Alopecia Areta y Vitíligo: la vía del Interferon gamma

Germans Trias i Pujol
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Conflictos de interés

- Ensayos Clínicos (Incyte, Pfzier,Abvvie)
- Advisory Board (Incyte)
- Asistencia curso (Lilly)

Índice

VITILIGO y ALOPECIA AREATA

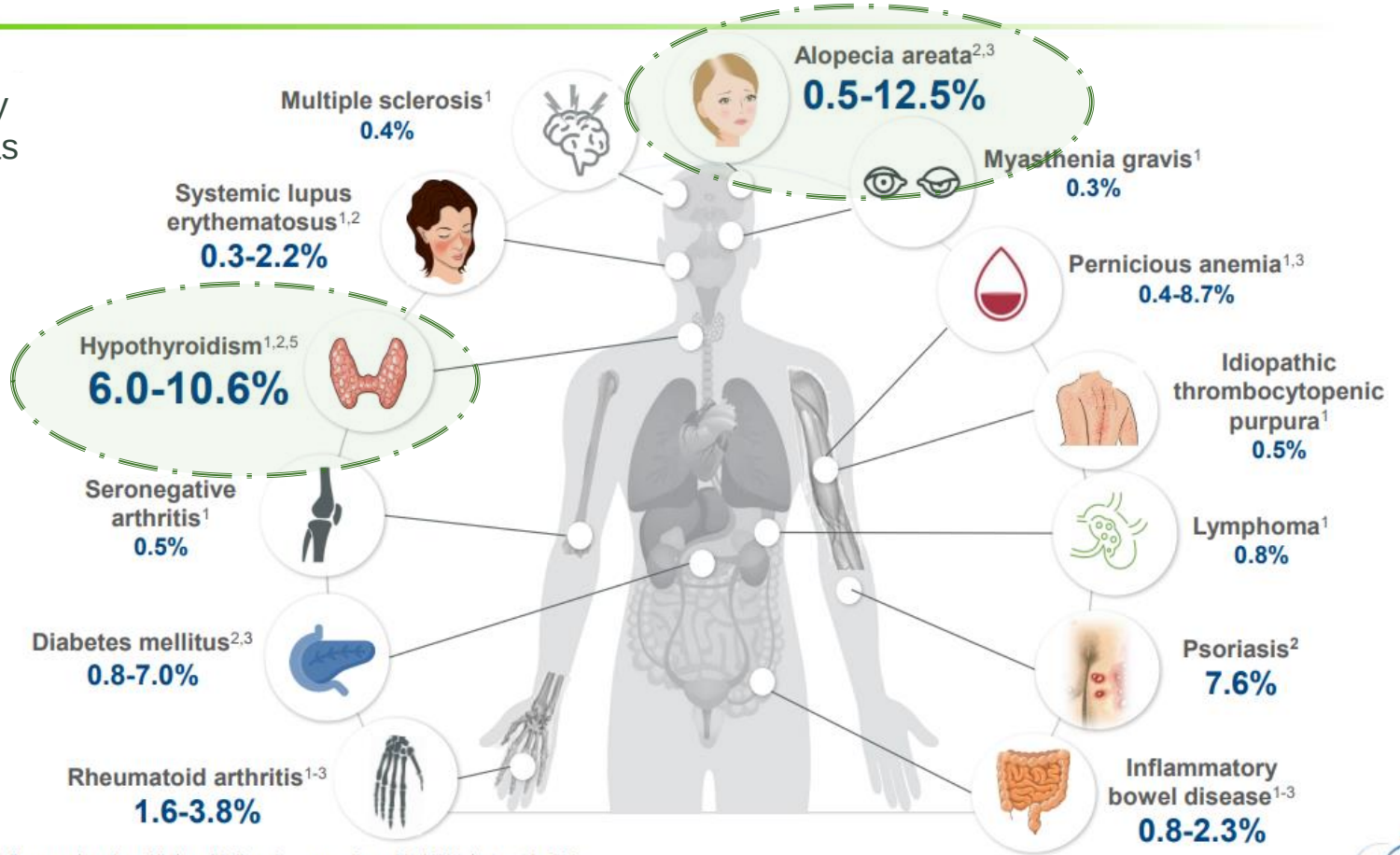
- Enfermedades de naturaleza autoinmune y base genética
- Prevalencia y edad de inicio similar
- Evolución crónica (e incierta)
- Similitud en la base patogénica (CD8 citotóxicos, vía INF-gamma, IL-15)
- Enfermedades "huérfanas" de tratamiento
- **Desarrollo de nuevas dianas terapéuticas /vías patogénicas**

VITILIGO

ALOPECIA AREATA

Ambas enfermedades se asocian con diversas comorbilidades autoinmunes

La enfermedad tiroidea y la alopecia areata son las comorbilidades autoinmunes más comunes



[a] Risk increases with larger affected BSA and disease duration. All thyroid disorders were found in NSV, but not in SV.

1. Hadi A, et al. *J Am Acad Dermatol*. 2020;82:628-633. 2. Sheth VM, et al. *Dermatol*. 2013;227:311-315. 3. Dahir AM, et al. *Int J Dermatol*. 2018;57:1157-1164. 4. Ma SH, et al. *J Am Acad Dermatol*. 2021;85:1465-1472. 5. Yuan J, et al. *Front Endocrinol* (Lausanne). 2019;9:803.

VITILIGO

ALOPECIA AREATA

Review > Am J Clin Dermatol. 2023 Nov;24(6):875-893. doi: 10.1007/s40257-023-00805-4.
Epub 2023 Jul 18.

Comorbid Conditions Associated with Alopecia Areata: A Systematic Review and Meta-analysis

Sophia Ly [1 2], Priya Manjaly [2 3], Kanika Kamal [2 4], Ali Shields [2 5], Bruna Wafae [2 4], Najiba Afzal [2 6], Lara Drake [2 7], Katherine Sanchez [2 8], Samantha Gregoire [2 9], Guohai Zhou [2], Carol Mita [10], Arash Mostaghimi [11 12]

Affiliations + expand

PMID: 37464249 DOI: 10.1007/s40257-023-00805-4

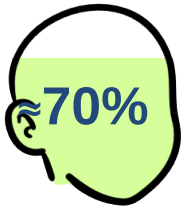
Deficit de vitamina D (OR 10.13)
LES (OR 5.53)
VITILIGO (OR 5.30)
Síndrome metabólico (OR %.03)
Tiroiditis de Hashimoto (OR 4.31)

VITILIGO

Ezzedine K et al. American Journal of Clinical Dermatology (2021) 22:757–774

Facial involvement is reflective of patients' global perception of vitiligo extent

Samar Merhi,[1,2] Pascale Salameh,[3,4,5,6] Mounya Abboud,[1] Julien Seneschal,[7,8] Viktoria Eleftheriadou,[9] Isabelle Pane,[10] Viet-Thi Tran,[10,11] Jason Shourick[12] and Khaled Ezzedine[1,13]



Afectación facial

JAMA Dermatol. 2022; 158(1): 1–9.

ALOPECIA AREATA

Clinical, Cosmetic and Investigational Dermatology
Dovepress
open access to scientific and medical research
Open Access Full Text Article
REVIEW

Epidemiology and burden of alopecia areata: a systematic review

Received: 12 August 2022 | Accepted: 5 January 2023
DOI: 10.1111/jdv.18921
ORIGINAL ARTICLE
JEADV

Exploring the overlap between alopecia areata and major depressive disorder: Epidemiological and genetic perspectives

Dermatol Ther (Heidelb) (2023) 13:3121–3135
https://doi.org/10.1007/s13555-023-01057-0
Check for updates
ORIGINAL RESEARCH

Physician- and Patient-Reported Severity and Quality of Life Impact of Alopecia Areata: Results from a Real-World Survey in Five European Countries

Sergio Vañó-Galván · Ulrike Blume-Peytavi · Paul Farrant · Pascal Reygagne · Erin Johansson · Catherine Reed · Simran Marwaha · Frederick Durand · Bianca Maria Piraccini

Calidad de vida

Baja autoestima

Depresión Estigma Ansiedad

Estrés

Medidas –índice de gravedad VITILIGO

Vitiligo Area Scoring Index

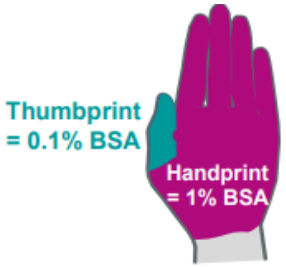
VASI

T-VASI

F-VASI

VASI[b]

A validated quantitative scale that measures the extent of vitiligo involvement as a % of BSA multiplied by the degree of depigmentation[2,3,6]

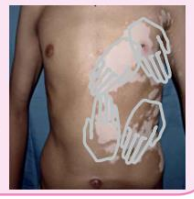


Total BSA (T-BSA) takes into account the depigmented areas for each of the following body regions:
head/neck (incl. F-BSA), upper limbs (incl. hands), trunk, lower limbs (incl. feet)[2]

Example:

T-BSA with skin lesions
= [(½ handprint x 3) + 1 handprint] × 1% BSA

→ **T-BSA = 2.5**



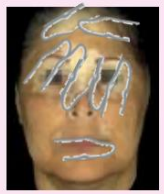
Facial BSA (F-BSA) takes into account the depigmented areas on the face as a % of the total body area[2,a]

Example:

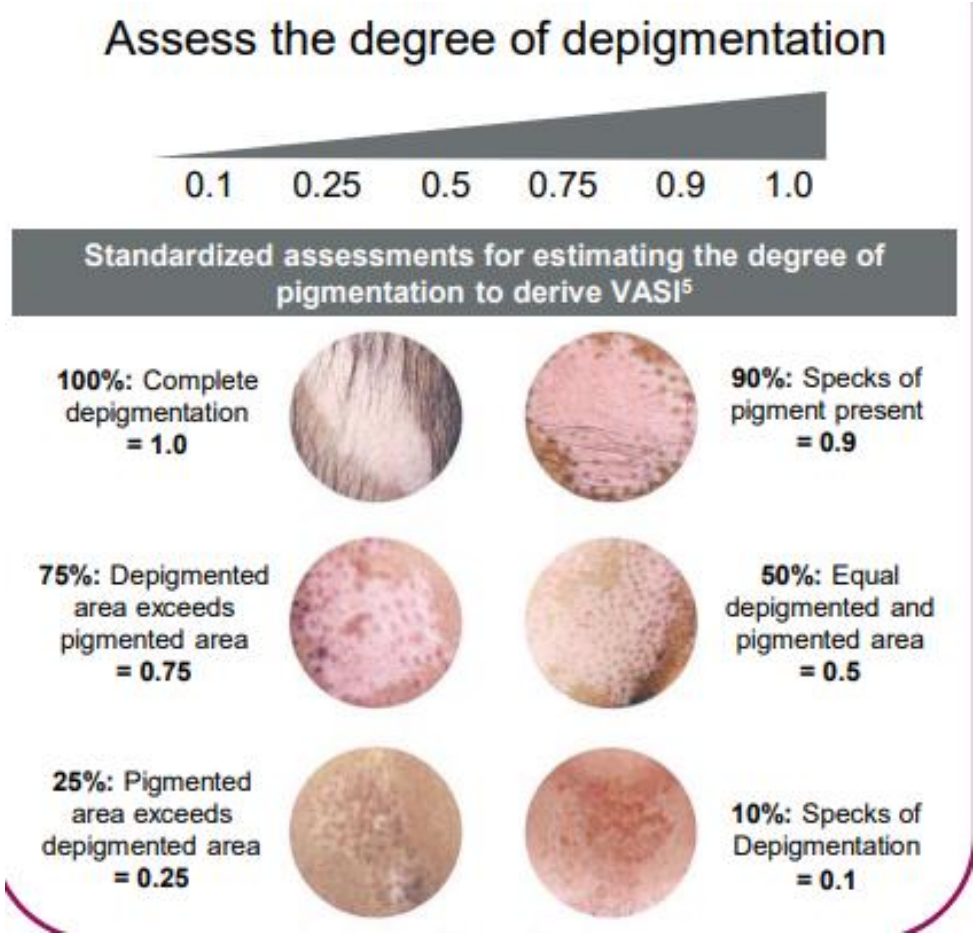
F-BSA with skin lesions
=6.5 thumbprints ×0.1% BSA

→ **F-BSA = 0.65**

Note: Max. F-BSA =3
(i.e. depigmentation on 100% of the face)



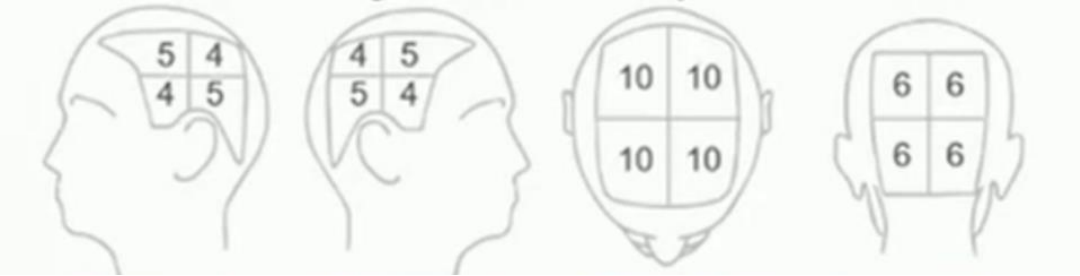
$$\text{VASI} = \sum_{\text{All Body Sites}} [\text{Hand Units}] \times [\text{Residual Depigmentation}]$$



Medidas –índice de gravedad ALOPECIA AREATA

Severity of Alopecia Tool

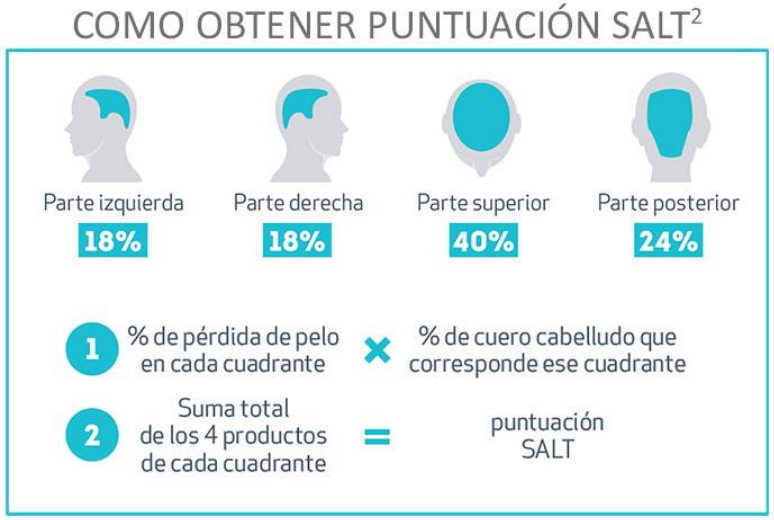
SALT



Alopecia Areata Investigator Global Assessment™ (AA-IGA™)

	None 0	Limited 1	Moderate 2	Severe 3	Very Severe 4
Please rate the patient's **scalp hair loss**, as it looks **today**.	0%	1-20%	21-49%	50-94%	95-100%

The Severity of Alopecia Tool (SALT; Olsen et al 2004) is recommended to assess the extent (0-100%) of scalp hair loss.

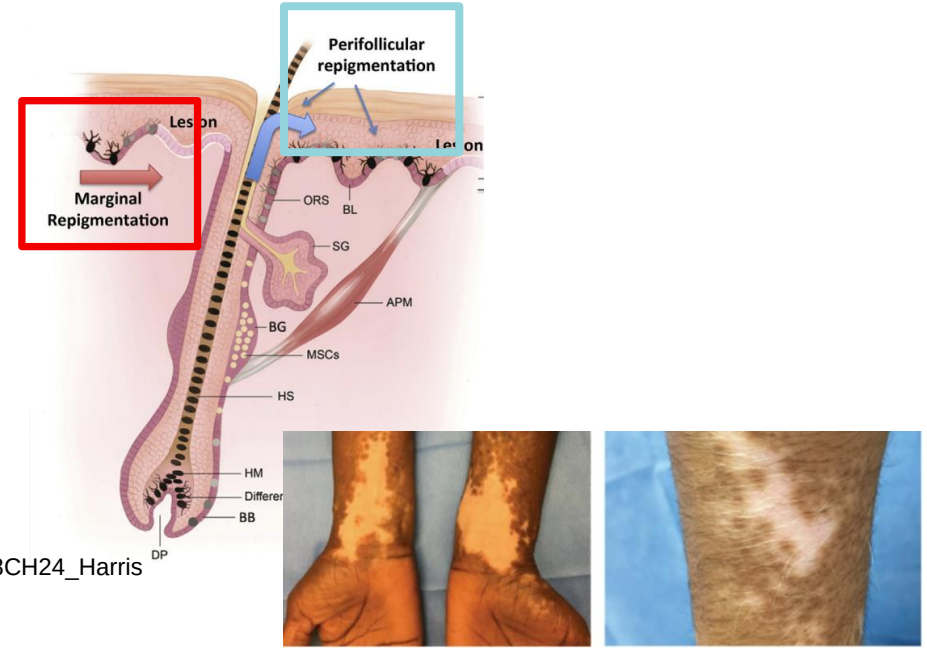


Calculadora

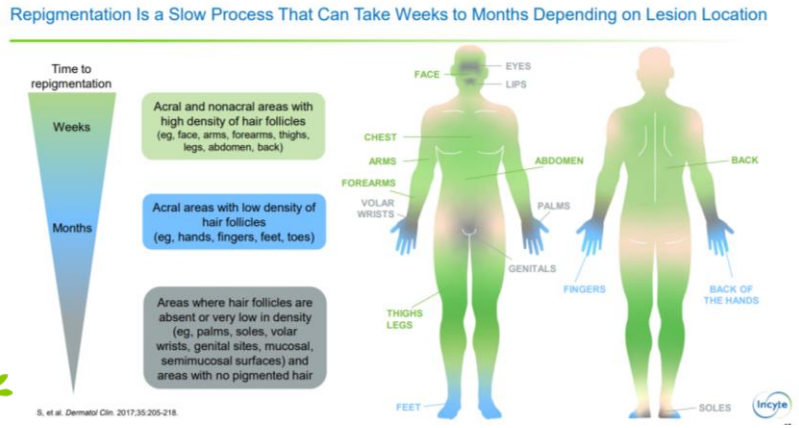
Wyrwich. BJD 2020

Olsen et al. J Am Acad Dermatol. 2004;51(3):440-7

Repigmentación Vitíligo



IY38CH24_Harris



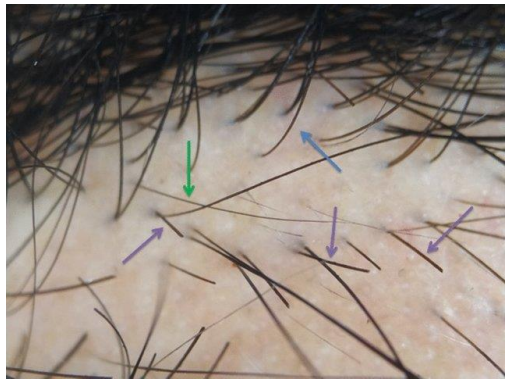
Repoblación AA

Signos dermatoscópicos de repoblación capilar

Pigtail hairs

Pelos vellosos

Pelos rectos en crecimiento



Sibbald. J Cutan Med Surg. 2023

Gómez-Quispe y cols.ACTAS Dermo-Sifiliográficas 114 (2023) 25-32

Metwally et al. Arch Dermatol Res. 2022;314(2):167-182.

Patogénesis

MOLECULAR MEDICINE REPORTS 22: 3111-3116, 2020

IFN-γ induces apoptosis in human melanocytes by activating the JAK1/STAT1 signaling pathway

QIANYA SU, FEI WANG, ZHENGBANG DONG, MEI CHEN and RONG CAO

Department of Dermatology, School of Medicine, Zhong Da Hospital, Southeast University, Nanjing, Jiangsu 210009, P.R. China

Received October 10, 2019; Accepted March 27, 2020

DOI: 10.3892/mmr.2020.11403

See related commentary on pg 1752

ORIGINAL ARTICLE

A Mouse Model of Vitiligo with Focused Epidermal Depigmentation Requires IFN-γ for Autoreactive CD8$^+$ T-Cell Accumulation in the Skin

John E. Harris[1], Tajie H. Harris[2], Wolfgang Weninger[3,4], E. John Wherry[5], Christopher A. Hunter[2] and Laurence A. Turka[6]

DERMATOLOGIC THERAPY

Original Article

Interferon-gamma serum level and immunohistochemical expression of CD8 cells in tissue biopsies in patients with alopecia areata in correlation with trichoscopic findings

Naglaa Agamia, Zoe Apalla, Samar El Achy, Eman Abdelmaksoud, Noha Kandil, Sami Abozeid

First published: 29 May 2020 | https://doi.org/10.1111/dth.13718 | Citations: 9

Moléculas JAK-STAT

Moléculas intracitoplasmáticas
Fosforilación –desfosforilación
Transcripción IL proinflamatorias

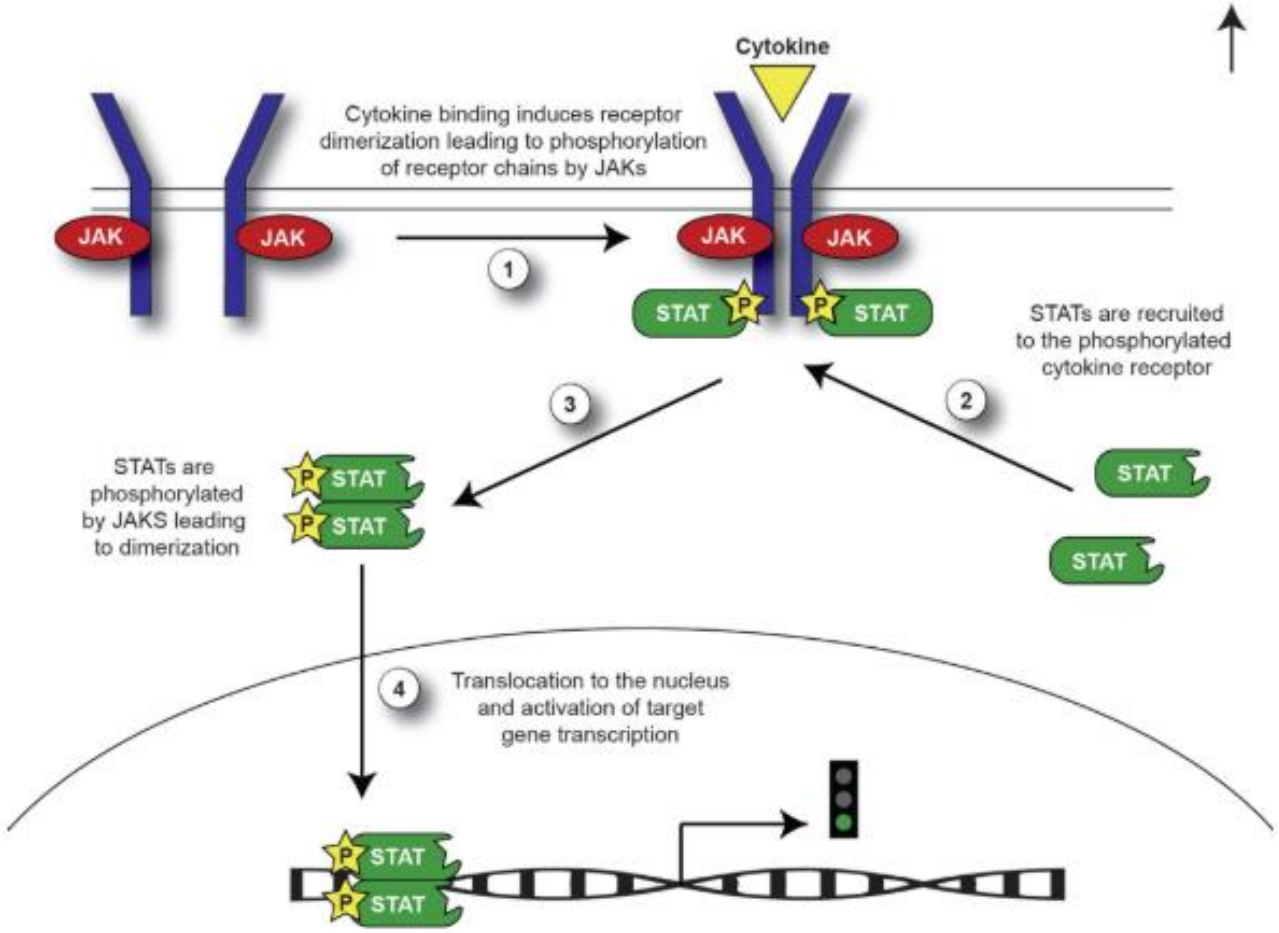


Figure 1.
JAK-STAT signaling pathway. JAK inhibitors antagonize JAK protein function and prevent activation of the pathway.

Damsky.J Am Acad Dermatol. 2017 Apr;76(4):736-744

Vía IFN gamma –JAK STAT

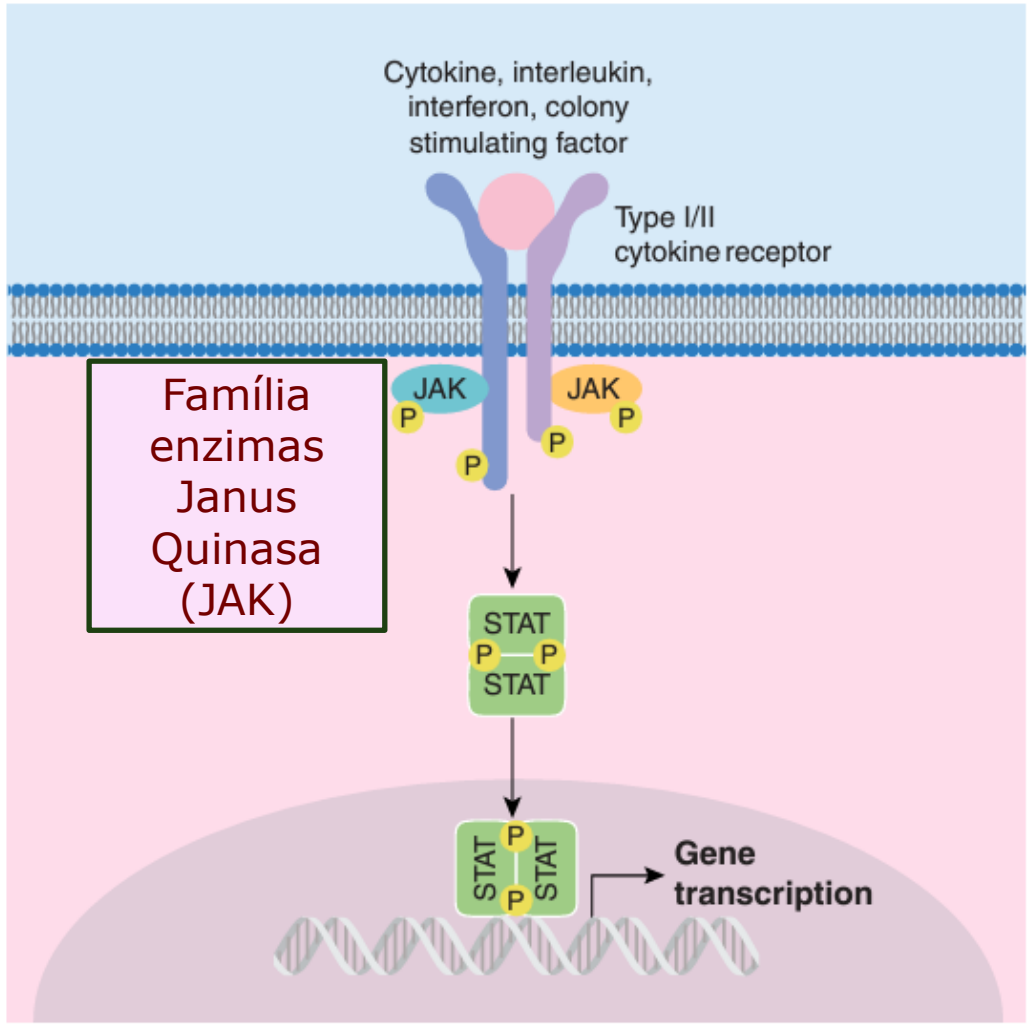
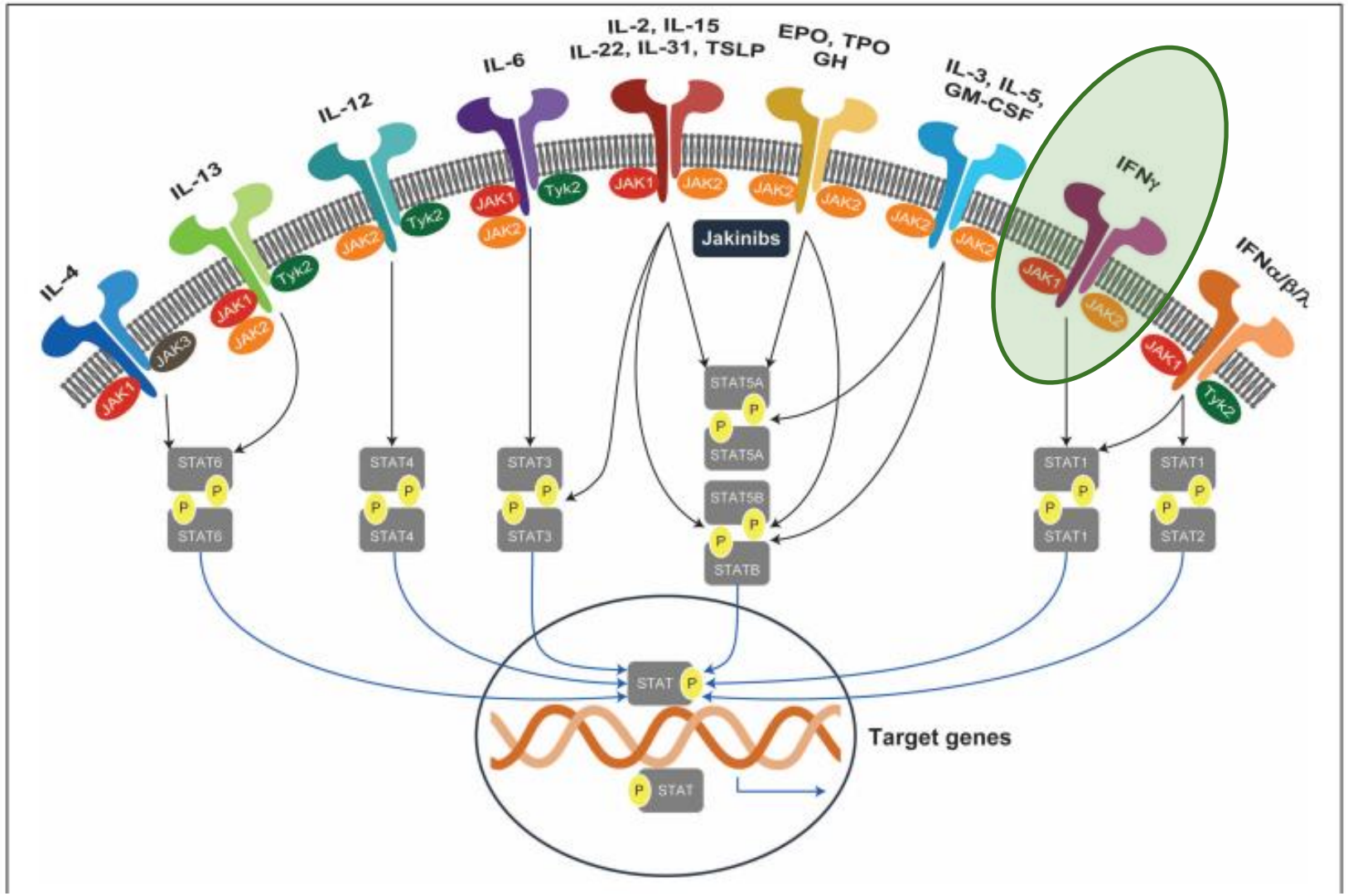


TABLE 1 Summary of usage of JAKs by various cytokines

JAK	CYTOKINE
JAK1	γc cytokines: (IL-2,-4,-7,-9,-15,-21); IL-13 TSLP gp130 cytokine family: IL-6, IL-11, IL-31, OSM, CNTF, LIF, CT-1, NNT-1 IFN-γ, IFNα, IFNβ, IFNλ, IL-10-like cytokines (L-10, IL-19, IL-20, IL- 22, IL-24, and IL-26)
JAK2	βc cytokines: (IL-3, IL-5, GM-CSF), TSLP gp130 cytokine family: (IL-6, IL-11, IL-31, OSM, CNTF, LIF, CT-1, NNT-1) Leptin, GH, Prolactin, EPO, TPO, IFNγ, IL-13 IL-12, IL-23
JAK3	γc cytokines: IL-2,-4,-7,-9,-15,-21
TYK2	IFNα, IFNβ, IFNλ, gp 130 cytokines * IL-10-like cytokines (L-10, IL-19, IL-20, IL- 22, IL-24, and IL-26), IL-12 IL-13 IL-23, IL-27

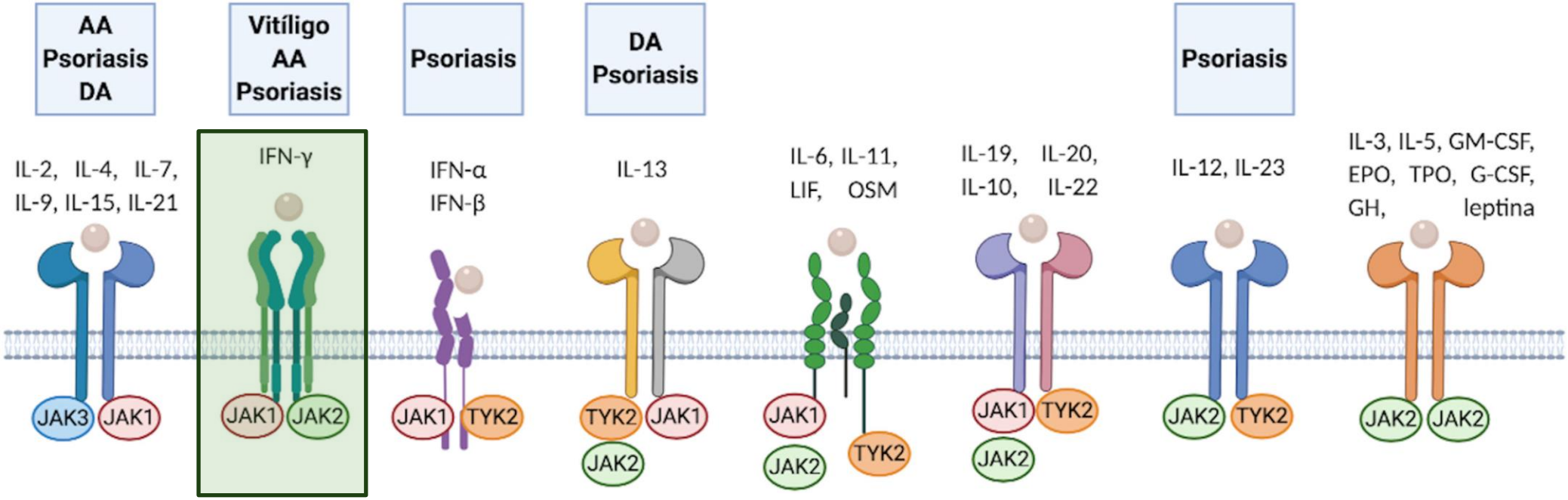
Gadina et al.J Leukoc Biol. 2018;104(3):499-514.

Hay cuatro enzimas Janus Quinasa (JAK) conocidas:
JAK1, JAK2, JAK3 y TYK2
-cada miembro es utilizado por receptores diferentes-



Howell. Front Immunol. 2019;10:2342.

Vía señalización JAK STAT



ACTAS Dermo-Sifiliográficas 112 (2021) 503–515

ACTAS
Dermo-Sifiliográficas

Full English text available at
www.actasdermo.org

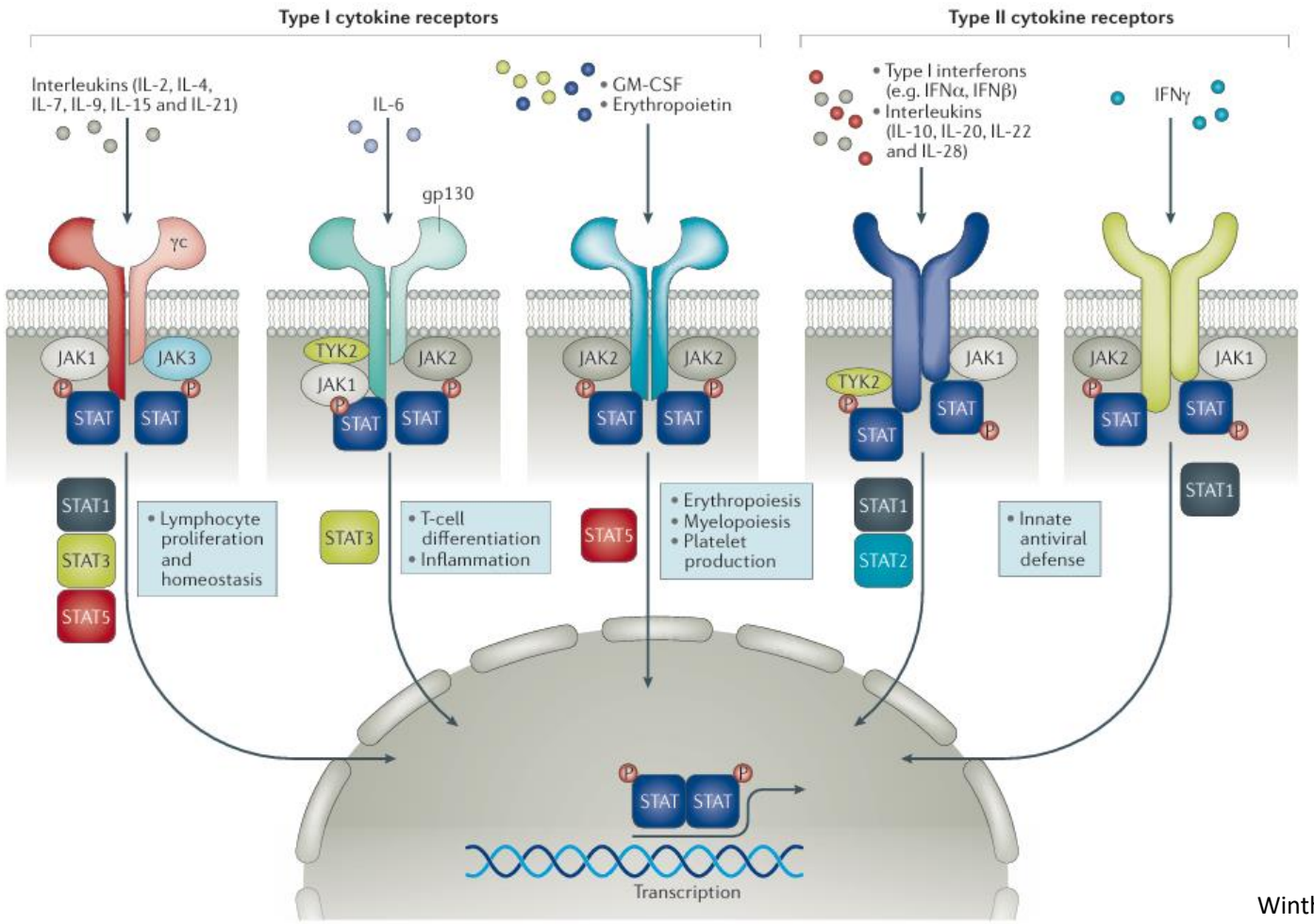
REVISIÓN

Inhibidores de JAK: usos en dermatología. Parte 1: generalidades, aplicaciones en vitíligo y en alopecia areata

C. García-Melendo*, X. Cubiró y L. Puig

Vía IFN gamma – JAK STAT

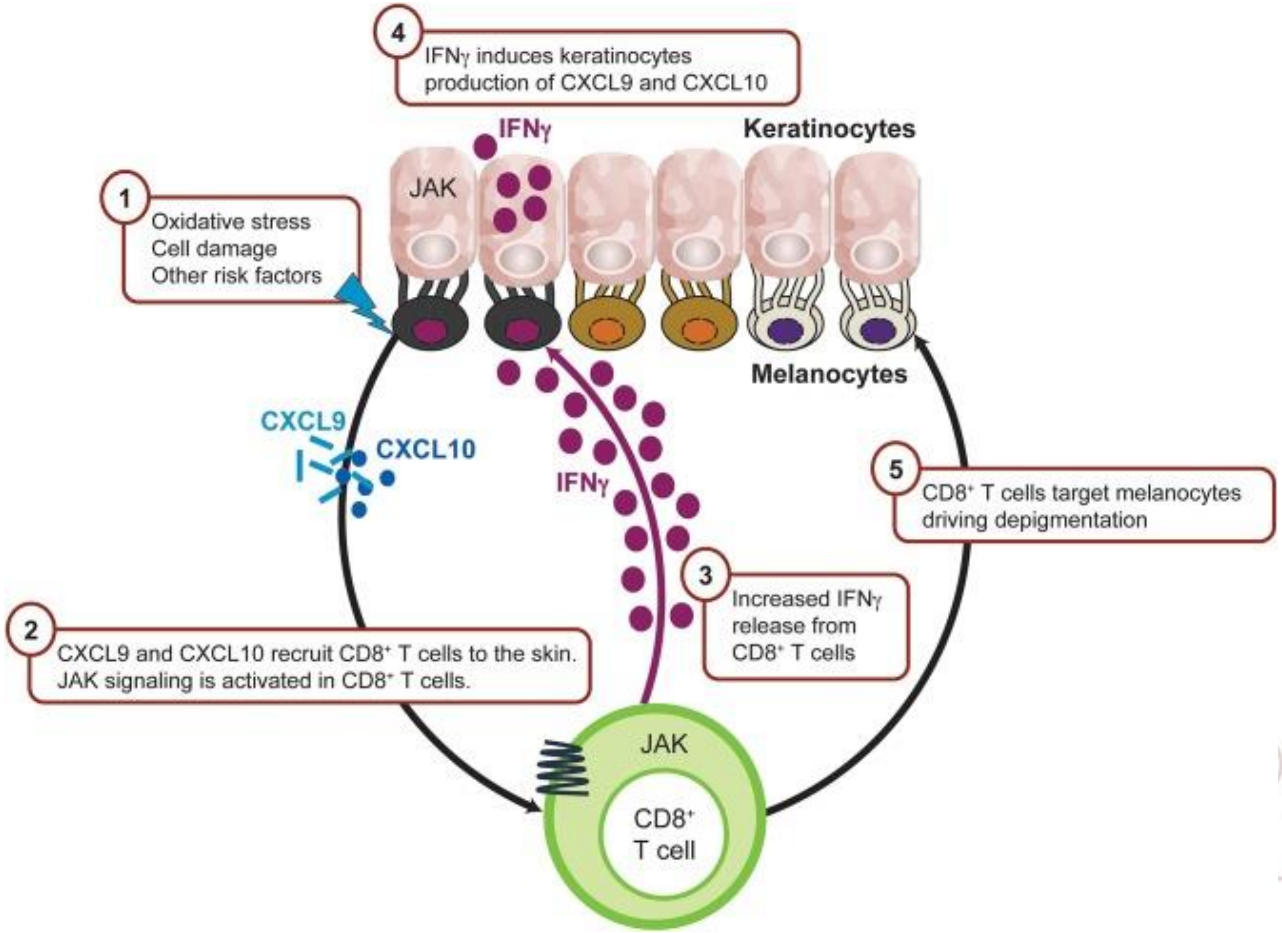
Hematopoyesis y función inmune



Winthrop KL.Nat Rev Rheumatol. 2017;13(4):234-243.

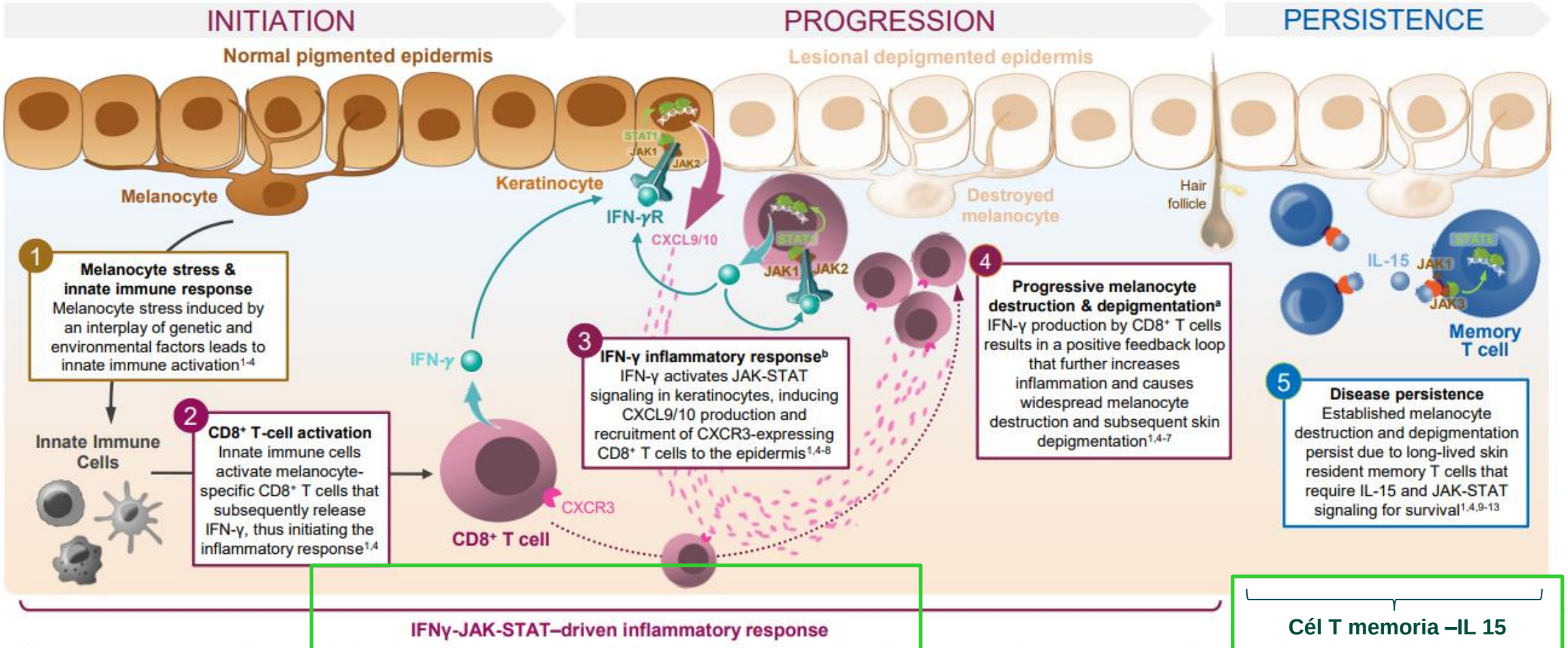
VITILIGO

ALOPECIA AREATA



Howell MD, et al. Front Immunol. 2019

Depigmentation in Vitiligo Is The Result of T-Cell–Mediated Autoimmune Destruction of Melanocytes[1-13]



Cél T memoria –IL 15

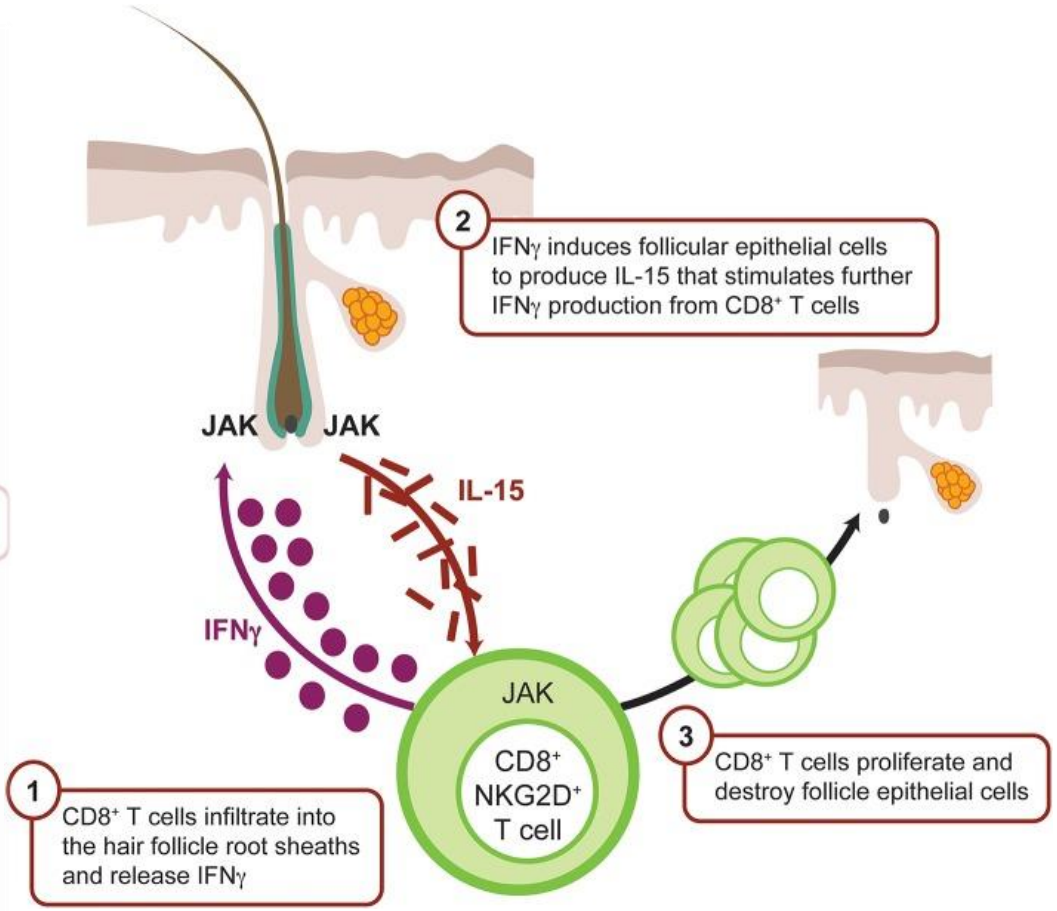
[a] Vitiligo may be more complex than previously thought, with prominent combined activities of both Th1- and Th2-related cytokines inducing inflammatory responses. Moreover, melanocytes may not only be a target of T cells but could actively contribute to perpetuate inflammation.[8]

CXCL, C-X-C motif chemokine ligand; CXCR, C-X-C motif chemokine receptor.

1. Bergqvist C, Ezzedine K. *J Dermatol*. 2021;48:252-270. 2. Strassner JP and Harris JE. *Curr Opin Immunol*. 2016;43:81-88. 3. Richmond JM, et al. *Curr Opin Immunol*. 2013;25:676-682. 4. Frisoli ML, et al. *Annu Rev Immunol*. 2020;38:621-648. 5. Howell MD, et al. *Front Immunol*. 2019;10:2342. 6. Rashighi M and Harris JE. *Dermatol Clin*. 2017;35:257-265. 7. Rosmarin D, et al. *Lancet*. 2020;396:110-120. 8. Martins C, et al. *J Invest Dermatol*. 2022;142:1194-1205. 9. Chen X, et al. *Free Radical Biology Med*. 2019;139:80-91. 10. Richmond JM, et al. *Sci Transl Med*. 2018;10:eaam7710. 11. Atwa MA, et al. *J Cosmet Dermatol*. 2021;20:2640-2644. 12. Nolz JC and Richer MJ. *Mol Immunol*. 2020;117:180-188. 13. Riding RL, Harris JE. *J Immunol*. 2019;203:11-19.

VITILIGO

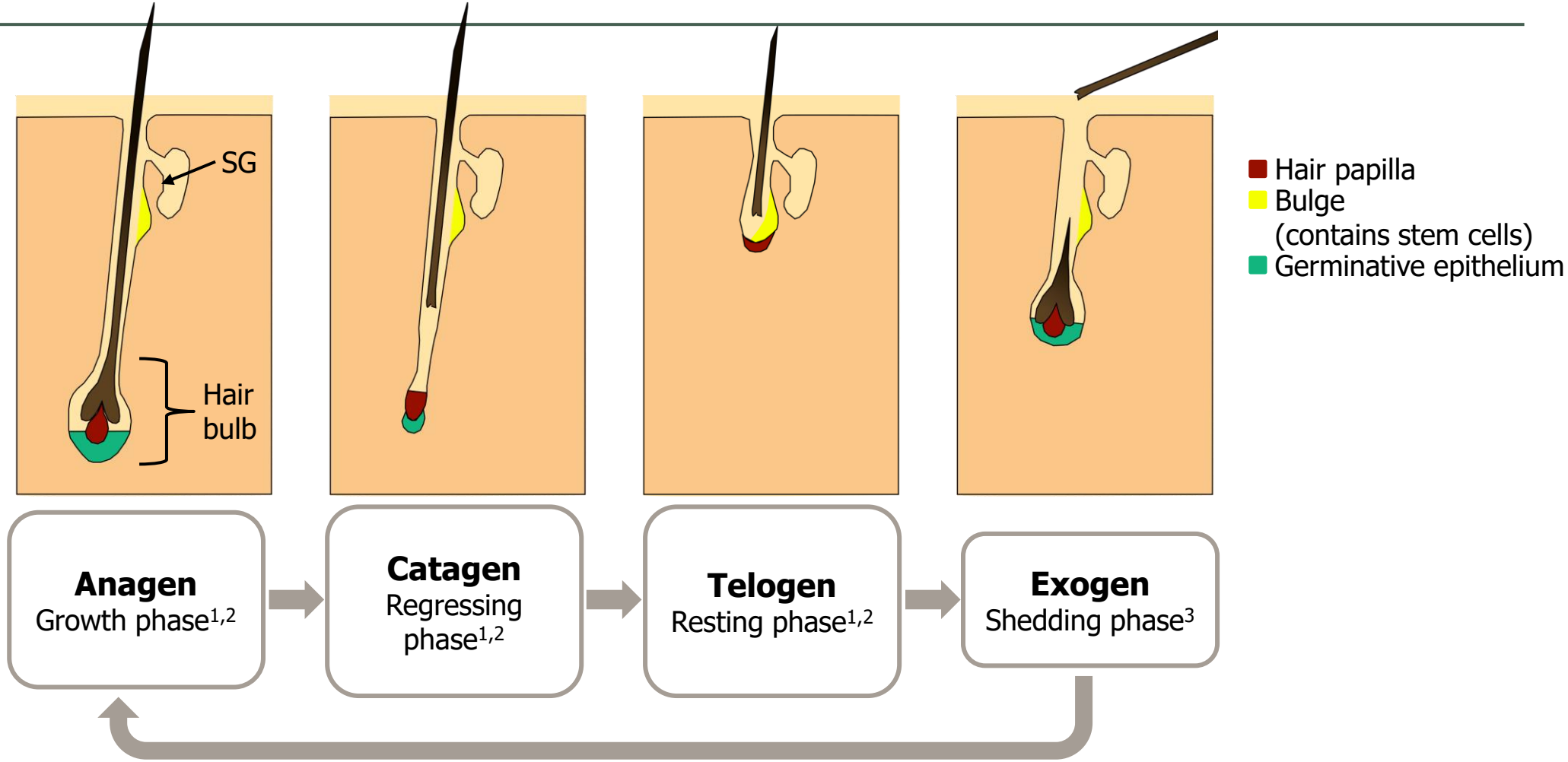
ALOPECIA AREATA



Howell MD, et al. Front Immunol. 2019

ALOPECIA AREATA

Las células inflamatorias atacan los folículos pilosos anágenos, induciéndolos prematuramente a la fase catágena

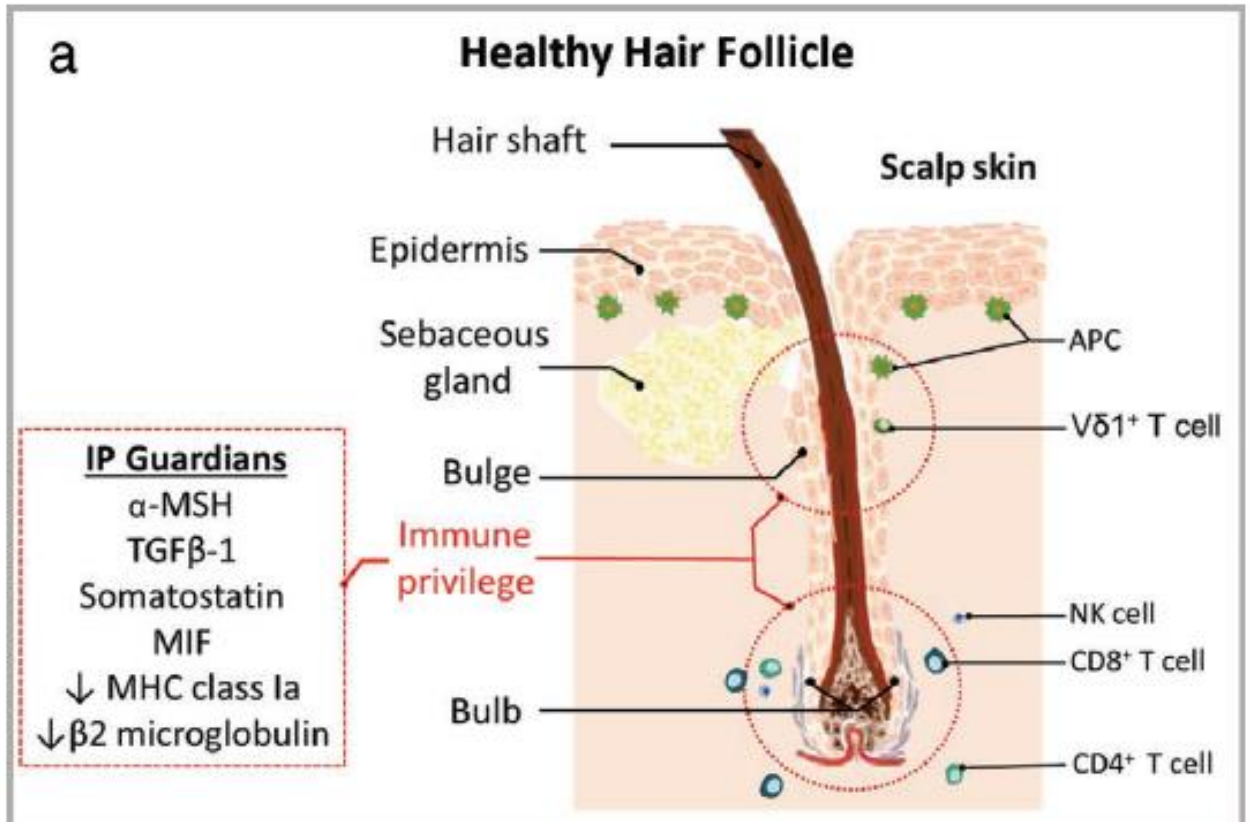


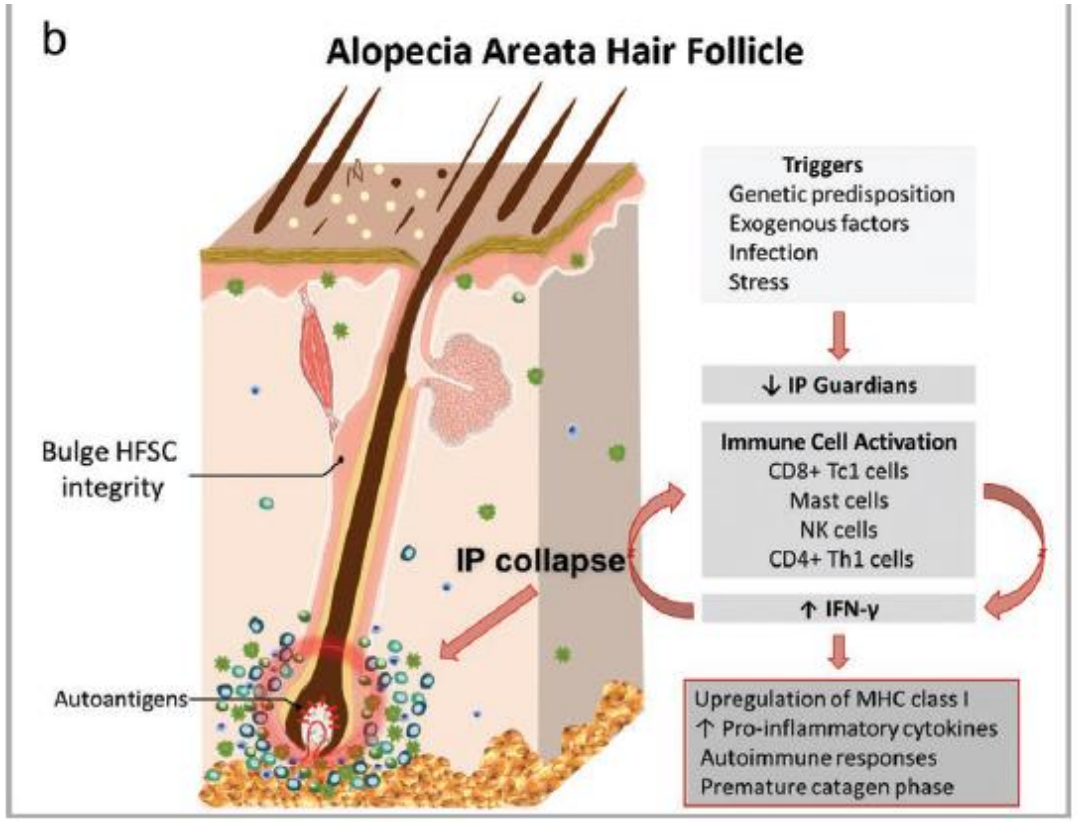
SG=sebaceous gland

1. Waters JM et al. *Semin Cell Dev Biol* 2007;18(2):245-54; 2. Juárez-Rendón KJ et al. *Arch Argent Pediatr* 2017;115(6):e404-11; 3. Santos Z et al. *Expert Opin Drug Discov* 2015;10(3):269-92;

ALOPECIA AREATA

Patogénesis: pérdida del " privilegio inmunológico del folículo"





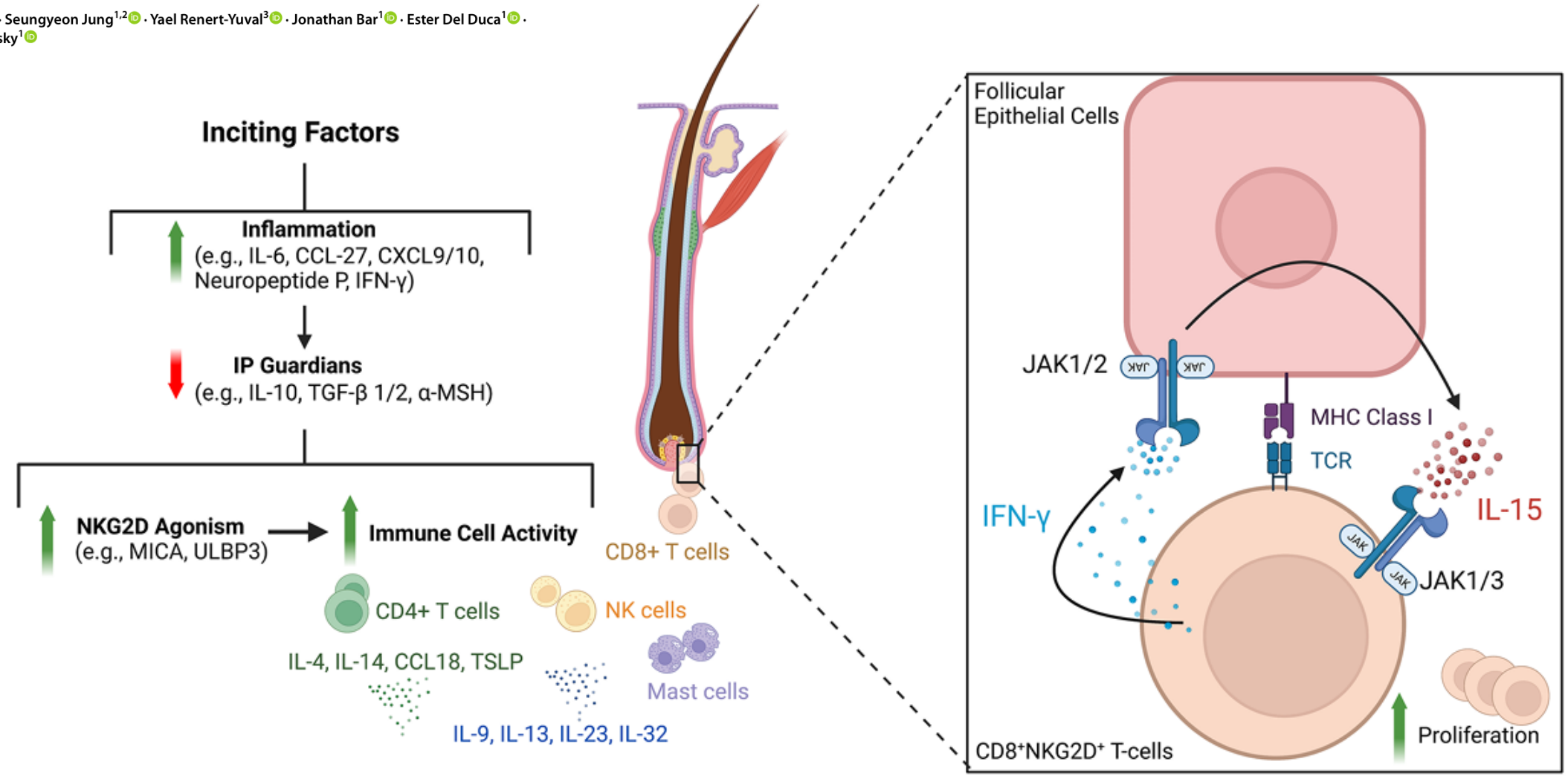
Litzeri DA et al . J Dtsch Dermatol Ges. 2022;20(1):59-90.

American Journal of Clinical Dermatology (2023) 24:895–912
https://doi.org/10.1007/s40257-023-00808-1

REVIEW ARTICLE

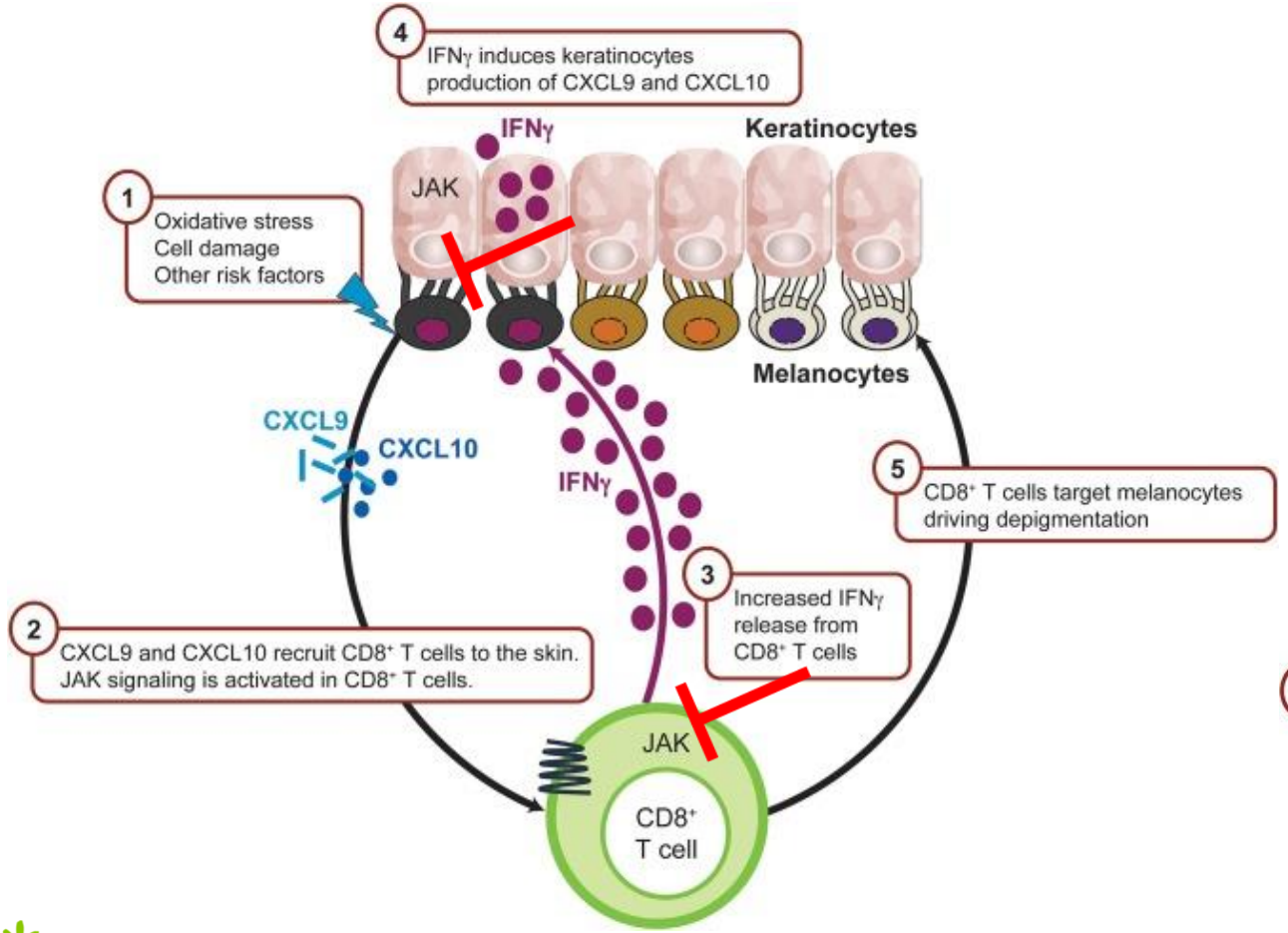
Alopecia Areata: Current Treatments and New Directions

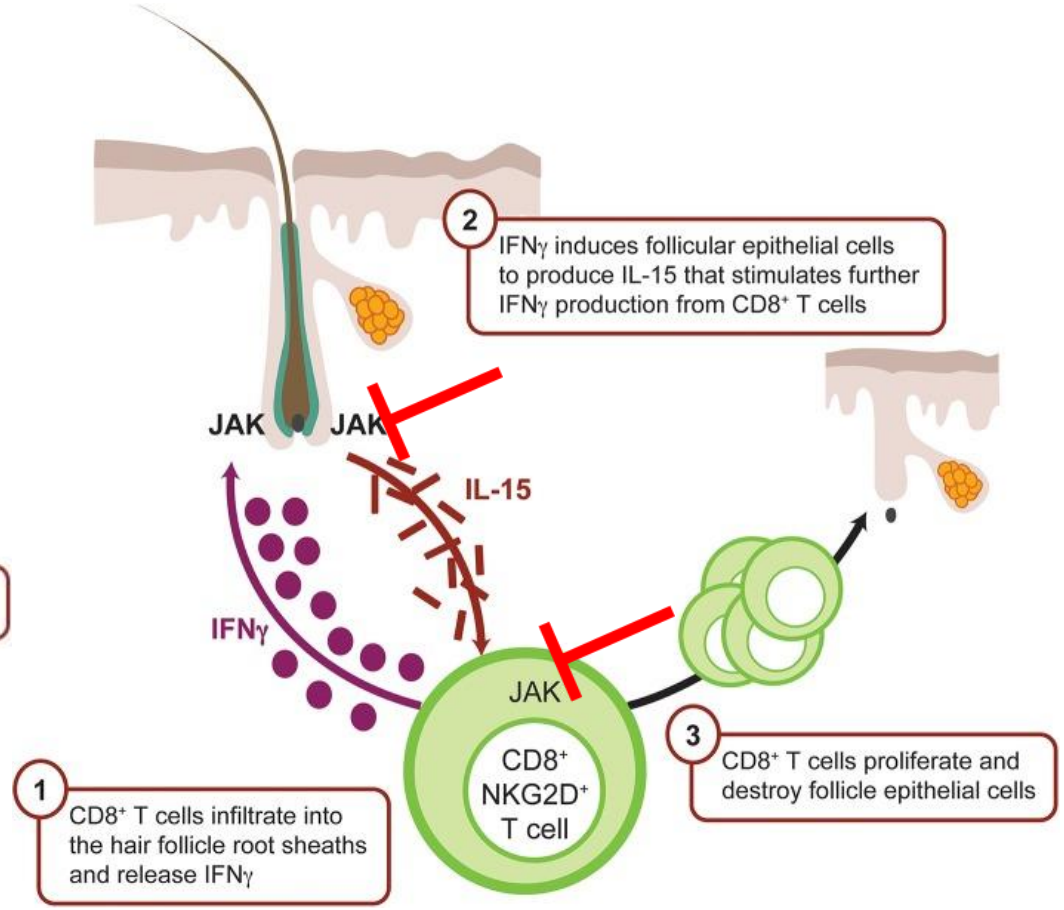
Dante Dahabreh[1] · Seungyeon Jung[1,2] · Yael Renert-Yuval[3] · Jonathan Bar[1] · Ester Del Duca[1] · Emma Guttman-Yassky[1]



VITILIGO

ALOPECIA AREATA





VITILIGO

ALOPECIA AREATA

REVIEWS

JAK inhibitors in dermatology: The promise of a new drug class

William Damsky, MD, PhD, and Brett A. King, MD, PhD
New Haven, Connecticut

REVIEW

JAK-STAT pathway inhibitors in dermatology☆

Hélio Amante Miot [a,*], Paulo Ricardo Criado [b,c], Caio César Silva de Castro [d,e], Mayra Ianhez [f], Carolina Talhari [g], Paulo Müller Ramos [a]

H.A. Miot, P.R. Criado,

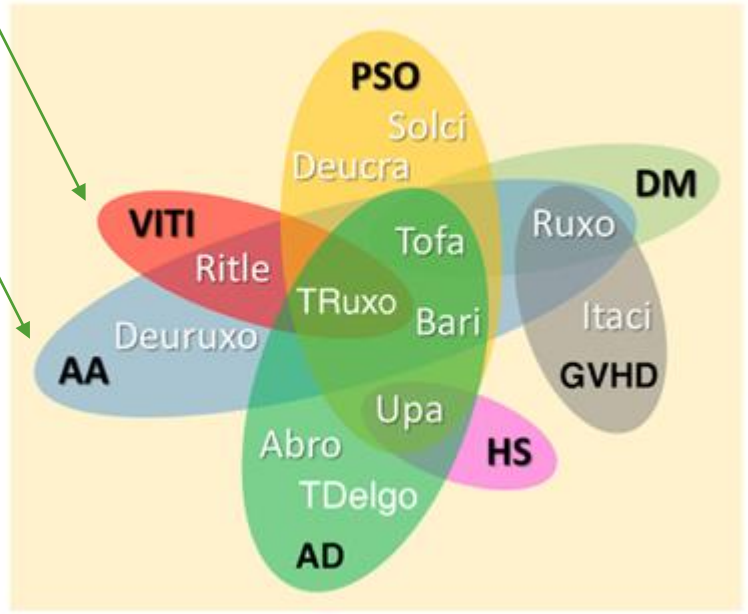
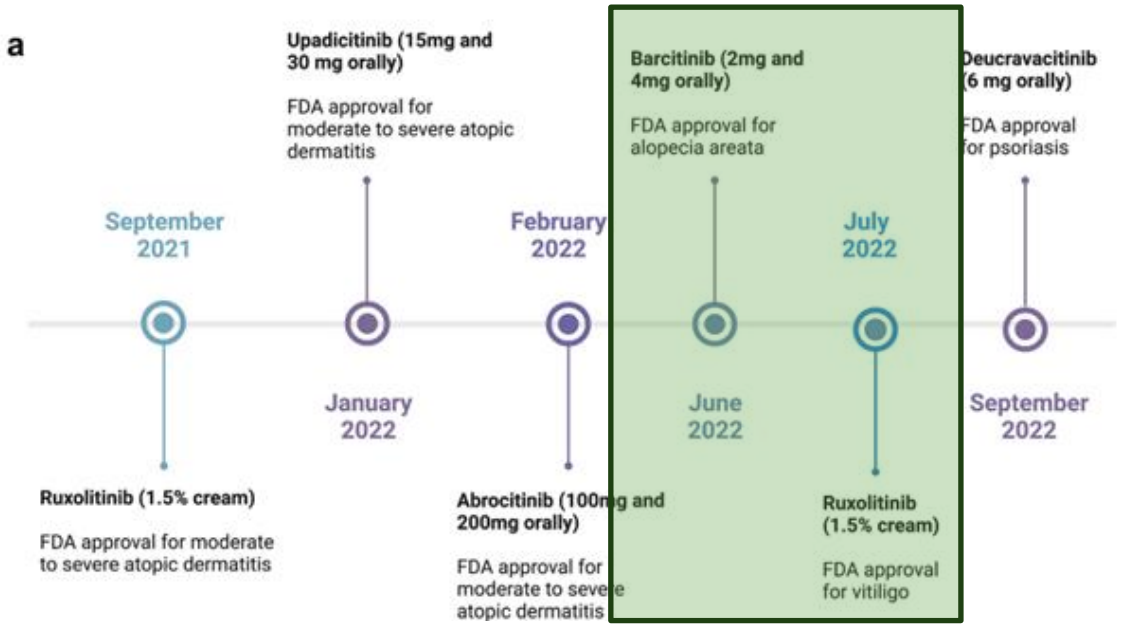


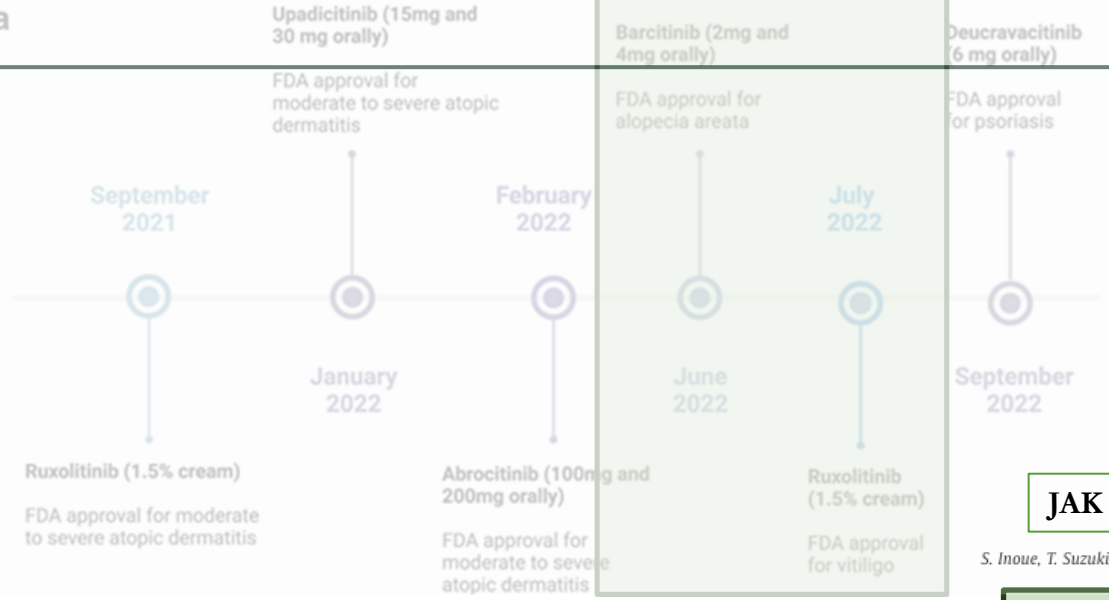
Figure 2 Diagram representing the main JAKi that show favorable results in clinical studies for inflammatory and autoimmune

Dermatol Ther (Heidelb) (2023) 13:729–749



Dermatol Ther (Heidelb) (2023) 13:729–749

a



JAK 1/2

JAK 1/2

JAK 3/TEC

S. Inoue, T. Suzuki, S. Sano et al.

Journal of Dermatological Science 113 (2024) 86–92

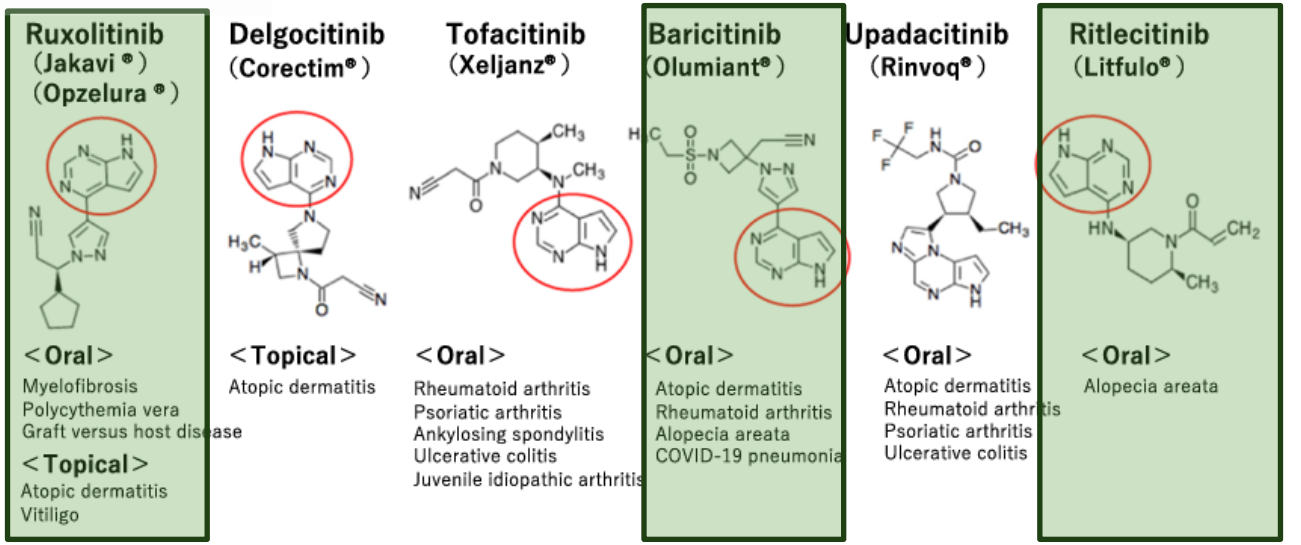


Fig. 1. Chemical structures and indications of typical JAK inhibitors. Pyrrolopyrimidine skeletal structure circled in red.

VITILIGO

ALOPECIA AREATA

VITILIGO

Received: 13 February 2023 | Accepted: 4 August 2023
DOI: 10.1111/jdv.19451

POSITION STATEMENT

Worldwide expert recommendations for the diagnosis and management of vitiligo: Position statement from the International Vitiligo Task Force Part 1: towards a new management algorithm

Received: 13 February 2023 | Accepted: 4 August 2023
DOI: 10.1111/jdv.19450

POSITION STATEMENT

Worldwide expert recommendations for the diagnosis and management of vitiligo: Position statement from the international Vitiligo Task Force—Part 2: Specific treatment recommendations

Topical JAK-inhibitors

The topical JAK-inhibitor ruxolitinib is now the first treatment approved for the repigmentation of vitiligo. Two randomized, double-blind, phase III studies were conducted in 674 patients. Response rates were much better than placebo, with 50.3% and 74.6% of patients achieving a Facial-VASI (F-VASI) 75 and 50, respectively, at week 52. Moreover, 51.1% of patients achieved a total VASI (T-VASI) of 50 at week 52. Treatment-related adverse events (AEs) occurred in 13.7% of patients who applied ruxolitinib cream over the course of the study, with the most common AEs being application site acne (4.4%) or pruritus (3.5%).[12]

Other immunomodulating agents

Methotrexate, cyclosporine, azathioprine and minocycline can be used in patients with progressive vitiligo, although strong evidence for efficiency and safety is lacking.[40–42] Immunosuppressants such as methotrexate, cyclosporine and azathioprine have not been studied in combination with phototherapy. No biologics can currently be recommended for vitiligo (e.g. anti-TNF-α and anti-IL-17).[43,44]

Systemic JAK inhibitors are promising, and their use can be considered when available and approved by regulatory agencies.

JAMA Dermatology | Consensus Statement

Expert Recommendations on Use of Topical Therapeutics for Vitiligo in Pediatric, Adolescent, and Young Adult Patients

Yael Renert-Yuval, MD, MSc; Khaled Ezzedine, MD, PhD; Pearl Grimes, MD; David Rosmarin, MD; Lawrence F. Eichenfield, MD; Leslie Castelo-Soccio, MD, PhD; Victor Huang, MD; Seemal R. Desai, MD; Samantha Walsh, MLS, MA; Jonathan I. Silverberg, MD, PhD, MPH; Amy S. Paller, MD; Michele Rodrigues, MD; Mark Weingarten, BA; Shanthi Narla, MD; Jackie Gardner, BA; Michael Siegel, PhD;

Figure. Therapeutic Paradigm for Pediatric, Adolescent, and Young Adult Patients With Vitiligo

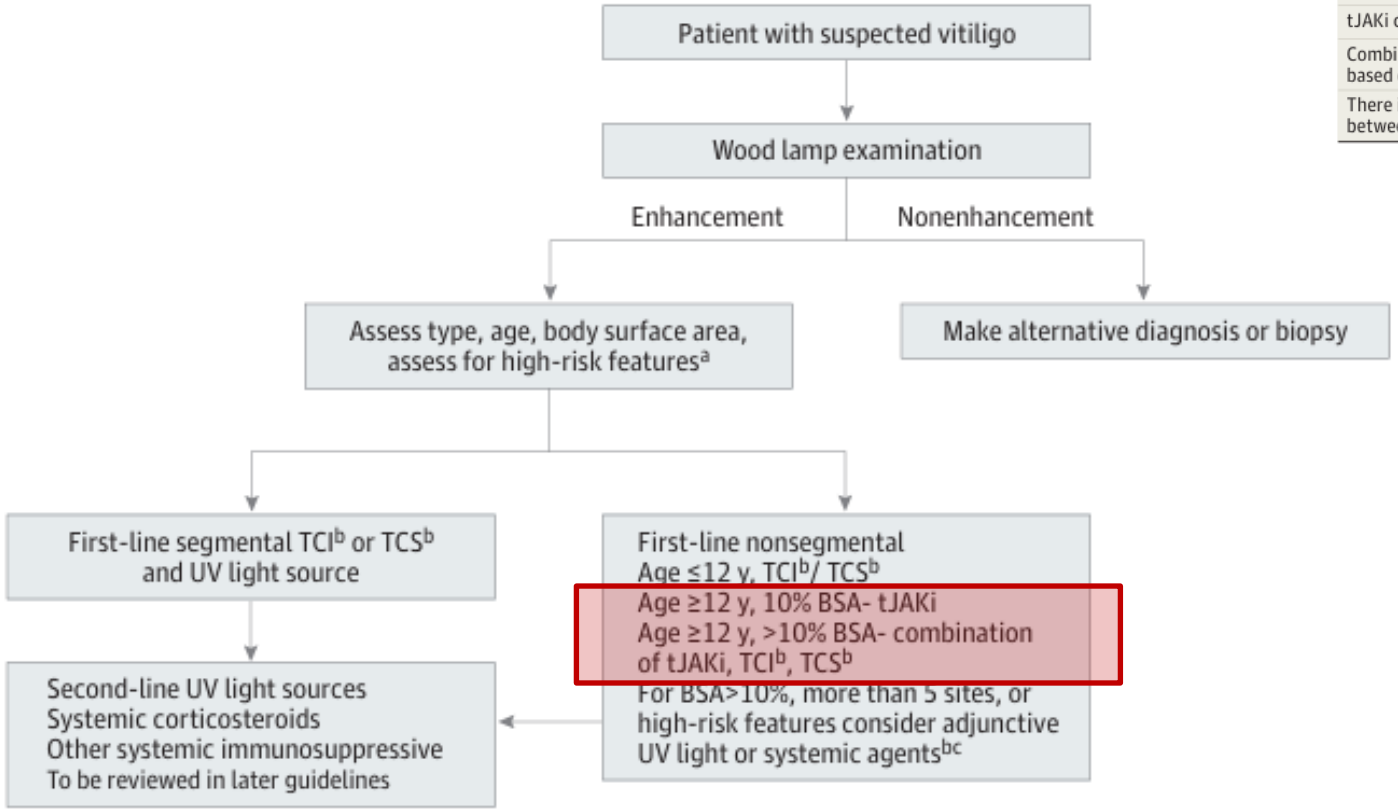


Table 4. Topical JAK Inhibitor (tJAKi) Recommendations and Pseudocatalase Recommendations

Statement	Evidence grade SORT	OXFORD
tJAKi should be considered as first-line or second-line therapy at 12 y of age and older, and at younger ages with lesser evidence.[59-61]	EC	5
tJAKi may be used off label in younger children but has limited evidence and should be used with limited BSA until absorption data are better understood.[61,62]	C3	5
Patients may need more than 3 mo to see initial repigmentation with use of tJAKi. Patients may need to be treated with tJAKi beyond 1 y before maximal repigmentation is achieved.[59-65]	A1	1
Counseling patients treated with tJAKi includes mention of the label adverse events, which are derived from trials of systemic tJAKi, with focus on common adverse events including acne and application site reactions.[59,60,66] (product label)	EC	1
tJAKi can be applied to areas with risk of atrophy including face, eyelids, and groin.[67,68]	A1	1
Combination of tJAKi and phototherapy (natural sunlight or NB-UV-B) may be synergistic based on evidence in adults but needs to be confirmed in pediatric patients.[69-73]	EC	1
There is not enough evidence to recommend pseudocatalase due to extreme variability between formulations.[67-71]	EC	5

Inh JAK en vitíligo … inicio

Journal of the American Academy of Dermatology
Volume 74, Issue 2, February 2016, Pages 370-371

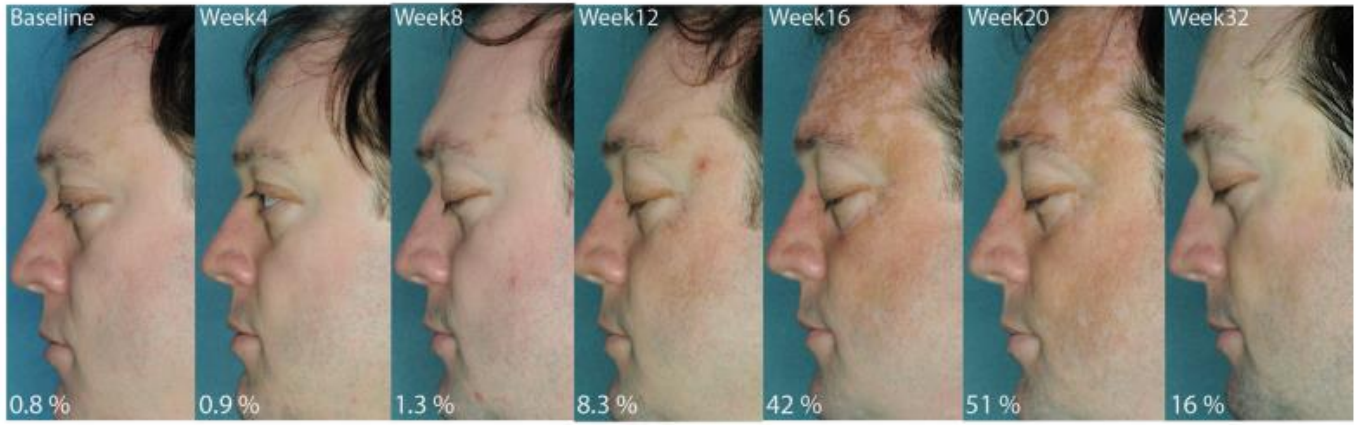
Letter

Rapid skin repigmentation on oral ruxolitinib in a patient with coexistent vitiligo and alopecia areata (AA)

John E. Harris MD, PhD [a], Mehdi Rashighi MD [a], Nhan Nguyen MD [b], Ali Jabbari MD, PhD [b], Grace Ulerio BA [b], Raphael Clynes MD, PhD [b], Angela M. Christiano PhD [b, c], Julian Mackay-Wiggan MD, MS [b]

CASO CLÍNICO

- Hombre 35 años con AA y vitíligo.
- Estudio Fase 2 para evaluar la eficacia de ruxolitinib (Jakafi,Incyte,Wilmington, DE) en AA moderada-severa
- **Ruxolitinib oral:** 20 mg/12h durante 20 sem
- **Resultados: Semana 20 repigmentación facial del 51%**
- 12 semanas tras suspensión: repigmentación regresó.



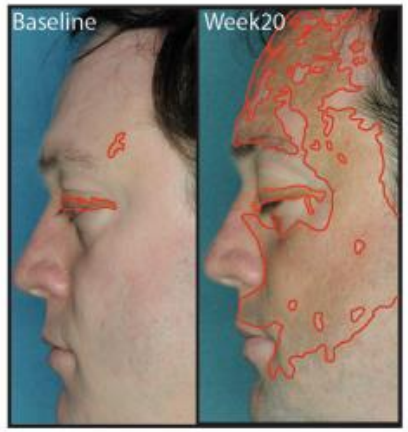
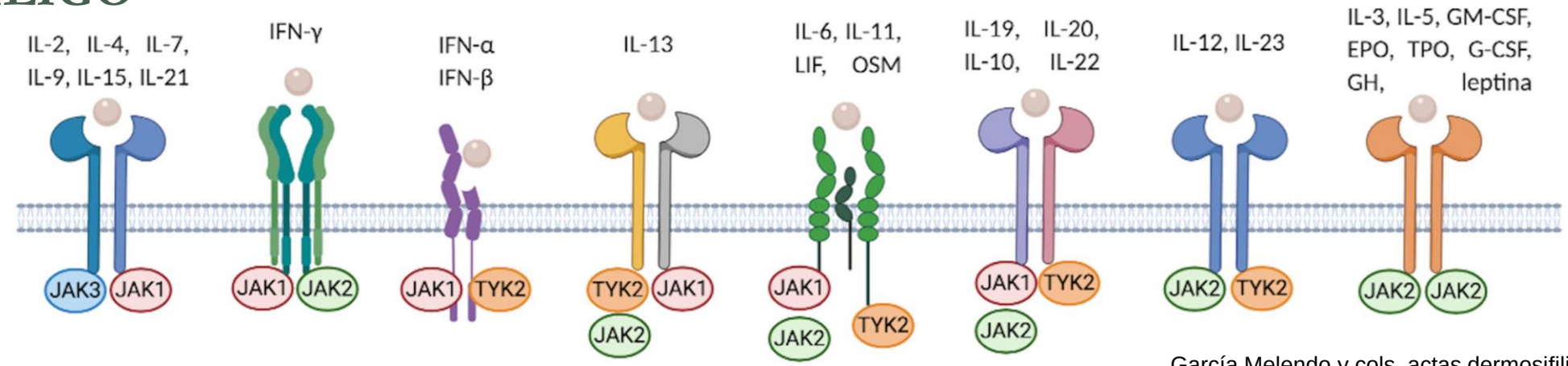


Fig 1. Vitiligo repigmentation during treatment with ruxolitinib. Screening skin examination reveals near-complete depigmentation of the patient's face at baseline. The first evidence of skin repigmentation appeared after 12 weeks of therapy, which continued until week 20, when ruxolitinib was discontinued. Follow-up visit 12 weeks after stopping the treatment shows recurrent depigmentation in the majority of previously repigmented areas. Pigmented areas of the face were outlined using the freehand selection tool followed by calculation of the percent selected area using ImageJ software (National Institutes of Health, Bethesda, MD).

VITILIGO



García Melendo y cols. actas dermosifiliogr 2021; 112: 503-15

	JAK 1	JAK 2	JAK 3	TYK 2	OTROS
Tópicos	RUXOLITINIB **(**aprobado** FDA/EMA)				
	CERDULATINIB				SYK
Orales	INCB54707				
	UPADACITINIB				
	TOCAFITINIB				
	BREPOCITINIB			BREPOCITINIB	
			RITLECITINIB		TEC

Qui. Inmunol frontal. 2021; 12: 790125.

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 OCTOBER 20, 2022 VOL. 387 NO. 16

Two Phase 3, Randomized, Controlled Trials of Ruxolitinib Cream for Vitiligo

David Rosmarin, M.D., Thierry Passeron, M.D., Ph.D., Amit G. Pandya, M.D., Pearl Grimes, M.D., John E. Harris, M.D., Ph.D., Seemal R. Desai, M.D., Mark Lebwohl, M.D., Mireille Ruer-Mulard, M.D., Julien Seneschal, M.D., Ph.D., Albert Wolkerstorfer, M.D., Ph.D., Deanna Kornacki, Ph.D., Kang Sun, Ph.D., Kathleen Butler, M.D., and Khaled Ezzedine, M.D., Ph.D., for the TRuE-V Study Group*

Eligibility Criteria

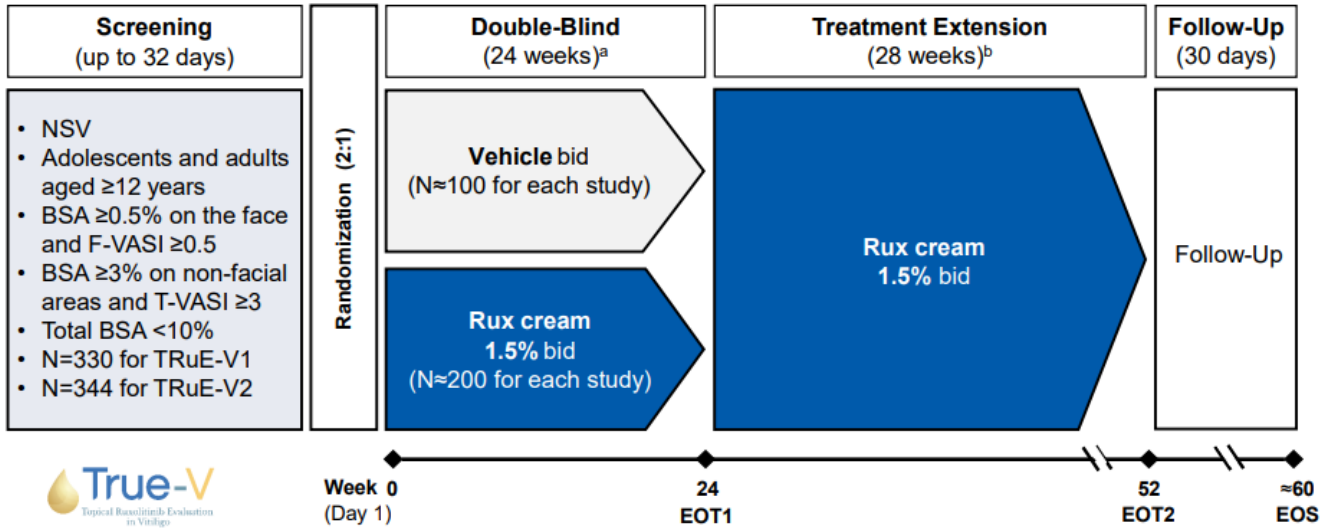
Key Inclusion Criteria

- Patients aged ≥12 years with nonsegmental vitiligo
- Depigmented areas including the following
  - ≥0.5% of total BSA on the face and ≥3% of total BSA on nonfacial areas
  - Scores ≥0.5 on F-VASI and ≥3 on T-VASI

Hospital Universitario Fundación Alcorcón **(Madrid)**
Hospital Universitari Germans Trias i Pujol **(Barcelona)**
Clínica Universitaria de Navarra **(Navarra/Madrid**)

TRuE-V
Diseño del estudio1-3

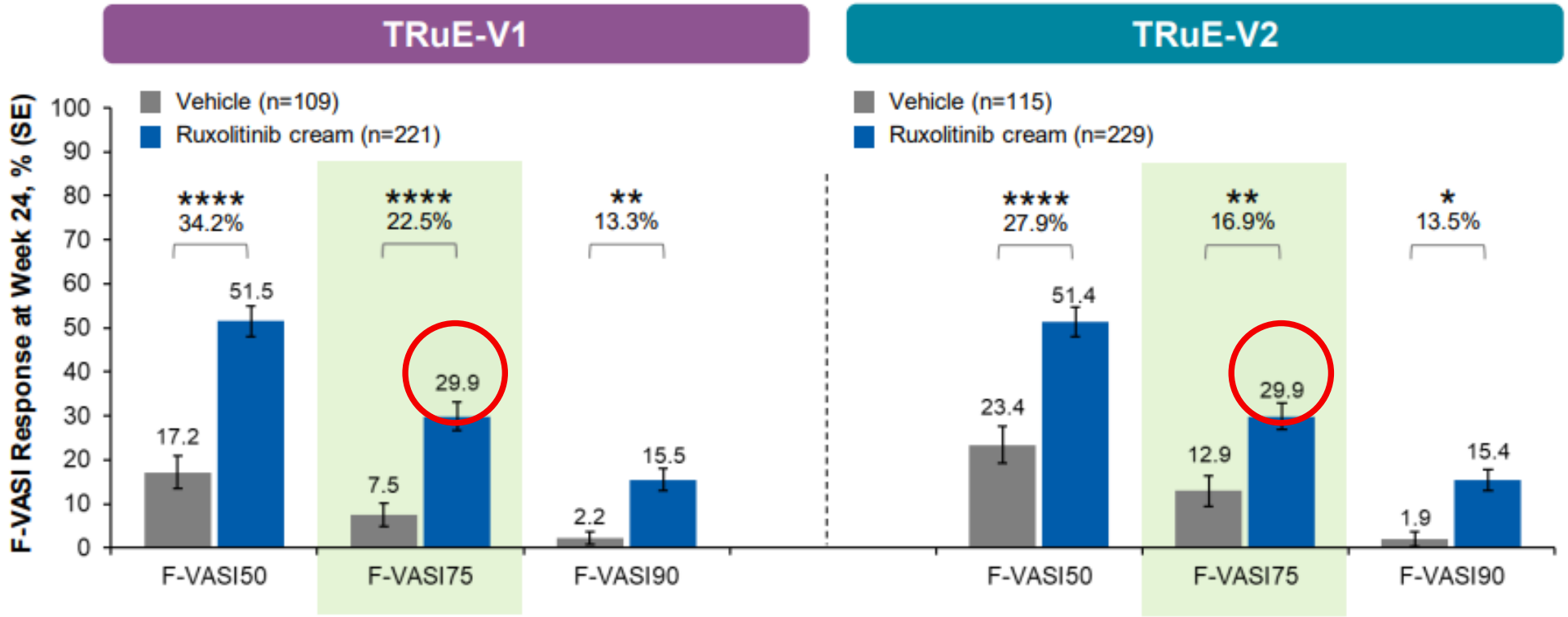
TRuE-V1 and TRuE-V2
Two Phase 3, Randomized, Double-Blind, 52-Week, Vehicle-Controlled Studies of Ruxolitinib Cream[1-3]



F-VASI Responses at Week 24

VITILIGO

- F-VASI75 (primary endpoint), F-VASI50, and F-VASI90 responses at week 24 were achieved by a significantly greater proportion of patients applying ruxolitinib cream vs vehicle[1,a,b]



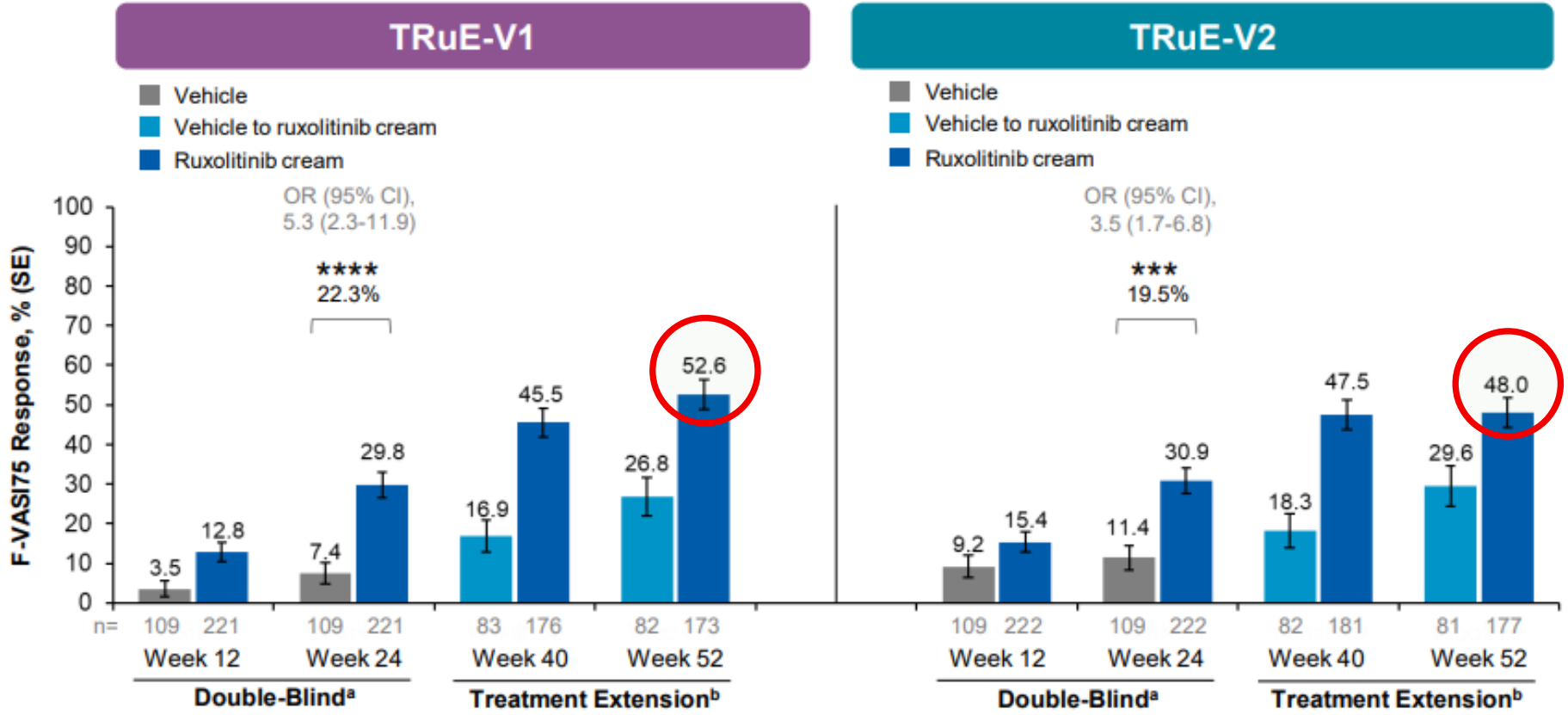
* $P<0.05$, ** $P<0.01$, **** $P<0.0001$ for response rate difference for ruxolitinib cream vs vehicle.
[a] Statistical analysis at week 24 used multiple imputation to account for any missing values. [b] A ≥50% improvement in facial repigmentation was considered clinically meaningful by patients based on analysis of TRuE-V1 and TRuE-V2 exit interviews.[2]

1. Rosmarin D, et al. EADV 2021. Oral presentation 2931. 2. Pandya AG, et al. Maui Derm 2022. ePoster.

F-VASI75 Responses
Individual Study Analyses Through 52 Weeks

VITILIGO

Aproximadamente **1/2** de los pacientes que aplicaron ruxolitinib crema desde el día 1 alcanzaron F-VASI75 en la semana 52

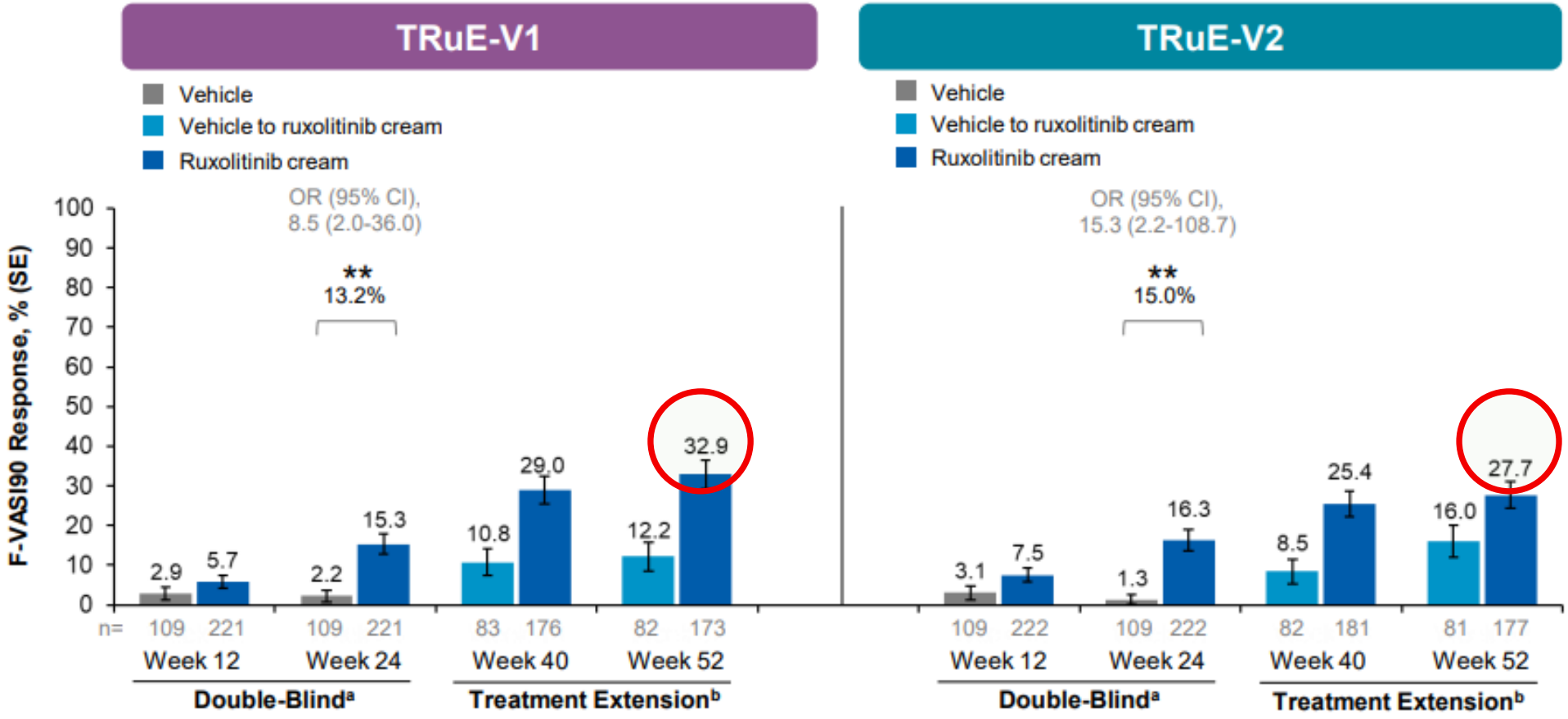


*** $P<0.001$, **** $P<0.0001$ for response rate difference for ruxolitinib cream vs vehicle.
[a] During the double-blind period (up to week 24), multiple imputation was applied to account for missing values. [b] During the open-label extension (after week 24), responses were reported as observed. Rosmarin D, et al. AAD 2022. Late-breaking oral presentation.

F-VASI90 Responses
Individual Study Analyses Through 52 Weeks

VITILIGO

Aproximadamente 1 de cada 3 pacientes que aplicaron ruxolitinib crema desde el día 1 alcanzaron F-VASI90 en la semana 52

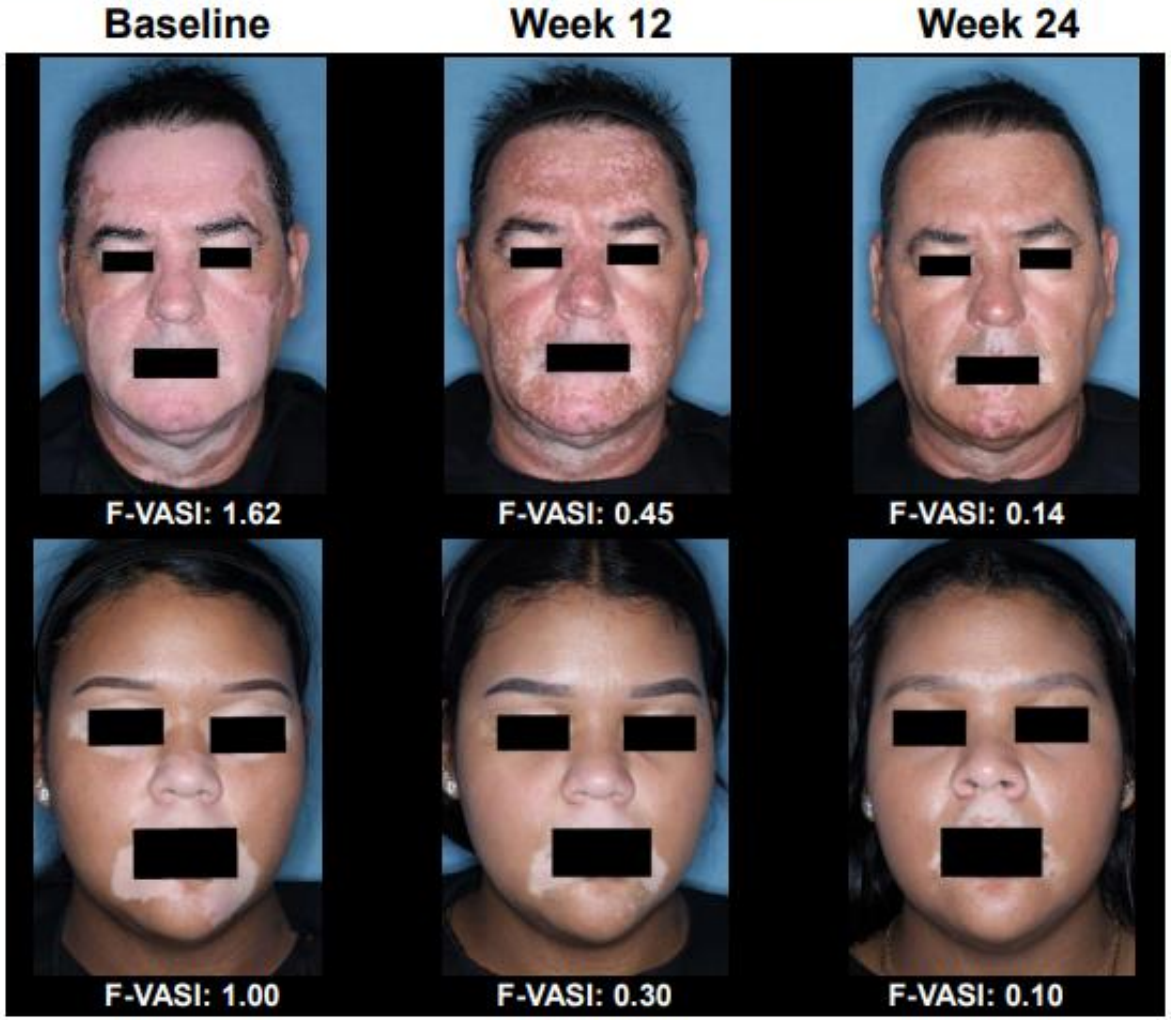


** *P*<0.01 for response rate difference for ruxolitinib cream vs vehicle.
[a] During the double-blind period (up to week 24), multiple imputation was applied to account for missing values. [b] During the open-label extension (after week 24), responses were reported as observed.
Rosmarin D, et al. AAD 2022. Late-breaking oral presentation.

VITILIGO

Representative Clinical Images Showing F-VASI Response

Ruxolitinib Cream 1.5% bid



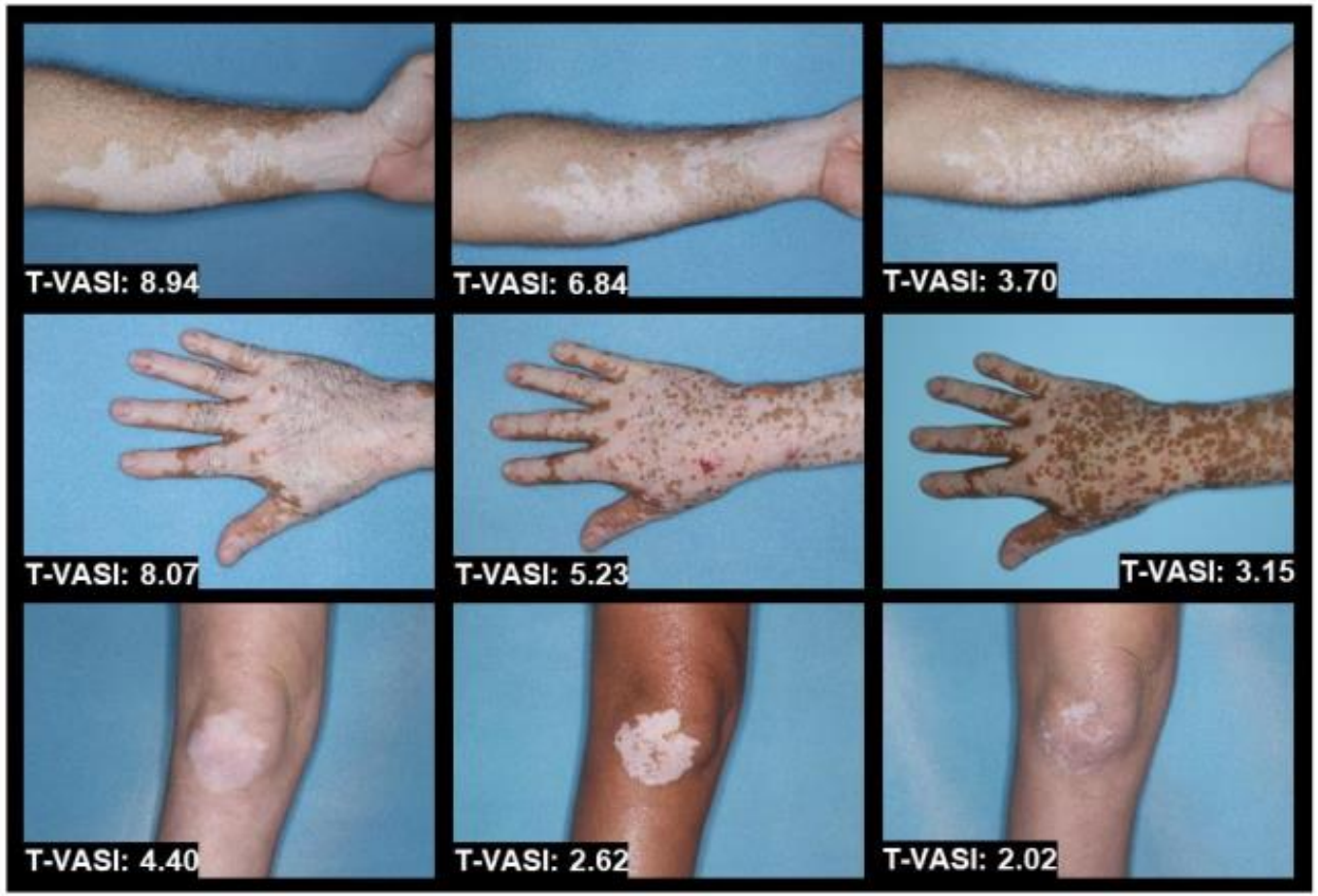
Rosmarin D, et al. EADV 2021. Oral presentation 2931.

N Engl J Med . 2022 20;387(16):1445-55

VITILIGO

Clinical Images Showing Repigmentation of Body Regions

Ruxolitinib Cream 1.5% bid



VASI improvement from baseline at week 52

T-VASI[a]: **58.6%**
VASI of upper extremities: **45.8%**

T-VASI[a]: **60.9%**
VASI of hands: **50.0%**

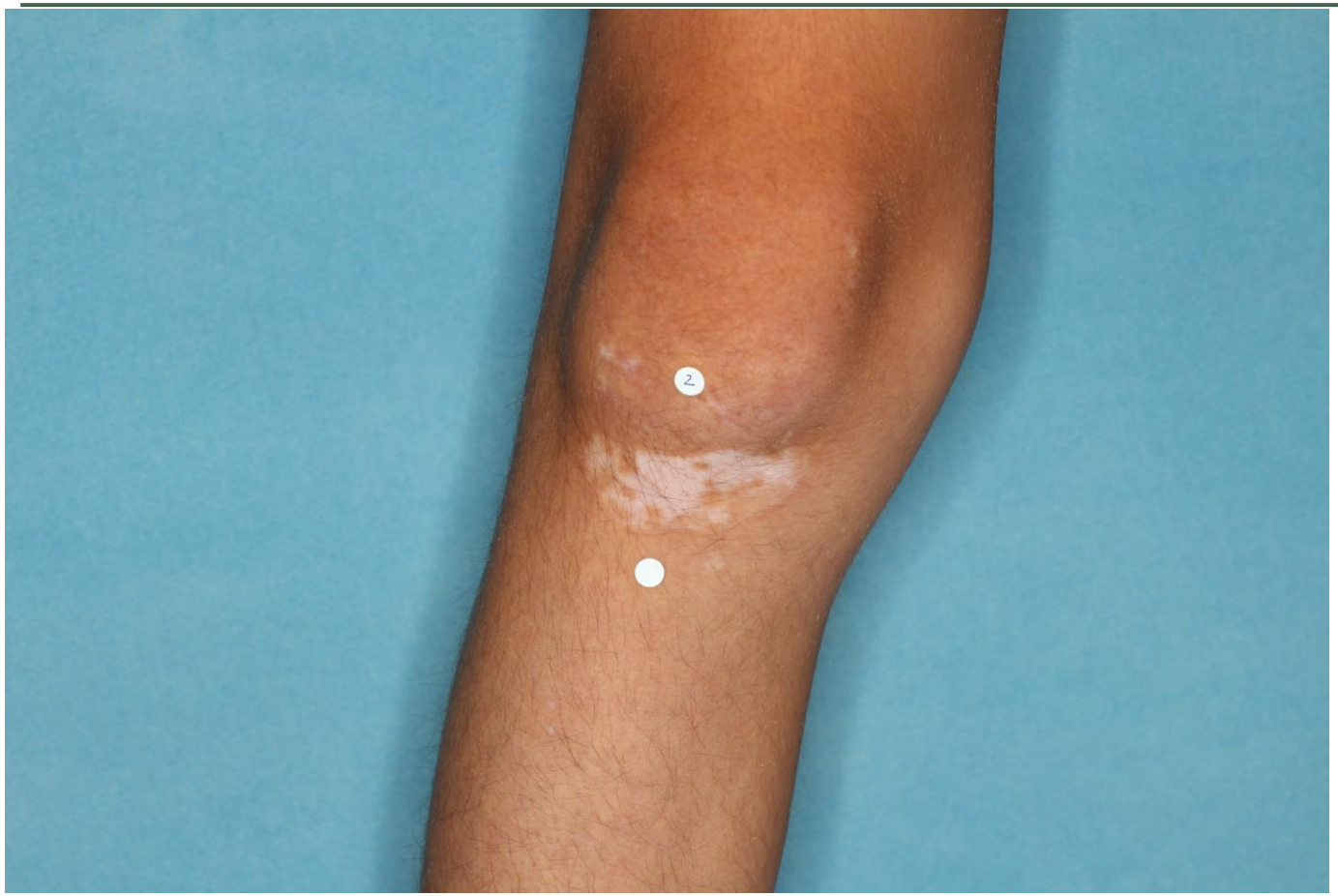
T-VASI[a]: **54.0%**
VASI of lower extremities: **86.4%**

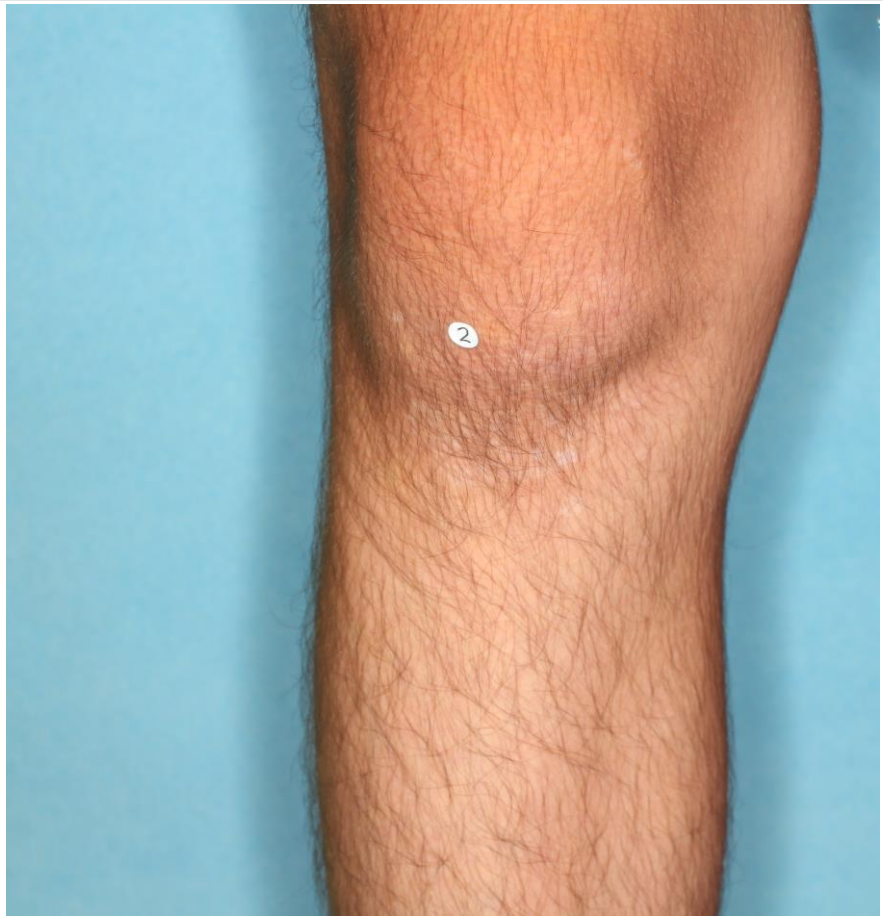
T-VASI scores (including face) that are indicated on the figure reflect the whole body of the patients and not only the body parts shown on the pictures.
Passeron T, et al. EADV 2022. Oral presentation 3640.

Nuestra experiencia... Dentro del EC

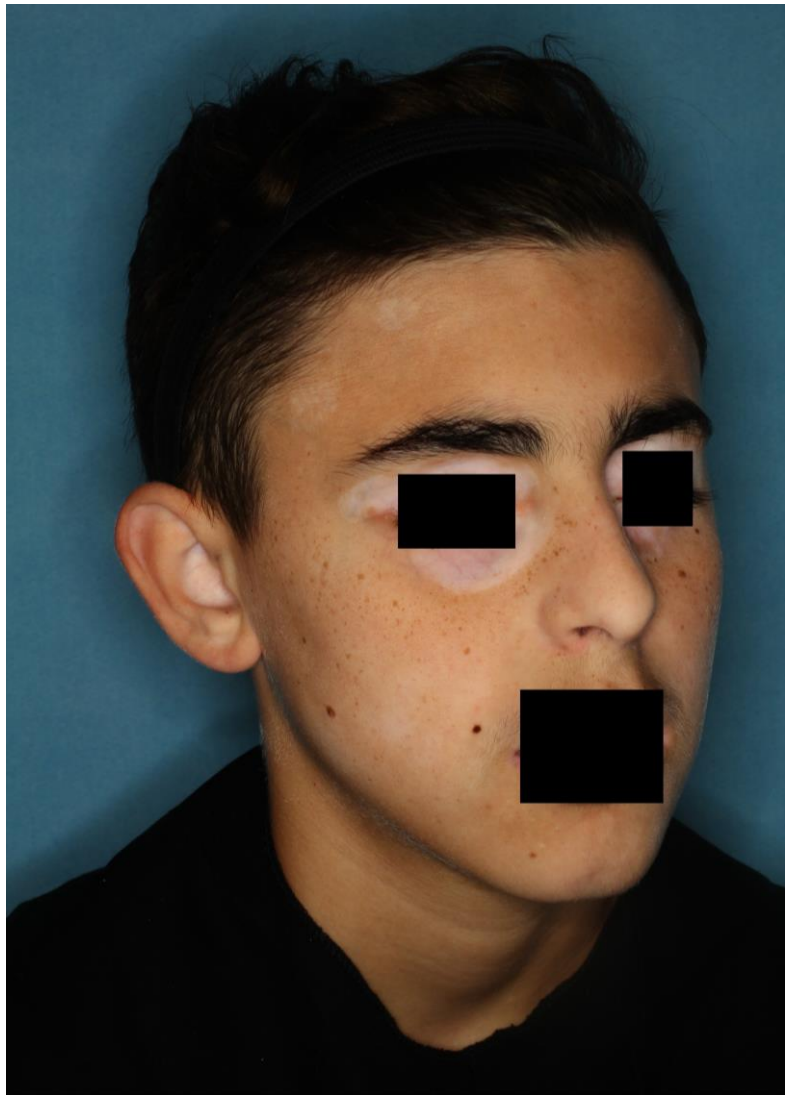
Baseline

Semana 52

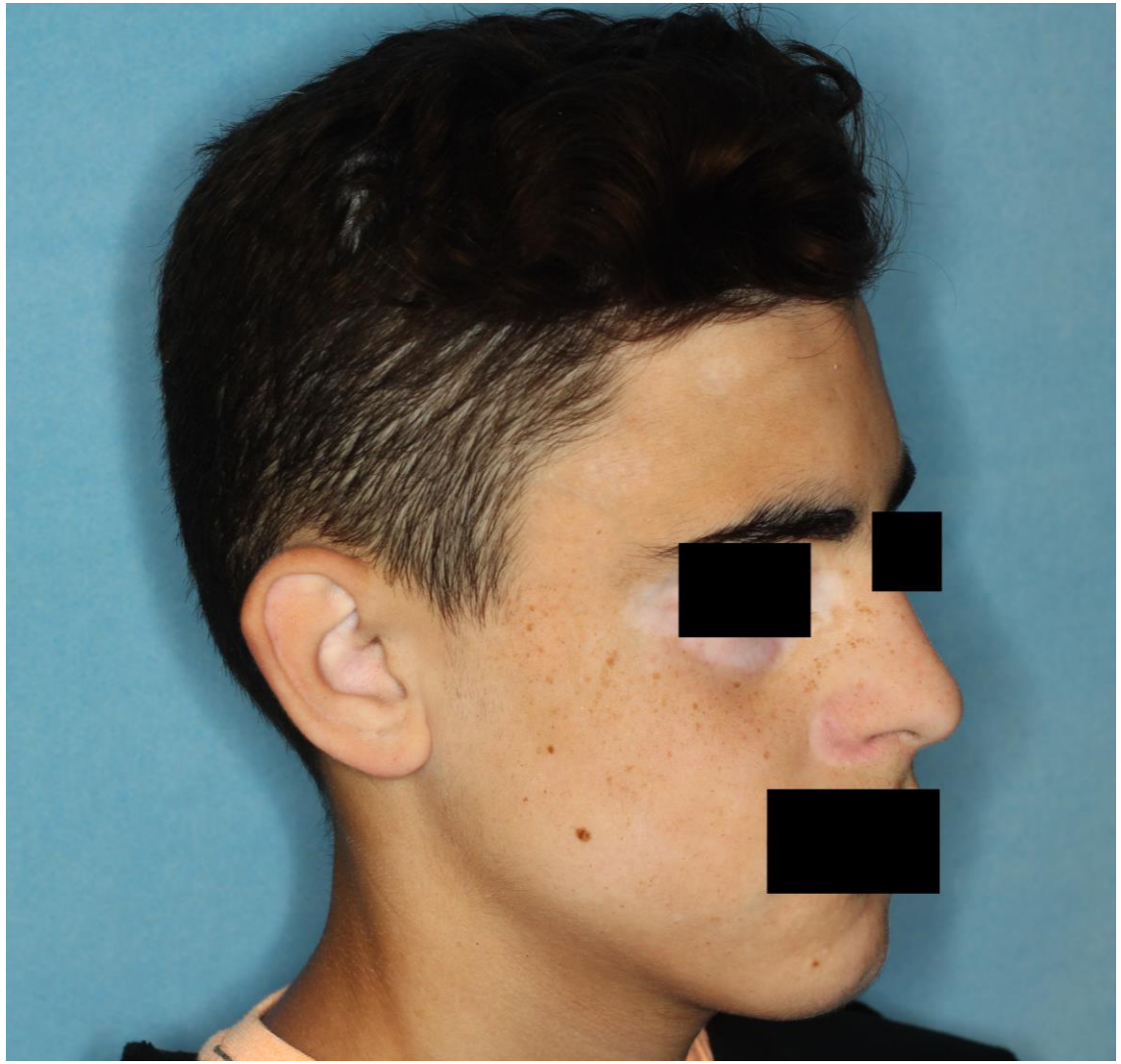




Baseline



Semana 52



Safety
Pooled Analysis Through 52 Weeks

VITILIGO

- Application site reactions, including acne and pruritus, were all mild or moderate
- No serious TEAEs were considered related to treatment with ruxolitinib cream

Characteristic, n (%)	Vehicle up to week 24 (n=224)	Ruxolitinib cream up to week 52[a] (n=637)
Patients with TEAE	81 (36.2)	332 (52.1)
Most common TEAEs[b]		
COVID-19	7 (3.1)	39 (6.1)
Application site acne	3 (1.3)	34 (5.3)
Nasopharyngitis	5 (2.2)	31 (4.9)
Application site pruritus	6 (2.7)	25 (3.9)
Headache	6 (2.7)	25 (3.9)
Upper respiratory tract infection	5 (2.2)	20 (3.1)
Patients with treatment-related TEAE	16 (7.1)	87 (13.7)
Most common treatment-related TEAEs[b]		
Application site acne	2 (0.9)	28 (4.4)
Application site pruritus	6 (2.7)	22 (3.5)
Patients with serious TEAE	1 (0.4)	14 (2.2)
Patients with TEAE leading to discontinuation	1 (0.4)	3 (0.5)

[a] Including patients who crossed over from vehicle to ruxolitinib cream after week 24. [b] Occurring in ≥3% of patients in any treatment group.
1. Wolkerstorfer A, et al. EADV 2022. Oral presentation FC01.04. 2. Passeron T, et al. EADV 2022. Oral presentation 3640.

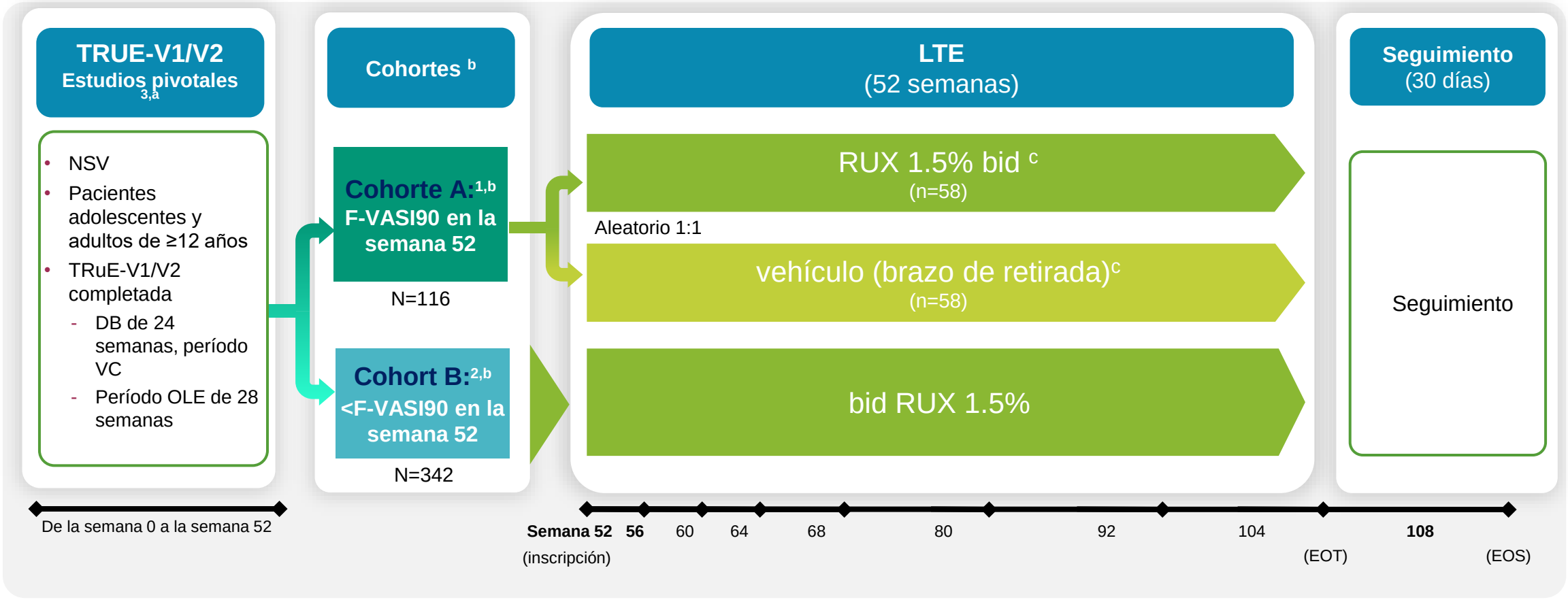
Incyte

N Engl J Med . 2022 20;387(16):1445-55

ESTUDIO DE EXTENSIÓN

VITILIGO

Diseño del estudio [1-4] TRuE-V LTE



a Los pacientes deben haber completado y tolerado 52 semanas de tratamiento con crema de ruxolitinib en los estudios iniciales TRuE-V1/V2 sin problemas de seguridad, a juicio de los investigadores, y con un buen cumplimiento. Los tratamientos concomitantes para el vitíligo, como la fototerapia, no se permitieron durante el estudio TRuE-V LTE. b La inscripción de la cohorte se basó en la respuesta clínica en la semana 52 de los estudios parentales. Cohorte A: pacientes que lograron una repigmentación facial casi completa (F-VASI90, es decir, una mejoría del ≥90% desde el inicio [día 1 del estudio parental] en F-VASI) al final de los estudios parentales TRuE-V1/V2; Cohorte B: pacientes que no lograron una repigmentación facial casi completa (respuesta <F-VASI90) al final de TRuE-V1/V2. c Todos los pacientes de la cohorte A utilizarían su tratamiento asignado al azar (ya sea vehículo o RUX 1,5% dos veces al día) tanto en la cara como en todo el cuerpo. El paciente de la cohorte A, que perdería, en cualquier momento, una respuesta clínicamente significativa en la cara (<F-VASI75) podría aplicar el tratamiento de rescate RUX 1,5% hasta la semana 104.

DB: doble ciego; EOS, fin de estudio; EOT, fin del tratamiento; LTE, extensión a largo plazo; OLE, extensión abierta; RUX, crema de ruxolitinib; VC, controlado por vehículo.

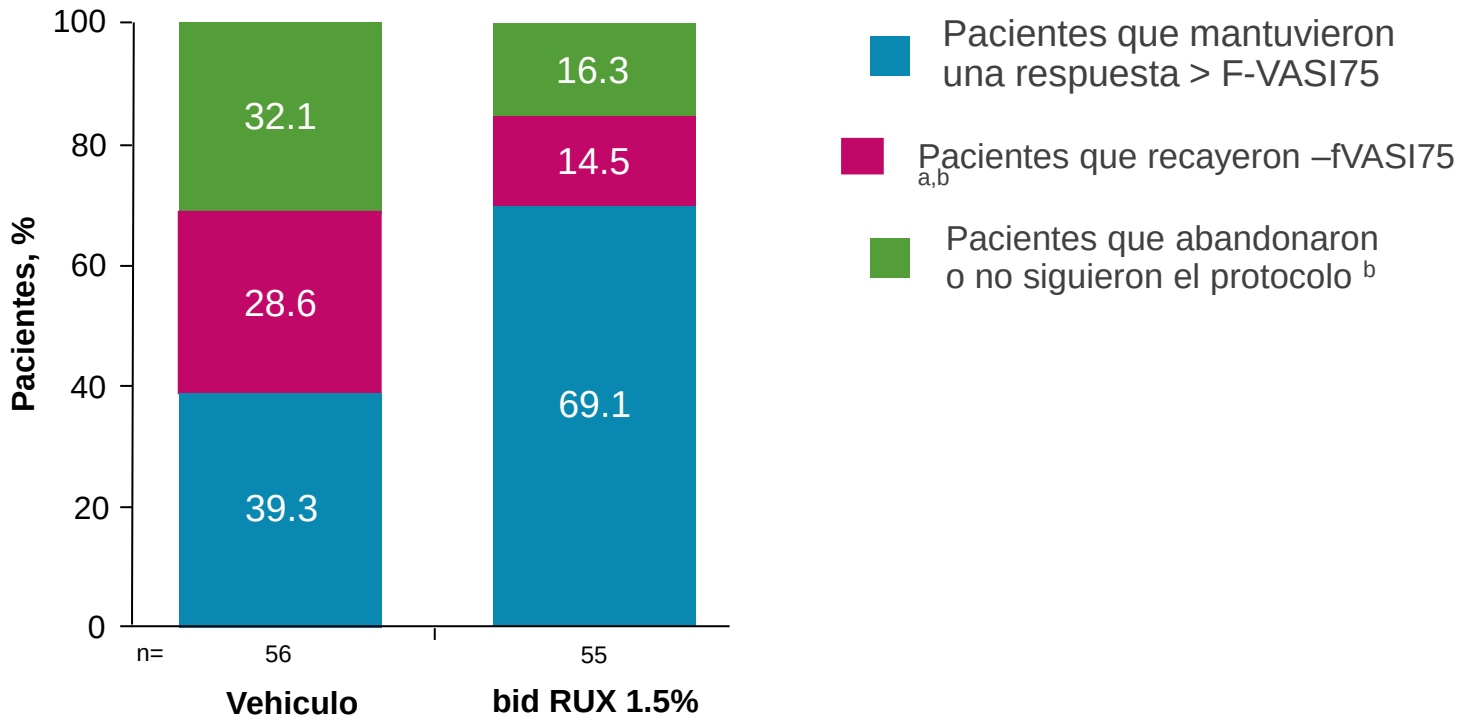
1. Harris JE, et al. AAD 2023. Presentación de última hora. 2. Rosmarin D, et al. AAD 2023. Presentación de última hora. 3. Rosmarina D, et al. *N Engl J Med.* 2022;387:1445-1455. 4. ClinicalTrials.gov. JIFE, 18424-308. Consultado en octubre de 2023. https://clinicaltrials.gov/study/NCT04530344.

Proporción de pacientes que mantuvieron una respuesta a **F-VASI75** en la semana 104 [1]
TRuE-V LTE – COHORTE A

~ El 69 % de los pacientes que continuaron la aplicación de la crema de ruxolitinib al 1,5 % dos veces al día mantuvieron una respuesta de F-VASI75 en la semana 104 [1,2]

Entre los pacientes que interrumpieron el tratamiento, se mantuvo una respuesta de F-VASI75 en ~39% en la semana 104 1,2

Proporciones de pacientes en la semana 104 [1,2]



a Un evento de "recaída" se definió como una pérdida de la respuesta de F-VASI75, y una respuesta de F-VASI75 se definió como una mejoría del ≥75% en F-VASI desde el inicio (día 1 del estudio inicial). b Se excluyó a los pacientes del análisis del tiempo transcurrido hasta la recaída en ausencia de recaída, si interrumpían el tratamiento o si aplicaban tratamiento de rescate sin recaída.

1. Harris JE, et al. AAD 2023. Presentación de última hora. 2. Datos en archivo, Incyte Corporation.

Proporción de pacientes que mantuvieron una respuesta a **F-VASI75** en la semana 104 [1]
TRuE-V LTE – COHORTE A

~ El 69 % de los pacientes que continuaron la aplicación de la crema de ruxolitinib al 1,5 % dos veces al día mantuvieron una respuesta de F-VASI75 en la semana 104 [1,2]

Entre los pacientes que interrumpieron el tratamiento, se mantuvo una respuesta de F-VASI75 en ~39% en la semana 104 1,2

La mayoría de los pacientes que experimentaron una recaída pudieron recuperar una repigmentación facial clínicamente significativa (F-VASI75)

El 75% de los pacientes **recuperaron F-VASI75**

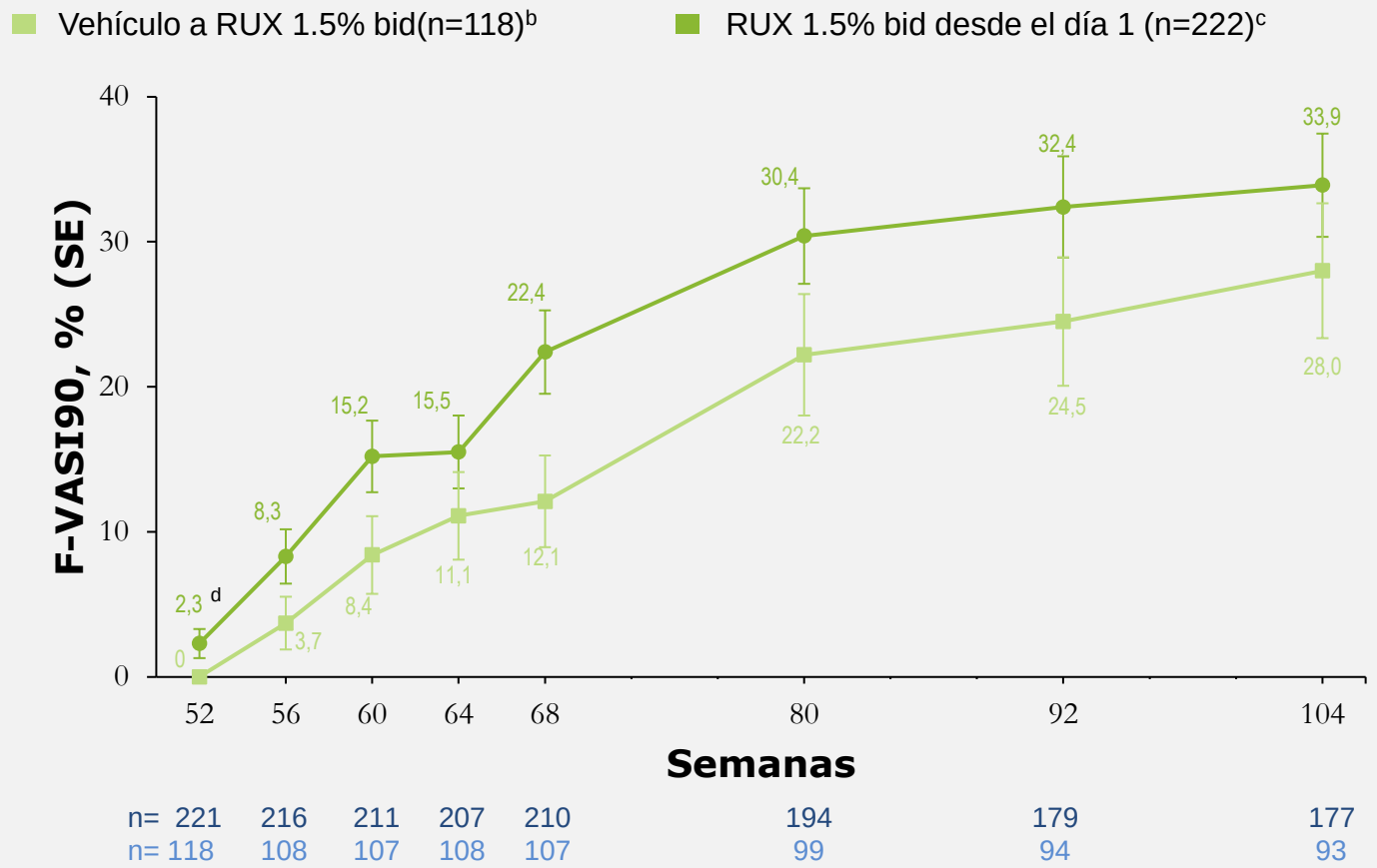
Mediana del tiempo necesario para recuperar el F-VASI75

fue de **12 semanas** después de reiniciar RUXb

a Un evento de "recaída" se definió como una pérdida de la respuesta de F-VASI75, y una respuesta de F-VASI75 se definió como una mejoría del ≥75% en F-VASI desde el inicio (día 1 del estudio inicial). b Se excluyó a los pacientes del análisis del tiempo transcurrido hasta la recaída en ausencia de recaída, si interrumpían el tratamiento o si aplicaban tratamiento de rescate sin recaída.

1. Harris JE, et al. AAD 2023. Presentación de última hora. 2. Datos en archivo, Incyte Corporation.

F-VASI90 Semanas de respuesta 52-104
TRuE-V LTE – **Cohorte B** [a]



Se observó una mejoría continua en las respuestas de F-VASI90 con la monoterapia con crema de ruxolitinib hasta la semana 104

El 33,9% de los pacientes que aplicaron crema de ruxolitinib al 1,5% dos veces al día desde el día 1 en los estudios parentales alcanzaron F-VASI90 en la semana 104

a Los pacientes que no lograron una repigmentación facial completa o casi completa (≥F-VASI90) al final del estudio parental (es decir, en la semana 52) fueron asignados a la cohorte B (± retirada del tratamiento) en el estudio TRuE-V LTE. b El grupo de vehículo a ruxolitinib crema al 1,5% dos veces al día corresponde a pacientes que aplicaron el vehículo crema durante el estudio TRuE-V inicial e iniciaron el tratamiento con ruxolitinib crema al 1,5% dos veces al día al inicio del estudio 308 LTE (semana 52). c El grupo de crema de ruxolitinib al 1,5 % dos veces al día corresponde a los pacientes que aplicaron crema de ruxolitinib al 1,5 % dos veces al día desde el día 1 del estudio TRuE-V hasta el estudio 308 LTE. d Cinco pacientes fueron asignados incorrectamente a la cohorte B al inicio del LTE.

Rosmarin D, et al. AAD 2023. Late-breaker presentation.

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← Home / Drugs / News & Events for Human Drugs / FDA approves topical treatment addressing repigmentation in vitiligo in patients aged 12 and older

07/2022

FDA approves topical treatment addressing repigmentation in vitiligo in patients aged 12 and older

2022

TWICE A DAY—EVERY DAY

2x

Consistently apply OPZELURA two times each day to the affected skin on up to 10% of body surface area, perhaps as part of your morning and evening routines.

NIH U.S. National Library of Medicine

ClinicalTrials.gov

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Home > Search Results > Study Record Detail

Save this study

Topical Ruxolitinib Evaluation in Vitiligo Study 1 (TRuE-V1)

Topical Ruxolitinib Evaluation in Vitiligo Study 2 (TRuE-V2)

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2023

Opzelura

ruxolitinib

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Page contents

Overview

Opzelura is a medicine used for treating non-segmental vitiligo, a disease that causes patches of skin to lose colour on both sides of the body. In patients with vitiligo, the immune system (the body's natural defences) attacks melanocytes (the skin cells that make pigment), causing patches of pale pink or white skin (depigmentation). Opzelura is used in adults and adolescents from 12 years of age with non-segmental vitiligo that also affects the face.

Opzelura contains the active substance ruxolitinib.

VITILIGO

Pérdida de respuesta al suspender el tratamiento.....

IL-15

La IL-15 estimula la proliferación de células T humanas de memoria

Células T CD8+ de memoria efectoras anti- melanocito

VITILIGO

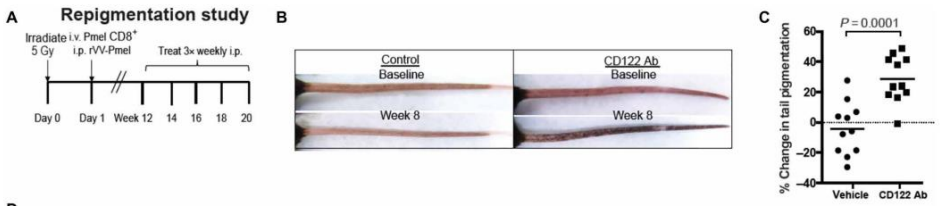
Published in final edited form as:
Sci Transl Med. 2018 July 18; 10(450): . doi:10.1126/scitranslmed.aam7710.

Antibody blockade of IL-15 signaling has the potential to durably reverse vitiligo

Jillian M. Richmond[1], **James P. Strassner**[1], **Lucio Zapata Jr.**[1], **Madhuri Garg**[1], **Rebecca L. Riding**[1], **Maggi A. Refat**[1], **Xueli Fan**[1], **Vincent Azzolino**[1], **Andrea Tovar-Garza**[2], **Naoya Tsurushita**[3], **Amit G. Pandya**[2], **J. Yun Tso**[3], and **John E. Harris**[1,*]

[1]Department of Dermatology, University of Massachusetts Medical School, Worcester, MA 01605, USA.

SCIENCE TRANSLATIONAL MEDICINE | RESEARCH ARTICLE



Row	Saved	Status	Study Title	Conditions	Interventions
1	☐	Completed	Effect of NB-UVB on the Tissue Level of **IL 15** and **IL-15**Rα in Active Non Segmental **Vitiligo** Cases.	• Active Non Segmental **Vitiligo**	• Radiation: Narrow band ultraviolet B
2	☐	Unknown †	Evaluation of Serum **Interleukin-15** and Interleukin-22 Levels in Patients With Non-segmental **Vitiligo**	• **Vitiligo**	• Diagnostic Test: **Interleukin-15** and Interleukin-22
3	☐	Recruiting	Evaluation of AMG 714 for **Vitiligo**	• **Vitiligo**	• Biological: AMG 714 • Biological: Placebo • Procedure: nbUVB phototherapy

Auremolimab

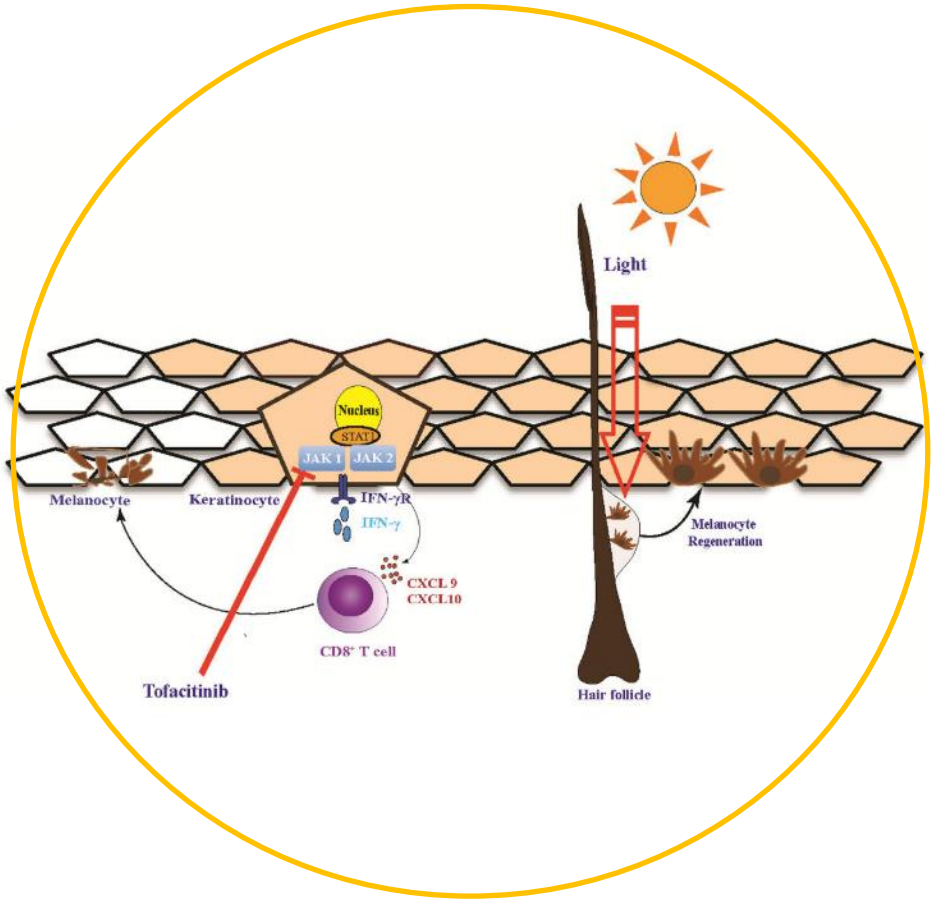
VITILIGO

Inhibidores JAK y fotoactivación

Repigmentation in vitiligo using the Janus kinase inhibitor tofacitinib may require concomitant light exposure

Lucy Y. Liu, BA • James P. Strassner, BS • Maggi A. Refat, MD • John E. Harris, MD, PhD • Brett A. King, MD, PhD

La repigmentación requiere tanto la supresión de la inflamación en la piel (inhibidores de JAK), como la **estimulación de los melanocitos mediante la exposición a la luz solar**



Beneficio iJAK asociados a UVBBE

Addition of Narrow-Band UVB Phototherapy to Ruxolitinib Cream in Patients With Vitiligo

Journal of Investigative Dermatology (2022) **142**, 3352–3355; doi:10.1016/j.jid.2022.05.1093

News · March 19, 2024

AAD 2024: Narrow Band Ultraviolet B Add-On Phototherapy Enhances Effectiveness of Ritlecitinib

VITILIGO

ALOPECIA AREATA

NEWS AND VIEWS

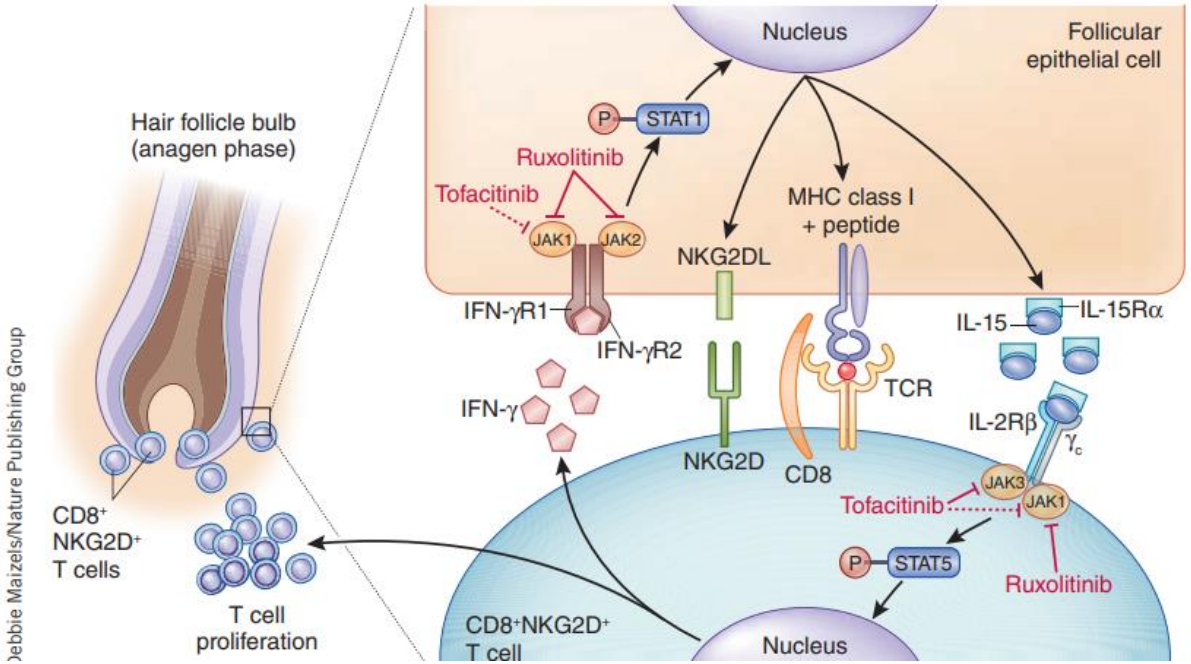
ALOPECIA AREATA

Inhibiting Janus kinases to treat alopecia areata

Sherrie J Divito & Thomas S Kupper

Alopecia areata is an immune-mediated, nonscarring form of hair loss. A new study using human clinical samples and a mouse model demonstrates that CD8αβ+NKG2D+ T effector memory cells mediate alopecia areata in part through Janus kinase (JAK) signaling and that alopecia areata might be treated with JAK inhibitors.

NEWS AND VIEWS



Received: 7 October 2023 | Accepted: 27 November 2023
DOI: 10.1111/jdv.19768

JEADV JOURNAL OF THE EUROPEAN ACADEMY OF DERMATOLOGY & VENEREOLOGY

REVIEW ARTICLE

European expert consensus statement on the systemic treatment of alopecia areata

L. Rudnicka[1] | M. Arenbergerova[2] | R. Grimalt[3] | D. Ioannides[4] | A. C. Katoulis[5] | E. Lazaridou[5] | M. Olszewska[1] | Y. S. Ovcharenko[6] | B. M. Piraccini[7,8] | A. Prohic[9] | A. Rakowska[1] | P. Reygagne[10] | M. A. Richard[11] | R. O. Soares[12] | M. Starace[7,8] | S. Vañó-Galvan[13] | A. Waskiel-Burnat[1]

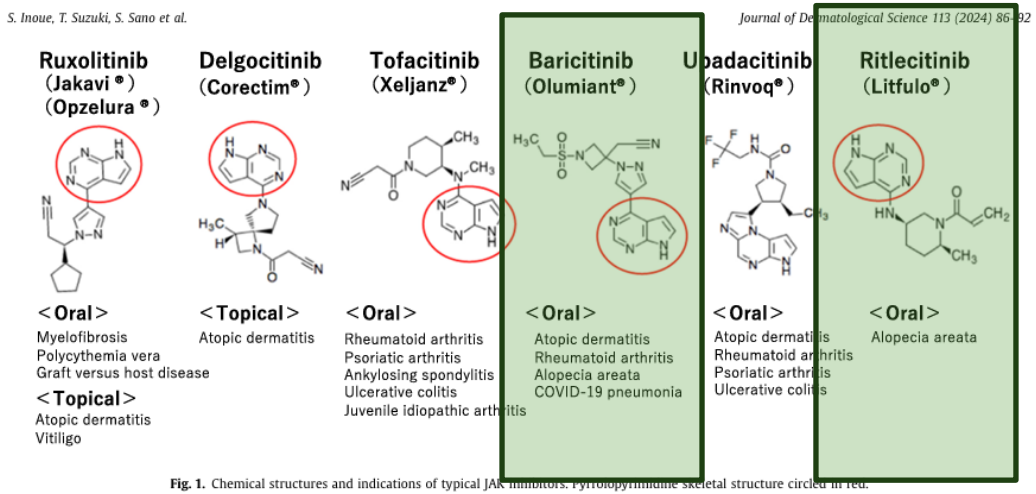
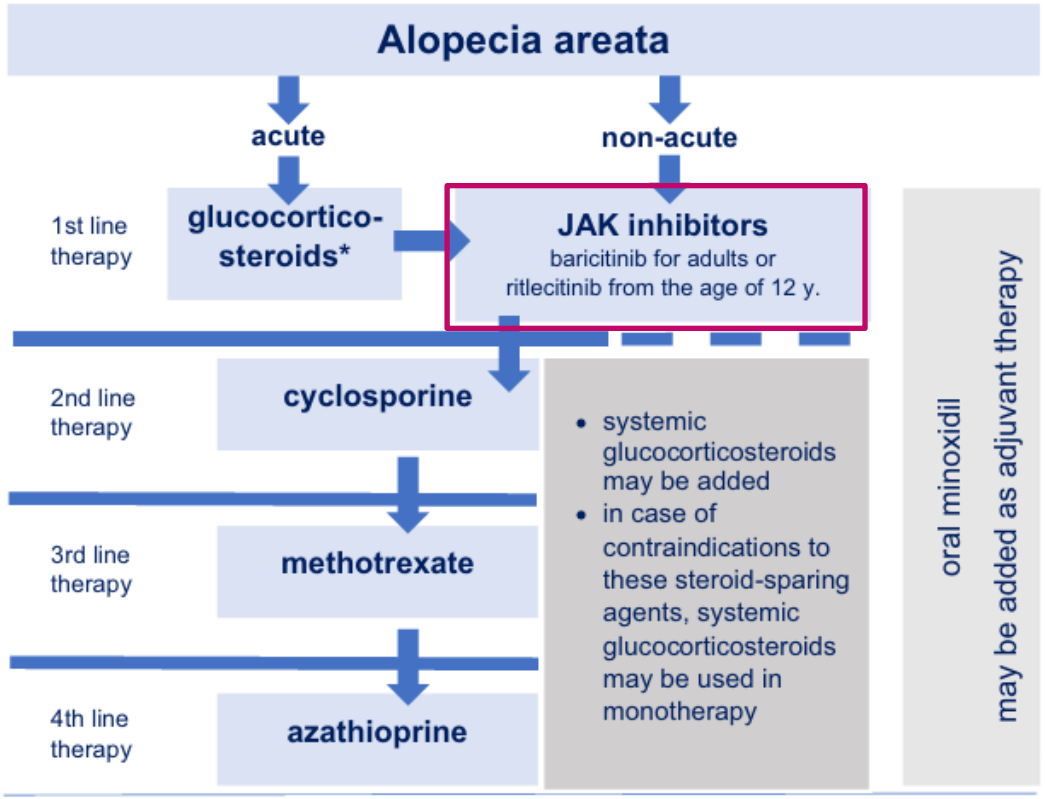


Fig. 1. Chemical structures and indications of typical JAK inhibitors. Pyrrolopyrimidine skeletal structure circled in red.

ALOPECIA AREATA



ggested therapeutic algorithm for the systemic treatment of alopecia areata.

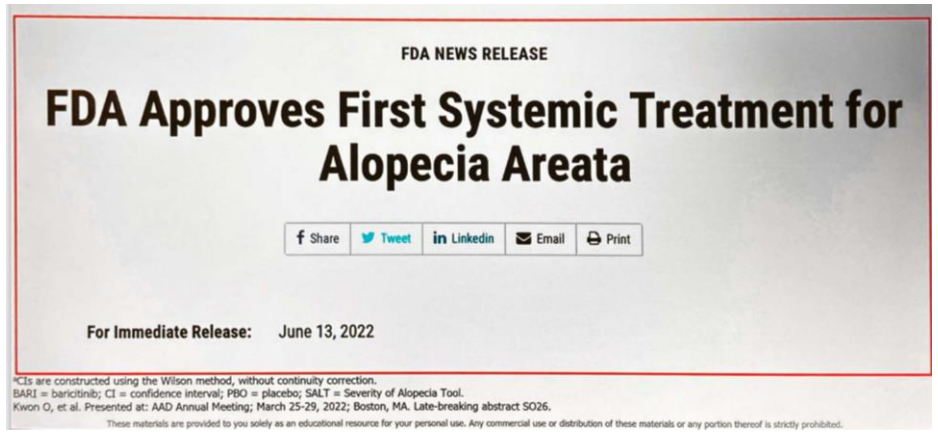
ALOPECIA AREATA

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 MAY 5, 2022 VOL. 386 NO. 18

Two Phase 3 Trials of Baricitinib for Alopecia Areata

Brett King, M.D., Ph.D., Manabu Ohyama, M.D., Ph.D., Ohsang Kwon, M.D., Ph.D., Abraham Zlotogorski, M.D., Justin Ko, M.D., Natasha A. Mesinkovska, M.D., Ph.D., Maria Hordinsky, M.D., Yves Dutronc, M.D., Wen-Shuo Wu, M.D., Jill McCollam, Pharm.D., Chiara Chiasserini, Sc.D., Guanglei Yu, Ph.D., Sarah Stanley, Ph.D., Katrin Holzwarth, M.D., Amy M. DeLozier, M.P.H., and Rodney Sinclair, M.D., for the BRAVE-AA Investigators*



FDA NEWS RELEASE

FDA Approves First Systemic Treatment for Alopecia Areata

Share | Tweet | LinkedIn | Email | Print

For Immediate Release: June 13, 2022

*CIs are constructed using the Wilson method, without continuity correction.
BARI = baricitinib; CI = confidence interval; PBO = placebo; SALT = Severity of Alopecia Tool.
Kwon O, et al. Presented at: AAD Annual Meeting; March 25-29, 2022; Boston, MA. Late-breaking abstract SO26.

Received: 31 March 2023 | Accepted: 20 October 2023

DOI: 10.1111/jdv.19665

JEADV JOURNAL OF THE EUROPEAN ACADEMY OF DERMATOLOGY & VENEREOLOGY

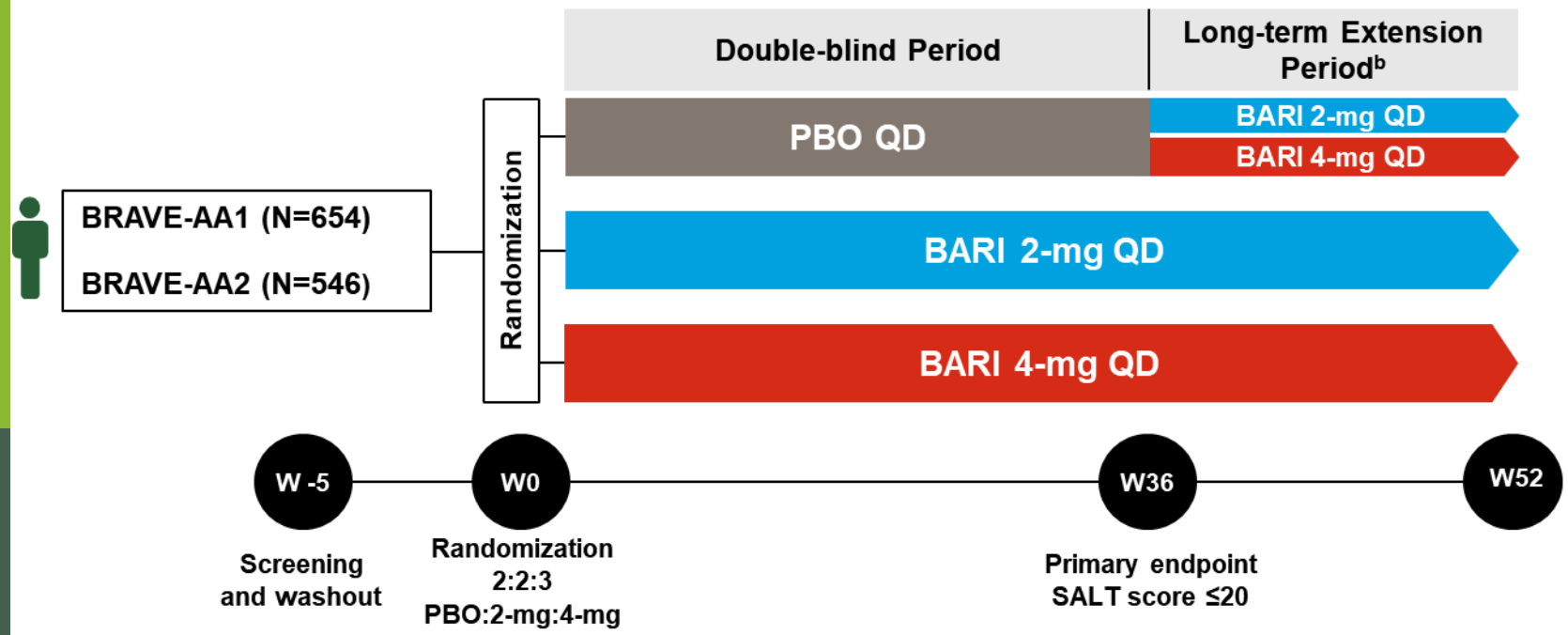
ORIGINAL ARTICLE

Long-term efficacy and safety of baricitinib in patients with severe alopecia areata: 104-week results from BRAVE-AA1 and BRAVE-AA2

M. Senna[1] | A. Mostaghimi[2] | M. Ohyama[3] | R. Sinclair[4] | Y. Dutronc[5] | W. S. Wu[5] | G. Yu[5] | C. Chiasserini[5] | N. Somani[5] | K. Holzwarth[5] | B. King[6]

ALOPECIA AREATA

Study Design[a], BRAVE-AA1 and BRAVE-AA2



Key Eligibility Criteria

- Male or female ≥18 years old; ≤60 years for males and ≤70 years for females
- Hair loss involving ≥50% of the scalp, as measured by the SALT score
- Current episode of AA >6 months to <8 years[c]
- No spontaneous improvement in the 6 months prior to screening

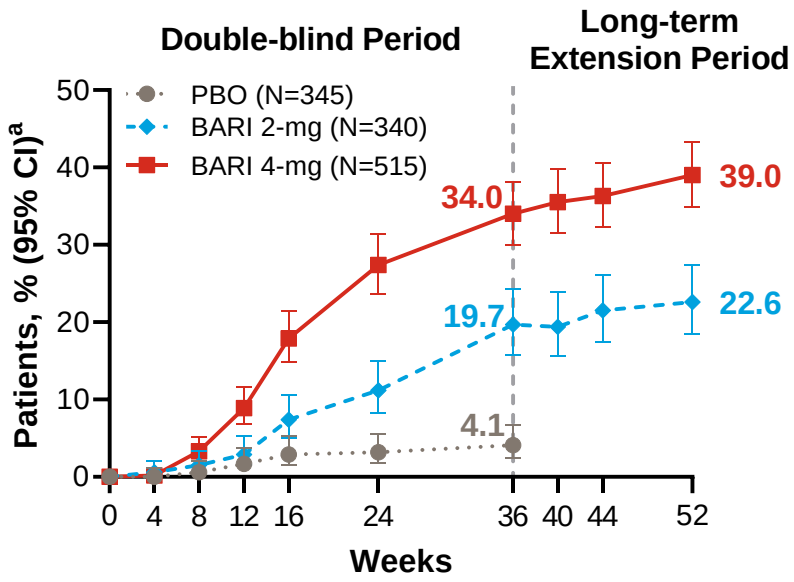
[a] Figure is not the full study design, but only the Double-blind Period and the Long-term Extension Period of both trials; [b] Patients randomized to BARI (4-mg or 2-mg QD) at baseline retained their treatment allocation through W52, whereas PBO non-responders were rescued at W36; [c] Patients who had AA for ≥8 years could be enrolled if episodes of regrowth (spontaneous or under treatment) had been observed on the affected areas over the past 8 years

AA=alopecia areata; BARI=baricitinib; PBO=placebo; QD=once daily; SALT=Severity of Alopecia Tool; W=Week

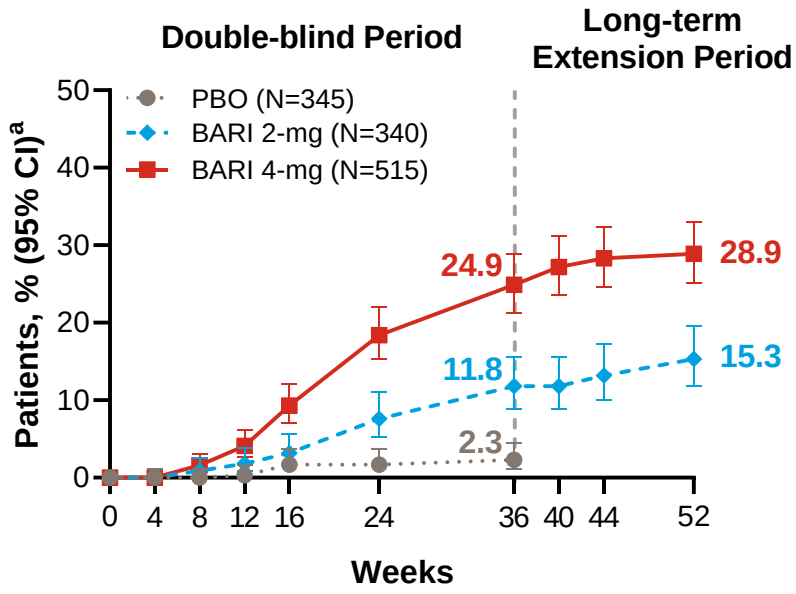
ALOPECIA AREATA

Proportion of Patients Achieving SALT Score ≤20 and SALT Score ≤10 Increased Over 52 Weeks of BARI Treatment

SALT Score ≤20



SALT Score ≤10



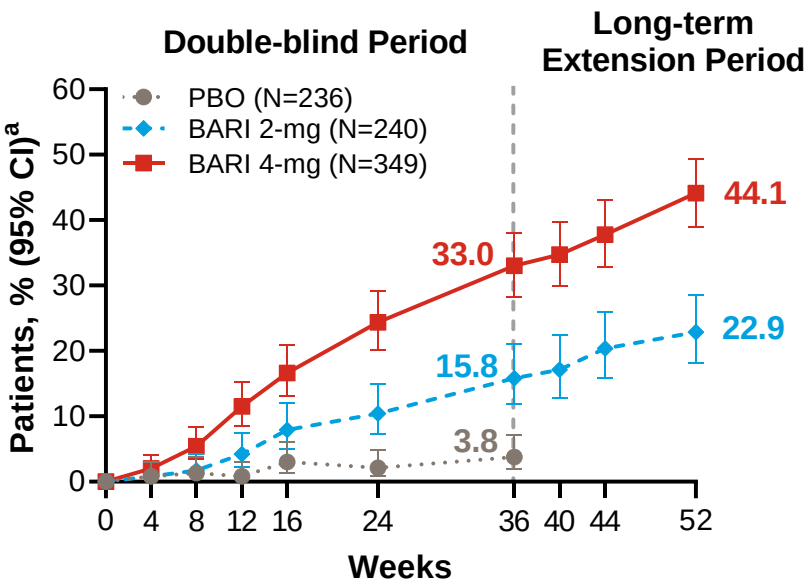
- Proportions of patients achieving SALT score ≤20 and SALT score ≤10 were higher for patients treated with BARI 4-mg vs. BARI 2-mg

Non-responder imputation used for missing data
Patients randomized to BARI (4-mg or 2-mg QD) at baseline retained their treatment allocation through W52, whereas PBO non-responders were rescued at W36
[a] CIs are constructed using the Wilson method, without continuity correction
BARI=baricitinib; CI=confidence interval; PBO=placebo; SALT=Severity of Alopecia Tool

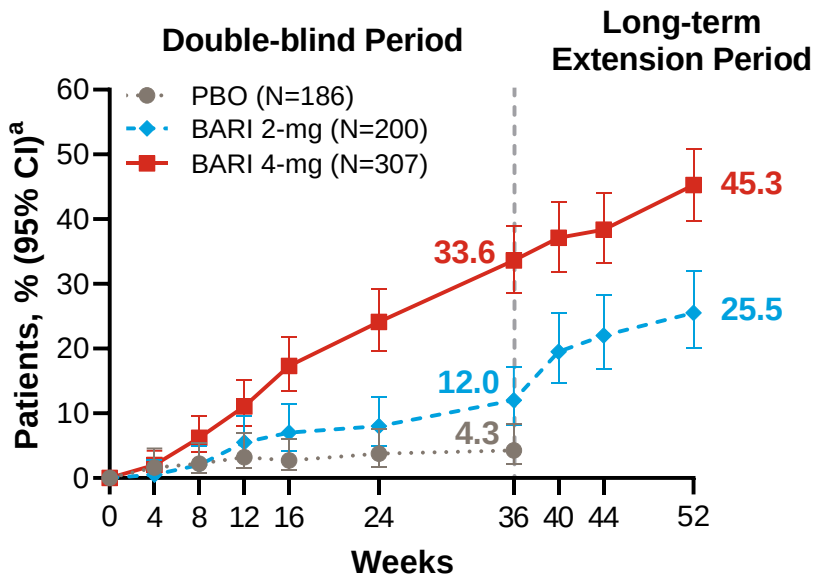
Continued Improvements in Eyebrow and Eyelash Hair Regrowth Were Observed Over 52 Weeks of BARI Treatment

ALOPECIA AREATA

ClinRO Measure for EB Hair Loss 0-1 With ≥2-Point Improvement From Baseline Among Patients With ClinRO EB ≥2 at Baseline



ClinRO Measure for EL Hair Loss 0-1 With ≥2-Point Improvement From Baseline Among Patients With ClinRO EL ≥2 at Baseline

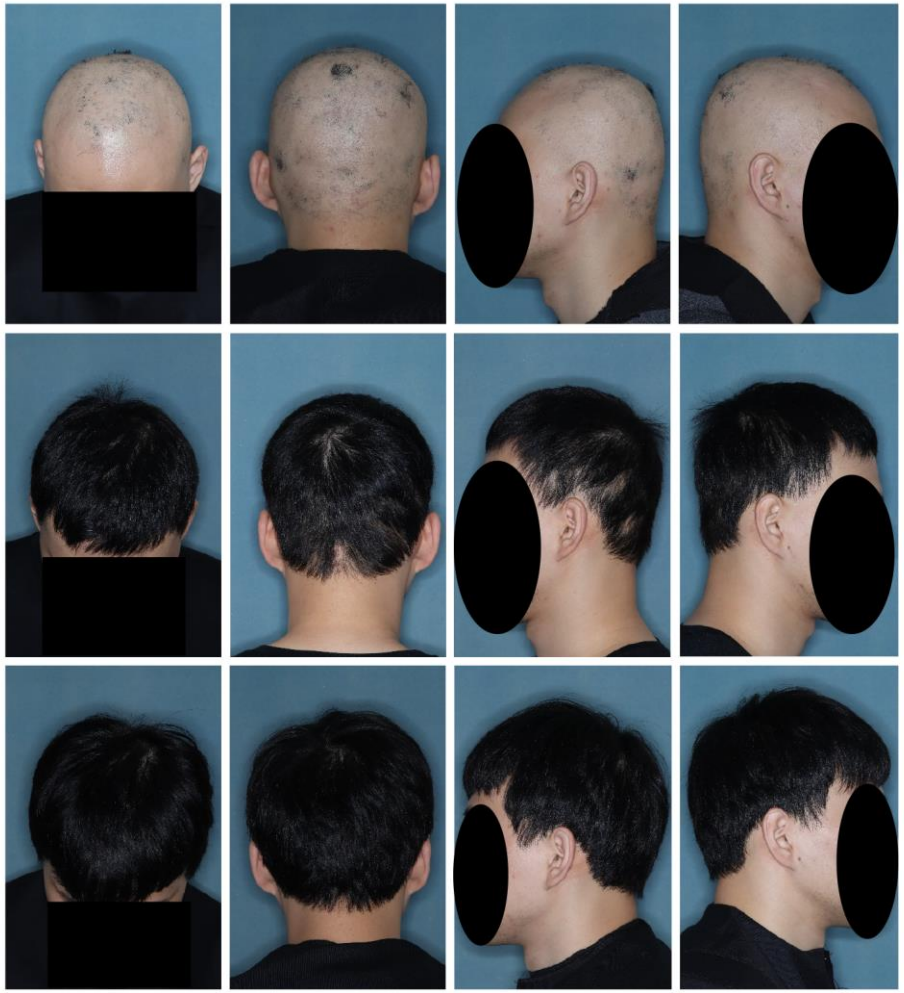


Non-responder imputation used for missing data. A score of 0 or 1 indicates full coverage or minimal gaps in eyebrows and eyelashes
Patients randomized to BARI (4-mg or 2-mg QD) at baseline retained their treatment allocation through W52, whereas PBO non-responders were rescued at W36
[a] CIs are constructed using the Wilson method, without continuity correction
BARI=baricitinib; CI=confidence interval; ClinRO=clinician-reported outcome; EB=eyebrow; EL=eyelash; PBO=placebo

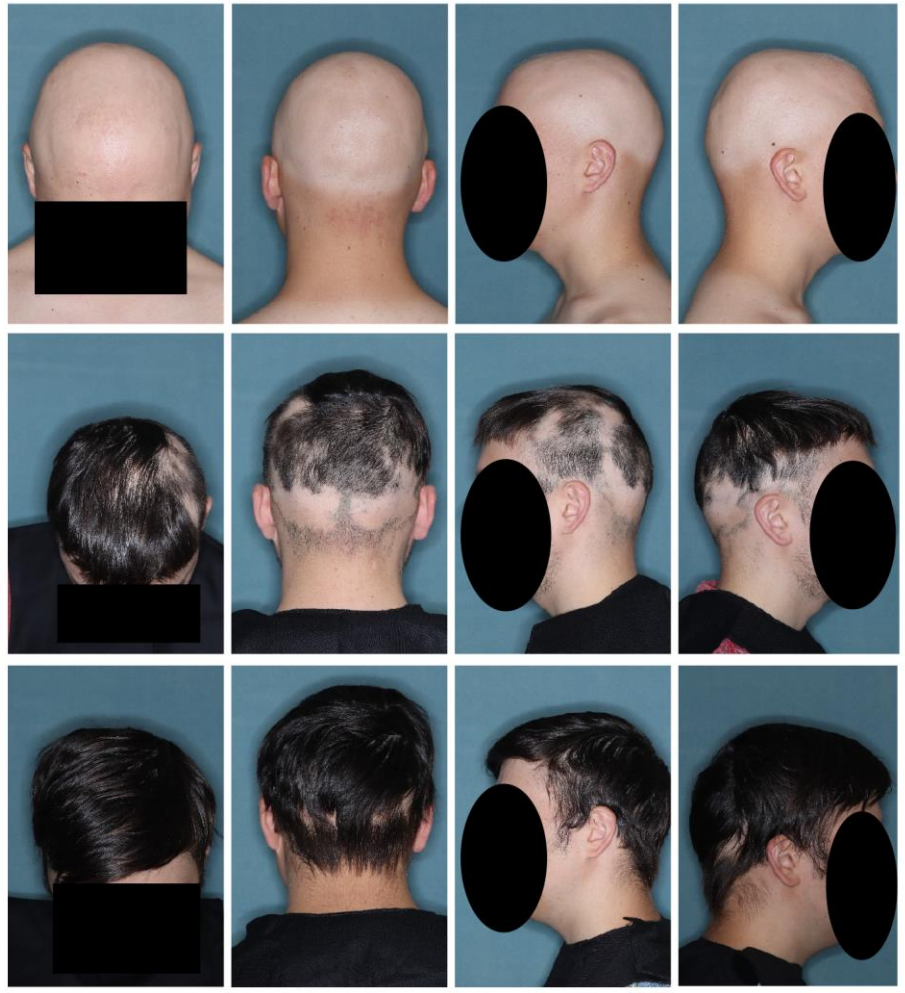
ALOPECIA AREATA

Representative Images of Scalp Hair Regrowth After 52 Weeks of BARI 4-mg Treatment

Patient 1



Patient 2



BARI=baricitinib; SALT=Severity of Alopecia Tool

Table 3. Safety Outcomes.*

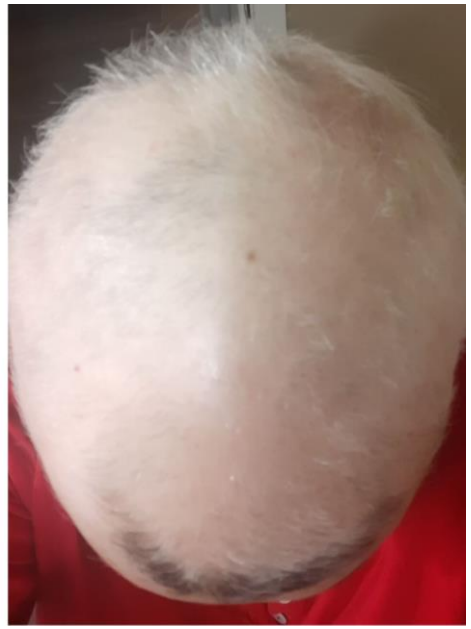
Outcome	BRAVE-AA1			BRAVE-AA2		
	Placebo (N=189)	Baricitinib, 2 mg (N=183)†	Baricitinib, 4 mg (N=280)†	Placebo (N=154)†	Baricitinib, 2 mg (N=155)†	Baricitinib, 4 mg (N=233)†
At least one adverse event — no. (%)	97 (51.3)	93 (50.8)	167 (59.6)	97 (63.0)	106 (68.4)	154 (66.1)
Severity of adverse event — no. (%)						
Mild	49 (25.9)	60 (32.8)	106 (37.9)	65 (42.2)	60 (38.7)	81 (34.8)
Moderate	41 (21.7)	31 (16.9)	54 (19.3)	28 (18.2)	42 (27.1)	60 (25.8)
Severe	7 (3.7)	2 (1.1)	7 (2.5)	4 (2.6)	4 (2.6)	13 (5.6)
Serious adverse event — no. (%)	3 (1.6)	4 (2.2)	6 (2.1)	3 (1.9)	4 (2.6)	8 (3.4)
Death — no. (%)	0	0	0	0	0	0
Adverse event leading to permanent discontinuation of baricitinib or placebo — no. (%)	2 (1.1)	3 (1.6)	5 (1.8)	4 (2.6)	4 (2.6)	6 (2.6)
Adverse events occurring in ≥5% of patients in any group — no. (%)						
Upper respiratory tract infection	10 (5.3)	9 (4.9)	21 (7.5)	11 (7.1)	12 (7.7)	15 (6.4)
Headache	9 (4.8)	8 (4.4)	14 (5.0)	10 (6.5)	12 (7.7)	21 (9.0)
Nasopharyngitis	12 (6.3)	12 (6.6)	21 (7.5)	7 (4.5)	2 (1.3)	15 (6.4)
Acne	1 (0.5)	10 (5.5)	16 (5.7)	3 (1.9)	9 (5.8)	11 (4.7)
Urinary tract infection	3 (1.6)	2 (1.1)	7 (2.5)	2 (1.3)	12 (7.7)	11 (4.7)
Blood creatine kinase increased	3 (1.6)	3 (1.6)	16 (5.7)	2 (1.3)	0	7 (3.0)
Infectious adverse event — no. (%)						
At least one infection	53 (28.0)	46 (25.1)	88 (31.4)	45 (29.2)	58 (37.4)	69 (29.6)
Serious infection	0	0	0	0	2 (1.3)	1 (0.4)
Opportunistic infection	0	0	0	0	0	0
Herpes zoster	1 (0.5)	1 (0.5)	2 (0.7)	1 (0.6)	3 (1.9)	3 (1.3)
Herpes simplex	4 (2.1)	0	5 (1.8)	8 (5.2)	6 (3.9)	2 (0.9)
Tuberculosis	0	0	0	0	0	0
Infection leading to permanent discontinuation of baricitinib or placebo	0	0	0	0	1 (0.6)	0
Adverse events of special interest — no. (%)						
Major adverse cardiovascular event	0	1 (0.5)‡	0	0	0	0
Venous thromboembolism	0	0	0	0	0	0
Cancer other than nonmelanoma skin cancer	0	0	0	1 (0.6)	0	1 (0.4)
Nonmelanoma skin cancer	0	0	0	0	0	0
Gastrointestinal perforations	0	0	0	0	0	0

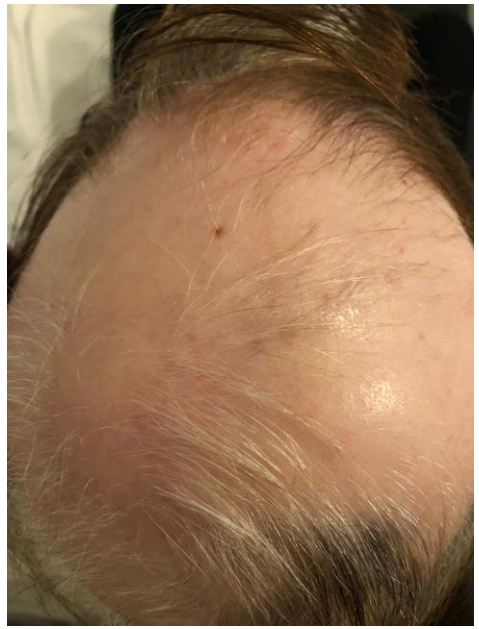
- Los efectos adversos más communes fueron el acne, las infecciones de vías respiratorias altas, infecciones del tracto urinario y aumento de la CK.
- Infecciones por herpes zóster ocurrieron en un porcentaje bajo de pacientes.
- No hubo eventos de tromboembolismo venoso, tuberculosis, infección oportunista o perforación gastrointestinal (GI).

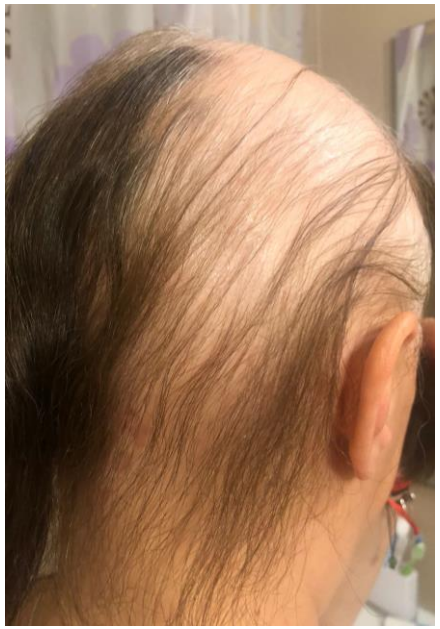
Nuestra experiencia …

Caso clínico

- Mujer de 54 años
- AA desde 2017
- Tratamientos previos: Corticoides tópicos, infiltrados y sistémicos (terapia pulsátil), ciclosporina y metotrexato (mala tolerancia)
- SALT 85%

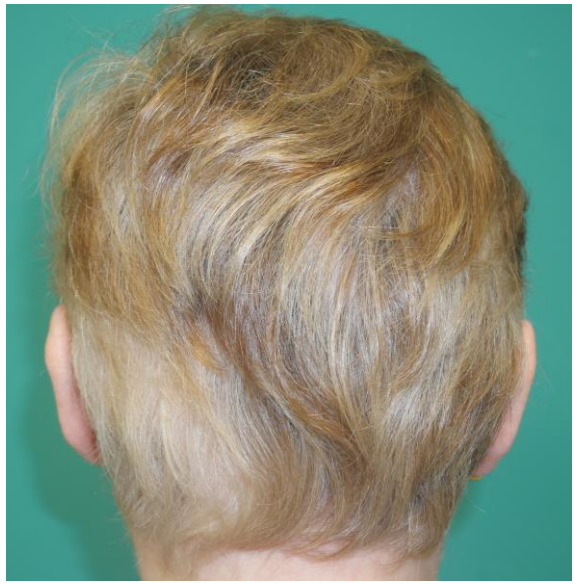


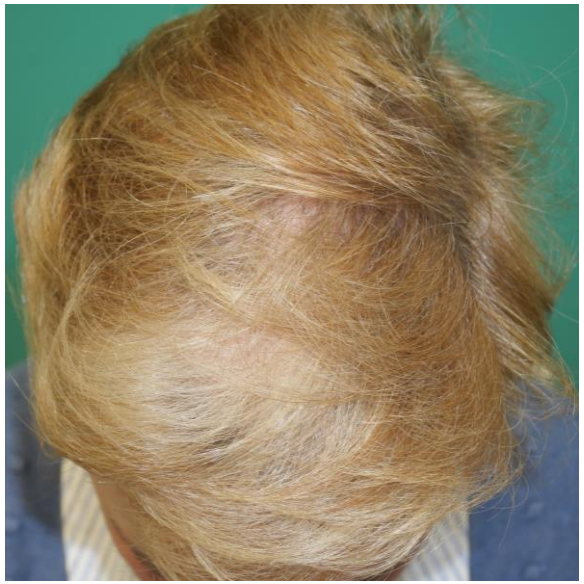


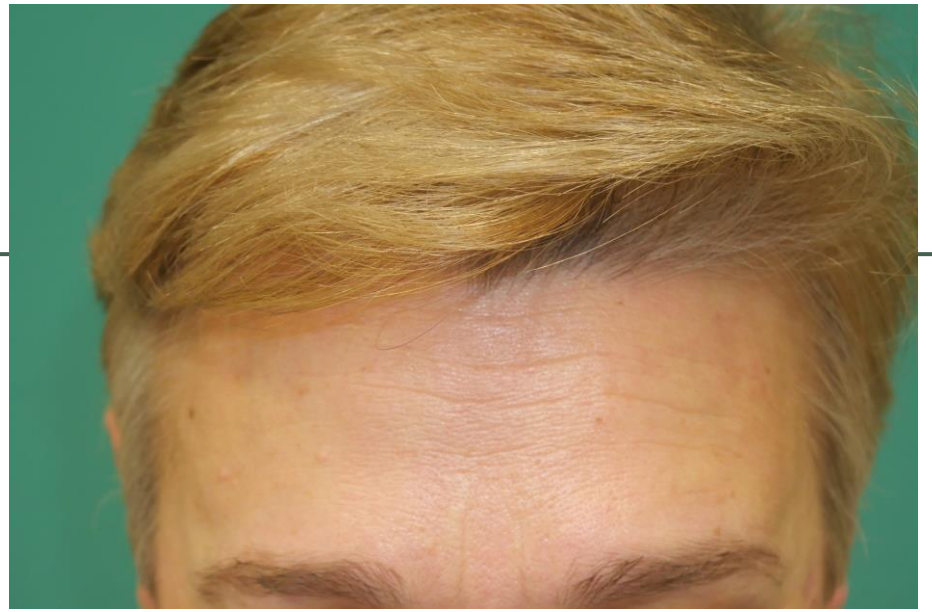


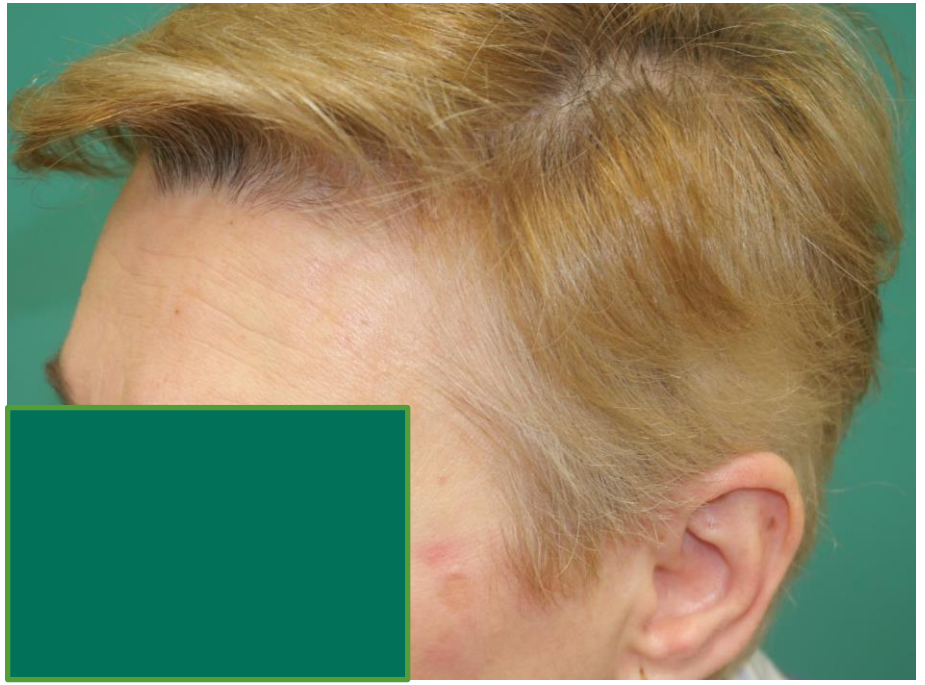
Caso clínico

- Inicio de baricitinib 4mg/día en nov 2023









ALOPECIA AREATA

Randomized Controlled Trial > Lancet. 2023 May 6;401(10387):1518-1529.
doi: 10.1016/S0140-6736(23)00222-2. Epub 2023 Apr 14.

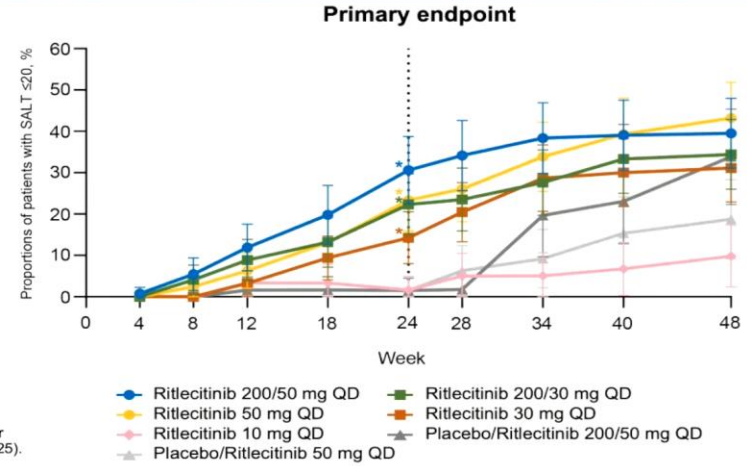
Efficacy and safety of ritlecitinib in adults and adolescents with alopecia areata: a randomised, double-blind, multicentre, phase 2b-3 trial

Brett King [1], Xingqi Zhang [2], Walter Gubelin Harcha [3], Jacek C Szepietowski [4], Jerry Shapiro [5], Charles Lynde [6], Natasha A Mesinkovska [7], Samuel H Zwillich [8], Lynne Napatalung [9], Dalia Wajsbrot [10], Rana Fayyad [10], Amy Freyman [10], Debanjali Mitra [10], Vivek Purohit [10], Rodney Sinclair [11], Robert Wolk [8]

Affiliations + expand

PMID: 37062298 DOI: 10.1016/S0140-6736(23)00222-2

- The primary endpoint of SALT score ≤20 at Week 24 was met for the 200/50 mg, 200/30 mg, 50 mg, and 30 mg ritlecitinib groups
- SALT score ≤20 responses continued to increase up until Week 48
- At Week 48, response rates for 200/50 mg and 50 mg were numerically higher vs 200/30 mg and 30 mg; response rates for 10 mg remained low



* Indicates statistical significance compared to placebo for overall study (P<0.05), EMA (P<0.01) and FDA (P<0.00125). QD=once daily; SALT=Severity of Alopecia Tool

American Journal of Clinical Dermatology (2024) 25:299–314
https://doi.org/10.1007/s40257-024-00846-3

ORIGINAL RESEARCH ARTICLE

Integrated Safety Analysis of Ritlecitinib, an Oral JAK3/TEC Family Kinase Inhibitor, for the Treatment of Alopecia Areata from the ALLEGRO Clinical Trial Program

Brett King[1] · Jennifer Soung[2] · Christos Tziotzios[3] · Lidia Rudnicka[4] · Pascal Joly[5] · Melinda Gooderham[6] · Rodney Sinclair[7] · Natasha A. Mesinkovska[8] · Carle Paul[9] · Yankun Gong[10] · Susan D. Anway[11] · Helen Tran[10] · Robert Wolk[11] · Samuel H. Zwillich[11] · Alexandre Lejeune[12]

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Page contents
Overview
Product information
Product details

Overview

Litfulo is a medicine used to treat adults and adolescents over 12 years of age with severe alopecia areata, an autoimmune disease (a disease caused by the body's own defence system attacking normal tissue) causing hair loss of the scalp or other parts of the body.

Litfulo contains the active substance ritlecitinib.

> 12 años

Tratamiento tópico en alopecia areata..

ALOPECIA AREATA

Meta-Analysis > Front Immunol. 2023 Apr 17:14:1152513. doi: 10.3389/fimmu.2023.1152513. eCollection 2023.

Efficacy and safety of different JAK inhibitors in the treatment of alopecia areata: a network meta-analysis

Dongfan Wei [1], Yi Chen [2], Yuqing Shen [2], Bo Xie [3], Xiuzu Song [3]

Conclusion: Oral baricitinib and ruxolitinib are excellent options for the treatment of AA owing to their good efficacy and safety profiles. In contrast, non-oral JAK inhibitors do not appear to have satisfactory efficacy in treating AA. However, further studies are required to verify the optimal dose of JAK inhibitors for AA therapy.

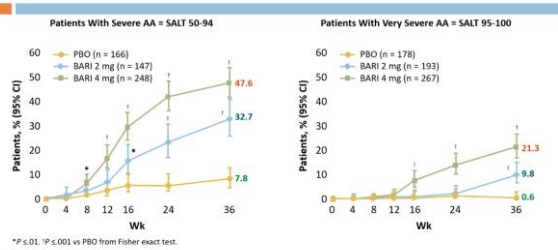
Factors That May Influence Response to JAK Inhibitors

Dosing of JAK Inhibitors

Dose of JAK inhibitor used

Baseline severity scalp hair loss

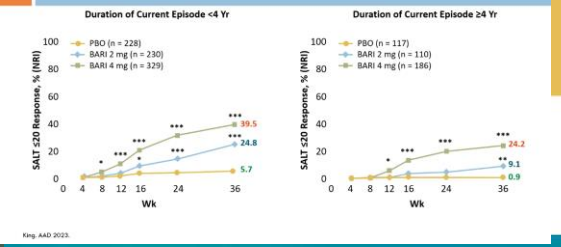
Severe AA Patients versus Very Severe AA Patients: Baricitinib Data



Duration of current episode

Concomitant oral minoxidil

Duration of Current Episode: Baricitinib Data



Adjuvant oral minoxidil for the treatment of alopecia areata refractory to Janus kinase inhibitors

Tratamento adjuvante com minoxidil oral para tratamento de alopecia areata refratária a inibidores de JAK

DOI: http://www.dx.doi.org/10.5935/scd1984-8773.20201211512

Maryanne M. Senna

Are new treatments for AA a real breakthrough ?

Dr. Maryanne M. Senna
Winchester, United States

Cuánto tiempo mantener el tratamiento con iJAK en alopecia areata..

2020 **The Alopecia Areata Consensus of Experts (ACE) study: Results of an international expert opinion on treatments for alopecia areata**

- Systemic treatment is best discontinued once complete regrowth has been achieved and maintained for 6 months or when regrowth is sufficient to be managed topically.
- If vellus regrowth fails to convert to terminal hair, systemic treatment should continue for 6 months, but not longer.

FICHA TECNICA BARICITINIB CIMA-AEMPS

Se debe considerar una dosis de 2 mg una vez al día para los pacientes que hayan logrado un control sostenido de la actividad de la enfermedad con 4 mg una vez al día y sean aptos para reducción de dosis . Una vez alcanzada una respuesta estable, se recomienda continuar el tratamiento durante al menos varios meses, para evitar recaídas.

Se debe considerar la interrupción del tratamiento en pacientes que no muestren evidencia de beneficio terapéutico después de 36 semanas de tratamiento.

Otros iJAK en alopecia areata

ALOPECIA AREATA

Fase III

Criterios inclusión:

- > 50% extensión (SALT)
- Ritlecitinib > 12 años
- Baricitinib y deuruxolitinib > 18 años

Table 1 Common traditional and emerging treatments for alopecia areata

Newly approved/advanced pipeline treatments	Janus kinase inhibitors	Baricitinib[a] Ritlecitinib[a] Deuruxolitinib[b] (CTP-543)
Experimental treatments and treatments in phase I–II clinical trials	Janus kinase inhibitors	Tofacitinib[c] Brepocitinib[c] Ivarmacitinib (SHR0302) Upadacitinib Topical: Tofacitinib Ruxolitinib Delgocitinib (LEO 124249) Ifidancitinib (ATI-50002) Jaktinib
	Th2 pathway inhibitors	Dupilumab[c] Tralokinumab[c,d]
	Targeting IL-23	Ustekinumab
	Targeting Th17/IL-17	Secukinumab[d] Apremilast[d]
	Immune checkpoint modulators	Rosnilimab (ANB030) Abatacept
	Targeting IL-9/IL-15	EQ101 (BNZ-1)
	Prostaglandin analogs	Latanoprost[d] Bimatoprost[d]
	Other treatments	Low-dose IL-2[b,d] Platelet-rich plasma Daxdilimab Etrasimod

American Journal of Clinical Dermatology (2023) 24:895–912
https://doi.org/10.1007/s40257-023-00808-1

REVIEW ARTICLE

Alopecia Areata: Current Treatments and New Directions

Dante Dahabreh[1] · Seungyeon Jung[1,2] · Yael Renert-Yuval[3] · Jonathan Bar[1] · Ester Del Duca[1] · Emma Guttman-Yassky[1]

ALOPECIA AREATA

ClinicalTrials.gov

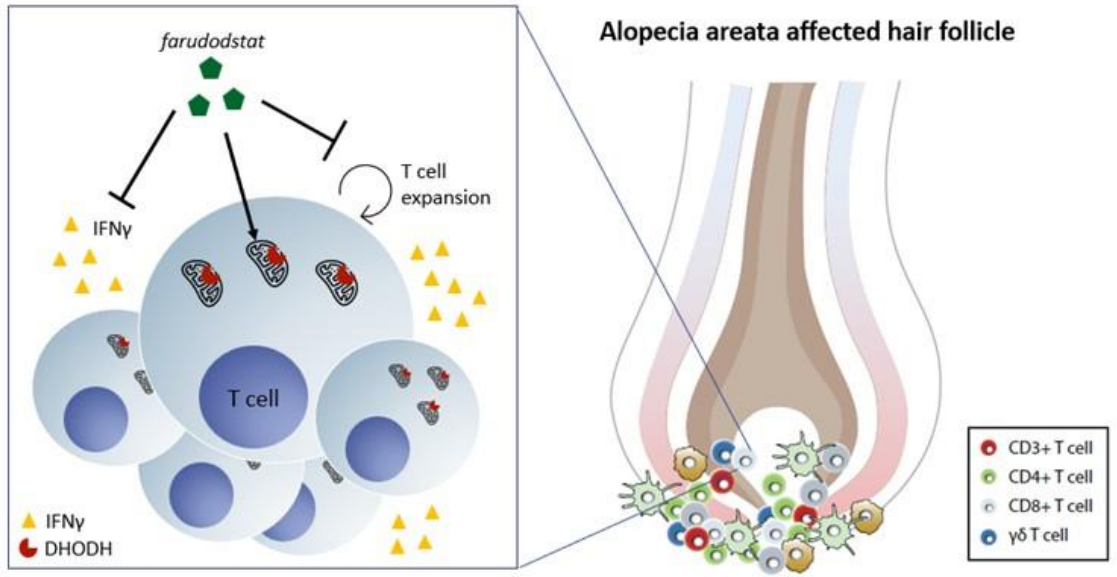
Find Studies ▾ About Studies ▾ Submit Studies ▾ Resources ▾ About Site ▾ PRS Login

Home > Search Results > Study Record Detail ☐ Save this study

Investigate the Efficacy and Safety of Farudodstat Compared With Its Placebo in Adult Alopecia Areata Participants (FAST-AA)

ClinicalTrials.gov Identifier: NCT05865041

Inhibidor de la enzima dihidroorotato deshidrogenasa (DHODH), que suprime la proliferación de células T y la secreción de interferón gamma (IFNγ)



Seguridad iJAK

ALOPECIA AREATA

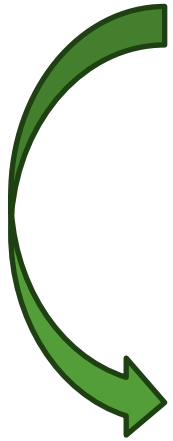
VITILIGO

DRUG SAFETY MATTERS

FDA requires warnings about increased risk of serious heart-related events, cancer, blood clots, and death for JAK inhibitors that treat certain chronic inflammatory conditions

FDA Drug Safety Podcast

- **Infecciones graves**
- **Mortalidad**
- **Cáncer**
- **Eventos CV (MACE)**
- **Trombosis**



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Cardiovascular and Cancer Risk with Tofacitinib in Rheumatoid Arthritis

Steven R. Ytterberg, M.D., Deepak L. Bhatt, M.D., M.P.H., Ted R. Mikuls, M.D., M.S.P.H., Gary G. Koch, Ph.D., Roy Fleischmann, M.D., Jose L. Rivas, M.D., Rebecca Germino, Ph.D., Sujatha Menon, Ph.D., Yanhui Sun, Ph.D., Cunshan Wang, Ph.D., Andrea B. Shapiro, M.D., Keith S. Kanik, M.D., and Carol A. Connell, R.N., Ph.D., for the ORAL Surveillance Investigators*

Pacientes con AR >50 años
MTX concomitante
FR cardiovascular preexistentes

Original Investigation

November 1, 2023

Cardiovascular and Venous Thromboembolic Risk With JAK Inhibitors in Immune-Mediated Inflammatory Skin Diseases

A Systematic Review and Meta-Analysis

Jenne P. Ingrassia, BA[1,2]; Muhammad Haisum Maqsood, MD[3]; Joel M. Gelfand, MD[4]; et al

» Author Affiliations

JAMA Dermatol. 2024;160(1):28-36. doi:10.1001/jamadermatol.2023.4090

Conclusions and relevance: This meta-analysis did not identify a significant increase in the risk of MACE and VTE in dermatology patients receiving JAK-STATi for median duration of 16 weeks. The results of this review suggest there is insufficient evidence that JAK-STATi confer an increased risk of cardiovascular complications in dermatological patients, especially when used for short time frames.

Adv Ther (2023) 40:1867–1883
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

What was learned from this study?

Incidence of AESI in patients treated with baricitinib who were younger than 65 years without risk factors were reduced compared with the population of patients with risk factors for all indications, and the number of AESI is also minimal for patients with atopic dermatitis and alopecia areata who have risk factors.

Individual disease burden, risk factors, and response to treatment should be considered to make informed decisions for individual patients treated with baricitinib.

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

Key Summary Points

Oral Janus kinase (JAK) inhibitors had low rates of venous thromboembolism, major adverse cardiovascular events, and malignancy compared with similarly low rates in the placebo in their use in clinical trials in dermatology.

Most patients who developed serious adverse events had risk factors specific to the event.

The most common treatment emergent adverse events observed in ≥ 5% of patients on oral JAK inhibitors included upper respiratory tract infection, nasopharyngitis, nausea, headache, and acne.

A comprehensive evaluation of a patient's baseline risk factors for complications and comorbid diseases is critical in assessing the net benefit of JAK inhibitors on a case-by-case basis.

ACTAS Dermo-Sifiliográficas 114 (2023) T784–T801

ACTAS Dermo-Sifiliográficas

Full English text available at www.actasdermo.org

REVISIÓN

[Artículo traducido] Perfil de seguridad a largo plazo y usos fuera de indicación de los inhibidores de JAK en dermatología

L. Corbella-Bagot[a], C. Riquelme-McLoughlin[a] y D. Morgado-Carrasco[a,b,*]

Conclusion

JAK inhibitors pose an important step forward toward precision medicine. Their safety is largely influenced by patient characteristics, disease being treated, route of administration, specific JAK inhibitor, and dosage. When compared to traditional immunosuppressant therapies, overall, JAK inhibitors demonstrate improved safety profiles. These agents hold promise as treatments for various inflammatory dermatoses that greatly impact quality of life.

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

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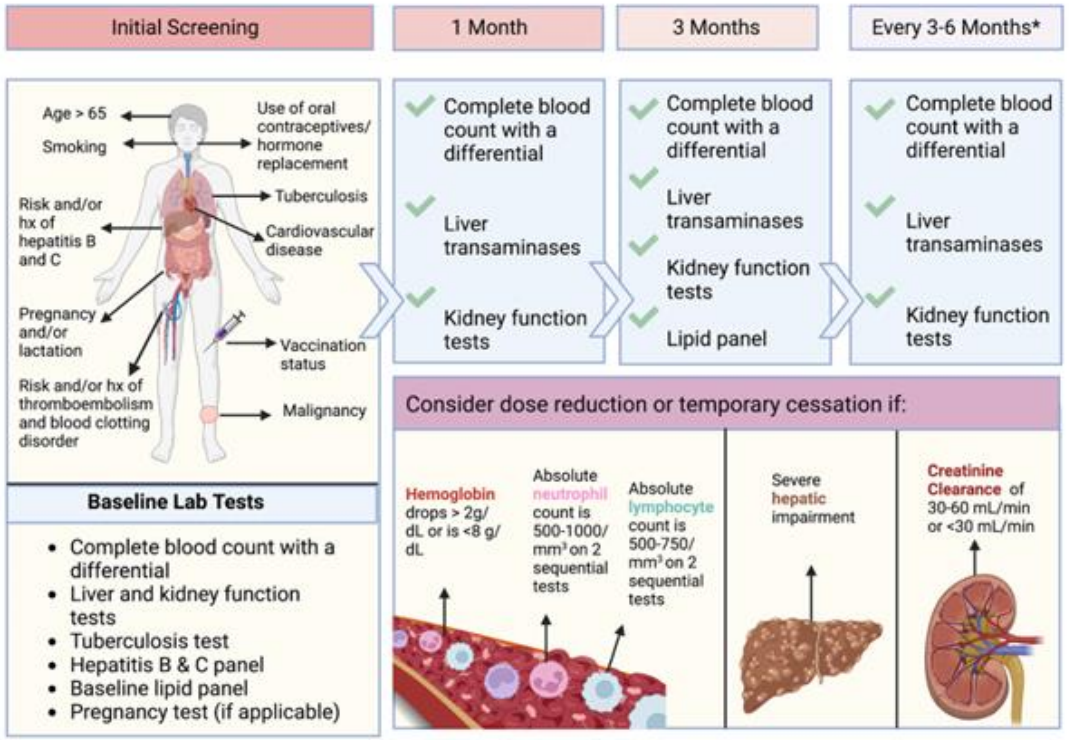
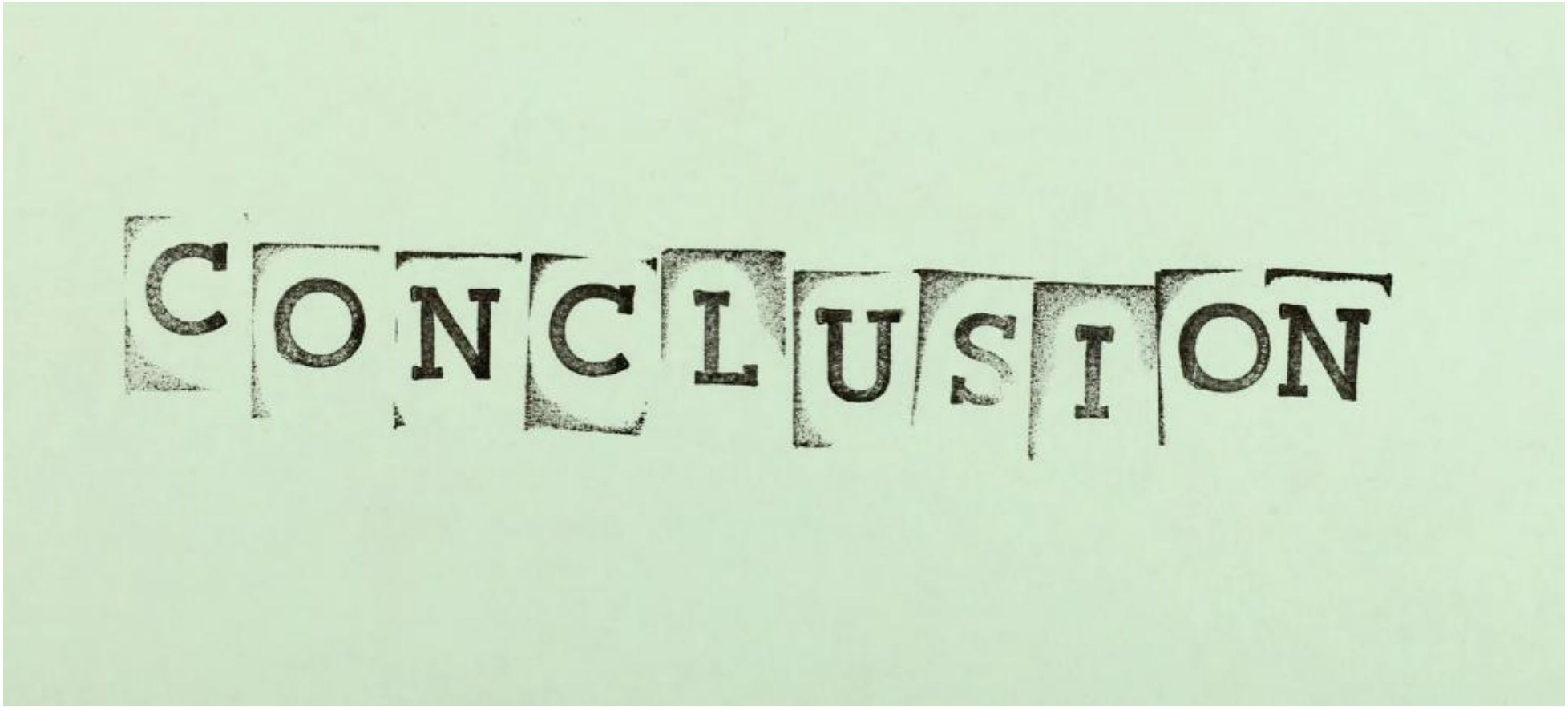


Table 3 Conditions where JAK inhibitor use is not appropriate

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 hospitalizations 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


CONCLUSION

Conclusiones

- Vitíligo y AA presentan puntos de similitud patogénica (IFG gamma/ CD8/IL15)
- Similitud en el desarrollo terapéutico a partir de inhibidores de JAK
- Reto terapéutico : Recaída al suspender el fármaco
  - Posibles dianas adicionales específicas de cada enfermedad en el futuro

Inmunoterapia en dermatología

V EDICIÓN

25 de abril de 2024

Casa de Convalescència, Barcelona

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Ane Jaka

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Gràcies,