Master 2024

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BEST CONTENT, BEST FACULTY

¿Por qué es importante lograr una respuesta rápida en el paciente con enfermedad psoriásica?

PP-BA-MX-1100
Septiembre 2024

Número de slides: 50

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- Egresada de la Universidad Autónoma de Guadalajara.
- Especialidad en Dermatología en Centro Médico Nacional Siglo XXI
- Subespecialidad en Dermapatología del Hospital General de México
- Adscrita al servicio de Dermatología del Hospital de Especialidades del Centro Médico Nacional Siglo XXI, Bernardo Sepúlveda del IMSS
- Miembro del Colegio Ibero Latinoamericano de Dermatología
- Coautora de las Guías de tratamiento en Psoriasis y Dermatitis Atópica

Conflicto de intereses: Speaker para Abbvie, Janseen, Novartis, Eli Lilly, Novartis, Leo Pharma, UCB

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Dr. Valente Armando Maldonado Ríos

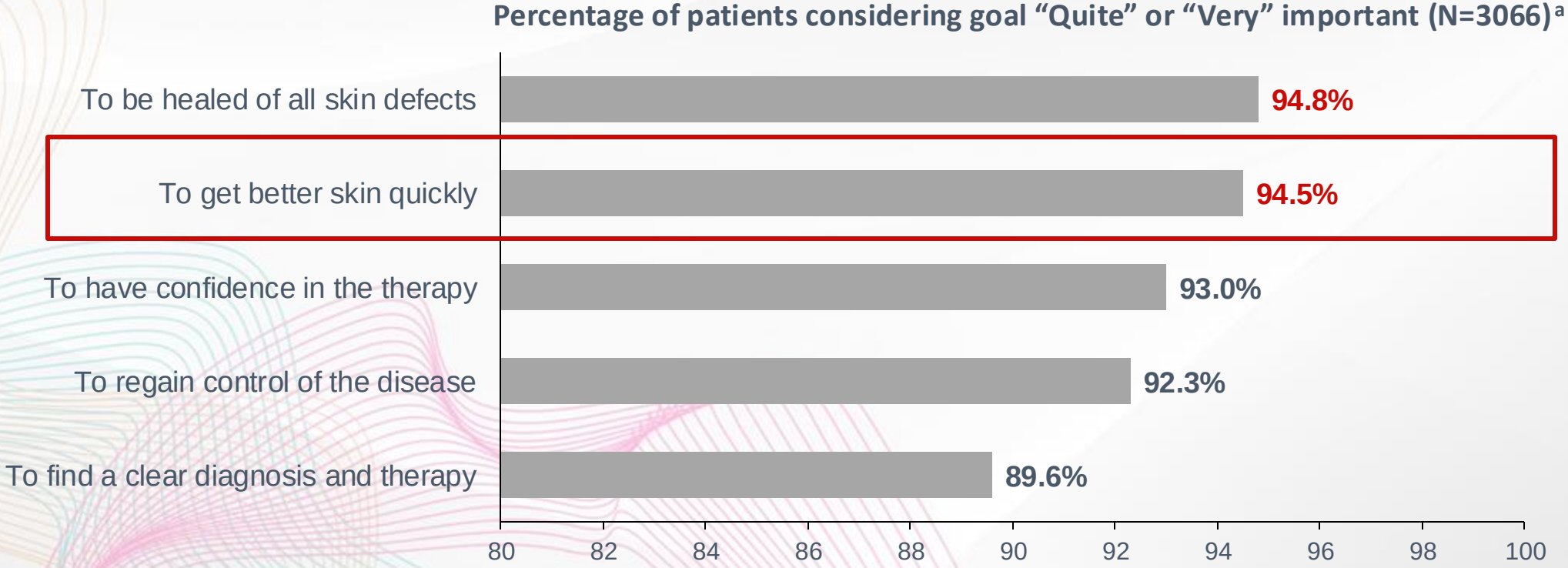
- Médico internista
- Subespecialista en inmunología clínica y alergia
- Maestría en Farmacología Clínica
- Médico adscrito al servicio de Alergia e Inmunología Clínica del Centro Médico Nacional Siglo XXI. IMSS

- Conflicto de intereses: Participación como ponente y en asesorías para Laboratorio Carnot SA de CV, participación como ponente para Laboratorio Astra Zeneca, Eli Lilly y Pfizer

Patient needs from psoriasis treatment in the order of importance

Data From the PsoBest German Psoriasis Registry

Top 5 ranked



Note: Data presented in this slide are the top 5 ranked out of 10 dataset. [a]Importance of treatment goals according to the PBI-S Patient Needs Questionnaire, ordered by % of patients stating "Quite" or "Very" important. Patients could score treatment goals from 0–4, with 0=not at all important or not applicable to 4=very important.
PBI-S=Patient Benefit Index–Standard Version for Chronic Skin Diseases.
Modified from Blome C, et al. Arch Dermatol Res. 2016;308(2): 69–78.

Patients with moderate-to-severe psoriasis have certain expectations regarding treatment

How many days would you expect a systemic psoriasis treatment to take in order to deliver each of the following[1,2]

16.4 (19.2)

Number of days to achieve 50% clearer skin, mean (SD)

33.8 (44.4)

Number of days to achieve completely clear skin, mean (SD)

To reach clinical goals, it is important that physicians recognize patient expectations[3]

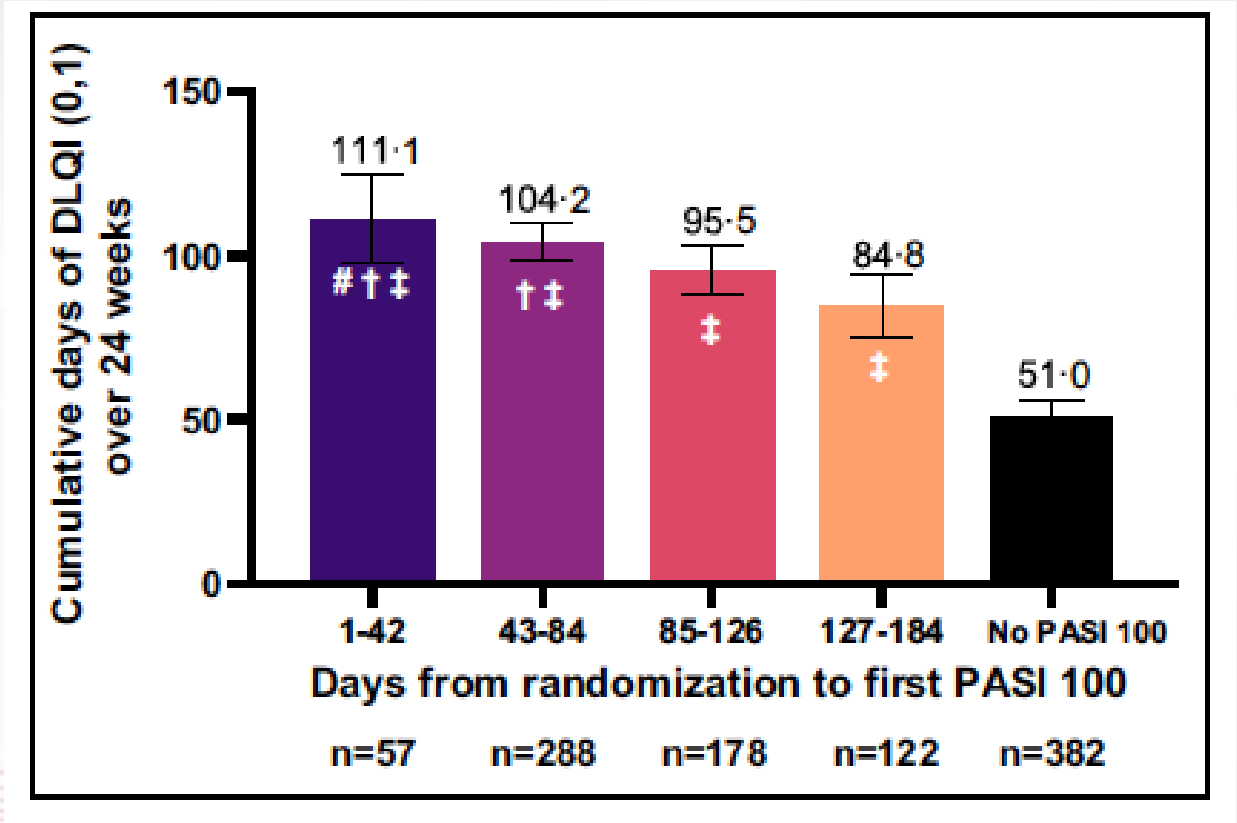
SD=Standard Deviation.

1. Gorelick J, et al. Dermatol Ther (Heidelb). 2019;9(4): 785–797. 2. Gorelick J, et al. Poster presented at: *EADV* 2019. P1620. 3. Strober BE, et al. Dermatol Ther (Heidelb). 2019;9(1): 5–18.

PASI 100 en tiempo y DLQI 0-1

Los pacientes que logran DLQI 0-1

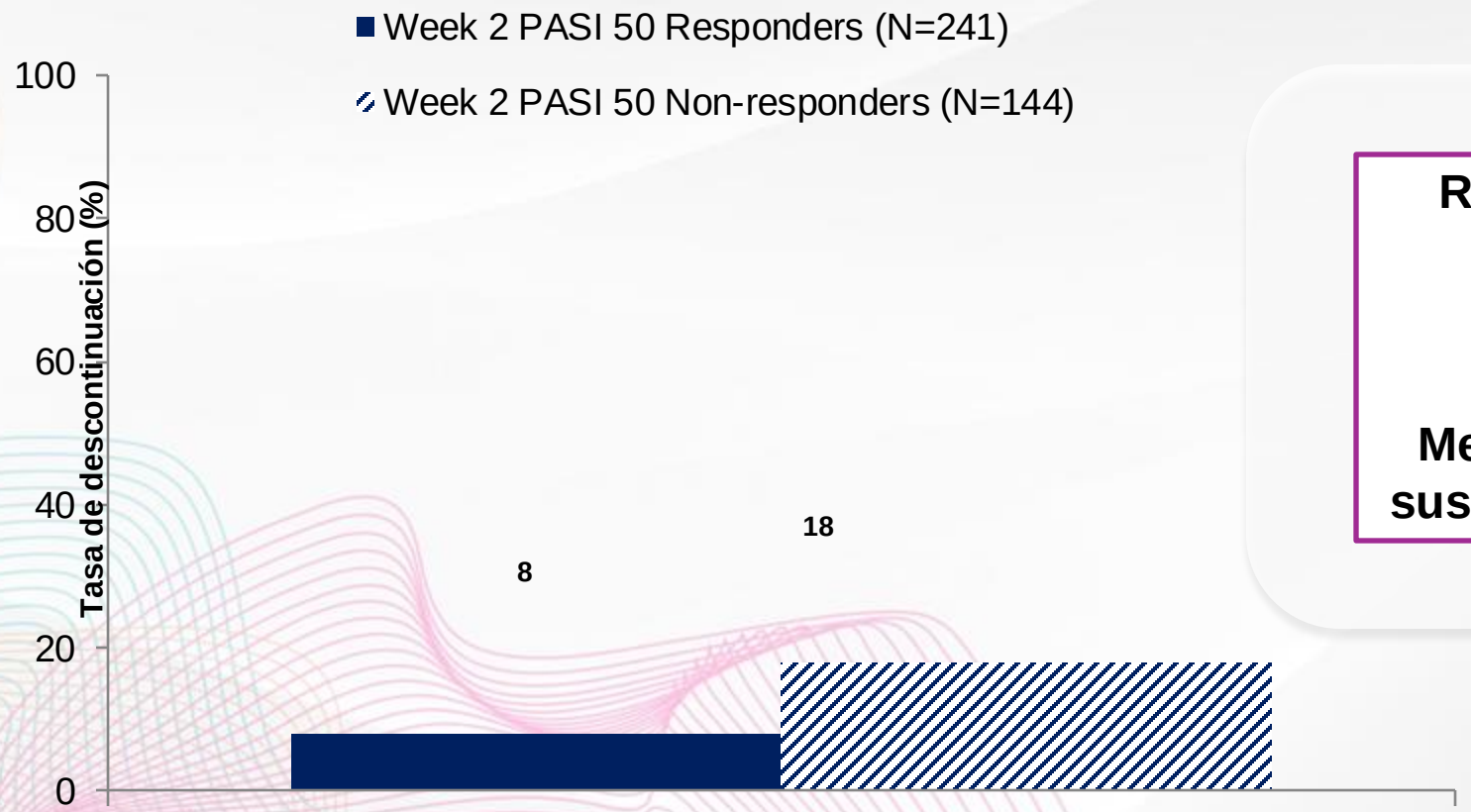
Lograron más rápidamente obtener un PASI 100



Blauvelt A, Leonardi C, Elewski B, Crowley JJ, Guenther LC, Gooderham M, Langley RG, Vender R, Pinter A, Griffiths CEM, Tada Y, Elmaraghy H, Lima RG, Gallo G, Renda L, Burge R, Park SY, Zhu B, Papp K; IXORA-R Study Group. A head-to-head comparison of ixekizumab vs. guselkumab in patients with moderate-to-severe plaque psoriasis: 24-week efficacy and safety results from a randomized, double-blinded trial. Br J Dermatol. 2021 Jun;184(6):1047-1058

Respondedor rápido y respuesta a un año

(*post-hoc análisis UNCOVER-3*)



Respuesta temprana

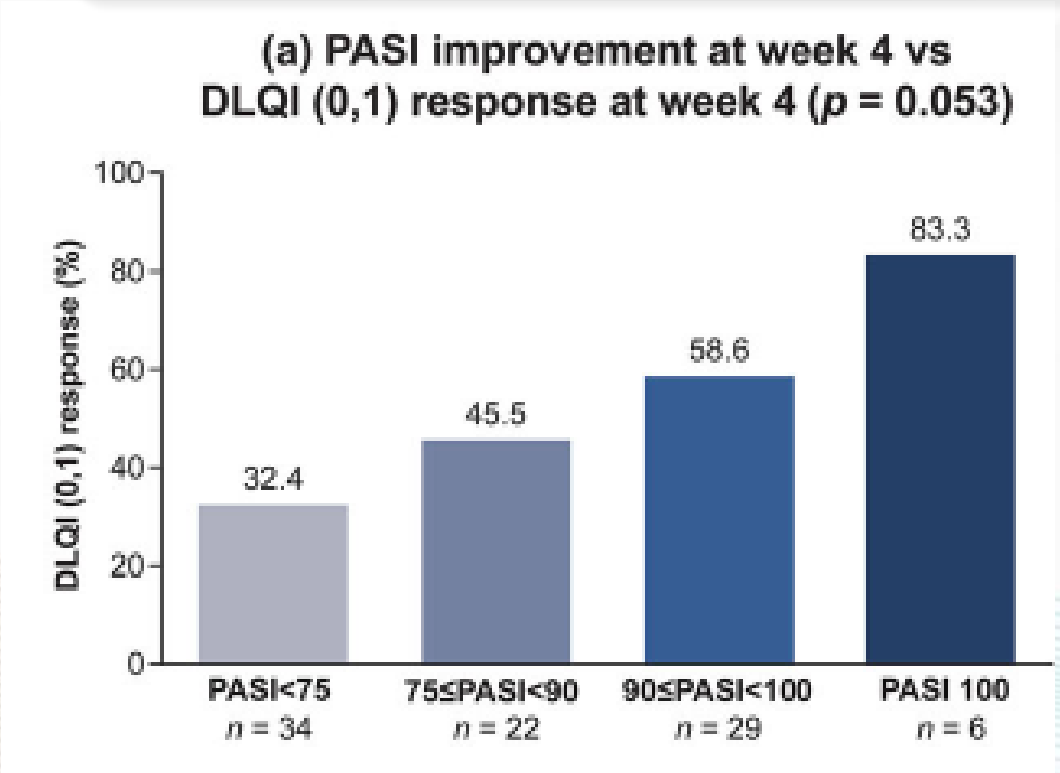
=

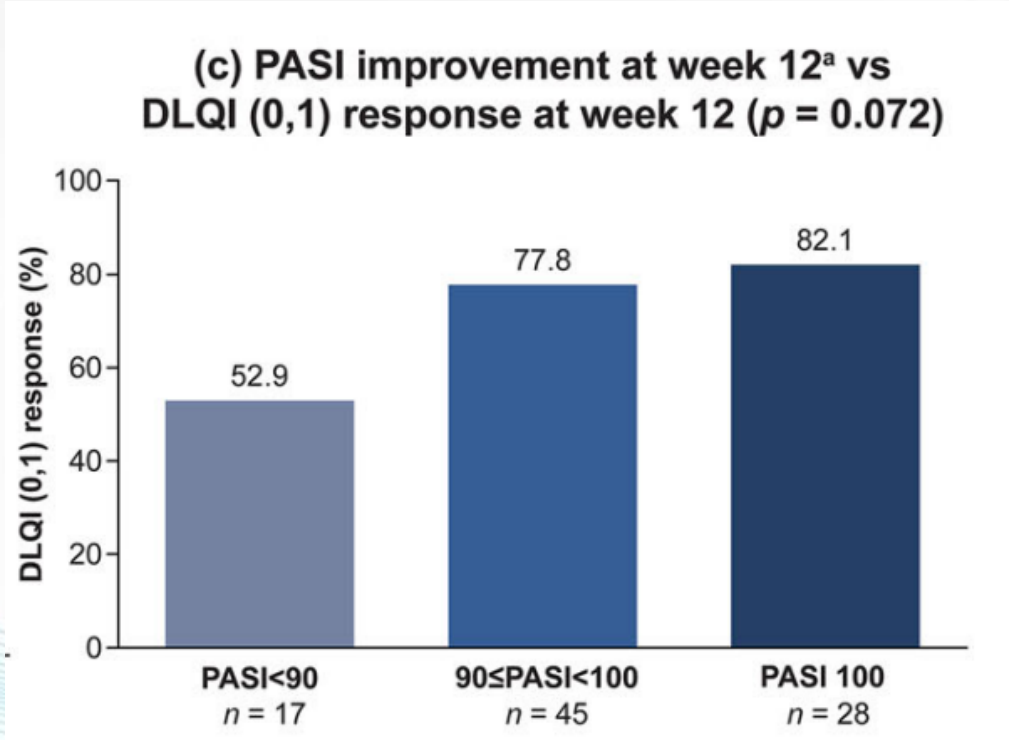
Menor probabilidad de suspender el tratamiento

Egeberg A, et al. Sustained Resolution of Nail Psoriasis Through 5 Years with Ixekizumab: A Post-Hoc analysis from UNCOVER-3. Acta Der Venerol 2022.

Si la piel mejora, la calidad de vida también (uncover-J)

Buscar los resultados para reestablecer al paciente cuanto antes





Honma M, Cai Z, Burge R, Zhu B, Yotsukura S, Torisu-Itakura H. Relationship Between Rapid Skin Clearance and Quality of Life Benefit: Post Hoc Analysis of Japanese Patients with Moderate-to-Severe Psoriasis Treated with Ixekizumab (UNCOVER-J). Dermatol Ther (Heidelb). 2020 Dec;10(6):1397-1404.

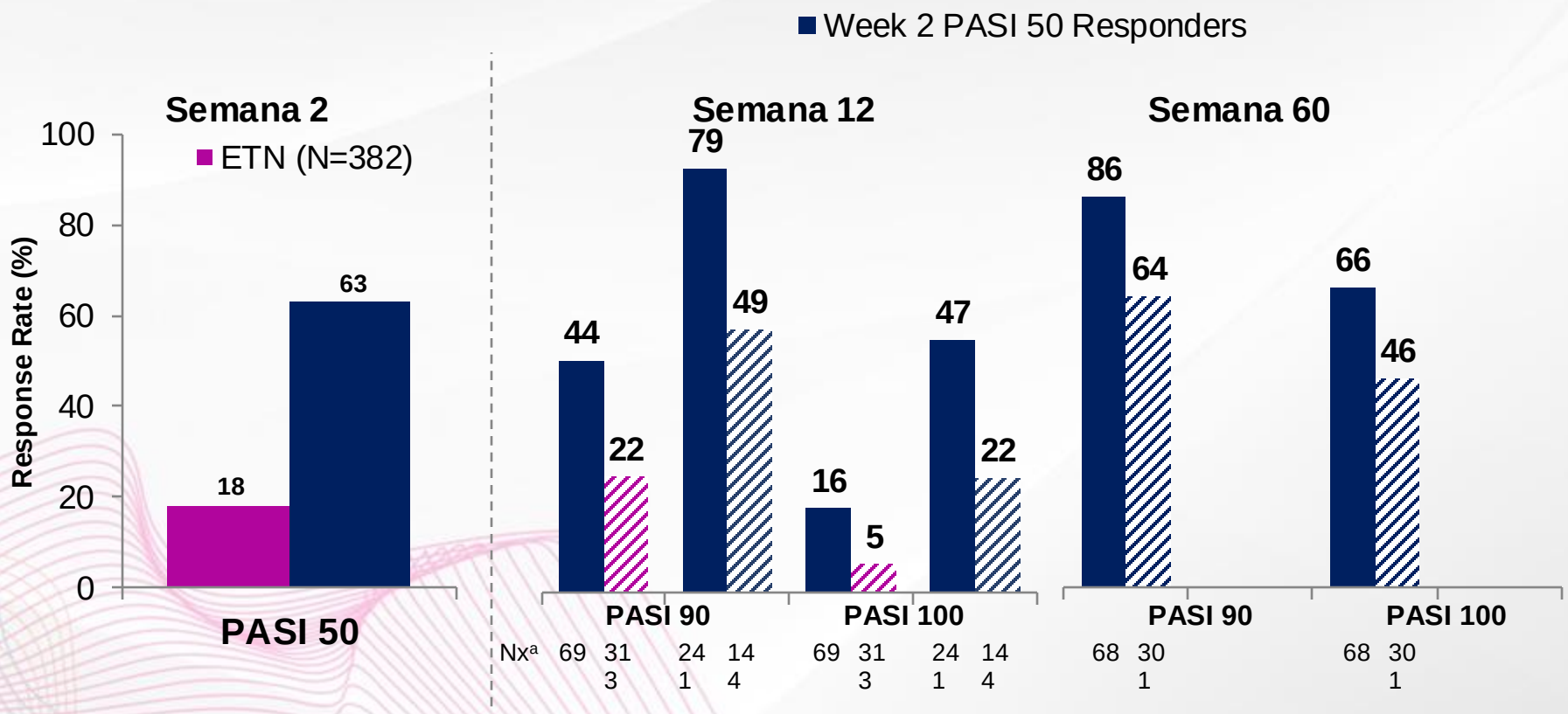
Lograr respuesta rápida y evaluación al año (Uncover-3)

RESPUESTA

PASI 50 en la semana 2

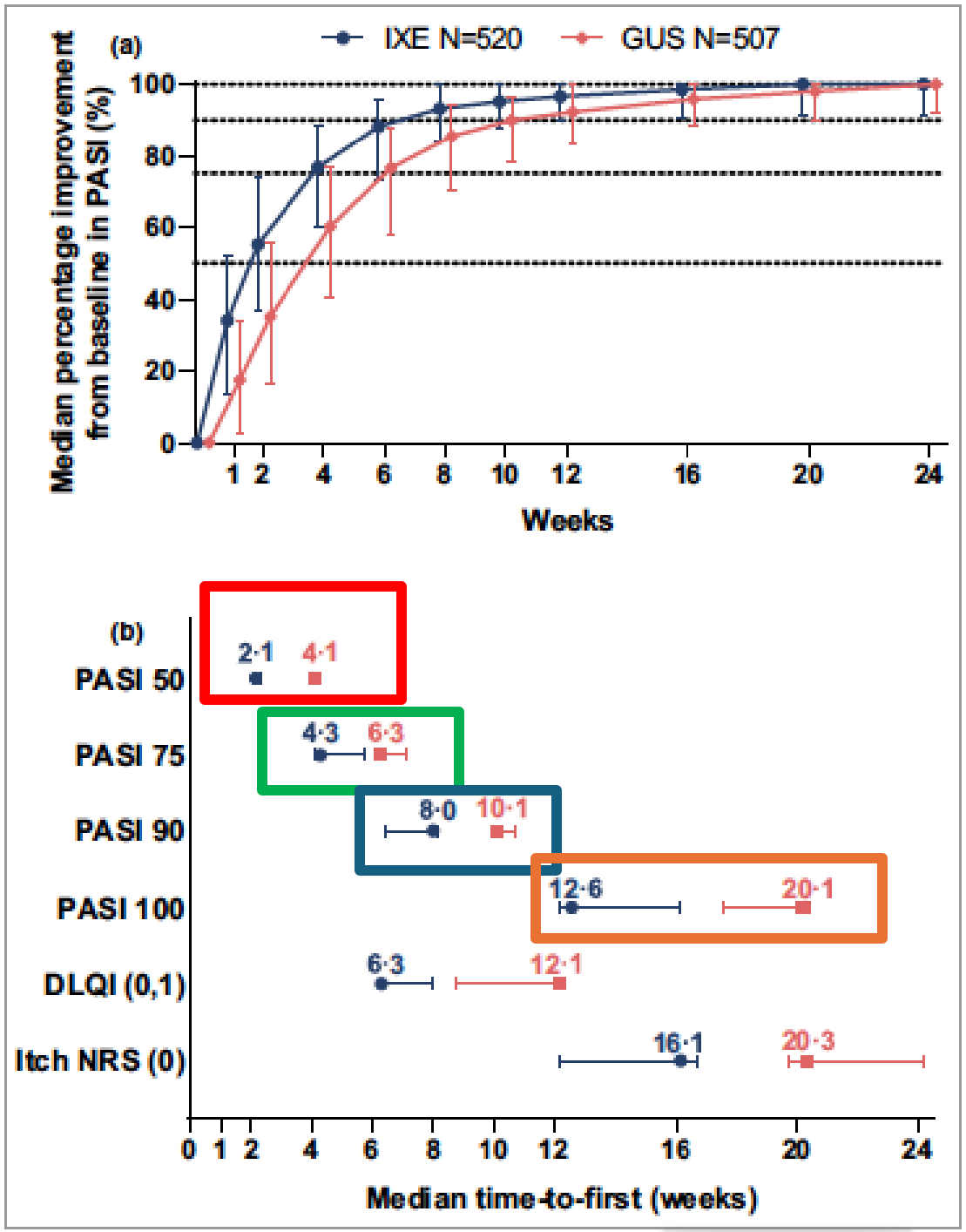
PASI 90 y 100
→ en las semanas 12 y 60

Respondedores rápidos vs respondedores



Rapid responders treated with IXE or ETN had a higher response rates at Weeks 12 and 60

[a]Week 2 PASI 50 Responders/Non-Responders in the ITT or LTE Populations.
Gordon KB, et al. Phase 3 Trials of Ixekizumab in Moderate-to-Severe Plaque Psoriasis. N Engl J Med 2016;375:345-356. Post hoc



Ixekizumab had a Faster Onset of Response than Guselkumab

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Estudio Ixora-R

Búsqueda del PASI de manera rápida con Ixekizumab

PASI 50 es de 2 semanas

PASI 75 es de 4 semanas

PASI 90 es de 8 semanas

PASI 100 es de 12 semanas

Blauvelt A, Leonardi C, Elewski B, Crowley JJ, Guenther LC, Gooderham M, Langley RG, Vender R, Pinter A, Griffiths CEM, Tada Y, Elmaraghy H, Lima RG, Gallo G, Renda L, Burge R, Park SY, Zhu B, Papp K; IXORA-R Study Group. A head-to-head comparison of ixekizumab vs. guselkumab in patients with moderate-to-severe plaque psoriasis: 24-week efficacy and safety results from a randomized, double-blinded trial. Br J Dermatol. 2021 Jun;184(6):1047-1058

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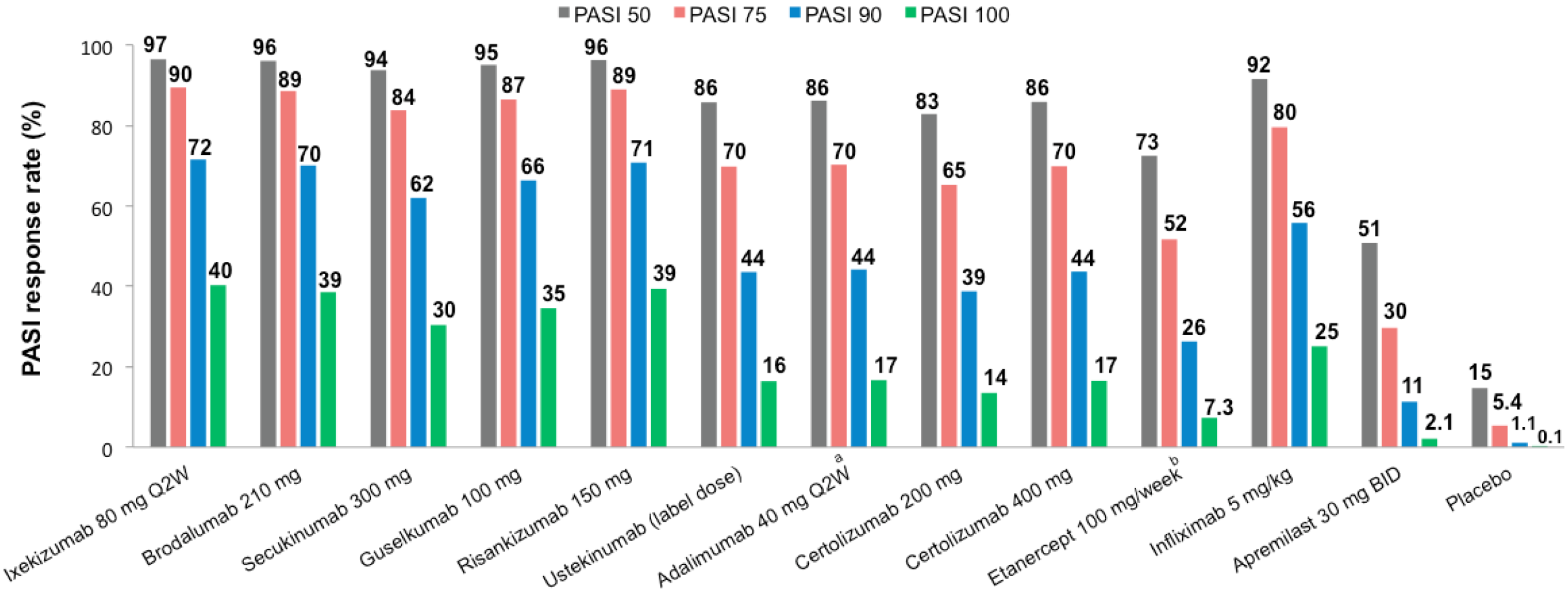
Effectiveness of the different systemic therapies for PSO treatment

NMA data for the treatment of 10 – 16 Wochen)*



a. Patients in the adalimumab group received an initial dose of adalimumab 80 mg at week 0, followed by adalimumab 40 mg Q2W

b. Patients in the etanercept group received etanercept 50 mg twice weekly during the induction period

* **This NMA was limited by the fact that it was not a head-to-head trial and included combined data from different timepoints (10–16 weeks).** The period of analysis was limited to the induction period of the different systemic therapies and considered PASI results only. Not all treatments may be approved in your country. Please refer to local prescribing information for your country

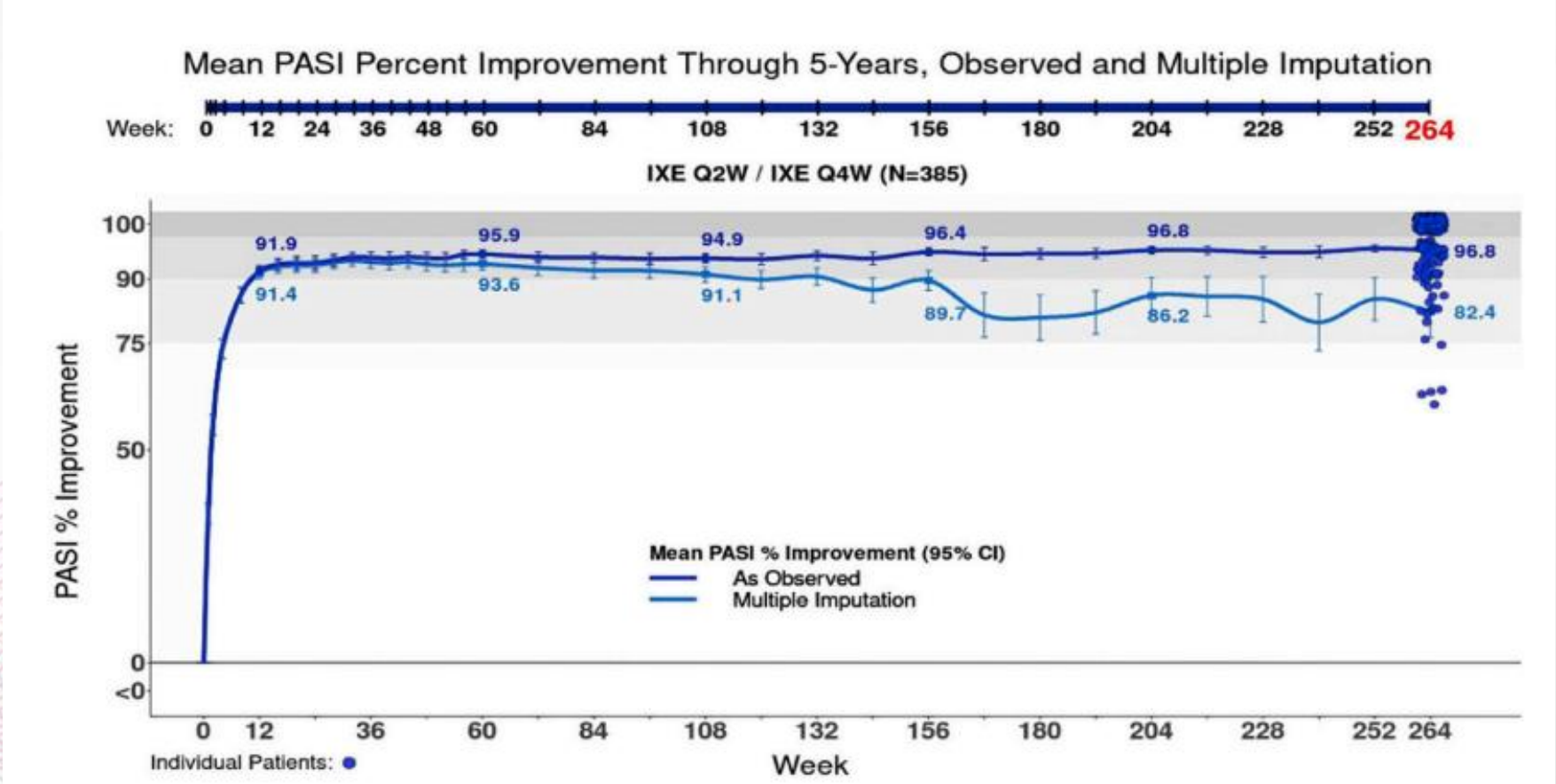
BID, twice daily; NMA, network meta-analysis; PASI, Psoriasis Area and Severity Index; Q2W, every 2 weeks

Sawyer LM, et al. Assessing the relative efficacy of interleukin-17 and interleukin-23 targeted treatments for moderate-to-severe plaque psoriasis: A systematic review and network meta-analysis of PASI response. *PLoS One* 2019;14(8):e0220868

Estudio UNCOVER - 3

EXPERIENCIA DE 5 AÑOS

El paciente que continúa con Ixekizumab va a mantener las metas de tratamiento

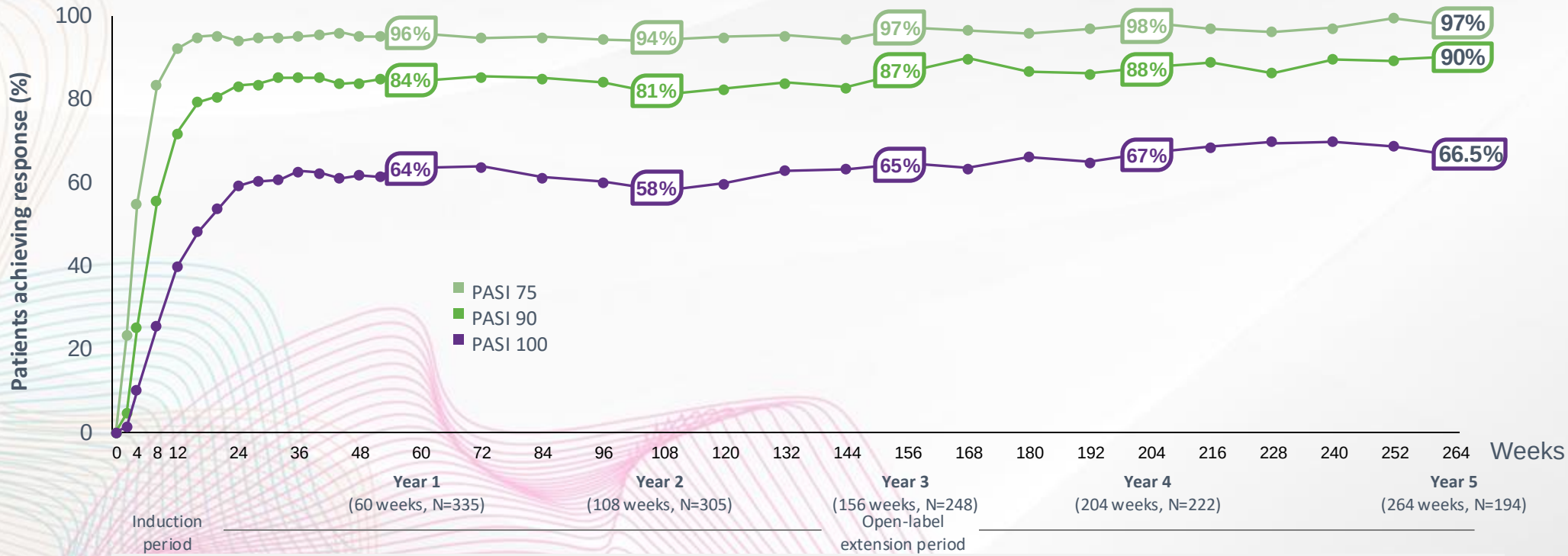


Blauvelt A, Lebwohl MG, Mabuchi T, Leung A, Garrelts A, Crane H, ElMaraghy H, Patel H, Ridenour T, See K, Gallo G, Paul C. Long-term efficacy and safety of ixekizumab: A 5-year analysis of the UNCOVER-3 randomized controlled trial. J Am Acad Dermatol. 2021 Aug;85(2):360-368.

Ixekizumab provided complete skin clearance sustained up to 5 years of treatment in adults with moderate-to-severe plaque psoriasis

UNCOVER-3: More than half of the patients on treatment (66%) achieved or maintained PASI 100 at Week 264

UNCOVER-3: PASI 75, PASI 90, and PASI 100 "as observed" results up to Week 264[1]



Ixekizumab achieved superiority in the coprimary endpoints: PASI 75 and sPGA score of clear or minimal (0/1) with at least a two-point reduction from baseline at Week 12 vs etanercept and placebo[2]

A post hoc analysis is shown in which a subset from UNCOVER-3 (n=385) received a 160-mg starting dose of ixekizumab at Week 0, followed by 80 mg Q2W through Week 12, followed by 80 mg Q4W. Data shown are "as observed", so only data from patients who completed the visit were analysed and no missing data imputation was performed.[1] For UNCOVER-2 and UNCOVER-3, respectively, in the ixekizumab every 2 weeks group, PASI 75 was achieved by 89.7%; [effect size 87.4% (97.5% CI 82.9–91.8) placebo; 48.1% (41.2–55.0) vs. etanercept] and 87.3%; [80.0% (74.4–85.7) vs. placebo; 33.9% (27.0–40.7) vs etanercept] patients; in the ixekizumab every 4 weeks group, by 77.5%; [75.1% (69.5–80.8) vs. placebo; 35·9% (28.2–43.6) vs. etanercept] and 84·2%; [76.9% (71.0–82.8) vs. placebo; 30.8% (23.7–37.9) vs. etanercept] patients; in the placebo group, by 2.4% and 7.3% patients; and in the etanercept group by 41.6% and 53.4% patients (all p<0.0001 vs. placebo or etanercept).[2] PASI 75/90/100=Psoriasis Area and Severity Index improvement of ≥75%/≥90%/100% from baseline; QxW=every x weeks; sPGA=static Physician's Global Assessment.

1. Modified from Blauvelt A, et al. J Am Acad Dermatol. 2021;85(2): 360–368. 2. Griffiths CEM, et al. Lancet. 2015;386(9993): 541–551.

Disease modification concept – Components

Early intervention

Change in PsO pathophysiology

Potential of treatment withdrawal

PsO=Psoriasis.

Eyerich K, et al. J Eur Acad Dermatol Venereol. 2024;38(5): e424–7.

A handful of studies have provided some data to show pathophysiology changes in patients with psoriasis

IL=Interleukin

1. Iversen L, et al. J Eur Acad Dermatol Venereol. 2023;37(5): 1004–16. 2. Garcet S, et al. J Am Acad Dermatol. 2023;89(3): Suppl (AB59). 3. Schäkel K, et al. J Eur Acad Dermatol Venereol. 2023;37(10): 2016–27.
4. Blauvelt A, et al. Oral Presentation presented at: American Academy of Dermatology (AAD) Meeting; March 8–12, 2024; San Diego, Califomia, USA. 5. Mehta H, et al. J Invest Dermatol. 2021;141(7): 1707–18.E9.

Main cytokines and cells involved in the pathogenesis of psoriasis

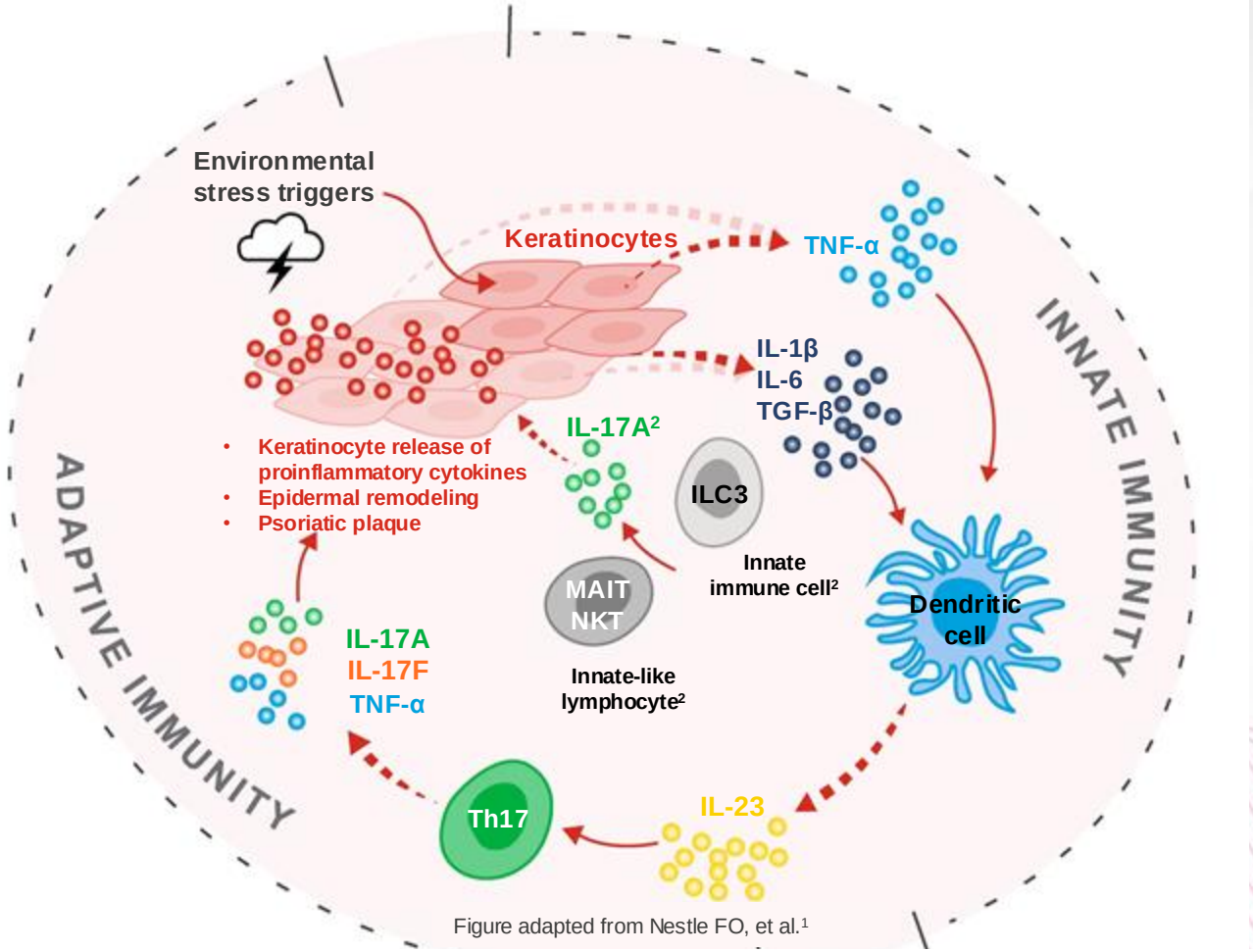
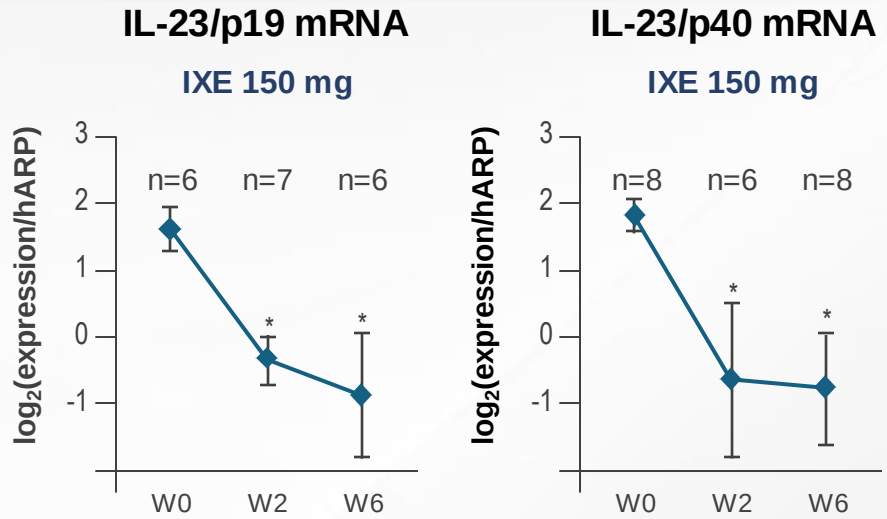


Figure adapted from Nestle FO, et al.[1]

Moreover, IL-17A signalling activates keratinocytes to produce IL-23[3]



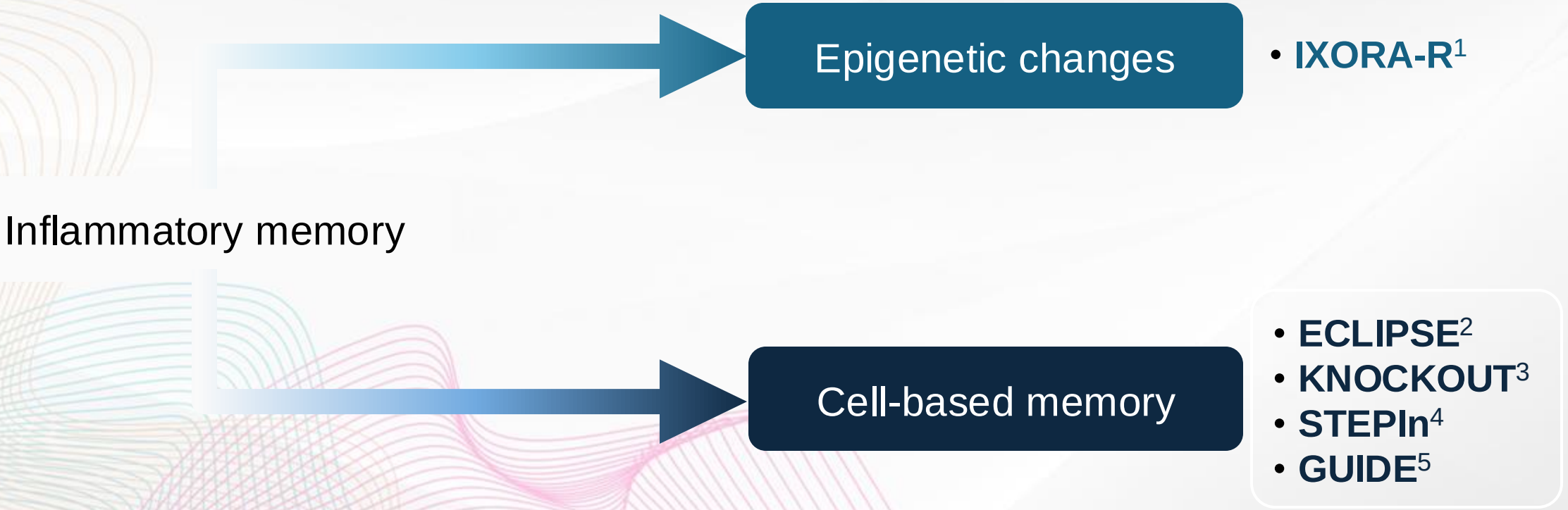
IL-17 neutralization with ixekizumab decreased expression of IL-23 mRNA from dendritic cells[4]

*p<0.05 vs baseline. Data of the line graph are shown as mean ± SEM.

IL=Interleukin; ILC=Innate Lymphoid Cell; IXE=Ixekizumab; MAIT=Mucosal-Associated Invariant T Cell; mRNA=Messenger Ribonucleic Acid; NKT=Natural Killer T Cell; SEM=Standard Error of Mean; TGF=Transforming Growth Factor; Th=T-Helper Cell; TNF=Tumor Necrosis Factor; W=Week.

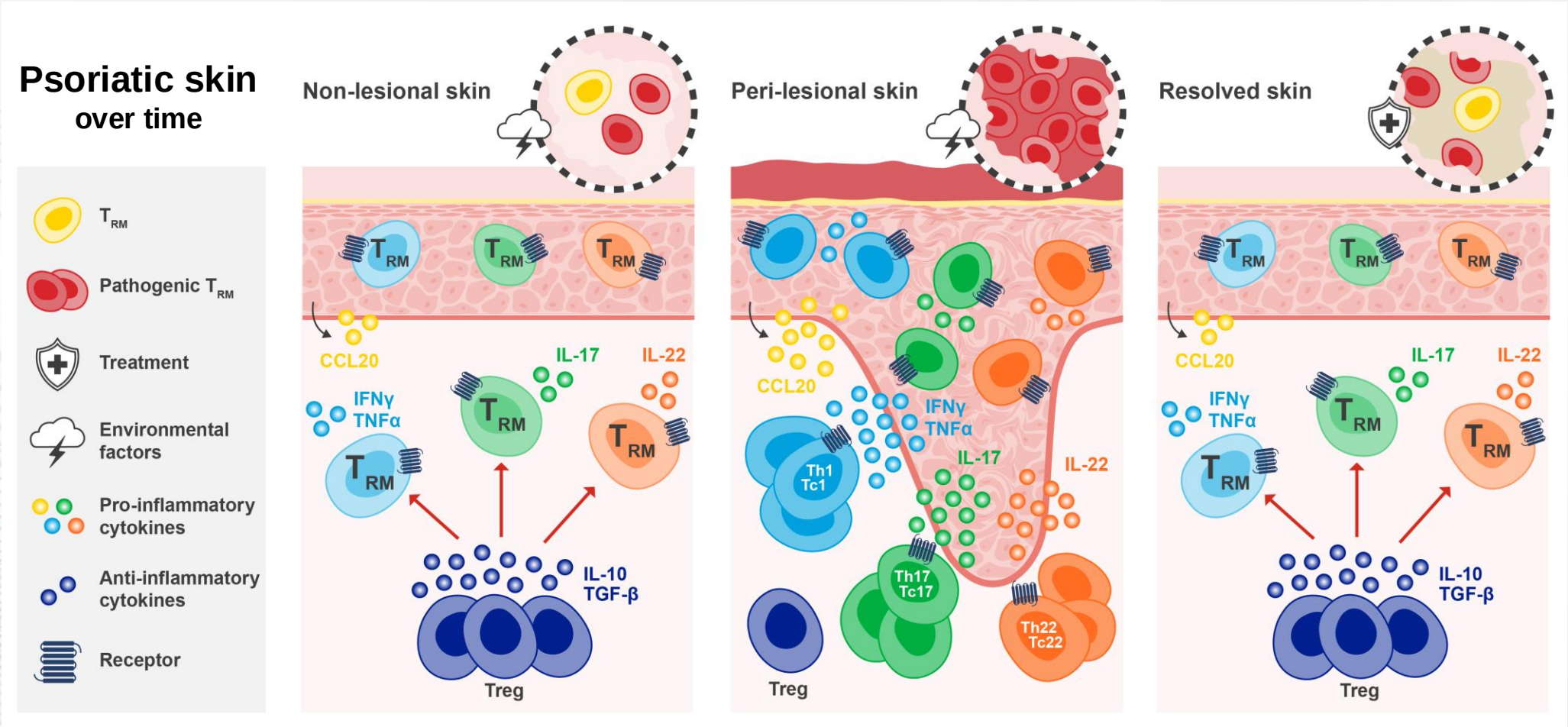
1. Nestle FO, et al. N Engl J Med. 2009;361(5): 496–509. 2. Navarro-Compán V, et al. Front Immunol. 2023;14: 1191782. 3. Cheuk S, et al. Exp Dermatol. 2017;26(9): 824–7. 4. Krueger JG, et al. J Allergy Clin Immunol. 2012;130(1): 145–54.e9.

Inflammatory memory – a mechanistic rationale



1. Gudjonsson JE, et al. Poster presented at: International Society for Investigative Dermatology (ISID); May 10–13, 2023; Tokyo, Japan.
2. Mehta H, et al. J Invest Dermatol. 2021;141(7): 1707–18.E9. 3. Blauvelt A, et al. Oral Presentation presented at: American Academy of Dermatology (AAD) Meeting; March 8–12, 2024; San Diego, California, USA.
4. Iversen L, et al. J Eur Acad Dermatol Venereol. 2023;37(5): 1004–16. 5. Schäkel K, et al. J Eur Acad Dermatol Venereol. 2023;37(10): 2016–27.

Cell-based memory in psoriasis: After treatment, T_{RM} cells persist in clinically healed skin and could participate in relapses

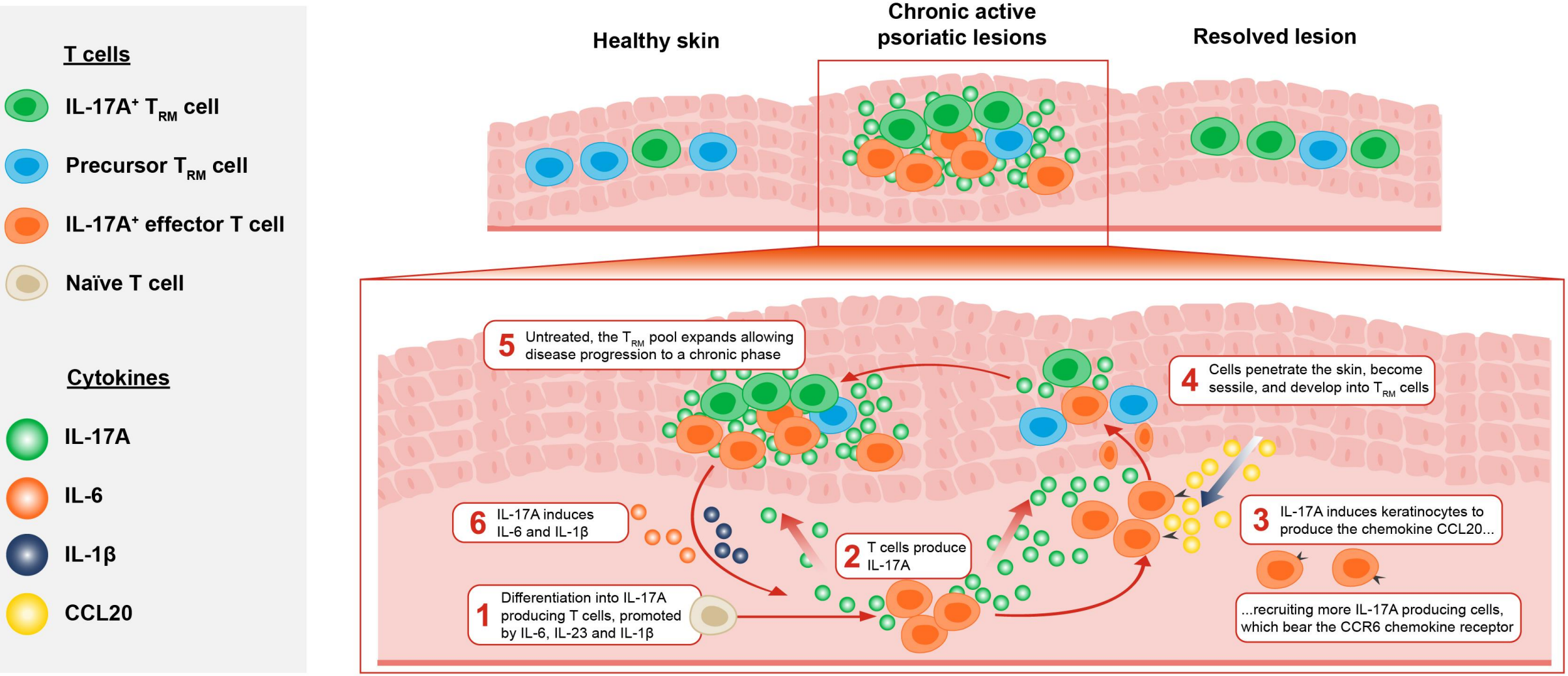


Normal-appearing skin in PsO has pathogenic T_{RM} cells that may lead to the development of new lesions if triggered by environmental factors. T_{RM} cells may persist after treatment in clinically cleared skin and contribute to later relapses

CCL=Chemokine Ligand; IFN=Interferon; IL=Interleukin; PsO=Psoriasis; Tc=Cytotoxic T Cell; TGF=Transforming Growth Factor; Th=T-Helper Cell; TNF=Tumor Necrosis Factor; Treg=Regulatory T Cell; T_{RM}=Tissue-Resident Memory T Cell.

Migayron L, et al. J Allergy Clin Immunol. 2024;153(3): 606–14.

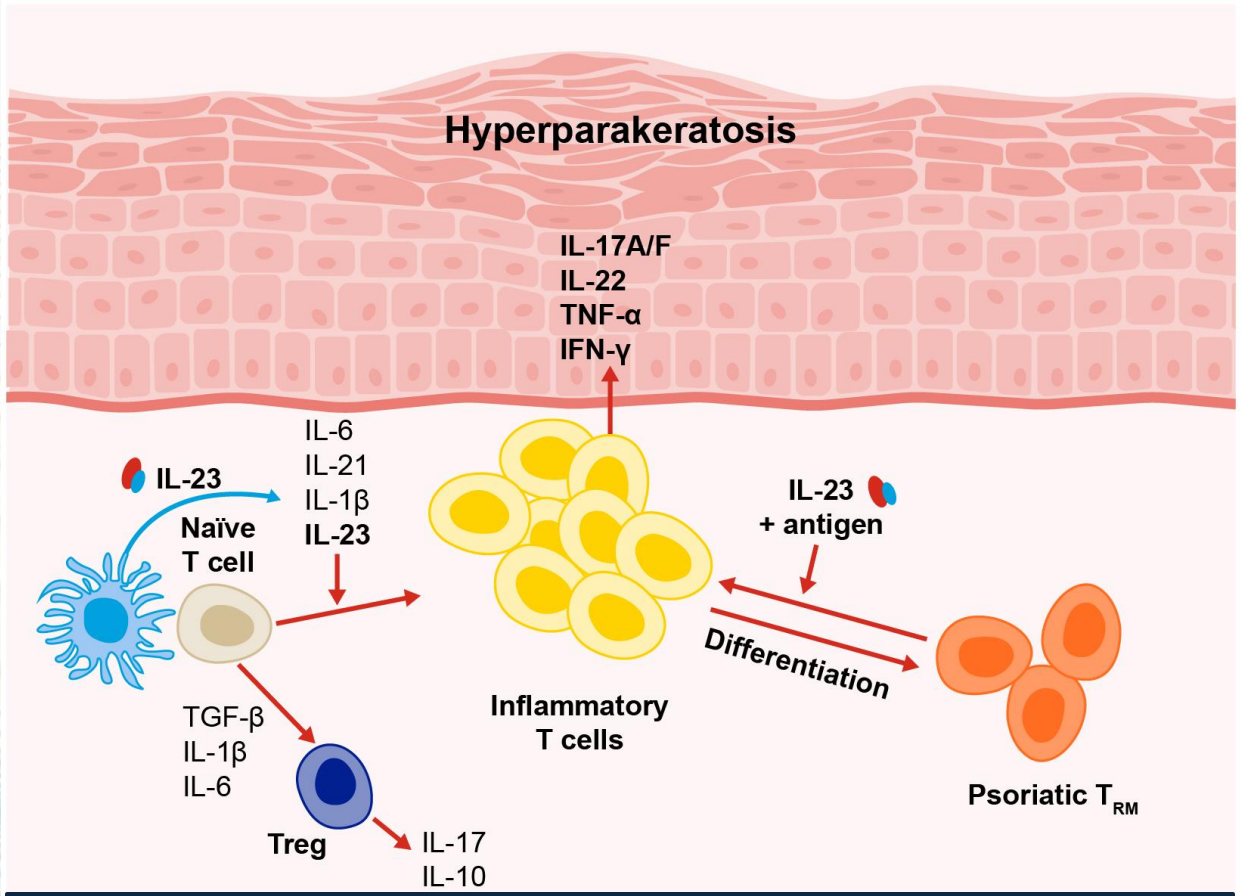
Key role of IL-17 in establishment of cell-based memory (T_{RM} cells)



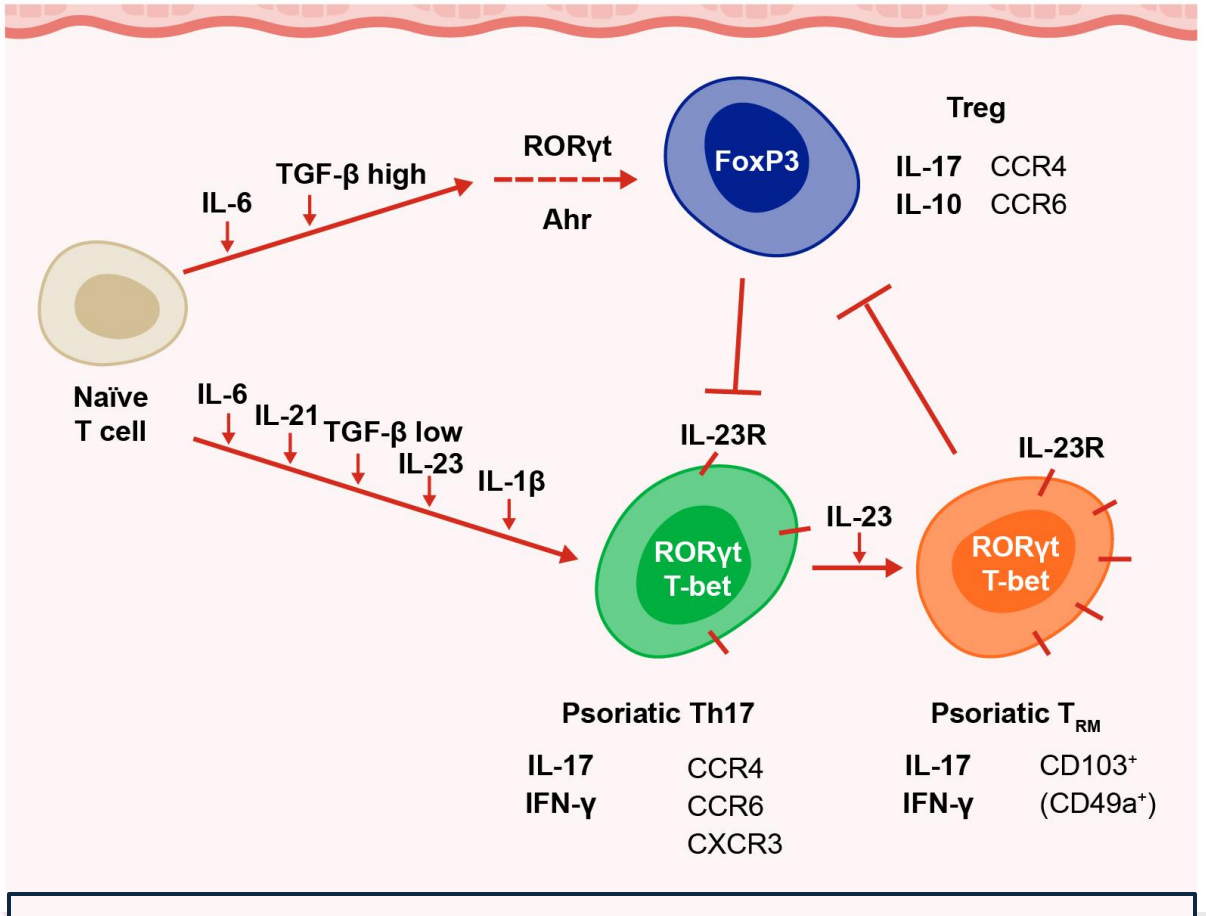
CCL=Chemokine Ligand; IL=Interleukin; T_{RM}=Tissue-Resident Memory T Cell.

Iversen L, et al. J Eur Acad Dermatol Venereol. 2018;32(11): 1930–9.

Theoretical development of T_{RM} and dysregulation of T_{reg} in psoriasis



TGF-β promotes IL-10 and IL-17, producing Treg differentiation, while IL-6, IL-1β and IL-23 promote Th17 cell differentiation



IL-23 in combination with low concentrations of TGF-β would promote IL-23R expression, increasing Th17 cell differentiation and suppressing Treg differentiation

CCL=Chemokine Ligand; CCR=Chemokine Receptor; CD=Cluster of Differentiation; IFN=Interferon; IL=Interleukin; TGF=Transforming Growth Factor; Th=T-Helper Cell; TNF=Tumor Necrosis Factor; Treg=Regulatory T Cell; T_{RM}=Tissue-Resident Memory T Cell.

Eyerich K, et al. BMJ Open. 2021;11(9): e049822.

IXORA-R study: Does Ixekizumab reduce IL-17 and IL-23 pathway genes more rapidly than Guselkumab?

A subanalysis of a Phase 3, randomized, double-blind, multicenter study (NCT03573323)

Objectives:

- To examine the effects of IXE and GUS on IL-17/IL-23 pathway gene expression in psoriatic lesions at Weeks 0, 1, 2 and 4

Healthy Control (N=26)

IXORA-R Addendum (N=72)

IXE (N=41)

GUS (N=31)

RNASeq (N=80)

Psoriasis (N=54)

IXE (N=32)

GUS (N=22)

Healthy Control RNASeq Samples=26

Week 0 Psoriasis RNASeq Samples=54

Week 1 Psoriasis RNASeq Samples=39

Week 2 Psoriasis RNASeq Samples=40

Week 4 Psoriasis RNASeq Samples=40

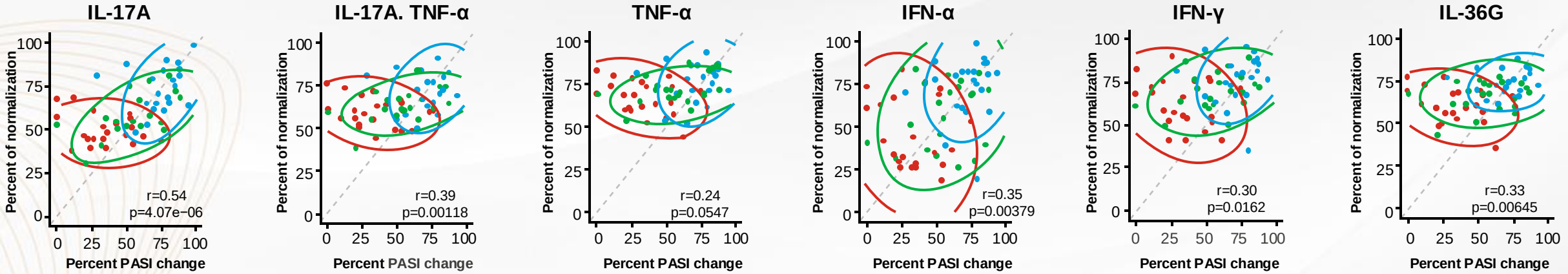
72 patients consented to have skin biopsies taken from lesions as well as blood samples at Weeks 0, 1, 2 and 4 in a study addendum.

GUS=Guselkumab; IL=Interleukin; IXE=Ixekizumab; RNA=Ribonucleic Acid.

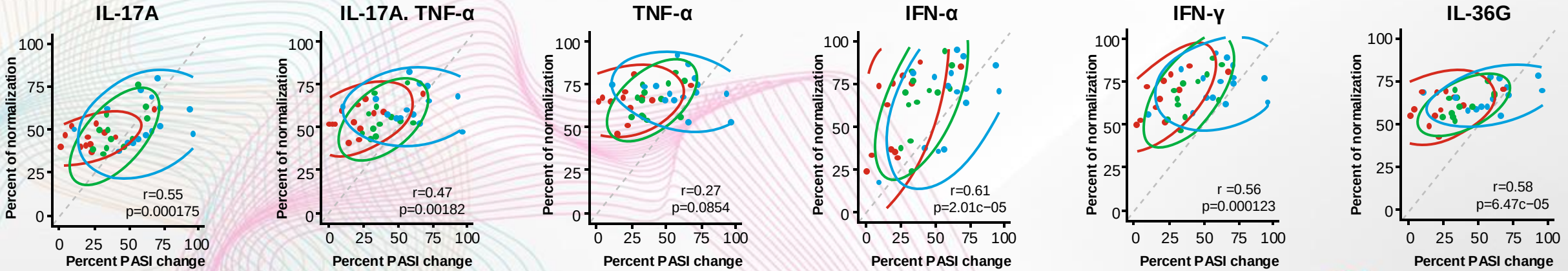
Gudjonsson JE, et al. Poster presented at: International Society for Investigative Dermatology (ISID); May 10–13, 2023; Tokyo, Japan.

IXORA-R correlation of early transcriptomic changes with PASI 100 at Week 24: Normalization of epidermal IL-17A and IL-36 responses correlated with PASI 100 at Week 24 earlier for IXE vs GUS

Ixekizumab



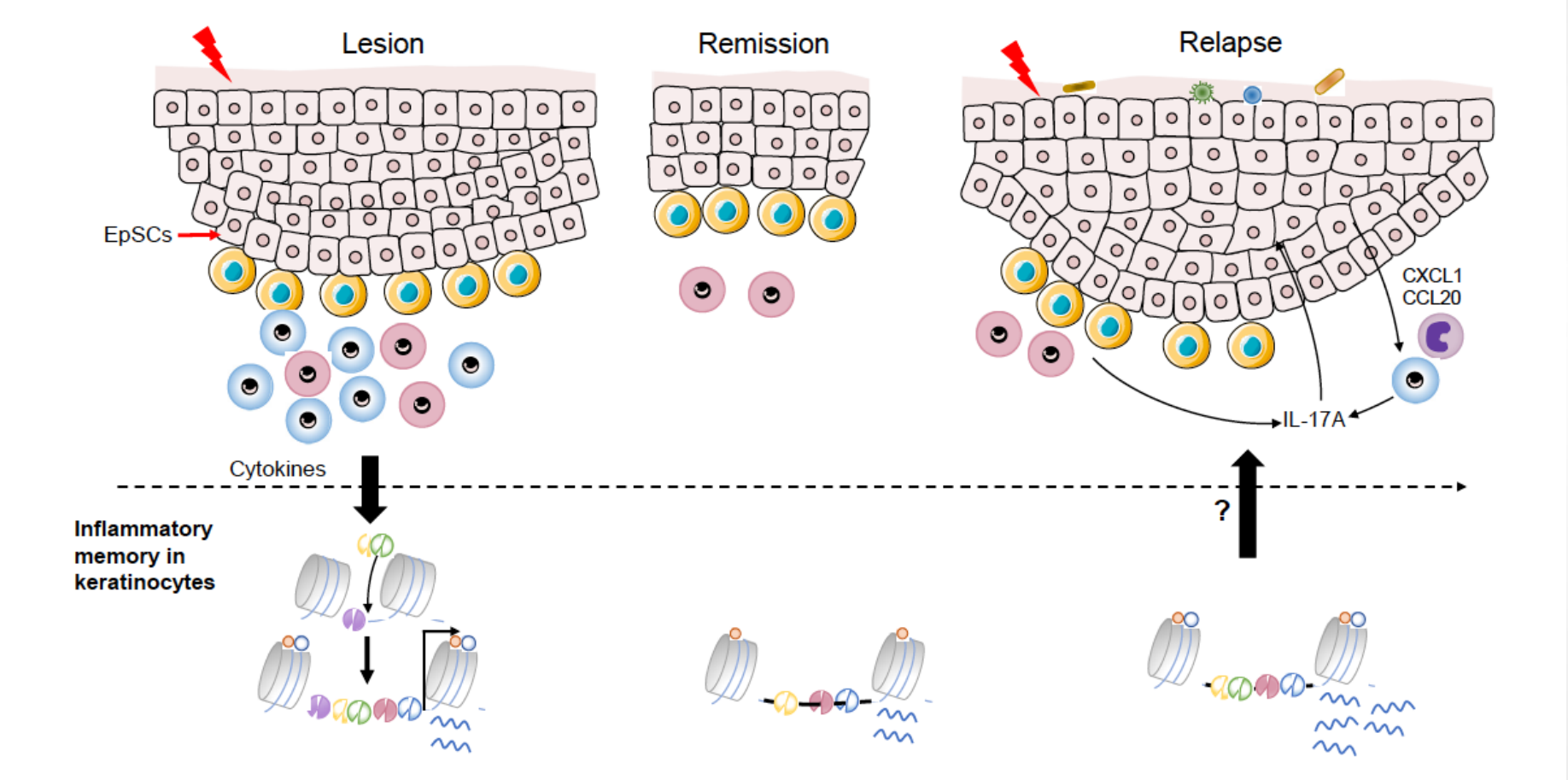
Guselkumab



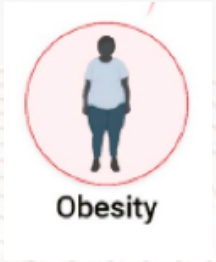
Week 1 Week 2 Week 4

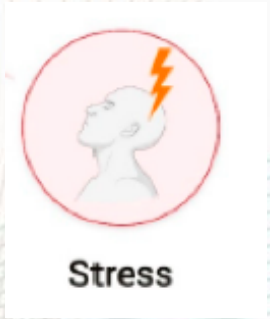
GUS=Guselkumab; IL=Interleukin; IFN=Interferon; IXE=Ixekizumab; PASI=Psoriasis Area and Severity Index; PASI 100=Percentage Change from PASI Baseline Score; TNF=Tumor Necrosis Factor.

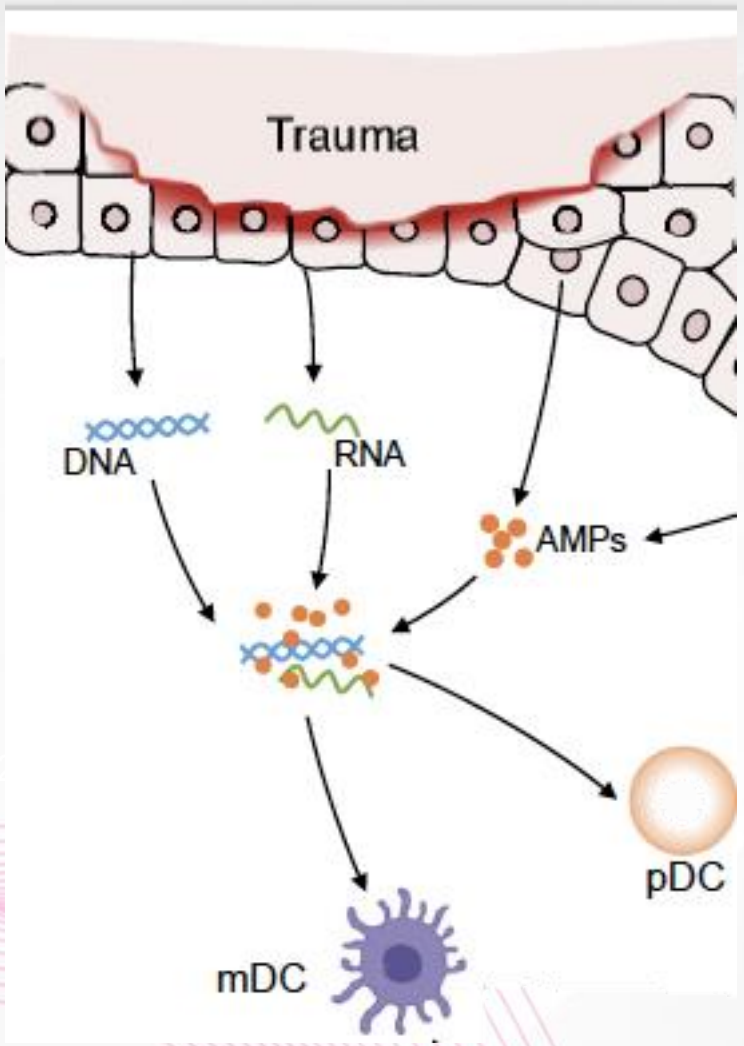
Gudjonsson JE, et al. Poster presented at: International Society for Investigative Dermatology (ISID); May 10–13, 2023; Tokyo, Japan.



Tian, D., & Lai, Y. (2022). The Relapse of Psoriasis: Mechanisms and Mysteries. *JID innovations : skin science from molecules to population health*, *2*(3), 100116. https://doi-org.pbidi.unam.mx:2443/10.1016/j.xjidi.2022.100116





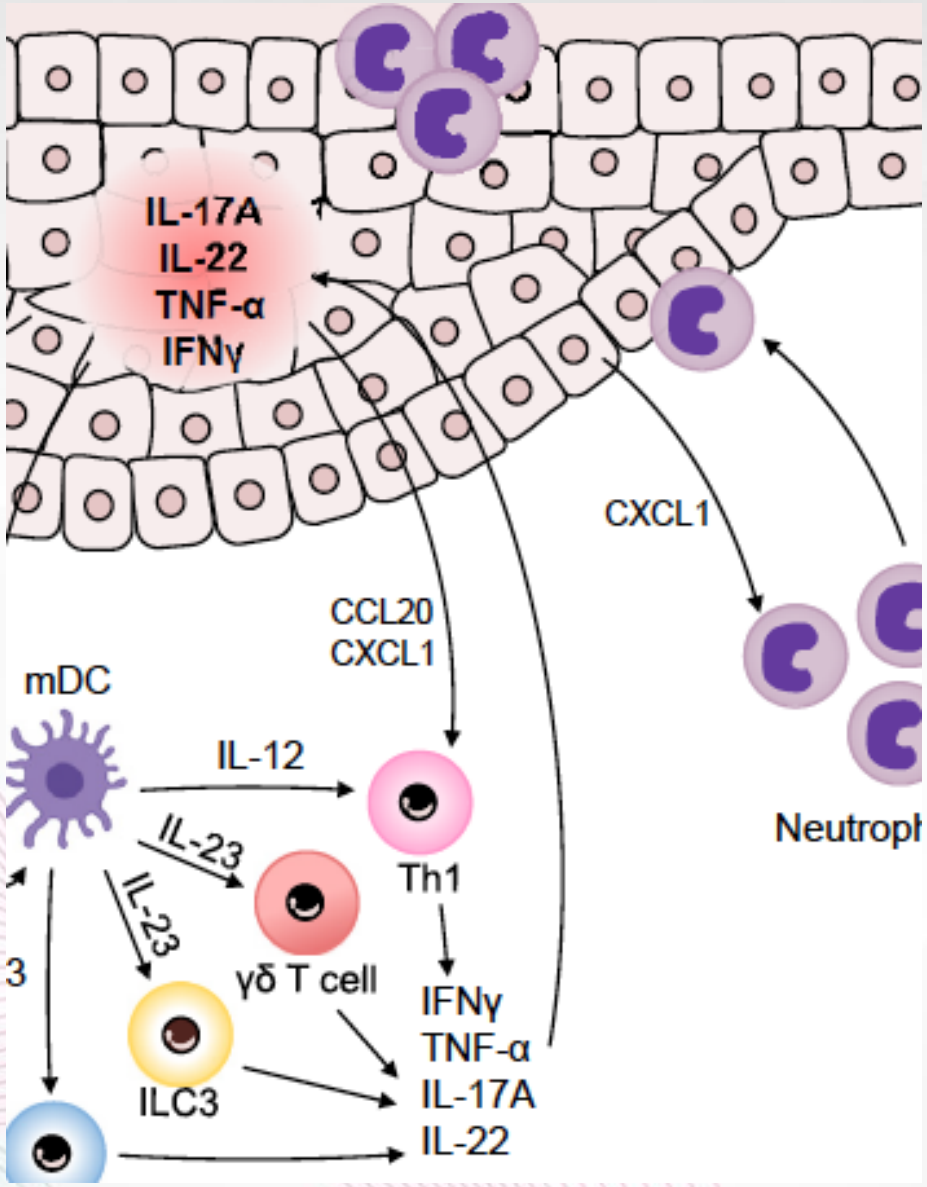


IL-12, IL-23, IL-22 IL-

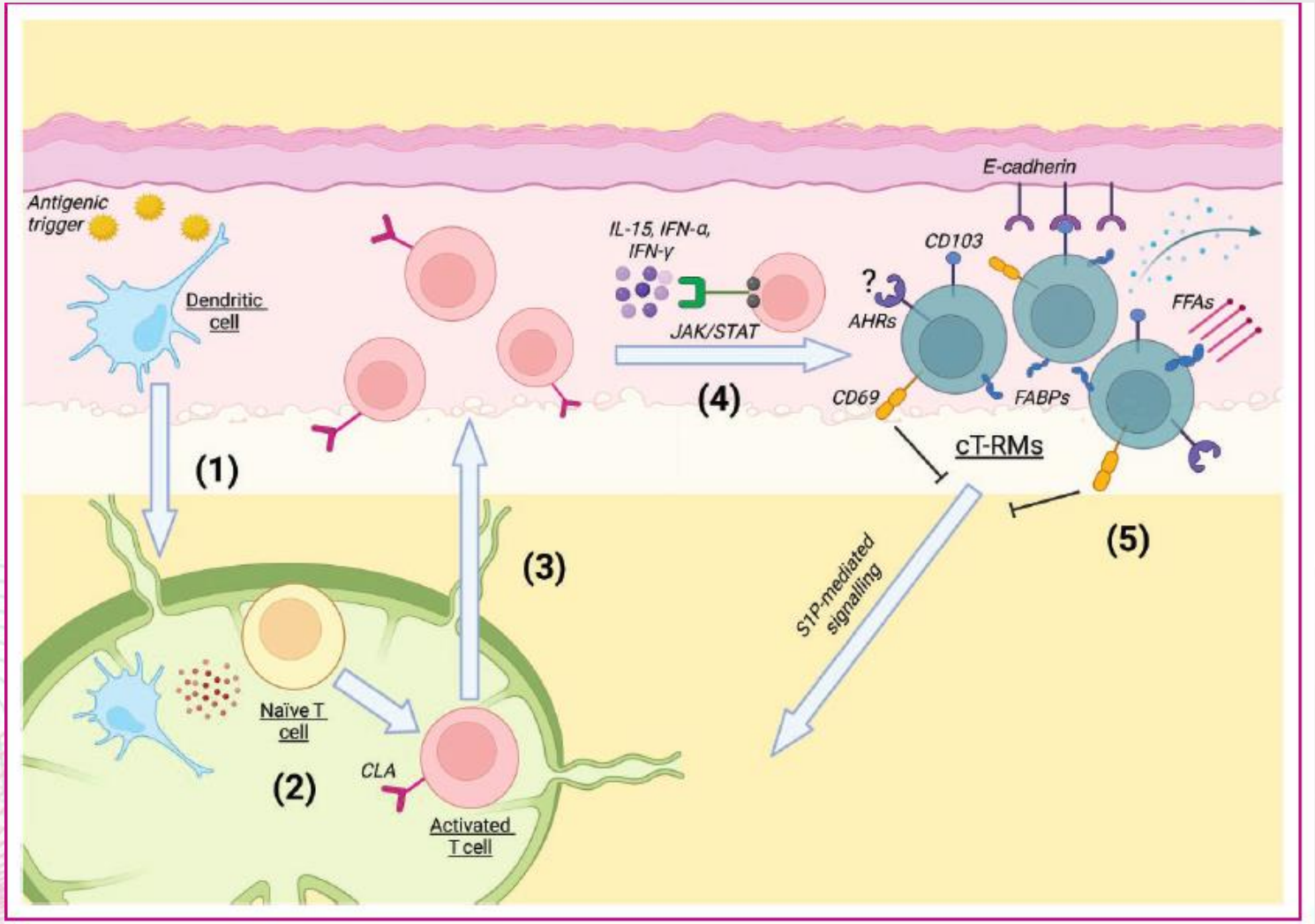
IFN I

TNF-α, IL-6
TGF-β

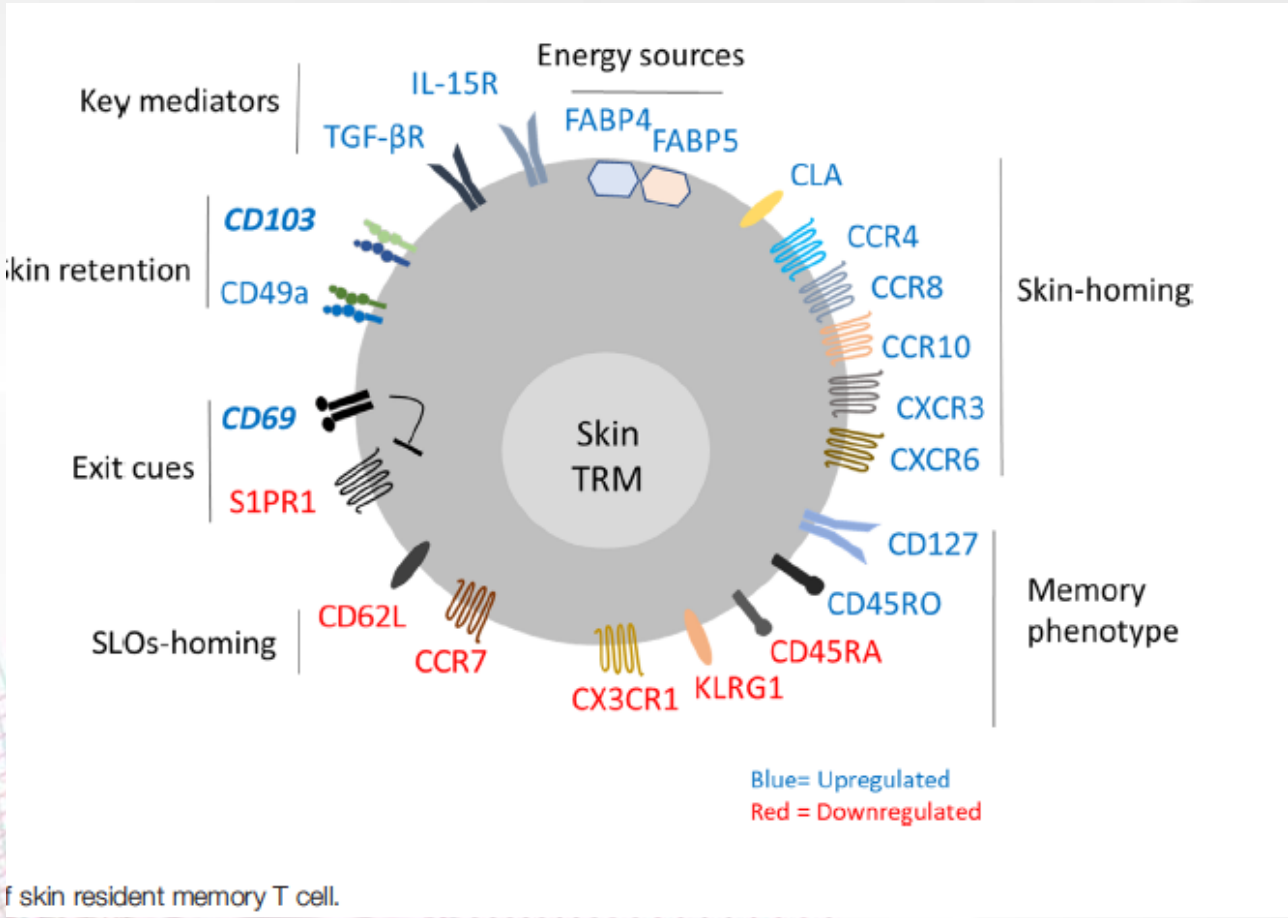
Tian, D., & Lai, Y. (2022). The Relapse of Psoriasis: Mechanisms and Mysteries. *JID innovations : skin science from molecules to population health*, *2*(3), 100116. https://doi-org.pbidi.unam.mx:2443/10.1016/j.xjidi.2022.100116



Tian, D., & Lai, Y. (2022). The Relapse of Psoriasis: Mechanisms and Mysteries. *JID innovations : skin science from molecules to population health*, *2*(3), 100116. https://doi-org.pbidi.unam.mx:2443/10.1016/j.xjidi.2022.100116

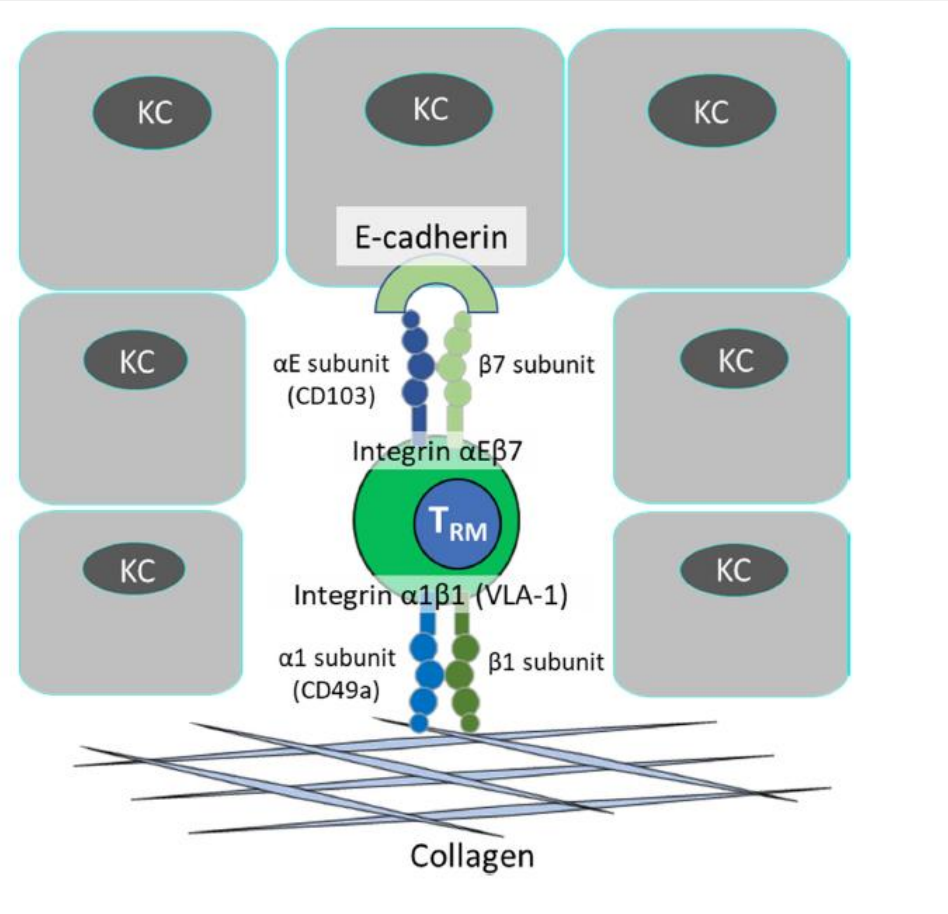


Pham, J. P., Wark, K. J. L., Woods, J., & Frew, J. W. (2023). Resident cutaneous memory T cells: a clinical review of their r ole in chronic inflammatory dermatoses and potential as therapeutic targets. *The British journal of dermatology*, *189*(6), 656–663. https://doi-org.pbidi.unam.mx:2443/10.1093/bjd/ljad303



f skin resident memory T cell.

Tokura, Y., Phadungsaksawasdi, P., Kurihara, K., Fujiyama, T., & Honda, T. (2021). Pathophysiology of Skin Resident Memory T Cells. *Frontiers in immunology*, *11*, 618897. https://doi-org.pbidi.unam.mx:2443/10.3389/fimmu.2020.618897



Tokura, Y., Phadungsaksawasdi, P., Kurihara, K., Fujiyama, T., & Honda, T. (2021). Pathophysiology of Skin Resident Memory T Cells. *Frontiers in immunology*, *11*, 618897. https://doi-org.pbidi.unam.mx:2443/10.3389/fimmu.2020.618897

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¿Por qué no todos los IL-17 son iguales?

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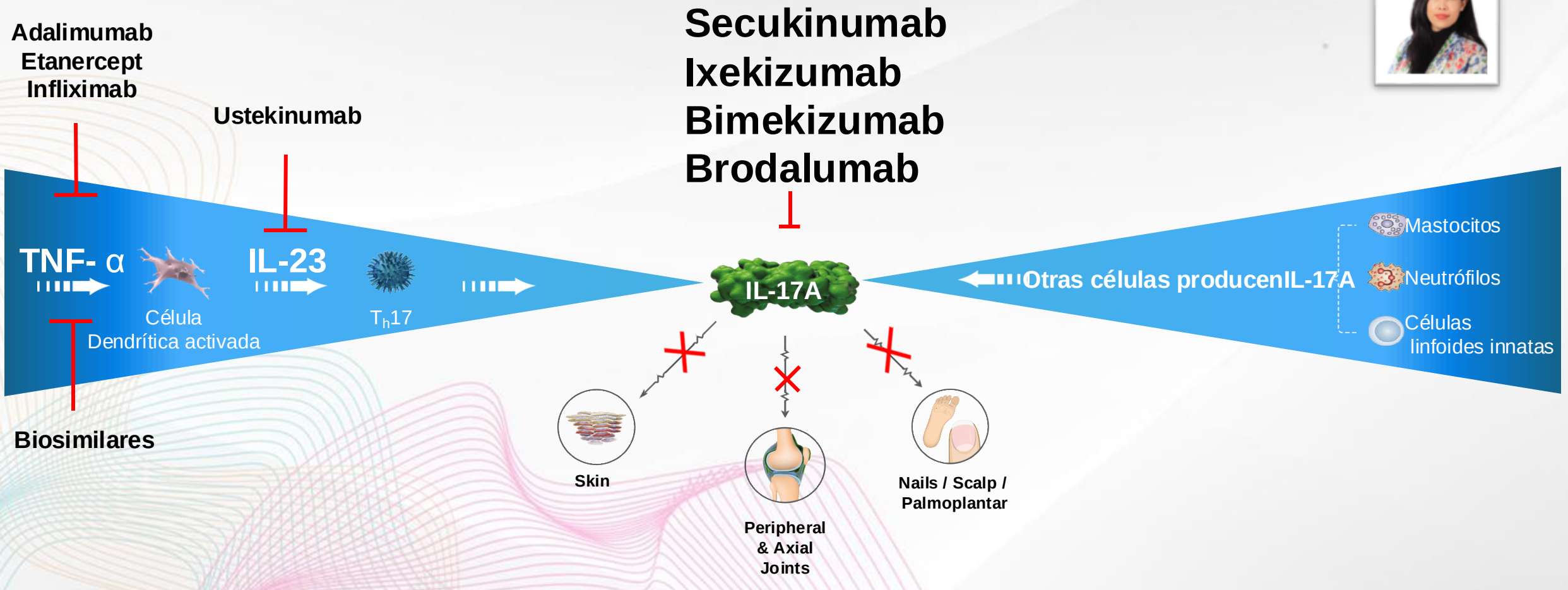
Blancos terapéuticos de terapia biológica para psoriasis



IL, interleukin; ILC3, type 3 innate lymphoid cells; Th17, T helper 17 cells

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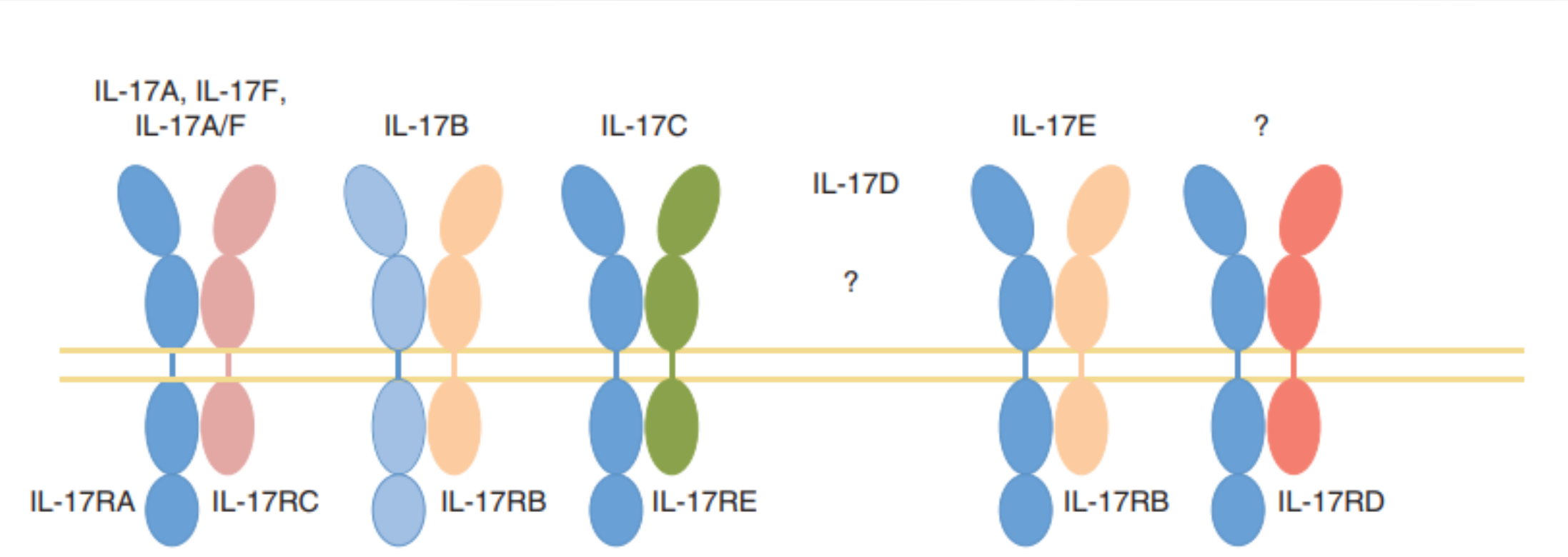
Girolomoni G, et al. Br J Dermatol 2012;167:717; 2. Secukinumab SmPC; 3. Kerdel FA, Strober BE. Semin Cutan Med Surg 2014;33(Suppl 2):S31; 4. Fotiadou C, et al. Psoriasis (Auckl) 2018 Jan 4;8:1

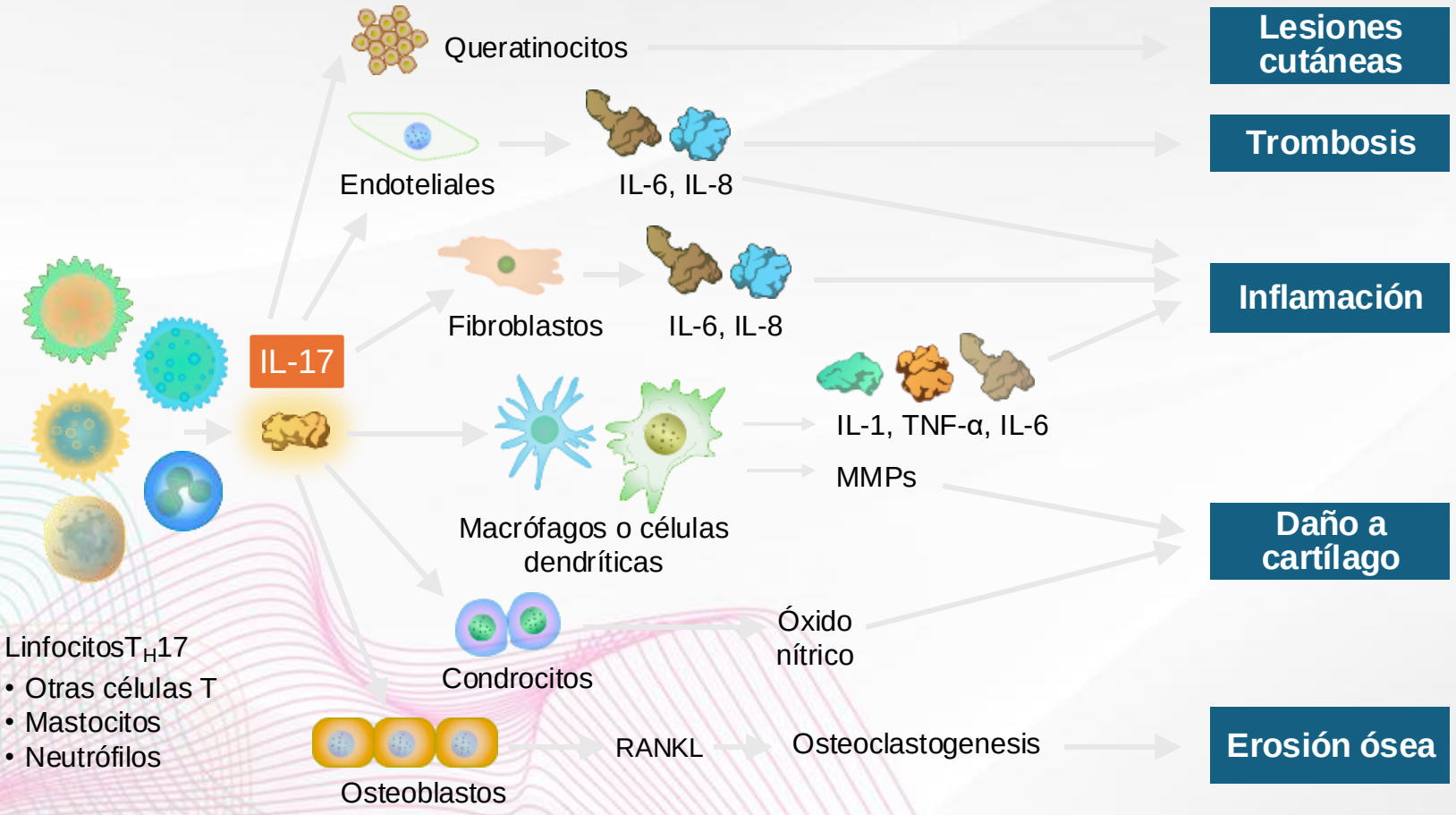
Familia de IL-17



Interleukin 17 (IL-17) family cytokines and their receptors. Most IL-17 family cytokines signal via a heterodimeric receptor composed of IL-17RA and a second chain that varies depending on ligand, as indicated

Cold Spring Harb Perspect Biol. 2018 Apr; 10(4): a028522.

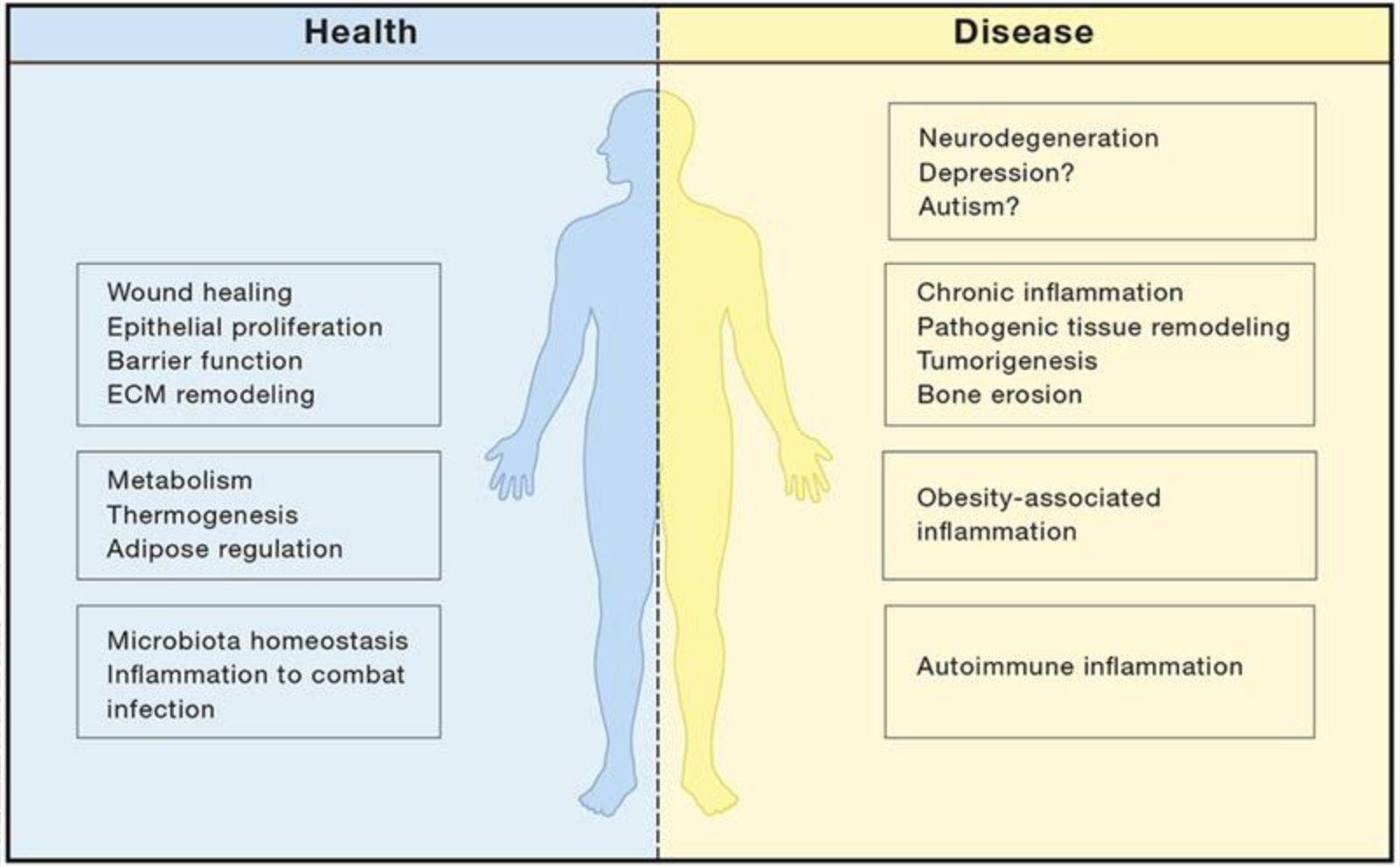
IL-17A juega un importante rol en diferentes tejidos



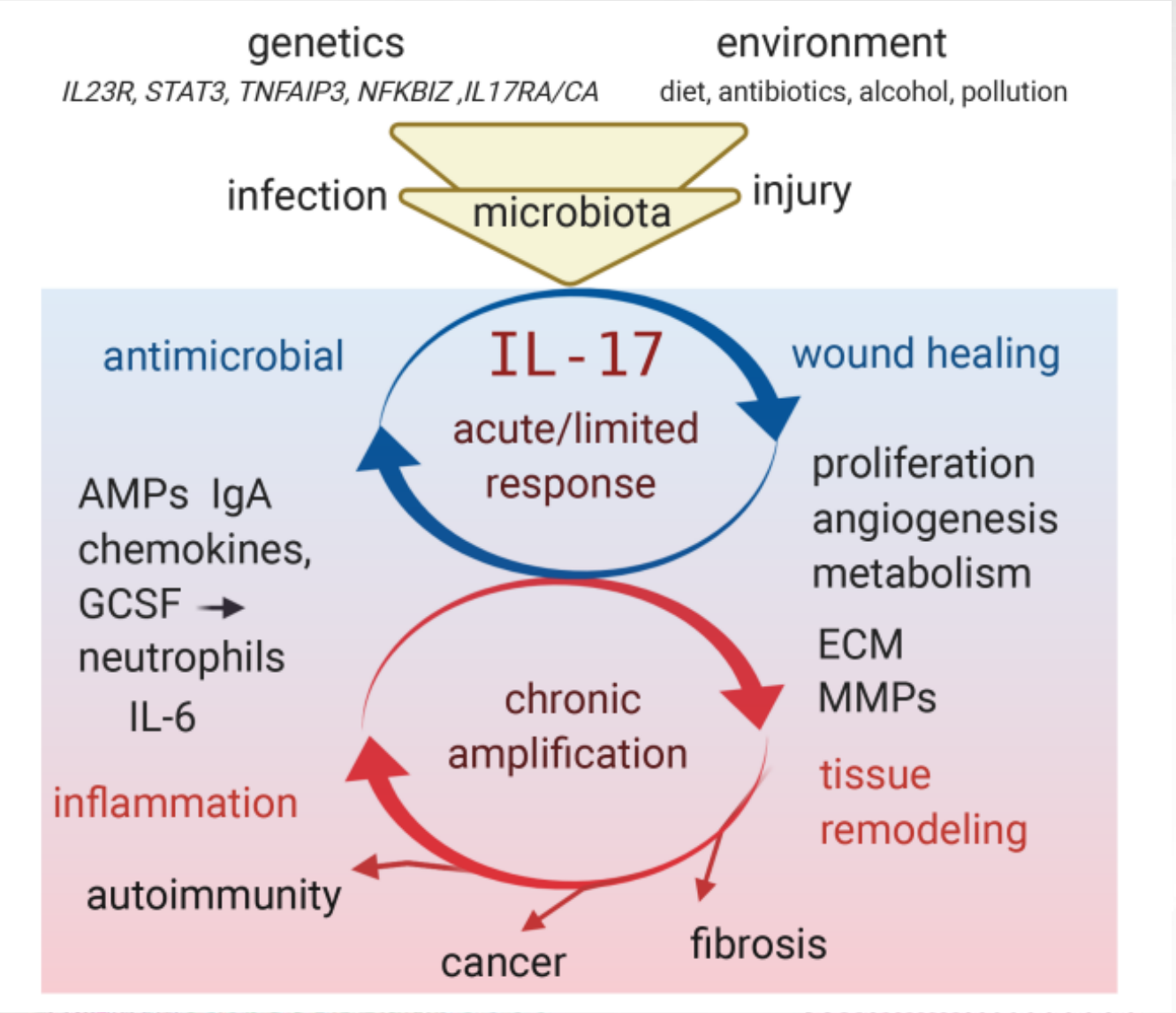
MMPs, matrix metalloproteins; RANKL, receptor activator of nuclear factor kappa-B ligand

Moissec P, et al. *Nat Rev Drug Discov* 2012;11:763; Suzuki E, at al. *Autoimmun Rev* 2014;13:496; Mease P, McInnes I. *Rheumatol Ther* 2016;3:5

IL-17A juega un importante rol en diferentes tejidos



Immunity. 2019 Apr 16; 50(4): 892–906

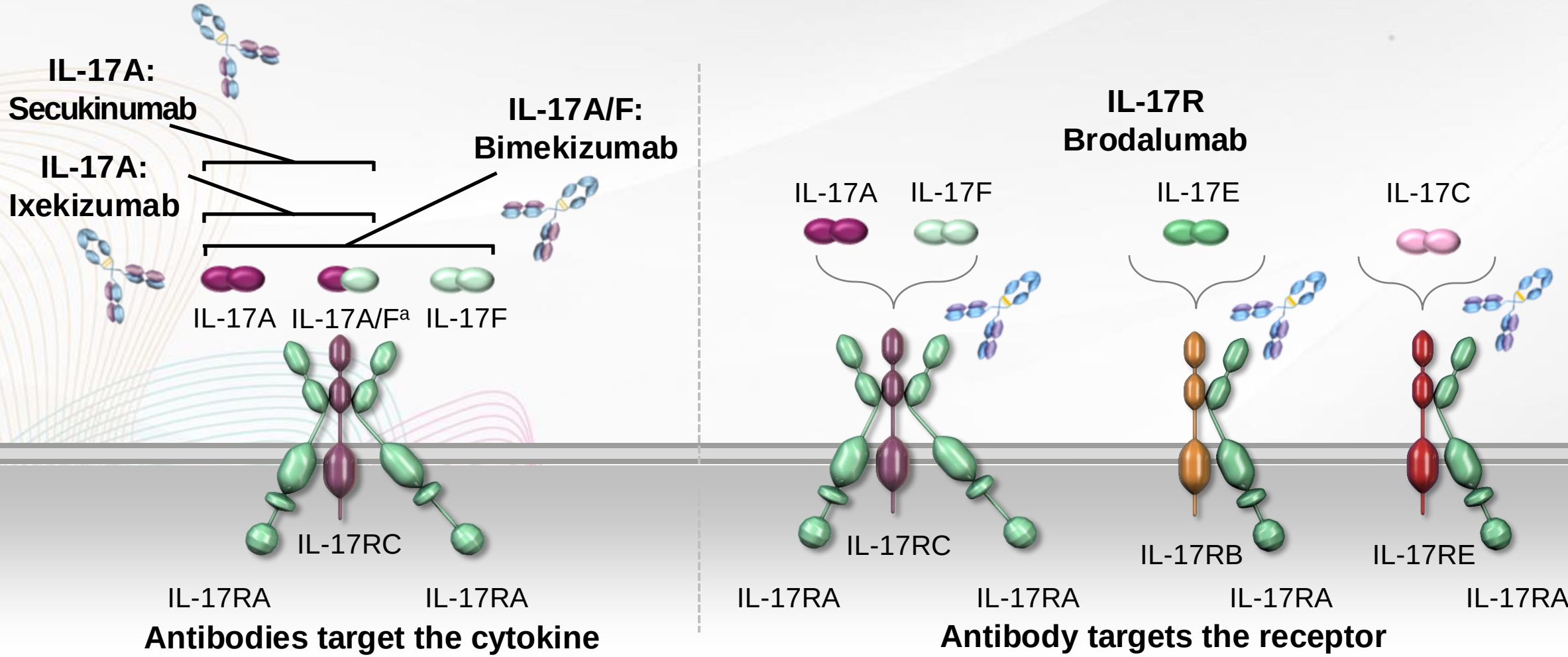


IL-17 production and signaling is multifactorially regulated by interplay between genetics, environment and resulting microbiota populations at barrier surfaces, leading to homeostatic maintenance in healthy individuals.

Majumder S, et al. Annu Rev Immunol. 2021 April 26; 39: 537–556.

Inhibidores de IL17. Mecanismo de acción

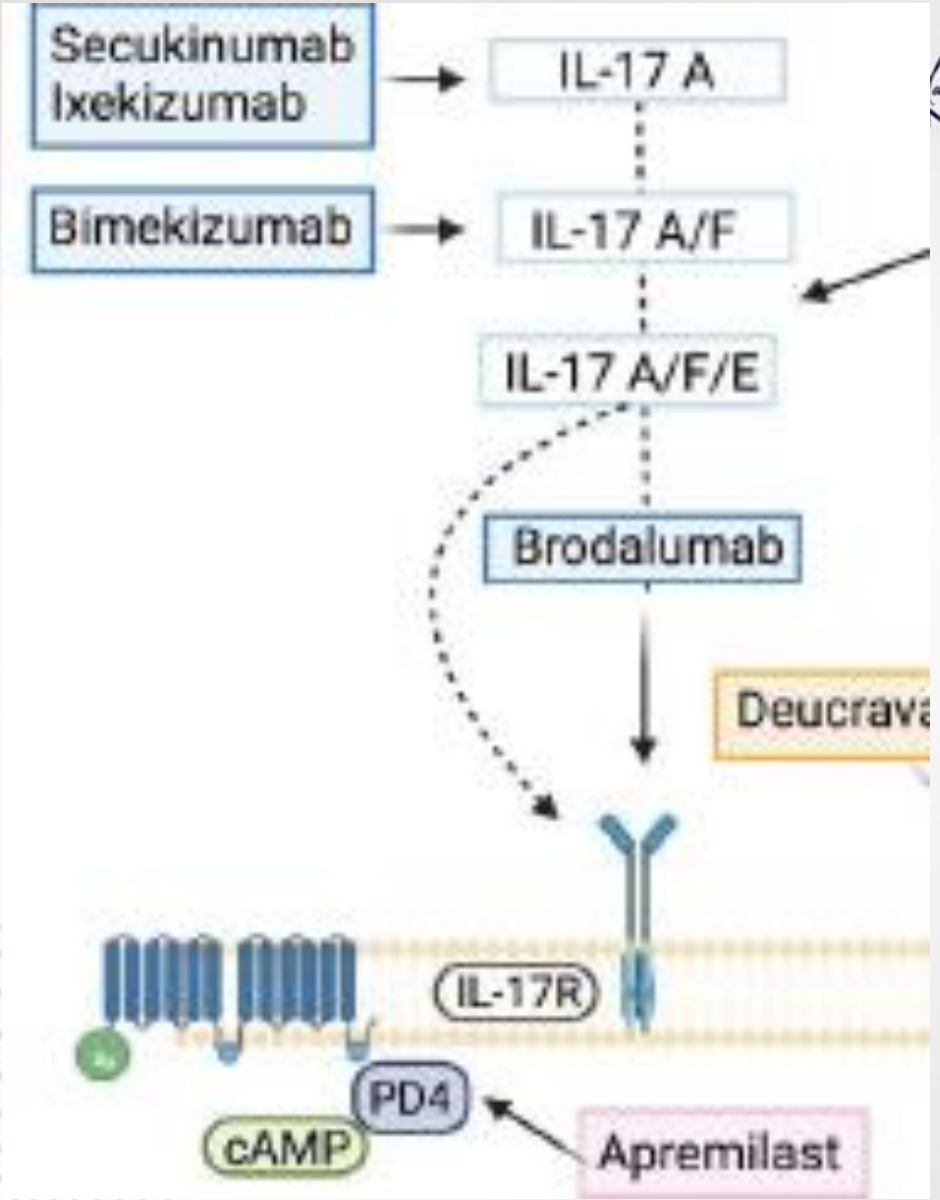
IL-17A, IL-17A/F, and IL-17R Inhibitors



[a]Binding of ixekizumab to the A/F heterodimer is included in the summary of product characteristics but not in the US prescribing information.[6,7] Binding of secukinumab to the A/F heterodimer is not included in the summary of product characteristics or the US prescribing information.[4,5] 1. Patel D, et al. *Ann Rheum Dis*. 2013;72(Suppl, 2):ii116-123. 2. Gaffen SL. *Nat Rev Immunol*. 2009;9(8):556-567. 3. Reis J, et al. *BioDrugs*. 2019;33(4):391-399. 4. Cosentyx [SmPC]. Dublin, Ireland: Novartis Europharm Limited, 2020. 5. Cosentyx [US PI]. East Hanover, NJ, USA: Novartis Pharmaceuticals Corporation, 2020 https://www.pharma.us.novartis.com/sites/www.pharma.us.novartis.com/files/cosentyx.pdf (Accessed June 30, 2022). 6. Taltz [SmPC]. Utrecht, The Netherlands: Eli Lilly Nederland B.V., 2022. 7. Taltz [US PI]. Indianapolis, IN, USA: Eli Lilly USA LLC, 2022. 8. Adams R, et al. *Front Immunol.* 2020;11:1894. 9. Schminke B, et al. *Eur J Immunol.* 2016;46:440-445. Brodalumab no ha sido aprobado por la agencia regulatoria local para Psoriasis

No todos los IL-17 son iguales

- Secukinumab IL17A IgG1
- Ixekizumab IL17A IgG4
- Brodalumab IL17 receptor
- Bimekizumab IL17A-F

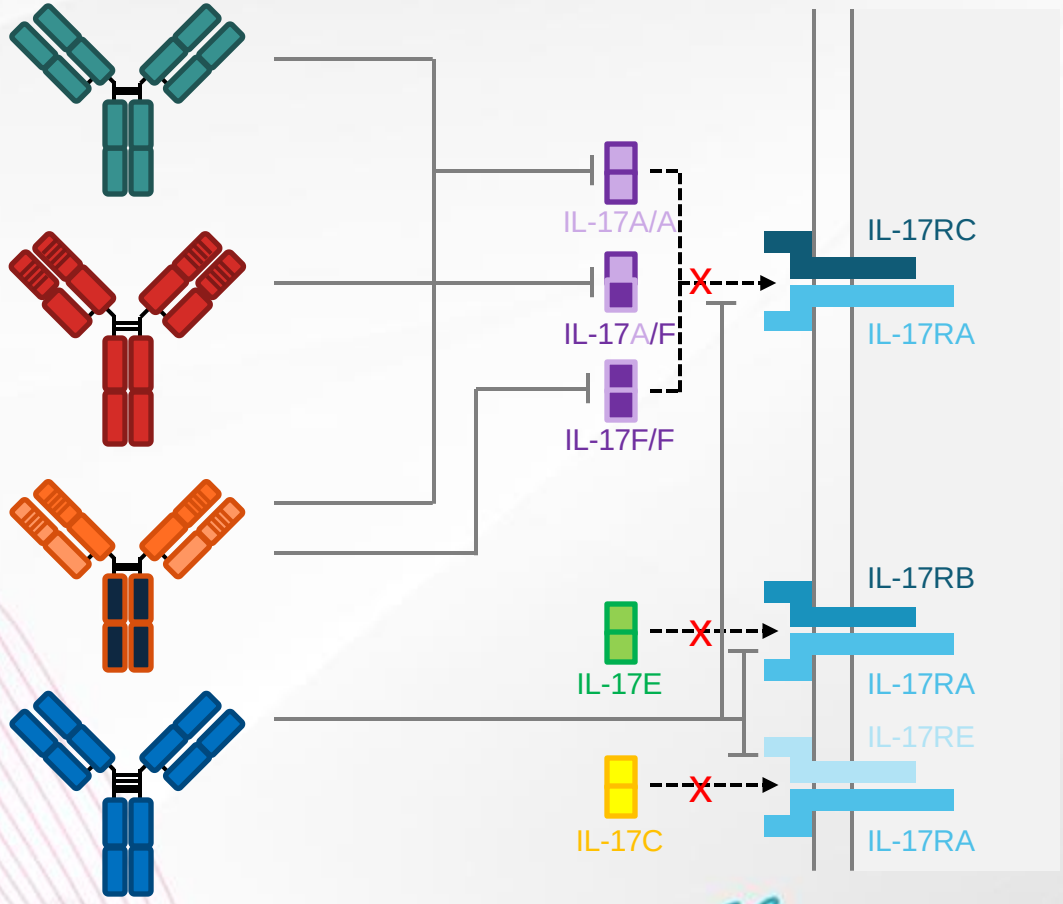


Azuaga AB, Ramírez J, Cañete JD. Psoriatic Arthritis: Pathogenesis and Targeted Therapies. Int J Mol Sci. 2023 Mar 3;24(5):4901.

Brodalumab no tiene la indicación de PsO en México

Mechanism of Action of IL-17 Inhibitors[a]

mAb	mAb type	Binding affinity (K_D)[b]	Half-life in PsO patients
Secukinumab[1,2]	Human IgG1κ	~200 pM	27 days
Ixekizumab[3,4]	Humanized IgG4	1.8 pM	13 days
Bimekizumab[5,6]	Humanized IgG1	IL-17A: 3.2 pM IL-17F: 23 pM	23 days
Brodalumab[7,8]	Human IgG2	239 pM	11 days

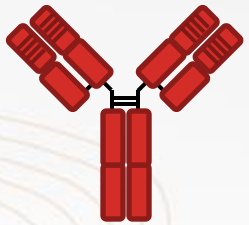


Brodalumab, Tildrakizumab y Deucravacitininb no tienen la aprobación regulatoria en México

[a]This slide reflects only the known information about the drug mechanism of action from published papers and regulatory documents and does not represent a safety or efficacy comparison; [b]Binding affinities obtained from published sources using different methodologies and cannot be directly compared. IgG=Immunoglobulin G; IL=Interleukin; K_D=Equilibrium Disassociation Constant; mAb=Monoclonal Antibody; PsO=Psoriasis.

1. Azevedo A, Torres T. *Dermatol Online J* 2018;24:13030/qt2qn1p4bz. 2. Cosentyx® [Summary of Product Characteristics 2023]. Novartis Europharm Limited. 3. Taltz® IPP-A.: 05-Oct-2022_v01. CDS-20220525 SPC. 4. Liu L, et al. J *Inflamm Res* 2016;9:39–50. 5. Adams R, et al. *Front Immunol* 2020;11:1894. 6. Bimzelx® [Summary of Product Characteristics 2023]. UCB Pharma S.A. 7. Timmermann S, Hall A. *Pharmacol* 2019;125:16–25. 8. Kyntheum® [Summary of Product Characteristics 2022]. Leo Laboratories Limited.

Ixekizumab[1]



IgG4 antibodies have a lower potential to activate complement and Fcγ receptor engagement compared with IgG1[3]

mAb type	**Humanized IgG4**
Target	IL-17A/A IL-17A/F
Binding affinity (K_D)[2]	1.8 pM
Half-life in PsO patients	13 days

Each human immunoglobulin class has specialized functions[4]

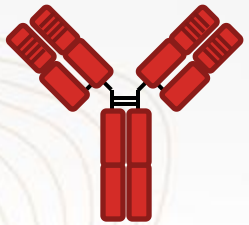
Functional Activity	IgG1	IgG2	IgG3	IgG4
Neutralization	++	++	++	++
Opsonization	++	*	++	+
Sensitization for killing by NK cells	++	-	++	-
Sensitization of mast cells	+	-	+	-
Activates complement system	++	+	+++	-

The major effector functions of each class (+++) are shaded in dark red, whereas lesser functions (++) are shown in dark pink, and very minor functions (+) in pale pink. *IgG2 can act as an opsonin in the presence of an Fc receptor of the appropriate allotype, found in about 50% of people of Caucasian descent.[4]

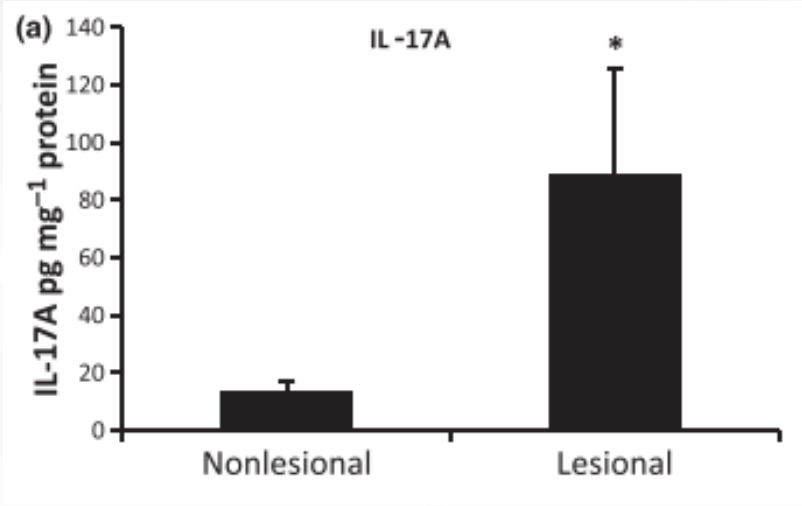
1. Taltz® IPP-A.: 05-Oct-2022_v01. CDS-20220525 SPC. 2. Liu L, et al. J Inflamm Res 2016;9:39–50. 3. Rispens & Huijbers. Nat Rev Immunol 2023 Apr 24:1–16; Epub ahead of print. 4. Adapted from "Janeways Immunobiology, 9th edition by Keneth Murphy and Casey Weaver, 2017

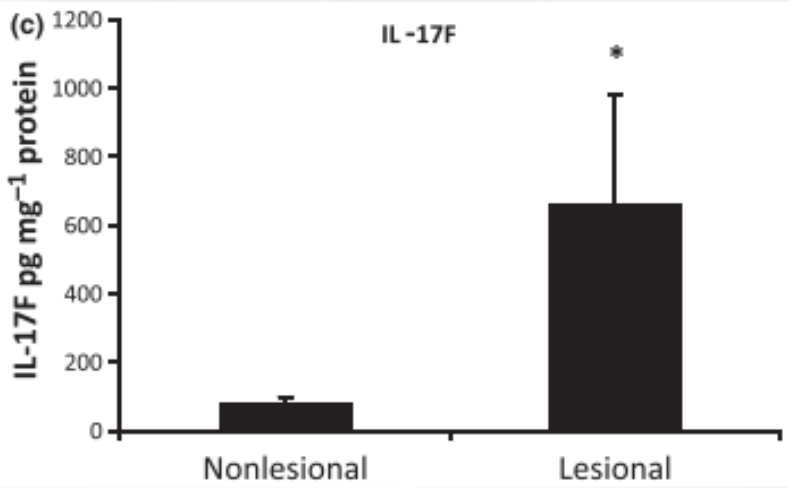
Ixekizumab[1]

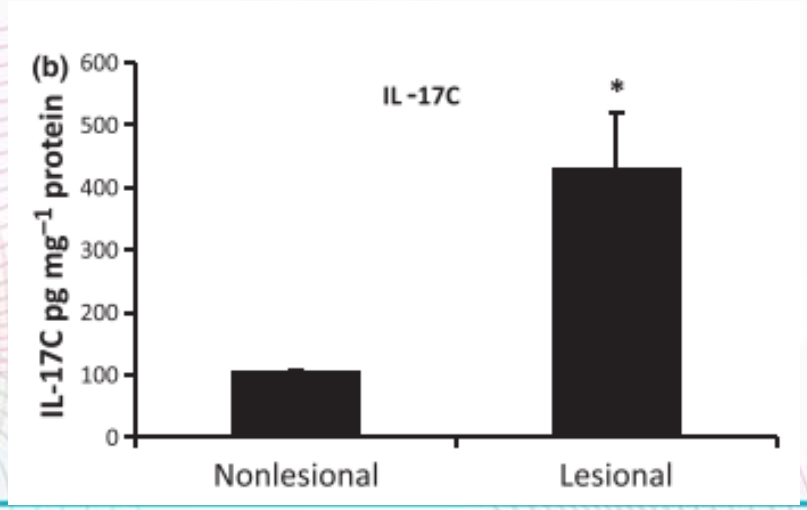
Interleukin (IL) 17-A, IL-17C, and IL-17F protein levels were increased in psoriatic skin.



mAb type	Humanized IgG4
Target	**IL-17A/A IL-17A/F**
Binding affinity (K_D)[2]	1.8 pM
Half-life in PsO patients	13 days



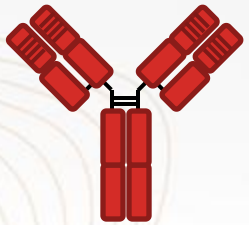




Whole call protein extracts were prepared from keratome biopsies taken from lesional and nonlesional psoriatic skin. The protein extracts were determined by ELISA. Results represent mean ± SD from five patients with psoriasis. All measurements were performed in duplicate. *p<0.05 compared with nonlesional psoriatic skin.

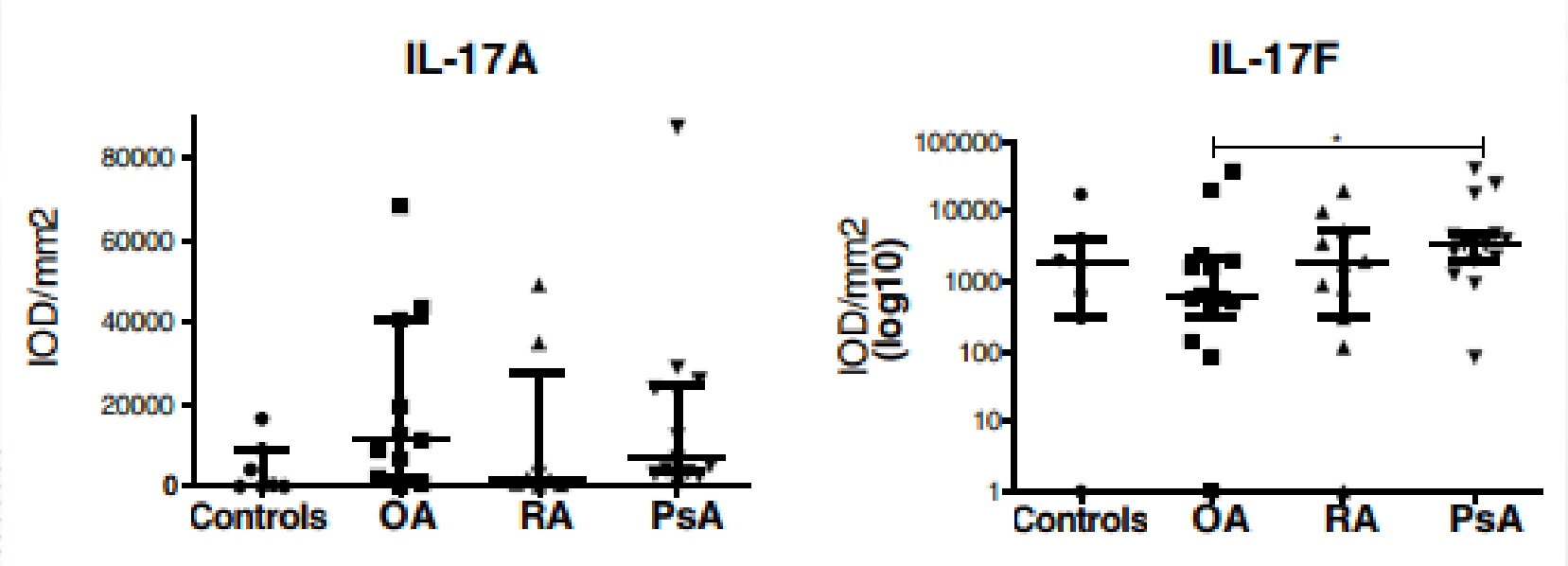
1 Taltz® IPP-A.: 05-Oct-2022_v01. CDS-20220525 SPC. 2. Liu L, et al. J Inflamm Res 2016;9:39–50. 3. Johansen C, Usher PA, Kjellerup RB, Lundsgaard D, Iversen L, Kragballe K. Characterization of the interleukin-17 isoforms and receptors in lesional psoriatic skin. Br J Dermatol. 2009 Feb;160(2):319-24. doi: 10.1111/j.1365-2133.2008.08902.x. Epub 2008 Oct 21. PMID: 19016708.

Ixekizumab[1]



mAb type	Humanized IgG4
Target	**IL-17A/A IL-17A/F**
Binding affinity (K_D)[2]	1.8 pM
Half-life in PsO patients	13 days

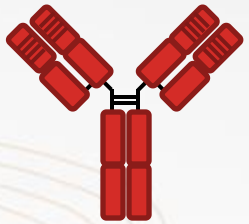
Expression of interleukins 17A and 17F in synovial tissue[3]



The expression of interleukin 17A (IL-17A), IL-17F, IL-17RA and IL-17RC in rheumatoid arthritis (RA), osteoarthritis (OA), psoriatic arthritis (PsA) and noninflamed synovial tissue was determined by immunohistochemistry using monoclonal antibodies. The intensity of staining was analysed using digital image analysis, and levels were compared between the noninflammatory and arthritis groups using a Mann-Whitney U test (B) and between OA, PsA and RA patients using a Kruskal-Wallis test with post hoc Dunn's multiple-comparisons tests (C). *P < 0.05. IOD, Integrated optical density

1. Taltz® IPP-A.: 05-Oct-2022_v01. CDS-20220525 SPC. 2. Liu L, et al. J Inflamm Res 2016;9:39–50. 3. van Baarsen, L.G., Lebre, M.C., van der Coelen, D. et al. Heterogeneous expression pattern of interleukin 17A (IL-17A), IL-17F and their receptors in synovium of rheumatoid arthritis, psoriatic arthritis and osteoarthritis: possible explanation for nonresponse to anti-IL-17 therapy?. Arthritis Res Ther 16, 426 (2014).

Ixekizumab[1]



mAb type	Humanized IgG4
Target	IL-17A/A IL-17A/F
Binding affinity (K_D)[2]	**1.8 pM**
Half-life in PsO patients	13 days

Binding affinities of secukinumab, ixekizumab and 496.g3 (bimekizumab) for human IL-17A, IL-17A/F, and IL-17F[3]

Cytokine	Secukinumab	Ixekizumab	469.g3 (Bimekizumab)
IL-17A	129†	1.8*	3.2†
IL-17A/F	2400**	1.8*	26†^
IL-17F	NB†	NB*	23†

Internal† and published*,** binding affinities (pM) of 496.g3 (Bimekizumab), secukinumab and ixekizumab for IL-17A, IL-17A/F, and IL-17F were generated by SPR. ^The kinetic parameters for binding to IL-17A/F are ka = 3.19E+06, kd = 8.17E-05 and KD = 2.56E-11. NB, no binding

1. Taltz® IPP-A.: 05-Oct-2022_v01. CDS-20220525 SPC 2. Liu L, et al. J Inflamm Res 2016;9:39–50. 3. Adams R, Maroof A, Baker T, et al. Bimekizumab, a Novel Humanized IgG1 Antibody That Neutralizes Both IL-17A and IL-17F. Front Immunol. 2020;11:1894.

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Caso clínico

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El caso Clínico pertenece a un paciente real y no presenta eventos adversos o quejas de calidad relacionadas a productos Lilly.

CASO CLÍNICO

- Hombre de 32 años
- APP: Negó enfermedades crónicas
- PA:
- Inicia con su dermatosis en 2012, con lesiones eritemato-escamosas en piel cabelluda.
- Posteriormente se disemina al tronco, predominio en región lumbar. Refiere fluctuaciones en la severidad asociadas a estrés
- Tratamiento en medio privado con emolientes
- En 2017 acude a servicio de Dermatogía de HGR Venados, con exacerabación. Inicia en este momento manejo con Ciclosporina 300 mg/día
- Suspende seguimiento y tratamiento debido a pandemia COVID-19.

LABORATORIO

- Hb: 19 g/dl, 48.9%, Plaquetas: 372 000, Leucocitos: 8,300,
- Glucosa: 90.5 mg/dl, Urea: 29.1 mg/dl, Creatinina: 0.81 mg/dl.
- FA: 116 U/L; TGO: 35.3 U/L, TGP: 52 U/L, DHL: 210 U/L; Acido úrico: 9.4 U/L,
- EGO: sin alteraciones.
- Panel viral no reactivo.
- Rx tórax: Datos de neumopatía restrictiva.
- Urocultivo: BLEE positivo..

¿QUÉ TRATAMIENTO RECOMENDARÍA?

- Ciclosporina
- Metotrexate SC
- bDMARDs (anti-TNF)
- bDMARDs (anti-IL 17)
- bDMARDS (anti-IL 23)

ELECCIÓN DE TRATAMIENTO

bDMARDs anti-IL 17: Secukinumab

Justificación

Psoriasis moderada a severa

Afección a zonas visibles

Necesidad de respuesta rápida

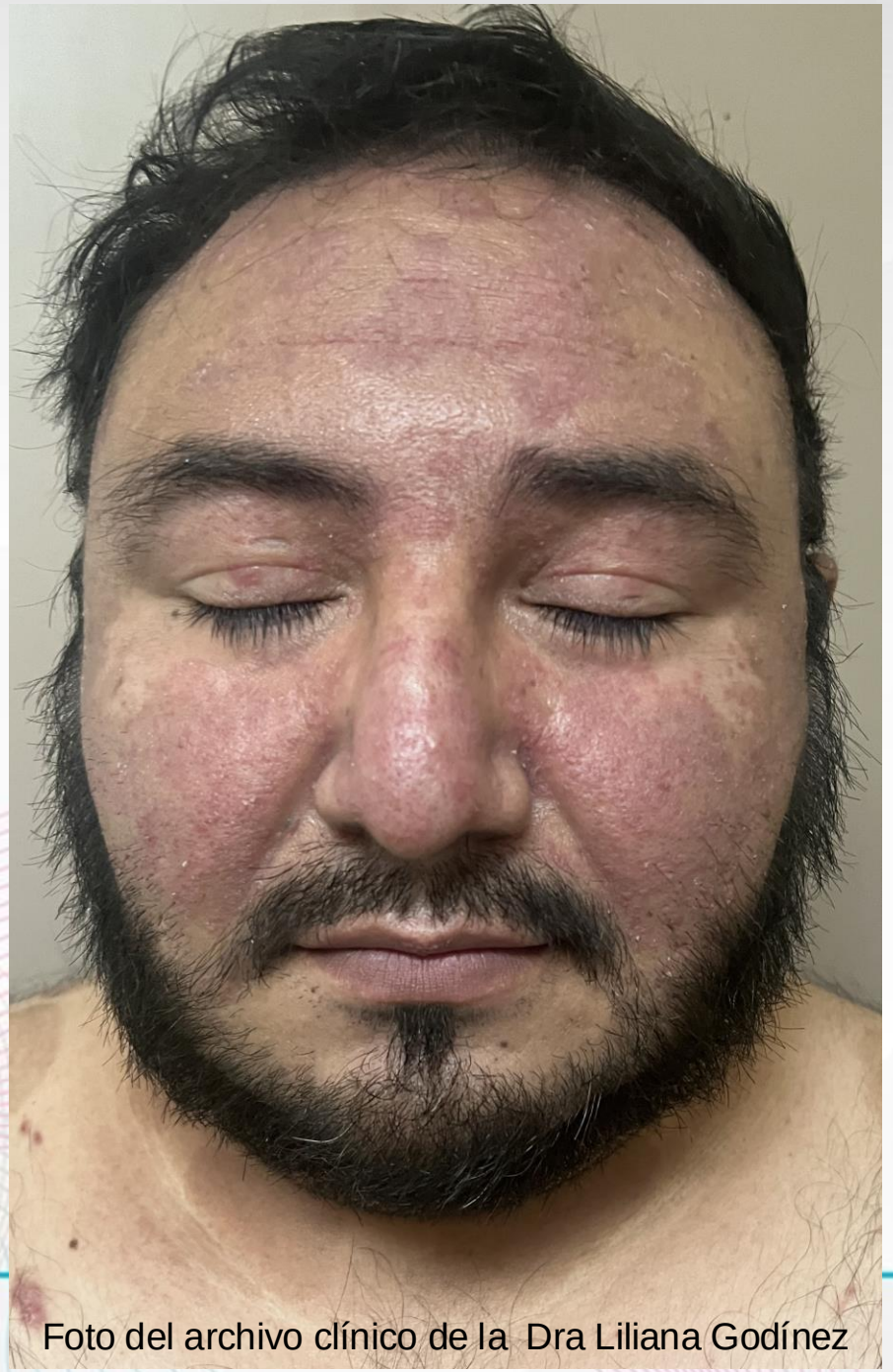

Foto del archivo clínico de la Dra Liliana Godínez

PASI 75 a las 5 semanas

- BSA <10%
- PASI: 5.5 pts
- DLQI: 2 pts

SEGUIMIENTO

- A las 16 semanas presenta recaída de la dermatosis con reactivación de las placas previas, y enrojemiento facial importante.
- Manejo: Se continua con secukinumab 300 mg/mensual + Ciclosporina 100 mg/día

- A las 24 semanas:
  - Persiste con actividad de la dermatosis a pesar de manejo combinado
  - Desarrolla efectos adversos asociados a uso de CyA (descontrol hipertensivo y cefalea)

SEGUIMIENTO

- Falla secundaria a uso de Secukinumab (PASI 75) + Uso de terapia combinada con CyA para mantener respuesta
- Se decide cambio de terapia a Ixekizumab
  - Dosis de impregnación 160 mg (plumas prellenadas) SC a las semanas 0, seguidos por 80 mg SC (1 pluma) en las semanas 2,4,6, 8, 10 y 12.
  - Dosis de mantenimiento: 80 mg SC (1 pluma) SC cada 4 semanas.

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¡GRACIAS!

Consulte la IPP de Taltz