urticaria; Sinusitis
Elarekibep	Phase II	AstraZeneca Pieris Australia Pty Ltd	Asthma
CBP-201	Phase II	Connect Biopharma	Atopic Dermatitis; Asthma
SHR-1819	Phase I	Atridia Pty Ltd; Jiangsu Hengrui Pharmaceuticals	Atopic Dermatitis; Asthma
LQ-036	Phase I	Shanghai Novamab Biopharmaceuticals; Syneos Health	Asthma
BA2101	Preclinical	Boan Biotech	Atopic Dermatitis; Asthma; Sinusitis;Itching; Hives

TQH2722 Phase I (NCT05409326)



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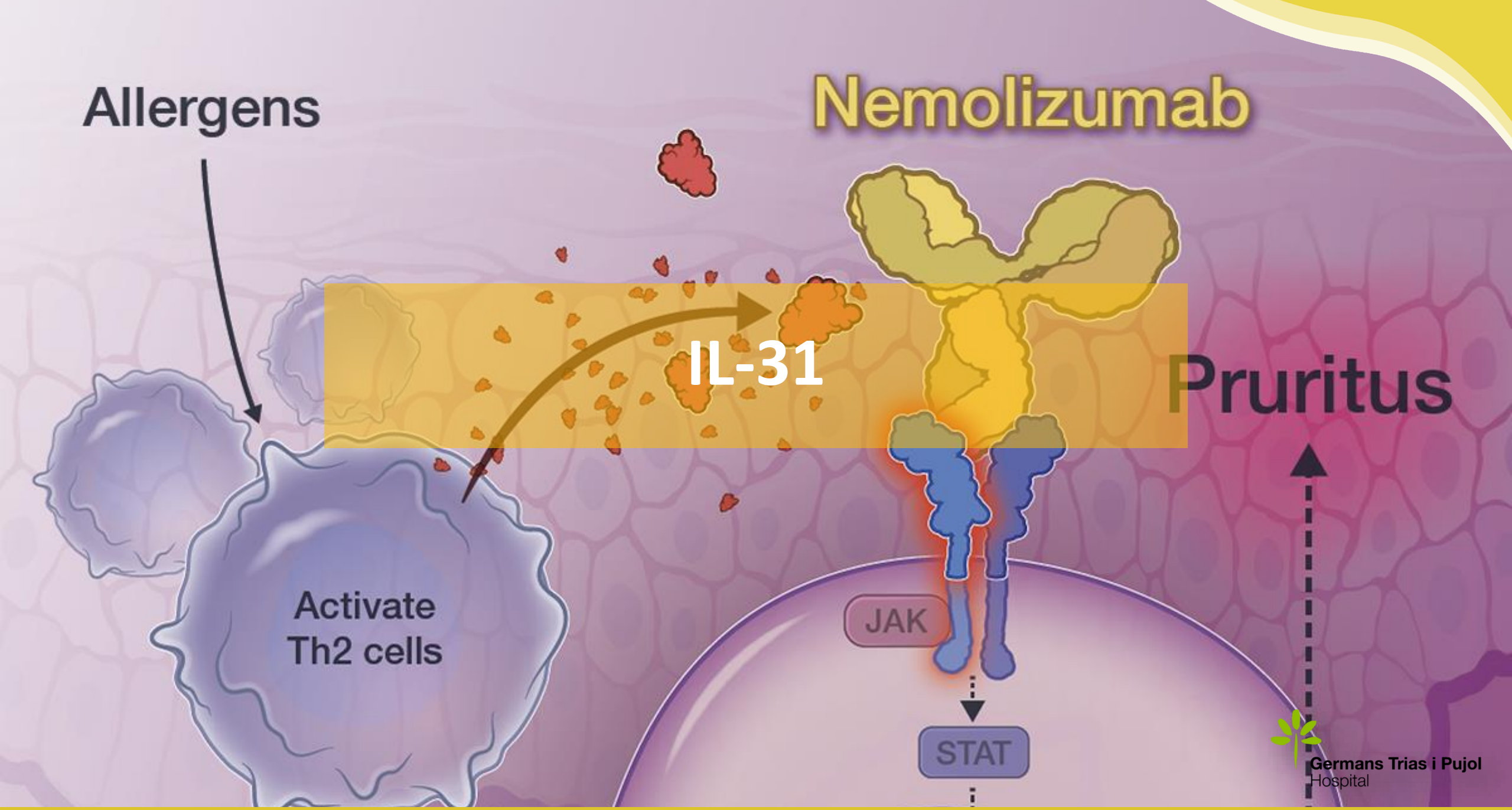
Allergens
Nemolizumab
IL-31
Pruritus
Activate
Th2 cells
JAK
STAT
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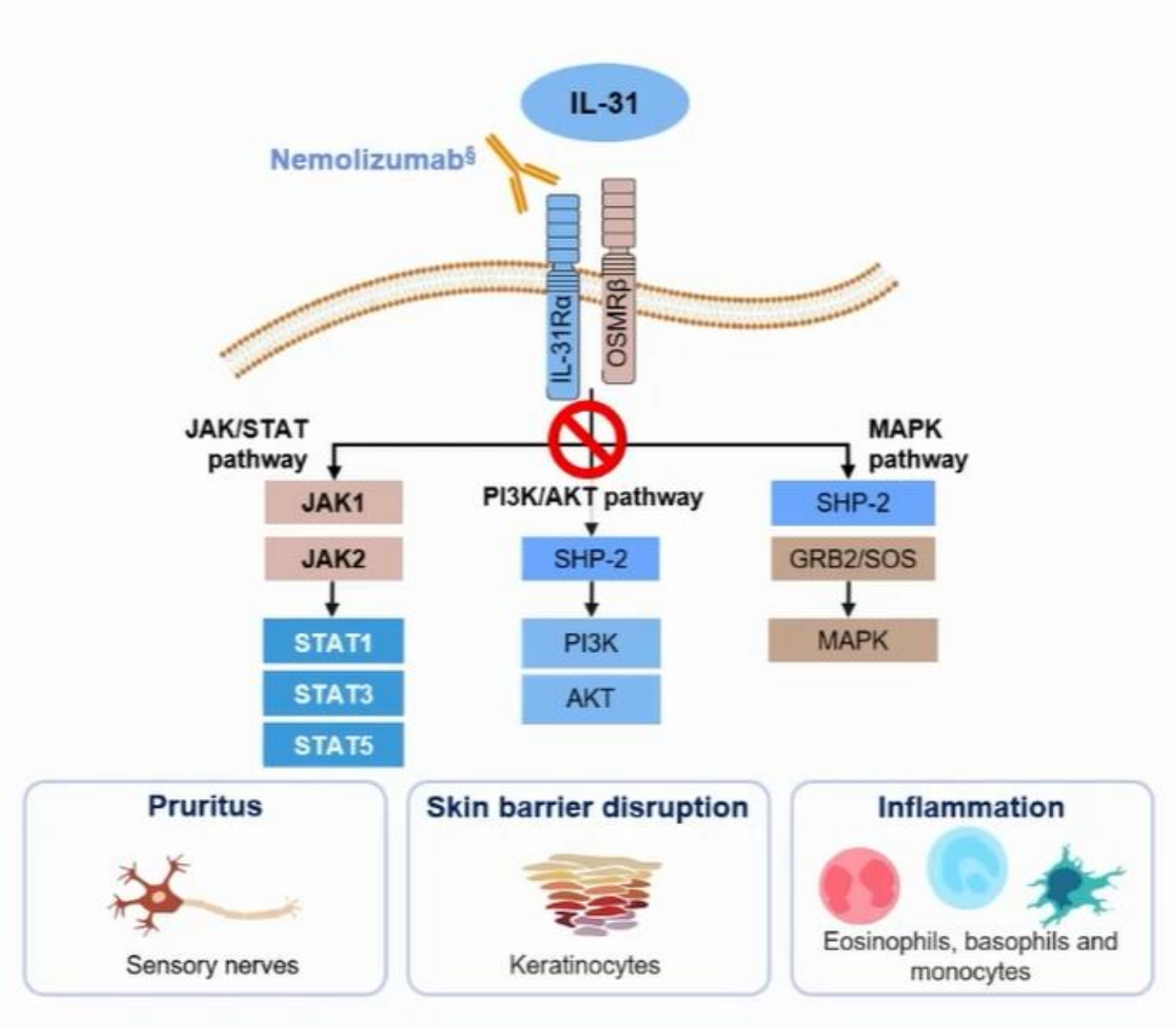
Hospital

ANTI-IL31Rα

NEMOLIZUMAB



- IL31: citoquina neuroinmune clave en DA. Prurito, disrupción de barrera y exacerbación de la inflamación.
- Señaliza a través del receptor heterodimérico compuesto por OSMRβ e IL-31Rα
- Nemolizumab es el primer antagonista de IL-31Rα que inhibe la unión de IL-31 a su receptor

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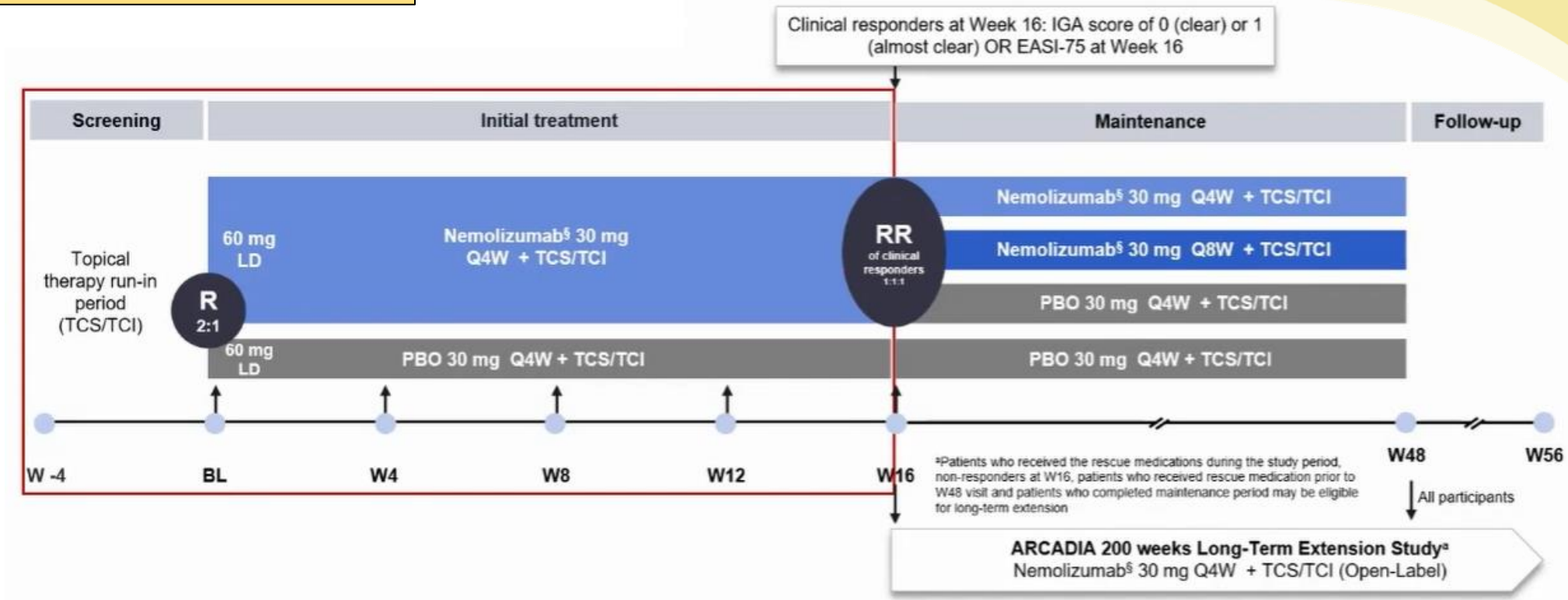
ANTI-IL31Rα

NEMOLIZUMAB



Key inclusion criteria

- Adults and adolescents (≥12 years) with chronic AD for ≥2 years
- EASI score ≥16
- IGA score ≥3
- AD involvement ≥10% of BSA
- PP NRS score ≥4

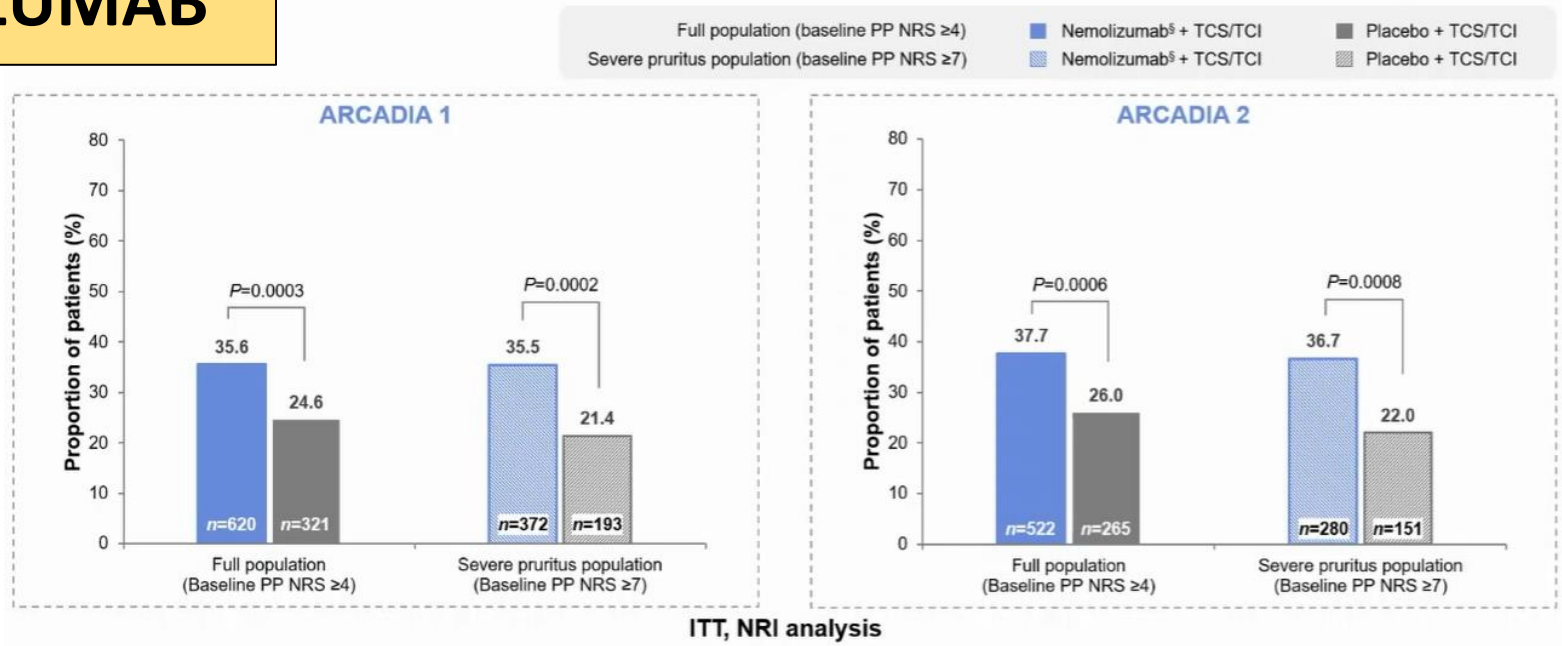
Key exclusion criteria

- Body weight <30 kg
- Exacerbation of asthma requiring hospitalization in the preceding 12 months
- Uncontrolled asthma in preceding 3 months
- History of COPD and/or chronic bronchitis

ANTI-IL31Rα

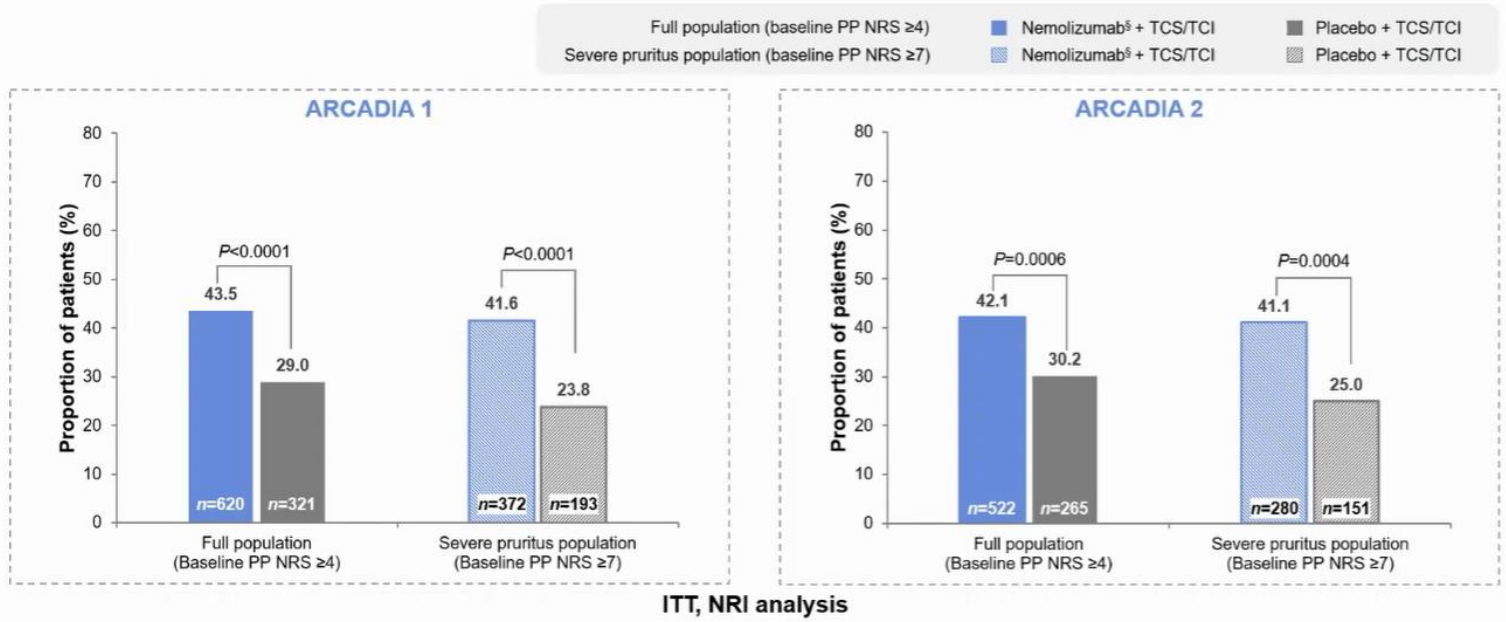
NEMOLIZUMAB

IGA 0/1



ITT, NRI analysis

EASI75



ITT, NRI analysis

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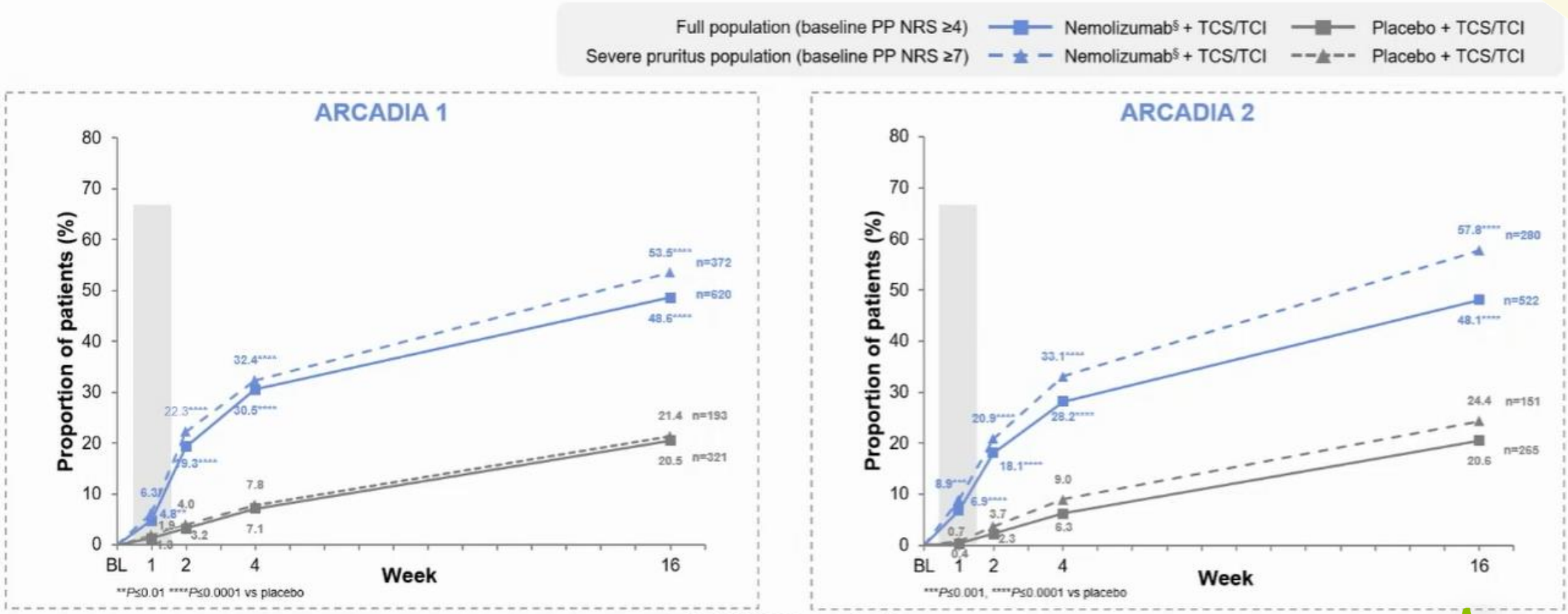
ANTI-IL31Rα

NEMOLIZUMAB

Reducción de ≥4 PP-NRS



ITT, MI MAR analysis

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ANTI-IL31Rα

NEMOLIZUMAB

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)

ANTI-IL31Rα

NEMOLIZUMAB

Acontecimientos adversos de interés

	ARCADIA 1		ARCADIA 2	
	Nemolizumab§ + TCS/TCI *N*=616	Placebo + TCS/TCI *N*=321	Nemolizumab§ + TCS/TCI *N*=519	Placebo + TCS/TCI *N*=263
Conjunctivitis allergic, *n* (%)	6 (1.0)	4 (1.2)	1 (0.2)	2 (0.8)
Nasopharyngitis, *n* (%)	9 (1.5)	8 (2.5)	19 (3.7)	12 (4.6)
COVID-19, *n* (%)	10 (1.6)	6 (1.9)	14 (2.7)	8 (3.0)
Upper respiratory tract infection, *n* (%)	9 (1.5)	14 (4.4)	6 (1.2)	5 (1.9)
Sinusitis, *n* (%)	4 (0.6)	3 (0.9)	5 (1.0)	2 (0.8)
Urinary tract infection, *n* (%)	9 (1.5)	3 (0.9)	4 (0.8)	2 (0.8)
Conjunctivitis, *n* (%)	2 (0.3)	0	3 (0.6)	3 (1.1)
Herpes infections, *n* (%)	16 (2.6)	9 (2.8)	10 (1.9)	7 (2.7)
Herpes zoster	4 (0.6)	0	1 (0.2)	0
Other Herpes infections	12 (1.9)	9 (2.8)	9 (1.7)	7 (2.7)
Neoplasms benign, malignant and unspecified (including cysts and polyps), *n* (%)	3 (0.5)	3 (0.9)	2 (0.4)	2 (0.8)

No se observa un incremento en el riesgo de conjuntivitis ni infecciones herpéticas.

ANTI-IL31Rα

NEMOLIZUMAB

Desarrollado por Chugai Pharmaceutical Co. Ltd, Maruho Co. Ltd y Galderma Pharma S.A.
Aprobado en Japón en marzo 2022 para adultos y niños ≥13 años para el tratamiento del prurito asociado a la DA

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

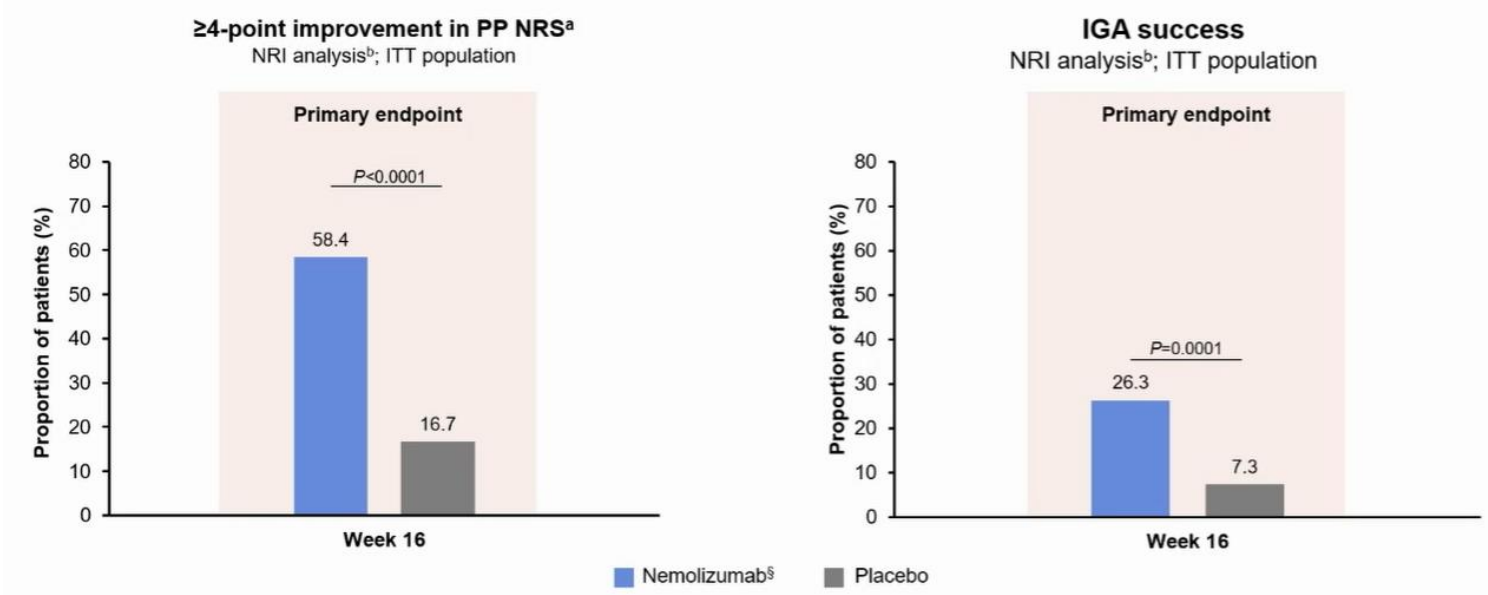
Phase 3 Trial of Nemolizumab in Patients with Prurigo Nodularis

Br J Dermatol 2024; **190**:20–28
https://doi.org/10.1093/bjd/ljad268
Advance access publication date: 31 July 2023

BJD
British Journal of Dermatology
Clinical Trial

Efficacy and safety of nemolizumab in paediatric patients aged 6–12 years with atopic dermatitis with moderate-to-severe pruritus: results from a phase III, randomized, double-blind, placebo-controlled, multicentre study

Atsuyuki Igarashi[1], Toshio Katsunuma[2], Takayo Matsumura[3] and Hiroshi Komazaki[3], for the Nemolizumab-JP04 Study Group



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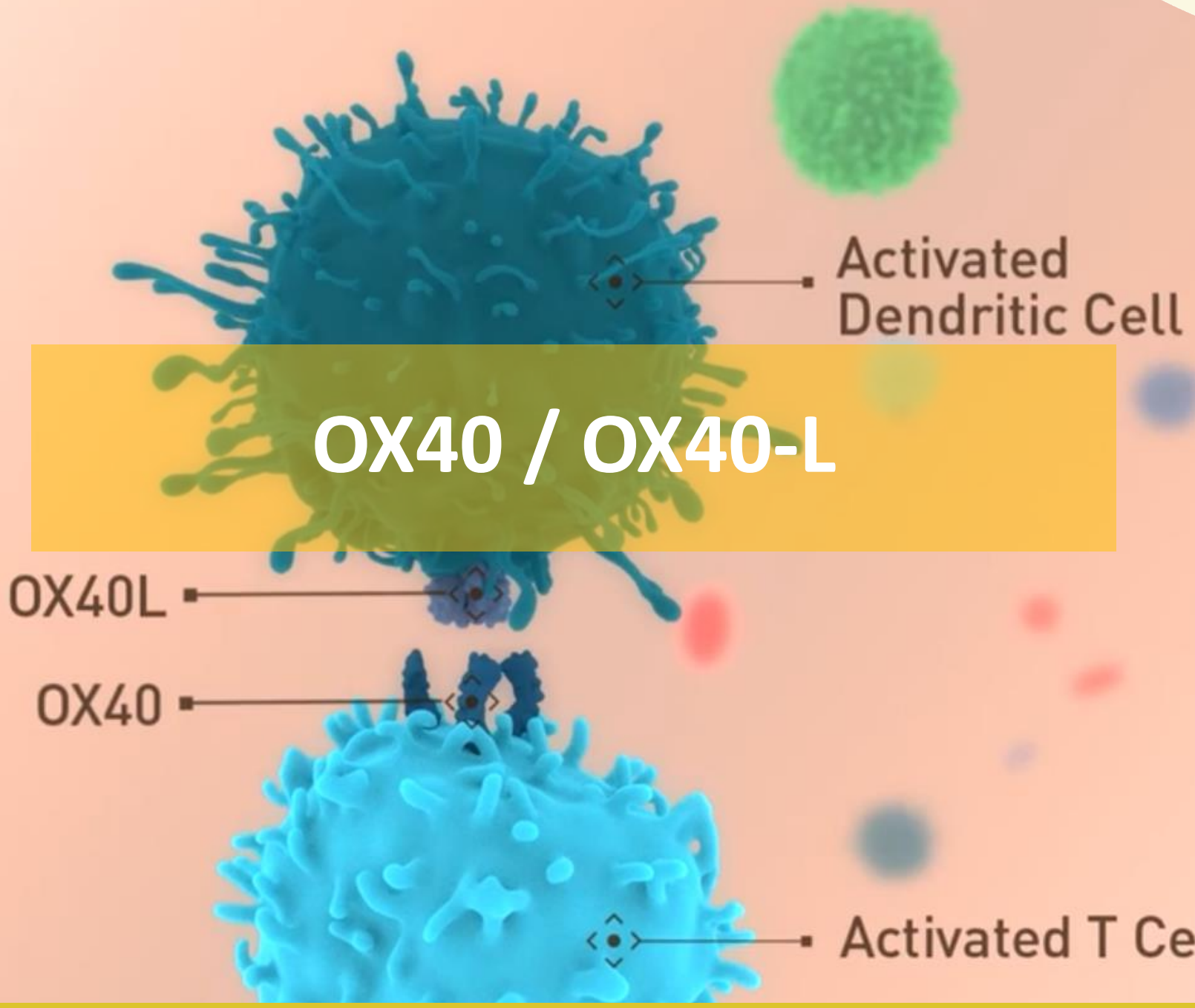
OX40 / OX40-L



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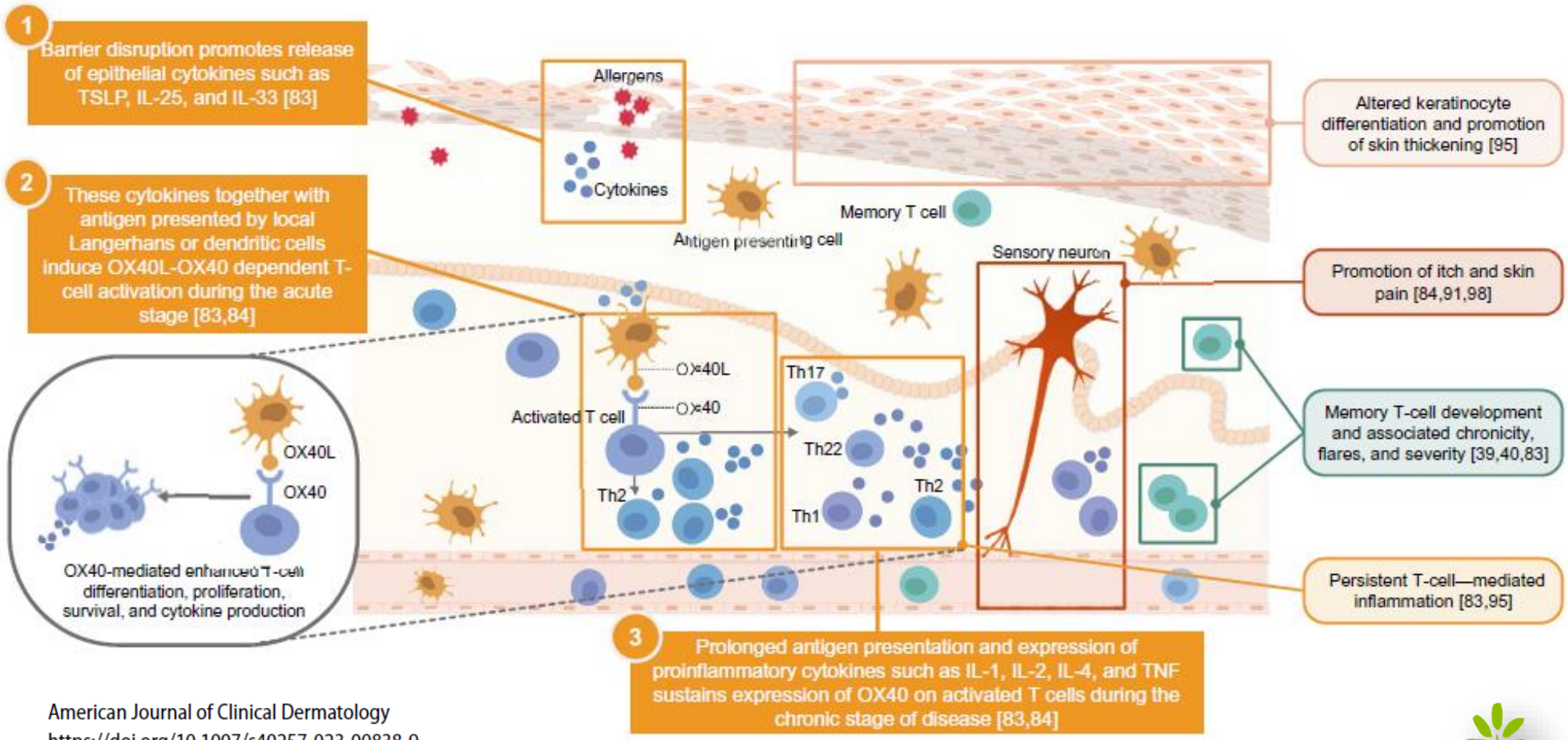
Vía OX40 / OX40-L

- Expansión de las células T
- Desarrollo de sus funciones efectoras
- Formación de células T de memoria



American Journal of Clinical Dermatology
https://doi.org/10.1007/s40257-023-00838-9

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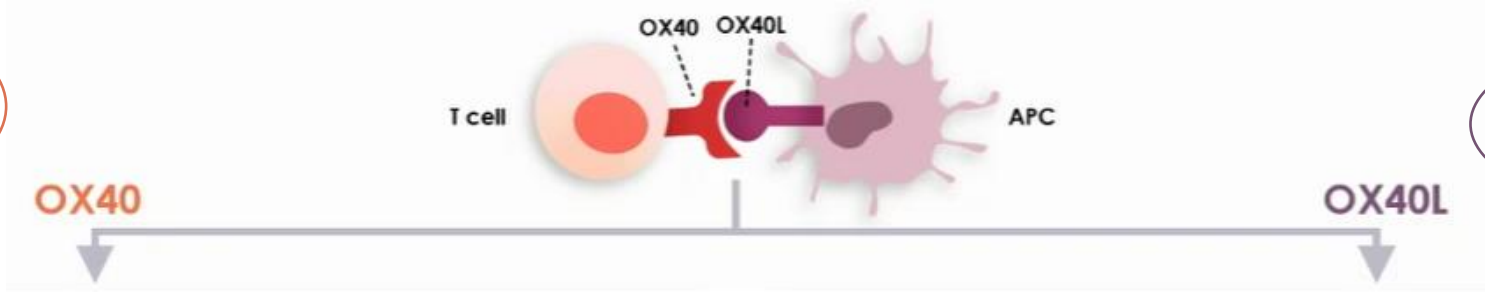
Vía OX40 / OX40-L

ROCATINLIMAB
TELAZORLIMAB



AMLITELIMAB

Descripción	**OX40** es un receptor co-estimulador	**OX40L** es una **molécula de superficie celular** que **se une a OX40**
Expresión	• Expresada en **células T efectoras activadas, células T reguladoras, células T de memoria** (pero no en células T naive). También en células **NKT, NK** y **neutrófilos.** • La expresión está **promovida por varias citoquinas** (IL-1, IL-2, I-4, TNF-α)	• Se encuentra sobre todo en **CPAs activadas**. También en céulas endoteliales, de músculo liso, mastocitos y NK • No diferencias en la expresión de OX40L en PBMs en pacientes con DA vs controles sanos
Señalización	• La vía OX40 dirige la **expansión, diferenciación, y supervivencia de las células T activadas patogénicas** • La señalización OX40 no necesita de la activación de la vía JAK/STAT	

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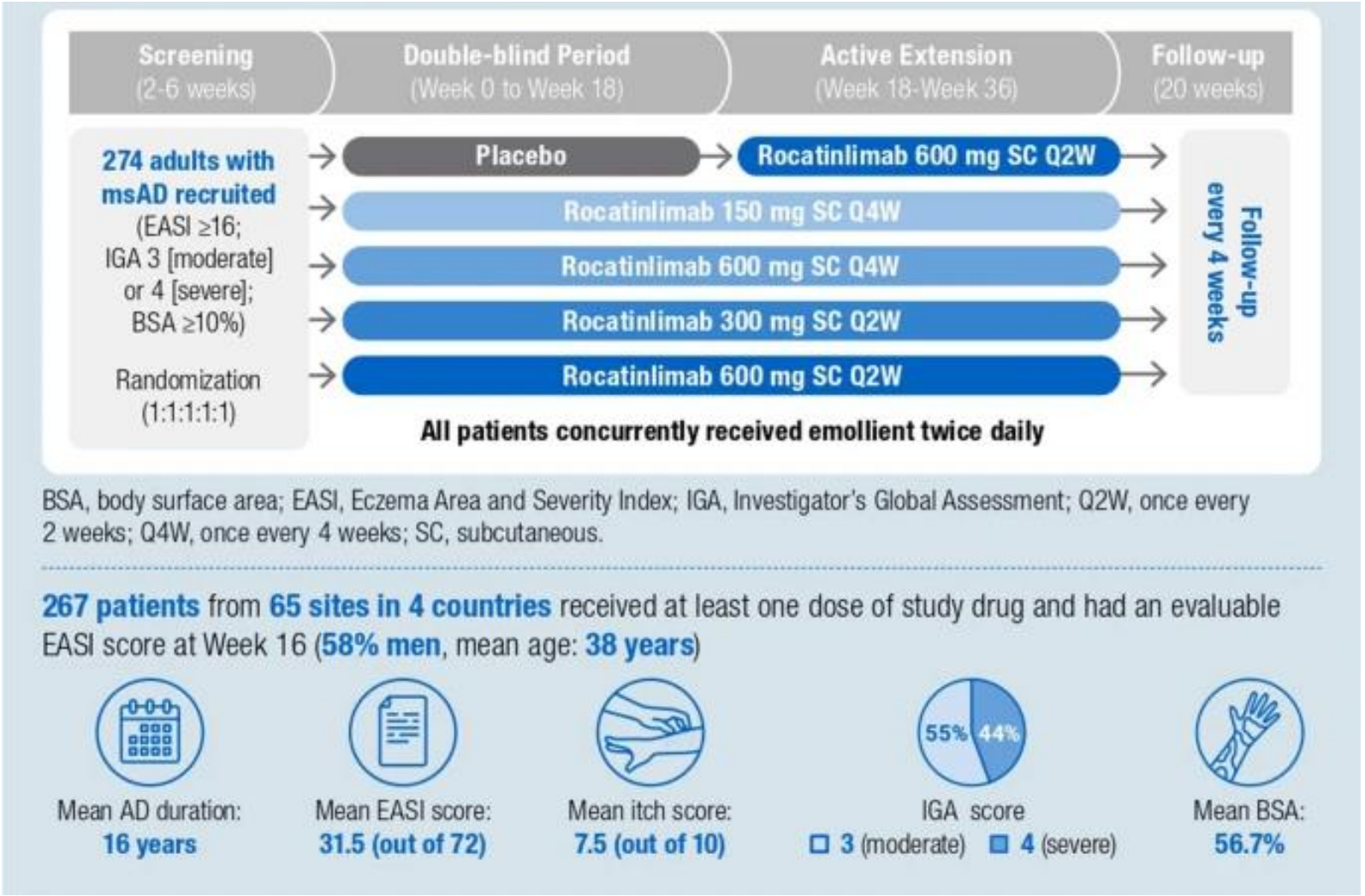
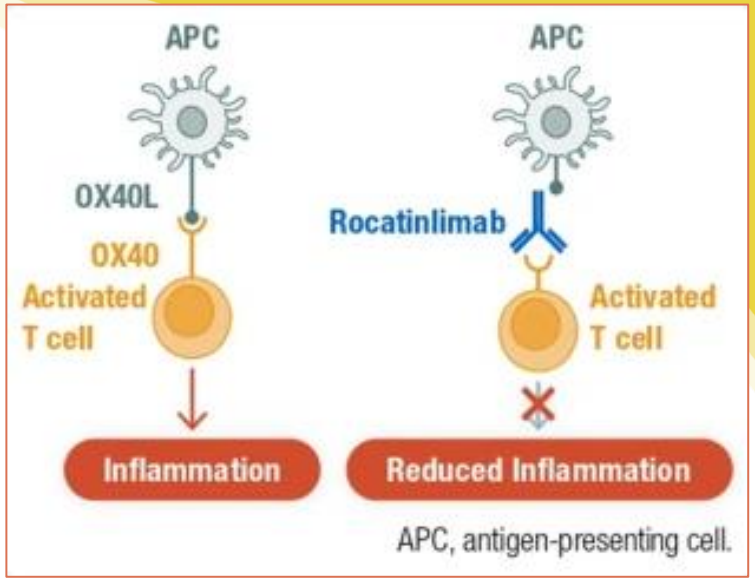
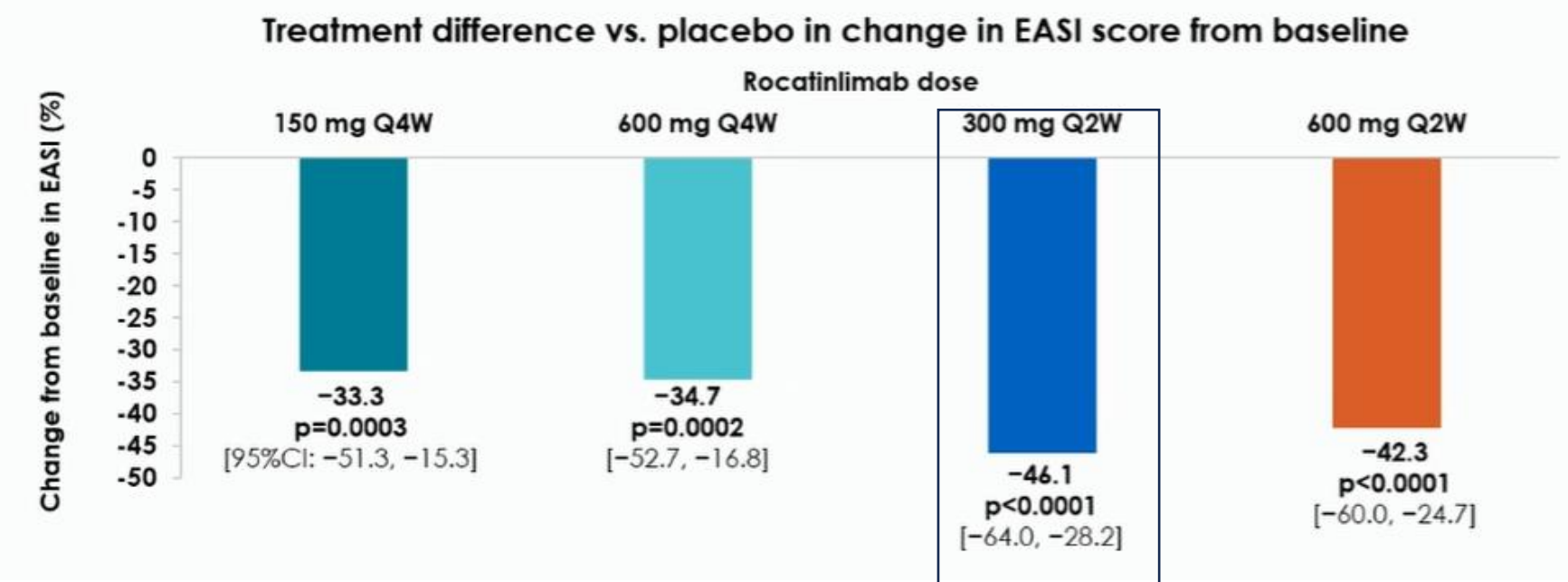
Rocatinlimab (AMG 451/KHK 4083)





Guttman-Yassky E, Simpson EL, Reich K, Kabashima K, Igawa K, Suzuki T, Mano H, Matsui T, Esfandiari E, Furue M. An anti-OX40 antibody to treat moderate-to-severe atopic dermatitis: a multicentre, double-blind, placebo-controlled phase 2b study. Lancet. 2023;401(10372):204–14. https://doi.org/10.1016/S0140-6736(22)02037-2.

Rocatinlimab (AMG 451/KHK 4083)



Rocatinlimab 300mg cada 2W
W16:

EASI75: 54% (vs. 11% placebo)
IGA 0/1: 31% (vs. 2% placebo)
Reducción NRS-P≥4p: 56%

- La **reducción en el EASI** desde la visita basal a W16 fue significativamente **mayor en todos los grupos de rocatinlimab vs placebo**
- La mayor diferencia se observó para la dosis de **300mg cada 2W**

Guttman-Yassky E, Simpson EL, Reich K, Kabashima K, Igawa K, Suzuki T, Mano H, Matsui T, Esfandiari E, Furue M. An anti-OX40 antibody to treat moderate-to-severe atopic dermatitis: a multicentre, double-blind, placebo-controlled phase 2b study. Lancet. 2023;401(10372):204–14. https://doi.org/10.1016/S0140-6736(22)02037-2.

Rocatinlimab (AMG 451/KHK 4083)

Secondary Endpoint Results at Week 16: Patient-Reported Outcomes

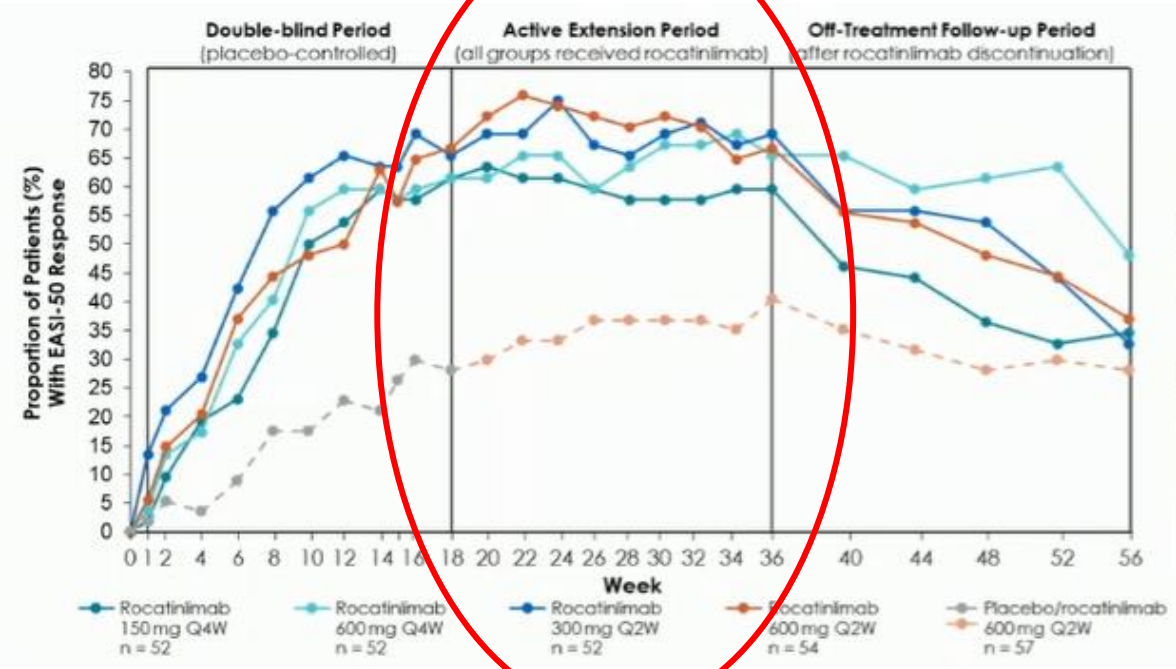
	Rocatinlimab 150 mg Q4W (n = 52)	Rocatinlimab 600 mg Q4W (n = 52)	Rocatinlimab 300 mg Q2W (n = 52)	Rocatinlimab 600 mg Q2W (n = 54)	Placebo (n = 57)
Change from baseline in **percent BSA**, LS mean (95% CI)	−22.9 (−30.3, −15.4)	−21.5 (−29.1, −13.9)	−27.9 (−35.3, −20.5)	−25.0 (−32.3, −17.8)	−7.9 (−15.0, −0.8)
Treatment difference (95% CI)	−15.0 (−24.3, −5.6)	−13.6 (−23.0, −4.3)	−20.1 (−29.4, −10.7)	−17.2 (−26.4, −8.0)	—
Percent change from baseline in **pruritus NRS**, LS mean (95% CI)	−25.6 (−39.5, −11.7)	−34.4 (−48.6, −20.2)	−48.0 (−61.7, −34.3)	−36.8 (−50.4, −23.3)	−6.2 (−19.4, 7.0)
Treatment difference (95% CI)	−19.4 (−36.8, −2.0)	−28.2 (−45.6, −10.8)	−41.8 (−59.2, −24.5)	−30.7 (−47.9, −13.4)	—
Change from baseline in **sleep disturbance NRS**, LS mean (95% CI)	−1.1 (−2.0, −0.2)	−1.9 (−2.9, −1.0)	−2.6 (−3.5, −1.7)	−2.0 (−2.9, −1.1)	−0.01 (−0.9, 0.9)
Treatment difference (95% CI)	−1.1 (−2.2, 0.1)	−1.9 (−3.1, −0.8)	−2.6 (−3.7, −1.4)	−2.0 (−3.1, −0.9)	—
Change from baseline in **DLQI**, LS mean (95% CI)	−2.6 (−4.7, −0.4)	−4.7 (−6.9, −2.4)	−6.3 (−8.4, −4.2)	−4.9 (−7.0, −2.8)	0.2 (−1.9, 2.3)
Treatment difference (95% CI)	−2.8 (−5.4, −0.1)	−4.9 (−7.6, −2.2)	−6.5 (−9.1, −3.8)	−5.1 (−7.8, −2.5)	—

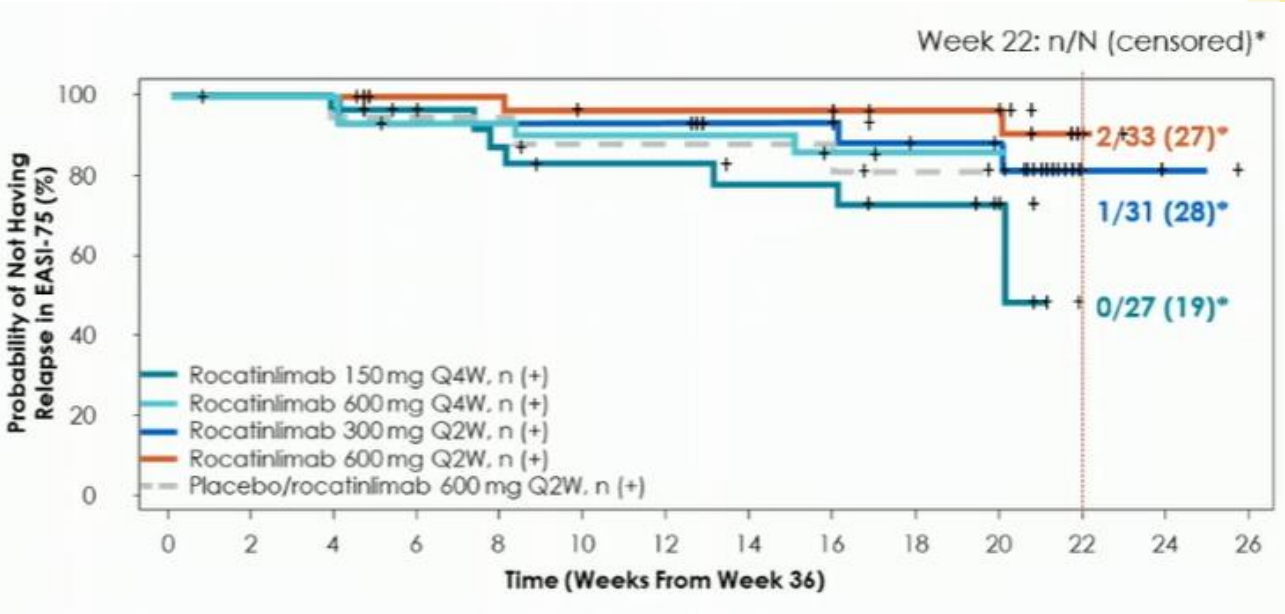
- Para todos los PROs (patient-reported outcomes), el grupo que recibió 300mg cada 2W presentó mejores resultados

Guttman-Yassky E, Simpson EL, Reich K, Kabashima K, Igawa K, Suzuki T, Mano H, Matsui T, Esfandiari E, Furue M. An anti-OX40 antibody to treat moderate-to-severe atopic dermatitis: a multicentre, double-blind, placebo-controlled phase 2b study. Lancet. 2023;401(10372):204–14. https://doi.org/10.1016/S0140-6736(22)02037-2.

Rocatinlimab (AMG 451/KHK 4083)

Rocatinlimab 300mg cada 2W W16:	W56 (tras suspensión a W36):
EASI75: 54% IGA 0/1: 31% Reducción NRS-P≥4p: 56%	EASI75: 31% IGA 0/1: 25% Reducción NRS-P≥4p: 29%





- La respuesta a W16 se mantuvo para todos los grupos de rocatinlimab a **W36**
- **Rocatinlimab 300mg cada 2W:**
  - **EASI75: 64%**
  - **IGA 0/1: 52%**

- Tras la suspensión del tratamiento, se mantuvo la respuesta EASI75 en la mayoría de pacientes (W36 a W56)
- **La probabilidad de mantener la respuesta tras la suspensión fue del 73 al 96% entre todos los grupos de rocatinlimab.**

↓TARC/CCL17 (Th2 signature)
↓ IL-22 (Th17/Th22 signature)

Guttman-Yassky E, Simpson EL, Reich K, Kabashima K, Igawa K, Suzuki T, Mano H, Matsui T, Esfandiari E, Furue M. An anti-OX40 antibody to treat moderate-to-severe atopic dermatitis: a multicentre, double-blind, placebo-controlled phase 2b study. Lancet. 2023;401(10372):204–14. https://doi.org/10.1016/S0140-6736(22)02037-2.

Rocatinlimab (AMG 451/KHK 4083)

Adverse events (safety analysis set) in the double-blind period

Adverse event, n (%)	Rocatinlimab 150 mg Q4W (n=54)	Rocatinlimab 600 mg Q4W (n=53)	Rocatinlimab 300 mg Q2W (n=55)	Rocatinlimab 600 mg Q2W (n=54)	Total rocatinlimab (n=216)	Placebo (n=57)
Any adverse event	37 (69)	45 (85)	47 (86)	46 (85)	175 (81)	41 (72)
Serious adverse events	3 (6)	1 (2)	3 (6)	1 (2)	8 (4)	1 (2)
Adverse events leading to treatment discontinuation	5 (9)	3 (6)	7 (13)	4 (7)	19 (9)	12 (21)
All deaths	0	0	0	0	0	0
Adverse events with severity grade of ≥3	6 (11)	1 (2)	5 (9)	4 (7)	16 (7)	2 (4)

Acontecimientos adversos más frecuentes:

- **Pirexia (17%** *vs. 4%)*
- **Escalofríos (11%** *vs. 0%)*
- Cefalea (9% *vs. 2%)*
- Aftas (7% *vs. 0%*)
- Náuseas (6% *vs. 2%*)

Guttman-Yassky E, Simpson EL, Reich K, Kabashima K, Igawa K, Suzuki T, Mano H, Matsui T, Esfandiari E, Furue M. An anti-OX40 antibody to treat moderate-to-severe atopic dermatitis: a multicentre, double-blind, placebo-controlled phase 2b study. Lancet. 2023;401(10372):204–14. https://doi.org/10.1016/S0140-6736(22)02037-2.

Rocatinlimab (AMG 451/KHK 4083)

COMING SOON

ROCKET Programme (programa de desarrollo de fase III)

Adult patients				Adolescent patients		Both
1 ROCKET ignite	2 ROCKET horizon	3 ROCKET shuttle	4 ROCKET voyager	5 ROCKET astro	6 ROCKET orbit	7 ROCKET ascend
• 24-week	• 24-week	• 24-week	• 24-week	• 52-week	• 52-week	• 104-week
• **Rocatinlimab** vs. PBO • **Two dosing regimens** (SC Q4W & LD at week 2)	• **Rocatinlimab** vs. PBO • **One dosing regimen** (SC Q4W & LD at week 2)	• **Rocatinlimab + TCS/TCI** vs. PBO • **Two dosing regimens** (SC Q4W & LD at week 2	• **Rocatinlimab** vs. PBO • **One dosing regimen** (SC Q4W & LD at week 2)	• **Rocatinlimab ± TCS/TCI** vs. PBO • **Two dosing regimens** (SC Q4W & LD at week 2 + open label extension)	• **Open-label rocatinlimab + TCS/TCI** • **One dosing regimen** (SC Q4W & LD at week 2)	• **Rocatinlimab** vs. PBO or open-label • **Two dosing regimens** (SC Q4W; Q8W)
• **Monotherapy; two dose regimens**	• **Monotherapy; one dose regimen**	• **Combination; two dose regimens**	• **Vaccine antibody response assessment**	• **PART 1 two dose regimens;** PART 2 dose 1 week 24–52 for non-responders	• Open-label **safety trial**	• **Long-term:** patients who completed a parent ROCKET trial

> 1000 pacientes reclutados

www.explorerockettrials.com

Germans Trias i Pujol Hospital

Telazorlimab (GBR830/ISB830)

Phase 2b randomized trial of OX40 inhibitor telazorlimab for moderate-to-severe atopic dermatitis

Barbara Rewerska, MD,[a] Lawrence D. Sher, MD,[b] Sady Alpizar, MD,[c] Sylvia Pauser, MD,[d] Grazyna Pulka, MD,[e] Neelufar Mozaffarian, MD, PhD,[f] Yacine Salhi, PhD,[f] Camille Martinet, MS,[g] Wafaa Jabert, MS,[f] Girish Gudi, PhD,[f] Vinu CA, MPharm, MSc,[f] Sunitha GN, PhD,[h] Julie Macoin, MSc,[f] Victor Anstett, MS,[f] Riccardo Turrini, PhD,[f] Marie-Agnès Doucey, PhD,[f] Stanislas Blein, PhD,[f] Cyril Konto, MD,[f] and Martina Machkova, MD[i]

Krakow, Poland; Rolling Hills Estates, Calif; Tampa, Fla; Osnabrück, Germany; New York, NY; Levallois-Perret, France; Mumbai, India; and Prague, Czech Republic

Characteristic	Variable	Part 1				Part 2	
		Telazorlimab				Telazorlimab	
		300 mg q2w (n = 76)	300 mg q4w (n = 78)	75 mg q4w (n = 77)	Placebo (n = 80)	600 mg q2w (n = 75)	Placebo (n = 74)
Primary end point	LS mean (SE) % change from baseline in EASI	−54.4 (5.1)	−48.6 (5.4)	−31.0 (5.7)	−34.2 (5.5)	−59.0 (4.6)	−41.8 (4.7)
	P value vs placebo	.008	.061	.691		.008	
	LS mean difference vs placebo (95% CI)	−20.2 (−34.9, −5.4)	−14.4 (−29.6, 0.7)	3.1 (−12.4, 18.7)		−17.2 (−29.9, −4.5)	
Secondary end points	EASI-75, no. (%)	18 (23.7)	16 (20.5)	9 (11.7)	9 (11.3)	19 (25.3)	14 (18.9)
	Odds ratio vs placebo (95% CI)	2.5 (1.0, 6.0)	2.1 (0.8, 5.0)	1.1 (0.4, 2.8)		1.4 (0.6, 3.2)	
	EASI-50, no. (%)	37 (48.7)	27 (34.6)	21 (27.3)	22 (27.5)	33 (44.0)	25 (33.8)
	Odds ratio vs placebo (95% CI)	2.5 (1.3, 5.0)	1.4 (0.7, 2.8)	1.0 (0.5, 2.0)		1.5 (0.8, 3.0)	
	IGA 0/1 response, no. (%)	10 (13.2)	8 (10.3)	5 (6.5)	4 (5.0)	9 (12.0)	4 (5.4)
	Odds ratio vs placebo (95% CI)	2.9 (0.9, 9.6)	2.2 (0.6, 7.8)	1.4 (0.3, 5.4)		2.5 (0.7, 8.6)	
	Pruritus NRS score improvement ≥4, no. (%)	6 (7.9)	9 (11.5)	4 (5.2)	8 (10.0)	10 (13.3)	7 (9.5)
	Odds ratio vs placebo (95% CI)	0.8 (0.3, 2.3)	1.2 (0.4, 3.3)	0.5 (0.1, 1.7)		1.5 (0.5, 4.1)	

Diferencias numéricas frente a placebo para las dosis altas (300mg y 600mg cada 2 semanas) pero no estadísticamente significativas

Telazorlimab (GBR830/ISB830)

Phase 2b randomized trial of OX40 inhibitor telazorlimab for moderate-to-severe atopic dermatitis

Barbara Rewerska, MD,[a] Lawrence D. Sher, MD,[b] Sady Alpizar, MD,[c] Sylvia Pauser, MD,[d] Grazyna Pulka, MD,[e] Neelufar Mozaffarian, MD, PhD,[f] Yacine Salhi, PhD,[f] Camille Martinet, MS,[g] Wafaa Jabert, MS,[f] Girish Gudi, PhD,[f] Vinu CA, MPharm, MSc,[f] Sunitha GN, PhD,[h] Julie Macoin, MSc,[f] Victor Anstett, MS,[f] Riccardo Turrini, PhD,[f] Marie-Agnès Doucey, PhD,[f] Stanislas Blein, PhD,[f] Cyril Konto, MD,[f] and Martina Machkova, MD[i] *Krakow, Poland; Rolling Hills Estates, Calif; Tampa, Fla; Osnabrück, Germany; New York, NY; Levallois-Perret, France; Mumbai, India; and Prague, Czech Republic*

TABLE IV. TEAE summary during double-blind period in safety population

	Part 1				Part 2	
	Telazorlimab					
TEAE	300 mg q2w (n = 76)	300 mg q4w (n = 78)	75 mg q4w (n = 77)	Placebo (n = 80)	Telazorlimab 600 mg q2w (n = 75)	Placebo (n = 74)
Any TEAE	52 (68.4)	45 (57.7)	56 (72.7)	58 (72.5)	49 (65.3)	37 (50.0)
Treatment discontinuation due to TEAE	1 (1.3)	2 (2.6)	1 (1.3)	3 (3.8)	0	2 (2.7)
Serious TEAE	3 (3.9)	2 (2.6)	2 (2.6)	1 (1.3)	1 (1.3)	0
TEAE > 5% in any treatment group						
Dermatitis atopic	14 (18.4)	19 (24.4)	17 (22.1)	18 (22.5)	13 (17.3)	12 (16.2)
Nasopharyngitis	3 (3.9)	9 (11.5)	7 (9.1)	7 (8.8)	6 (8.0)	7 (9.5)
Upper respiratory tract infection	6 (7.9)	4 (5.1)	7 (9.1)	4 (5.0)	4 (5.3)	5 (6.8)
Headache	6 (7.9)	5 (6.4)	2 (2.6)	8 (10.0)	5 (6.7)	5 (6.8)
Urinary tract infection	2 (2.6)	2 (2.6)	4 (5.2)	4 (5.0)	2 (2.7)	2 (2.7)
Pruritus	0	1 (1.3)	4 (5.2)	1 (1.3)	1 (1.3)	2 (2.7)
Fatigue	0	4 (5.1)	1 (1.3)	0	1 (1.3)	0

Data are presented as nos. (%). *q2w*, Every 2 weeks; *q4w*, every 4 weeks.

NO ENSAYOS EN CURSO
No ensayos previstos en DA

ACONTECIMIENTOS ADVERSOS MÁS FRECUENTES (dosis de 300 y 600 mg cada 2 semanas):

- **Nasofaringitis (16-21%)**
- **Infección del tracto respiratorio superior (8-16%)**
- **Cefalea (8-11%)**

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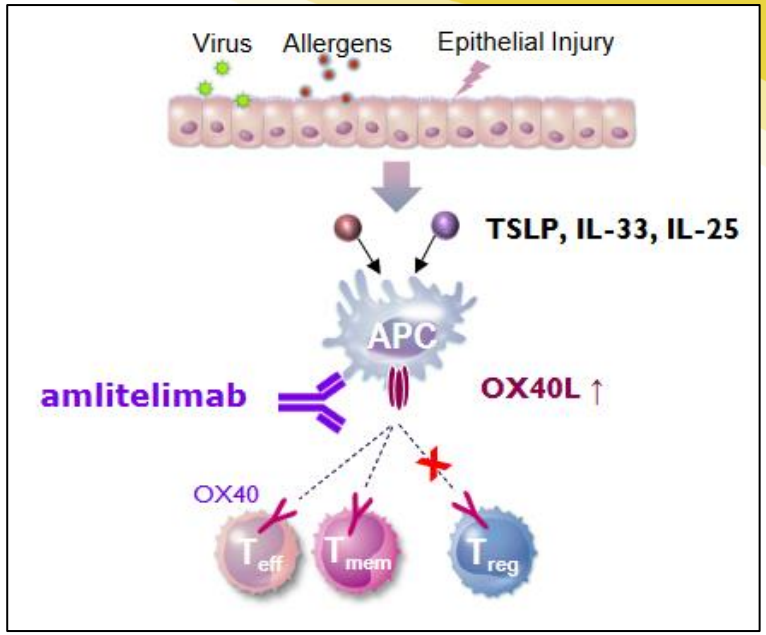
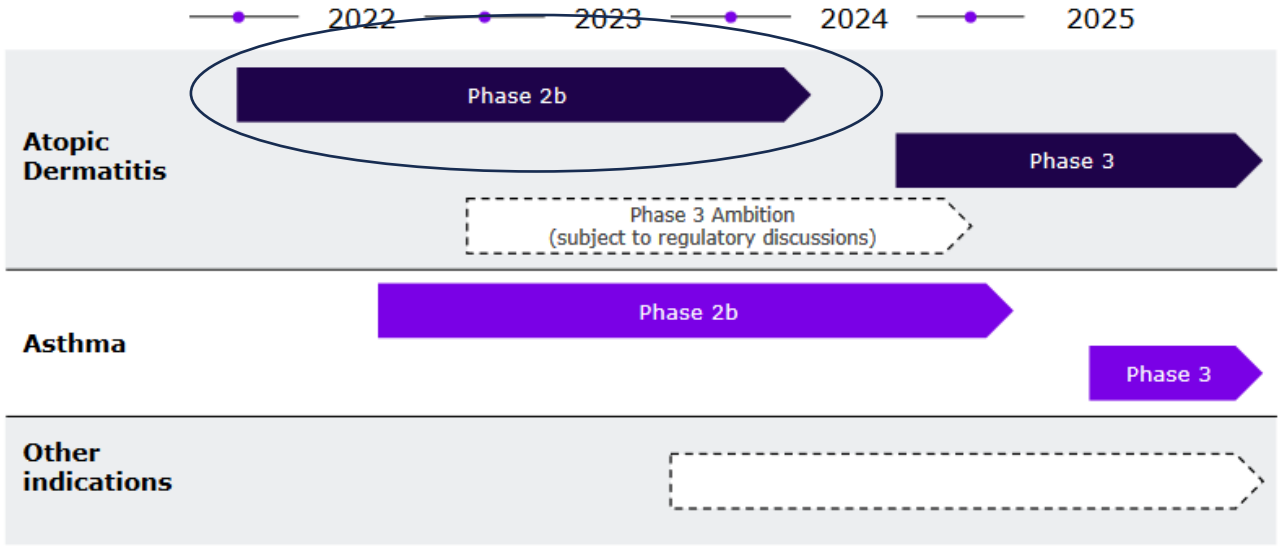
Amlitelimab (KY1005)

	OX40L Blocker	OX40 Depleter
Limited expression at sites of inflammation	✓	✗
Preserves T_{eff}, T_{mem} cells	✓	✗
Preserves and activates T_{reg}	✓	✗
Avoids cytokine release (fever, chills)	✓	✗





https://www.sanofi.com/en/media-room/press-releases/2023/2023-10-13-14-00-00-2760021

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Amlitelimab (KY1005)

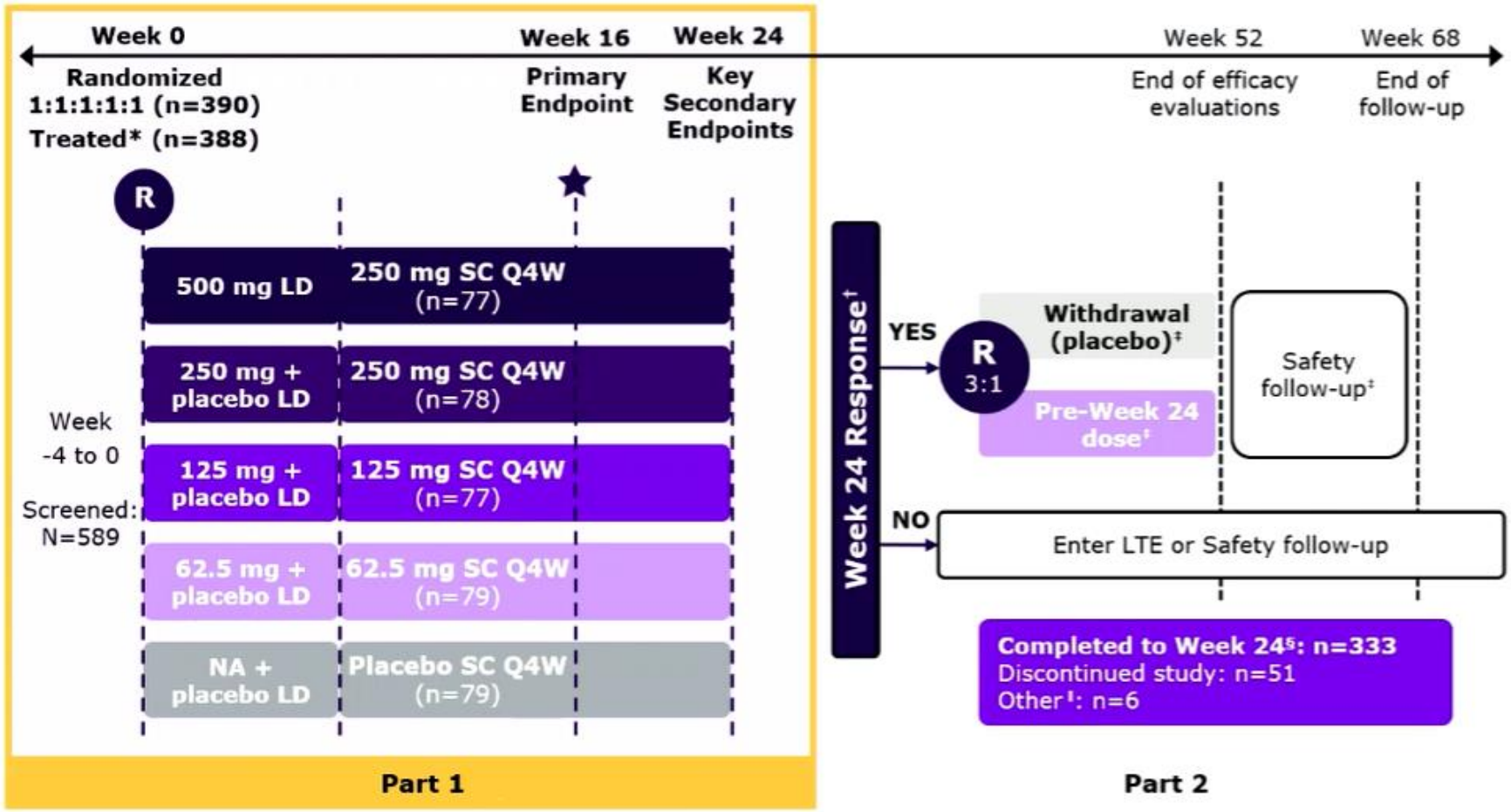
JOURNAL ARTICLE

523 - Efficacy and safety of amlitelimab (an anti-OX40 ligand antibody) in patients with moderate-to-severe atopic dermatitis: 24-week results from a phase 2b trial (STREAM-AD)

Stephan Weidinger, Andrew Blauvelt, Kim Papp, Adam Reich, Chih-Hung Lee, Margitta Worm, Charles Lynde, Yoko Kataoka, Peter Foley, Christine Weber

British Journal of Dermatology, Volume 190, Issue Supplement_2, February 2024, Pages ii24–ii26, https://doi.org/10.1093/bjd/ljad498.028

Published: 07 February 2024



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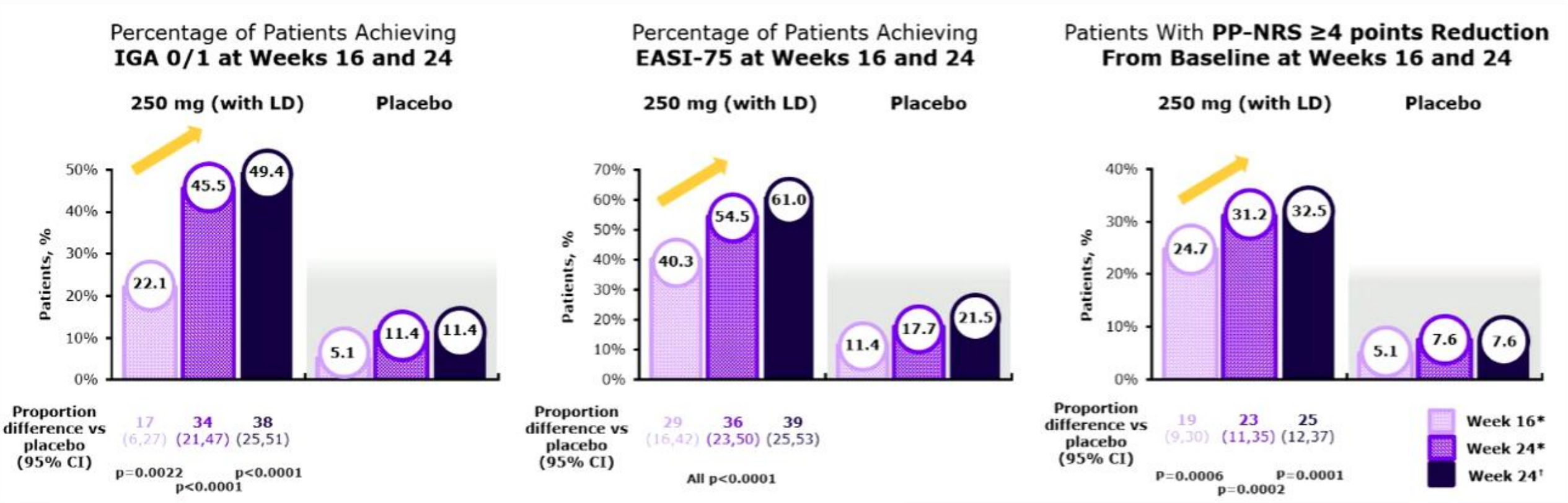
Amlitelimab (KY1005)



*Data collected after early treatment discontinuation due to reasons other than lack of efficacy prior to endpoint timepoint are included. Data on or after rescue medication or prohibited medications impacting efficacy start date or after the date of treatment discontinuation due to lack of efficacy prior to endpoint timepoint, were considered as non-responders. Any other unobserved values or other missing data are considered as non-responders at Week 16 and Week 24. †All data are used for analysis regardless of treatment discontinuation, regardless of rescue/prohibited concomitant medications use. Missing data are considered as non-responders at Week 16/Week 24.

AD, atopic dermatitis; CI, confidence interval; EASI, Eczema Area and Severity Index; IGA, investigator global assessment; LD, loading dose; PP-NRS, peak-pruritus numerical rating scale; Th, helper T cell.

Amlitelimab (KY1005)

JOURNAL ARTICLE

523 - Efficacy and safety of amlitelimab (an anti-OX40 ligand antibody) in patients with moderate-to-severe atopic dermatitis: 24-week results from a phase 2b trial (STREAM-AD)

Stephan Weidinger, Andrew Blauvelt, Kim Papp, Adam Reich, Chih-Hung Lee, Margitta Worm, Charles Lynde, Yoko Kataoka, Peter Foley, Christine Weber

British Journal of Dermatology, Volume 190, Issue Supplement_2, February 2024, Pages ii24–ii26, https://doi.org/10.1093/bjd/ljad498.028

Published: 07 February 2024

Seguridad

Summary of TEAEs through Week 24	Pooled amlitelimab dose groups	Placebo
Number (%) unique participants	N=310	N=78
Any TEAEs	209 (67.4%)	47 (60.3%)
Deaths	0	0
Any SAEs	8 (2.6%)	1 (1.3%)
Any AESIs	6 (1.9%)	1 (1.3%)
Any TEAE leading to treatment discontinuation	14 (4.5%)	5 (6.4%)
Proportion of TEAEs that were mild/moderate	196 (93.8%)	44 (93.6%)

Most frequent TEAEs by PT through Week 24 (≥5% in pooled amlitelimab groups)	Amlitelimab pooled dose groups	Placebo
Number (%) unique patients (N=388)	N=310	N=78
Worsening AD	53 (17.1%)	30 (38.5%)
Nasopharyngitis	34 (11.0%)	7 (9.0%)
COVID-19	24 (7.7%)	5 (6.4%)
Headache	19 (6.1%)	2 (2.6%)

There were no reports of:

- Parasitic infections or serious opportunistic infections
- Malignancy
- Severe injection site reactions
- Chills or aphthous ulcers as TEAEs
- Pyrexia or influenza/influenza-like illness within 72 hours of injection

There were overall low incidences of:

- Conjunctivitis*, balanced across treatment arms and placebo (1.6% pooled amlitelimab vs 3.8% placebo)
- Herpes infections† in pooled amlitelimab (2.3%) versus placebo (2.5%)

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Amlitelimab (KY1005)

EN MARCHA ENSAYO CLÍNICO DE FASE III

A Study to Evaluate the Efficacy and Safety of Subcutaneous Amlitelimab in Participants Aged 18 Years and Older With Moderate-to-severe Atopic Dermatitis on Background Topical Corticosteroids was last updated on Jan 25, 2024.

Property changed	Changes
Location	Avita Clinical Research Site Number : 8401073, Tampa, Florida, United States, 33613, Status: Recruiting

*Amlitelimab está siendo evaluado para otras indicaciones (Ph2): asma, hidradenitis supurativa y alopecia areata

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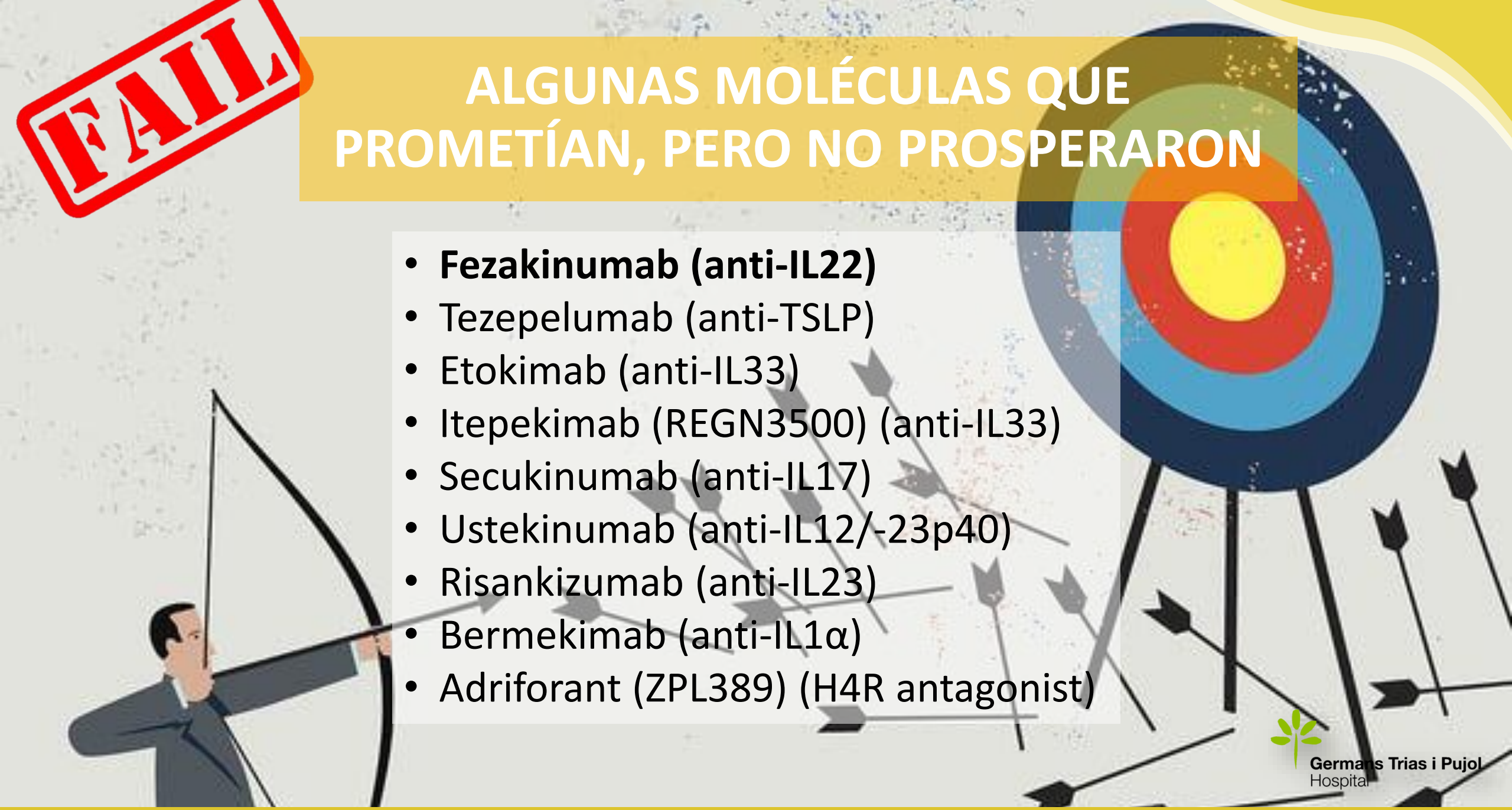

ALGUNAS MOLÉCULAS QUE PROMETÍAN, PERO NO PROSPERARON

- **Fezakinumab (anti-IL22)**
- Tezepelumab (anti-TSLP)
- Etokimab (anti-IL33)
- Itepekimab (REGN3500) (anti-IL33)
- Secukinumab (anti-IL17)
- Ustekinumab (anti-IL12/-23p40)
- Risankizumab (anti-IL23)
- Bermekimab (anti-IL1α)
- Adriforant (ZPL389) (H4R antagonist)

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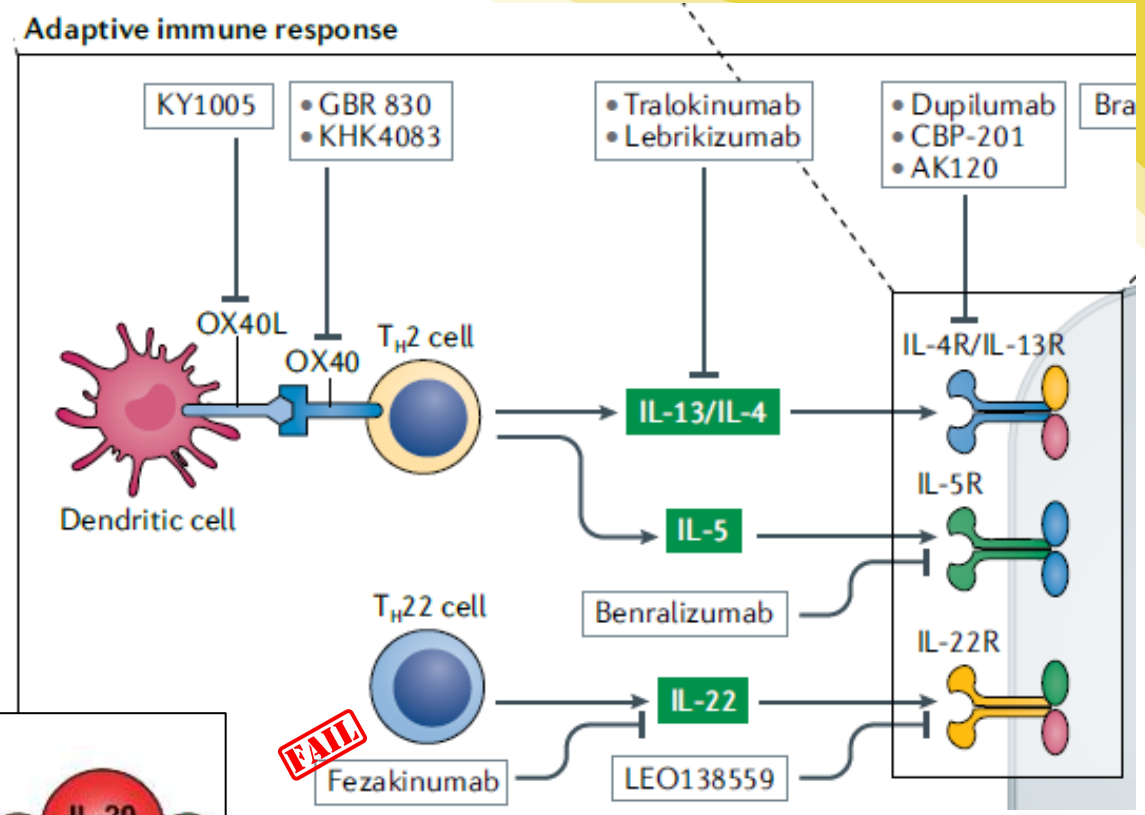
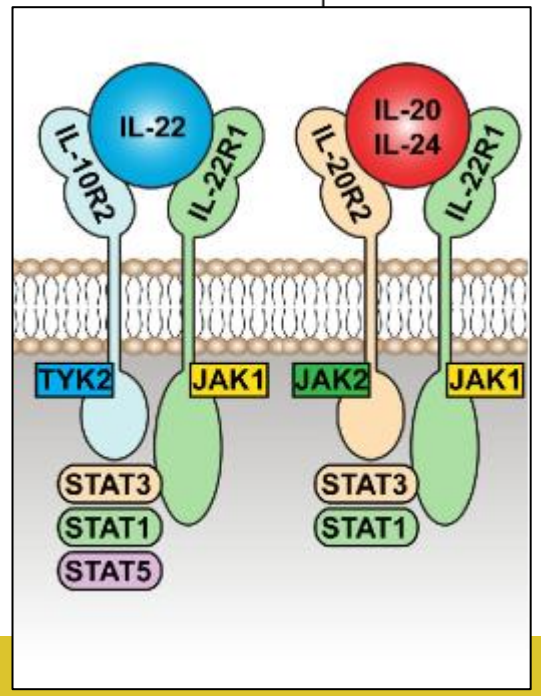
Anti-IL22

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

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	Complet
Anti-IL-22R1 antibody LEO 138559	NCT05099133	Phase I	Completed
Anti-IL-22R1 antibody LEO 138559	NCT05470114	Phase II	Recruiting





TEMTOKIBART (LEO138559) Anti-IL-22R1

Temtokibart W16 (CT 2a):

- EASI75: 41,6% (vs 13,7% PBO)
- EASI90: 30,8% (VS 3,5% PBO)
- EASI100: 20,9% (vs 0% PBO)
- IGA 0/1: 27,3% (vs 7% PBO)

Abstract N°: 4607 Efficacy and safety of IL-22RA1 inhibition in patients with moderate-to-severe atopic dermatitis: results from a Phase 2a monotherapy trial. EADV Congress 2023

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NUEVOS TÓPICOS Y PIPELINE

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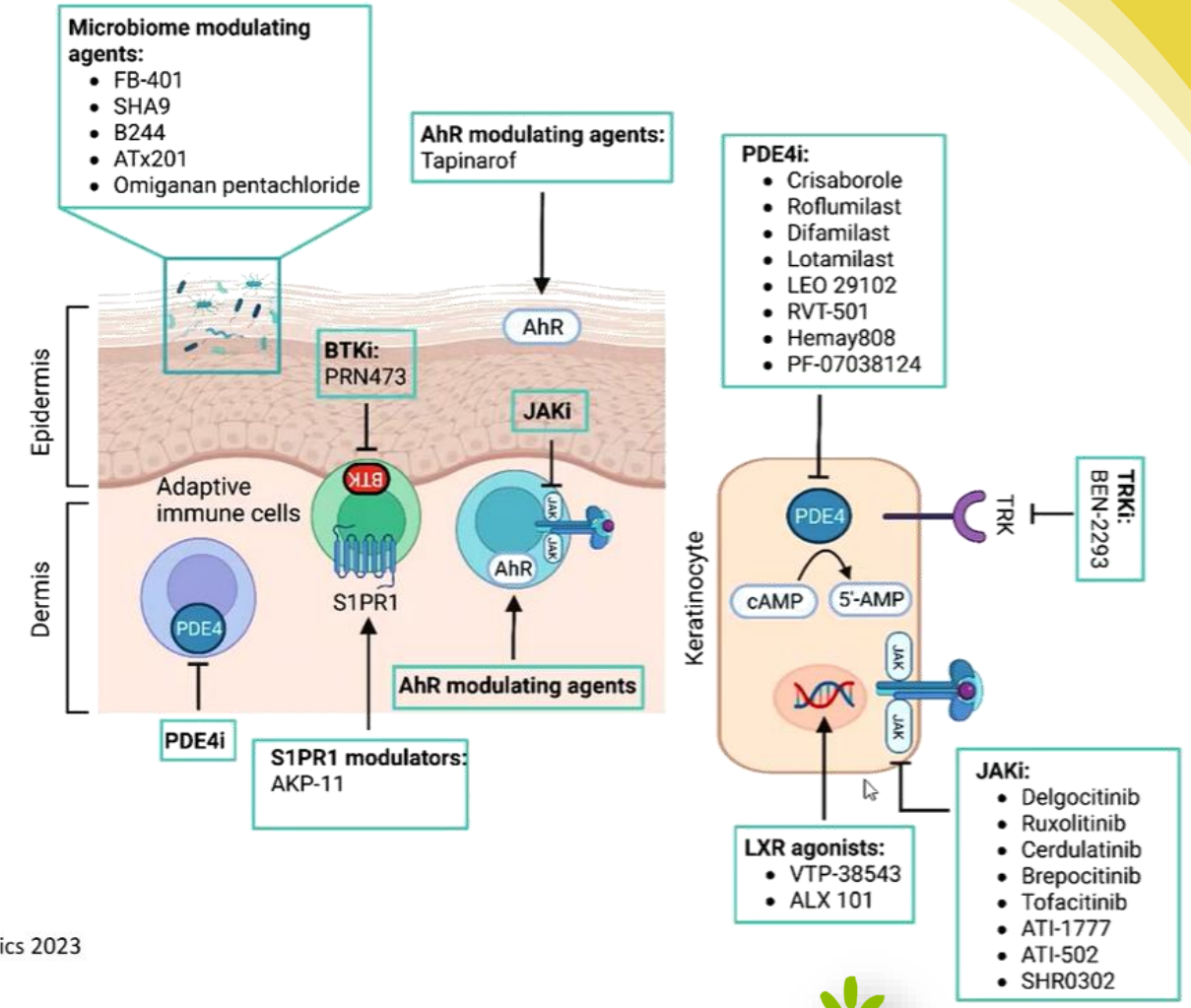
NUEVOS TÓPICOS Y PIPELINE

Approved topical treatments for AD

- **Topical corticosteroids (TCS)**
- **Topical calcineurin inhibitors (TCI)**
  - Tacrolimus
  - Pimecrolimus
- **Phosphodiesterase 4 inhibitors (PDE4i)**
  - Crisaborole
- **Janus kinase inhibitors (JAKi)**
  - Delgocitinib (pan-JAKi)
  - Ruxolitinib (JAK 1/2 inhibitor)

Emerging topical treatments in the pipeline for AD

- **Aryl hydrocarbon receptor (AhR) modulating agents**
  - Tapinarof
- **Phosphodiesterase 4 inhibitors (PDE4i)**
  - Roflumilast
  - Difamilast
  - Lotamilast
  - LEO 29102
  - RVT-501
  - Hemay808
  - PF-07038124
- **Janus kinase inhibitors (JAKi)**
  - Cerdulatinib (pan-JAKi and SYK)
  - Brepocitinib (JAK1/TYK2)
  - Tofacitinib (JAK1/3 inhibitor)
  - ATI-1777 (JAK1/3 inhibitor)
  - ATI-502 (JAK1/3 inhibitor)
  - SHR0302 (JAK1i)
- **Skin microbiome modulating agents**
  - FB-401
  - *Staphylococcus hominis A9* (SHA9)
  - Nitrosomonas eutropha (B244)
  - Niclosamide (ATx201)
  - Omiganan pentachloride
- **Liver X Receptor (LXR) agonists**
  - VTP-38543
  - ALX 101
- **Tropomyosin receptor kinase inhibitors (TRKi)**
  - BEN-2293
- **Nuclear transport modifiers (NTM)**
  - AMTX-100
- **Bruton tyrosine kinase inhibitors (BTKi)**
  - PRN473
- **Sphingosine-1-phosphate receptor subtype 1 (S1PR1) modulators**
  - AKP-11



Pinto LM, et al. Pharmaceutics 2023

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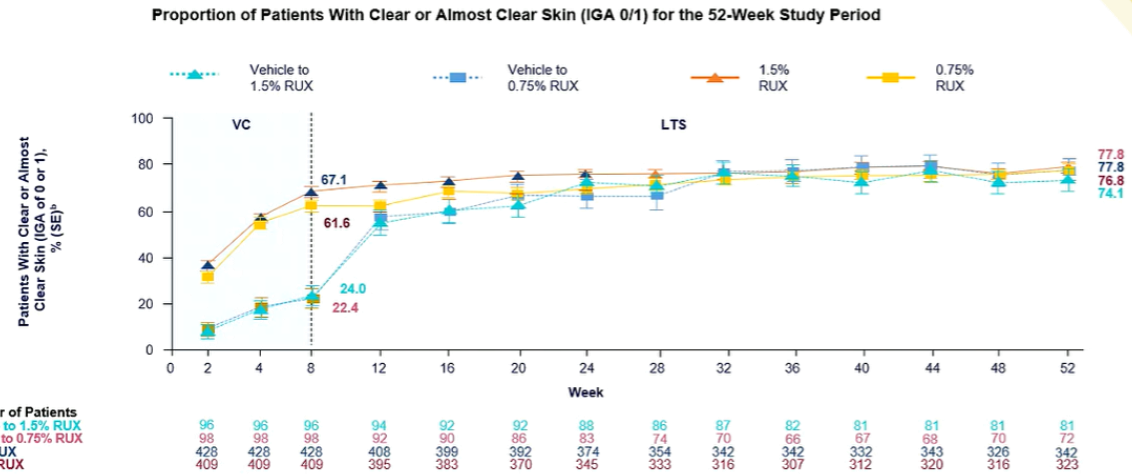
Mechanism of action	Name of topical agent	Stage of development	Intended use (BSA as per study design)
JAK-STAT inhibition	Ruxolitinib 1.5% cream (Opzelura™)*	Approved in the US in September 2021	Short term (up to 8 weeks) Mild-to-moderate AD BSA 3–20% (warning: maximum 20% BSA and/or 60 g/week) ≥ 12 years of age
	Delgocitinib 0.05% ointment (Corectim™)**	Approved in Japan in January 2020. *Not available in the US*	Evidence of long-term safety Any severity of AD BSA 5–30% ≥ 16 years of age
	Delgocitinib 0.025% ointment (Corectim™)**	Approved in Japan in March 2021. *Not available in the US*	Evidence of long-term safety Any severity of AD BSA 5–30% ≥ 2 years of age
	Delgocitinib cream	*Phase III began in May 2021*	*16-week trial* *Moderate-to-severe CHE* *> 18 years of age*
PDE4 inhibition	Crisaborole 2% ointment (Eucrisa™)*	Originally approved in the US in December 2016 for ages 2+ years. Extended approval in the US for ages 3+ months in March 2020	Evidence of long-term safety Mild-to-moderate AD ≥ 1% BSA ≥ 3 months of age
	Roflumilast 0.15% cream	*Phase III began in February 2021 for adults with AD.* Roflumilast 0.3% cream approved in US for psoriasis ages 12+ years	*4-week trial* *Mild-to-moderate AD* *> 3% BSA* *≥ 6 years of age*
	Roflumilast 0.05% cream	*Phase III began in April 2021 for pediatrics*	*4-week trial* *Mild-to-moderate AD* *> 3% BSA* *≥ 2 years of age*
	Difamilast 0.03% and 1% ointment (Moizerto™)**	Approved in Japan in September 2021. *Not available in the US*	4-week trial Mild-to-moderate AD 5–40% BSA ≥ 2 years of age
AHR modulation	Tapinarof 1% cream	*Phase III began in August 2021 for AD.* Approved in US for psoriasis ages 18+ years	*8-week trial + 48-week long-term extension* *Moderate-to-severe AD* *5–35% BSA* *≥ 2 years of age*
Microbial-based interventions	*Roseomonas-based medication (FB-401)*	*Phase II trial results did not meet statistical significance*	*Mild-to-moderate AD*
	ShA9	*Phase I*	*Moderate-to-severe AD*
Novel targeted therapies	*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*

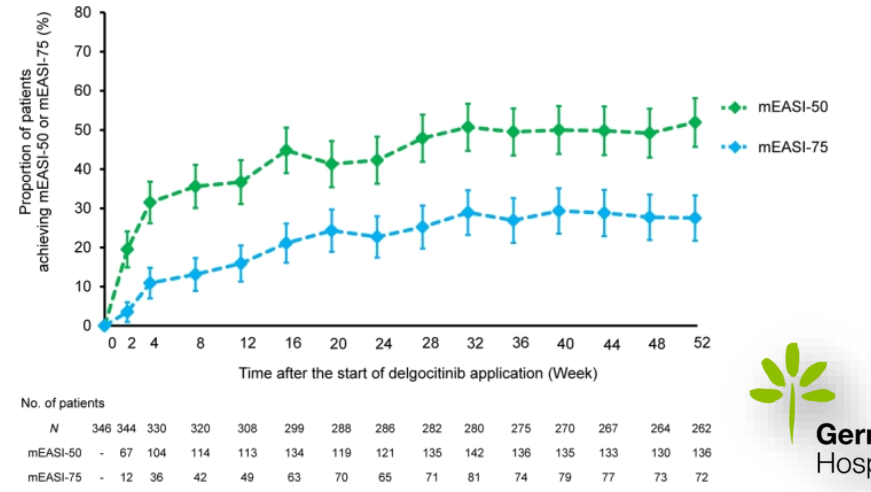
American Journal of Clinical Dermatology (2022) 23:595–603
https://doi.org/10.1007/s40257-022-00712-0

LEADING ARTICLE

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]





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MUCHAS GRACIAS