IV EDICIÓN

INMUNOTERAPIA EN DERMATOLOGÍA

MoAb/JAKinh en Dermatitis Atópica: Evidencia en RCT y RWE, aquí y ahora

Mónica Munera
Servei de Dermatologia
Hospital Universitari Germans Trias i Pujol

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

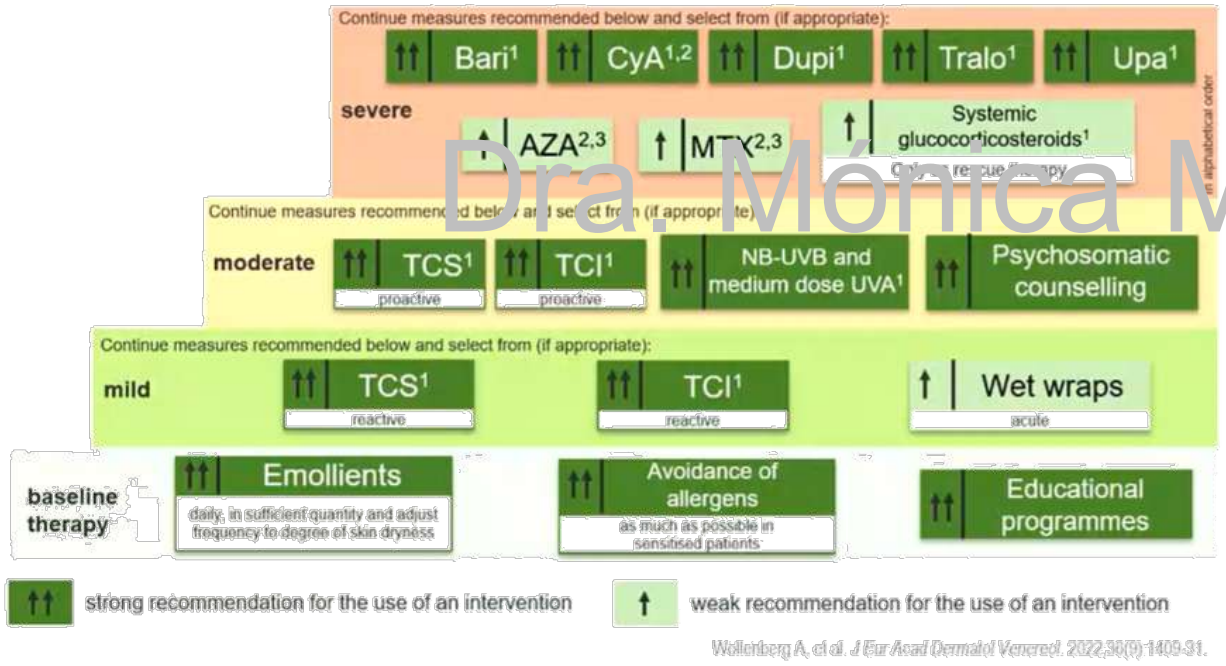
Escogiendo el camino hacia el tratamiento más óptimo

DOI: 10.1111/jdv.18345 JEADV

GUIDELINE

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

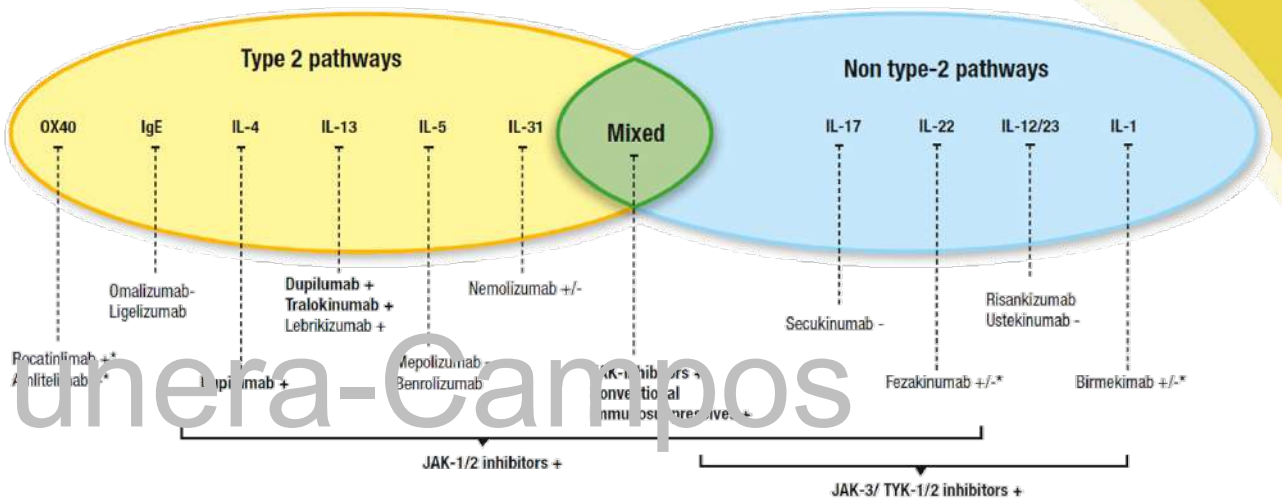
A. Wollenberg,[1,2,*] M. Kinberger,[3] B. Arents,[4] N. Aszodi,[1] G. Avila Valle,[3] S. Barbarot,[5] T. Bieber,[6] H.A. Brough,[7,8] P. Calzavara Pinton,[9] S. Christen-Zäch,[10] M. Deleuran,[11] M. Dittmann,[3] C. Dressler,[3] A.H. Fink-Wagner,[12] N. Fosse,[13] K. Gáspár,[14] L. Gerbens,[15] U. Gieler,[16] 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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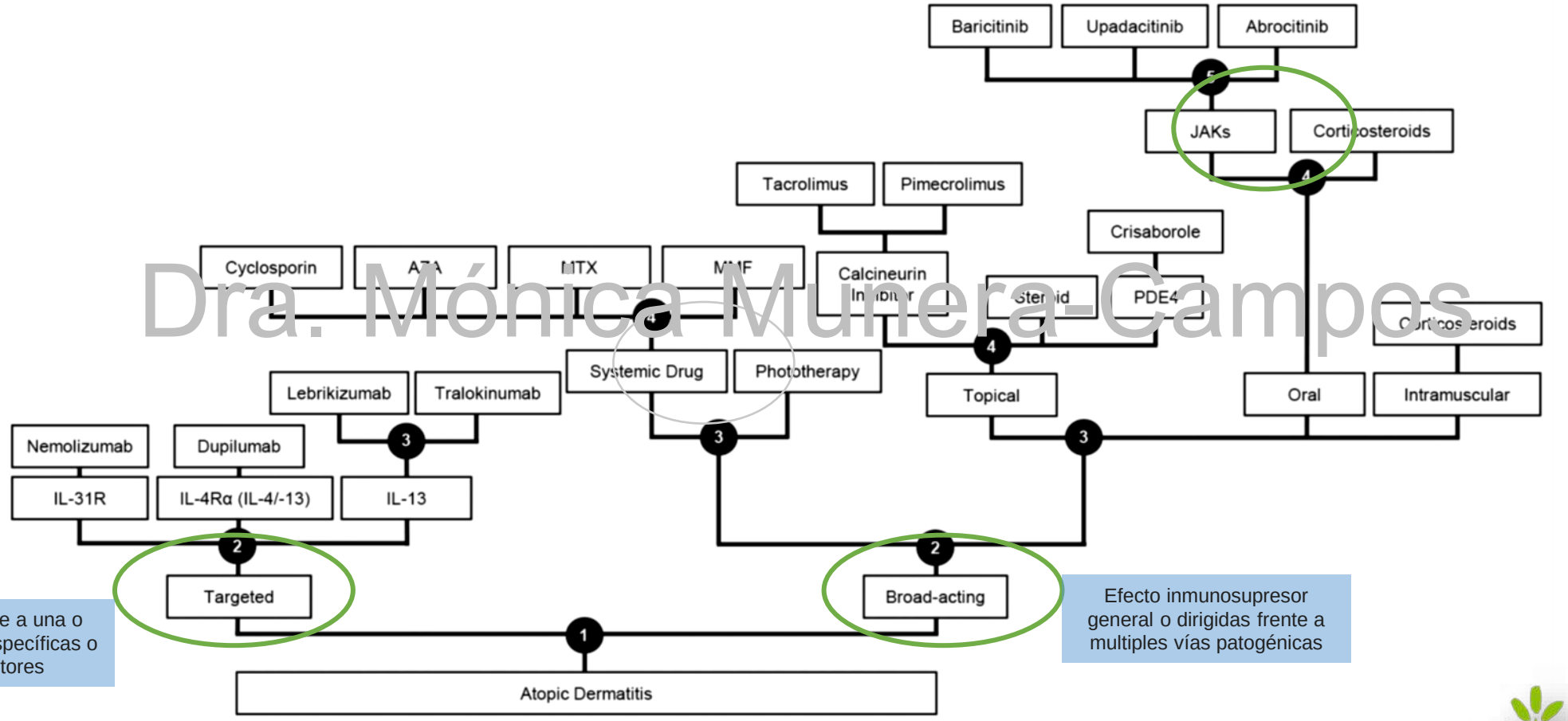
DOI: 10.1111/jdv.18225 JEADV
REVIEW ARTICLE

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]

Escogiendo el camino hacia el tratamiento más óptimo



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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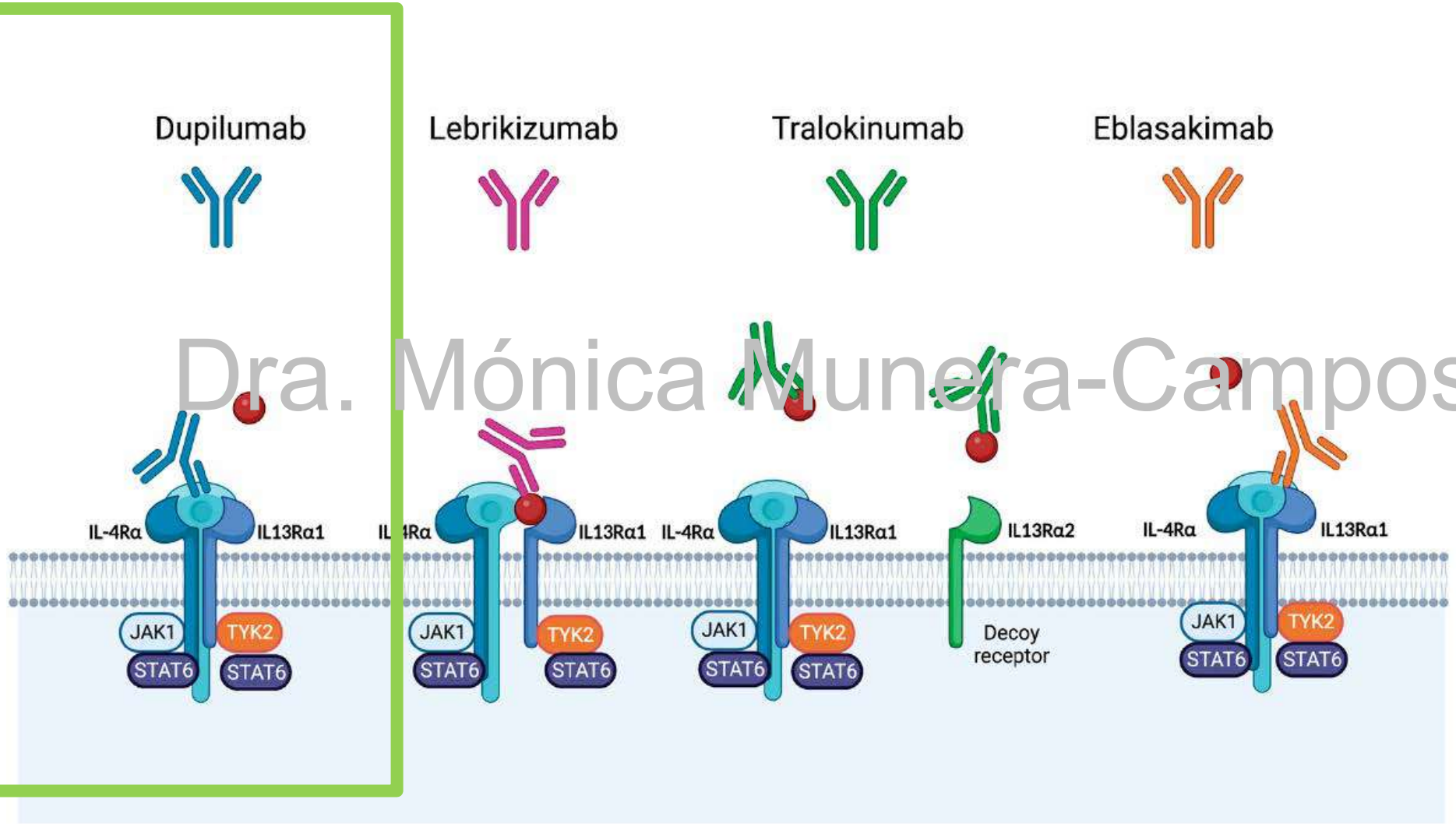
Anticuerpos monoclonales

Dra. Mónica Munera-Campos

Germans Trias i Pujol
Hospital

DUPILUMAB



DUPILUMAB: RCT

American Journal of Clinical Dermatology
https://doi.org/10.1007/s40257-018-0370-9

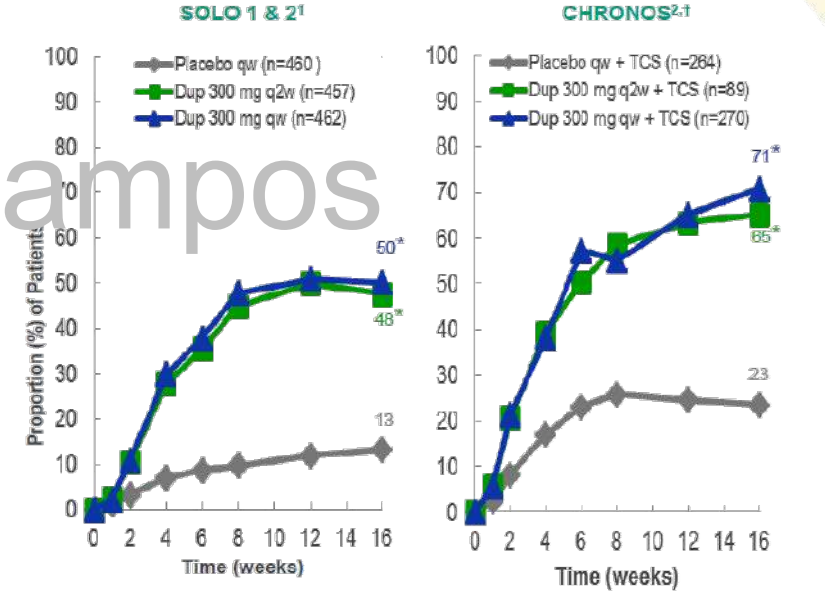
ADIS DRUG EVALUATION

Dupilumab: A Review in Moderate-to-Severe Atopic Dermatitis

James E. Frampton[1] · Hannah A. Blair[1]

Regimen (no. of pts[b])	Week	Responder rates (% pts)						
		IGA[c]	EASI 50	EASI 75	EASI 90	PNRS[d]	DLQI[d]	POEM[d]
SOLO 1 [26]								
DUP (224)	16	38*[e]	69*	51*[f]	36*	41*	64*[e]	68*[e]
PL (224)	16	10[e]	25	15[f]	8	12	31	27
SOLO 2 [26]								
DUP (233)	16	36*[e]	65	44*[f]	30*	6*	73*[e]	72*[e]
PL (236)	16	8[e]	22	12[f]	7	0	28	24
CAFÉ [28]								
DUP+TCS (107)	16	40.2*	85.0*[h,i]	62.6*[e]	45.8*[h,i]	45.7*	87.6*[e,g]	84.0*[e,g]
PL+TCS (108)	16	13.9	43.5[h]	29.6[e]	12.0[h]	14.3	44.2[g]	42.1[g]
CHRONOS [27][g]								
DUP+TCS (106)	16	39**[e]	80**[h,i]	69**[e]	40**[h,i]	59**	81**[e,g]	77**[e,g]
PL+TCS (315)	16	12[e]	37[h]	23[e]	11[h]	20	43[g]	37[g]
DUP+TCS (106)	52	36**	79**[h,i]	65**	51**[h,i]	51**	80**[e,g]	76**[e,g]
PL+TCS (315)	52	13	30[h]	22	16[h]	13	30[g]	26[g]

Patients Achieving EASI-75 Through Week 16



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DUPILUMAB: RCT$_{+TCS, 52W}$

American Journal of Clinical Dermatology
https://doi.org/10.1007/s40257-018-0370-9

ADIS DRUG EVALUATION

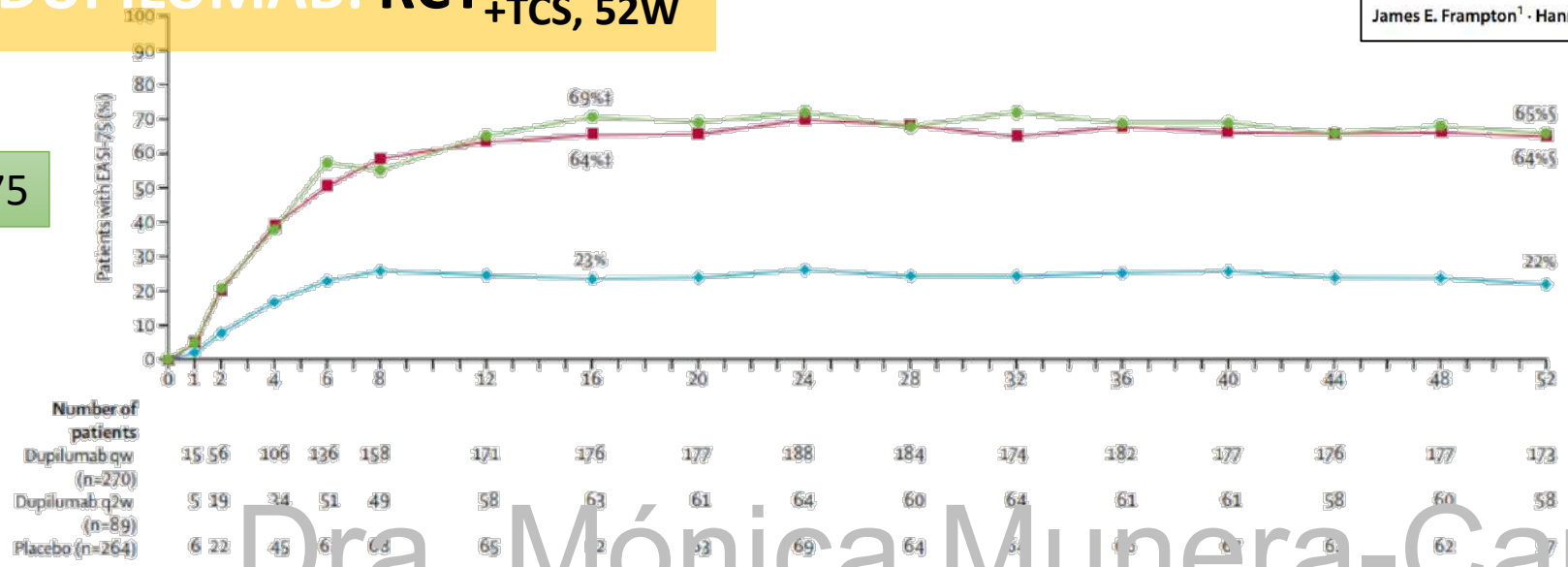
Dupilumab: A Review in Moderate-to-Severe Atopic Dermatitis

James E. Frampton[1] · Hannah A. Blair[1]

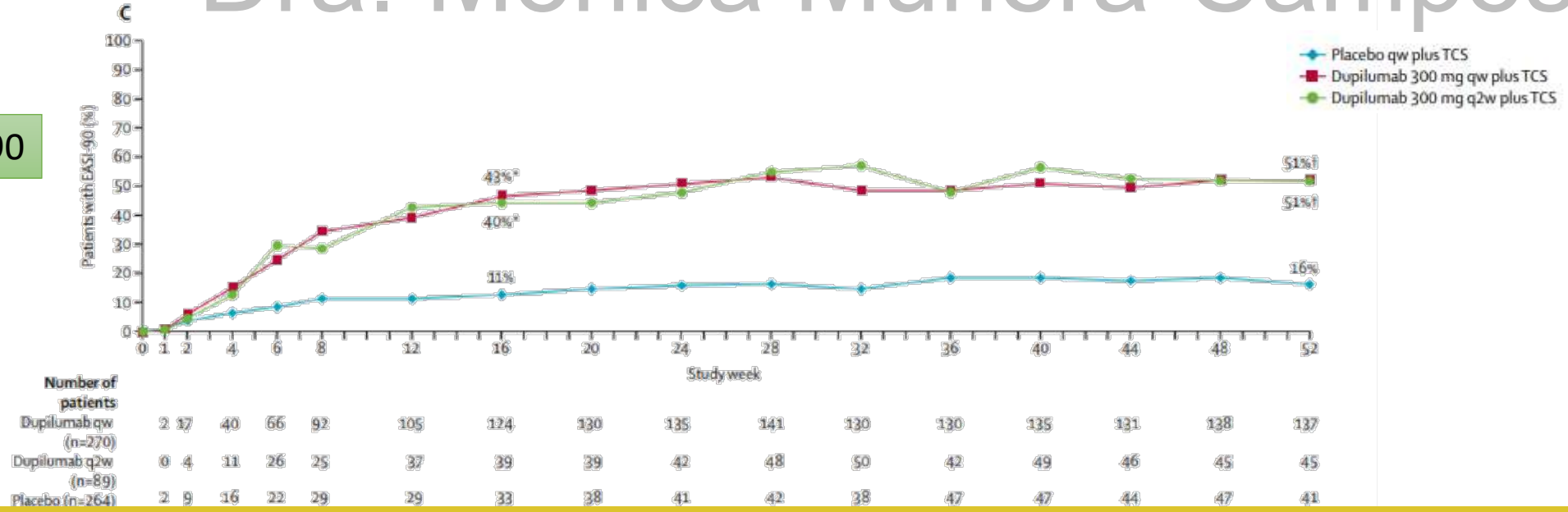
Long-term management of moderate-to-severe atopic dermatitis with dupilumab and concomitant topical corticosteroids (LIBERTY AD CHRONOS): a 1-year, randomised, double-blinded, placebo-controlled, phase 3 trial

Andrew Blauvelt, Marjolein de Bruin-Weller, Melinda Gooderham, Jennifer C Cather, Jamie Weisman, David Pariser, Eric L Simpson, Kim A Papp, H Chih-Ho Hong, Diana Rubel, Peter Foley, Errol Prens, Christopher E M Griffiths, Takafumi Etoh, Pedro Herranz Pinto, Ramon M Pujol, Jacek C Szepietowski, Karel Ettler, Lajos Kemény, Xiaoping Zhu, Bolanle Akinlade, Thomas Hultsch, Vera Mastey, Abhijit Gadkari, Laurent Eckert, Nikhil Amin, Neil M H Graham, Gianluca Pirozzi, Neil Stahl, George D Yancopoulos, Brad Shumel

EASI75



EASI90



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DUPILUMAB: RCT SEGURIDAD-LARGO PLAZO

- Of 2677 patients enrolled and treated, 352 (13.1%) completed week 204 (end of efficacy assessments) and 202 (7.5%) completed safety follow-up through week 244.

American Journal of Clinical Dermatology (2022) 23:393–408
https://doi.org/10.1007/s40257-022-00685-0

ORIGINAL RESEARCH ARTICLE

Dupilumab Provides Acceptable Safety and Sustained Efficacy for up to 4 Years in an Open-Label Study of Adults with Moderate-to-Severe Atopic Dermatitis

Lisa A. Beck[1] · Mette Deleuran[2] · Robert Bissonnette[4] · Marjolein de Bruin-Weller[4] · Ryszard Galus[5] · Takeshi Nakahara[6] · Seong Jun Seo[7] · Faisal A. Khokhar[8] · Jignesh Vakil[9] · Jing Xiao[8] · Ainara Rodriguez Marco[10] · Noah A. Levit[8] · John T. O'Malley[11] · Arsalan Shabbir[8]

Accepted: 10 March 2022 / Published online: 3 May 2022

Table 4. Analysis of most common TEAEs

TEAEs reported in ≥ 5% of patients by PT	OLE Dupilumab 300 mg qw (N = 2677)		CHRONOS Week 52, final data set: Placebo + TCS (N = 315)		CHRONOS Week 52, final data set: Dupilumab 300 mg qw + TCS (N = 315)	
	Patients ≥ 1 event, n (%)	nP/100PY	Patients ≥ 1 event, n (%)	nP/100PY	Patients ≥ 1 event, n (%)	nP/100PY
Nasopharyngitis	773 (28.9)	17.95	62 (19.7)	24.9	62 (19.7)	24.2
Conjunctivitis[a]	536 (20.0)	11.4	25 (7.9)	9.24	61 (19.4)	23.37
Atopic dermatitis	444 (16.6)	8.95	147 (46.7)	74.32	55 (17.5)	20.7
Upper respiratory tract infection	362 (13.5)	7.15	32 (10.2)	12.0	43 (13.7)	15.8
Headache	218 (8.1)	4.14	19 (6.0)	7.0	25 (7.9)	9.0
Oral herpes	199 (7.4)	3.77	9 (2.9)	3.2	15 (4.8)	5.2
Injection site reaction	138 (5.2)	2.54	25 (7.9)	9.4	61 (19.4)	24.5

[a]Includes the following PTs: conjunctivitis, conjunctivitis allergic, conjunctivitis bacterial, conjunctivitis viral and atopic keratoconjunctivitis.
MedDRA, Medical Dictionary for Regulatory Activities; PT, MedDRA Preferred Term.

Table 5. Assessment of conjunctivitis

Assessment of conjunctivitis[a]	OLE Dupilumab 300 mg qw (N = 2677)		CHRONOS Week 52, final data set: Placebo + TCS (N = 315)		CHRONOS Week 52, final data set: Dupilumab 300 mg qw + TCS (N = 315)	
Number of events	888		29		91	
Not recovered/not resolved	83 (9.3)		1 (3.4)		7 (7.7)	
Recovered/resolved	775 (87.3)		27 (93)		81 (89)	
Recovered/resolved with sequelae	10 (1.1)		0		1 (1.1)	
Recovering/resolving	18 (2.0)		1 (3.4)		2 (2.2)	
	n (%)	nP/100PY	n (%)	nP/100PY	n (%)	nP/100PY
Number of patients with ≥ 1 event of conjunctivitis	536 (20)	11.4	25 (7.9)	9.2	61 (19.4)	22.6
Related to study drug	258 (9.6)	4.9	5 (1.6)	1.8	15 (4.8)	5.2
Mild	248 (9.3)	4.7	15 (4.8)	5.4	31 (9.8)	11.0
Moderate	262 (9.8)	5.0	9 (2.9)	3.2	28 (8.9)	10.0
Severe	26 (1.0)	0.5	1 (0.3)	0.4	2 (0.6)	0.7
Resulting in permanent discontinuation of study drug	14 (0.5)	0.2	0	0	0	0

[a]Includes the following PTs: conjunctivitis, conjunctivitis allergic, conjunctivitis bacterial, conjunctivitis viral, and atopic keratoconjunctivitis.

20% (11,4nP-100P-Y)
85%leve-moderada
0,5% discontinuación

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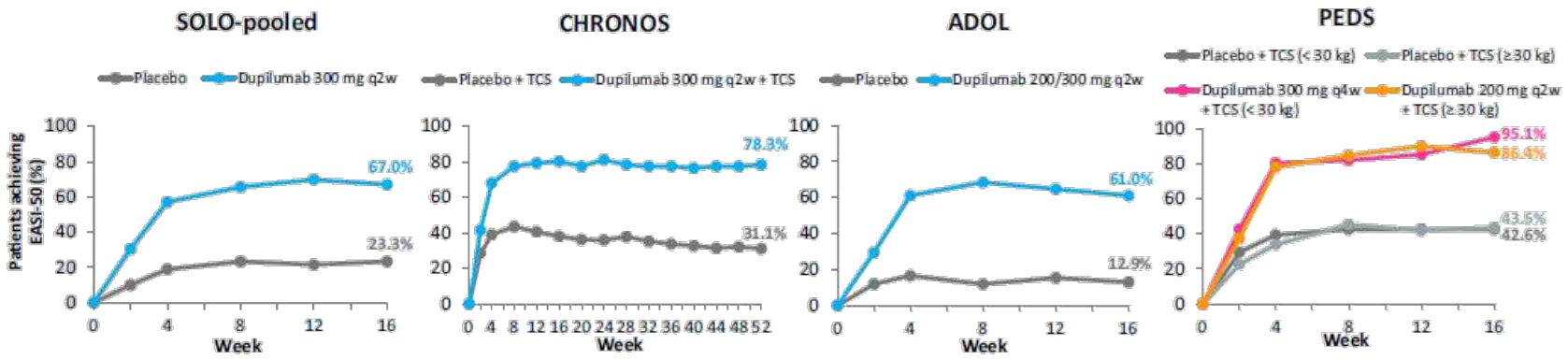

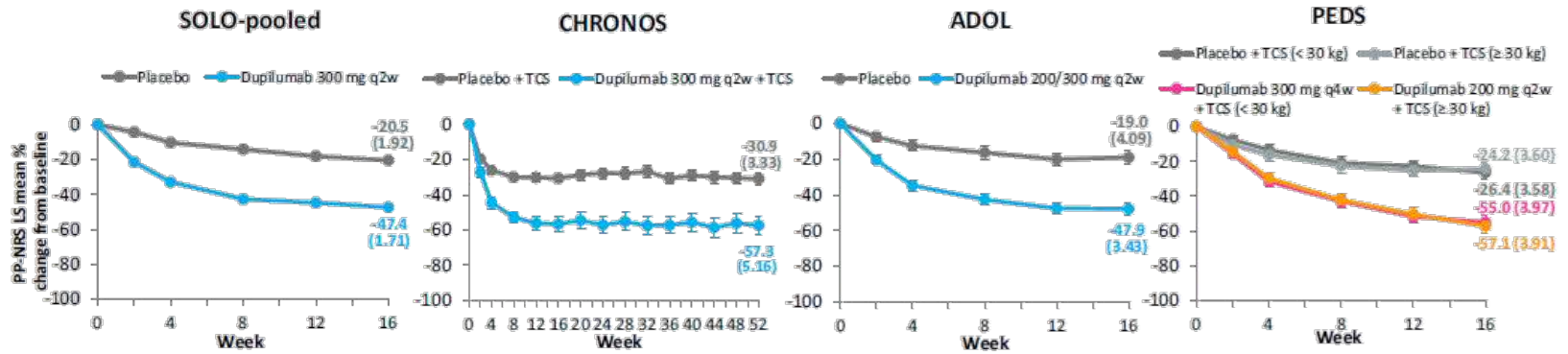

https://doi.org/10.1007/s13555-022-00778-y
REVIEW

A Review of Phase 3 Trials of Dupilumab for the Treatment of Atopic Dermatitis in Adults, Adolescents, and Children Aged 6 and Up

Jennifer Cather · Melodie Young · Douglas C. DiRuggiero · Susan Tofte · Linda Williams · Tayler Gonzalez

demonstrate that dupilumab provides rapid improvements (in as little as 1 week) and sustained efficacy (up to 4 years) when used as a treatment for moderate-to-severe AD. Dupilumab not only improves skin signs and symptoms, but also provides multiple health benefits beyond the skin, including improvements in quality of life, itch, sleep disturbances, and pain/discomfort. Dupilumab is generally well tolerated, has a favorable safety profile in adults, adolescents, and children, has no serious drug–drug interactions, does not require routine laboratory testing, and is not an immunosuppressant. Taken together, phase 3 trials demonstrate that dupilumab provides rapid and sustained efficacy and is generally well tolerated for the treatment of moderate-to-severe AD across age groups.

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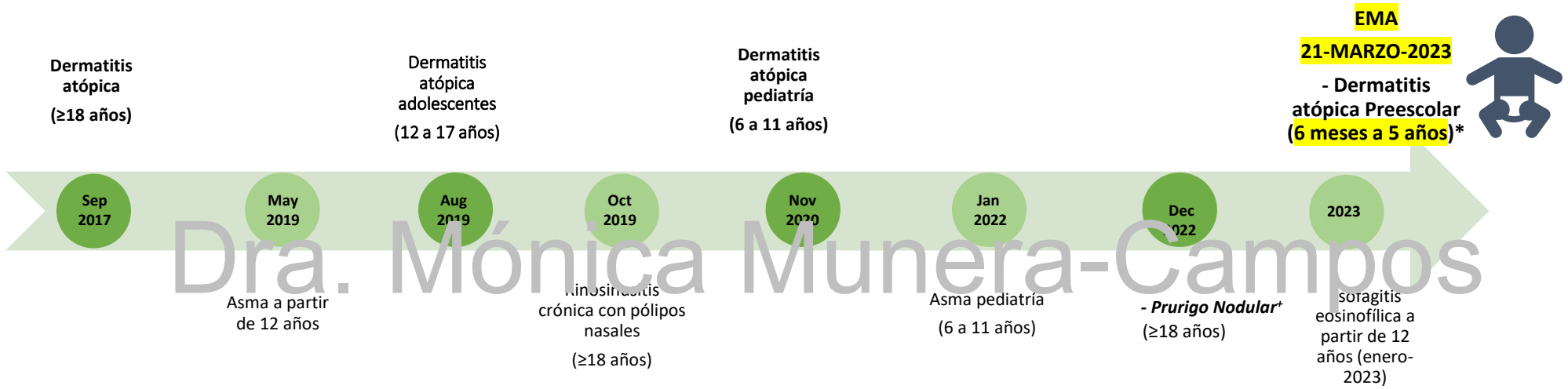
DUPILUMAB

Press Release: Dupixent® (dupilumab) approved by European Commission as first and only targeted medicine for children as young as six months old with severe atopic dermatitis

Dupilumab: Aprobaciones por la Agencia Europea del Medicamento (EMA)



Indicaciones en proceso de aprobación:

- **Urticaria crónica espontánea:** aceptado para revisión por la FDA (adultos y adolescentes) el 07-MARZO-2023
- **Esofagitis eosinofílica de 1 a 11 años (aprobado en >12 años)**

Estudios en marcha:

- **Prurito de origen desconocido:** NCT05263206
- **Eccema crónico** de manos (vesicular recurrente o fisurado crónico) refractario/no tolerancia a alitretinoína: NCT04512339
- **Urticaria inducible por frío:** NCT04681729

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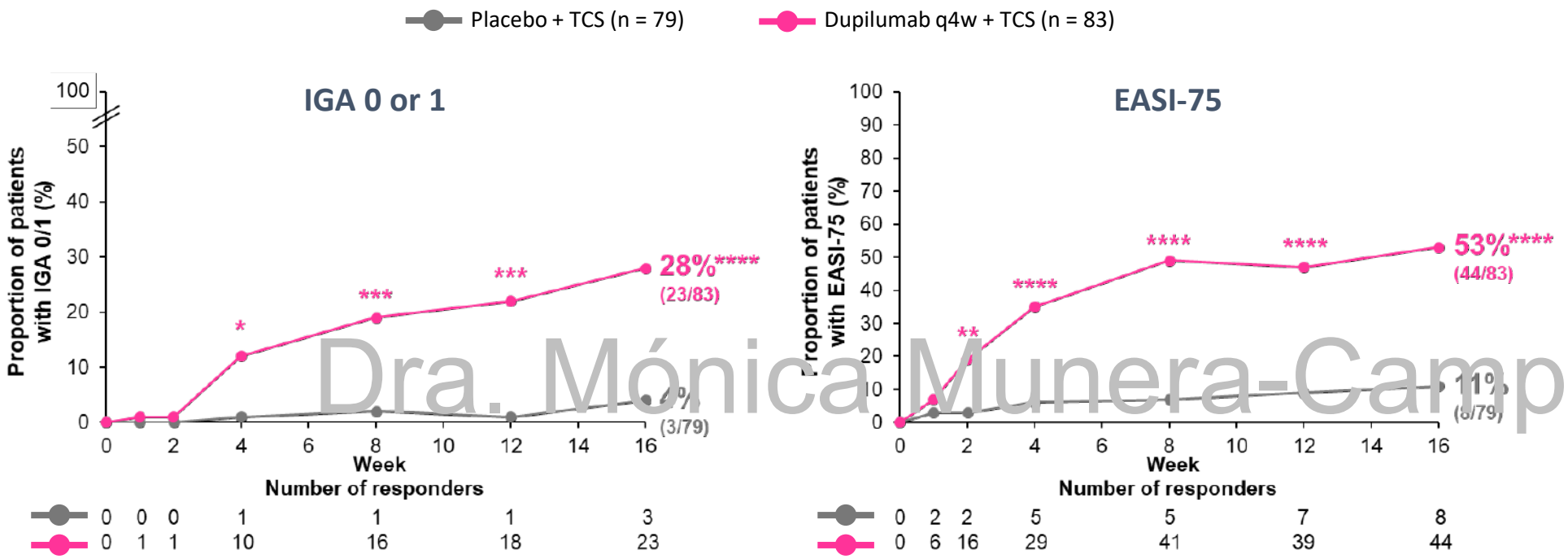
DUPILUMAB: RCT PEDIATRÍA



*$P < 0.05$; **$P < 0.01$; ***$P < 0.001$; ****$P < 0.0001$ vs placebo. *P*-values are nominal at all time points except Week 16.
Values after first rescue treatment use were set to missing. Patients with missing values at Week 16 due to rescue treatment, withdrawn consent, adverse event, and lack of efficacy were considered as non-responders. Patients with missing values due to other reasons including COVID-19 were imputed by multiple imputation (MI).

≥6 meses

Paller AS et al. Dupilumab in children aged 6 months to younger than 6 years with uncontrolled atopic dermatitis: a randomised, double-blind, placebo-controlled, phase 3 trial. Lancet. 2022 Sep 17;400:908-919. doi: 10.1016/S0140-6736(22)01539-2. PMID: 36116481.

DUPILUMAB: RCT PEDIATRÍA

*Conjuntivitis: 5 pacientes (2,8%) (nP/100P-Y: 3,71)

	Total Patients (N = 180)
Patient who completed up to	
Week 16	122 (67.8%)
Week 24	74 (41.1%)
Week 26	68 (37.8%)
Week 52	30 (16.7%)
Week 78	30 (16.7%)
Week 104	29 (16.1%)
Week 156	15 (8.3%)
Patients ongoing	167 (92.8%)

AAD annual MEETING
MARCH 17–21, 2023 | NEW ORLEANS, LA

	AD-1434 (N = 180)		AD-1539B Placebo+TCS (N = 78)		AD-1539B Dupi 200/300 Q4W+TCS (N = 83)	
Patients with any TEAE	109 (60.6%)		58 (74.4%)		53 (63.9%)	
Patients with any drug related TEAE	15 (8.3%)		5 (6.4%)		9 (10.8%)	
Patients with any TEAE leading to Permanent Study Drug Discontinuation	1 (0.6%)[a]		1 (1.3%)		1 (1.2%)	
Patients with any TEAE with Maximum Intensity						
Mild	50 (27.8%)		22 (28.2%)		30 (36.1%)	
Moderate	56 (31.1%)		26 (33.3%)		21 (25.3%)	
Severe	3 (1.7%)		10 (12.8%)		2 (2.4%)	
Patients with TEAE resulting in Death	0		0		0	
Patients with any Serious TEAE	2 (1.1%) [b]		4 (5.1%)		0	
PT > 5% [c]	**N**	**nP/PY (nP/100 PY)**	**N**	**nP/PY (nP/100 PY)**	**N**	**nP/PY (nP/100 PY)**
Nasopharyngitis	23 (12.8%)	23/109.0 (21.09)	7 (9.0%)	7/23.3 (29.99)	7 (8.4%)	7/25.3 (27.67)
Upper respiratory tract infection	21 (11.7%)	21/116.5 (18.02)	7 (9.0%)	7/23.6 (29.72)	5 (6.0%)	5/25.6 (19.49)
Cough	15 (8.3%)	15/122.9 (12.21)	5 (6.4%)	5/23.5 (21.31)	0	0/26.6
Rhinorrhoea	11 (6.1%)	11/129.3 (8.51)	1 (1.3%)	1/24.3 (4.11)	4 (4.8%)	4/26.0 (15.36)
Urticaria [a]	13 (7.2%)	13/124.7 (10.42)	4 (5.1%)	4/24.2 (16.50)	1 (1.2%)	1/26.2 (3.81)
Dermatitis atopic	12 (6.7%)	12/119.8 (10.02)	25 (32.1%)	25/19.3 (129.69)	12 (14.5%)	12/24.1 (49.69)
Pyrexia	21 (11.7%)	21/111.0 (18.91)	7 (9.0%)	7/23.4 (29.96)	1 (1.2%)	1/26.3 (3.80)
Food allergy	9 (5.0%)	9/128.5 (7.00)	0	0/24.6	1 (1.2%)	1/26.3 (3.80)

≥6 meses

Treatment-Emergent Adverse Events in Patients Aged 6 Months to 5 Years With Moderate-to-Severe Atopic Dermatitis Treated With Dupilumab in an Open-Label Extension Clinical Trial

DUPILUMAB: RWE ADULTOS

A Literature Review of Real-World Effectiveness and Safety of Dupilumab for Atopic Dermatitis

Masahiro Kamata[1] and Yayoi Tada[1]

Table 1. Real-World Evidence of the Effectiveness and Safety of Dupilumab Treatment for AD

Publication	Country	Time (wk)	Number of Patients	EASI-75, %	Other Outcomes
Ariëns et al. (2020)	The Netherlands	16	138	62	The most frequently reported side effect was conjunctivitis, occurring in 47 patients (34%).
Ariëns et al. (2021)	The Netherlands	52	210	70.3	The most frequently reported adverse effect was conjunctivitis (34%).
Armario-Hita et al. (2019)	Spain	24	70	ND	EASI decreased to 6.5 (79.3% reduction), SCORAD diminished to 15 (69.3% reduction), and pruritus VAS decreased to 2.4 (69.9% reduction). The safety profile was favorable, with six reported cases of mild conjunctivitis.
Faiz et al. (2019)	France	3.8 mo (median)	241	48.8	Conjunctivitis was reported in 84 (38.2%) of 241 patients.
Fargnoli et al. (2019)	Italy	[illegible]	109	60.[illegible]	Adverse events were experienced by 19.[illegible] (21/109) of the patients and they were all mild in intensity, conjunctivitis being the most common side effect.
Fargnoli et al. (2020)	Italy	48	[illegible]	[illegible].9	Conjunctivitis was diagnosed in 20.5% (21/102) at wk 24 and 8.1% (8/98) at wk 48, suggesting remission in most cases.
Ferrucci et al. (2020)	Italy	16	117	72.7	The majority of adverse events were mild in severity and included blepharoconjunctivitis (n = 14; 11.9%), facial redness (n = 6; 5.1%), and paradoxical psoriasis (n = 1; 0.8%).
Jang et al. (2020)	Korea	16	101	63.6	Adverse events from treatment included facial erythema (9.9%) and conjunctivitis (5.0%).
Jo et al. (2020b)	Canada	16	93	ND	A total of 51 (55%) patients reached IGA of 0/1, and 38 (41%) experienced ≥1 adverse events.
Jo et al. (2020a)	Canada	52	52	ND	IGA 0/1 was achieved by 28 (54%) of 52 patients at wk 52, similar to the proportion of patients achieving IGA 0/1 at wk 16 (30/48, 63%). Conjunctivitis (n = 4, 8%) was the most commonly reported adverse event.
Kim et al. (2020)	Canada	ND	34	ND	Of 34 patients, 33 showed some clinical improvement on initiating dupilumab. The most frequently reported adverse events were nasopharyngitis (n = 4, 11.8%) and conjunctivitis (n = 4, 11.8%).
Kreeshan et al. (2021)	United Kingdom	30	164	75.31	The most common side effects were eye symptoms, occurring in 43.1% of patients, with 16.3% developing conjunctivitis.
Matsutani et al. (2020)	Japan	16	53	ND	EASI score, DLQI, and POEM decreased by 73.1%, 73.6%, and 72.1%, respectively. Conjunctivitis was the most common side effect (15/53 patients, 28%).

Posibles predictores de respuesta

- **No parece haber diferencias en el fenotipo ni en las distintas localizaciones afectadas**, aunque la respuesta podría ser más lenta en las formas tipo prurigo nodular y eccema numular.
- Los pacientes con otras comorbilidades T2 presentan un inicio de respuesta más lento, pero más sostenido en el largo plazo.
- **La obesidad podría asociarse a una menor probabilidad de respuesta**
- Los niveles elevados de LDH podrían predecir una peor respuesta

Journal of Clinical Medicine
MDPI
Brief Report

Blood Cells Count Derived Inflammation Indexes as Predictors of Early Treatment Response to Dupilumab in Patients with Moderate-to-Severe Atopic Dermatitis

Angelo Zinellu [1], Federica Sucato [2], Viviana Piras [3], Gian Mario Addis [4], Gabriele Biondi [2], Maria Antonia Montesu [2], Arduino A. Mangoni [5,6], Ciriaco Carru [1], Pietro Pirina [2], Panagiotis Paliogiannis [2], Alessandro G. Fois [2,*] and Rosanna Satta [2]

Germans Trias i Pujol Hospital

Original Article

Dupilumab Improves Clinical Scores in Children and Adolescents With Moderate to Severe Atopic Dermatitis: A Real-World, Single-Center Study

Angel D. Pagan, BS[a], Eden David, BA[a], Benjamin Ungar, MD[a], Sabrina Ghalili, BS[a], Helen He, MD[a], and Emma Guttman-Yassky, MD, PhD[a] *New York, NY*

Pediatric Drugs (2022) 24:671–678
https://doi.org/10.1007/s40272-022-00531-0

ORIGINAL RESEARCH ARTICLE

Dupilumab Treatment in Children Aged 6–11 Years With Atopic Dermatitis: A Multicentre, Real-Life Study

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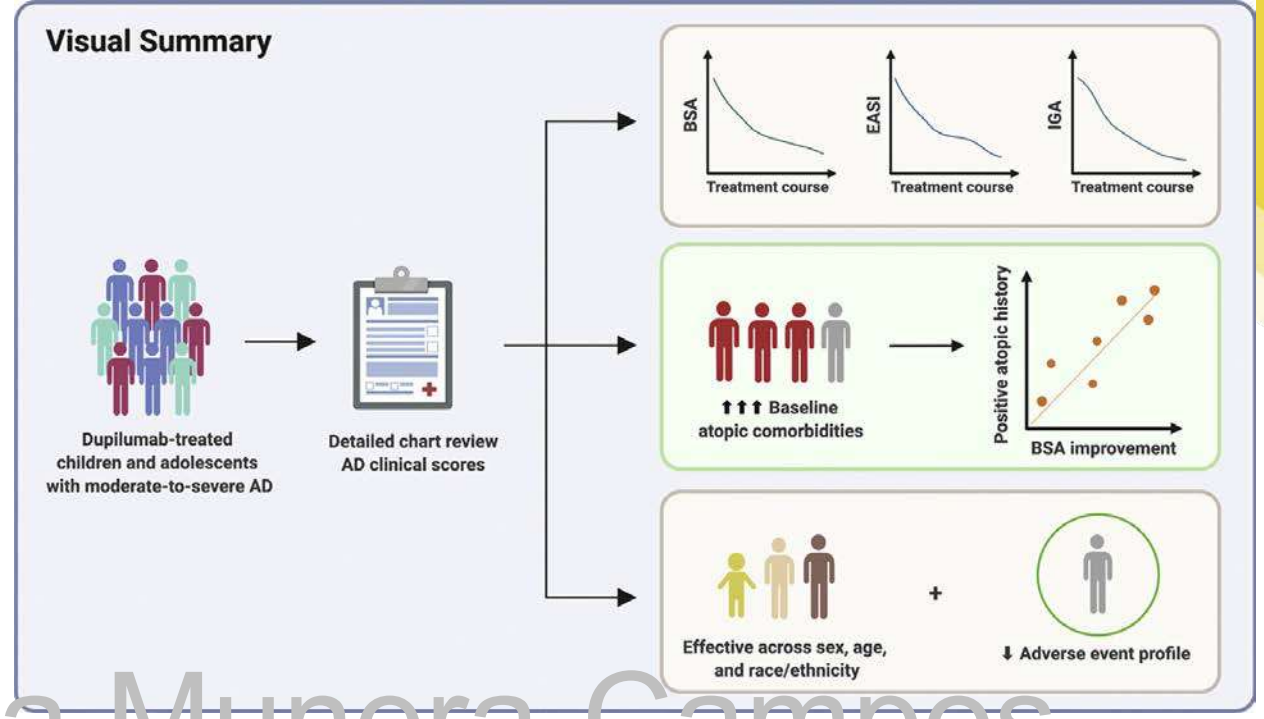

	N	Edad (años)	Tiempo de tratamiento	Reducción media EASI (%)	Respuesta EASI75	Conjuntivitis	Eritema facial	Reacción punto de inyección
Treister AD, et al. (2018)[1]	6	7-15	34W	ND Red. media BSA: 45%	ND	No	No	No
Mareschal A, et al. (2020)[2]	4	16-17	52W	ND Red. 84%	ND	7,5% (3)	No	No
Igelman S, et al. (2020)[3]	11	3-18	36W	ND	ND *Red IGA ≥2p en W16	9% (10)	5,4%	2,7% (3)
Hansel K, et al.[4]	9	14-17	32W	84,7%	1100%	11% (1)	No	No
Chia SY, et al. (2021)[5]	12	6-18	16W	59,9%	68%	8% (2)	0,5% (1)	No
Stingeni L, et al. (2021)[6]	19	12-17	16W	ND	78,9%	0,5% (1)	No	No
Napolitano M, et al. (2022)	55	6-11	16W	77,58%	74m54%	5,45% (3)	0	5,25%
Pagan AD[7]	89	<18	52W	ND	100%	5,6%	No	No *Dolor articular (2,2%)

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JAMA Dermatology | Original Investigation

Dupilumab Drug Survival and Associated Predictors in Patients With Moderate to Severe Atopic Dermatitis

Long-term Results From the Daily Practice BioDay Registry

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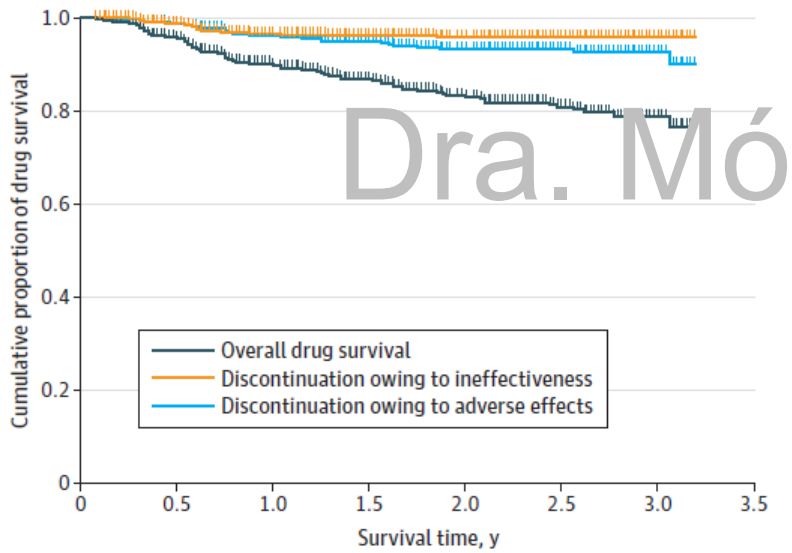
- 715 adultos con DA
- Media [SD] edad: 41.8 [16.0] años
- Hombres: 418 [58.5%]

Supervivencia global de dupilumab:

- 1 año: 90.3%
- 2 años: 85.9%
- 3 años: 78.6%

Figure 1. Dupilumab Drug Survival and Split for Reasons for Discontinuation



Predictores de discontinuación por falta de eficacia

- Uso de tratamiento inmunosupresor al inicio de dupilumab (HR: 2.64; 95% CI, 1.10-6.37)
- Falta de respuesta en W4 (HR: 8.68; 95% CI, 2.97-25.35)

Predictores de discontinuación por efectos adversos

- Uso de tratamiento inmunosupresor al inicio de dupilumab (HR: 2.69; 95% CI, 1.32-5.48)
- Edad ≥65 años (HR, 2.94; 95% CI, 1.10-7.87)
- IGA muy grave (HR, 3.51; 95%CI, 1.20-10.28)

Adverse effects as reason for discontinuation		
Ocular-related complaints	20 (2.8)	32 (17-41)
Conjunctivitis (DAOSD)	14 (2.0)	31 (18-41)
Uveitis	3 (0.4)	28 (4-97)
Limbitis (DAOSD)	2 (0.3)	39 (39-39)
Cornea perforation (DAOSD)	1 (0.1)	4 (4-4)
Skin-related complaints	10 (1.4)	63 (46-83)
Atypical lymphomatoid reaction	3 (0.4)	54 (27-85)
Worsening of MF[b]	1 (0.1)	60 (60-60)
Psoriasiform lesions	3 (0.4)	65 (16-83)
Rosacea	3 (0.4)	81 (46-91)

BioDay Eczema and Atopic Diseases Registry

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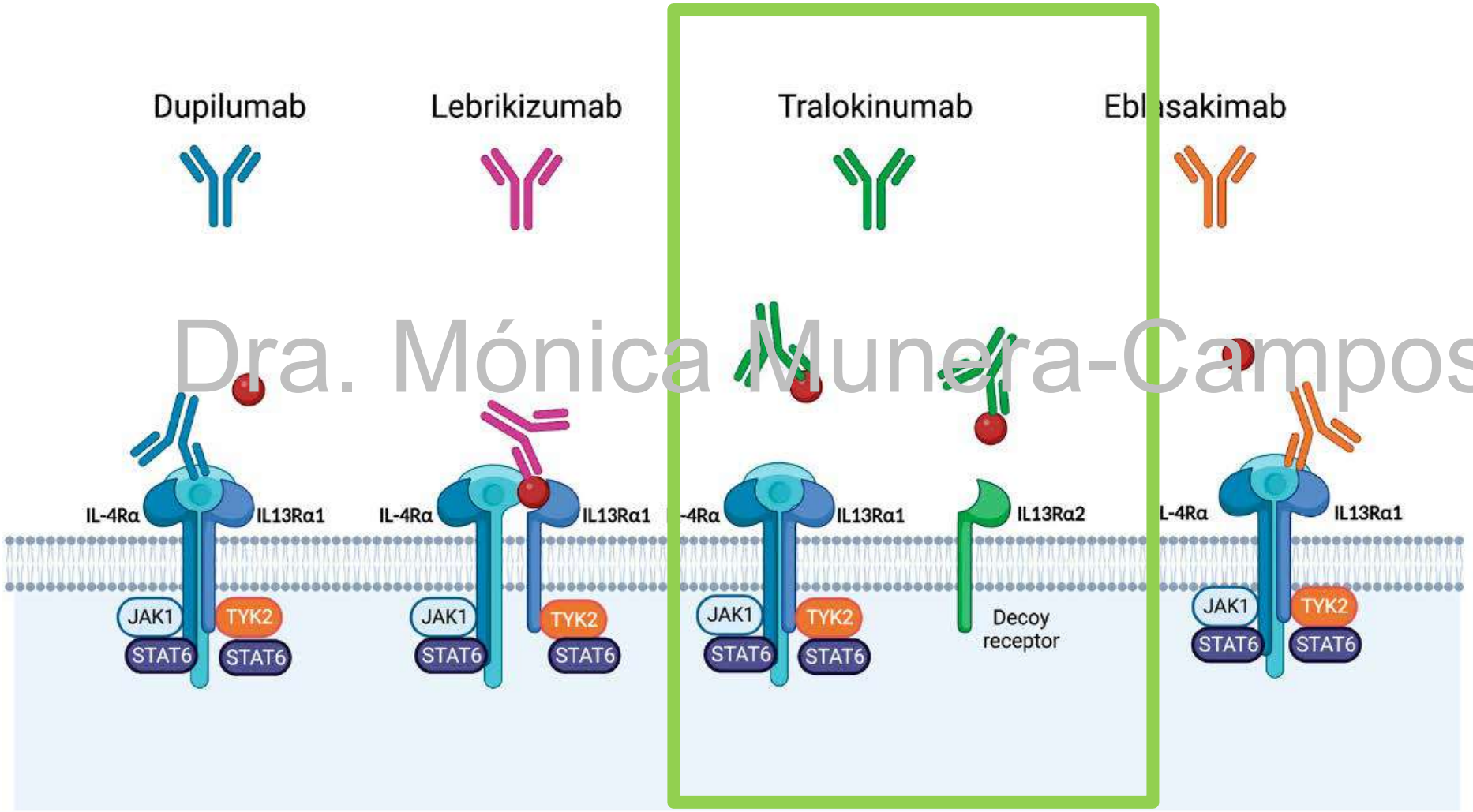
TRALOKINUMAB

pharmaceutics
MDPI
Review
Targeting Interleukin 13 for the Treatment of Atopic Dermatitis
Yuliya Lytvyn [1] and Melinda Gooderham [2,3,4,*]

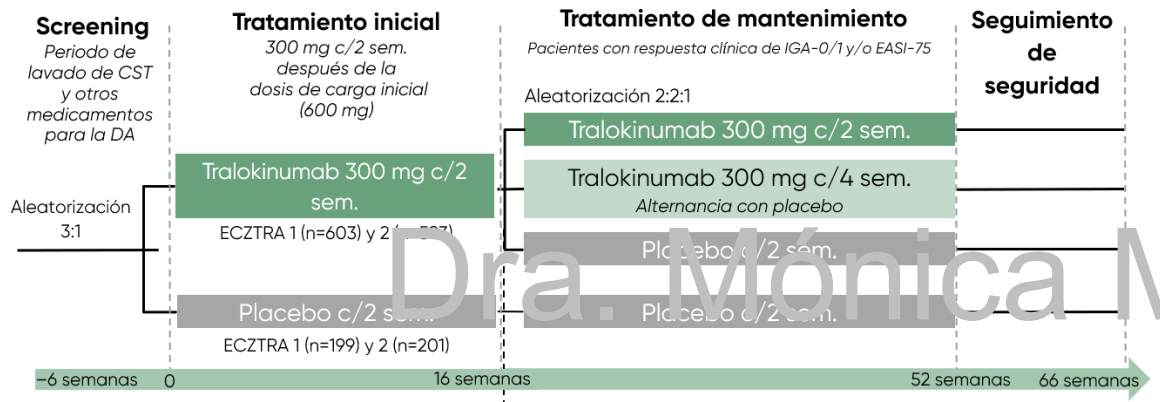


TRALOKINUMAB: RCT monoterapia

pharmaceutics
MDPI
Review
Targeting Interleukin 13 for the Treatment of Atopic Dermatitis
Yuliya Lytvyn [1] and Melinda Gooderham [2,3,4,*]

CLINICAL TRIAL
BJD British Journal of Dermatology
Tralokinumab for moderate-to-severe atopic dermatitis: results from two 52-week, randomized, double-blind, multicentre, placebo-controlled phase III trials (ECZTRA 1 and ECZTRA 2)*
A. Wollenberg, A. Blauvelt, E. Guttman-Yassky, M. Worm, C. Lynde, J.-P. Lacour, L. Spelman, N. Katoh, H. Saeki, Y. Poulin, A. Lesiak, L. Kircik, S.H. Cho, P. Herranz, M.J. Cork, K. Peris, L.A. Steffensen, B. Bang, A. Kuznetsova, T.N. Jensen, M.L. Ørsterdal, E.L. Simpson and on behalf of the ECZTRA 1 and ECZTRA 2 study investigators

Ensayos en monoterapia ECZTRA1 y ECZTRA2



Criterios de inclusión claves

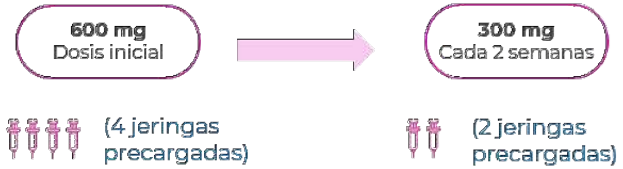
- Diagnóstico de DA de >1 año
- Afectación de BSA ≥10 %
- Puntuación de EASI ≥12 en el screening y 16 en el basal
- Puntuación de IGA ≥3 en la screening y en el basal
- Puntuación promedio del peor prurito diario en NRS ≥4 previo al basal

Tratamiento abierto (open-label)

Tralokinumab 300 mg c/2 sem.
CST opcional y uso óptimo en el domicilio

- Pacientes que no alcanzan IGA-0/1 ni EASI-75 en la semana 16
- Pacientes transferidos del tratamiento de mantenimiento

Clinical Trial	Eligibility (Sample Size)	Treatment Groups (Duration)	EASI	EASI 90	EASI 75	IGA 0 or 1
		Tralokinumab				
ECZTRA 1 (NCT03131648)	≥18 years BSA ≥ 10% (N = 802)	Tralokinumab 300 mg Q2W (16 weeks)	−15.5 ($p < 0.001$)	14.5% ($p < 0.001$)	25.0% ($p < 0.001$)	15.8% ($p = 0.002$)
		Placebo (16 weeks)	−9.0	4.1%	12.7%	7.1%
		Tralokinumab 300 mg Q2W (52 weeks)	N/A	N/A	59.6% ($p = 0.056$)	51.3% ($p = 0.68$)
		Tralokinumab 300 mg Q4W (52 weeks)	N/A	N/A	49.1% ($p = 0.27$)	38.95% ($p = 0.50$)
		Placebo (52 weeks)	N/A	N/A	33.3%	47.4%
ECZTRA 2 (NCT03160885)	≥18 years BSA ≥ 10% (N = 794)	Tralokinumab 300 mg Q2W (16 weeks)	−16.9 ($p < 0.001$)	18.3% ($p < 0.001$)	33.2% ($p < 0.001$)	22.2% ($p < 0.001$)
		Placebo (16 weeks)	−7.0	5.5%	11.4%	10.9%
		Tralokinumab 300 mg Q2W (52 weeks)	N/A	N/A	55.8% ($p < 0.001$)	59.3% ($p = 0.004$)
		Tralokinumab 300 mg Q4W (52 weeks)	N/A	N/A	51.4% ($p = 0.001$)	44.9% ($p = 0.084$)
		Placebo (52 weeks)	N/A	N/A	21.4%	25.0%



Tralo 300mg Q2W 16W

- IGA 0/1: 15,8% - 22,2%
- EASI75: 25% - 33,2%

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TRALOKINUMAB: RCT$_{+TCS}$

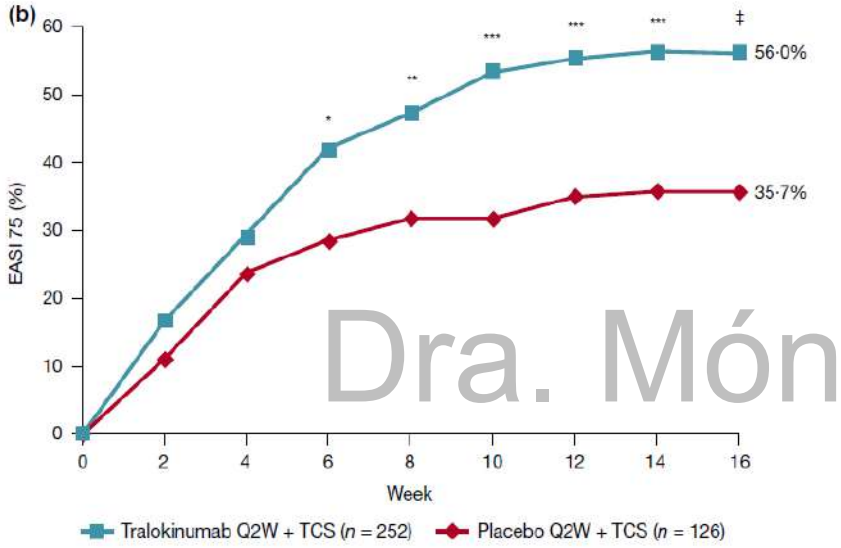
CLINICAL TRIAL
BJD British Journal of Dermatology

Tralokinumab plus topical corticosteroids for the treatment of moderate-to-severe atopic dermatitis: results from the double-blind, randomized, multicentre, placebo-controlled phase III ECZTRA 3 trial*

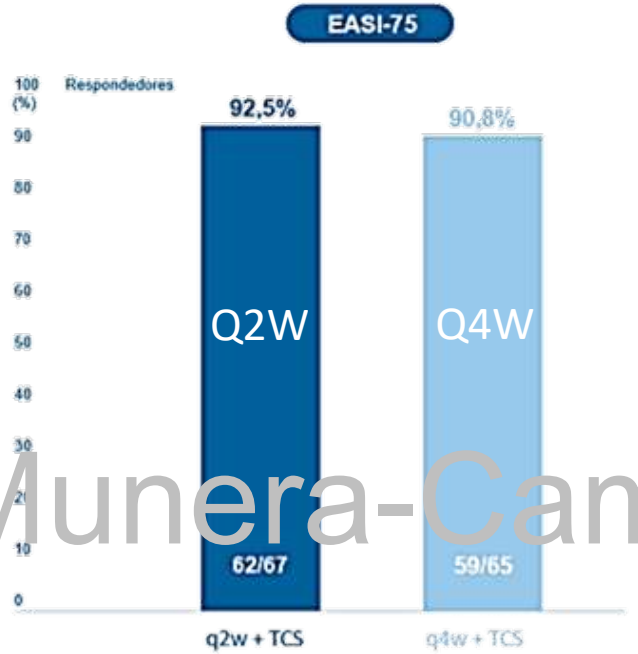
J.I. Silverberg,[1] D. Toth,[2] T. Bieber,[3] A.F. Alexis,[4] B.E. Elewski,[5] A.E. Pink,[6] D. Hijnen,[7] T.N. Jensen,[8] B. Bang,[8] C.K. Olsen,[8] A. Kurbasic,[8] S. Weidinger[9] and on behalf of the ECZTRA 3 study investigators

ECZTRA3

Tralo 300mg Q2W + TCS. Evaluación EASI75 W16



Tralo 300mg Q2W o Q4W + TCS . Evaluación EASI75 W32



Respuesta mantenida ECZTRA 3

9/10

Nueve de cada diez respondedores que alcanzaron EASI 75 a semana 16 mantuvieron esta respuesta a semana 32 en el brazo continuo de tralokinumab + TCS

Clinical Trial	Eligibility (Sample Size)	Treatment Groups (Duration)	EASI	EASI 90	EASI 75	IGA 0 or 1	NRS Change	DLQI Change
ECZTRA 3 (NCT03363854)	≥18 years BSA ≥ 10% (N = 380)	Tralokinumab 600 mg loading dose + 300 mg Q2W + TCS (16 weeks)	−21.0 ($p < 0.001$)	32.9% ($p = 0.022$)	56.0% ($p < 0.001$)	38.9% ($p = 0.015$)	−4.1 ($p < 0.001$)	−11.7 ($p < 0.001$)
		Placebo + TCS (16 weeks)	−15.6	21.4%	35.7%	26.2%	−2.9	−8.8
		Tralokinumab 600 mg loading dose + 300 mg Q2W + TCS (32 weeks)	N/A	N/A	92.5%	89.6%	N/A	N/A
		Tralokinumab 600 mg loading dose + 300 mg Q4W + TCS (32 weeks)	N/A	N/A	90.8%	77.6%	N/A	N/A

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

pharmaceutics
MDPI
Review
Targeting Interleukin 13 for the Treatment of Atopic Dermatitis
Yuliya Lytvyn [1] and Melinda Gooderham [2,3,4,*]

Ensayo ECZTEND: 3 años (Tralo 300mg Q2W)

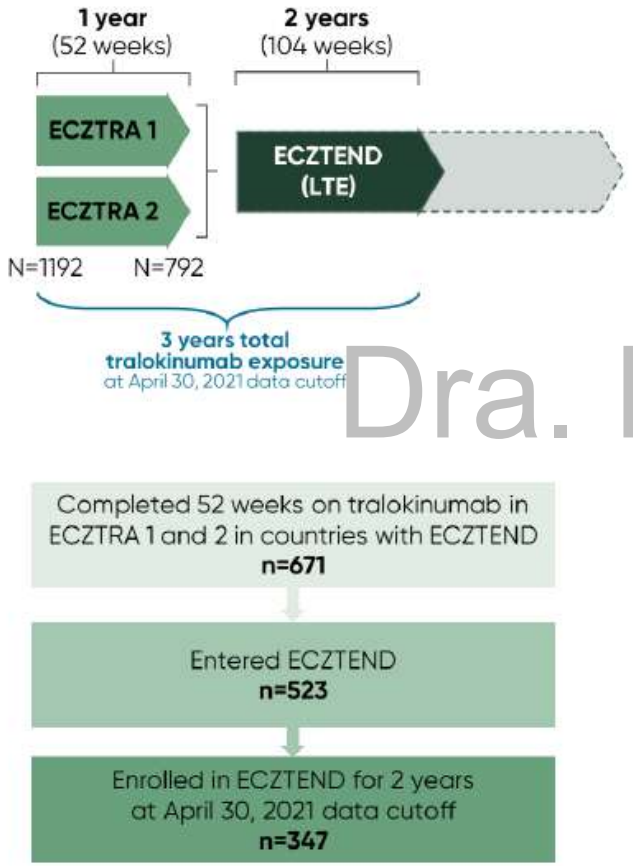
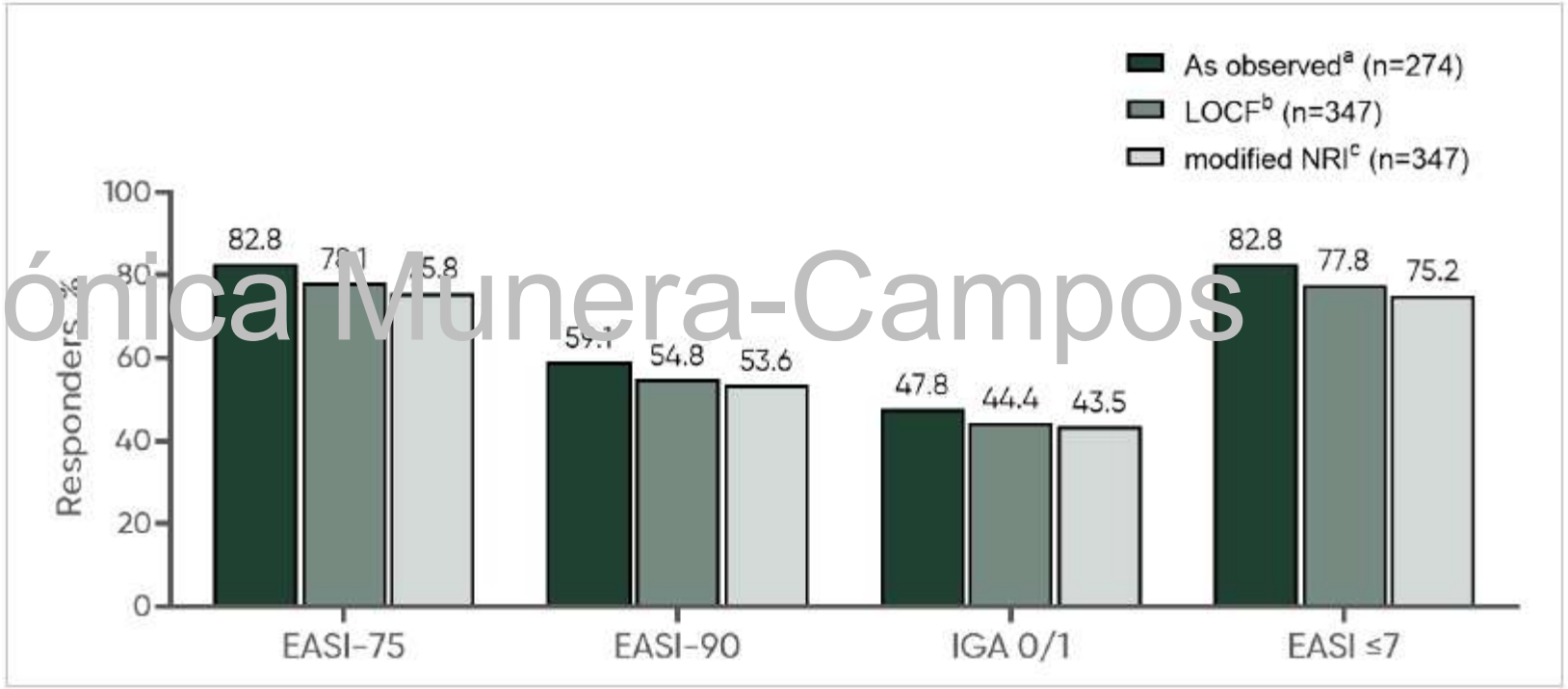


Figure 2. Proportion of patients with 3 years total tralokinumab treatment achieving EASI-75, EASI-90, IGA 0/1, and EASI ≤7



Presented at RAD DEC-2022. 3 years of tralokinumab treatment provides long-term disease control as demonstrated by clinically meaningful outcomes in moderate-to-severe atopic dermatitis. SKIN The Journal of Cutaneous Medicine. 6. s78. 10.25251/skin.6.supp.78.

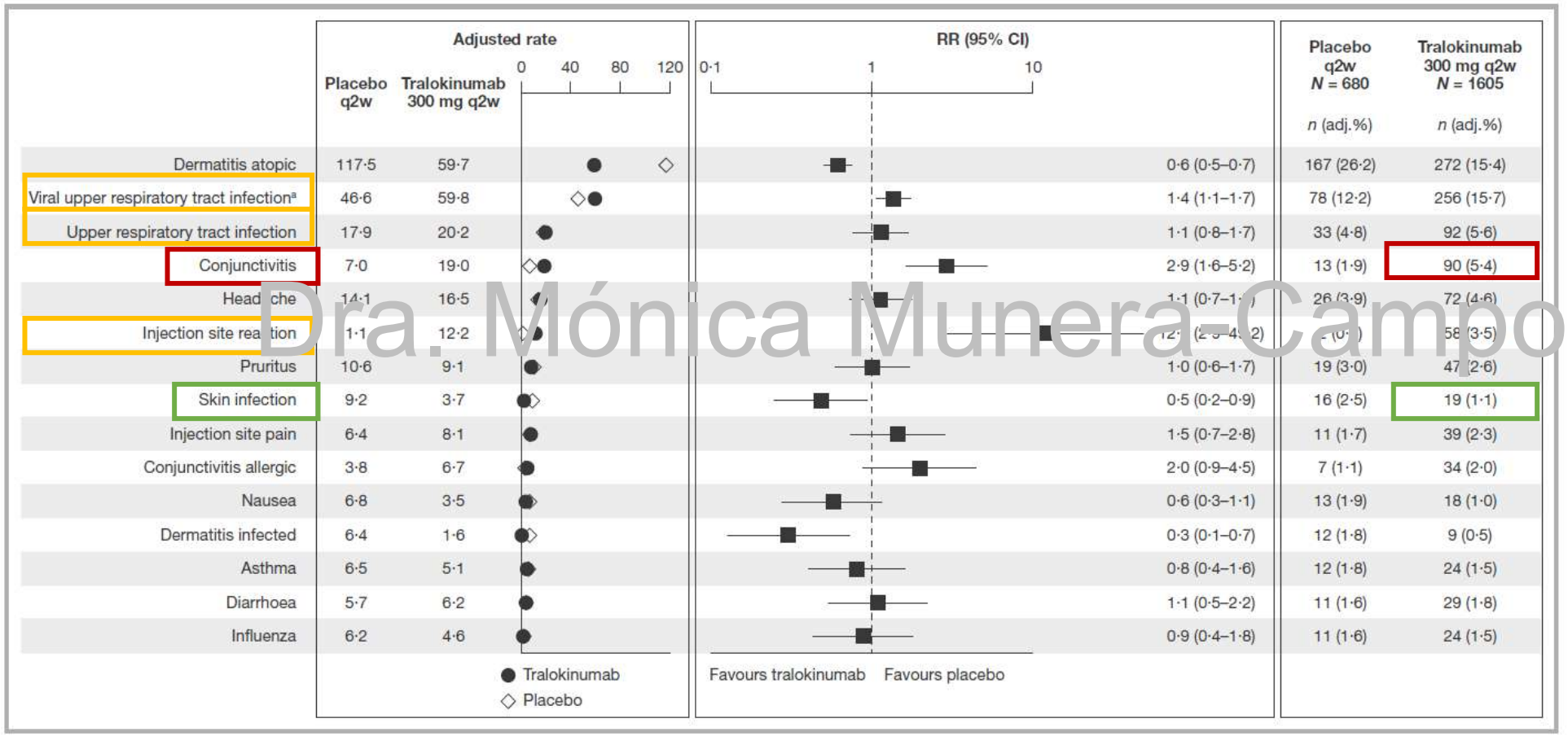
TRALOKINUMAB: RCT SEGURIDAD (datos agregados)

CLINICAL TRIAL
BJD British Journal of Dermatology

Safety of tralokinumab in adult patients with moderate-to-severe atopic dermatitis: pooled analysis of five randomized, double-blind, placebo-controlled phase II and phase III trials*

Eric L. Simpson,[1] Joseph F. Merola,[2] Jonathan I. Silverberg,[3] Kristian Reich,[4] Richard B. Warren,[5] Delphine Staumont-Sallé,[6] Giampiero Girolomoni,[7] Kim Papp,[8] Marjolein de Bruin-Weller,[9] Jacob P. Thyssen,[10] Rebecca Zachariae,[11] Christiana K. Olsen[11] and Andreas Wollenberg[12]

SEGURIDAD: datos agregados a 16W frente a placebo



5,4%

Los datos agrupados incluyen datos de fase 2b y ECZTRA 1, 2, 3 y 5 para el periodo de tratamiento inicial (12 semanas en el ensayo de búsqueda de dosis y 16 semanas en los ensayos ECZTRA).

TRALOKINUMAB: RCT SEGURIDAD (largo plazo)

SEGURIDAD: ECZTEND hasta 3,5 años

Long-term 2-year safety and efficacy of tralokinumab in adults with moderate-to-severe atopic dermatitis: Interim analysis of the ECZTEND open-label extension trial

Andrew Blauvelt, MD, MBA,[a] Richard G. Langley, MD,[b] Jean-Philippe Lacour, MD, PhD,[c] Darryl Toth, MD,[d] Vivian Laquer, MD,[e] Stefan Beissert, MD,[f] Andreas Wollenberg, MD,[g] Pedro Herranz, MD, PhD,[h] Andrew E. Pink, PhD, MBBS,[i] Ketty Peris, MD,[j] Stine Fangel, MSc,[k] Le Gjerum, MD, PhD,[k] Joshua Corriveau, PharmD, MBA,[l] Hidehisa Saeki, MD,[m] Richard B. Warren, MBChB, PhD,[n] Eric Simpson, MD, MCR,[o] and Kristian Reich, MD[p]

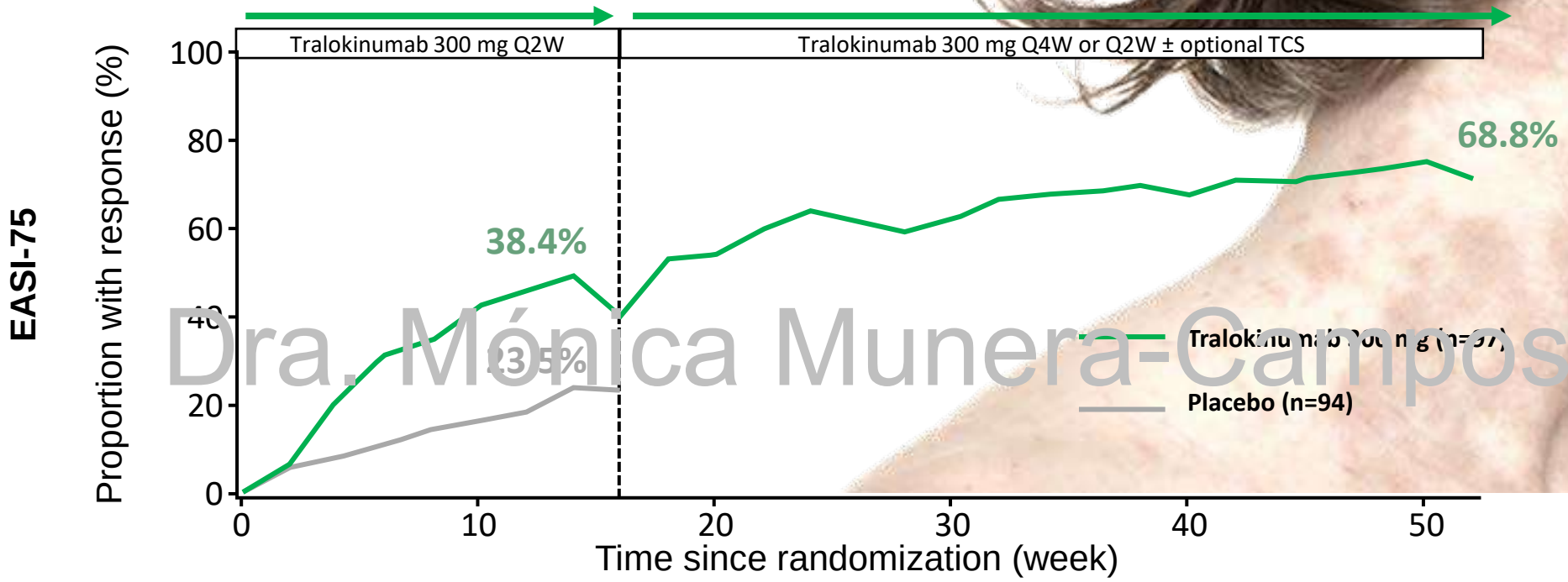
	AEs in ECZTEND interim safety analysis set		AEs Week 12-16 in parent trials[a]			
	Tralokinumab Q2W + optional TCS (*n* =1442; PYE=2446.2)		Tralokinumab Q2W ± TCS (*n* =1605; PYE=473.2)		Placebo Q2W ± TCS (n=680; PYE=193.1)	
	n (%)	Rate (nE/100 PYE)	*n (adj. %)*	Rate (nE/100 PYE)	*n (adj. %)*	Rate (nE/100 PYE)
All AEs	**1127 (78.2)**	**198.7**	**1080 (65.7)**	**639.5**	**449 (67.2)**	**678.3**
Severity						
Mild	956 (66.3)	132.6	881 (53.2)	429.8	326 (49.0)	391.0
Moderate	628 (43.6)	69.5	[illegible] (31.5)	[illegible]	[illegible] (39.0)	[illegible]
Severe	102 (7.1)	6.6	[illegible] 4.6)	[illegible]	[illegible] 6.[illegible])	33.[illegible]
Serious AEs	**101 (7.0)**	**4.9**	**37 (2.1)**	**7.4**	**18 (2.8)**	**11.9**
Leading to drug withdrawal	**34 (2.4)**	**1.4**	**38 (2.3)**	**9.9**	**20 (2.8)**	**13.3**
Outcome						
Not recovered/ not resolved	378 (26.2)	24.9	232 (14.3)	65.4	90 (13.5)	65.2
Recovering/resolving	190 (13.2)	11.0	79 (5.0)	18.9	36 (5.4)	22.7
Recovered/resolved	1052 (73.0)	160.1	997 (60.2)	544.5	416 (62.4)	585.4
Recovered/resolved with sequelae	20 (1.4)	0.9	18 (1.0)	3.5	2 (0.3)	1.7
Unknown	32 (2.2)	1.6	27 (1.7)	7.0	6 (0.9)	3.3

	AEs in ECZTEND interim safety analysis set		AEs Week 12-16 in parent trials[a]			
	Tralokinumab Q2W + optional TCS (*n* =1442; PYE=2446.2)		Tralokinumab Q2W ± TCS (*n* =1605; PYE=473.2)		Placebo Q2W ± TCS (n=680; PYE=193.1)	
	n (%)	*Rate (nE/100 PYE)*	*n (adj. %)*	*Rate (nE/100 PYE)*	*n (adj. %)*	*Rate (nE/100 PYE)*
Viral upper respiratory tract infection[b]	295 (20.5)	18.2	256 (15.7)	65.1	78 (12.2)	51.3
Dermatitis atopic	257 (17.8)	17.9	272 (15.4)	68.0	167 (26.2)	139.7
Upper respiratory tract infection	101 (7.0)	5.8	92 (5.6)	20.8	33 (4.8)	18.5
Headache	79 (5.5)	4.4	72 (4.6)	21.6	26 (3.9)	19.6
Conjunctivitis	77 (5.3)	3.8	90 (5.4)	21.0	13 (1.9)	6.9

Blauvelt A, Lacour J-P, Toth D, et al. Long-term improvements observed in tralokinumab-treated patients with moderate-to-severe atopic dermatitis: an ECZTEND interim analysis. Poster presented at: American Academy of Dermatology Association Virtual Meeting Experience (AAD VMX); April 23-25, 2021.

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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TRALOKINUMAB: RCT ADOLESCENTES

ECTZTEND (tralokinumab Q2W, 12-17 años, a 3 años)

	ECZTRA 6 Initial treatment period Week 0-16				ECZTRA 6 Week 16-52		ECZTEND	
	Tralokinumab 150/300 mg Q2W (n=195; PYE=58.81)		Placebo Q2W (n=94; PYE=27.93)		Tralokinumab 150 mg/300 mg Q4W/Q2W ± optional TCS (n=266; PYE=176.6)		Tralokinumab 300 mg Q2W ± optional TCS (n=127; PYE=201.5)	
	N (%)	nE/100 PYE	N (%)	nE/100 PYE	N (%)	nE/100 PYE	N (%)	nE/100 PYE
Adverse events (AEs)	129 (66.2)	518.6	58 (61.7)	479.7	181 (68.0)	328.4	83 (65.4)	137.0
Severity								
Mild	95 (48.7)	323.1	40 (42.6)	275.7	136 (51.1)	217.4	64 (50.4)	91.3
Moderate	65 (33.3)	[illegible]	3 (33.0)	[illegible]	[illegible]	108.1	[illegible]	[illegible]
Severe	[illegible]	23.8	[illegible]	25.1	5 (9)	[illegible]	3 (2.4)	[illegible]
Serious AEs	4 (2.1)	6.8	5 (5.3)	17.9	7 (2.6)	4.0	3 (2.4)	1.5
AEs leading to drug withdrawal	1 (0.5)	1.7	0 (0)	-	2 (0.8)	1.1	1 (0.8)	0.5
Most frequently reported AEs (≥5% of patients)								
Viral URTI[a]	31 (15.9)	64.6	8 (8.5)	35.8	48 (18.0)	37.4	17 (13.4)	11.9
Dermatitis atopic	20 (10.3)	40.81	12 (12.8)	57.3	22 (8.3)	16.4	13 (10.2)	7.4
URTI	19 (9.7)	35.7	4 (4.3)	17.9	29 (10.9)	22.1	7 (5.5)	4.5
Headache	11 (5.6)	18.7	3 (3.2)	10.7	12 (4.5)	9.6	5 (3.9)	2.5
Asthma	3 (1.5)	5.1	5 (5.3)	21.5	2 (0.8)	1.7	1 (0.8)	0.5
Conjunctivitis (AESI)[b]	7 (3.6)	11.9	2 (2.1)	10.7	15 (5.6)	10.2	4 (3.1)	3.0

[a]Mainly reported as common cold. [b]Conjunctivitis category includes several preferred terms, such as conjunctivitis, conjunctivitis allergic, conjunctivitis bacterial, and conjunctivitis viral.
PYE, patient-years of exposure.
%, percentage of patients; AE, adverse event; AESI, adverse event of special interest; n, number of patients achieving the indicated metric, or with ≥1 event; N, number of patients with recorded observation; nE, number of events; PYE, patient-years of exposure; Q2W, every 2 weeks; Q4W, every 4 weeks; TCS, topical corticosteroids; URTI, upper respiratory tract infection.

TRALOKINUMAB: RWE

Clin Exp Dermatol 2023; **00**:1–8
https://doi.org/10.1093/ced/llad038
Advance access publication date: 26 January 2023

CED
Clinical and Experimental Dermatology
Original Article

Tralokinumab treatment for patients with moderate-to-severe atopic dermatitis in daily practice

Anne R. Schlösser, Madena Shareef, Jill Olydam, Tamar E.C. Nijsten and Dirk Jan Hijnen

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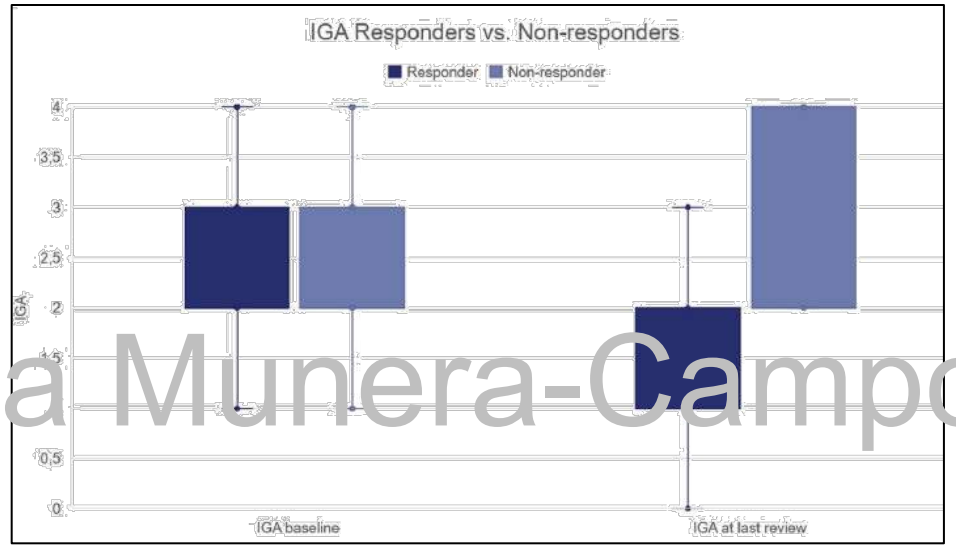
- **37 pacientes**
- Edad media 31 años (15-66 años)
- 46% (17/37) hombres
- Tratamientos previos: CsA 78%, CS orales (46%).

- **Tratamientos innovadores previos:**
  - Dupilumab: 76% (28)
  - Baricitinib: 16% (6)
  - Upadacitinib: 11% (4)
  - Abrocitinib: 11% (4)

Definición de respuesta / respondedor:
Cualquier disminución en el IGA y el NRS-itch 7d y paciente satisfecho con el tratamiento y que quisiera continuar



Fecha de publicación	Enero 2023
Tipo de datos	Cohorte prospectiva
País / países	Países Bajos (1 centro)
Evaluación	Mejoría IGA/ NRS prurito
Período de evaluación	Última visita
N.º de pacientes	37

- **De los 28 pacientes tratados previamente con dupilumab, 14 (50%) presentaron buena respuesta a tralokinumab.**
  - 5 casos habían suspendido dupilumab por **conjuntivitis**, que no presentaron con tralokinumab
  - Otros 5 casos habían presentado **dermatitis de cabeza y cuello**, de los que 4/5 tuvieron buena respuesta con tralokinumab

- **15/37 pacientes (41%) supendieron tralokinumab tras una media de 14W (1-36W).**
  - 12/15 (80%) por falta de respuesta
  - 3/15 (20%) discontinuaron por efectos adversos: 1 blefaritis anterior, 1 monoartritis, 1 dolor a la inyección

Germans Trias i Pujol Hospital

TRALOKINUMAB: **RWE**

Received: 19 September 2022 | Accepted: 9 November 2022
DOI: 10.1111/jdv.18753

LETTER TO THE EDITOR

Tralokinumab in the treatment of resistant atopic dermatitis: An open-label, retrospective case series study

- **Estudio retrospectivo**
- **12 pacientes adultos** tratados con tralokinumab **tras fallo a dupilumab (no respuesta EASI50 a W16)**
- 50% H, Edad media: 42,58 (19-82 años)
- 8 pacientes dermatitis flexural clásica, 2 pacientes DA tipo prurigo nodular, 1 paciente eccema numular, 1 paciente afectación de cabeza y cuello.

- **A W8 todos habían alcanzado respuesta EASI75**
- **EASI basal medio 27,58** (20-35) → **EASI a W12 4,67** (0-13)
- **NRS-prurito basal 8,42** (7-10) → **NRS-prurito a Q12 2,92** (0-5)

- Buena respuesta en CyC y manos
- Buena respuesta en DA tipo prurigo nodular (2)
- **4 pacientes habían presentado conjuntivitis con dupilumab, que no recurrió con el tratamiento con tralokinumab**

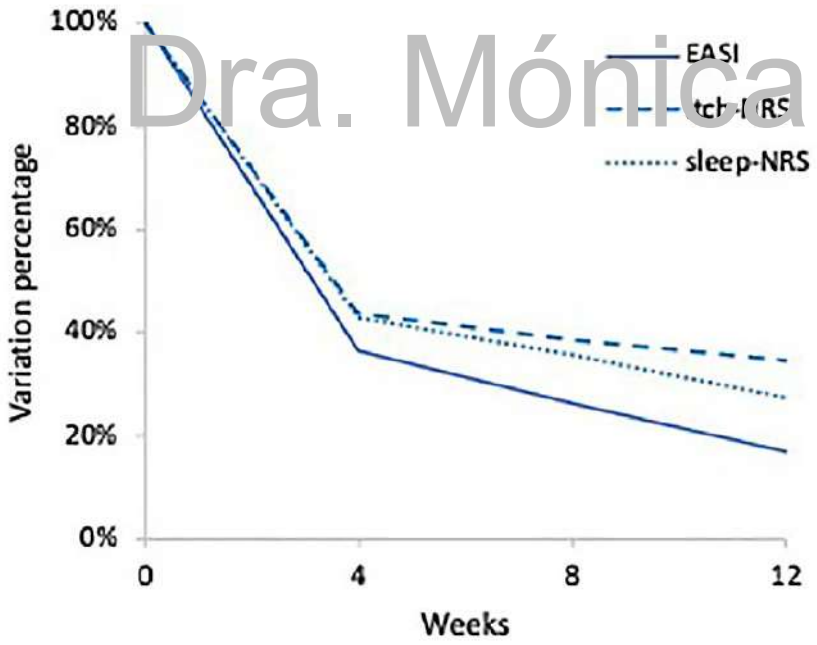


FIGURE 1 Severity variations of atopic dermatitis estimated through EASI, itch-NRS and sleep-NRS after 12-week treatment with tralokinumab. Initial values were measured at least 4 weeks after discontinuation of previous therapies and before treatment with tralokinumab.

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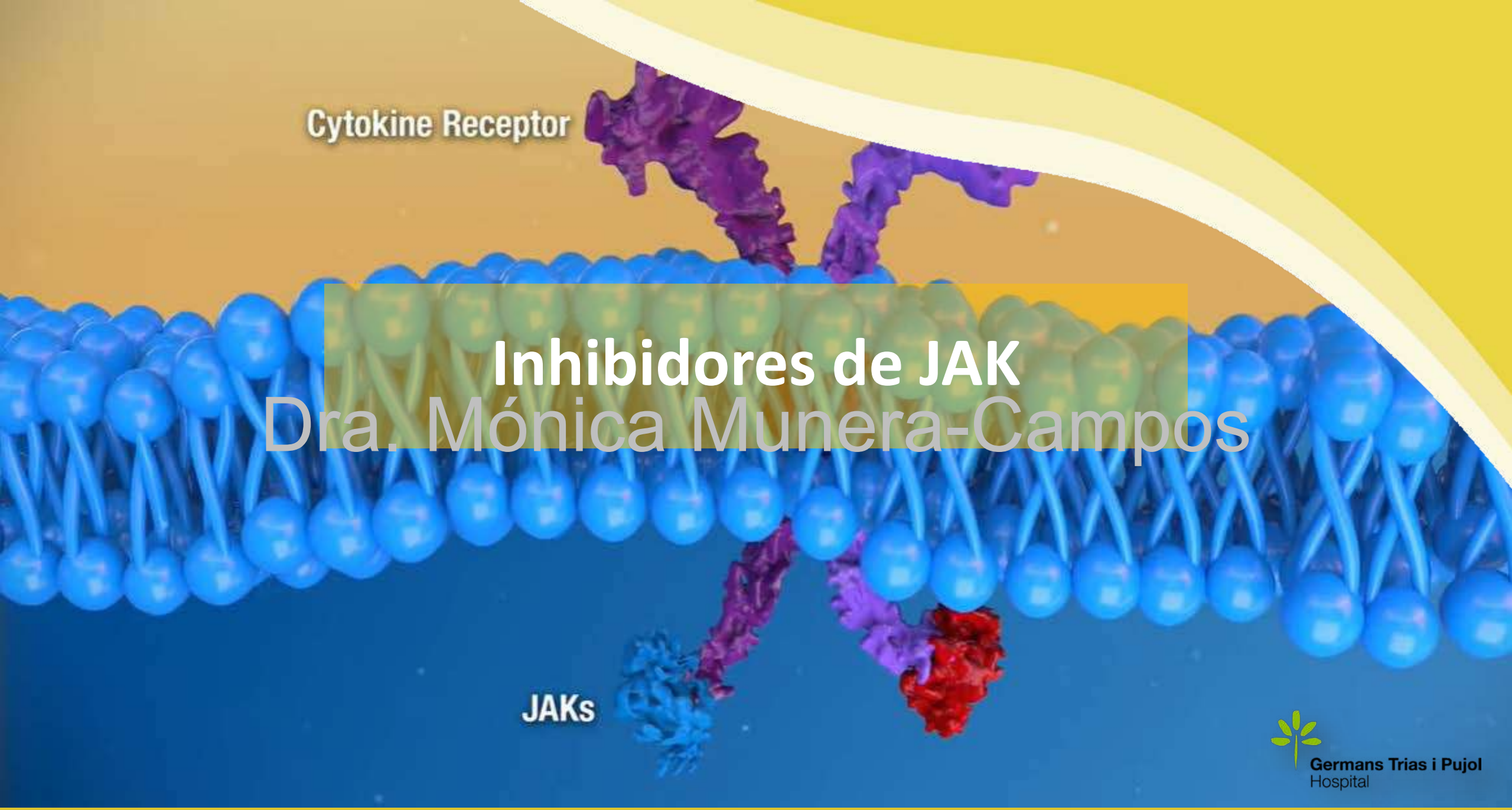


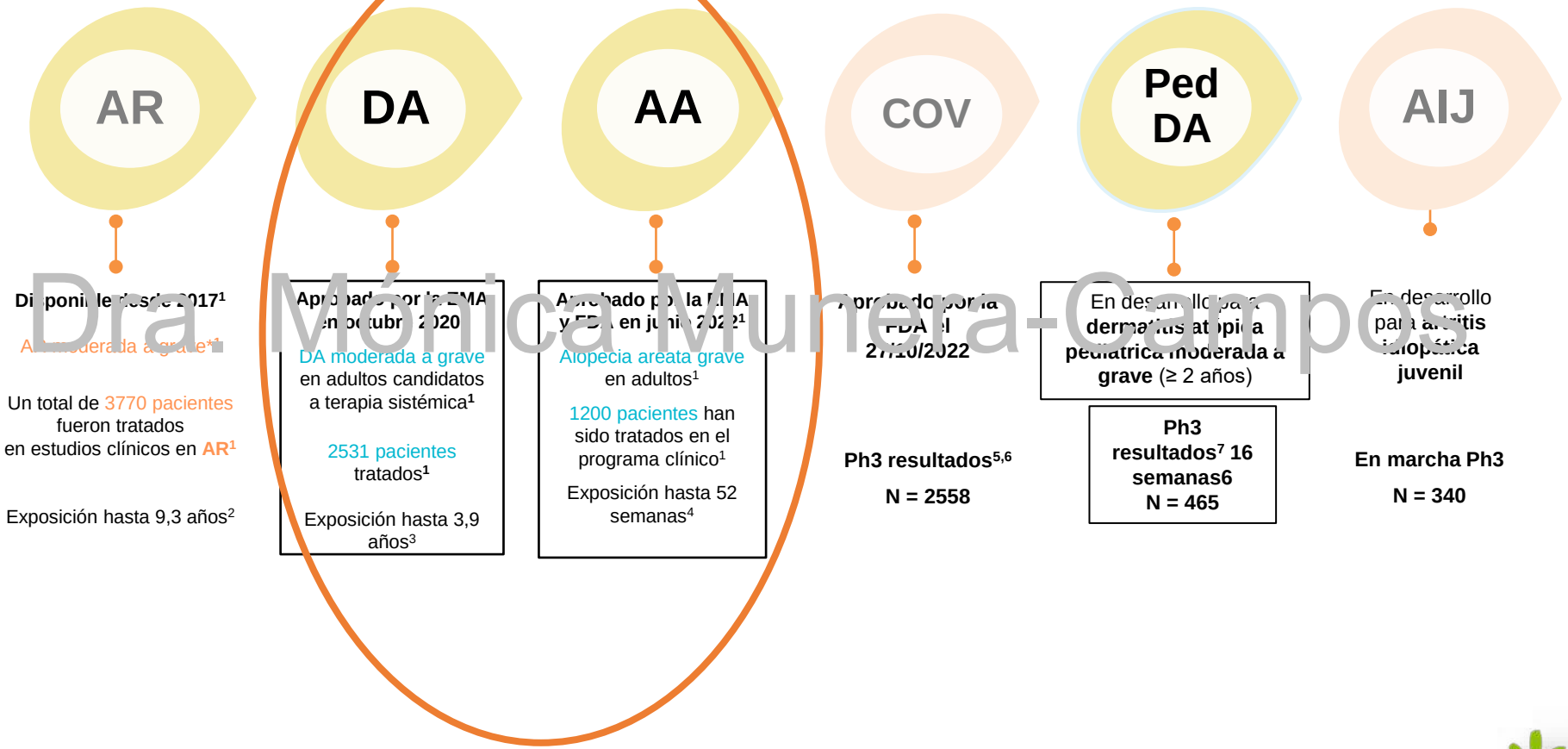
Inhibidores de JAK

Dra. Mónica Munera-Campos

Germans Trias i Pujol Hospital

BARICITINIB: RCT

JAK1 JAK2



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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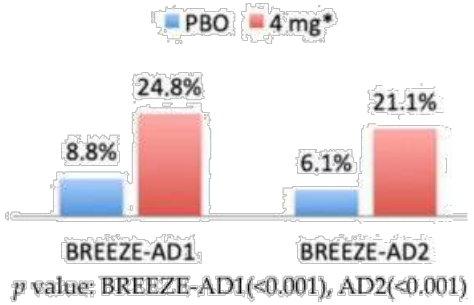
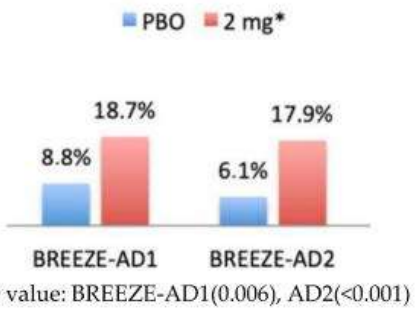
BARICITINIB: RCT$_{ADULTOS}$

BREEZE-AD1 y BREEZE-AD2 (monoterapia)

EASI75

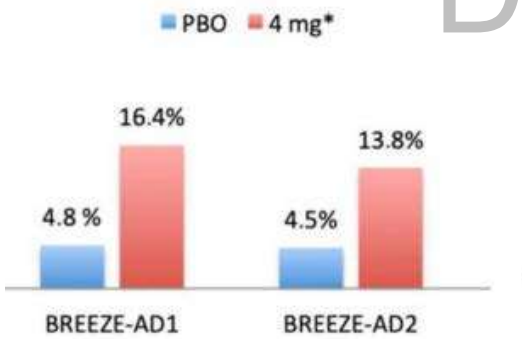


p value: BREEZE-AD1(<0.001), AD2(<0.001)

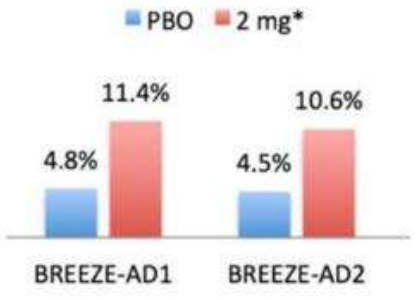


p value: BREEZE-AD1(0.006), AD2(<0.001)

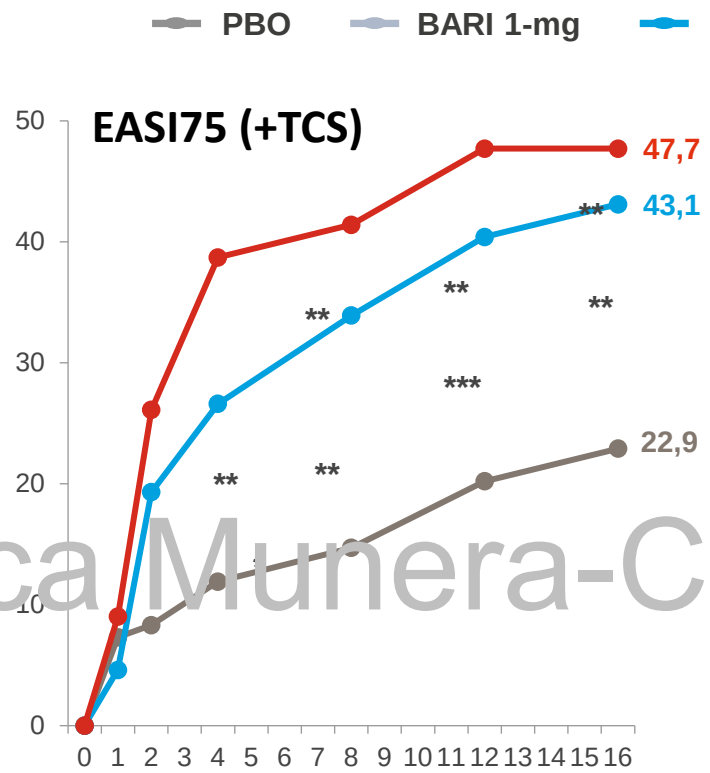
IGA 0/1

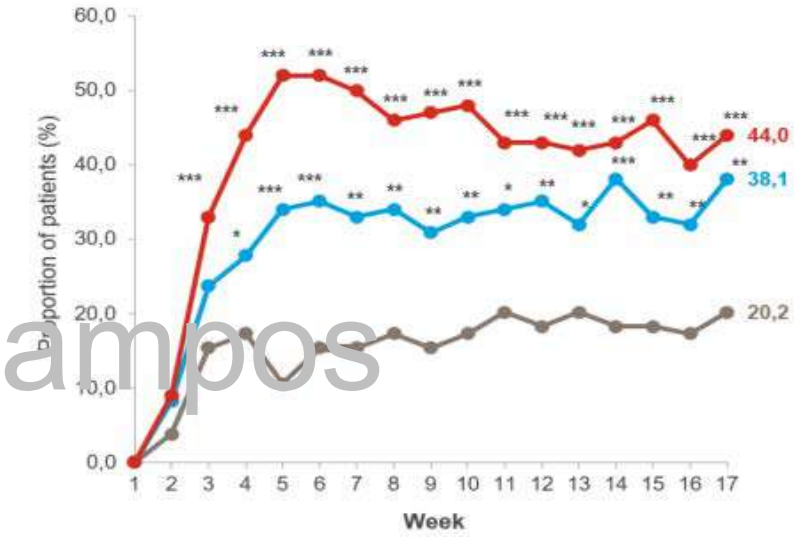


p value: BREEZE-AD1(<0.001), AD2(0.001)



p value: BREEZE-AD1(0.020), AD2(0.026)





p-value vs. PBO (unadjusted analyses for AD7) ***p≤0,001; **p≤0,01; *p≤0,05

BREEZE AD7 TCS Combo

Simpson, E.; Lacour, J.; Spelman, L.; Galimberti, R.; Eichenfield, L.; Bissonnette, R.; King, B.; Thyssen, J.; Silverberg, J.; Bieber, T.; et al. Baricitinib in patients with moderate-to-severe atopic dermatitis and inadequate response to topical corticosteroids: Results from two randomized monotherapy phaseIIItrials. Br. J. Dermatol. 2020, 183, 242–255.

Reich, K.; Kabashima, K.; Peris, K.; Silverberg, J.I.; Eichenfield, L.F.; Bieber, T.; Kaszuba, A.; Kolodsick, J.; Yang, F.E.; Gamalo, M.; et al. Efficacy and Safety of Baricitinib Combined with Topical Corticosteroids for Treatment of Moderate to Severe Atopic Dermatitis. JAMA Dermatol. 2020, 156, 1333.

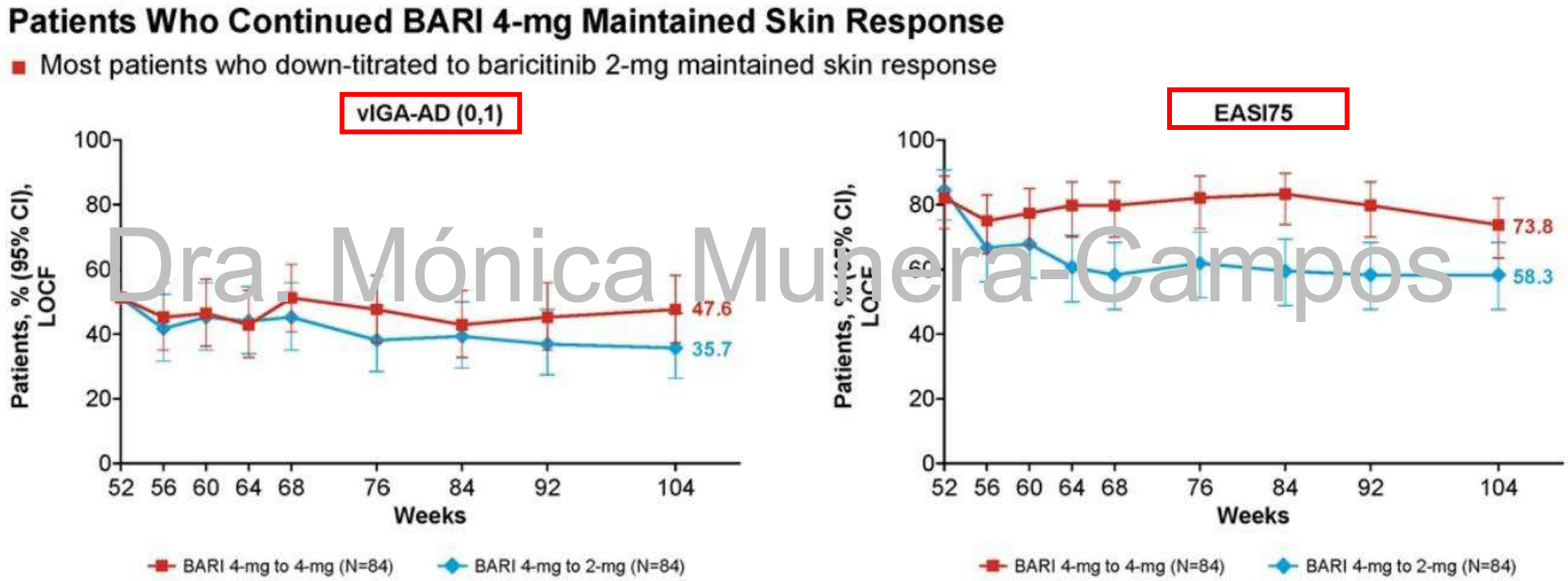
Germans Trias i Pujol Hospital

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)



Póster0816. **Maintained Improvement With Baricitinib In Adult Patients With Moderate To Severe Atopic Dermatitis Who Were Treated For Up To 104 Weeks In a Randomised Trial: Physician Assessments.** A. Wollenberg et al. EADV Congress September 2022

Germans Trias i Pujol Hospital

BARICITINIB: RCT$_{ADULTOS}$

SEGURIDAD

Datos de seguridad integrados (8 ensayos clínicos)

Exposición de hasta 3,9 años en adultos con DA

JOURNAL OF DERMATOLOGICAL TREATMENT
2023, VOL. 34, NO. 1, 2161812
https://doi.org/10.1080/09546634.2022.2161812

Taylor & Francis
Taylor & Francis Group

RESEARCH ARTICLE

OPEN ACCESS Check for updates

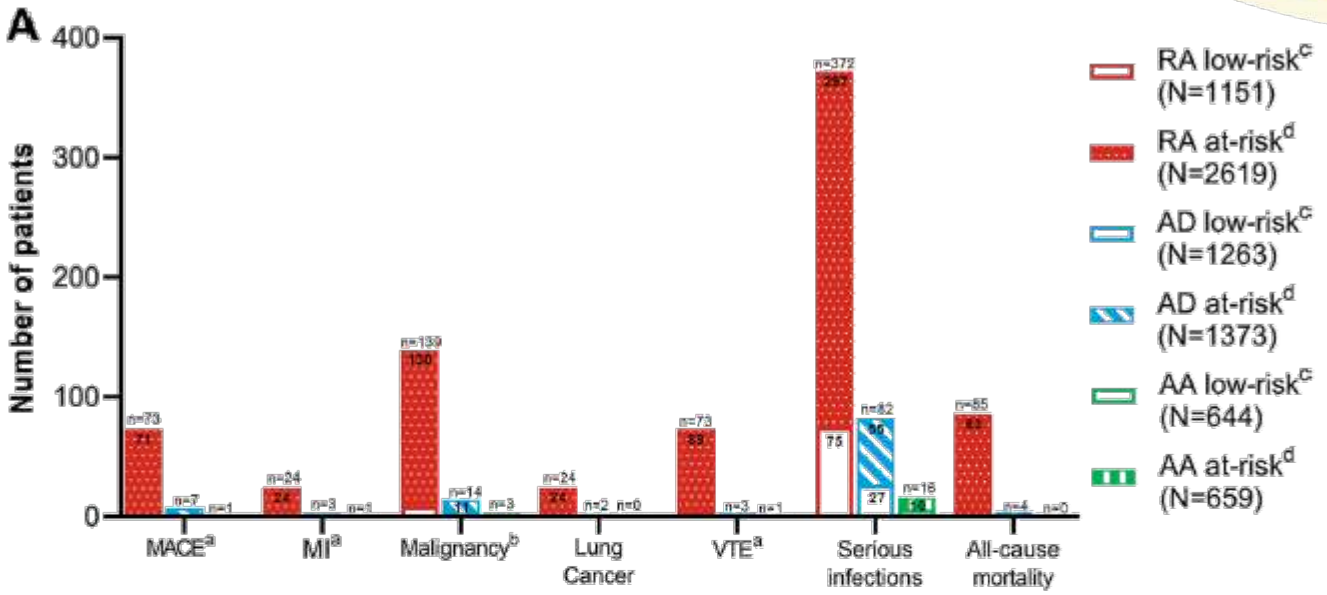
Safety of baricitinib for the treatment of atopic dermatitis over a median of 1.6 years and up to 3.9 years of treatment: an updated integrated analysis of eight clinical trials

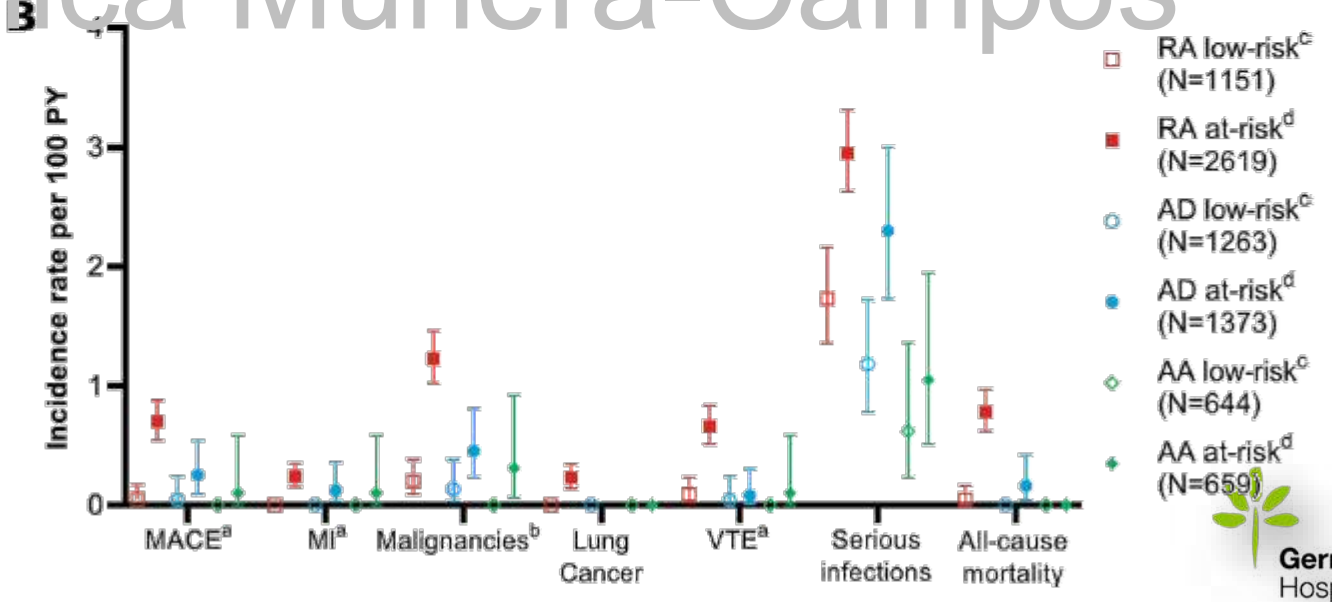
Thomas Bieber[a,b], Norito Katoh[c], Eric L. Simpson[d], Marjolein de Bruin-Weller[e], Diamant Thaçi[f], Antonio Torrelo[g], Angelina Sontag[h], Susanne Grond[h], Maher Issa[h], Xiaoyu Lu[i], Tracy Cardillo[h], Katrin Holzwarth[h] and Jacob P. Thyssen[j]

	Placebo-controlled (to week 16)			2-mg – 4-mg extended		All-bari-AD
	Placebo ($N = 743$) [PYE = 212]	Bari 2 mg ($N = 576$) [PYE = 169]	Bari 4 mg ($N = 489$) [PYE = 147]	Bari 2 mg ($N = 584$) [PYE = 727]	Bari 4 mg ($N = 497$) [PYE = 800]	($N = 2636$) [PYE = 4628]
TEAE occurring in ≥2% of patients in any group in the placebo-controlled datasets, n (adj %) [adj IR]						
Nasopharyngitis	83 (9.5) [34.9]	67 (9.5) [34.1]	67 (11.3) [40.8]	121 [21.0]	129 [22.3]	530 [13.8]
Headache	28 (3.3) [11.9]	37 (5.9) [21.1]	35 (6.3) [21.4]	58 [8.6]	55 [7.4]	2169 [4.9]
Blood creatine phosphokinase increased	6 (0.8) [2.7]	8 (1.1) [3.5]	17 (2.9) [9.6]	15 [2.0]	27 [3.3]	90 [1.9]
Diarrhea	15 (1.8) [6.2]	10 (1.3) [4.3]	15 (2.7) [9.0]	18 [2.3]	25 [3.3]	107 [2.3]
Herpes simplex	8 (0.9) [3.2]	13 (2.0) [7.1]	15 (2.6) [8.6]	22 [3.1]	36 [4.9]	120 [2.6]
Upper respiratory tract infection	14 (1.4) [4.8]	23 (3.2) [11.0]	15 (2.5) [8.3]	34 [5.1]	45 [5.8]	206 [4.7]
Upper abdominal pain	10 (1.2) [4.1]	10 (1.6) [5.3]	14 (2.5) [8.5]	18 [2.4]	18 [2.5]	55 [1.2]
Influenza	8 (1.0) [3.4]	13 (1.7) [5.7]	12 (2.2) [7.2]	33 [4.4]	30 [4.7]	135 [3.0]
Oral herpes	9 (1.2) [4.1]	10 (1.2) [4.2]	12 (2.0) [6.7]	21 [2.9]	33 [4.7]	140 [3.1]
Urinary tract infection	8 (0.8) [2.6]	9 (1.1) [3.8]	11 (2.0) [6.5]	17 [2.4]	21 [2.9]	104 [2.3]
Folliculitis	11 (1.2) [4.0]	14 (1.8) [6.2]	10 (1.5) [4.9]	28 [3.9]	19 [2.4]	109 [2.4]
Nausea	8 (0.8) [2.7]	14 (1.8) [5.8]	4 (0.8) [2.5]	18 [2.3]	9 [1.1]	61 [1.3]

BARICITINIB: RCT$_{ADULTOS}$

BAJO RIESGO
• <65 años y no FR cardiovascular
EN RIESGO (≥1 criterio)
• ≥65 años • Enfermedad cardiovascular • DM • HTA • Tabaquismo • HDL<40mg/dl • IMC ≥39 • Baja movilidad • Historia de neoplasia





Adv Ther
https://doi.org/10.1007/s12325-023-02445-w

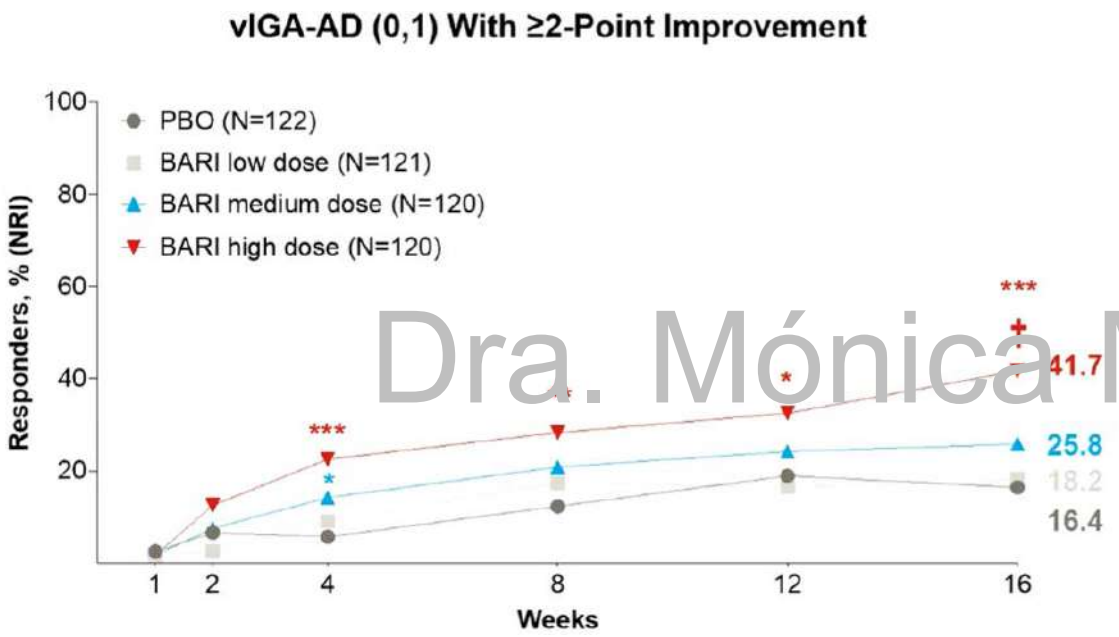
BRIEF REPORT

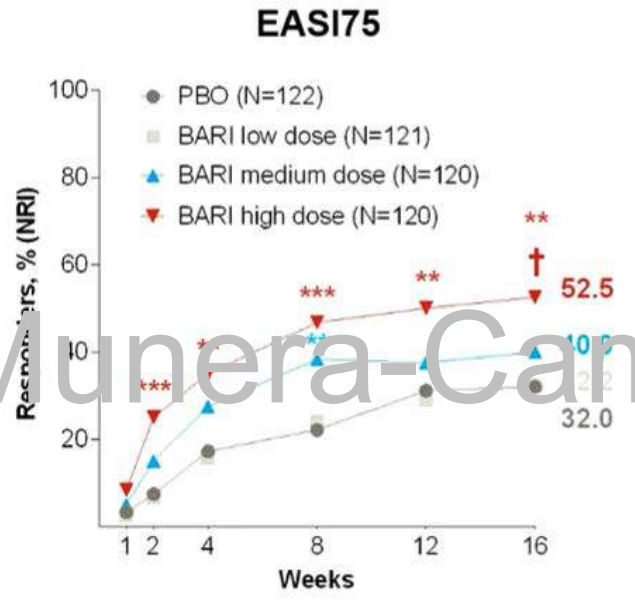
Baricitinib Safety for Events of Special Interest in Populations at Risk: Analysis from Randomised Trial Data Across Rheumatologic and Dermatologic Indications

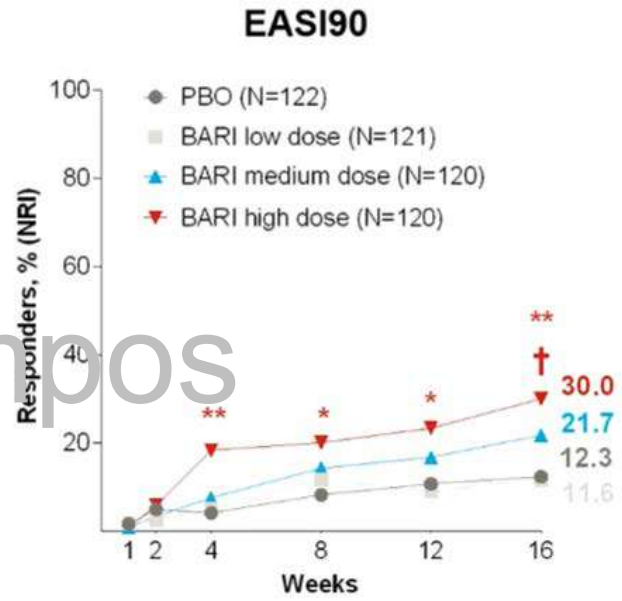
Received: December 5, 2022 / Accepted: January 25, 2023

BARICITINIB: RCT PEDIATRÍA

NIÑOS Y ADOLESCENTES (2-17 años)







Presentation D3T01.1E. Dr. A. Torrelo. **Efficacy and Safety of Baricitinib in a Phase 3, Randomized, Double-Blind, Placebo-Controlled Study in Pediatric Patients with Moderate-to-Severe Atopic Dermatitis. (BREEZE-AD-PEDS)** (NCT03952559).EADV Congress 2022

Germans Trias i Pujol Hospital

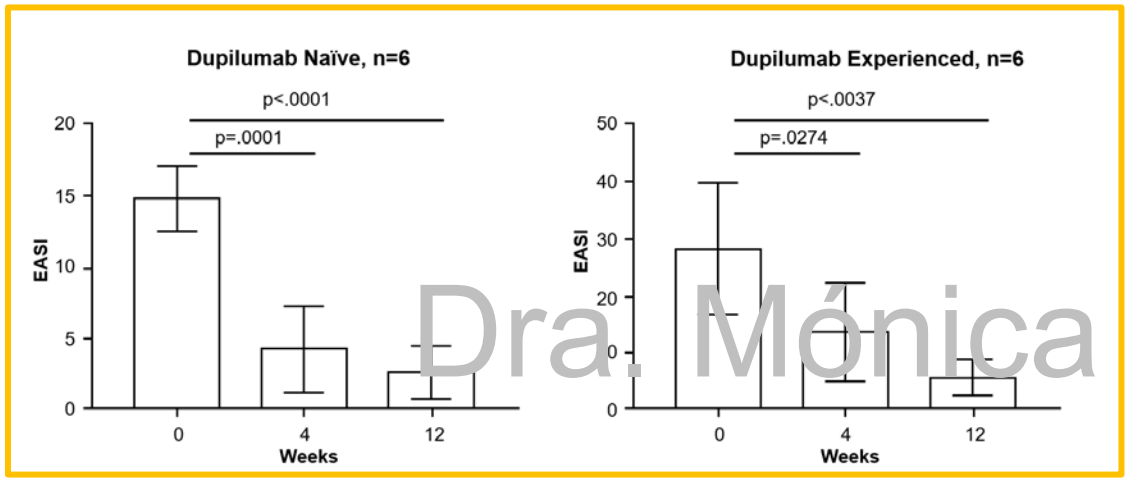
BARICITINIB: RWE

ActaDV

SHORT COMMUNICATION

Treatment of Atopic Dermatitis with Baricitinib: First Real-life Experience

Danielle ROGNER, Tilo BIEDERMANN and Felix LAUFFER
Department of Dermatology, Technical University of Munich, DE-80802 Munich, Germany.
Accepted Dec 2, 2021; Epub ahead of print Jan 27, 2022
Acta Derm Venereol 2022; 102: adv00677. DOI: 10.2340/actadv.v102.1088

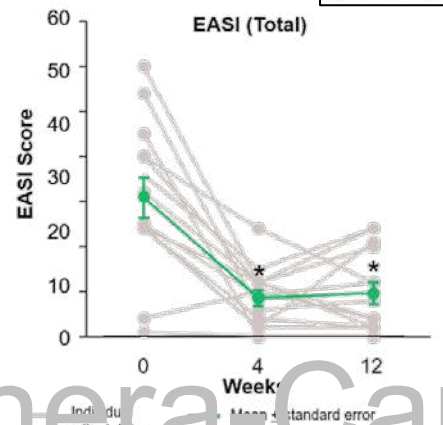


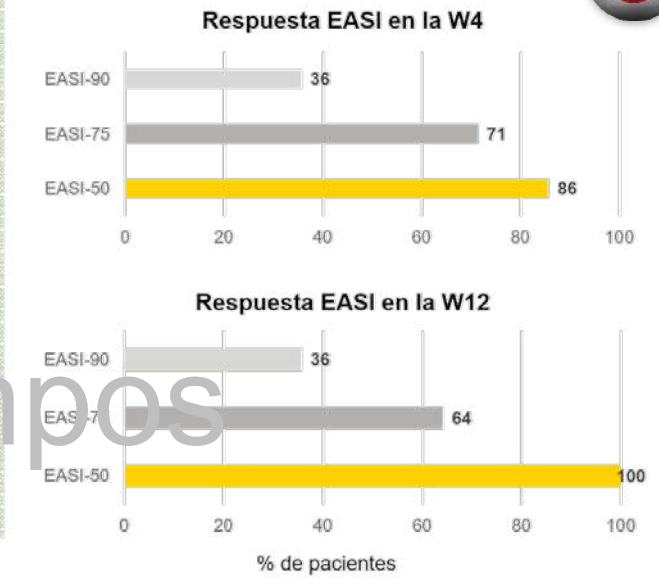
Received: 2 January 2022 | Accepted: 21 February 2022
DOI: 10.1111/1346-8138.16350

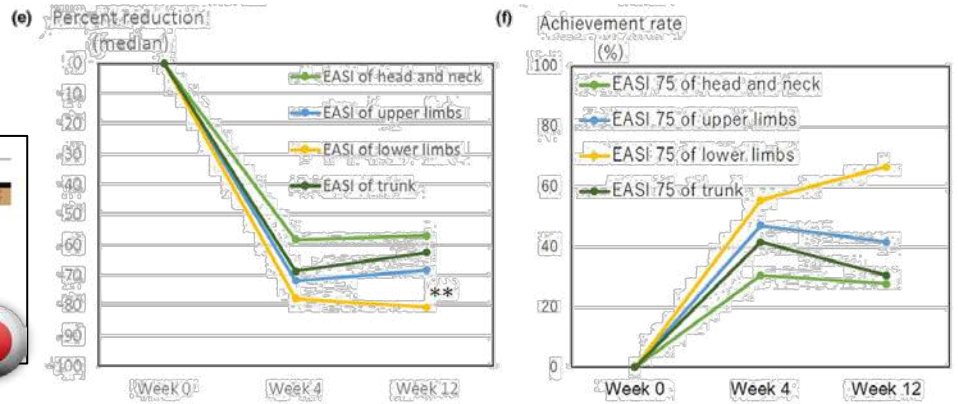
RESEARCH NOTE

Real-world effectiveness and safety of baricitinib in Japanese patients with atopic dermatitis: A single-center retrospective study

Akihiko Uchiyama | Chisako Fujiwara | Yuta Inoue | Sei-ichiro Motegi
Department of Dermatology, Gunma University Graduate School of Medicine, Maebashi, Japan







Received: 6 January 2023 | Accepted: 18 February 2023
DOI: 10.1111/1346-8138.16763

ORIGINAL ARTICLE

Efficacy and safety of baricitinib treatment for moderate to severe atopic dermatitis in real-world practice in Japan

Teppei Hagino[1] | Hidehisa Saeki[2] | Eita Fujimoto[3] | Naoko Kanda[1]

Received: 24 August 2022 | Accepted: 29 November 2022
DOI: 10.1111/jdv.18804

LETTER TO THE EDITOR

Short-term real-world experience with baricitinib treatment in Danish adults with moderate–severe atopic dermatitis

En el análisis agrupado:
Respuesta EASI75:
- W4: 53%
- W16: 33%

Germans Trias i Pujol Hospital

BARICITINIB: RWE

BioDay Eczema and Atopic Diseases Registry

ORIGINAL ARTICLE

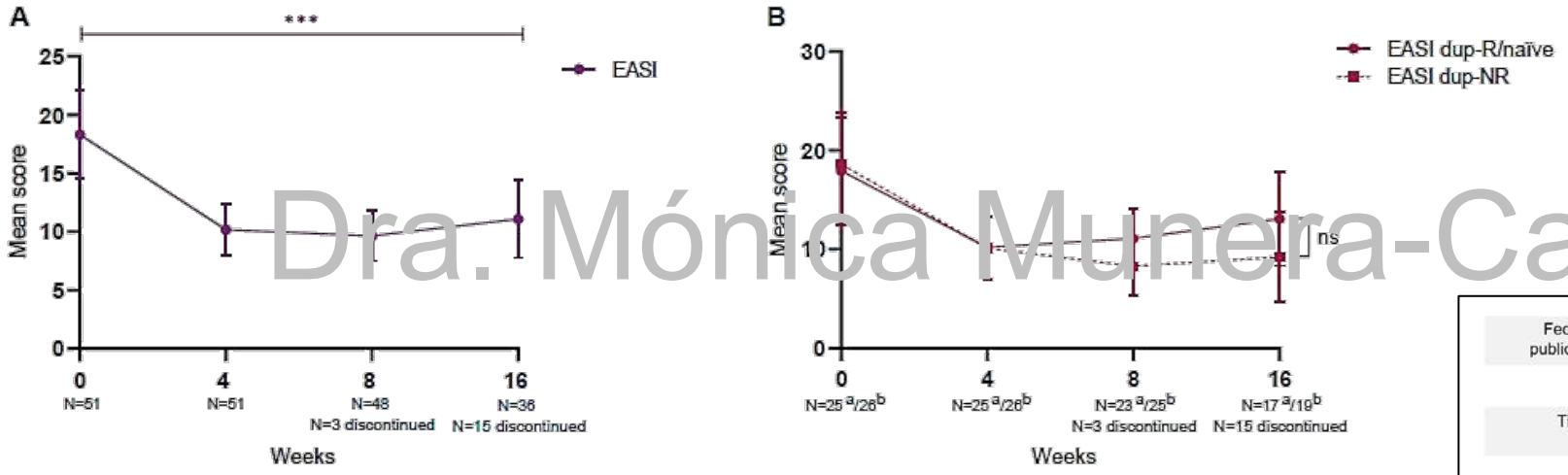
ActaDV

Daily Practice Experience of Baricitinib Treatment for Patients with Difficult-to-Treat Atopic Dermatitis: Results from the BioDay Registry

Celeste M. BOESJES[1#], Esmé KAMPHUIS[2#], Nicolaas P. A. ZUITHOFF[3], Daphne S. BAKKER[2], Laura LOMAN[2], Lotte S. SPEKHORST[1], Inge HAECK[4], Marijke KAMSTEEG[5], Anneke M. T. VAN LYNDEN-VAN NES[6], Floor M. GARRITSEN[7], Klaziena POLITIEK[8], Maria OLDHOFF[2], Marlies DE GRAAF[1], Marie L. A. SCHUTTELAAR[2§] and Marjolein S. DE BRUIN-WELLER[1§]

EFECTIVIDAD

	Baseline ($n=51$)	Week 4 ($n=51$)	Week 8 ($n=48$)	Week 16 ($n=36$)	p-value[a]
Patients who discontinued treatment, n (%)	0 (0)	3 (5.9)	12 (23.5)	8 (15.6)	
Concomitant immunosuppressive therapy, n (%)	28 (54.9)	20 (39.2)	4 (8.3)	3 (8.3)	
Primary endpoints, mean (95% CI)					
EASI score	18.3 (14.5–22.1)	10.2 (8.0–12.4)	9.7 (7.5–11.8)	11.1 (7.8–14.4)	<0.0001



- **51 pacientes adultos** (66,7% H)
- Edad media: 39,5
- **49 recibieron BARI 4mg/24h** y 2 pacientes BARI 2mg/24h (edad>75a, y obesidad + FRCV)
- 76,5% asociado a corticoides tópicos de alta o muy alta potencia
- **38 (74,5%) habían recibido dupilumab previamente.** Retirado por ineficacia (16; 42,1%), EAs (12; 31,6%) o ambos (10; 26,3%)

La mayoría de pacientes mantuvo la dosis de 4mg/24h

- 2 pacientes cambiaron a 2mg/24h por buen control de la enfermedad
- 2 pacientes pasaron a 2mg/24h por AEs

La mayoría de pacientes discontinó su tratamiento concomitante inmunosupresor/inmunomodulador

- 2 pacientes mantuvieron prednisolona
- 1 paciente mantuvo metotrexato

A W16, 22,2% no precisaban corticoides tópicos, y la mayoría usaban <10g/semana

Fecha de publicación	Noviembre 2022
Tipo de datos	Registro prospectivo (multicéntrico)
País / países	Países Bajos
Evaluación	IGA/EASI/BSA/ NRS prurito/ POEM, DLQI
Período de evaluación	W4/W8/W16
N.º de pacientes	51

Germans Trias i Pujol Hospital

UPADACITINIB: RCT

JAK1

*Upadacitinib: M16-049 (Phase 1; Pediatric Atopic Dermatitis)
https://clinicaltrials.gov/ct2/show/NCT03646604

Características principales

Inhibidor selectivo y reversible de JAK1

Indicado en adultos y adolescentes a partir de 12 años*

*Y peso corporal >30kg

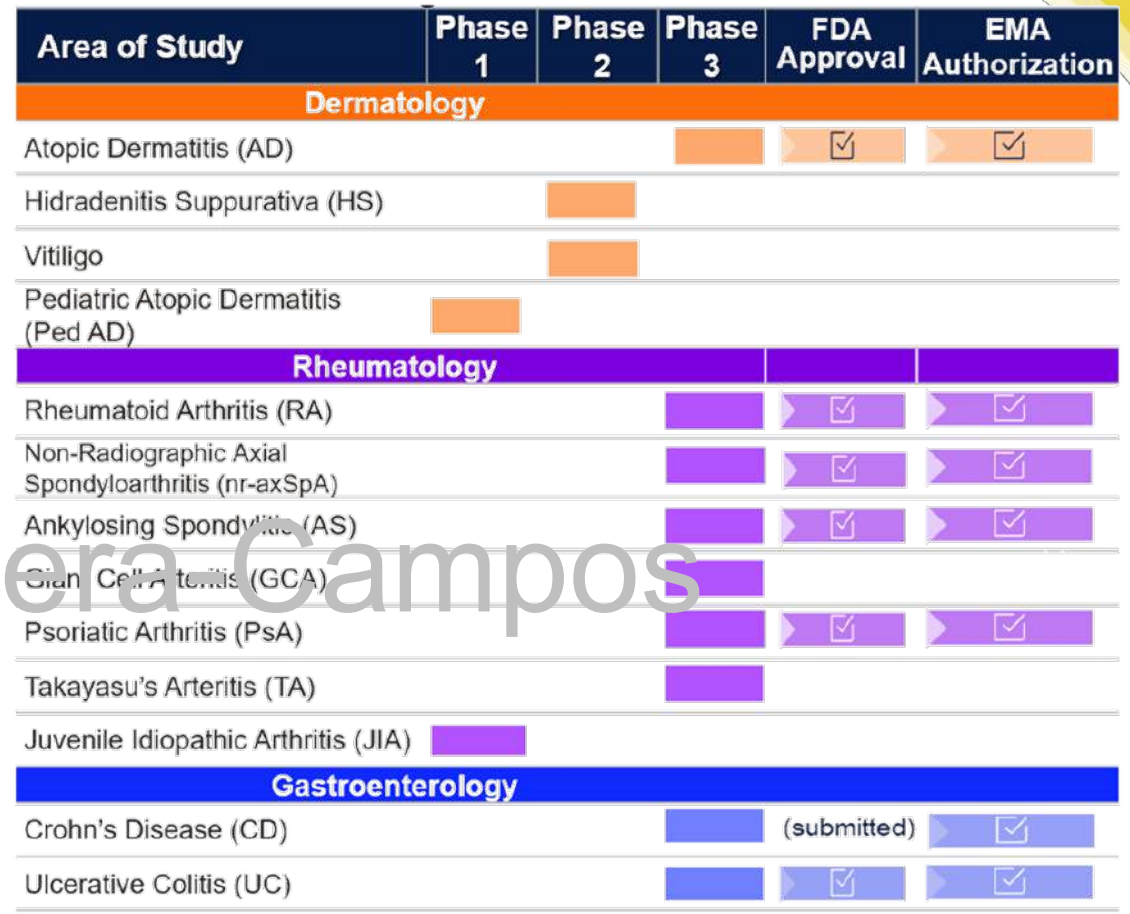
Administración oral y rápida absorción

- 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%)



*Datos limitados en >75 años: utilizar con precaución

Germans Trias i Pujol Hospital

UPADACITINIB: RCT

Análisis integrado de Measure Up 1 y 2 (monoterapia)

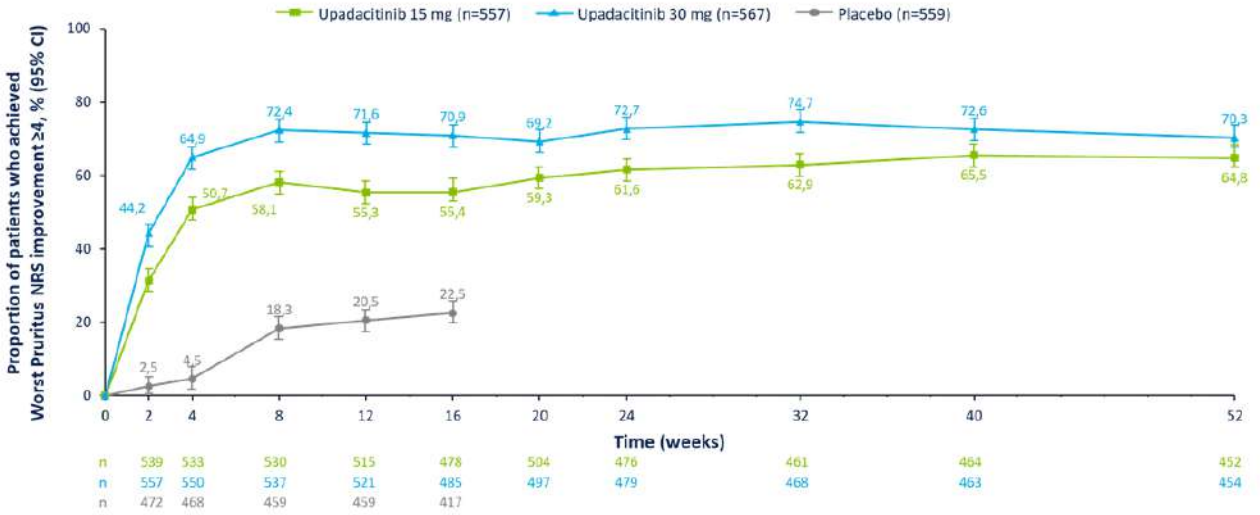
JAMA Dermatology | Original Investigation

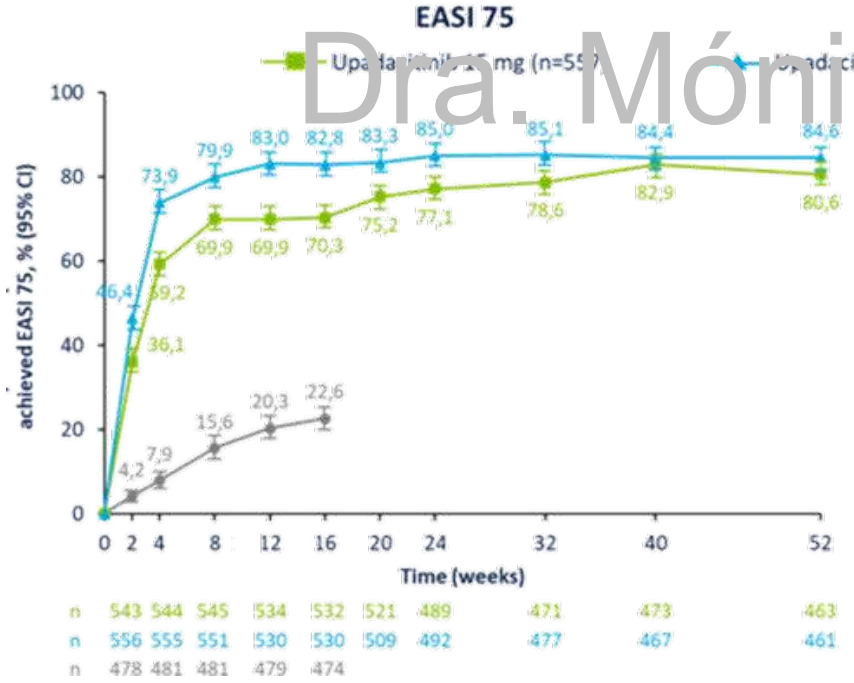
Efficacy and Safety of Upadacitinib in Patients With Moderate to Severe Atopic Dermatitis

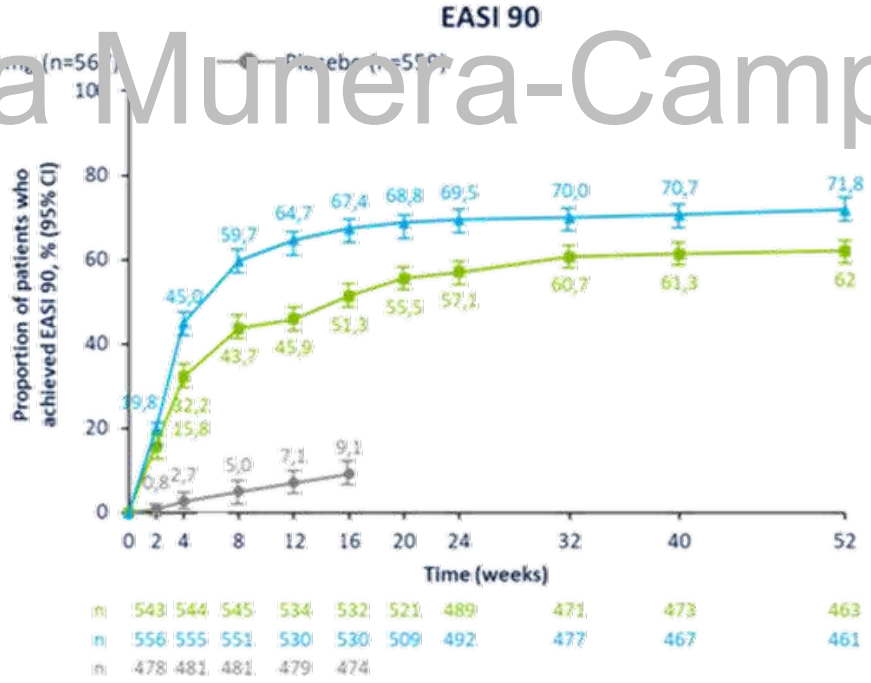
Analysis of Follow-up Data From the Measure Up 1 and Measure Up 2 Randomized Clinical Trials

Eric L. Simpson, MD; Kim A. Papp, MD; Andrew Blauvelt, MD; Chia-Yu Chu, MD, PhD; H. Chih-ho Hong, MD; Norito Katoh, MD; Brian M. Calimlim, DrPH; Jacob P. Thyssen, MD, PhD, DMSc; Albert S. Chiou, MD, MBA; Robert Bissonnette, MD; Linda F. Stein Gold, MD; Colleen Wegzyn, PharmD; Xiaofei Hu, PhD; Meng Liu, PhD; John Liu, MD; Allan R. Tenorio, MD; Alvina D. Chu, MD; Emma Guttman-Yassky, MD

➢ Mejoría de ≥ 4p en NRS-prurito







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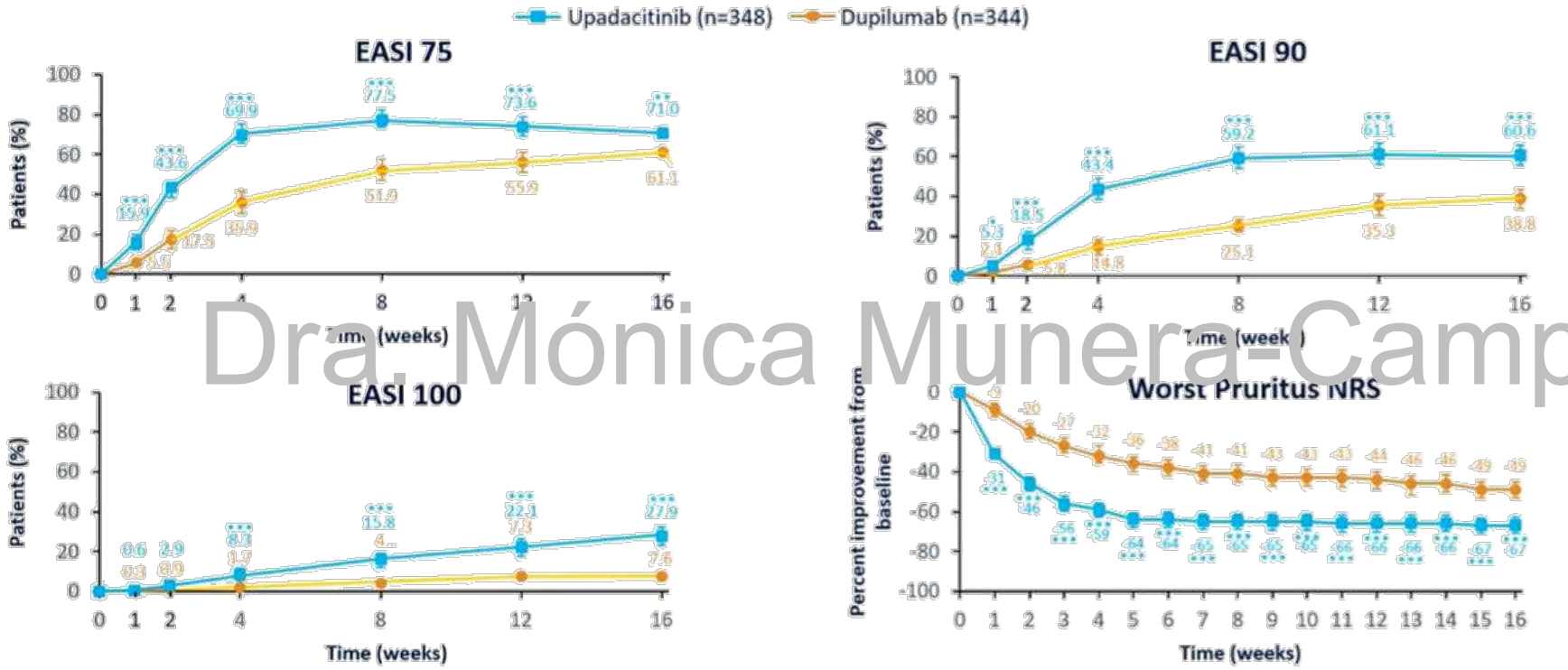
UPADACITINIB: RCT

Heads Up

JAMA Dermatology | Original Investigation

Efficacy and Safety of Upadacitinib vs Dupilumab in Adults With Moderate-to-Severe Atopic Dermatitis
A Randomized Clinical Trial

Andrew Blauvelt, MD, MBA; Henrique D. Teixeira, PhD, MBA; Eric L. Simpson, MD, MCR; Antonio Costanzo, MD; Marjolein De Bruin-Weller, MD; Sebastien Barbarot, MD, PhD; Vimal H. Prajapati, MD; Peter Lio, MD; Xiaofei Hu, PhD; Tianshuang Wu, PhD; John Liu, MD, MS; Barry Ladizinski, MD, MPH, MBA; Alvina D. Chu, MD; Kilian Eyerich, MD



*p≤0.05; **p≤0.01; ***p≤0.001; error bars indicate 95% confidence interval
[a]Percent improvement in Worst Pruritus NRS from baseline vs dupilumab at Weeks 1, 4, and 16 were ranked secondary endpoints, as were EASI 90, EASI 100, and proportion of subjects achieving ≥4-point improvement in Worst Pruritus NRS from baseline at Week 16
DUPI, dupilumab; EASI 75/90/100, ≥75%/90%/100% reduction in Eczema Area and Severity Index; EOW, every other week; NRS, numeric rating scale

UPADACITINIB: RCT

Safety of upadacitinib in moderate-to-severe atopic dermatitis: An integrated analysis of phase 3 studies

Emma Guttman-Yassky, MD, PhD,[a] Jacob P. Thyssen, MD, PhD, DmSci,[b] Jonathan I. Silverberg, MD, PhD, MPH,[c] Kim A. Papp, MD, PhD,[d] Amy S. Paller, MD,[e] Stephan Weidinger, MD,[f] H. Chih-ho Hong, MD,[g] Barbara Hendrickson, MD,[h] Deanne Dilley, MPH,[h] Allan R. Tenorio, MD,[h] Barry Ladizinski, MD, MPH, MBA,[h] Alvina D. Chu, MD,[h] John Liu, MD, MS,[h] and Alan D. Irvine, MD, DSc[i]

New York, NY; Copenhagen, Denmark; Washington, DC; Waterloo, Ontario, and Vancouver and Surrey, British Columbia, Canada; Chicago and North Chicago, Ill; Kiel, Germany; and Dublin, Ireland

	16-week analysis			All upadacitinib exposure	
	UPA 15 mg (n = 899) (PY = 271.2)	UPA 30 mg (n = 906) (PY = 273.3)	PBO (n = 902) (PY = 255.0)	UPA 15 mg (n = 1239) (PY = 1373.4)	UPA 30 mg (n = 1246) (PY = 1414.2)
TEAEs (E/100 PY) [95% CI]					
All TEAEs	1542 (568.6)	1813 (663.5)	1179 (462.3)	3771 (274.6) [265.9, 283.5]	4411 (311.9) [302.8, 321.2]
AE with reasonable possibility of being drug related	611 (225.3)	763 (279.2)	318 (124.7)	1308 (95.2) [90.1, 100.5]	1663 (117.6) [112.0, 123.4]
Severe AEs	55 (20.3)	51 (18.7)	49 (19.2)	170 (12.4) [10.6, 14.4]	215 (15.2) [13.2, 17.4]
SAEs	25 (9.2)	21 (7.7)	31 (12.2)	98 (7.1) [5.8, 8.7]	109 (7.7) [6.3, 9.3]
AEs leading to discontinuation	23 (8.5)	41 (14.3)	36 (14.1)	60 (4.4) [3.3, 5.6]	81 (5.7) [4.5, 7.1]
Deaths*	0	0	0	0	1 (<0.1) [0.0, 0.4]
Most commonly reported AEs, no. events (E/100 PY)†					
Acne	90 (33.2)	145 (53.1)	20 (7.8)	183 (13.3)	286 (20.2)
Nasopharyngitis	92 (33.9)	106 (38.8)	82 (32.2)	211 (15.4)	192 (13.6)
URTI	74 (27.3)	102 (37.3)	66 (25.9)	161 (11.7)	165 (11.7)
Headache	58 (21.4)	64 (23.4)	43 (16.9)	102 (7.4)	94 (6.6)
CPK elevation	44 (16.2)	52 (19.0)	22 (8.6)	97 (7.1)	153 (10.8)
Oral herpes	27 (10.0)	52 (19.0)	12 (4.7)	68 (5.0)	124 (8.8)
Diarrhea	34 (12.5)	32 (11.7)	23 (9.0)	46 (3.3)	62 (4.4)
Folliculitis	20 (7.4)	31 (11.3)	12 (4.7)	51 (3.7)	58 (4.1)
Cough	31 (11.4)	28 (10.2)	14 (5.5)	70 (5.1)	52 (3.7)
Nausea	28 (10.3)	25 (9.1)	5 (2.0)	41 (3.0)	44 (3.1)
Dermatitis atopic	31 (11.4)	15 (5.5)	80 (31.4)	120 (8.7)	81 (5.7)

PBO, Placebo; *UPA*, upadacitinib; *URTI*, upper respiratory tract infection.
*Reported as EAIR (n/100 PY, number of patients with at least 1 E/100 PY).
†AEs reported for ≥10 E/100 PY in any treatment group.

- Incidencia de SAEs similar en todos los grupos
- La incidencia de eventos cardiovasculares y tromboembólicos fue <0,1 por 100PY.
- La incidencia de neoplasias malignas fue similar a la esperada para la población general
- La incidencia de anemia o neutropenia graves fue infrecuente
- La elevación de LDL y HDL se estabiliza en el tiempo

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UPADACITINIB: RCT

RMD Open
Rheumatic & Musculoskeletal Diseases
ORIGINAL RESEARCH

Safety profile of upadacitinib over 15 000 patient-years across rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis and atopic dermatitis

Table 2 Exposure and overview of TEAEs

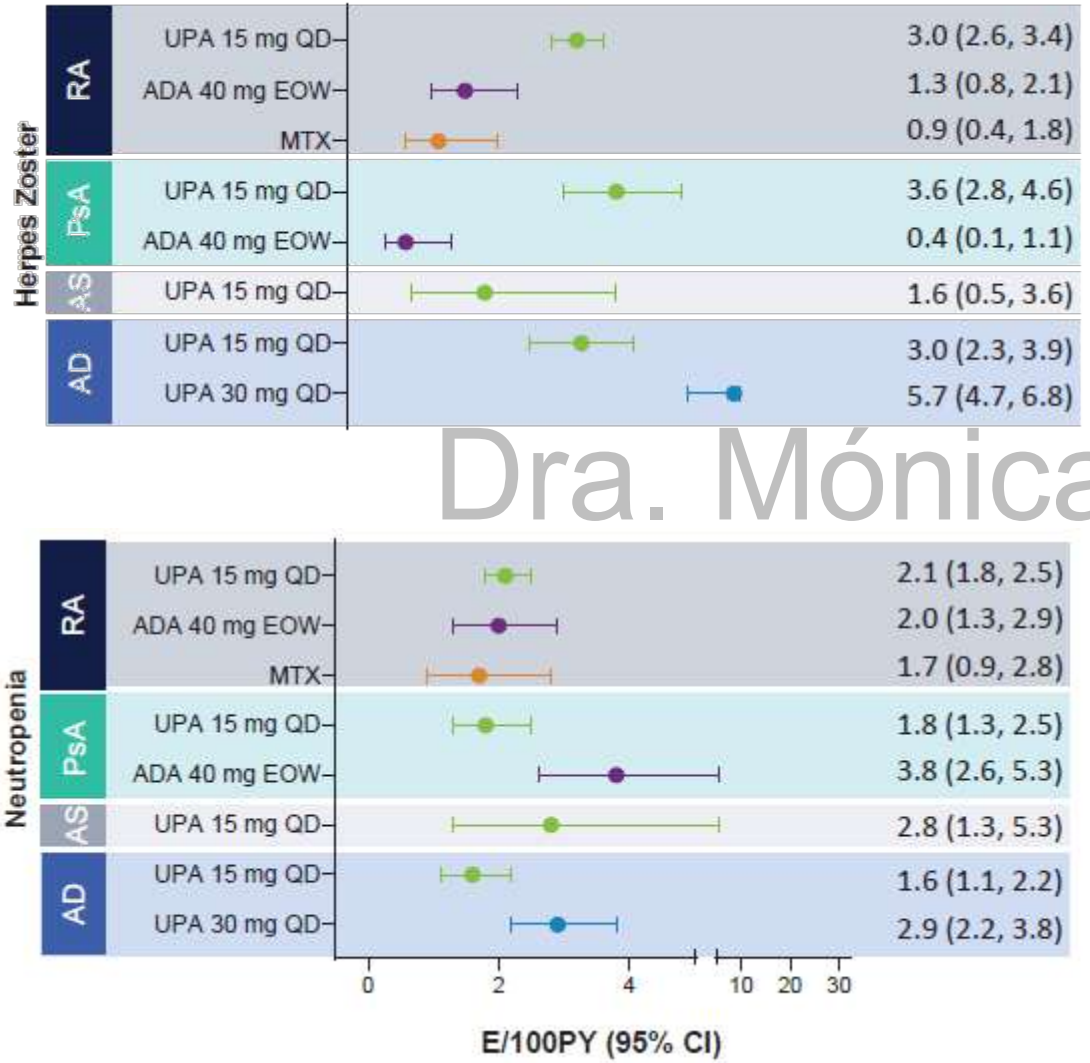
Parameter	RA			PsA		AS	AD	
	UPA 15 mg QD N=3209	ADA 40 mg EOW N=579	MTX N=314	UPA 15 mg QD N=907	ADA 40 mg EOW N=429	UPA 15 mg QD N=182	UPA 15 mg QD N=1340	UPA 30 mg QD N=1353
Exposure								
Total (PY)	9079.1	1307.7	781.7	1872.3	903.7	320.1	2035.8	2118.0
Median (minimum, maximum) (years)*	3.46 (0, 5.45)	2.23 (0.04, 5.44)	2.57 (0.02, 5.15)	2.25 (0, 3.9)	1.5 (0.04, 3.22)	1.76 (0.02, 3.26)	1.62 (0, 2.75)	1.65 (0, 2.84)
Overall TEAEs, E/100 PYs (95% CI)								
Any AE	205.5 (202.5, 208.5)	208.3 (196.0, 221.5)	209.9 (196.9, 223.7)	244.3 (237.3, 252.0)	259.9 (240.3, 280.0)	241.2 (224.5, 259.8)	260.5 (248.7, 272.5)	278.1 (271.0, 285.2)
Any serious AE	12.4 (11.7, 13.2)	13.7 (11.8, 15.8)	9.6 (7.5, 12.0)	11.1 (9.7, 12.7)	9.0 (7.1, 11.1)	6.6 (4.1, 10.0)	7.1 (6.0, 8.4)	8.2 (7.0, 9.5)
Any AE leading to discontinuation	4.9 (4.4, 5.3)	5.9 (4.6, 7.4)	5.8 (4.2, 7.7)	5.4 (4.4, 6.6)	5.5 (4.1, 7.3)	5.3 (3.1, 8.5)	4.5 (3.6, 5.5)	5.3 (4.4, 6.4)
Deaths,† E/100 PY (95% CI)	0.8 (0.6, 1.0)	0.9 (0.5, 1.6)	0.8 (0.3, 1.7)	0.8 (0.4, 1.3)	0.1 (0.0, 0.6)	0	0	0.1 (0.0, 0.4)

*Minimum in days are as follows: RA: UPA 15 mg, 2 days; ADA 40 mg, 14 days; MTX, 7 days. PsA: UPA 15 mg, 1 day; ADA 40 mg, 14 days. AS: UPA 15 mg, 6 days. AD: UPA 15 mg, 1 day; UPA 30 mg, 1 day.
†Non-treatment emergent deaths included.
AD, atopic dermatitis; ADA, adalimumab; AE, adverse event; AS, ankylosing spondylitis; EOW, every other week; MTX, methotrexate; PsA, psoriatic arthritis; E/100 PY, exposure-adjusted rates per 100 patient years; PY, patient-years; QD, once a day; RA, rheumatoid arthritis; TEAE, treatment-emergent adverse event; UPA, upadacitinib.

- SAEs: más frecuentes en AR.
- En DA, la incidencia de SAEs fue superior para la dosis de 30mg frente a 15mg.

UPADACITINIB: RCT

RMD Open
Rheumatic & Musculoskeletal Diseases
ORIGINAL RESEARCH
Safety profile of upadacitinib over 15 000 patient-years across rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis and atopic dermatitis



- El **acné** fue uno de los TEAEs más frecuente en AD, con muy baja incidencia en el resto de grupos (edad, evaluación por dermatólogos)
- **Infección por VHZ dosis-dependiente**. Fueron leves-moderados.
- Las alteraciones hematológicas fueron en su mayoría de grado 1 o 2 y transitorias
- Las neoplasias (excluyendo NMSC), MACEs y eventos tromboembólicos ocurrieron con una incidencia similar a la de los comparadores activos adalimumab y metotrexato
- Estas fueron numéricamente inferiores en DA comparado con AR.

UPADACITINIB: RWE

Upadacitinib for the Treatment of Atopic Dermatitis in a Spanish Cohort—Real Life: Fifty-Two–Week Follow-up Results

Jose-Juan Pereyra-Rodriguez, Pedro Herranz, Ignasi Figuras-Nart, Bibiana Perez, Marta Elosua, Monica Munera-Campos, Javier Melgosa-Ramos, Violeta Zaragoza Ninet, Juan Francisco Silvestre, Minia Campos-Dominguez, Antonio Guilabert, Javier Miquel, Sara Alcantara-Luna, Pablo de la Cueva, Esther Serra-Baldrich, and Jose Carlos Armario-Hita

Published Online: 1 Dec 2022

TABLE 1. Demographic and Clinical Characteristics of the Patients Included in This Series (N = 22)

Characteristics	Values
Age, mean ± SD (range), y	32.5 ± 14.3 (12–71)
Adolescent (12–17 y), n (%)	2 (9.1)
Sex, male, n (%)	13 (59.1)
Disease duration, mean ± SD, y	19.8 ± 9.8
BMI	24.58 ± 4.87
Comorbidities, n (%)	
Obesity	1 (4.5)
Nasal polyps	0 (0.0)
Conjunctivitis	5 (22.7)
Extrinsic asthma	9 (40.9)
Allergic rhinitis	9 (40.9)
Alimentary allergies	7 (31.8)
Patch tests performed, n (%)	20 (90.9)
Clinically relevant patch tests, n (% of performed)	4 (20.0)
Previous treatments, n (%)	
Systemic corticosteroids	22 (100)
Oral cyclosporine (3–5 mg·kg^{-1}·d^{-1})	22 (100)
Phototherapy	11 (50.0)
Dupilumab*	18 (81.8)
Upadacitinib dose prescribed, 30 mg, n (%)	12 (54.5)
Baseline SCORAD, mean ± SD	60.1 ± 15.8
Baseline EASI, mean ± SD	27.8 ± 8.1
Baseline Peak Pruritus NRS, mean ± SD	8.0 ± 1.0
Baseline DLQI, mean ± SD	18.4 ± 5.8
Baseline PGA = 4	16, 72.7

*Two patients (11.1%) discontinued dupilumab because of adverse effects (severe conjunctivitis) and 16 patients (88.89%) because of lack of efficacy with a mean use of 35.7 weeks and a median of 24 weeks.

BMI, body mass index; DLQI, Dermatology Life Quality Index; EASI, Eczema Area and Severity Index; NRS, Numerical Rating Scale; PGA, patient global assessment; SCORAD, SCORing Atopic Dermatitis.

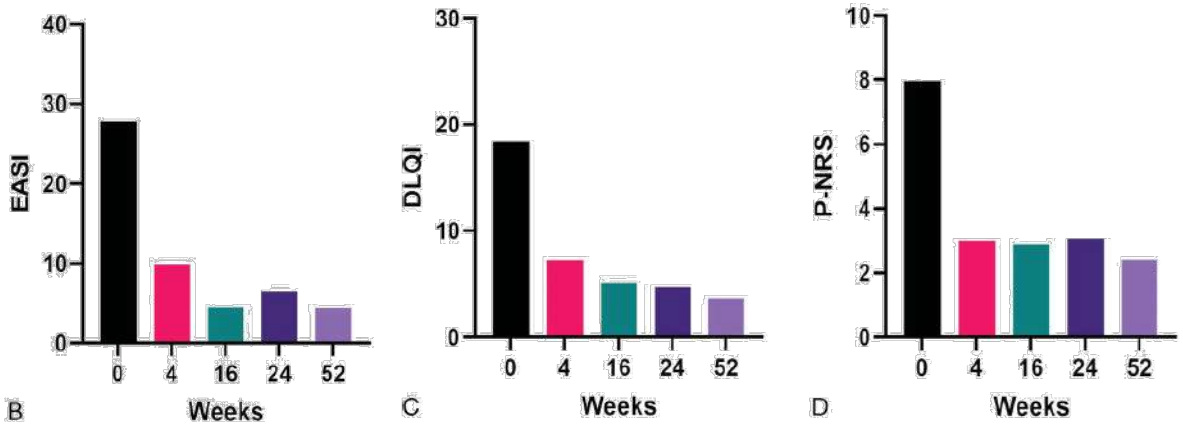
22 patients (13 male) were included
The mean age of our series was 34.40 ± 13.58 years old (2 adolescents).

- 100% of the patients had received previous systemic corticosteroids
- 100% cyclosporine
- 81,8% Dupilumab

- Peak pruritus NRS reduced to 2.4 (SD=2.9) (69.14% improvement)

- **EASI percentage change from baseline was -84,2%**
- **59,1% reached EASI75 at W52 and 55,5% EASI90.**
- **62.79% reached an IGA 0/1 at the end of the follow-up period.**

- The most frequent AE was acne (31,8%).
- 1 patient (2.33%) discontinued the drug due to adverse effects (loss of strength and asthenia).
- Only one patient had recurrent herpes
- Laboratory abnormalities were only found in 1 case (2-point drop in hemoglobin from 13,4 to 11,5g/dl) during follow-up.



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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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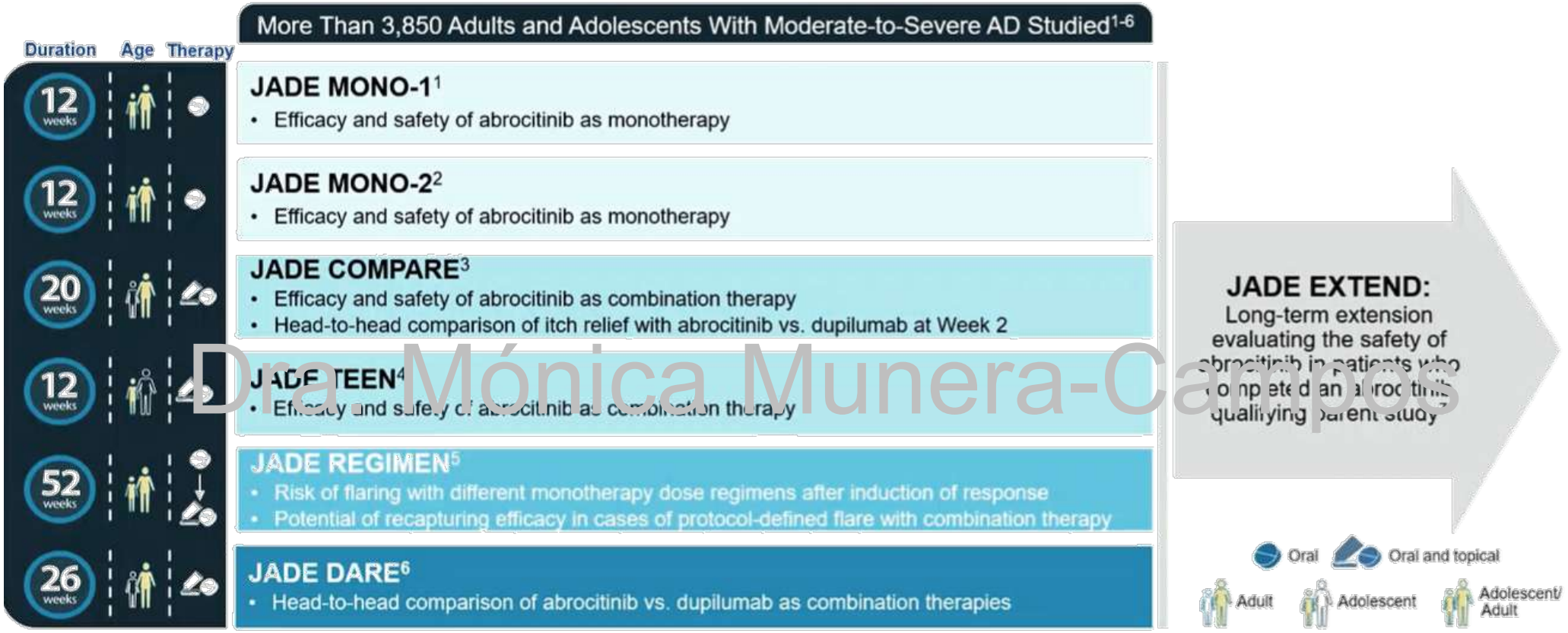
ABROCITINIB: RCT

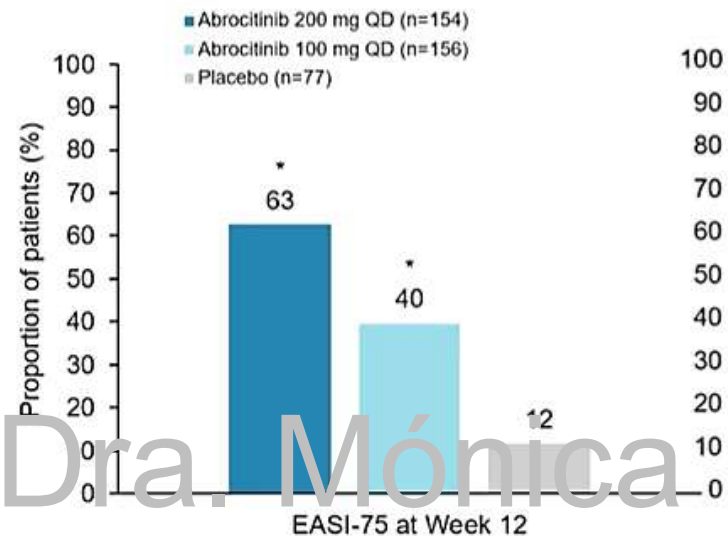


1. Simpson EL, et al. *Lancet*. 2020;396(10246):255-266. **2.** Silverberg JI, et al. *JAMA Dermatol*. 2020;156(8):863-873. **3.** Bieber T, et al. *N Engl J Med*. 2021;384(12):1101-1112. **4.** Eichenfield LF, et al. [published correction appears in *JAMA Dermatol*. 2021 Oct 1;157(10):1246]. *JAMA Dermatol*. 2021;157(10):1165-1173. **5.** Blauvelt A, et al. *J Am Acad Dermatol*. 2022;86(1):104-112. **6.** Reich K, et al. *Lancet*. 2022;400(10348):273-282. **7.** Shi VY, et al. *J Am Acad Dermatol*. 2022;S0190-9622(22)00608-9. **8.** Cibinqo Summary of Product Characteristics. Pfizer Europe MA EEIG; 2022.

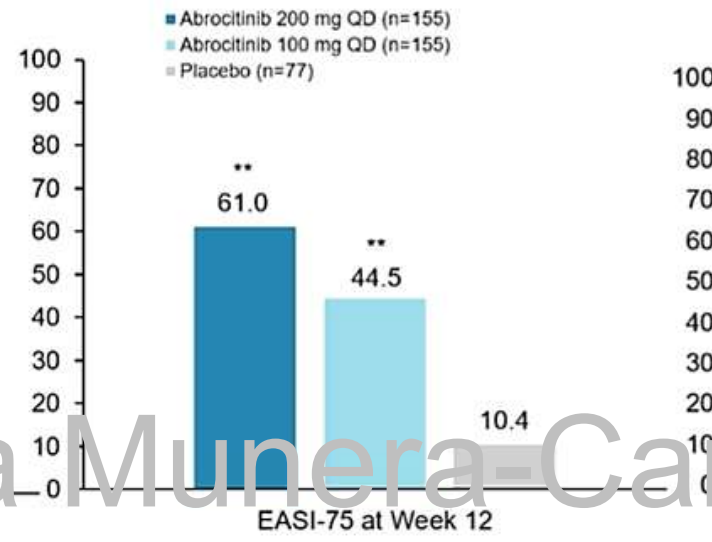
ABROCITINIB: RCT

Monotherapy

JADE MONO-1[1]

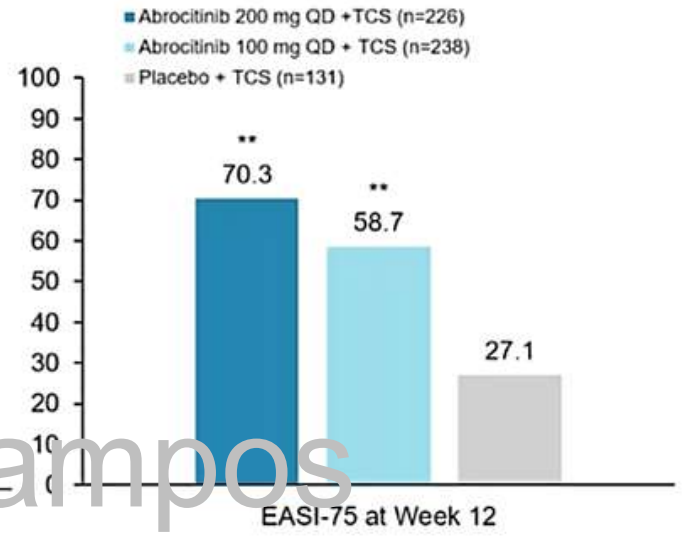


JADE MONO-2[2]

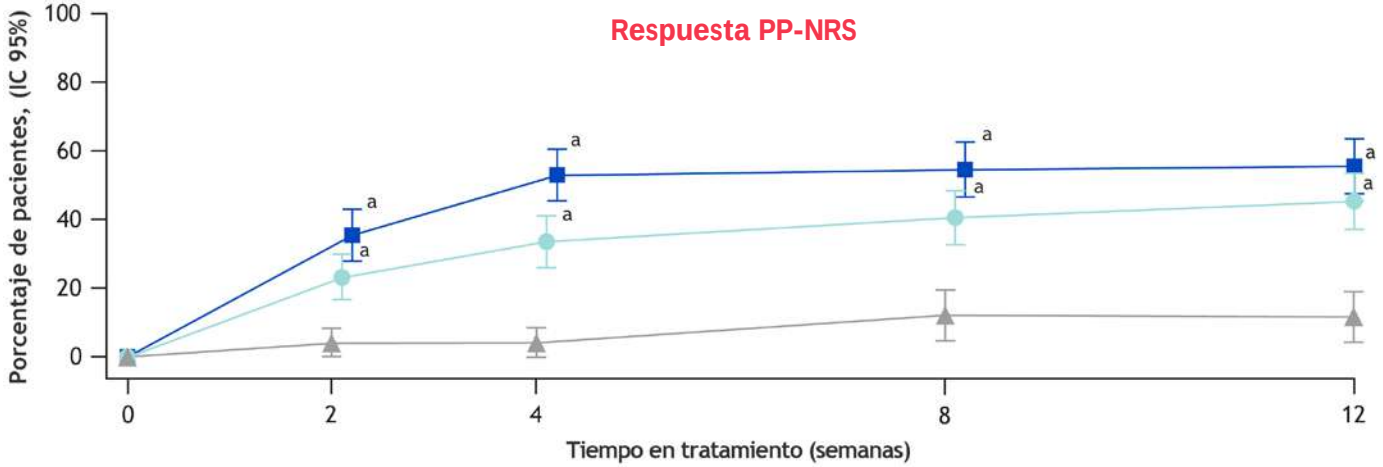


Combination therapy

JADE COMPARE[3]



Respuesta PP-NRS



1. Simpson EL, et al. Lancet. 2020;396(10246):255-266. **2.** Silverberg JI, et al. JAMA Dermatol. 2020;156(8):863-873. **3.** Bieber T, et al. *N Engl J Med*. 2021;384(12):1101-1112.

Germans Trias i Pujol Hospital

ABROCITINIB: RCT

JADE COMPARE:

- **Abrocitinib 100mg** QD + CST vs **200mg** QD + CST vs **Dupilumab** 300mg Q2W + CST vs **placebo** + CST

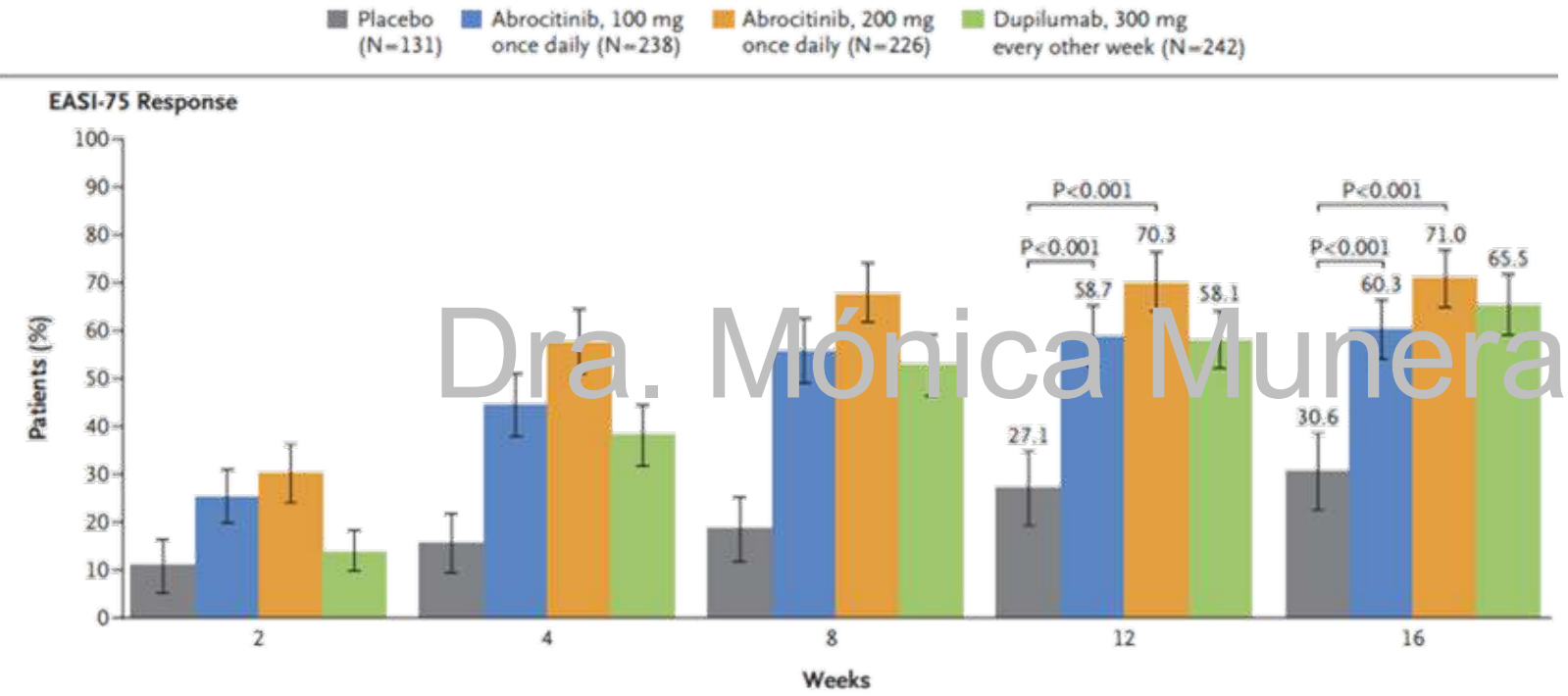
The NEW ENGLAND JOURNAL of MEDICINE

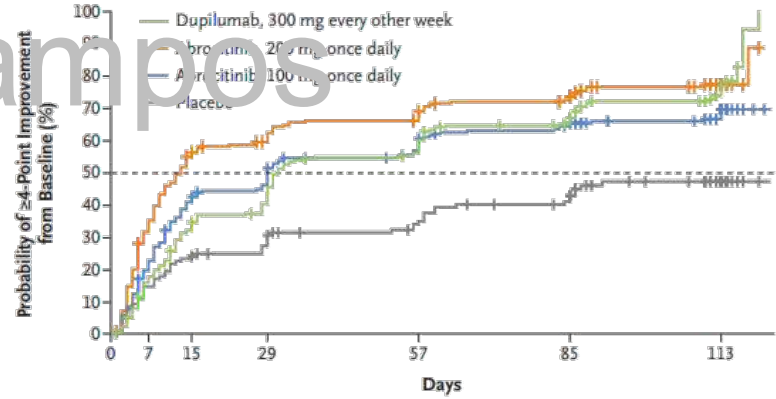
ORIGINAL ARTICLE

Abrocitinib versus Placebo or Dupilumab for Atopic Dermatitis

T. Bieber, E.L. Simpson, J.I. Silverberg, D. Thaçi, C. Paul, A.E. Pink, Y. Kataoka, C.-Y. Chu, M. DiBonaventura, R. Rojo, J. Antinew, I. Ionita, R. Sinclair, S. Forman, J. Zdybski, P. Biswas, B. Malhotra, F. Zhang, and H. Valdez, for the JADE COMPARE Investigators*

ABSTRACT





No. at Risk							
Dupilumab, 300 mg every other week	240	199	160	137	99	73	42
Abrocitinib, 200 mg once daily	226	153	100	86	70	53	24
Abrocitinib, 100 mg once daily	236	187	137	122	93	74	44
Placebo	130	110	99	89	76	65	29

Germans Trias i Pujol Hospital

ABROCITINIB: RCT

American Journal of Clinical Dermatology
https://doi.org/10.1007/s40257-021-00618-3

ORIGINAL RESEARCH ARTICLE

Integrated Safety Analysis of Abrocitinib for the Treatment of Moderate-to-Severe Atopic Dermatitis From the Phase II and Phase III Clinical Trial Program

Eric L. Simpson[1] · Jonathan I. Silverberg[2] · Audrey Nosbaum[3] · Kevin L. Winthrop[1] · Emma Guttman-Yassky[4] · Karin M. Hoffmeister[5,6] · Alexander Egeberg[7] · Hernan Valdez[8] · Min Zhang[9] · Saleem A. Farooqui[10] · William Romero[11] · Andrew J. Thorpe[12] · Ricardo Rojo[13] · Susan Johnson[12]

Accepted: 16 June 2021

Datos integrados de seguridad

- Efectos adversos más frecuentes

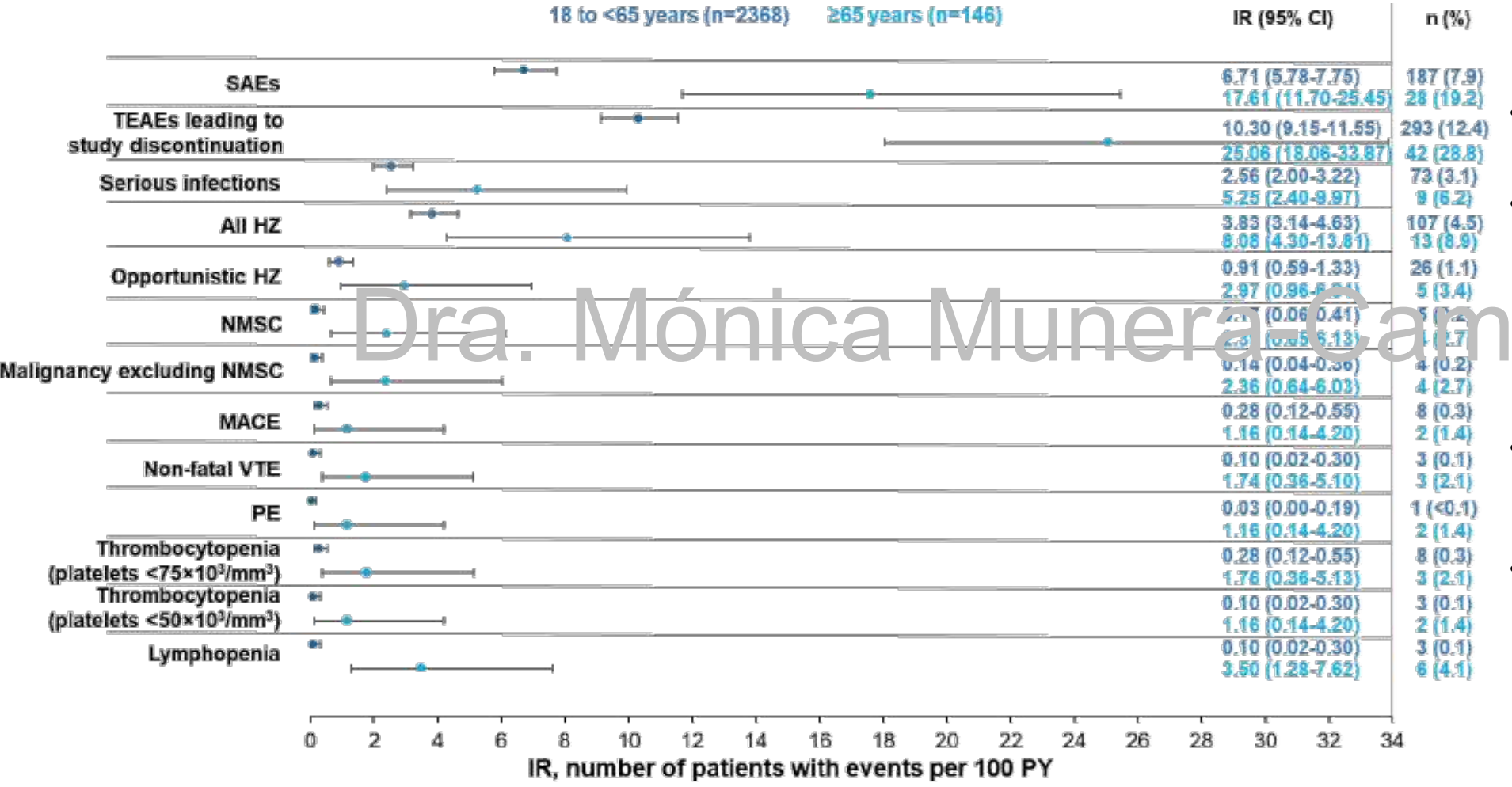
	Abrocitinib 100 mg (N=703)	Abrocitinib200 mg (N=684)	Placebo (N=438)
Nausea, n (%)	44 (**6.3**)	103 (**15.1**)	8 (1.8)
Headache, n (%)	40 (**5.7**)	54 (**7.9**)	19 (4.3)
Acne, n (%)	13 (**1.8**)	33 (**4.8**)	1 (0.2)
Herpes simplex, n (%)	2[illegible] (**2.8**)	29 (**4.2**)	6 (1.4)
Creatine phosphokinase increased >5 × ULN, n (%)	13 (1.8)	26 (3.8)	8 (1.8)
Vomiting, n (%)	13 (1.8)	24 (3.5)	2 (0.5)
Dizziness, n (%)	11 (1.6)	23 (3.4)	4 (0.9)
Abdominal pain upper, n (%)	4 (0.6)	15 (2.2)	0 (0.0)
Herpes zoster, n (%)	4 (0.6)	8 (1.2)	0 (0.0)

- La mayoría de efectos adversos frecuentes fueron dosis-dependiente
- Las náuseas eran en su mayoría leves a moderadas, y suelen resolverse hacia las 2 semanas de tratamiento. Se aconseja la toma con comida.

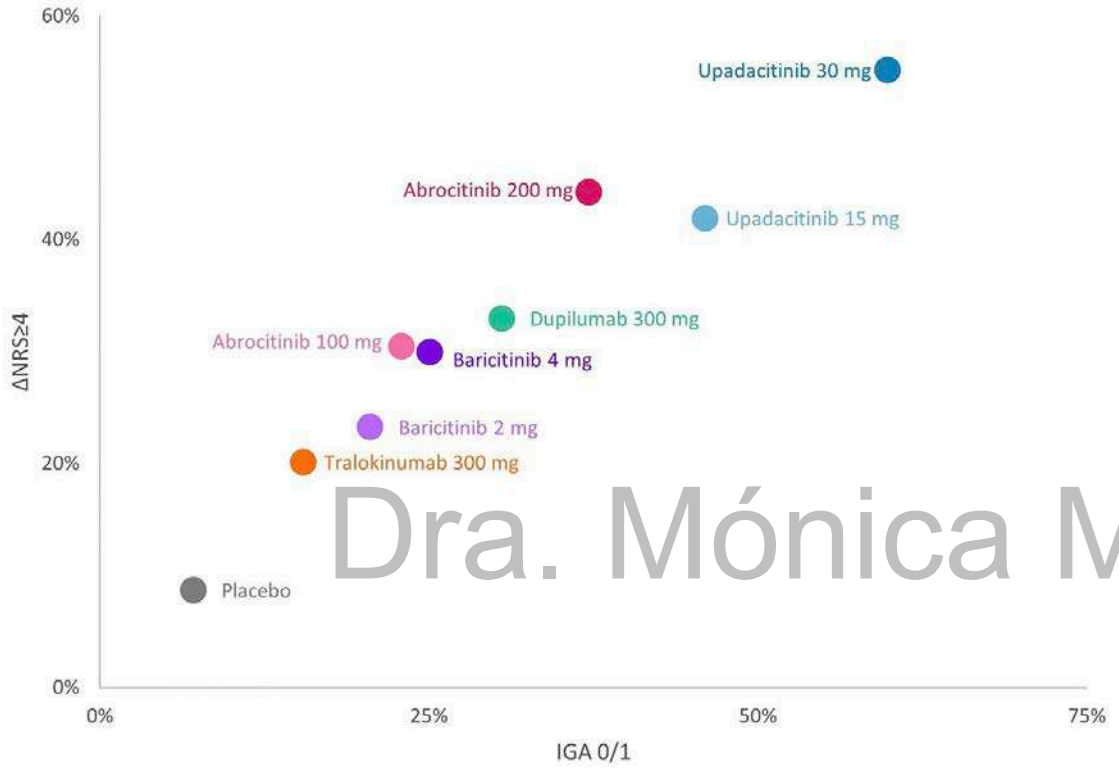
ABROCITINIB: RCT

Datos integrados de seguridad: largo plazo

3802 pacientes (exposición: 5213,9 pacientes-año) de 7 ensayos clínicos de fase 2/3 (**Fase 2b, MONO-1, MONO-2, COMPARE, TEEN, DARE y REGIMEN)** y un ensayo de extensión a largo plazo **(EXTEND).**



- **Infecciones graves más frecuentes:** herpes zoster, herpes simple y neumonía
- La mayoría de infecciones por **herpes zóster** fueron cutáneas; 2 (5%) fueron extracutáneas (1 caso de infección por VVZ diseminado, 1 caso de meningitis grave por VVZ). Hubo una tendencia, no significativa, a una asociación a infección por VVZ dosis-dependiente
- Las IRs para neoplasias y eventos cardiovasculares fueron superiores para los pacientes ≥65 años.
- Las IRs para trombocitopenia y linfopenia fueron superiores para los pacientes ≥65 años.



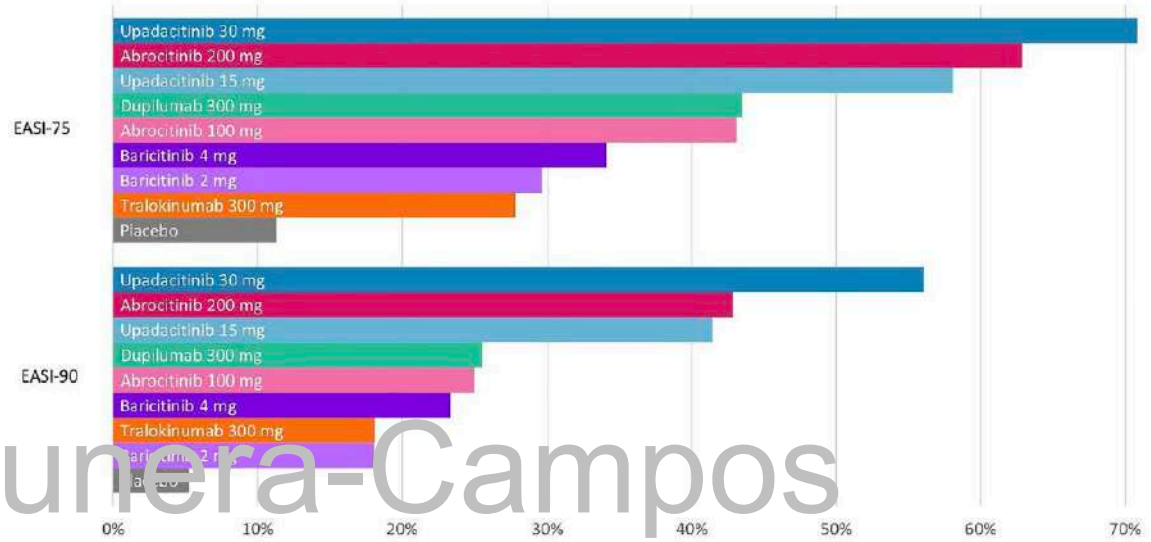


Fig. 3 EASI-75 and EASI-90 absolute response rate estimates for moderate to severe atopic dermatitis (primary endpoint timepoint). *EASI* Eczema Area and Severity Index

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 Dominguez-Cruz[3], Manuel Galán-Gutiérrez[4], Ricardo Ruiz-Villaverde[5], Samuel Vilar-Palomo[6] and José-Carlos Armario-Hita[7]

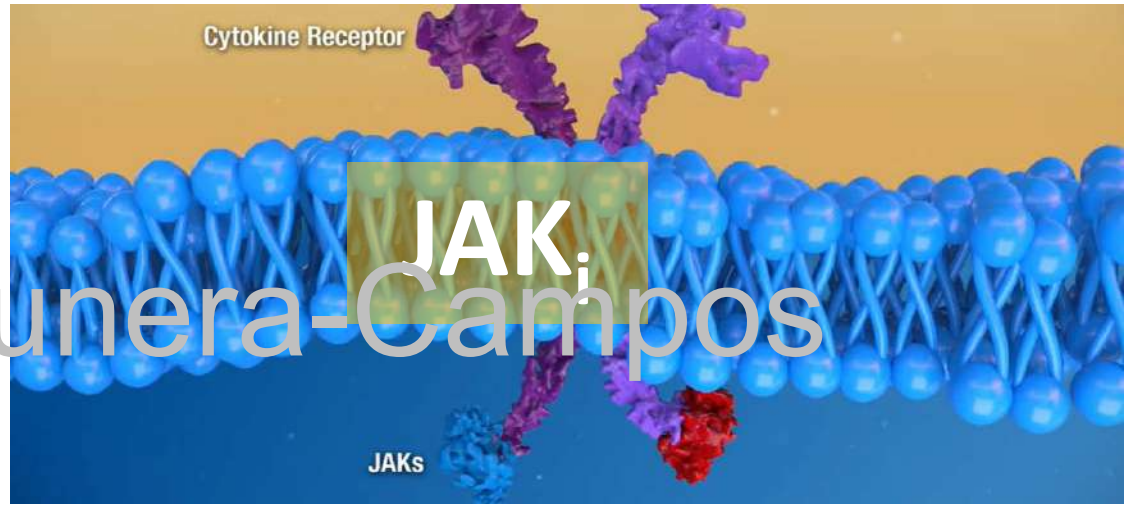
Dermatol Ther (Heidelb) (2022) 12:1181–1196
https://doi.org/10.1007/s13555-022-00721-1

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

Poblaciones y perfiles clínicos en DA



Germans Trias i Pujol Hospital

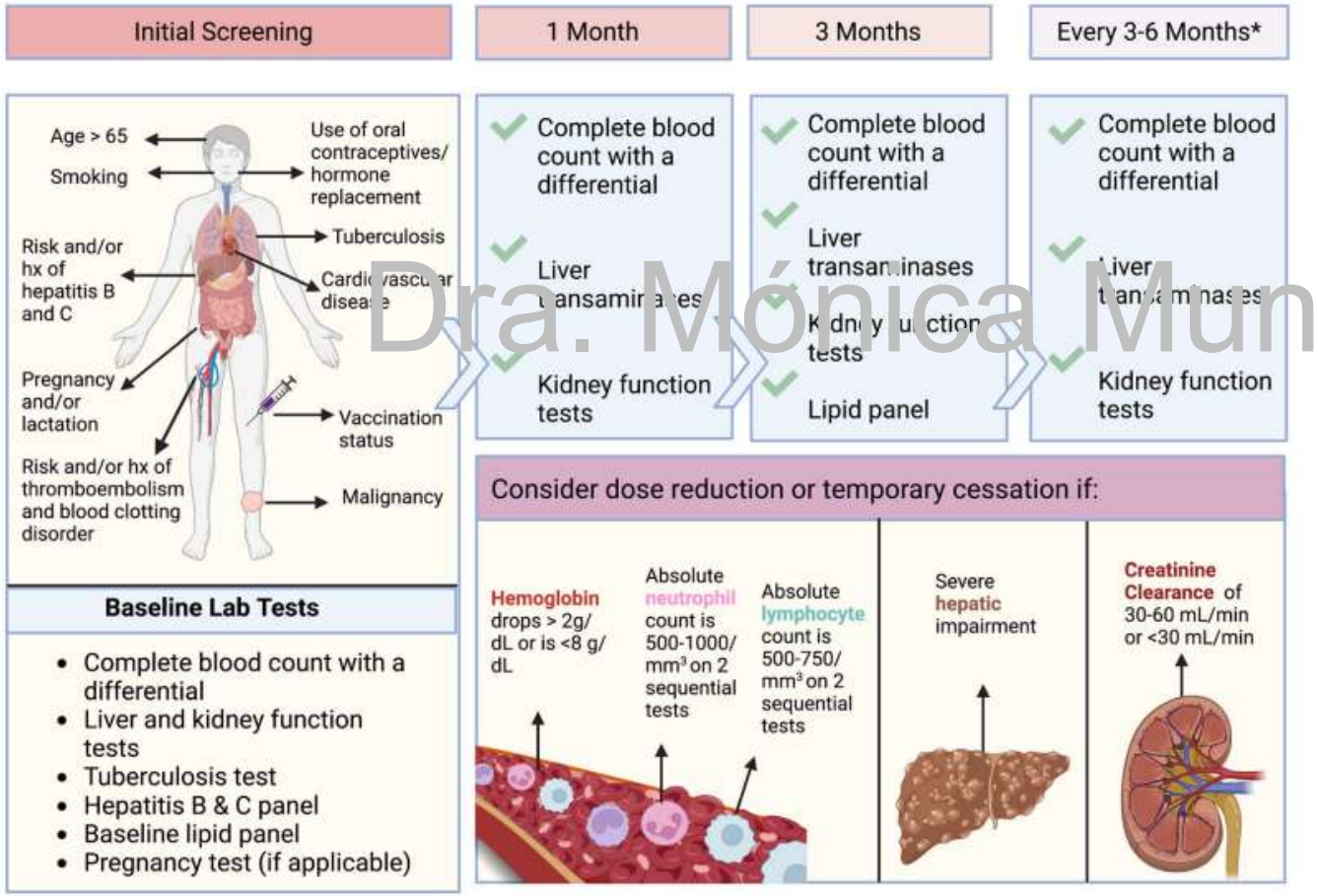
27 January 2023
EMA/27681/2023

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

EMA confirms measures to minimise risk of serious side effects with Janus kinase inhibitors for chronic inflammatory disorders

These medicines (Xeljanz, Cibinqo, Olumaint, Rinvoq and Jyseleca) should only be used in the following patients if no suitable treatment alternatives are available

- **aged 65 years or above**
- current or past long-time **smokers**
- history of **atherosclerotic cardiovascular disease or other cardiovascular risk factors**
- or those with **other malignancy risk**.



Dermatol Ther (Heidelb) (2023) 13:729–749
https://doi.org/10.1007/s13555-023-00892-5

REVIEW

A Review on the Safety of Using JAK Inhibitors in Dermatology: Clinical and Laboratory Monitoring

Christeen Samuel · Hannah Cornman · Anusha Kambala · Shawn G. Kwatra

Received: October 31, 2022 / Accepted: January 17, 2023 / Published online: February 15, 2023

Table 3 Conditions where JAK inhibitor use is not appropriate

JAK inhibitor use has higher risks in the following conditions:
Active cancer (or history of several cancers)
Active or recurrent shingles despite vaccination
Severe recurrent infections and/or frequent hospitalization for serious infections
Previous DVT and/or high risk for DVT without receiving anticoagulation
Pregnancy, breast-feeding, and/or patients considering pregnancy
Patients receiving other immunosuppressive therapies, such as transplant patients
Severe organ failure such as decompensated cirrhosis and end-stage renal disease requiring dialysis due to limited data in these populations

Germans Trias i Pujol Hospital

JOURNAL OF DERMATOLOGICAL TREATMENT
2022, VOL. 33, NO. 7, 3028–3033
https://doi.org/10.1080/09546634.2022.2102121

Taylor & Francis
Taylor & Francis Group

ARTICLE

Check for updates

Dupilumab for the treatment of adult atopic dermatitis in special populations

Cataldo Patruno[a], Luca Potestio[b], Massimiliano Scalvenzi[b], Teresa Battista[b], Flavia Raia[b], Vincenzo Picone[b], Gabriella Fabbrocini[b] and Maddalena Napolitano[c]

[a]Department of Health Sciences, University Magna Graecia of Catanzaro, Catanzaro, Italy; [b]Section of Dermatology – Department of Clinical Medicine and Surgery, University of Naples Federico II, Napoli, Italy; [c]Department of Medicine and Health Sciences Vincenzo Tiberio, University of Molise, Campobasso, Italy

27 January 2023
EMA/27681/2023

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Situaciones “No-JAK”

EMA confirms measures to minimise risk of serious side effects with Janus kinase inhibitors for chronic inflammatory disorders

Table 1. Clinical history and atopic dermatitis severity at baseline of SPs cohort (Group A).

Patient	Disease	Time*	Management	EASI	DLQI	P-NRS
1	Kidney Failure	7	C: Dialysis	25	25	10
2	Thyroid cancer	12	P: Surgery	32	25	10
3	Endometrial cancer	8	P: Surgery	32	26	9
4	Hepatitis C	9	P: Interferon + Ribavirine	30	30	10
5	Meningioma	22	P: Surgery	40	27	10
6	Kidney Failure	1	C: Dialysis	30	26	9
7	Hepatic transplant	17	C: Tacrolimus + Mycophenolate Mofetil	26	25	10
8	Monoclonal gammopathy	6	Follow up	30	30	10
9	Hepatitis C	1	P: Sofosbuvir + Ledipasvir	24	10	6
10	Parkinson disease	4	C: Levodopa	25	30	10
11	Acquired Immunodeficiency Syndrome	5	C: Emtricitabine + Tenofovir + Dolutegravir	30	25	10
12	Kidney Failure	2	C: Dialysis	24	20	10
13	Colorectal cancer	3	P: Surgery	25	10	18
14	Acquired Immunodeficiency Syndrome	4	C: Emtricitabine + Rilpivirine + Tenofovir	26	15	10
15	Kidney Failure	4	C: Dialysis	25	20	10
16	Osteosarcoma	6	P: Surgery	26	15	7
17	Hepatitis B	10	P: Tenofovir	24	20	10
18	Metastatic melanoma	1	C: Nivolumab	25	25	10
19	Kidney Failure	2	C: Dialysis	24	20	8
20	Renal cell carcinoma	2	C: Pembrolizumab	25	25	10
21	Renal Transplant	0	C: Everolimus + Tacrolimus	24	20	10
22	Hepatitis C	10	P: Interferon + Ribavirine	24	10	7
23	Multiple sclerosis	3	C: Dimethyl fumarate	30	28	10
24	Hepatitis B	4	C: Entecavir	25	26	10
25	Breast cancer	2	C: Tamoxifen	26	15	10

*Years between disease diagnosis and dupilumab starting. C: concomitant. P. previous. EASI: Eczema Area Severity Index; DLQI: Dermatology Life Quality Index; P-NRS: Pruritus—Numerical Rating Scale.

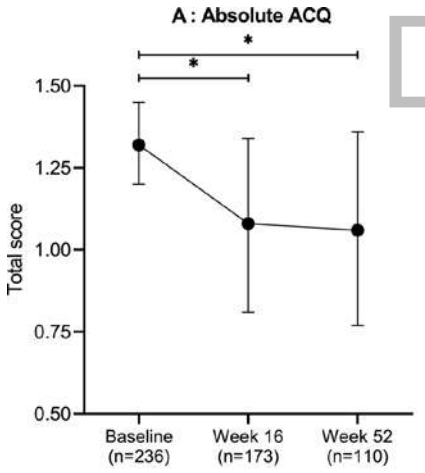
Germans Trias i Pujol Hospital

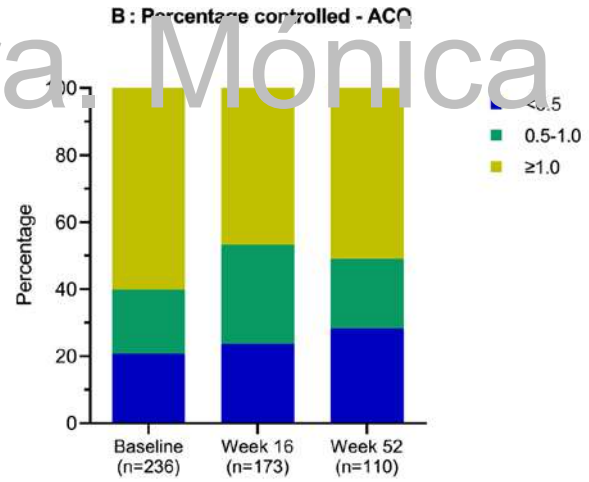
COMORBILIDADES: **ASMA**

CTA Clinical and Translational Allergy
LETTER | Open Access
The positive effect of dupilumab on comorbid asthma in patients with atopic dermatitis
Lotte S. Spekhorst, Marlies de Graaf, Lisa P. van der Rijst, Nicolaas P. A. Zuithoff, René C. Schweizer, Marijke Kamsteeg, Inge Haeck, Anneke M. T. van Lynden-van Nes, Paula van Lumig ... See all authors
First published: 16 January 2023 | https://doi-org.are.uab.cat/10.1002/clt2.12219

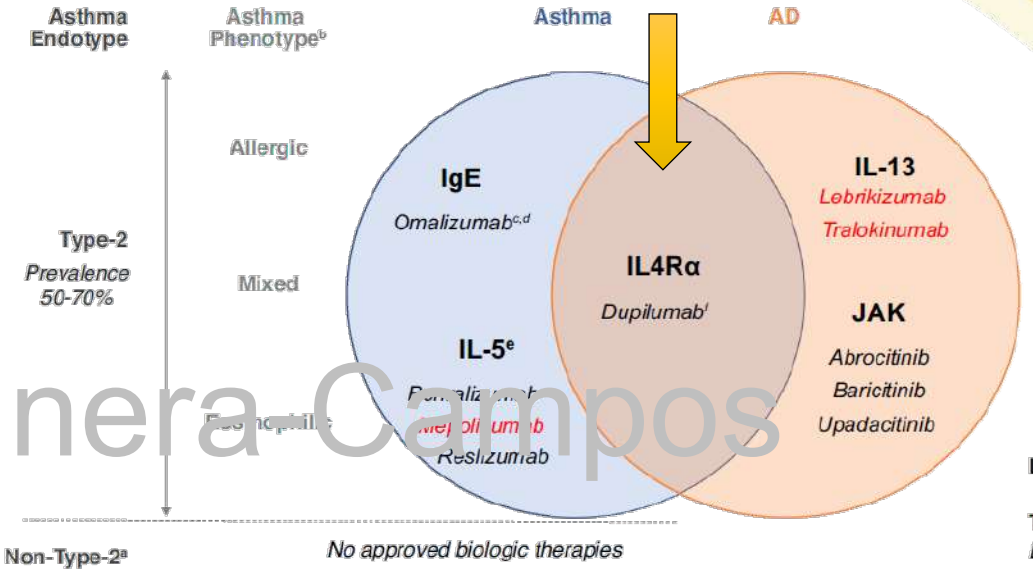
BioDay Eczema and Atopic Diseases Registry

304 pacientes con DA tratados con dupilumab, con asma





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



For patients with AD and comorbid asthma, inhibition of IL-4 and IL-13 via blockade of the IL-4 receptor (IL4R) is effective for both conditions. Medications singly targeting IL-4 or IL-13 have failed in asthma to date. Medications targeting IL-5 have failed in AD to date.

JAKis are in early phase studies for asthma management.

Apart from prednisone, traditional systemic medications used to treat patients with AD (AZA, CsA, MMF, and MTX) play no role in the treatment of comorbid asthma.

Germans Trias i Pujol Hospital

COMORBILIDADES: otras comorbilidades T2

ORIGINAL ARTICLE

Allergen-Specific Immunotherapy and Biologics

Efficacy of dupilumab in atopic comorbidities associated with moderate-to-severe adult atopic dermatitis

Original Article

Dupilumab Improves Asthma and Sinonasal Outcomes in Adults with Moderate to Severe Atopic Dermatitis

Mark Boguniewicz, MD[a,b], Lisa A. Beck, MD[c], Lawrence Sher, MD[d], Emma Guttman-Yassky, MD, PhD[e,f], Diamant Thaçi, MD[g], Andrew Blauvelt, MD, MBA[h], Margitta Worm, MD[i], Jonathan Corren, MD[j], Weily Soong, MD[k], Peter Lio, MD[l], Ana B. Rossi, MD[m], Yufang Lu, MD[n], Jingdong Chao, PhD[n], Laurent Eckert, PhD[o], Abhijit Gadkari, PhD[n], Thomas Hultsch, MD[m], Marcella Ruddy, MD[n], Leda P. Mannent, MD[n], Neil M.H. Graham, MD[n], Gianluca Pirozzi, MD[p], Zhen Chen, PhD[n,*], and Marius Ardeleanu, MD[n,*] *Denver, Colo; Rochester, Tarrytown, and New York, NY; Rolling Hills Estates and Los Angeles, Calif; Portland, Ore; Birmingham, Ala; Chicago, Ill; Cambridge, Mass; Bridgewater, NJ; Lübeck and Berlin, Germany; and Chilly-Mazarin, France*

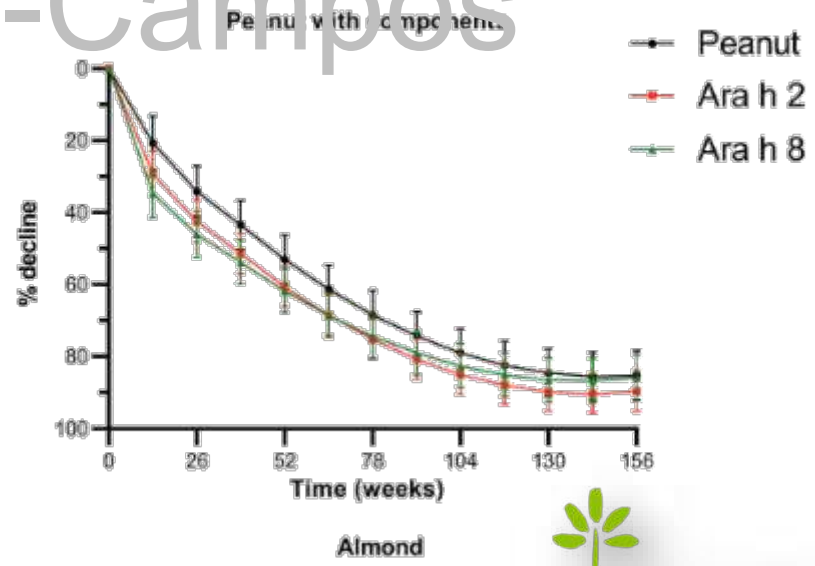
Anti–IL-4Rα	Dupilumab	NCT03793608 NCT04148352	II	Aged 6-17 y, with peanut allergy Aged 4-50 y, with cow's milk allergy	Proportion of patients treated with dupilumab monotherapy to pass DBPCFC with peanut protein (time frame: wk 24) Proportion of subjects treated with dupilumab plus milk protein OIT vs placebo plus milk protein OIT who tolerate at least 2040 mg (cumulative) of cow's milk protein during DBPCFC to milk at wk 18 (time frame: wk 18)
	Dupilumab + AR101 (peanut OIT)	NCT03682770	II	Aged 6-17 y, with peanut allergy	Proportion of patients who successfully complete an exit food challenge with 2044 mg of cumulative peanut protein (time frame: ≤40 wk)

Allergy. 2023 Mar;78(3):875-878. doi: 10.1111/all.15591. Epub 2022 Dec 3.

Dupilumab has a profound effect on specific-IgE levels of several food allergens in atopic dermatitis patients

BioDay Eczema and Atopic Diseases Registry

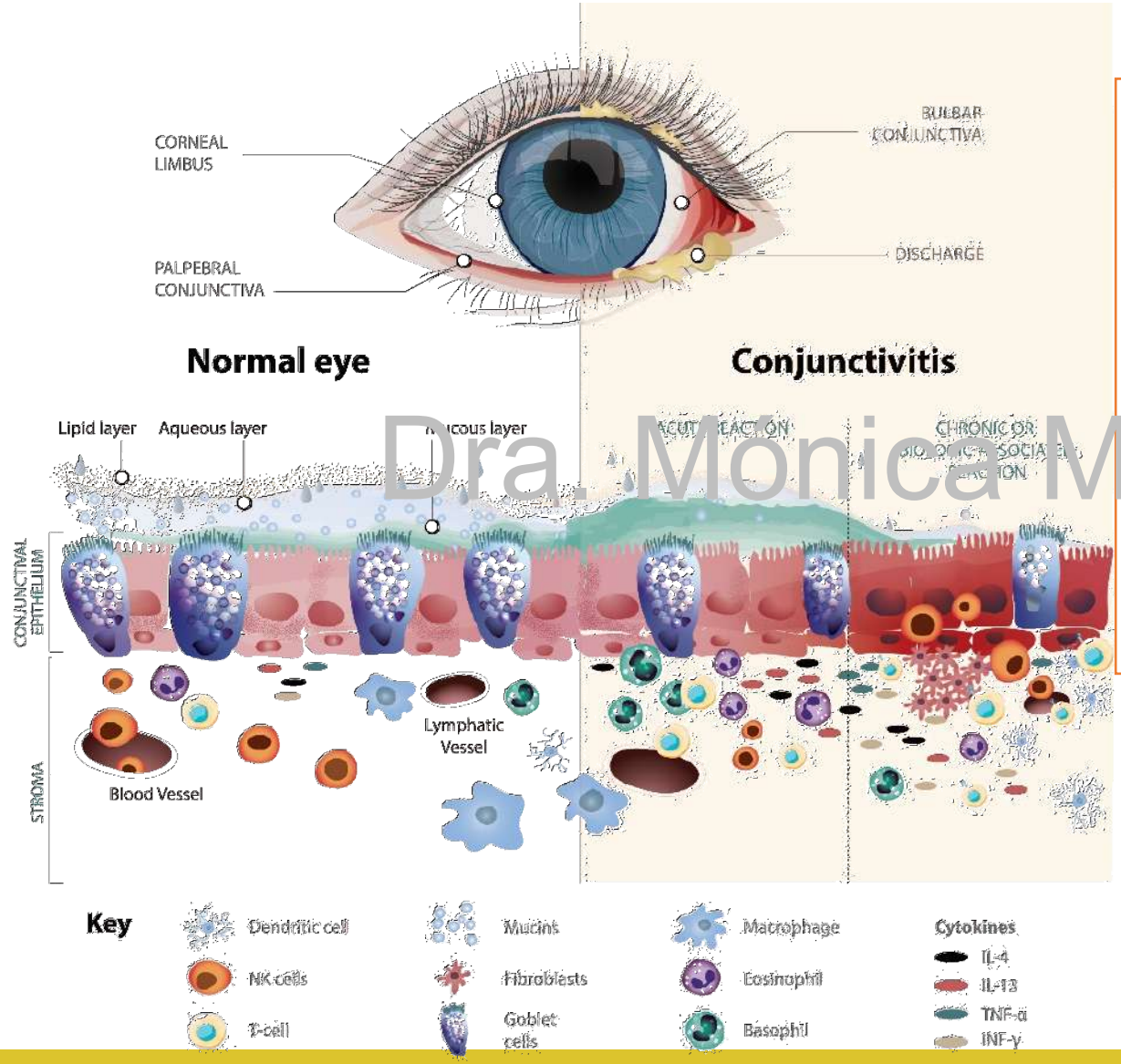
- **125 pacientes** con DA con alergia alimentaria.
- Cohorte a 3 años.
- Mayoría alérgicos a 1 (N=42; 33,6%) o 2 alimentos (N=35; 28%). Más frec: cacahuete (51,2%) y avellana (52%).
- **Observan una disminución de las IgE específicas.**
- **¿EFECTO CLÍNICO?**



Germans Trias i Pujol Hospital

Enfermedad de la Superficie Ocular

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

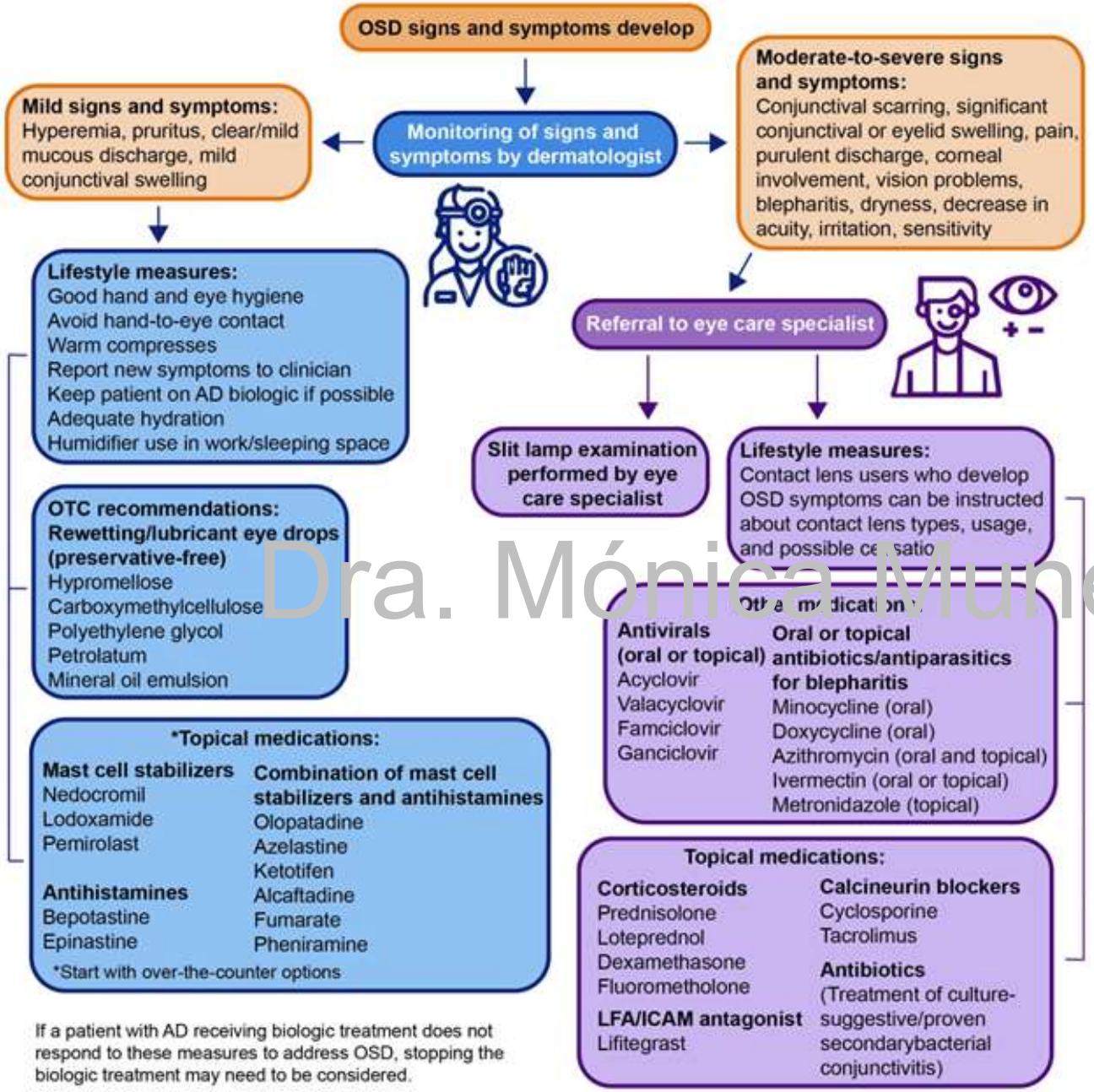
PATOGÉNESIS

- 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

Germans Trias i Pujol Hospital



REVIEW ARTICLE | ARTICLES IN PRESS

Practical management of ocular surface disease in patients with atopic dermatitis, with a focus on conjunctivitis: A review

Vivian Y. Shi, MD • Winston Chamberlain, MD, PhD • Elaine Siegfried, MD • ... Peter Lio, MD • Amy S. Paller, MD • Eric Simpson, MD • Show all authors

Published: February 14, 2023 • DOI: https://doi.org/10.1016/j.jaad.2023.01.043

PROFILAXIS

- **Ectoína**
- **Lágrimas artificiales con hialurónico**

Ej.: Hylo-Dual colirio lubricante (ectoína y hialurónico), Vidisan Alergia (ectoína), Aquoral, Monofresh.

CASOS LEVES

- **Anti-H1** (Zaditén 0,25mg/ml colirio –ketotifeno-)
- **Estabilizadores de los mastocitos** (Tebarat 0,5mg/ml, Afluon 0,5mg/ml – azelastina-)

CASOS MODERADOS-GRAVES

- **Derivar a OFT preferente**
- Corticoides (pautas descendentes)
- Tacrolimus colirio / pomada
- Ikervis (CsA oftálmica)

Germans Trias i Pujol Hospital

Enfermedad de la Superficie Ocular

n (%)	JADE COMPARE[3] PLACEBO (n=131)	ABROCITINIB 100 MG (n=238)	ABROCITINIB 200 MG (n=226)	DUPI 300 MG (n=242)
Common TEAEs[a]				
Nausea	2 (2)	10 (4)	25 (11)	7 (3)
Headache	6 (5)	10 (4)	15 (7)	13 (5)
Nasopharyngitis	9 (7)	22 (9.2)	15 (7)	23 (10)
Upper RTI	6 (5)	12 (5)	9 (4)	9 (4)
Dermatitis atopic	NR	NR	NR	NR
Herpes zoster	0	2 (1)	4 (2)	0
Eczema herpeticum	NR	NR	NR	NR
Acne	0	7 (3)	15 (7)	3 (1)
Vomiting	NR	NR	NR	NR
Conjunctivitis	3 (2)	2 (1)	3 (1)	15 (6)

n (%)	Heads Up[3] DUPI 300 MG (n=344)	UPA 30 MG (n=348)
Common TEAEs[a]		
Acne	9 (3)	55 (16)
Upper RTI	13 (4)	22 (6)
Nasopharyngitis	22 (6)	20 (6)
Headache	21 (6)	14 (4)
Dermatitis atopic	29 (8)	24 (7)
Eczema herpeticum	0	1 (0.3)
Herpes zoster	3 (1)	7 (2)
Blood CPK increased	10 (3)	23 (7)
Conjunctivitis	29 (8)	5 (1)

Ocular Adverse Events in Patients With Atopic Dermatitis Treated With Upadacitinib: A Real-Life Experience

Federica Gelato, Luca Mastorino, Pietro Quaglino, Giovanni Cavaliere, Michela Ortoncelli, and Simone Ribero

Published Online: 23 Jan 2023 | https://doi-org.are.uab.cat/10.1089/derm.2022.0063

- 14 pacientes que habían suspendido dupilumab por conjuntivitis, presentaron una resolución completa de la misma tras el cambio a upadacitinib (1 m de tratamiento)

Received: 11 January 2023 | Revised: 22 February 2023 | Accepted: 24 February 2023
DOI: 10.1111/cea.14305
RESEARCH LETTER
WILEY

Switching from dupilumab to tralokinumab in atopic dermatitis patients with ocular surface disease: Preliminary case series

- 3/4 pacientes mejoran al cambiar a tralokinumab

Th2 blockade with IL-4 and/or IL-13 inhibitors in patients with AD increases incidence of OSD; however, this increased incidence is not observed when these medications are used in other conditions including asthma, CRSwNP and EoE.

Although OSD may be induced or exacerbated by Th2 blockade with biologics, most cases are mild-to-moderate and do not warrant drug discontinuation.

When choosing a systemic treatment option for patients with a history of severe OSD, the treating dermatologist could consider starting with a JAKi or traditional systemic agent. If initiating an IL-4 and/or IL-13 inhibitor, consider an ophthalmology assessment prior to commencement of treatment.

JEADV
REVIEW ARTICLE

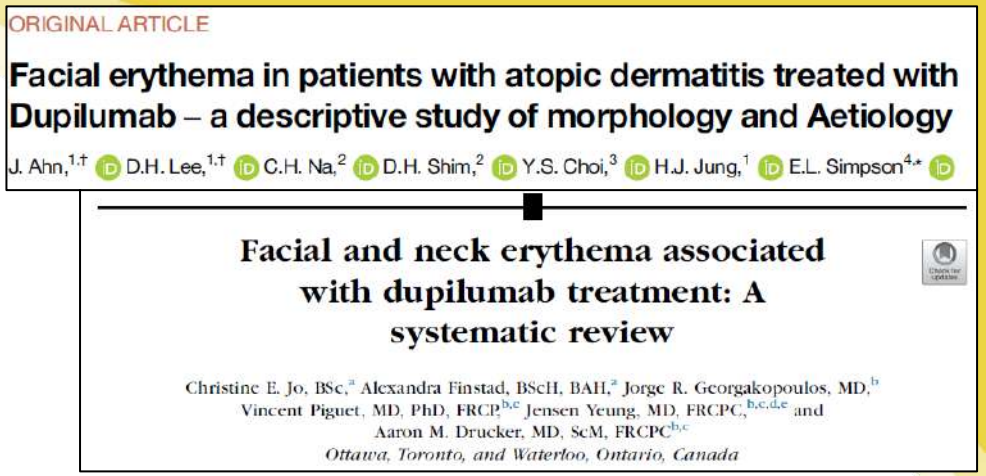
Expert consensus on the systemic treatment of atopic dermatitis in special populations

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]

Germans Trias i Pujol Hospital

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 frecuente post-pubertad.



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

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 • Some cases cleared with topical ketoconazole
Allergic contact dermatitis	• Some 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

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)
- …

Received: 7 July 2022 | Accepted: 29 November 2022

DOI: 10.1111/jdv.18849

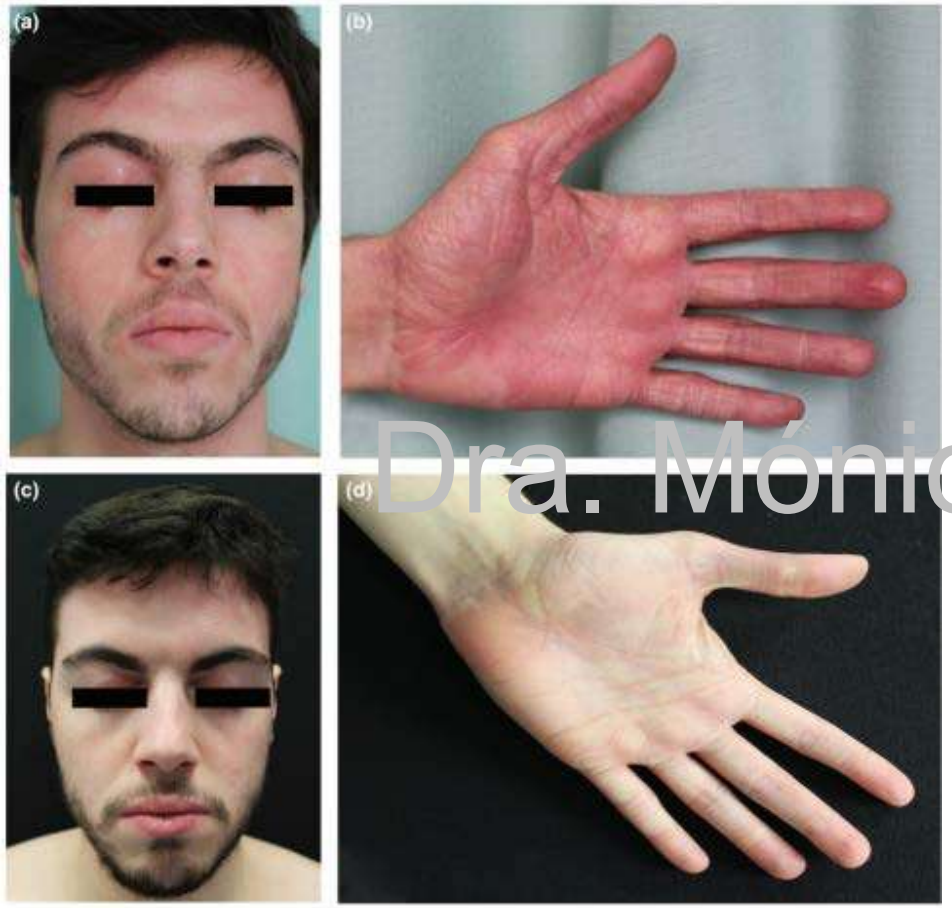
ORIGINAL ARTICLE

JEADV

A nationwide 104 weeks real-world study of dupilumab in adults with atopic dermatitis: Ineffectiveness in head-and-neck dermatitis

Germans Trias i Pujol Hospital

De novo o exacerbación: head and neck dermatitis



JEADV
JOURNAL OF THE EUROPEAN ACADEMY OF DERMATOLOGY & VENEREOLOGY

LETTER TO THE EDITOR

Newly developed erythema and red papules in the face and neck with detection of demodex during dupilumab treatment for atopic dermatitis improved by discontinuation of dupilumab, switching to upadacitinib or treatment with oral ivermectin: A report of two cases

RESEARCH LETTER | VOLUME 88, ISSUE 1, P255-257, JANUARY 2023

Dupilumab-associated head and neck dermatitis resolves temporarily with itraconazole therapy and rapidly with transition to upadacitinib, with *Malassezia*-specific immunoglobulin E levels mirroring clinical response

Emily Kozera, MD, MPH, MBeth • Akshay Flora, MD, MMed • Thomas Stewart, MBBS, MMed, MS • ...
Jennifer Xu • Mae Anne De La Vega, BSN, RN • John W. Frew, MBBS, MMed, MS, PhD

https://doi.org/10.1093/ced/llad040
Advance access publication date: 1 February 2023

Successful response to upadacitinib in the treatment of atopic dermatitis lesions involving sensitive and visible areas resistant to dupilumab treatment

Germans Trias i Pujol Hospital

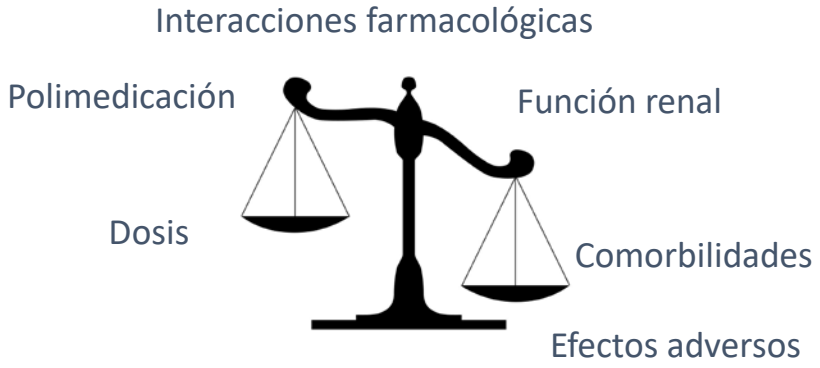
DA en mayores de >65

- **2-7%** ≥65 años tienen DA

MoAbs

- RCTs Dupilumab: 4% eran ≥ 65 años
- RCTs Tralokinumab: 4,8% eran ≥ 65 años

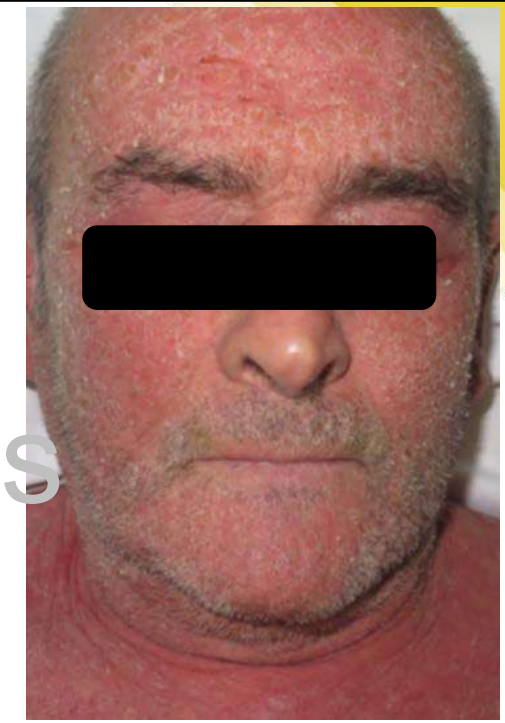
No diferencias en eficacia y seguridad



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

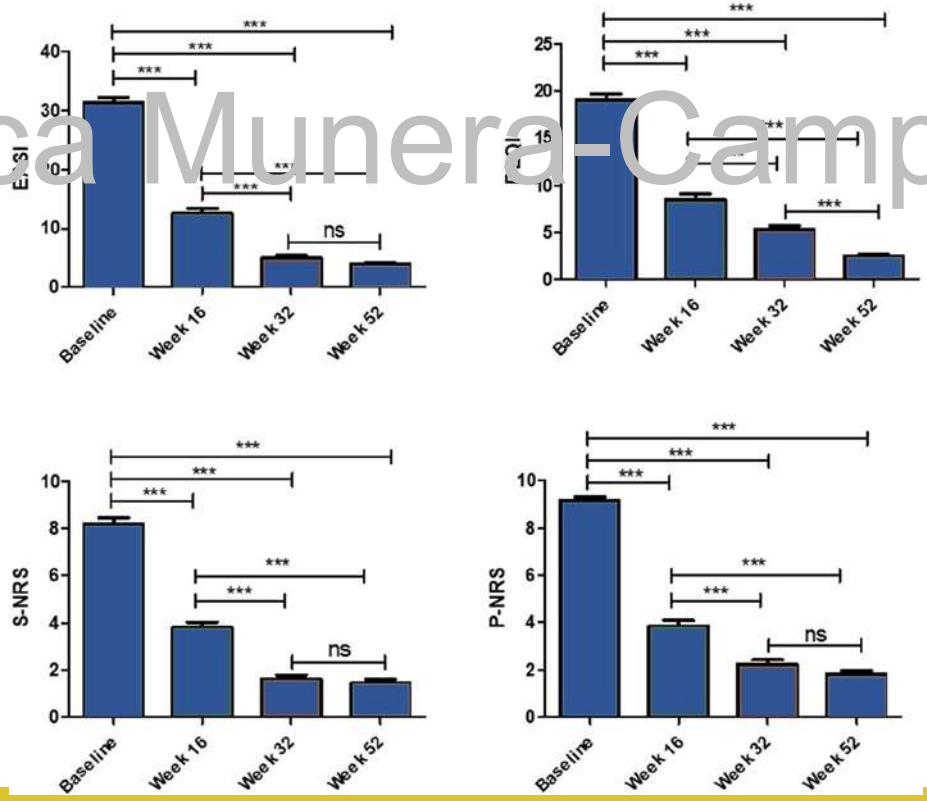
Expert consensus on the systemic treatment of atopic dermatitis in special populations

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]



Effectiveness and Safety of Long-Term Dupilumab Treatment in Elderly Patients with Atopic Dermatitis: A Multicenter Real-Life Observational Study

Cataldo Patruno[1] · Gabriella Fabbrocini[2] · Giuseppe Longo[3] · Giuseppe Argenziano[3] · Silvia Maniel Ferrucci[3] · Luca Stingeni[6] · Ketty Peris[7] · Michela Ortoncelli[8] · Annamaria Offidani[9] · Giuseppe Fabrizio Amoruso[10] · Marina Talamonti[11] · Giampiero Girolomoni[12] · Teresa Grieco[13] · Michela Iannone[14] · Eustachio Nettis[15] · Caterina Foti[16] · Franco Rongioletti[17] · Monica Corazza[18] · Michele Delli Veneri[3] · Maddalena Napolitano[19] · Dupilumab for Atopic Dermatitis of the Elderly (DADE) Study Group



- **105 pacientes**
- **Reducción media EASI: 87,2% (W52)**
- **AEs:** conjuntivitis (13,3%), eritema facial (4,8%), reacción en el punto de inyección (5,7%)
- **23,8% brotes transitorios**, tratados con corticoides tópicos

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DA en mayores de >65

	BARICITINIB	UPADACITINIB	ABROCITINIB
DOSIS	**≥75 años: 2mg/24h**	**≥65 años: 15mg/24h** *Datos limitados en >75 años: utilizar con precaución	**≥65 años: 100mg/24h** *Datos limitados en >75 años: utilizar con precaución
Ajuste ERC	**FGe >30-60ml/min:** 2mg/24h **FGe <30ml/min:** desaconsejado	**FGe >30-60ml/min:** no precisa ajuste de dosis **FGe 15-30ml/min:** 15mg/24h **FGe <15ml/min:** desaconsejado	**FGe >30-60ml/min:** 100mg/24h **FGe 15-30ml/min:** 50mg-100mg/24h **FGe <15ml/min:** desaconsejado

In elderly patients who require systemic treatment for AD, biologic therapy should be prioritized where possible. DUP has the most data supporting its use in elderly patients.

JAKis are indicated for elderly patients with AD, however elderly patients appear to be at a higher risk of adverse events compared to younger patients.

AZA and CsA are not recommended in elderly patients due to lack of data in AD and higher risk of toxicity.

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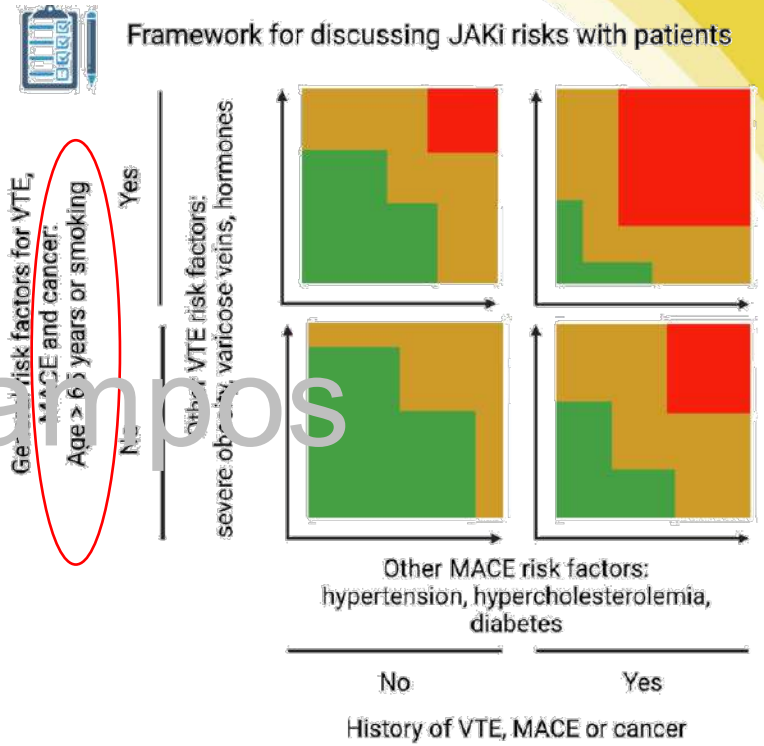

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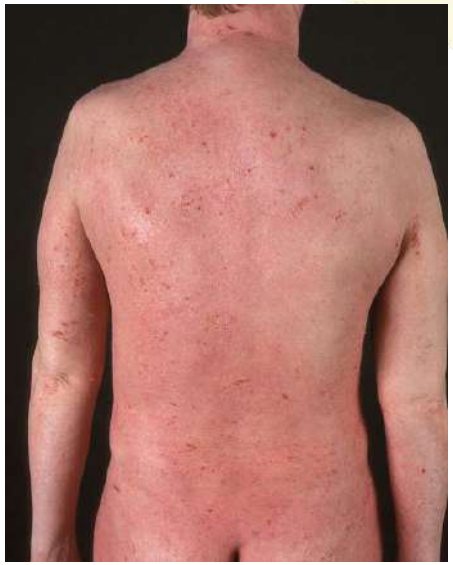
DA ERITRODÉRMICA

- 209 pacientes (adolescentes y adultos) con DA eritrodérmica
- 183 completaron 16W de tratamiento con dupilumab

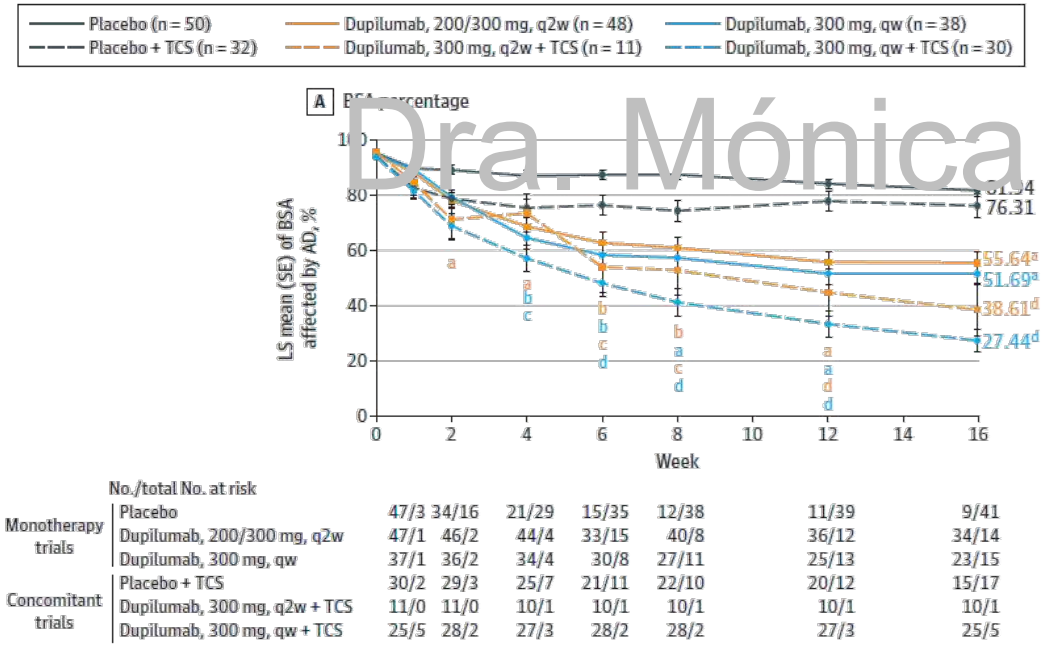


JAMA Dermatology | Original Investigation

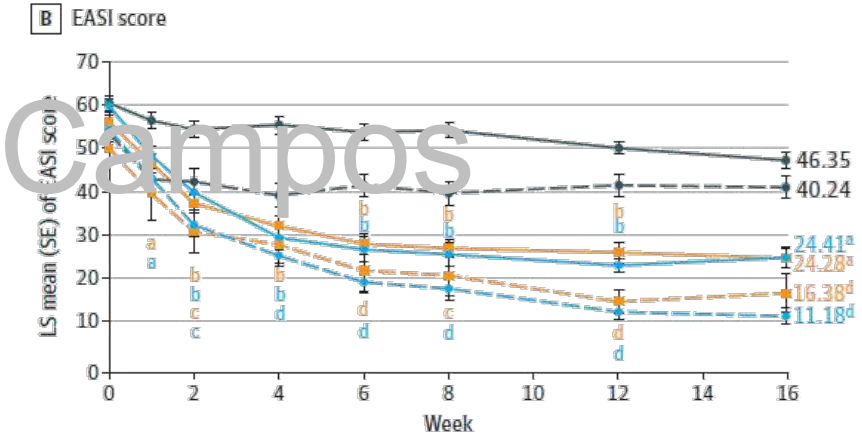
Efficacy and Safety of Dupilumab in Patients With Erythrodermic Atopic Dermatitis

A Post Hoc Analysis of 6 Randomized Clinical Trials

Amy S. Paller, MD; Jonathan I. Silverberg, MD, PhD; Michael J. Cork, PhD; Emma Guttman-Yassky, MD, PhD; Benjamin Lockshin, MD; Alan D. Irvine, MD; Moon Bum Kim, MD; Kenji Kabashima, PhD; Zhen Chen, PhD, MS, MA; Yufang Lu, MD, PhD; Ashish Bansal, MD; Ana B. Rossi, MD; Arsalan Shabbir, MD



	No./total No. at risk						
Monotherapy trials	Placebo	47/3 34/16	21/29	15/35	12/38	11/39	9/41
	Dupilumab, 200/300 mg, q2w	47/1 46/2	44/4	33/15	40/8	36/12	34/14
	Dupilumab, 300 mg, qw	37/1 36/2	34/4	30/8	27/11	25/13	23/15
Concomitant trials	Placebo + TCS	30/2 29/3	25/7	21/11	22/10	20/12	15/17
	Dupilumab, 300 mg, q2w + TCS	11/0 11/0	10/1	10/1	10/1	10/1	10/1
	Dupilumab, 300 mg, qw + TCS	25/5 28/2	27/3	28/2	28/2	27/3	25/5



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	Dupilumab, 200/300 mg, q2w	47/1 46/2	44/4	33/15	40/8	36/12	34/14
	Dupilumab, 300 mg, qw	37/1 36/2	34/4	30/8	27/11	25/13	23/15
Concomitant trials	Placebo + TCS	30/2 29/3	25/7	21/11	22/10	20/12	15/17
	Dupilumab, 300 mg, q2w + TCS	11/0 11/0	10/1	10/1	10/1	10/1	10/1
	Dupilumab, 300 mg, qw + TCS	28/2 28/2	27/3	28/2	28/2	27/3	25/5

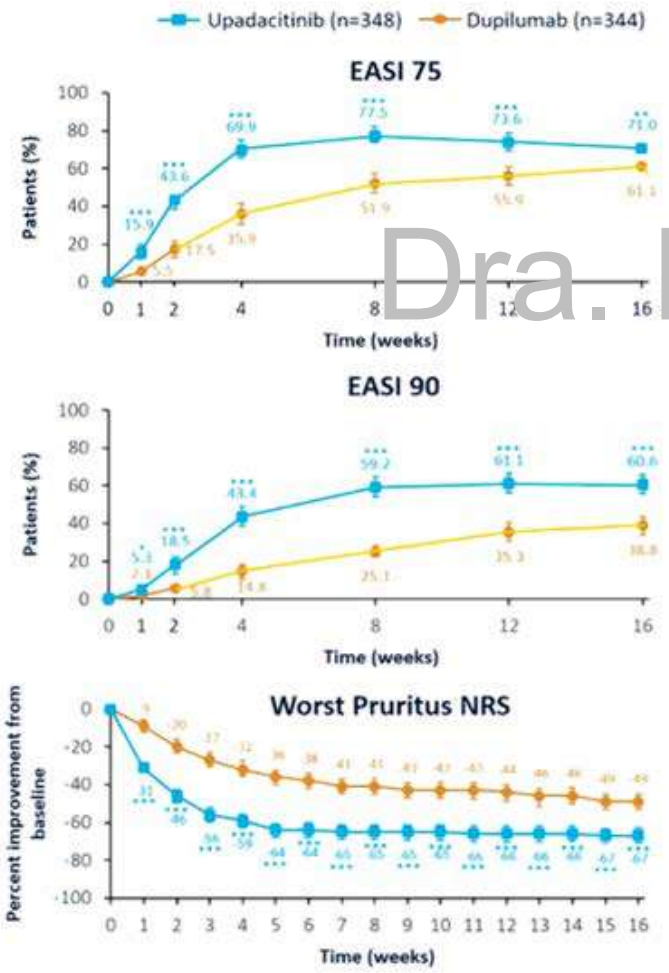
DA ERITRODÉRMICA

Heads Up

JAMA Dermatology | Original Investigation

Efficacy and Safety of Upadacitinib vs Dupilumab in Adults With Moderate-to-Severe Atopic Dermatitis
A Randomized Clinical Trial

Andrew Blauvelt, MD, MBA; Henrique D. Teixeira, PhD, MBA; Eric L. Simpson, MD, MCR; Antonio Costanzo, MD; Marjolein De Bruin-Weller, MD; Sebastien Barbarot, MD, PhD; Vimal H. Prajapati, MD; Peter Lio, MD; Xiaofei Hu, PhD; Tianshuang Wu, PhD; John Liu, MD, MS; Barry Ladizinski, MD, MPH, MBA; Alvina D. Chu, MD; Kilian Eyerich, MD



Opinion

EDITORIAL

Therapeutic Relief for Erythrodermic Atopic Dermatitis

Dawn Z. Eichenfield, MD, PhD

Received: 28 July 2022 | Accepted: 25 October 2022
DOI: 10.1111/jdv.18714

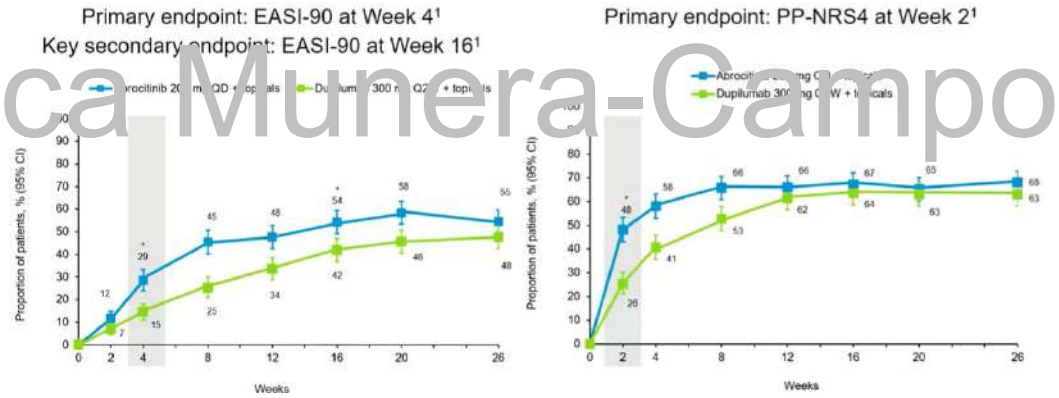
JEADV

LETTER TO THE EDITOR

Erythrodermic atopic dermatitis resistant to dupilumab and baricitinib successfully treated with upadacitinib

JADE DARE:

- **Abrocitinib** 200mg QD + CST vs **Dupilumab** 300mg Q2W + CST



THE LANCET

Efficacy and safety of abrocitinib versus dupilumab in adults with moderate-to-severe atopic dermatitis: a randomised, double-blind, multicentre phase 3 trial

Los inhibidores de JAK podrían ser útiles como primera opción cuando se requiera una mejoría rápida debido al riesgo de morbimortalidad, como en una DA eritrodérmica

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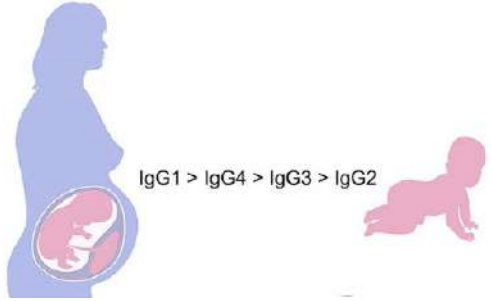
Embarazo/lactancia

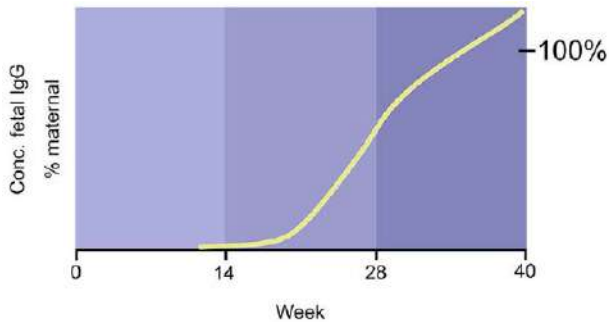


EAACI POSITION PAPER

Allergy WILEY

Biologicals in atopic disease in pregnancy: An EAACI position paper

Birgit Pfaller[1] | Juan José Yepes-Nuñez[2] | Ioana Agache[3] | Cezmi A. Akdis[4] | Mohammad Alsalamah[5,6,7] | Sevim Bavbek[8,9] | Apostolos Bossios[10,11] | Onur Boyman[12,13] | Adam Chaker[14] | Susan Chan[15,16] | Alexia Chatzipetrou[17,18,19,20] | George du Toit[21] | Marek Jutel[22,23] | Paula Kauppi[24] | Antonios Kolios[12,13] | Carmen Li[5] | Andrea Matucci[25] | Alanna Marson[5] | Sarah Bendien[26] | Oscar Palomares[27] | Barbara Rogala[28] | Zsolt Szepfalusi[29] | Eva Untersmayr[30] | Alessandra Vultaggio[24] | Thomas Elwegger[5,31,32]



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For pregnant or nursing women who require systemic treatment for AD, CsA has the most evidence supporting its use during pregnancy and lactation.

According to prescribing information, JAKis are contraindicated during pregnancy and lactation.

DUP is likely safe during pregnancy and lactation considering the pharmacology and data from a small number of pregnancies. Conclusions cannot be made for other biologics due to lack of data, although most biologics are anticipated to behave similarly in pregnancy and lactation due to their molecular weight.

	MUJER			HOMBRE
TRATAMIENTO	**PRE-CONCEPCIONAL**	**EMBARAZO**	**LACTANCIA**	**PRE-CONCEPCIONAL**
BIOLÓGICOS	No efectos conocidos en reproducción ni fertilidad	• El transporte de MoAbs aumenta a partir del 2T • Cualquier efecto potencial sería más probable en el 3T que en el 1T.	• Su excreción en leche materna es probablemente baja (gran tamaño) • La absorción intestinal por el bebé, probablemente también sea mínima.	No efectos conocidos en reproducción ni fertilidad
Dupilumab	NO restricciones	Probablemente Seguro. Evidencia limitada (no efectos teratogénico o perjudiciales conocidos) Puede considerarse en casos individuales (beneficio/riesgo)	Probablemente Seguro. Evidencia limitada (no efectos teratogénico o perjudiciales conocidos) Puede considerarse en casos individuales (beneficio/riesgo)	NO restricciones
Tralokinumab	NO restricciones	Evidencia limitada (no efectos teratogénico o perjudiciales conocidos)	Evidencia limitada (no efectos teratogénico o perjudiciales conocidos)	NO restricciones
INHIBIDORES DE JAK	No efectos conocidos en reproducción ni fertilidad. Precisa período de lavado	Efectos teratogénicos conocidos con dosis superiores (estudios animales)	Moléculas pequeñas: excreción en leche materna muy probable	No efectos conocidos en reproducción ni fertilidad
Baricitinib	1 week washout	CONTRAINDICADO	CONTRAINDICADO	NO restricciones
Upadacitinib	4 weeks washout	CONTRAINDICADO	CONTRAINDICADO	NO restricciones
Abrocitinib	4 weeks washout	CONTRAINDICADO	CONTRAINDICADO	NO restricciones

European Review for Medical and Pharmacological Sciences 2021; 25: 5448-5451

Safety profile of Dupilumab during pregnancy: a data mining and disproportionality analysis of over 37,000 reports from the WHO individual case safety reporting database (VigiBase™)

R. KHAMISY-FARAH[1], G. DAMIANI[2,3,4], J.D. KONG[5], J. WU[6], N.L. BRAGAZZI[5]

Concise Report

CED Clinical and Experimental Dermatology

Paternal and maternal use of dupilumab in patients with atopic dermatitis: a case series

A. L. Bosma,[1] L. A. A. Gerbens,[1] M. A. Middelkamp-Hup[1] and P. I. Spuls[1]

[1]Department of Dermatology, Amsterdam University Medical Centers (Amsterdam UMC), location Academic Medical Center, Amsterdam Public Health, Immunity and Infections, University of Amsterdam, Amsterdam, The Netherlands

doi:10.1111/ced.14725

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CONCLUSIONES

- **1 diana extracelular** (subunidad de R o IL): **ESPECIFICIDAD**
- **Catabolismo** (no dependiente de citocromo hepático): **menor potencial interacciones farmacológicas**
- **Tratamiento continuado**
- **Inicio de acción más lento**
- **Comorbilidades T2**
- **Necesidad de inyecciones, menos individualizable (intervalo de dosis)**
- **Riesgo de conjuntivitis, efectos adversos cutáneos** (eritema facial, psoriasis), **posibles EAs "Th1"**
- **No necesidad de monitorización analítica**
- **Riesgo teórico de AC anti-fármaco y pérdida de eficacia en el tiempo**

- **Diana intracelular: SELECTIVIDAD JAK1 o JAK1/2, supresión amplia de IL**
- **Metabolismo: interacciones farmacológicas potenciales**
- **Tratamiento intermitente**, p.ej. DA de curso estacional
- **Inicio de acción más rápido: lesiones y prurito (IL-31)**
- **Individualización: dosis, ciclos de tratamiento**
- **Otras comorbilidades (AA, vitíligo, artritis, EII)**
- **Mayor rango de EA: infecciones (herpéticas++), alteraciones hemograma y perfil lipídico. Riesgo potencial EA graves (bajo en población DA)**
- **Necesidad de controles analíticos periódicos**
- **Semivida de eliminación corta, aclaramiento rápido, no riesgo de AC anti-fármaco**

MUCHAS GRACIAS