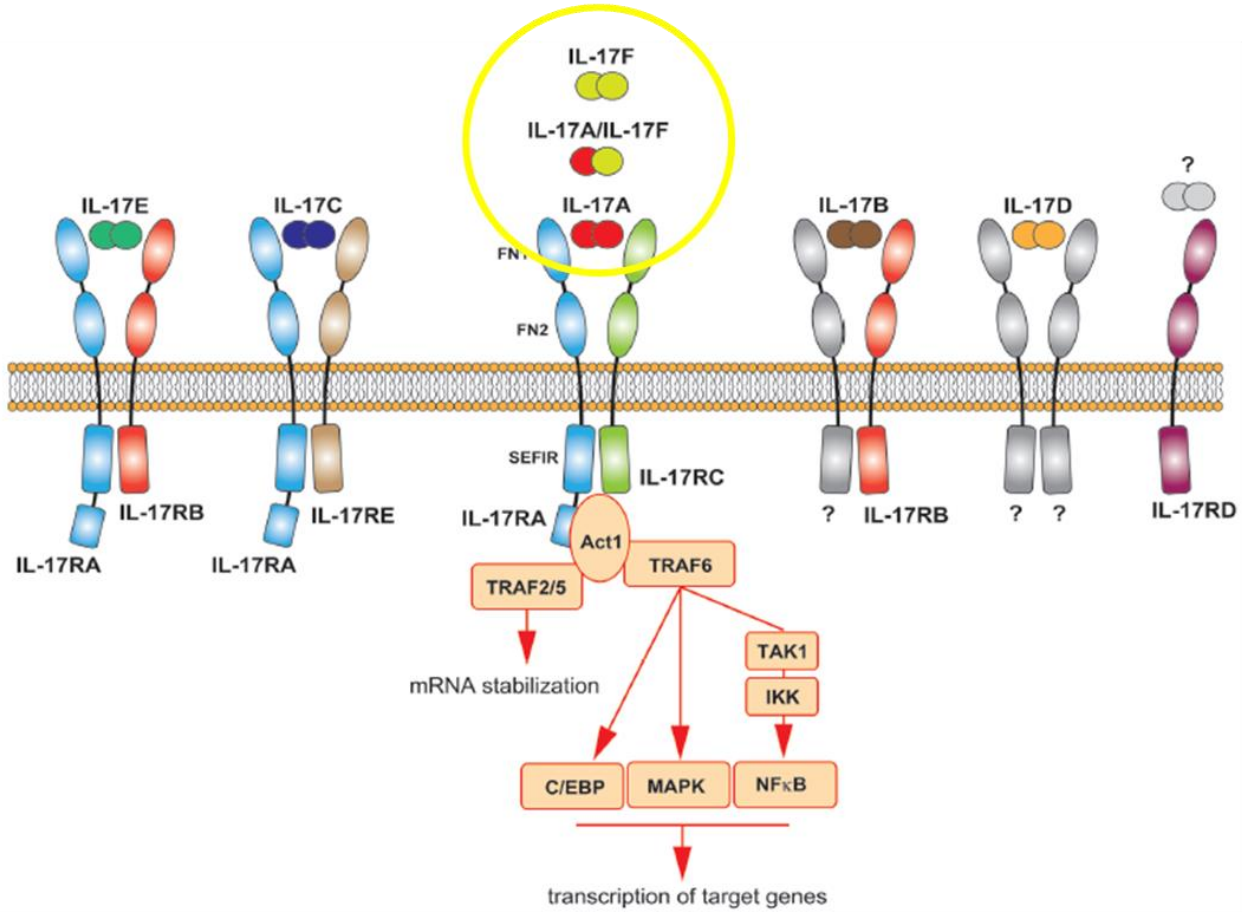
SCUOLA DERMATOLOGICA
SERGIO CHIMENTI
Roma, 1-2 Dicembre 2023 YES or NO CONTEST 3° INCONTRO
Dermatology Update

Giacomo Caldarola

Gli inibitori delle IL-17 (Secukinumab, Ixekizumab, Bimekizumab) e del loro recettore (Brodalumab)

The IL-17 family of cytokines[1]



SEFIR: IL-17Rs are categorized by a conserved cytoplasmic motif known as the 'similar expression of fibroblast growth factor and IL-17 receptor' or SEFIR domain, which is similar in structure to the Toll/interleukin-1 receptor (TIR) domain found in Toll-like receptors (TLRs) and IL-1 receptors

In the early 2000s, genomic sequencing led to the identification of several proteins structurally related to IL-17A or IL-17 or CTLA-8 (6 isoforms):

- IL-17B
- IL-17C
- IL-17D
- IL-17E (also called IL-25)
- IL-17F

Together, these cytokines are known as the IL-17 family.

IL-17F shares the highest homology with IL-17A (55%) and is often co-expressed with IL-17A.

Homodimers or heterodimers of IL-17A and IL-17F bind to a receptor composed of the RA and RC subunits, albeit with differing affinities.

IL-17RA and IL-17RC interact, via **SEFIR domains**, with the ***adaptor protein* Act1,** which contains two tumour necrosis factor (TNF) receptor-associated factor (TRAF)-binding motifs.

The pathway involving **TRAF6** leads to activation of the canonical *nuclear factor-kB (NF-kB)* and *mitogen activated protein kinase (MAPK)* pathways, and the *CCAAT/enhancer binding protein (C/EBP) transcription factors* resulting in pro-inflammatory gene expression.

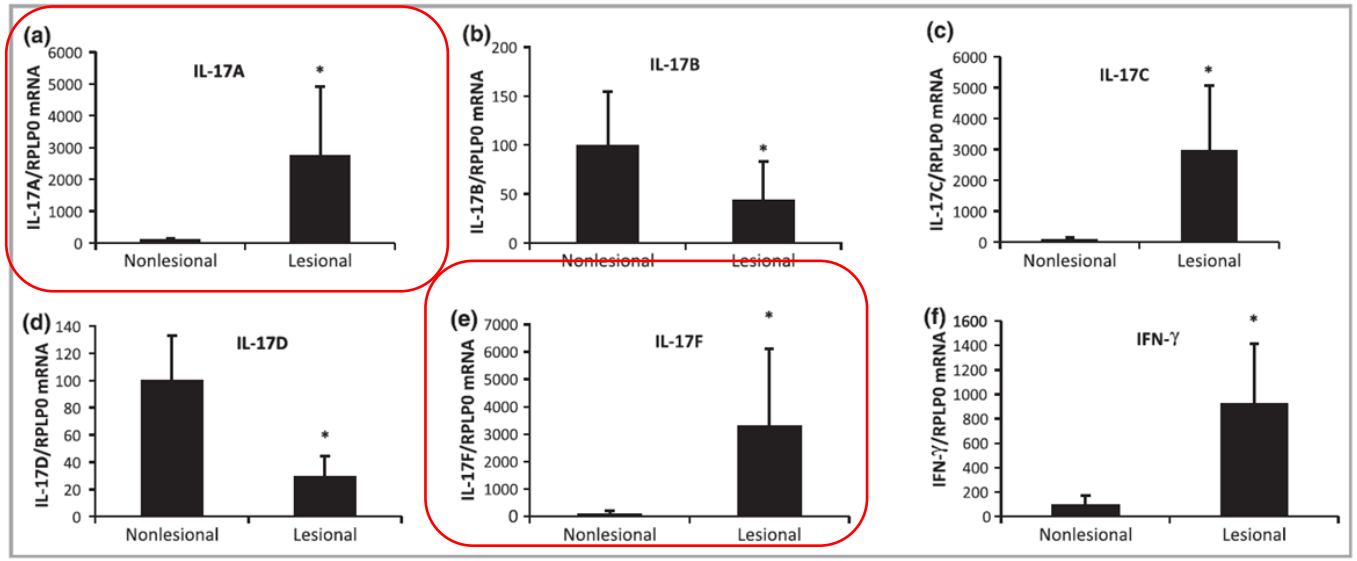
A TRAF6-independent, **TRAF2/5** signalling complex associated with IL-17Rs has also been identified that results in enhanced mRNA stability for the chemokine CXCL1.

Disruption of the relative balance of these two signalling pathways has been hypothesized to underlie autoimmune pathogenesis in certain cases.

1.Brembilla NC, et al., Front Immunol. 2018 Aug 2;9:1682; 2. Wang X, et al. Immunity 2012; 36: 23–31

IL-17 cytokines do not signal through the JAK–STAT pathway like signature TH1 or TH2 cytokines in the adaptive immune system.

mRNA expression profile of the interleukin-17 family members in psoriatic skin

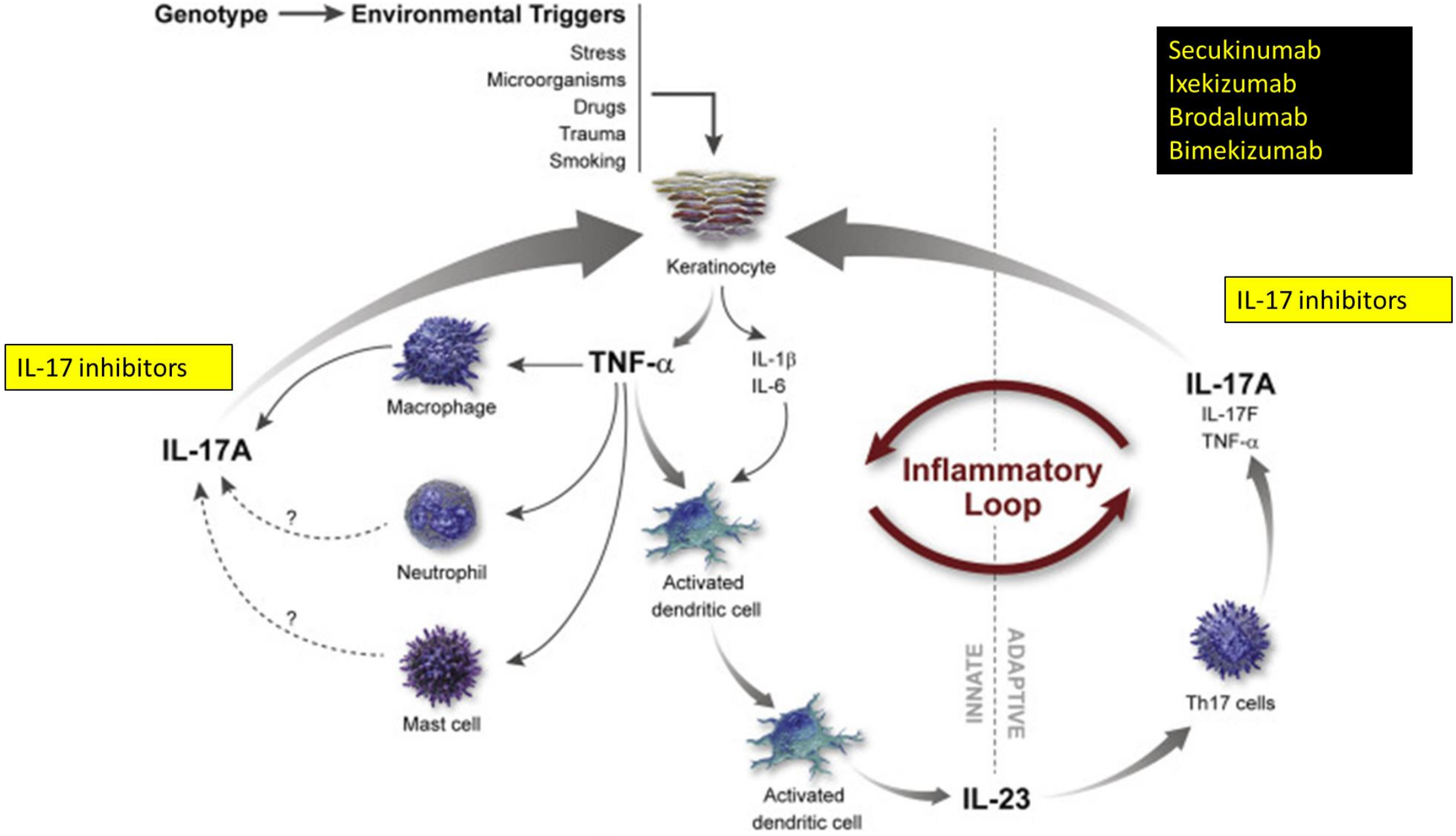


To investigate the mRNA expression profile of the IL-17 family members in psoriatic skin, RNA from punch **biopsies obtained from lesional and nonlesional psoriatic skin from 9 patients with PsO** was isolated and analysed by quantitative RT-PCR.

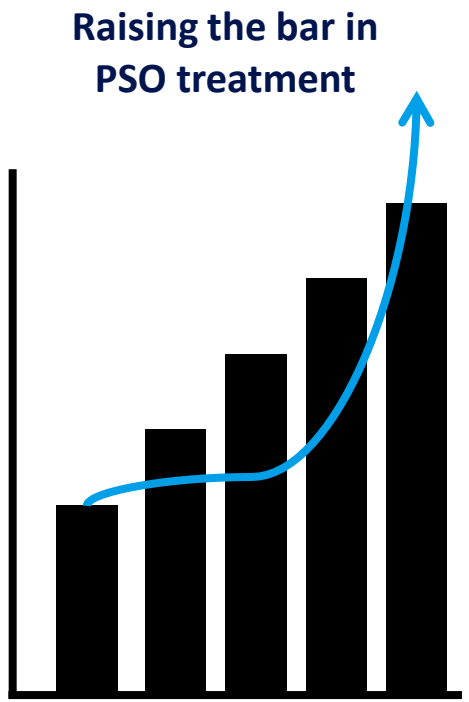
*P < 0.01compared with nonlesional psoriatic skin.

- ↑ in the **mRNA expression of IL-17A and IL-17F in psoriatic skin** of approximately **28-fold and 33-fold**, respectively, compared with nonlesional psoriatic skin.
- mRNA expression of **IL-17C** significantly ↑ in psoriatic skin (P = 0.0036) with a mean increase in the mRNA expression of approximately 30-fold compared with nonlesional psoriatic skin.
- In contrast, the mRNA expression of **IL-17B and IL-17D** significantly ↓ in psoriatic skin lesions (P = 0.0095 and P = 0.0003, respectively), with a mean decrease of approximately 2.3-fold and 3.4-fold, respectively.
- mRNA expression of **IFN-γ**, a Th1-derived cytokine known to be upregulated in psoriasis, significantly ↑ (P = 0.001) in psoriatic skin with a 9-fold induction compared with nonlesional psoriatic skin.

Johansen C, et al., Br J Dermatol 2009



Cambio di rotta

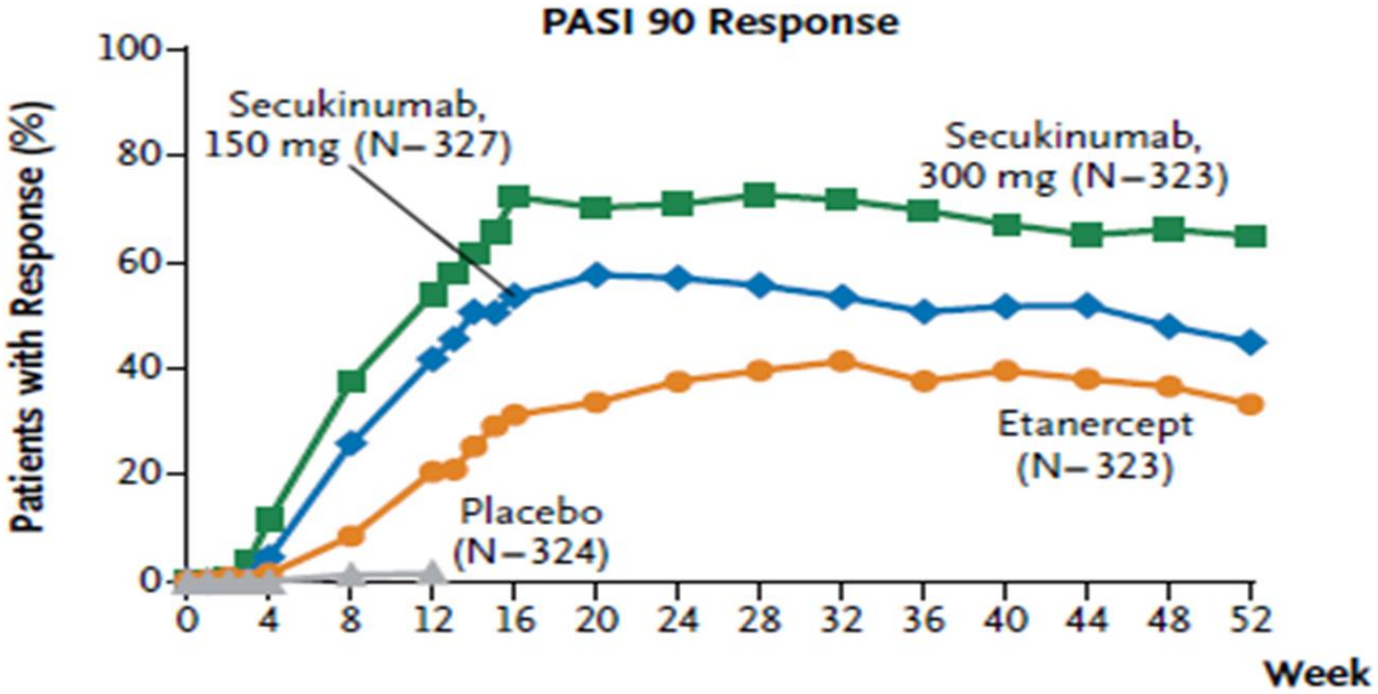


The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Secukinumab in Plaque Psoriasis — Results of Two Phase 3 Trials

Richard G. Langley, M.D., Boni E. Elewski, M.D., Mark Lebwohl, M.D., Kristian Reich, M.D., Ph.D., Christopher E.M. Griffiths, M.D., Kim Papp, M.D., Ph.D., Lluís Puig, M.D., Ph.D., Hidemi Nakagawa, M.D., Ph.D., Lynda Spelman, M.B., B.S., Bárður Sigurgeirsson, M.D., Ph.D., Enrique Rivas, M.D., Tsen-Fang Tsai, M.D., Norman Wasel, M.D., Stephen Tyring, M.D., Ph.D., Thomas Salko, B.A., Isabelle Hampele, Ph.D., Marianne Notter, M.S., Alexander Karpov, Ph.D., Silvia Helou, M.D., Ph.D., and Charis Papavassilis, M.D., Ph.D., for the ERASURE and FIXTURE Study Groups*



Comparison of ixekizumab with etanercept or placebo in moderate-to-severe psoriasis (UNCOVER-2 and UNCOVER-3): results from two phase 3 randomised trials

*Christopher E M Griffiths, Kristian Reich, Mark Lebwohl, Peter van de Kerkhof, Carle Paul, Alan Menter, Gregory S Cameron, Janelle Erickson, Lu Zhang, Roberta J Secrest, Susan Ball, Daniel K Braun, Olawale O Osuntokun, Michael P Heffernan, Brian J Nickoloff, Kim Papp, for the UNCOVER-2 and UNCOVER-3 investigators**

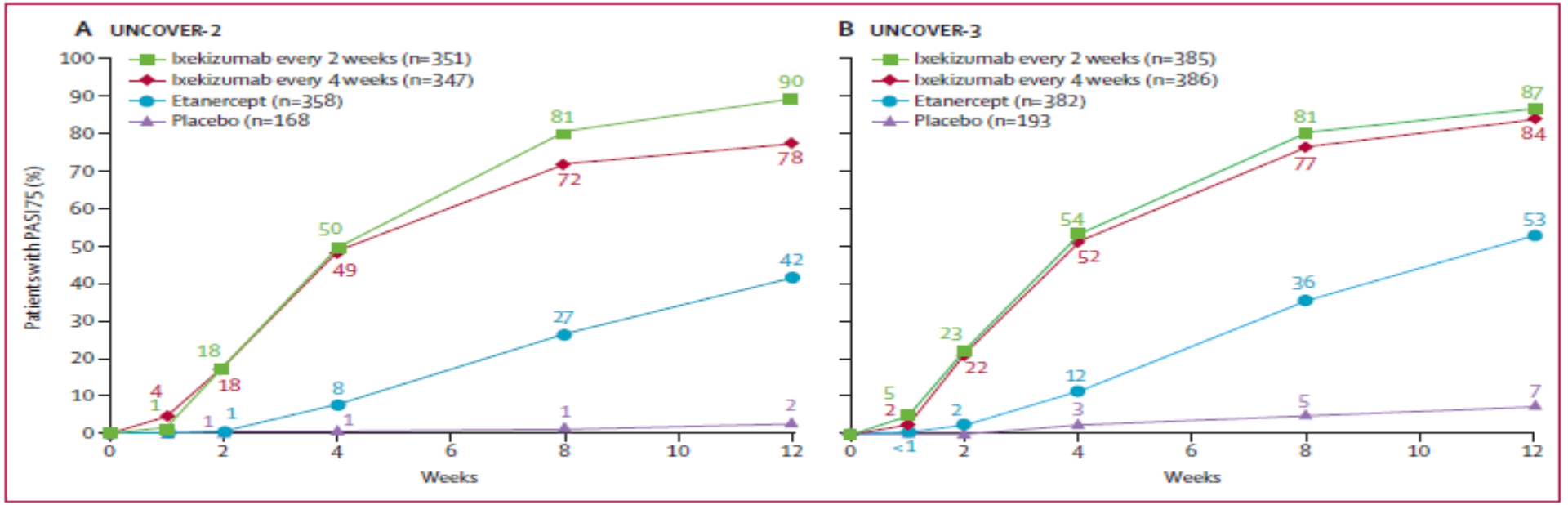


Figure 2: **Proportion of patients achieving PASI 75 from baseline through to week 12 in UNCOVER-2 (A) and UNCOVER-3 (B)**
Percentages for each timepoint are colour coded by treatment group, except for 0 values which are not labelled. PASI=psoriasis area and severity index score.

ORIGINAL ARTICLE

Phase 3 Studies Comparing Brodalumab with Ustekinumab in Psoriasis

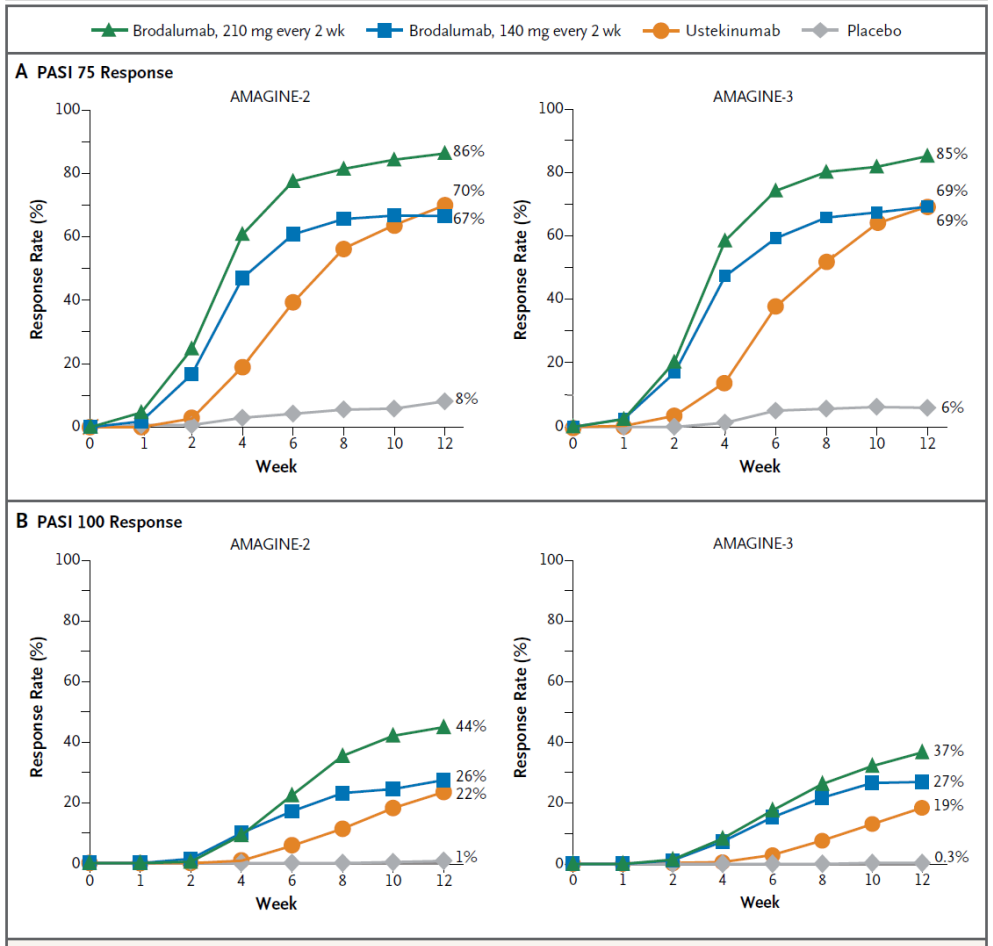
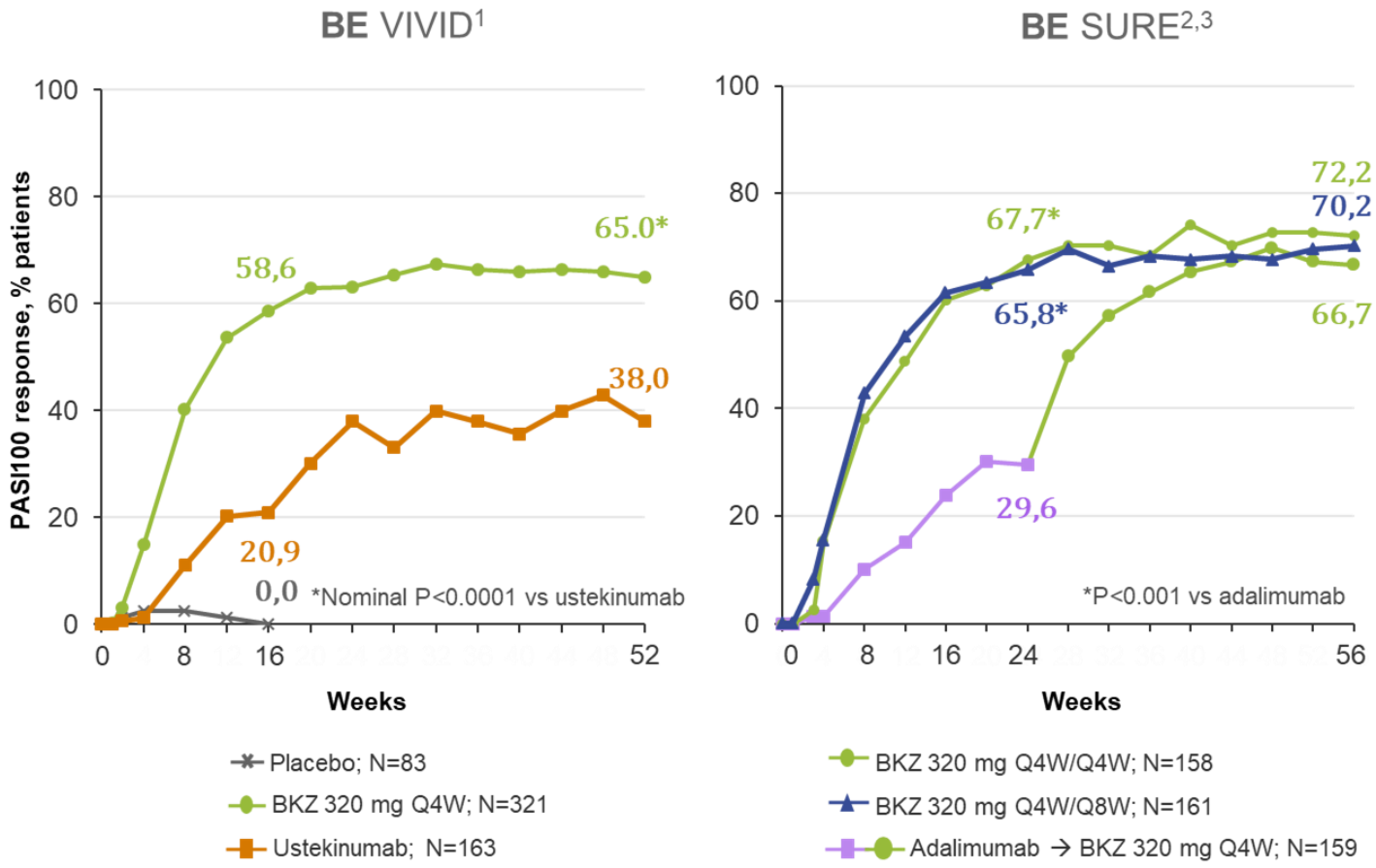


Figure 1. PASI 75 and PASI 100 Response Rates over Time.

Shown are the proportions of patients in each treatment group who had reductions in the psoriasis area-and-severity index (PASI) score of 75% or more (PASI 75) or of 100% (PASI 100) from baseline through the 12-week induction phase in the AMAGINE-2 and AMAGINE-3 studies. PASI scores range from 0 to 72, with higher scores indicating more severe disease. Missing values were imputed as indicating a lack of response.

BKZ demonstrated durable efficacy PASI100 during Year 1 with BKZ vs active comparators (NRI)



In BE SURE, PASI100 at Week 24 was a ranked secondary endpoint. In BE RADIANT, PASI100 at Week 48, was a ranked secondary endpoint. In BE SURE, patients in the BKZ Q4W/Q8W arm switched at Week 16 from Q4W to BKZ Q8W, and patients in the Adalimumab → BKZ Q4W arm switched at Week 24 from adalimumab to BKZ Q4W. †These data are taken from the maintenance set. All figures adapted from the cited reference(s). 1. Reich et al. Lancet 2021;397:487–98. 2. Warren et al. N Engl J Med 2021;385:130–41. 3. Warren et al. Presented at EADV 2020. 4. Reich et al. N Engl J Med 2021;385:142–52. 5. PS0015. Table 6.3.1.9.

European S3-Guidelines on the systemic treatment of psoriasis vulgaris

Supported by the EDF/EADV/IPC

D Pathirana, AD Ormerod, P Saiag, C Smith, PI Spuls, A Nast, J Barker, JD Bos, G-R Burmester, S Chimenti, L Dubertret, B Eberlein, R Erdmann, J Ferguson, G Girolomoni, P Gisondi, A Giunta, C Griffiths, H Hönigsmann, M Hussain, R Jobling, S-L Karvonen, L Kemeny, I Kopp, C Leonardi, M Maccarone, A Menter, U Mrowietz, L Naldi, T Nijsten, J-P Ortonne, H-D Orzechowski, T Rantanen, K Reich, N Reytan, H Richards, HB Thio, P van de Kerkhof, B Rzany*

Table 1 Proposal for treatment goals in psoriasis (adapted from [18])

	Skin symptoms	HRQoL
Treatment goals (assessment after 10 to 16 weeks, and every 8 weeks thereafter)	PASI 75 or, alternatively, PGA of 'clear' or 'almost clear'	DLQI of 0 or 1
Minimum efficiency; 'lowest hurdle'	PASI 50	DLQI < 5 or, alternatively, DLQI improvement of at least 5 points

Italian guidelines on the systemic treatments of moderate-to-severe plaque psoriasis

P. Gisondi,[1,*] G. Altomare,[2] F. Ayala,[3] F. Bardazzi,[4] L. Bianchi,[5] A. Chiricozzi,[6] A. Costanzo,[7] A. Conti,[8] P. Dapavo,[9] C. De Simone,[10] C. Foti,[11] L. Naldi,[12] A. Offidani,[13] A. Parodi,[14] S. Piaserico,[15] F. Prignano,[16] F. Rongioletti,[17] L. Stingeni,[18] M. Talamonti,[5] G. Girolomoni[1]

Table 2 Treatment goals in moderate-to-severe psoriasis

- Treatment goals should be agreed with the patient based on informed discussion
- PASI75
- PASI90
- There is a need to define the minimum absolute PASI (i.e. <1 or 2)
- DLQI < 5

doi: 10.1111/j.1346-8138.2011.01459.x

ORIGINAL ARTICLE

Dramatic impact of a Psoriasis Area and Severity Index 90 response on the quality of life in patients with psoriasis: An analysis of Japanese clinical trials of infliximab

Hideshi TORII,[1] Noriko SATO,[2] Toru YOSHINARI,[2] Hidemi NAKAGAWA,[3] The Japanese Infliximab Study Investigators*

[1]*Division of Dermatology, Social Insurance Central General Hospital Tokyo,* [3]*Department of Dermatology, The Jikei University School of Medicine, Tokyo, and* [2]*Mitsubishi Tanabe Pharma, Osaka, Japan*

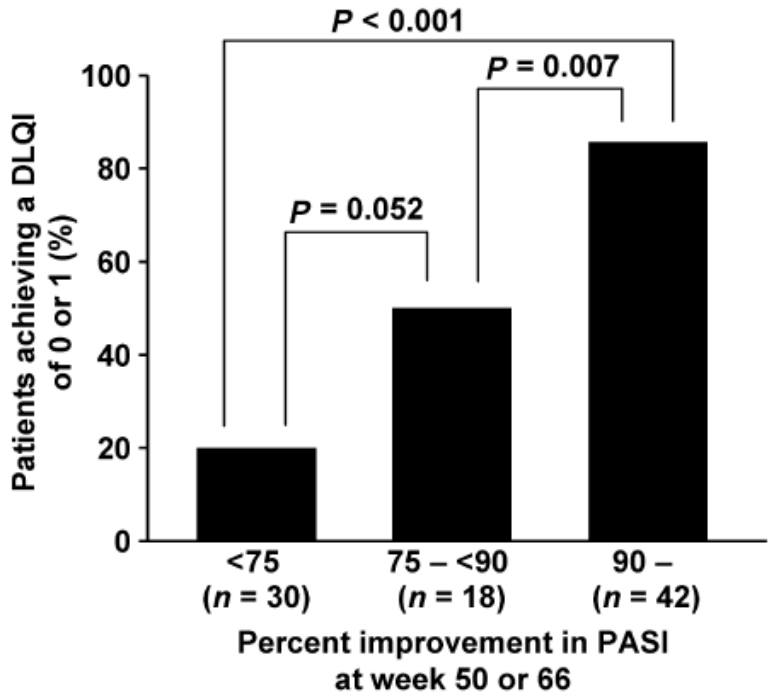


Figure 5. Percentage of patients achieving a Dermatology Life Quality Index (DLQI) of 0 or 1 according to percent improvement in Psoriasis Area and Severity Index (PASI) at the complete assessment (week 50 or 66).

Storia clinica

- Marcello, 68 anni
- Psoriasi volgare da circa 30 anni
- BMI: 30
- Fumatore di 20 sigarette/die da circa 40 anni

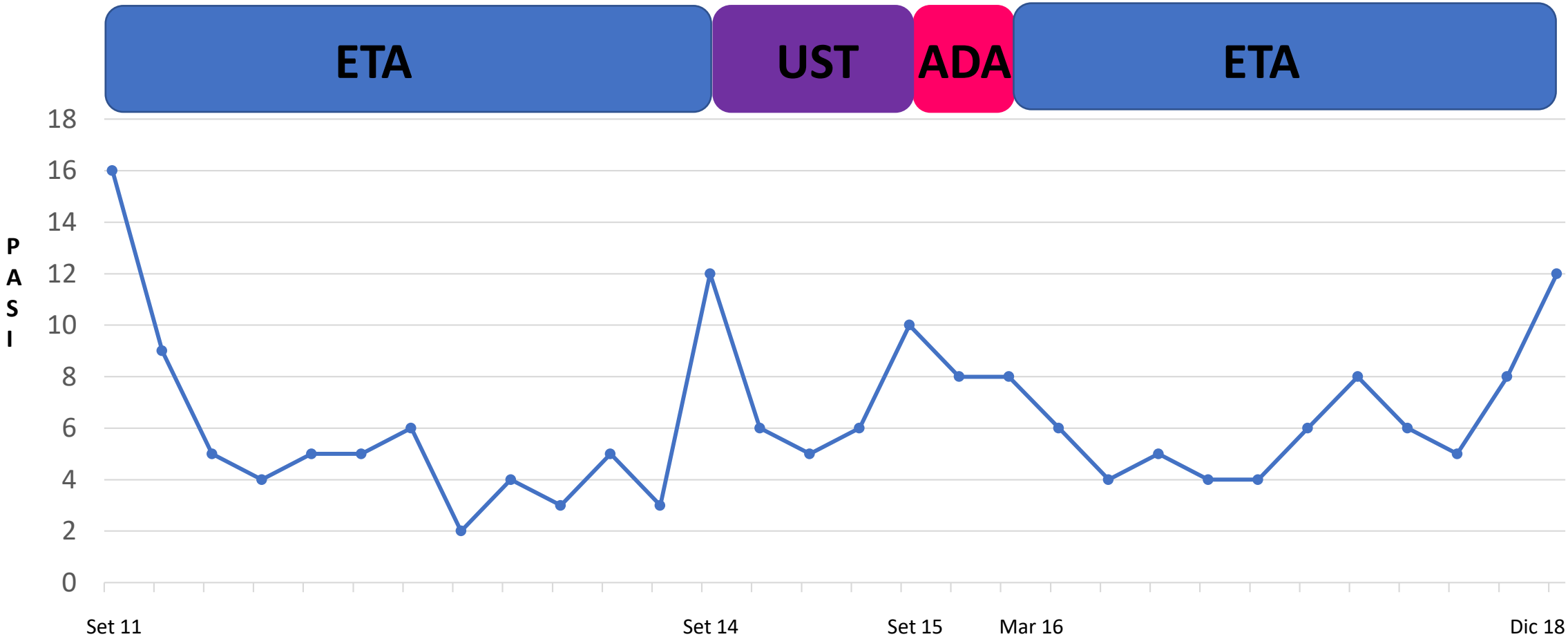
Storia clinica

- **Disturbo bipolare,** in terapia con risperidone, litio, acido valproico, carbamazepina, quetiapina, clonazepam
- **Dislipidemia,** in terapia con atorvastatina
- **Ipertensione arteriosa,** in terapia con amlodipina, ramipril, acido acetilsalicilico 100 mg
- **Diabete di tipo 2,** in terapia con metformina
- **Ipotiroidismo,** in terapia con levotiroxina

- Pregressa emorragia cerebrale per dissecazione aneurisma cerebrale (nel 1999)

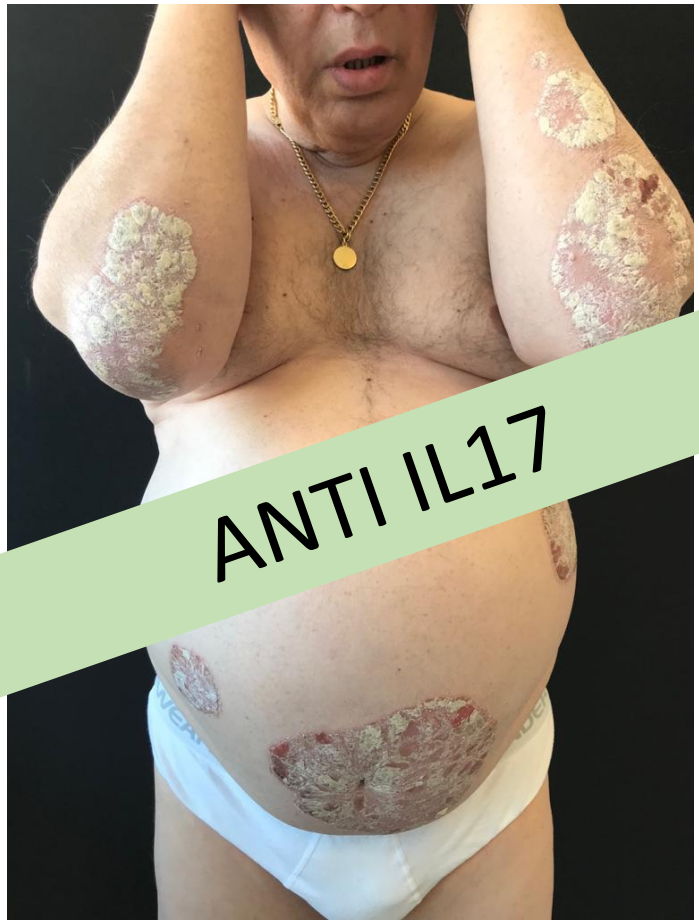
- TIA nel 2004

Storia clinica



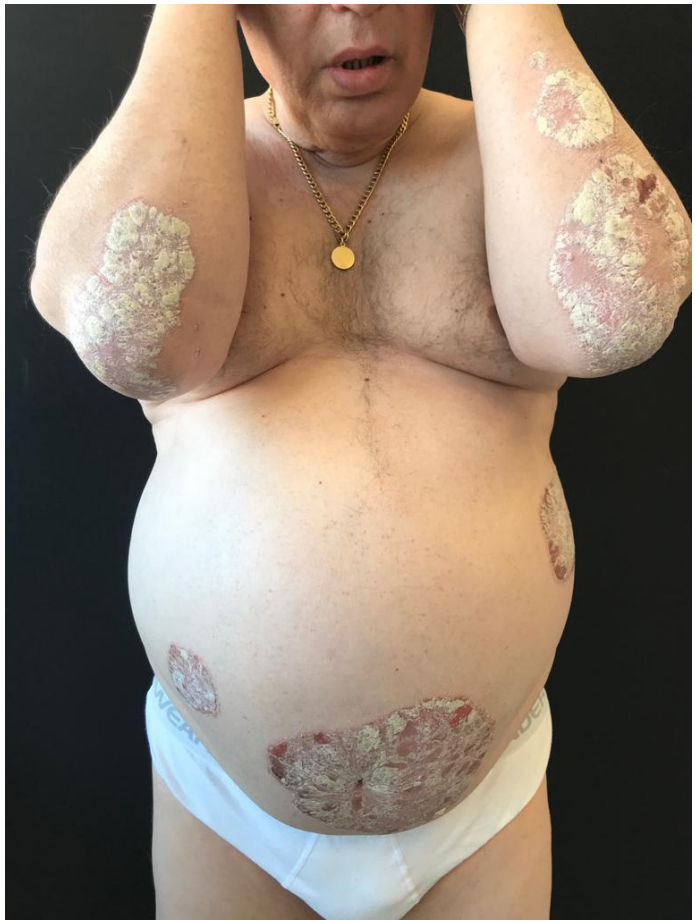
Caso 1 – Marcello

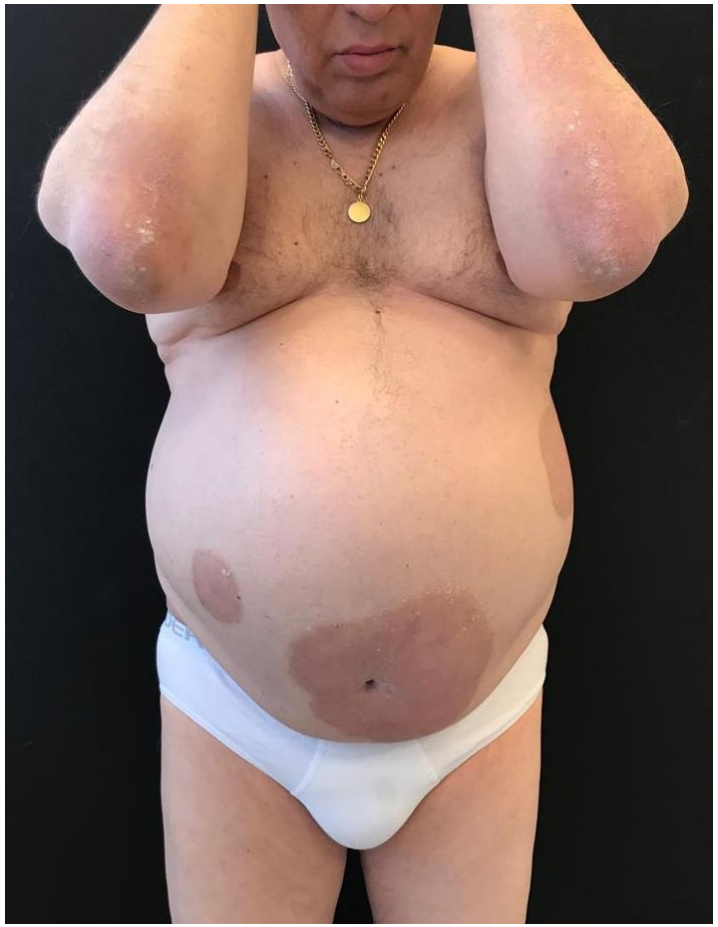
Week 0
PASI: 25
DLQI: 16



Caso 1 – Marcello

Week 0
PASI: 25
DLQI: 16

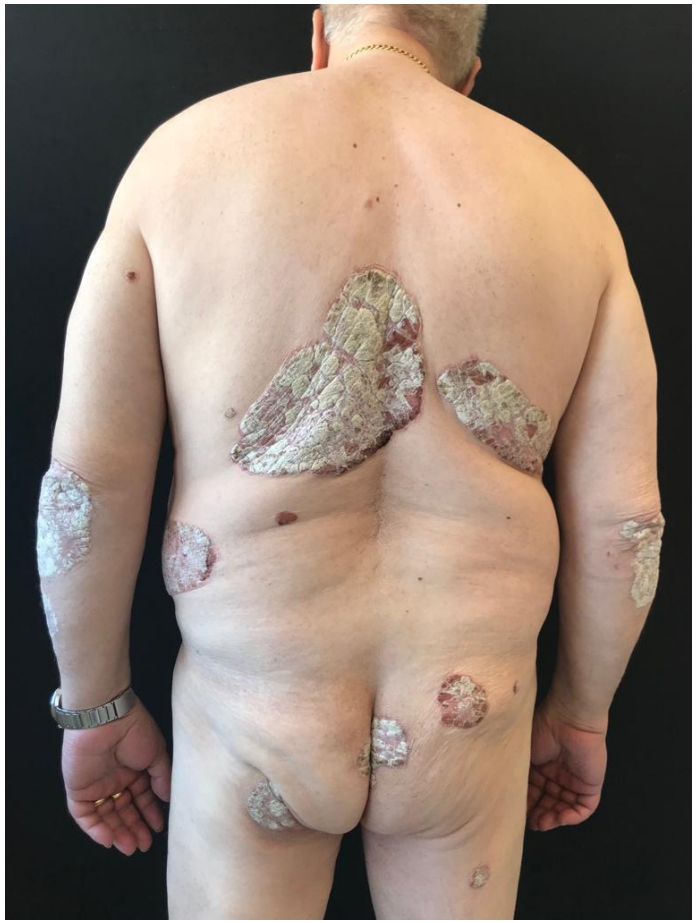




Week 4
PASI: 2
DLQI: 5

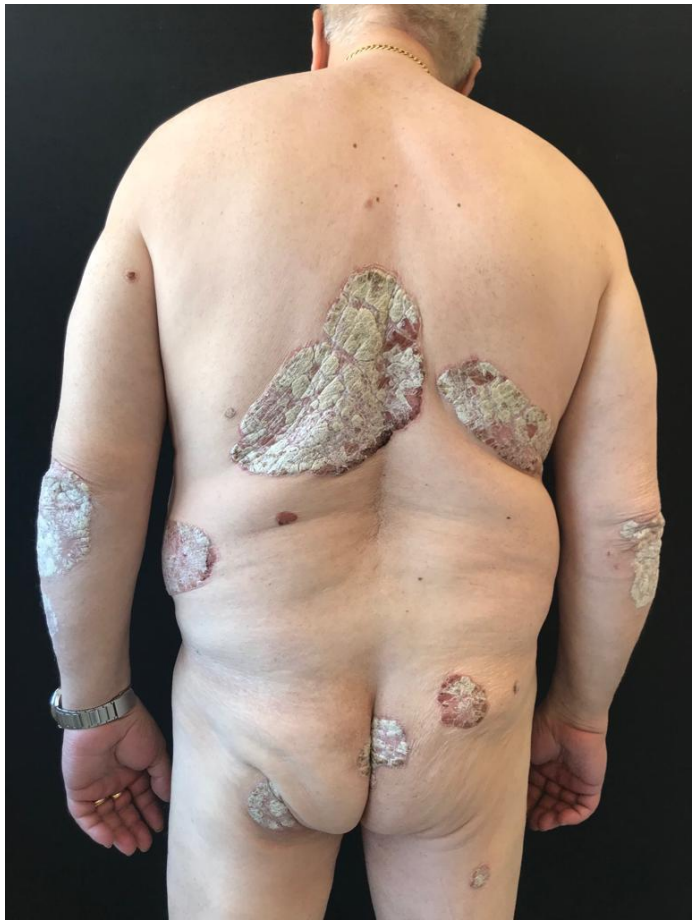
Caso 1 – Marcello

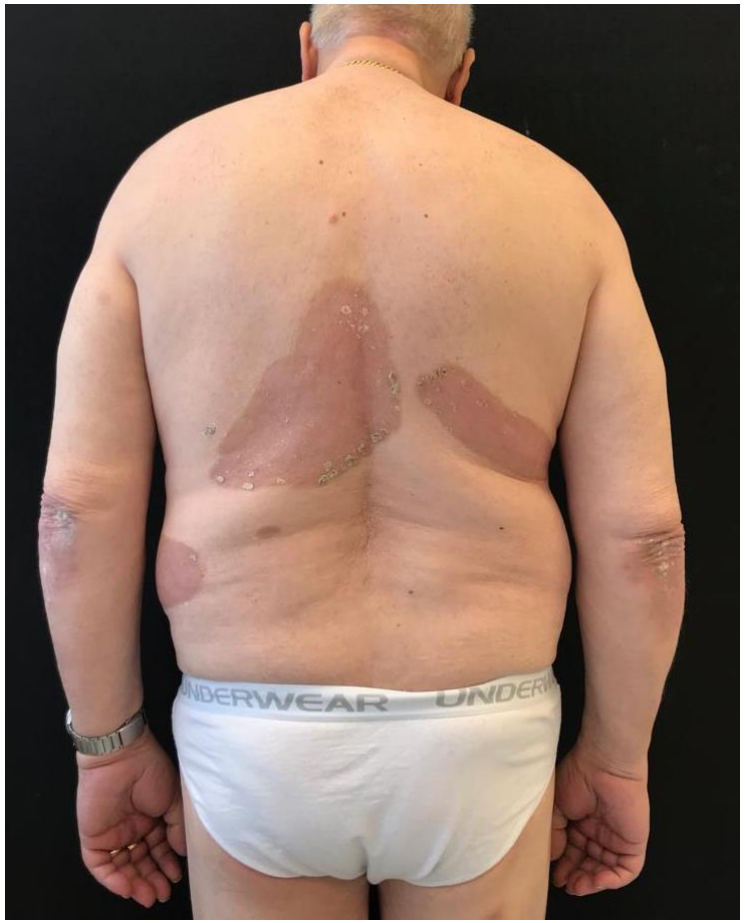
Week 0
PASI: 25
DLQI: 16



Caso 1 – Marcello

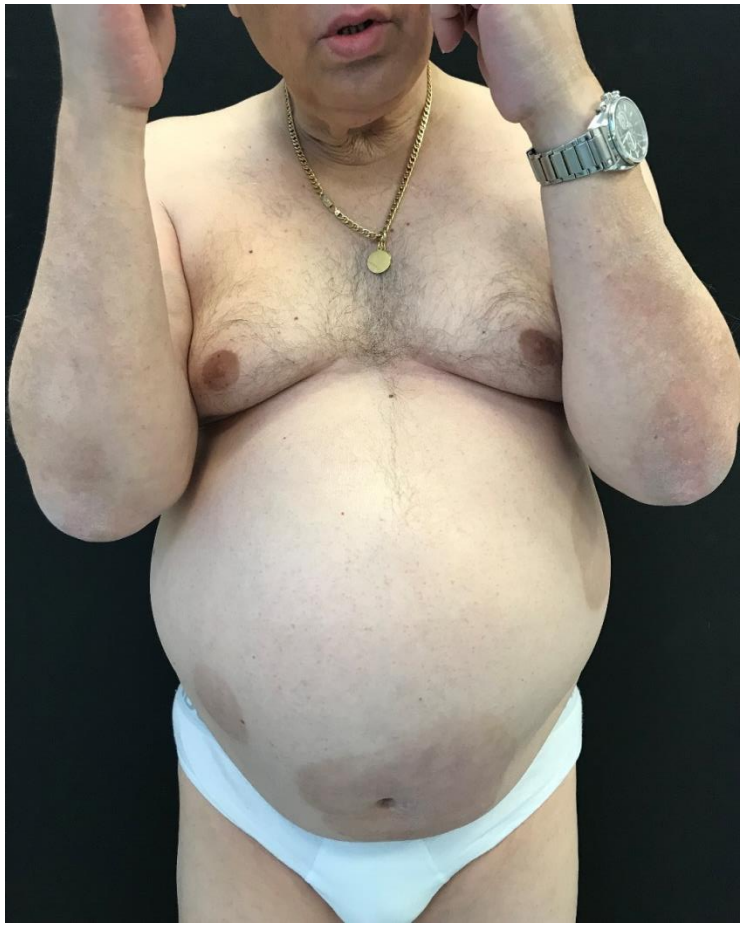
Week 0
PASI: 25
DLQI: 16

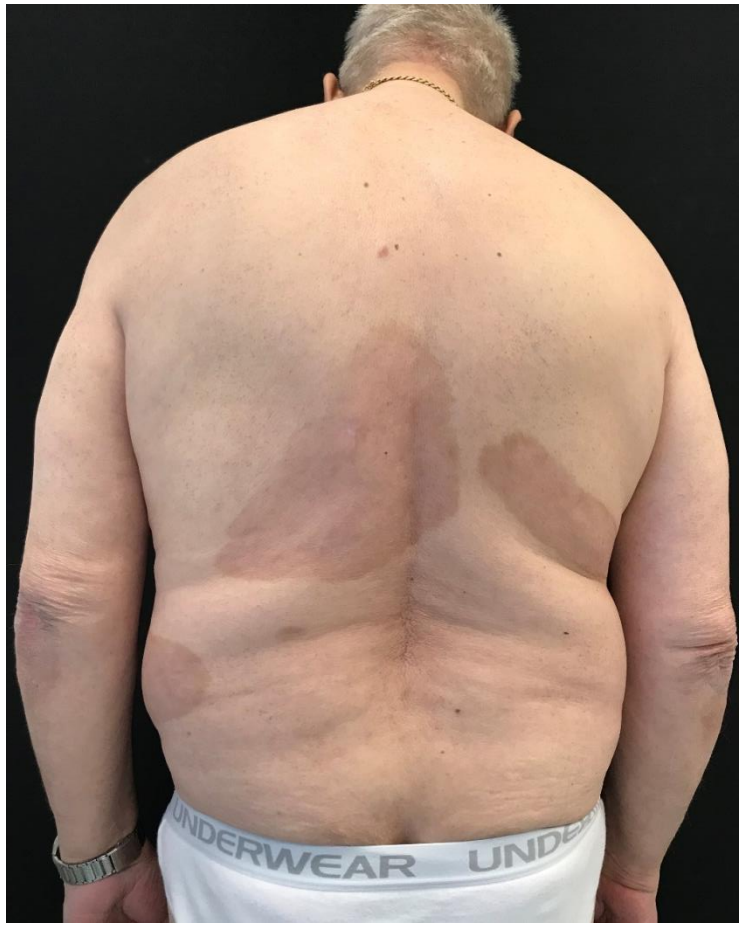




Week 4
PASI: 2
DLQI: 5

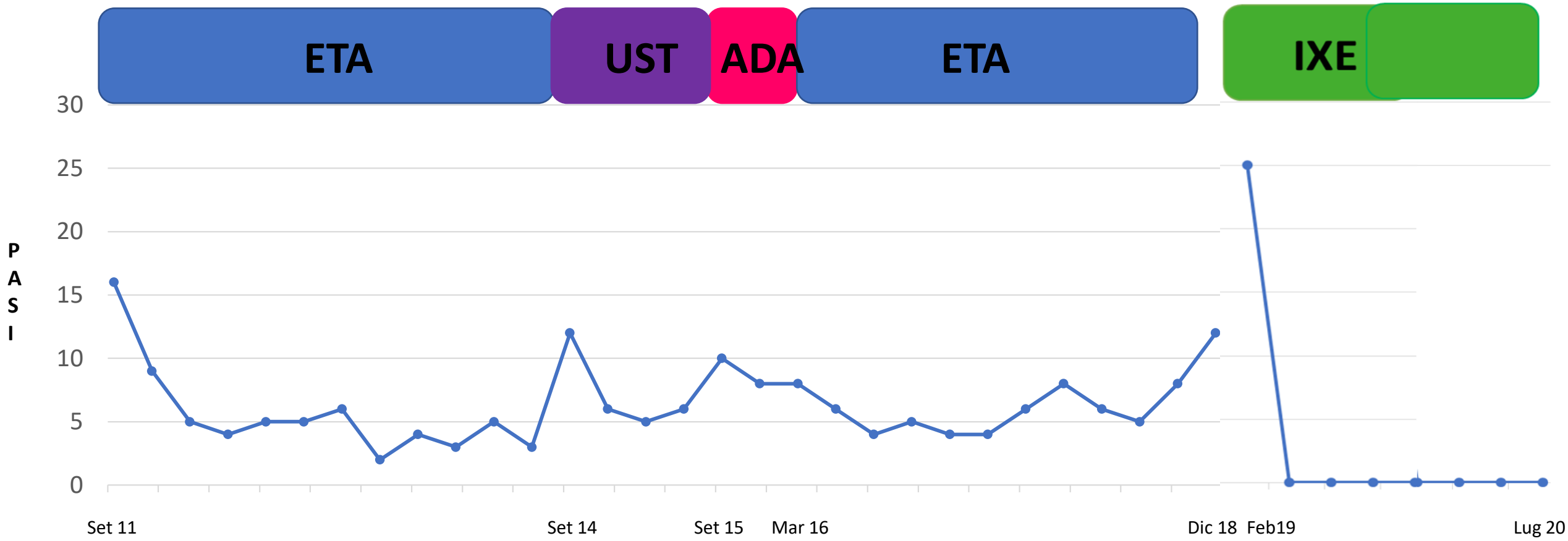
Caso 1 – Marcello



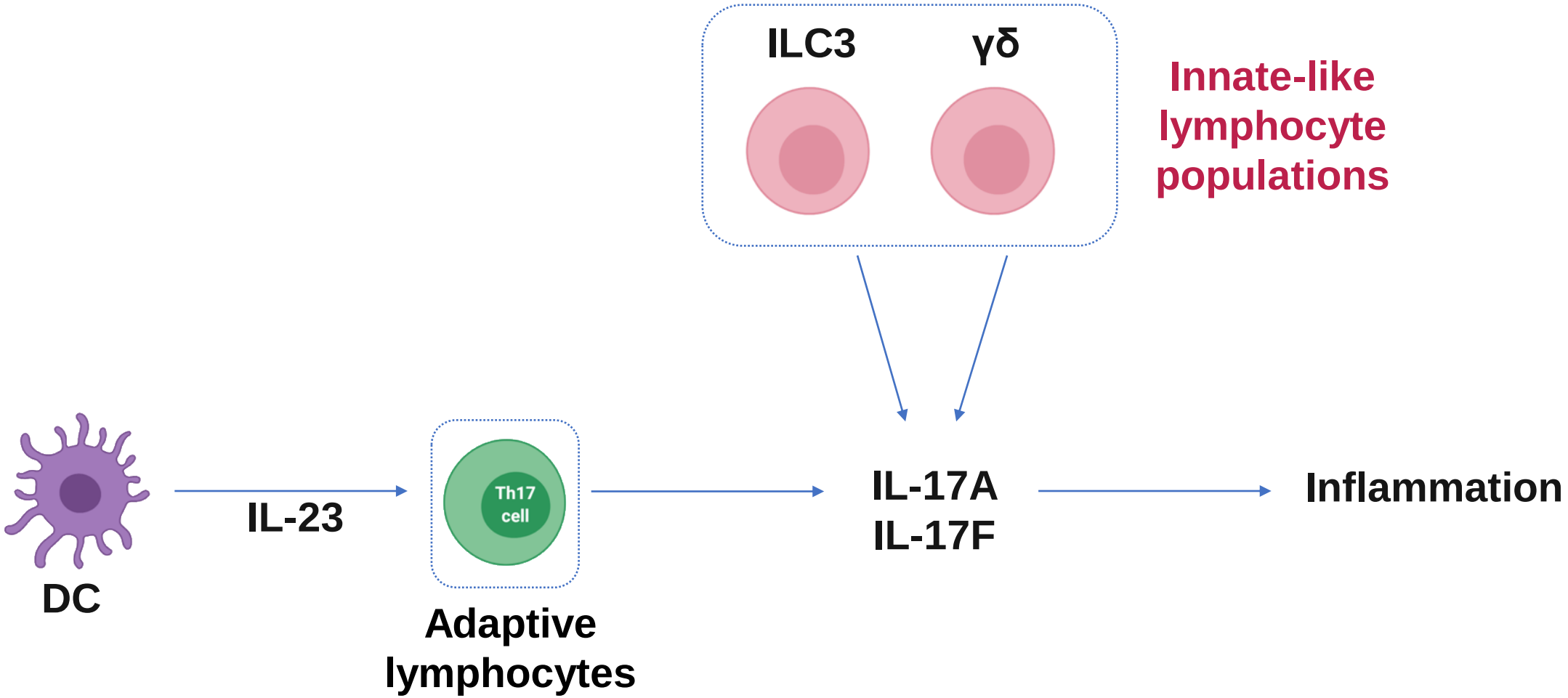


Week 16
PASI: 0
DLQI: 0
Nessun evento avverso

Caso 1 – Marcello

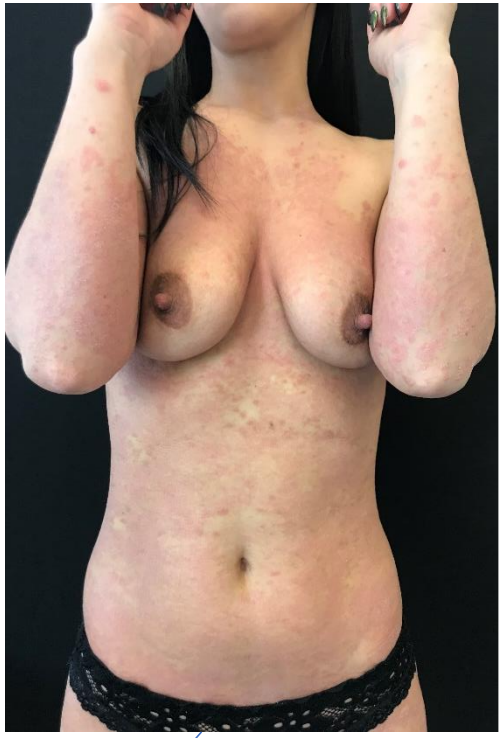


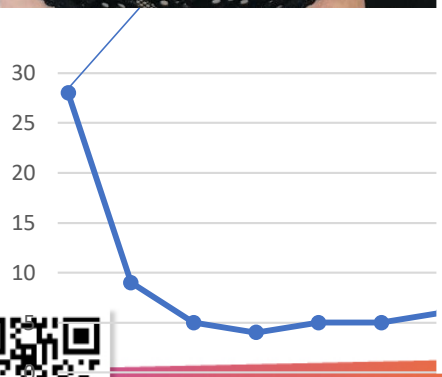
Cellular sources of IL-17A and IL-17F include both adaptive and innate-like lymphocyte populations[1]



DC, dendritic cell. 1. Cole et al. IGAS 2019;oral presentation.

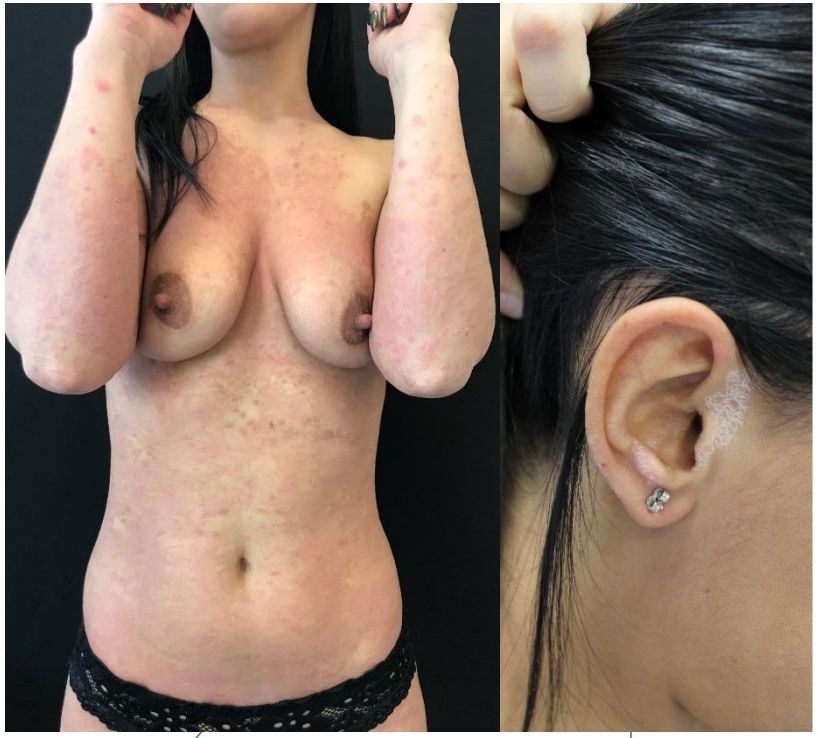
Caso 2 - Giulia

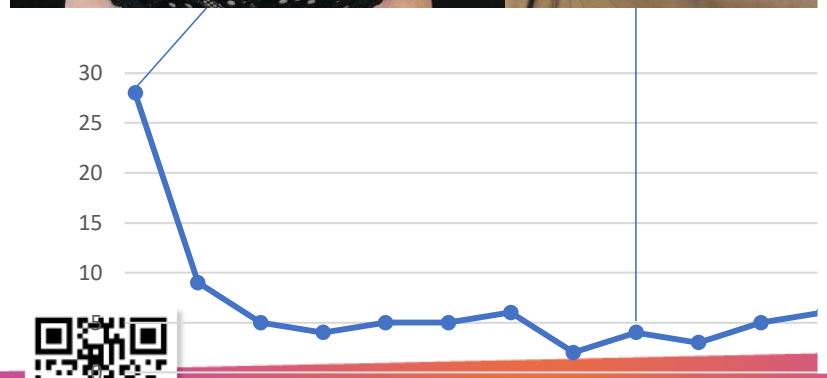




ANTI TNF ALFA

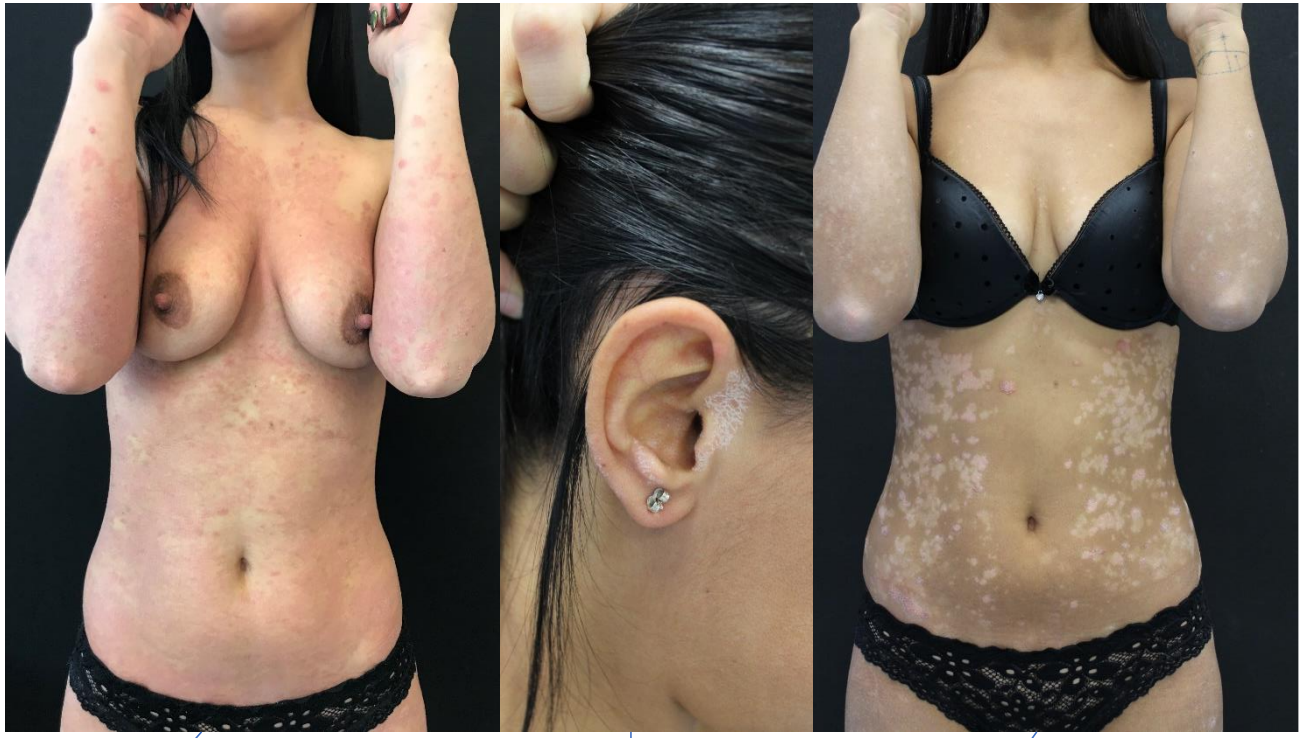
Caso 2 - Giulia

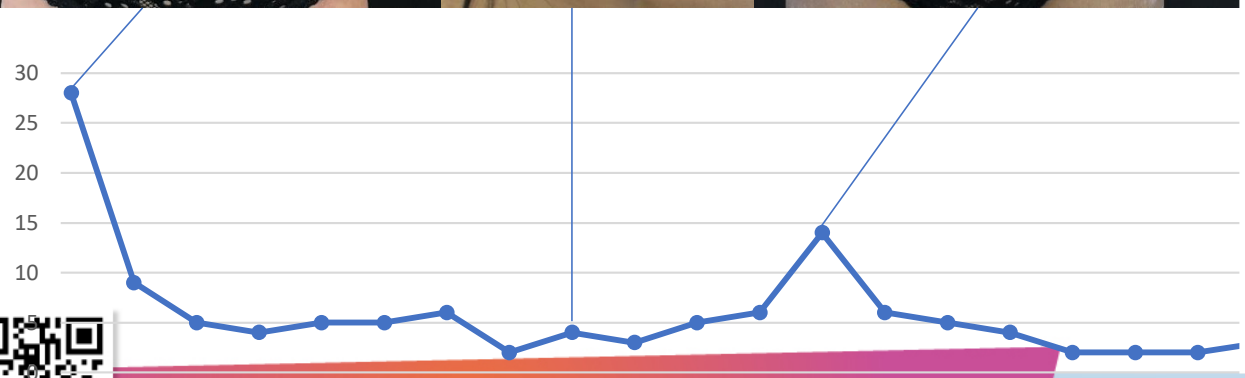




ANTI TNF ALFA

Caso 2 - Giulia

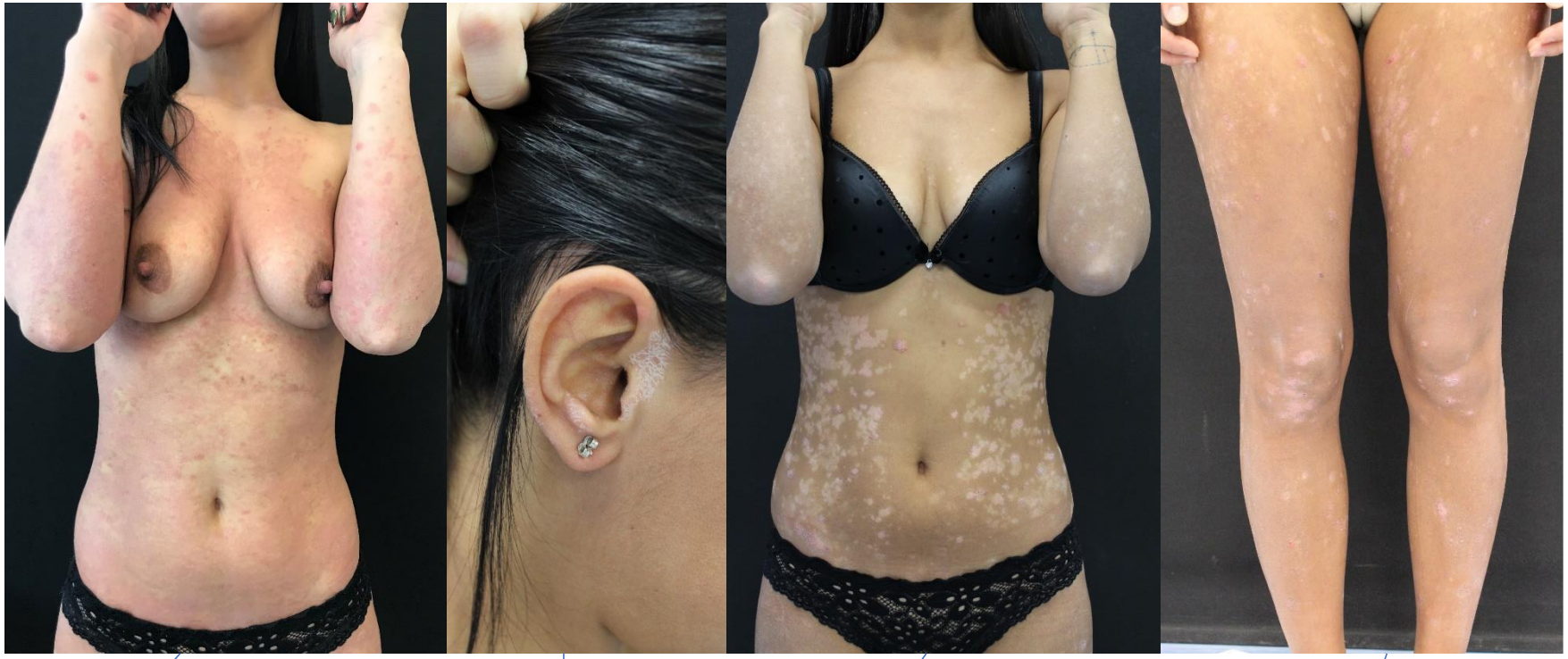


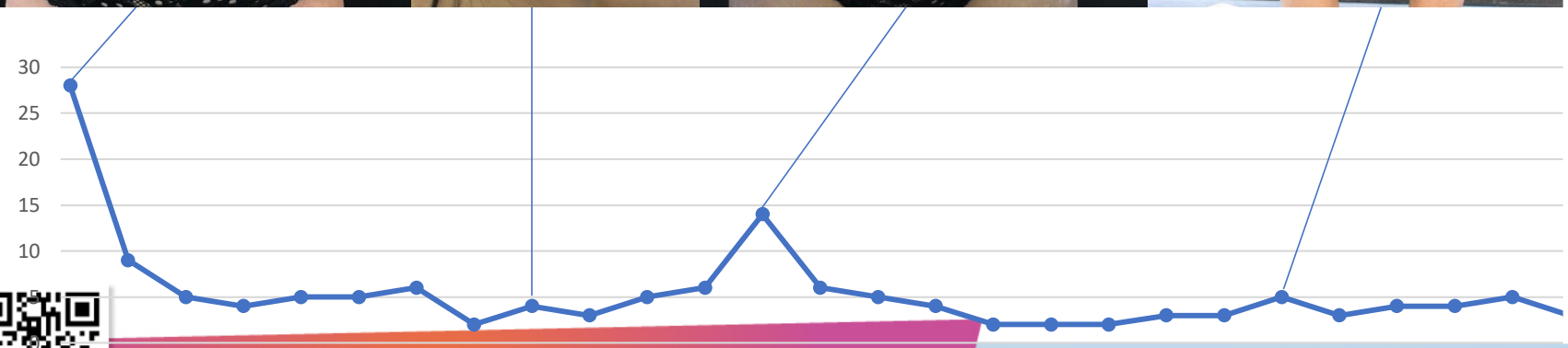


ANTI TNF ALFA

ANTI IL23

Caso 2 - Giulia

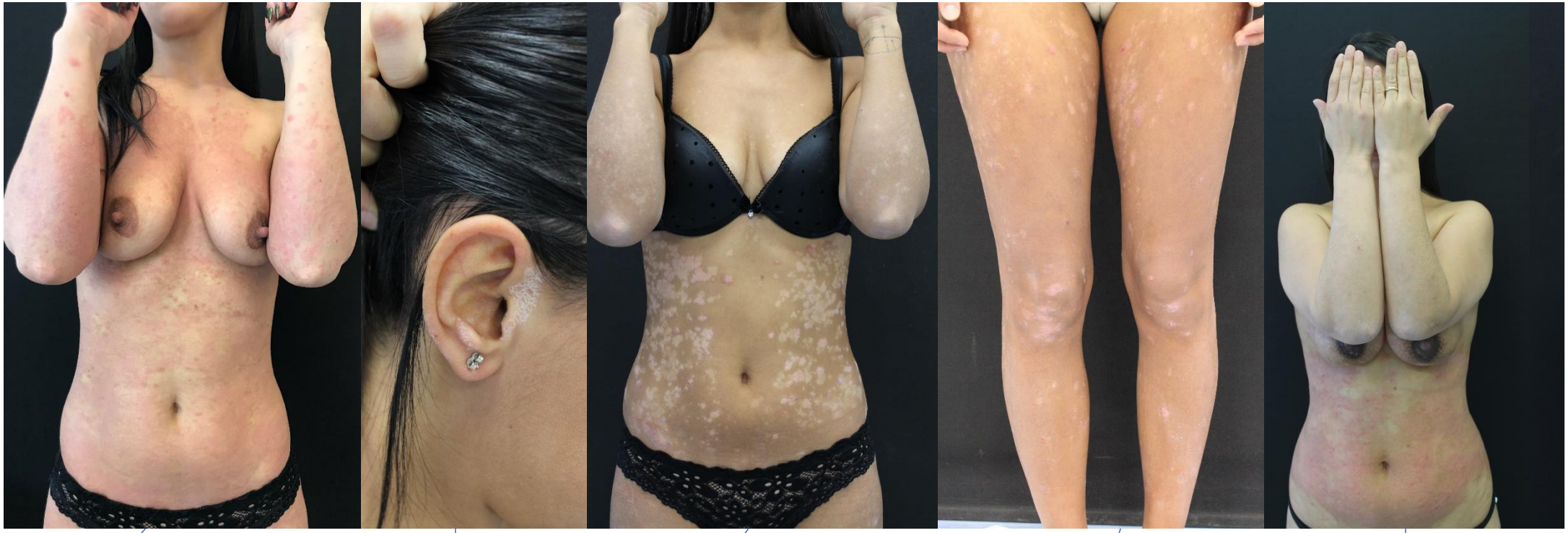


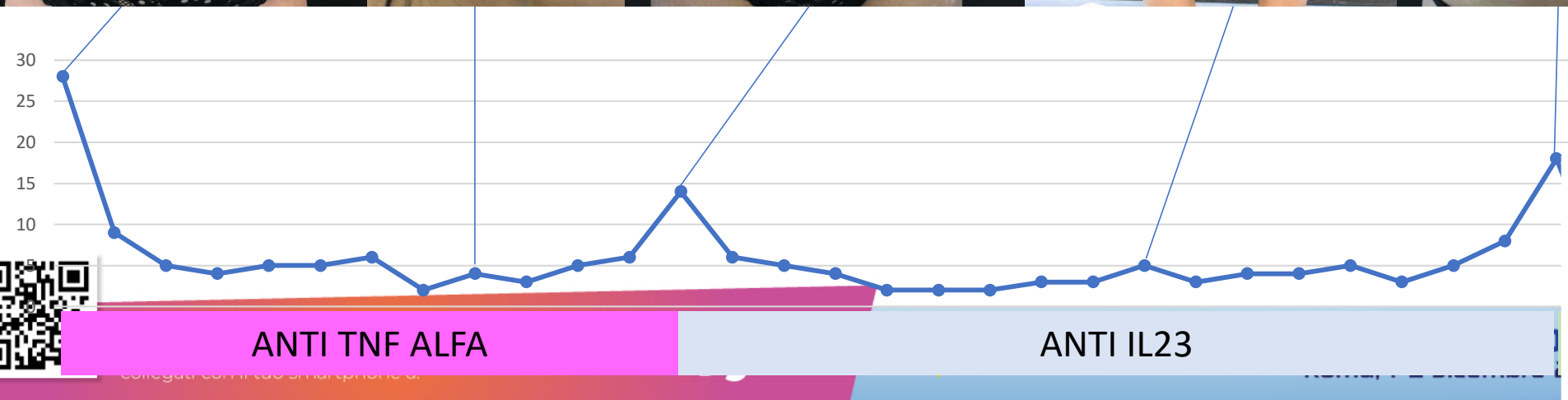


ANTI TNF ALFA

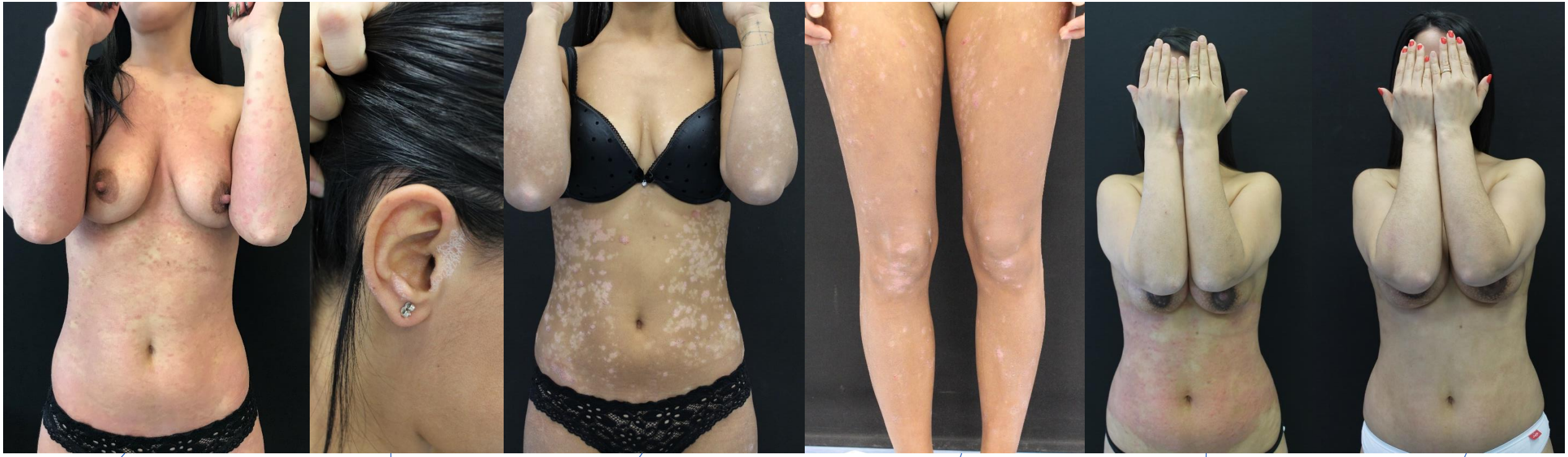
ANTI IL23

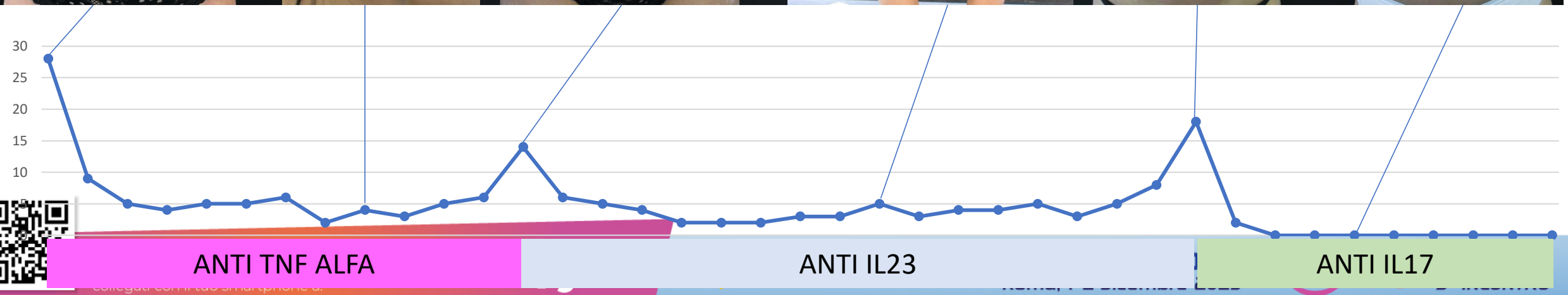
Caso 2 - Giulia



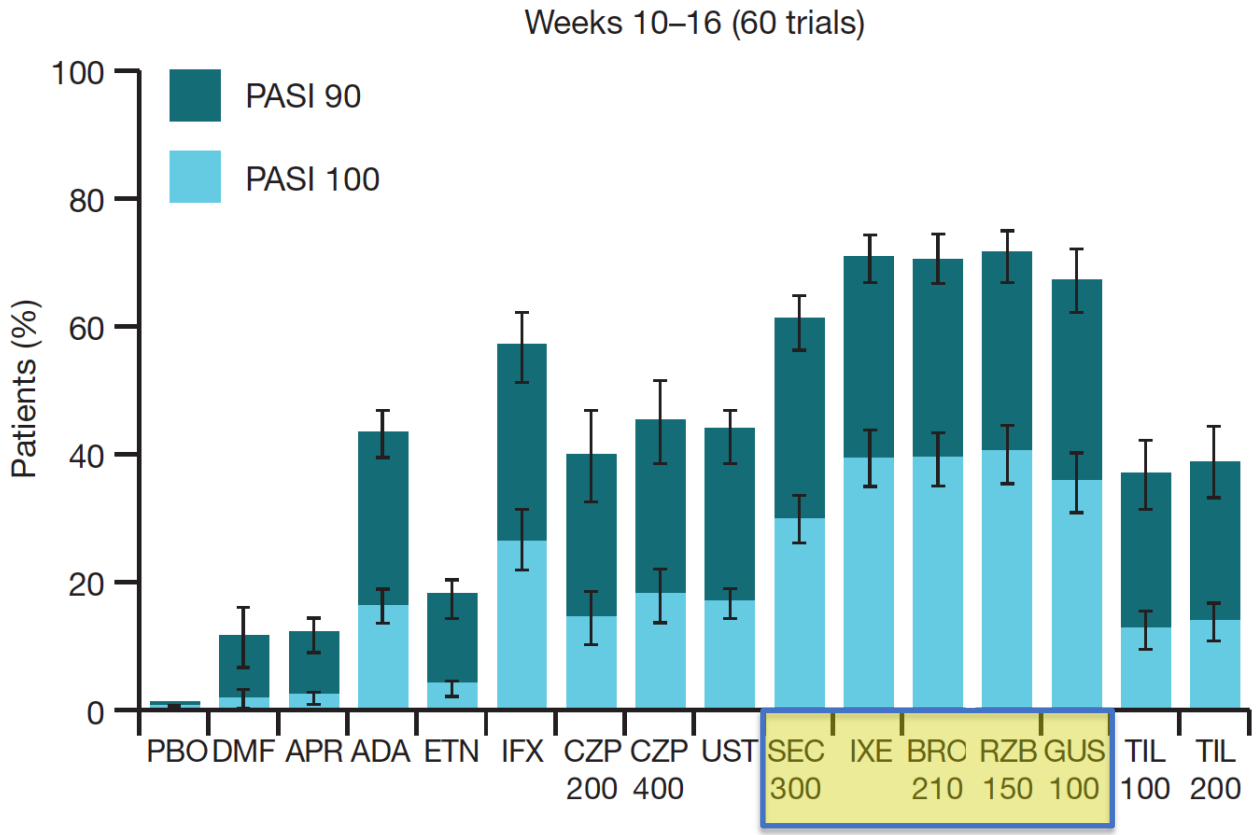


Caso 2 - Giulia





Efficacy in psoriasis: network meta-analysis favors IL-17A and p19 blockade



* $p < 0.05$ vs SEC. † $p < 0.05$ vs SEC and IXE. ‡ $p < 0.05$ vs GUS.
APR, apremilast; BRO, brodalumab; CZP, certolizumab pegol; DMF, dimethyl fumarate; ETN, etanercept; IFX, infliximab; IXE, ixekizumab; NMA, network meta-analysis; TIL, tildrakizumab.

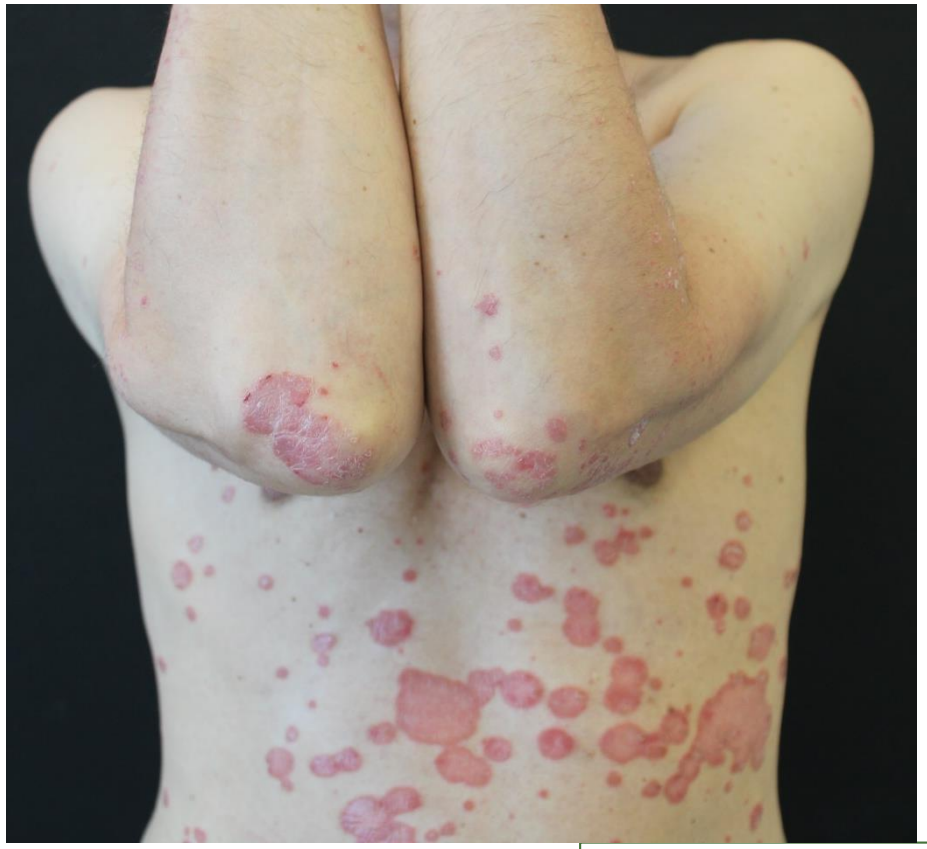
Armstrong AW, et al. JAMA Dermatol 2020; 156(3):258–269

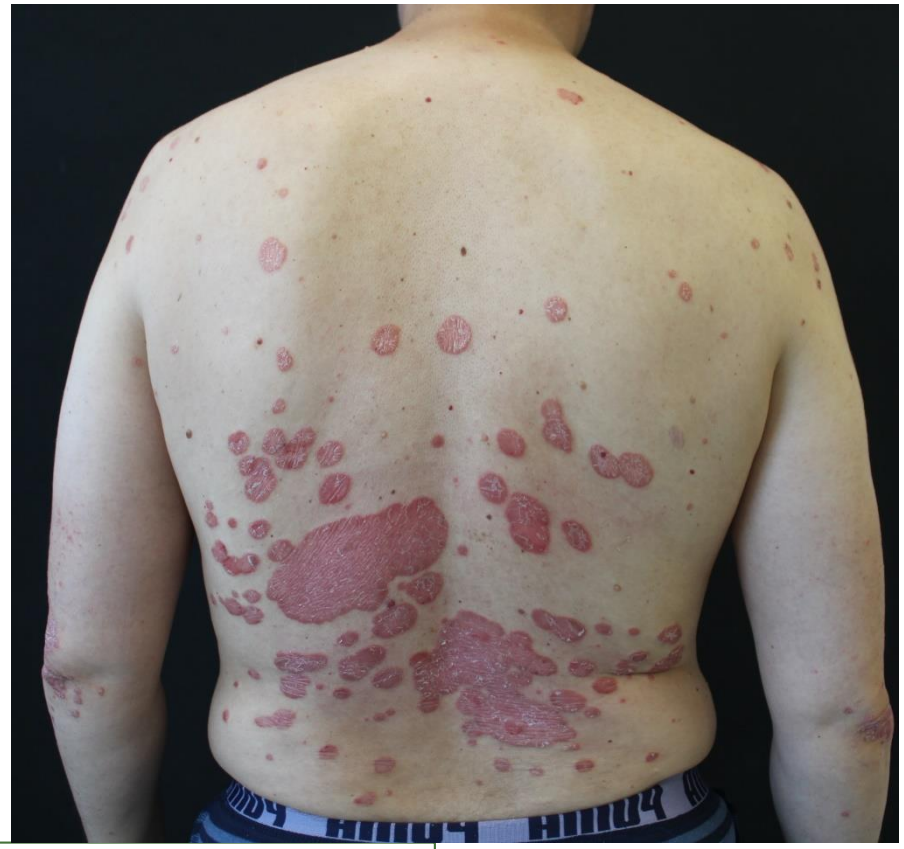
…ma quanto veloce?

Caso 3 - Alessandro

- 48 anni
- BMI 24
- Psoriasi dall'età di 25 anni
- Artrite psoriasica dall’età di 30 anni
- Precedenti terapie: Adalimumab (sospeso per perdita di efficacia a settembre 2021)

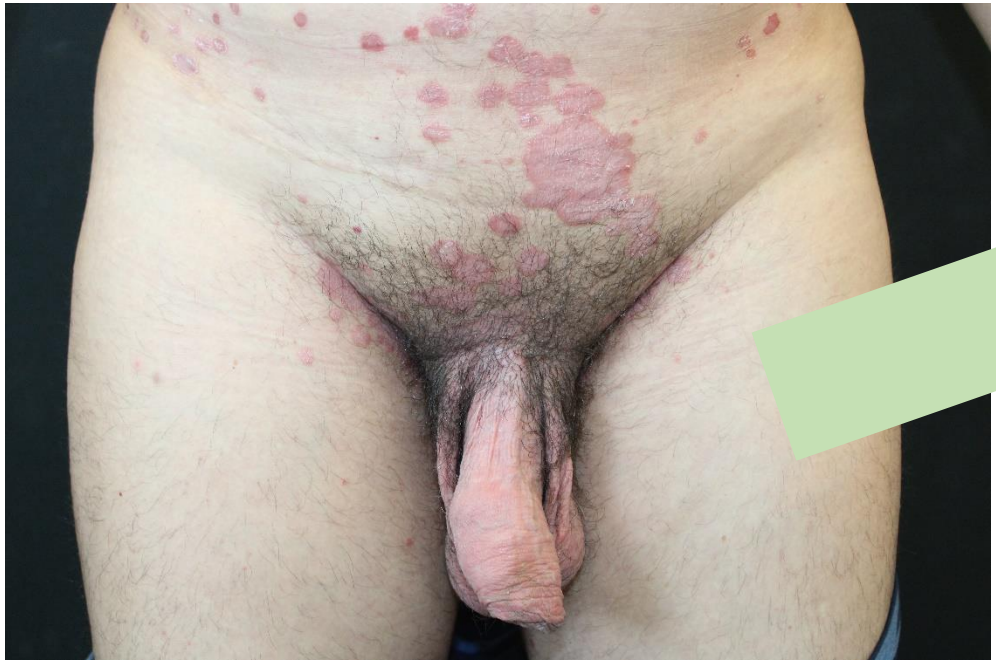
Caso 3 - Alessandro

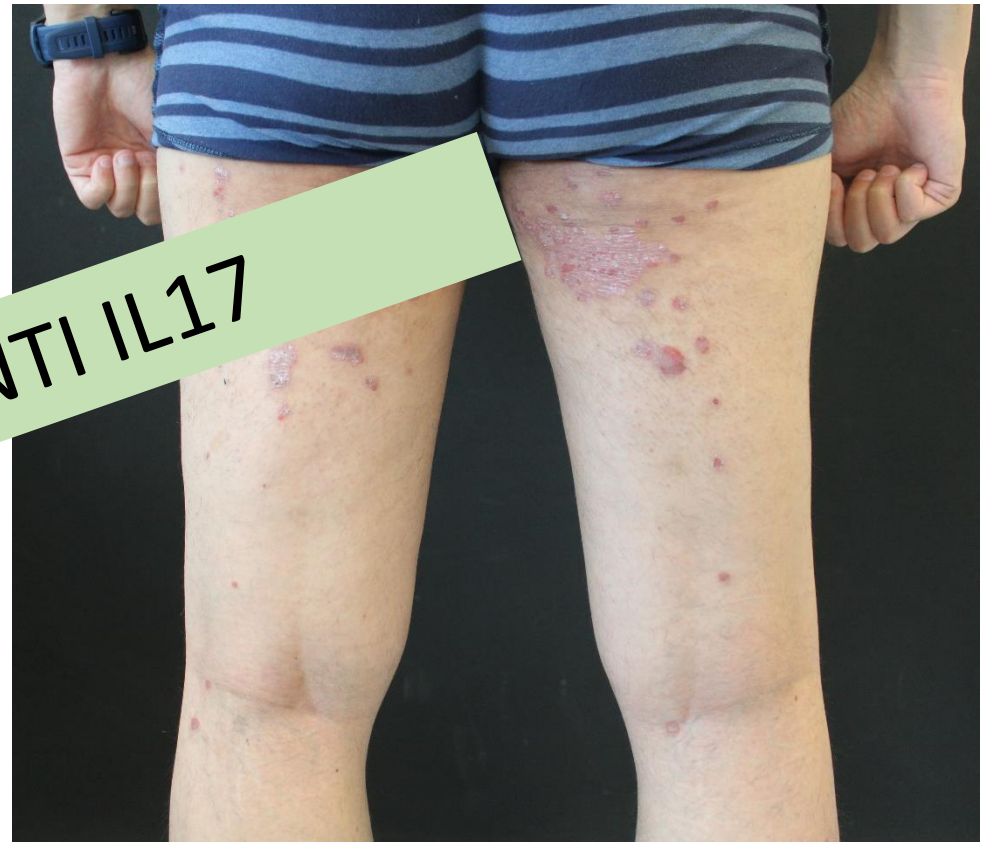




PASI 22 VAS dolore 3/10

Caso 3 - Alessandro



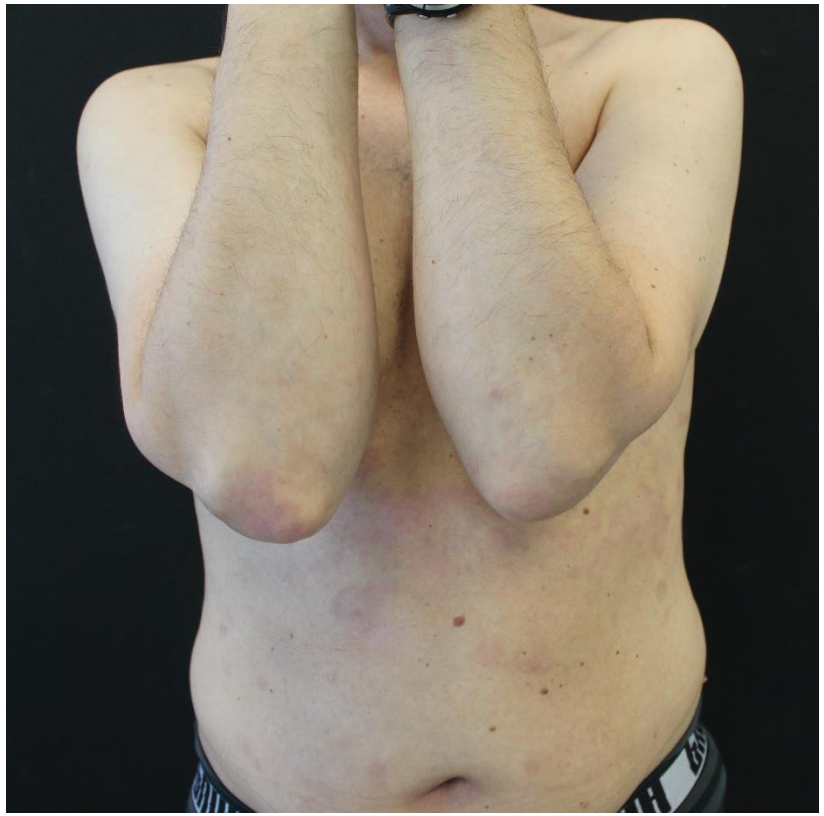


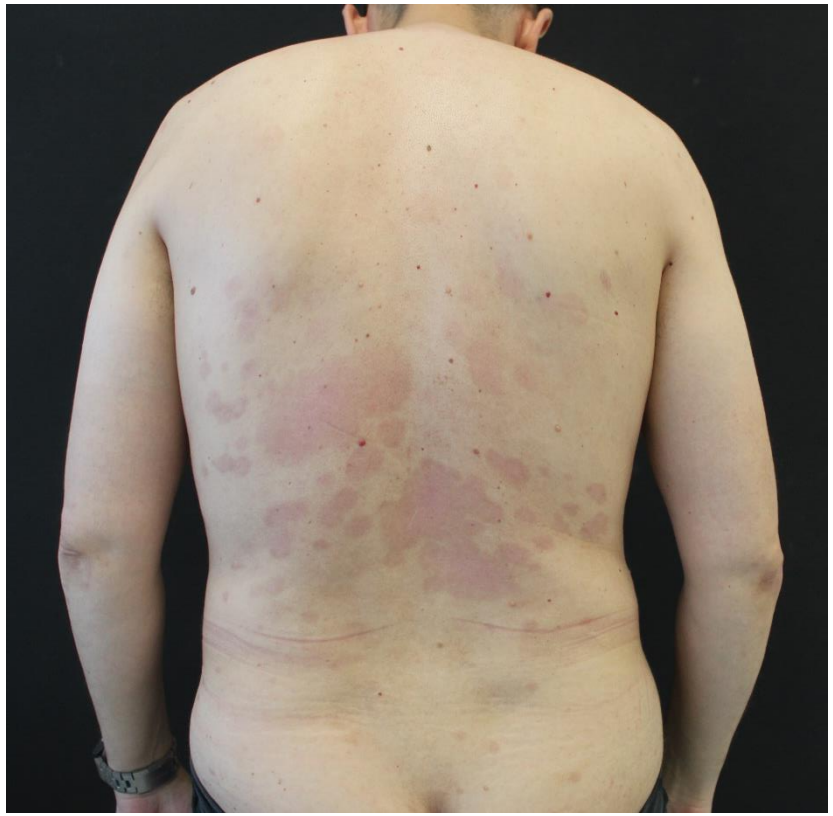
ANTI IL17

PASI 22 VAS dolore 3/10

Caso 3 - Alessandro

Week 4

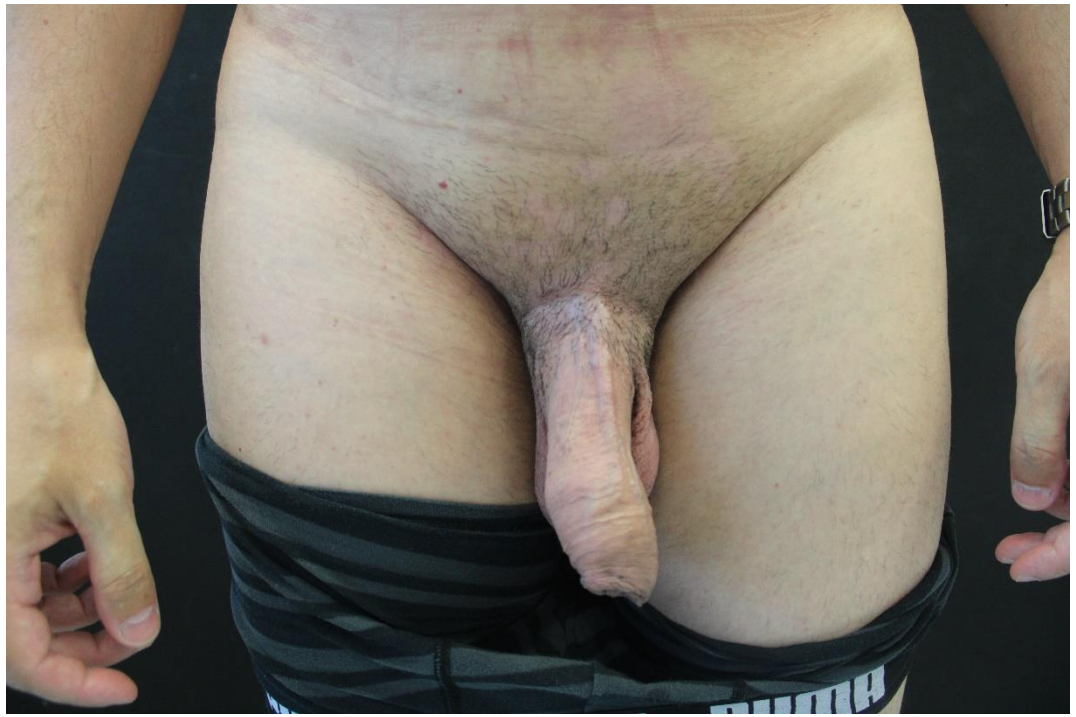


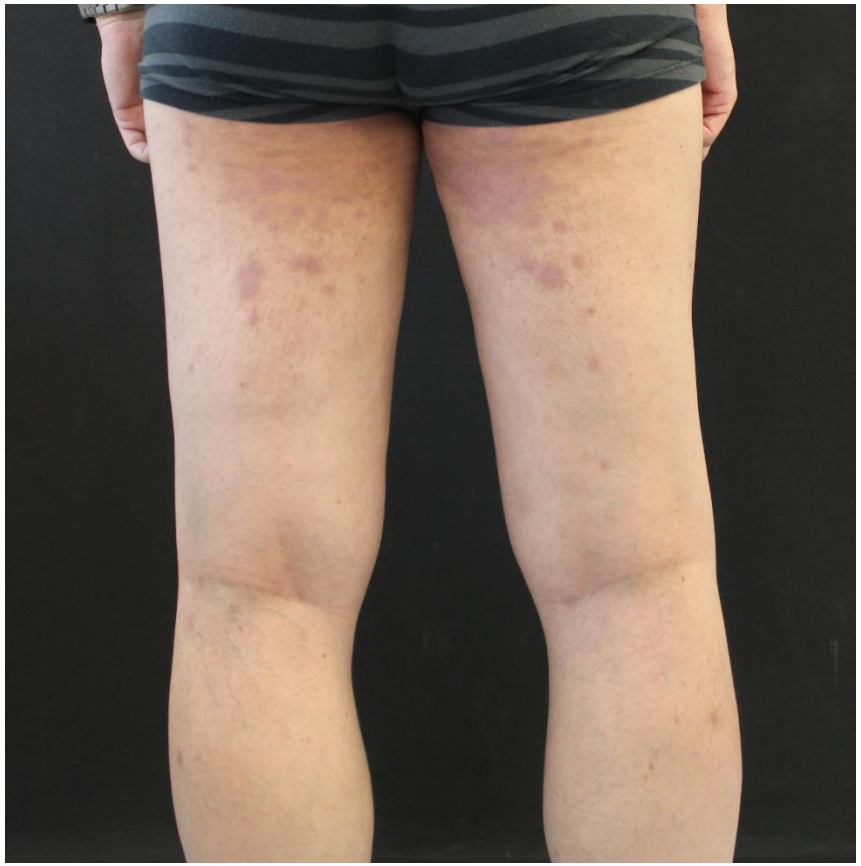


PASI 1,2 VAS dolore 0/10

Caso 3 - Alessandro

Week 4





PASI 1,2 VAS dolore 0/10

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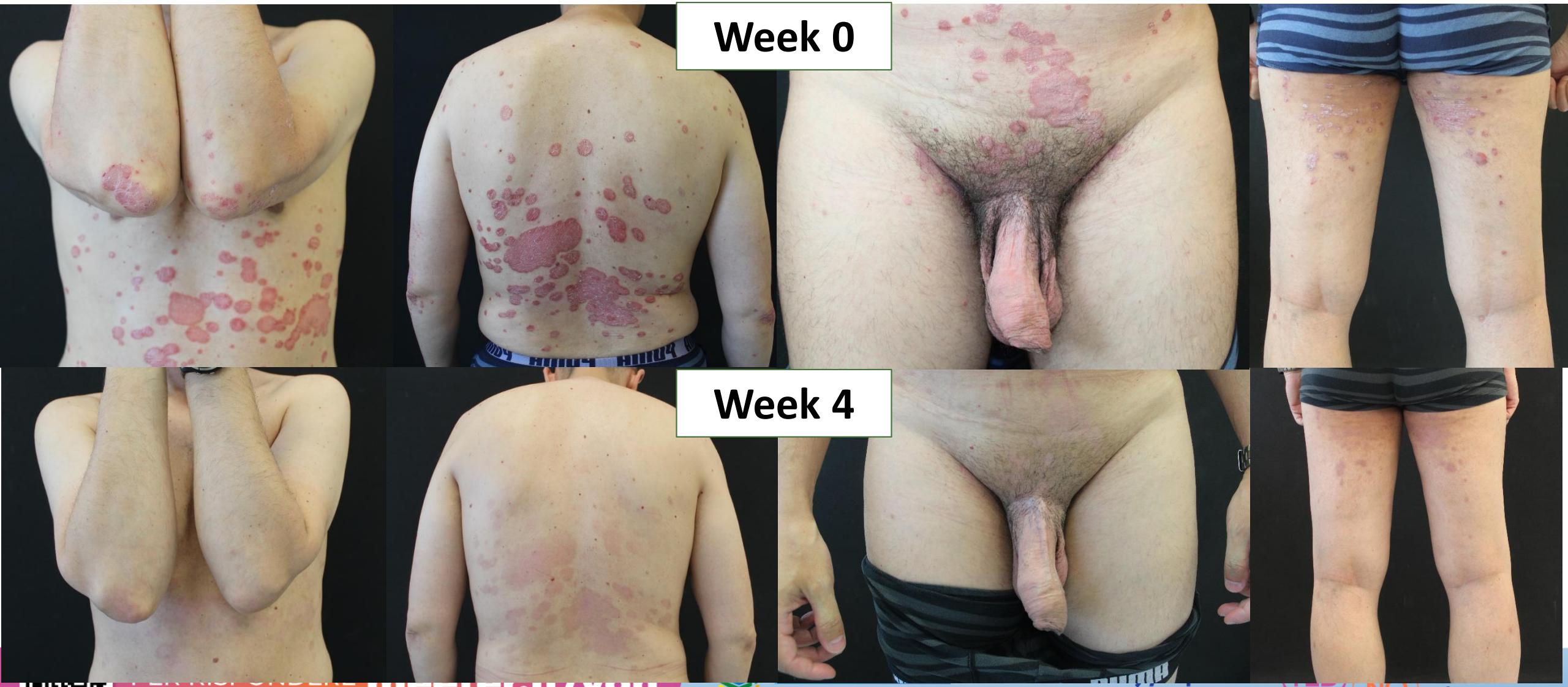

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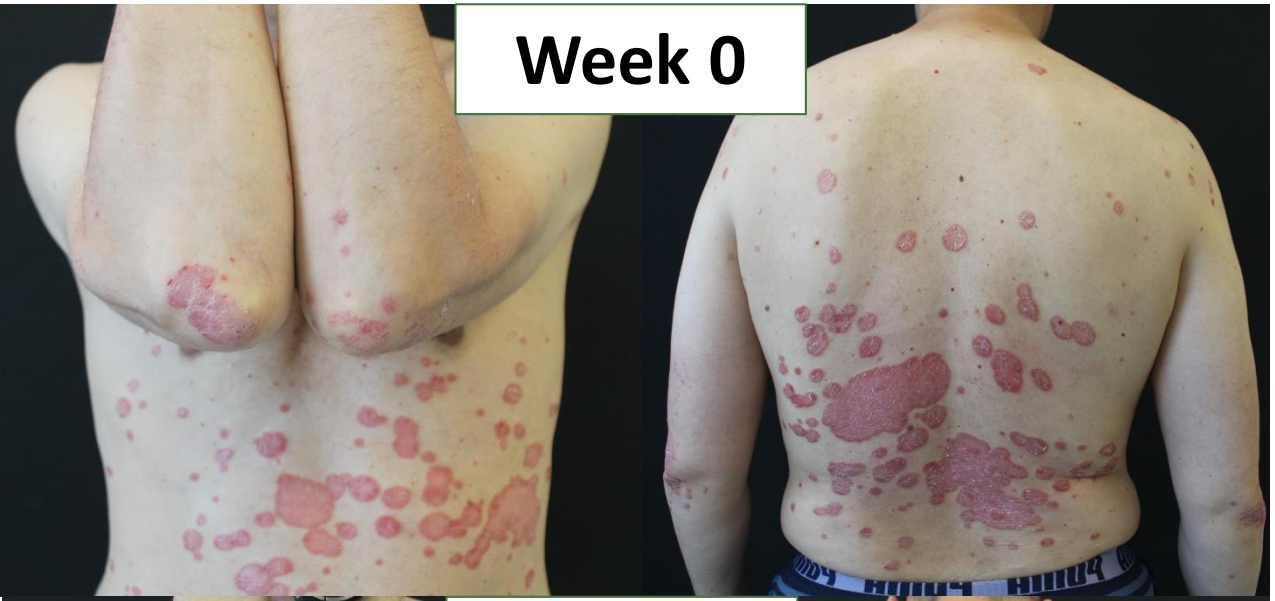
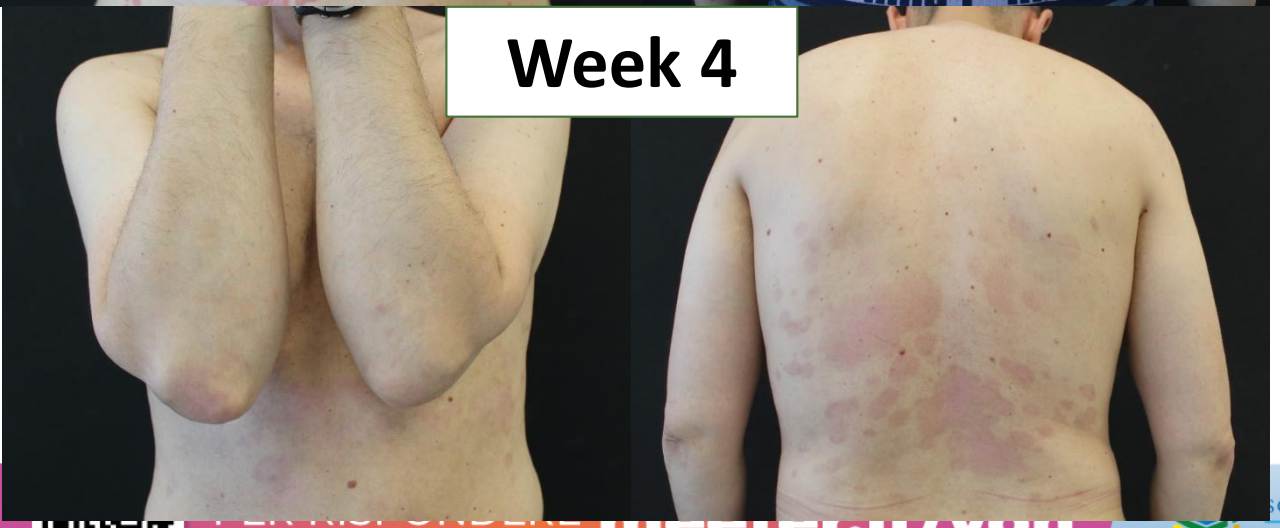
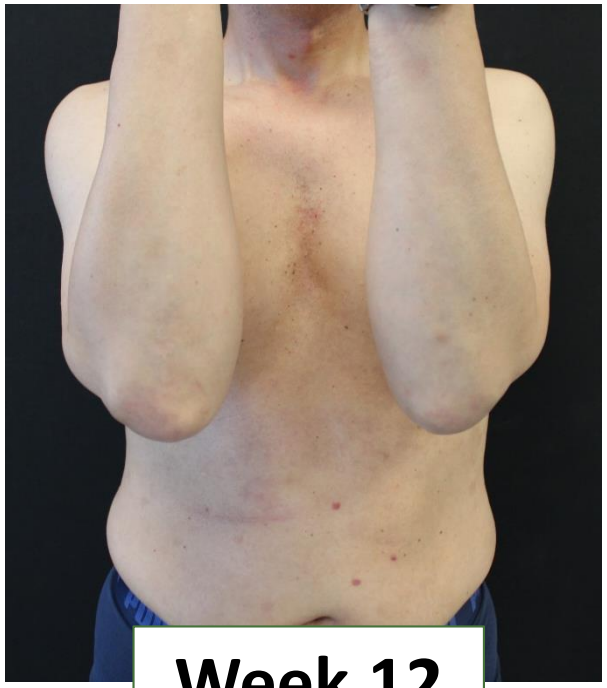
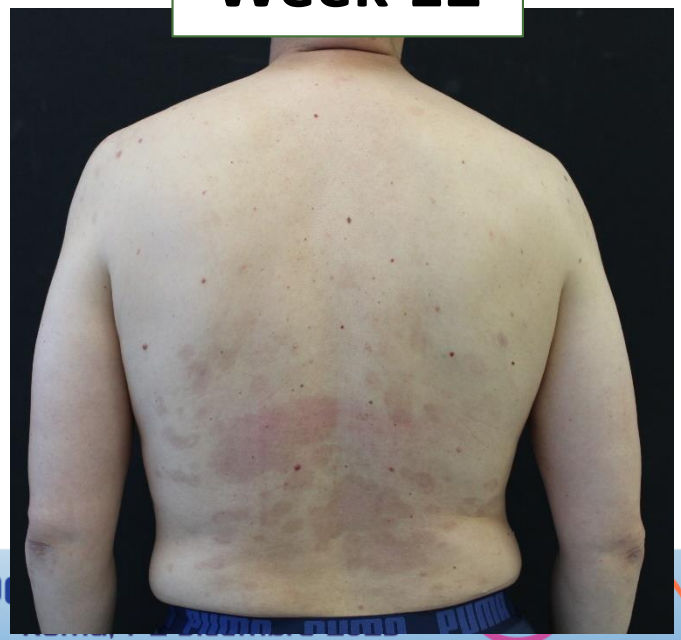
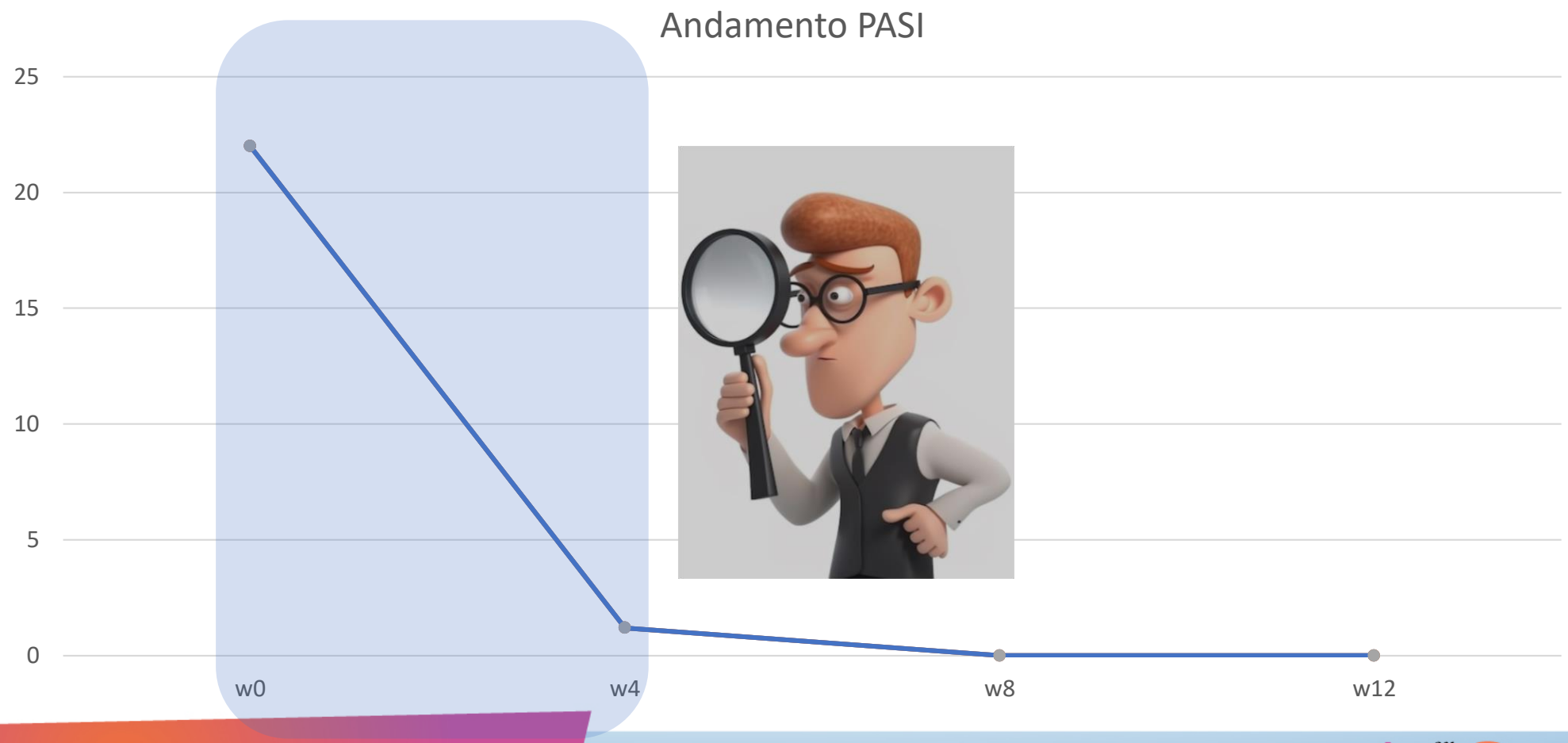








Caso 3 - Alessandro



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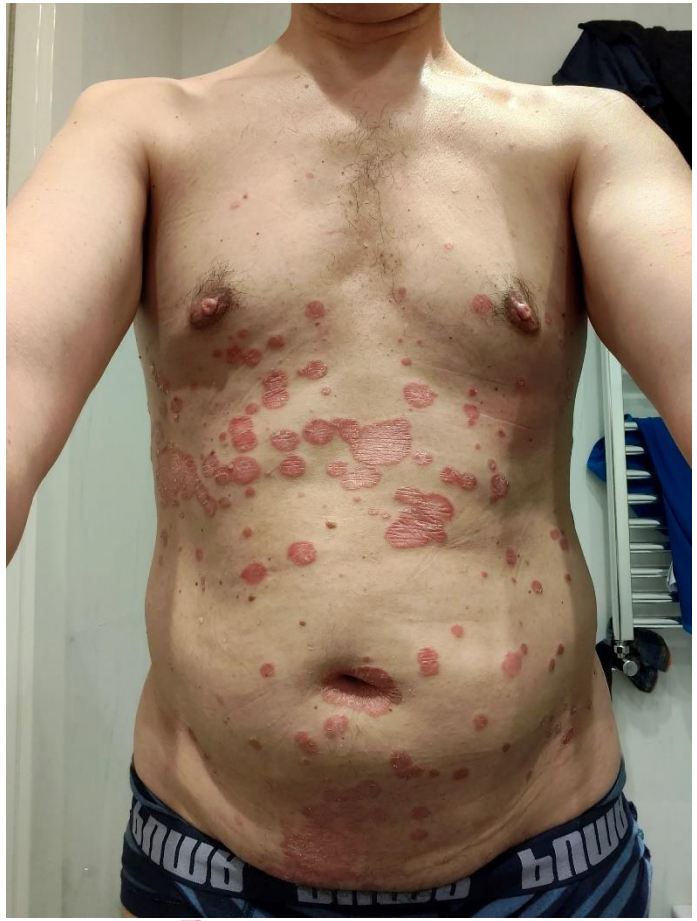

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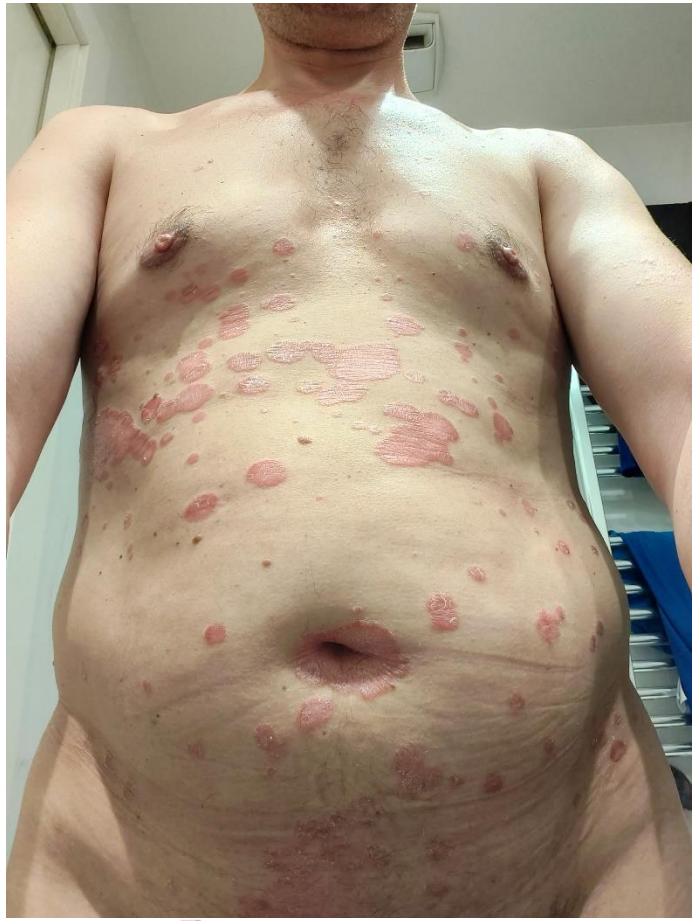

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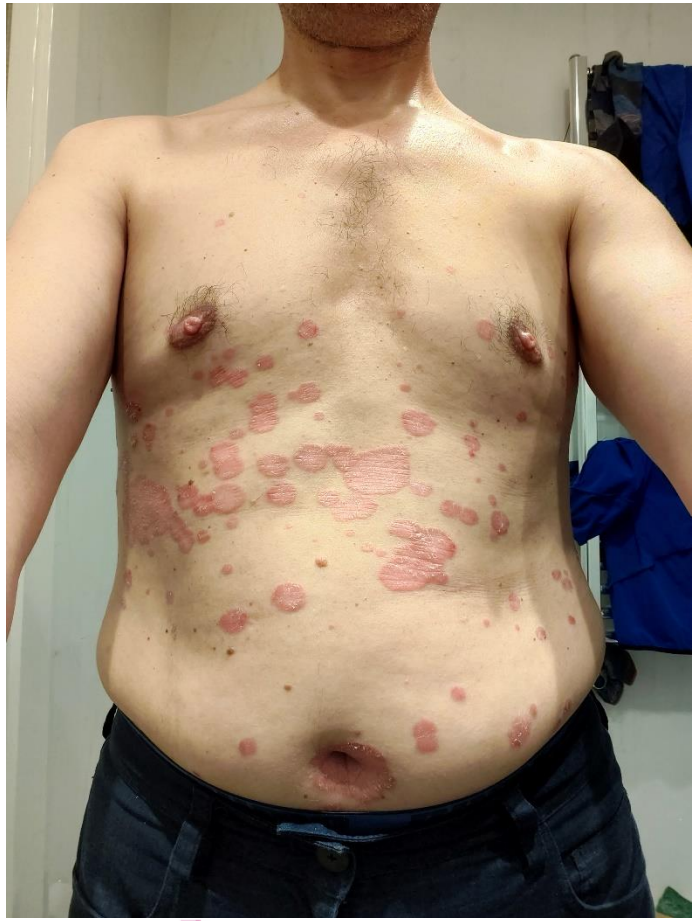

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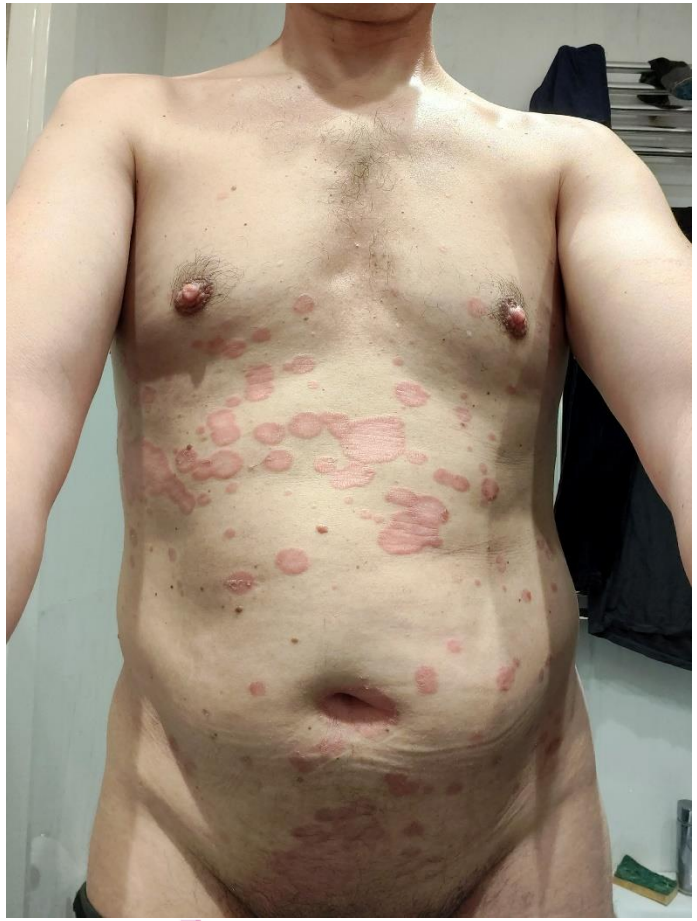

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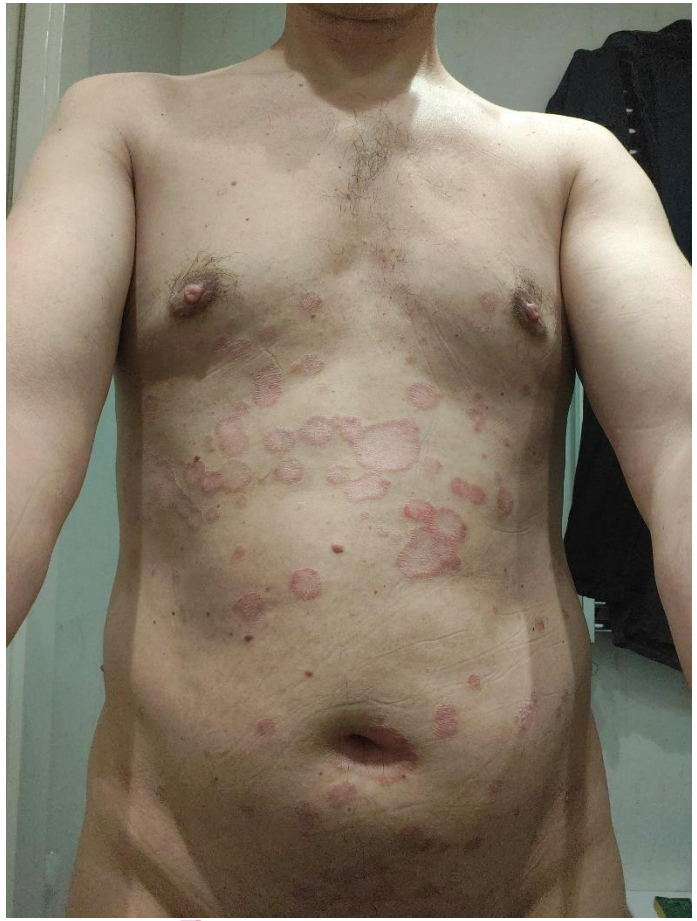

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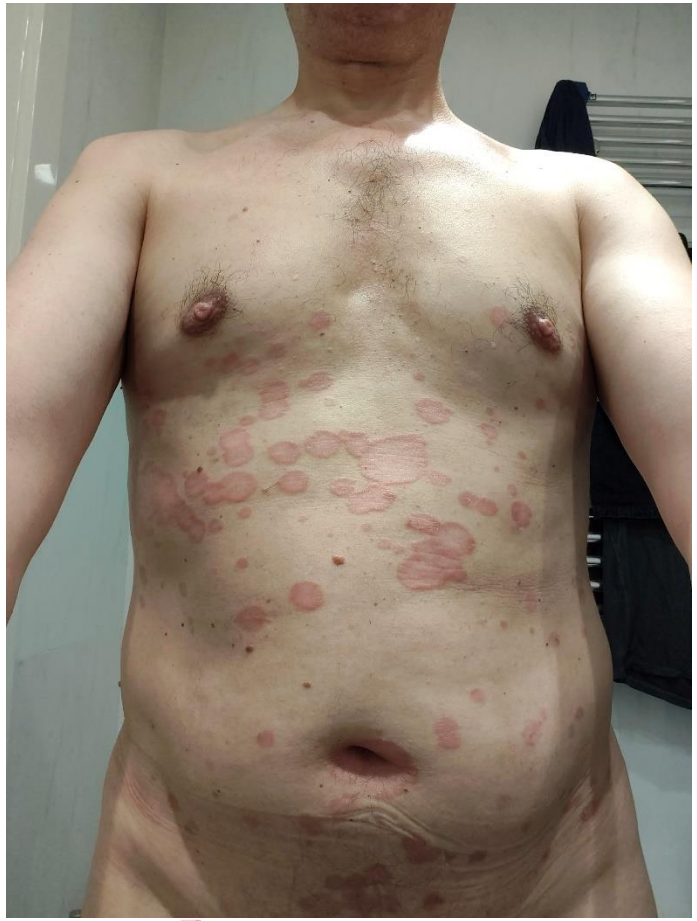

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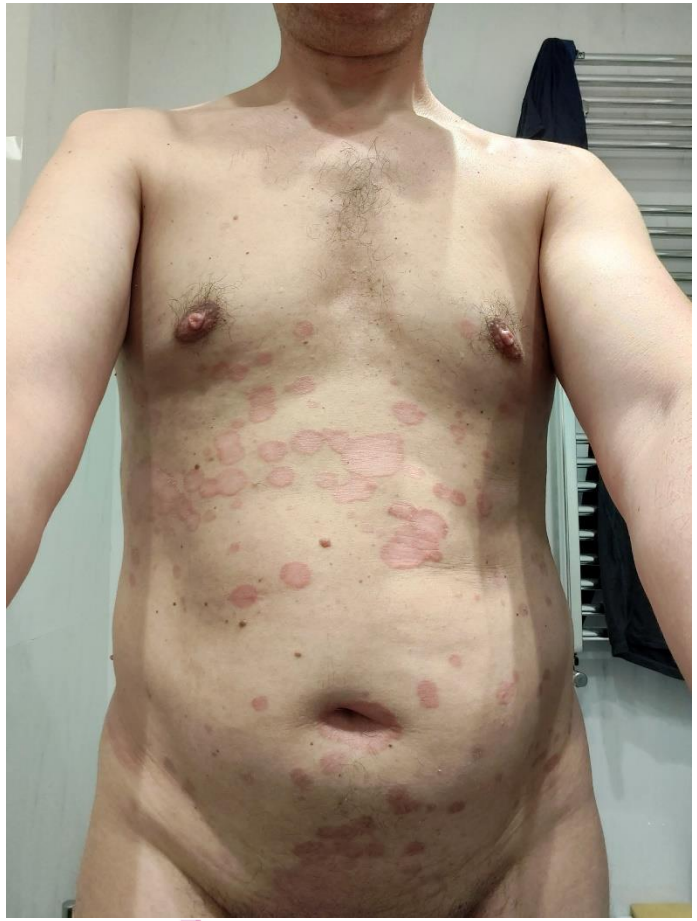

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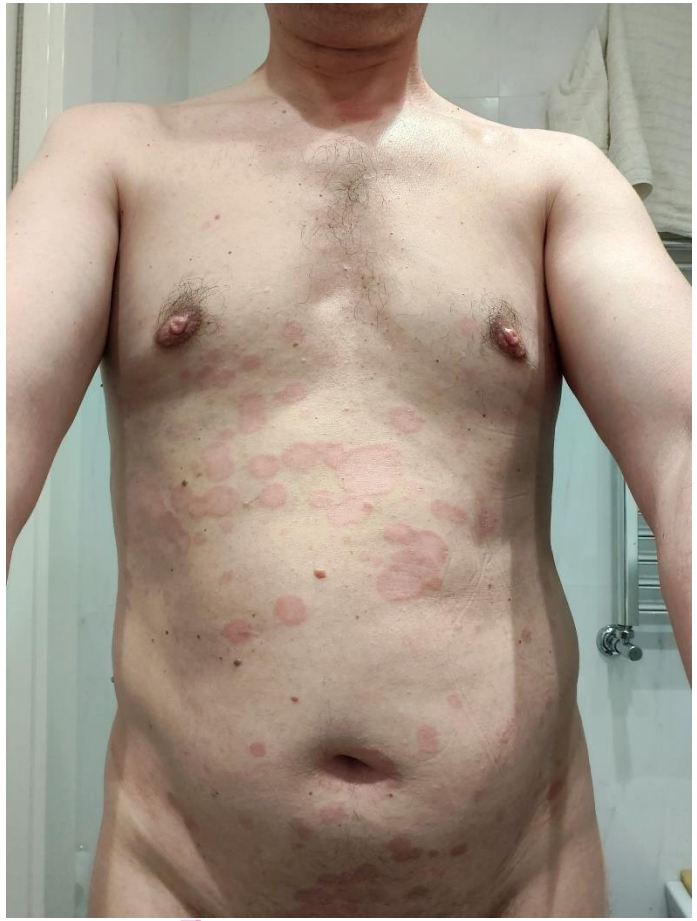

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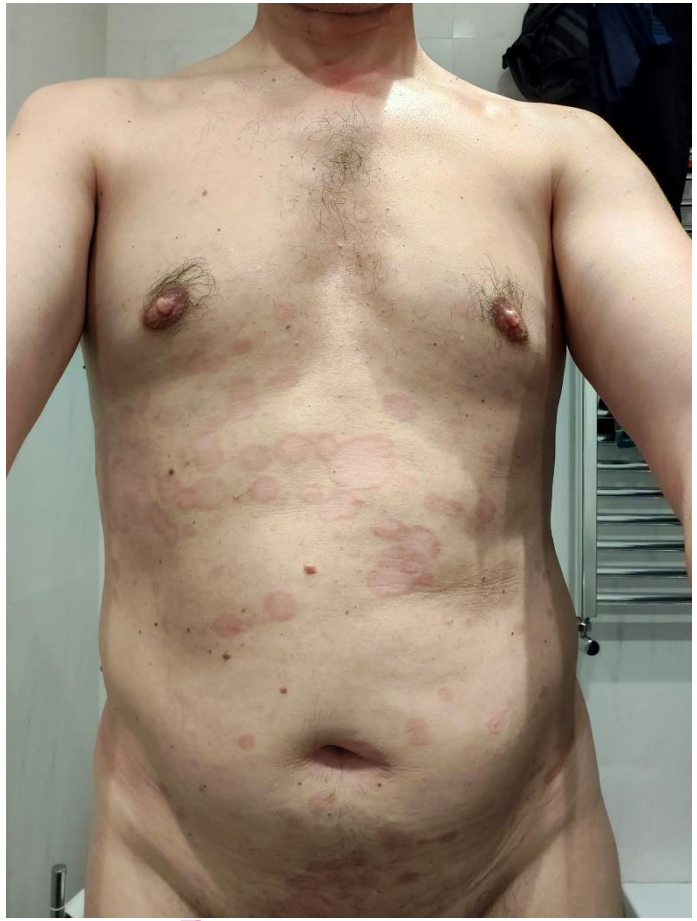

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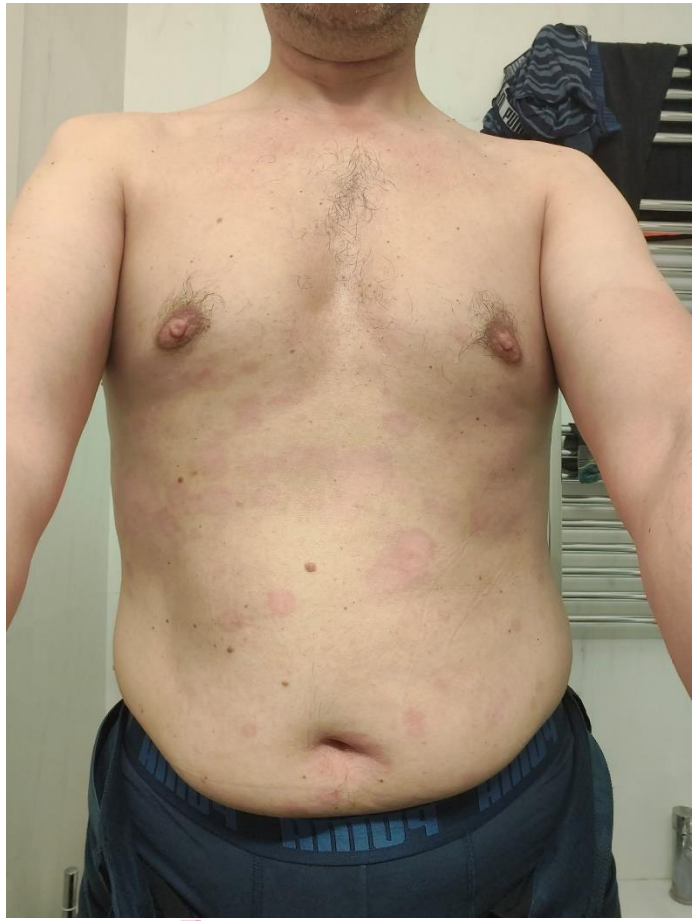
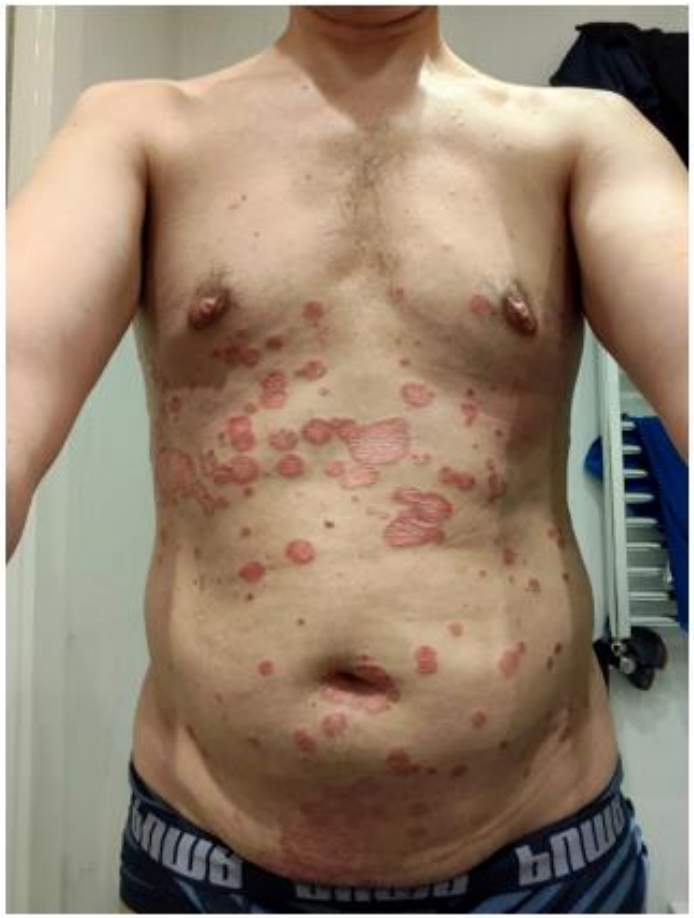


DAY 1



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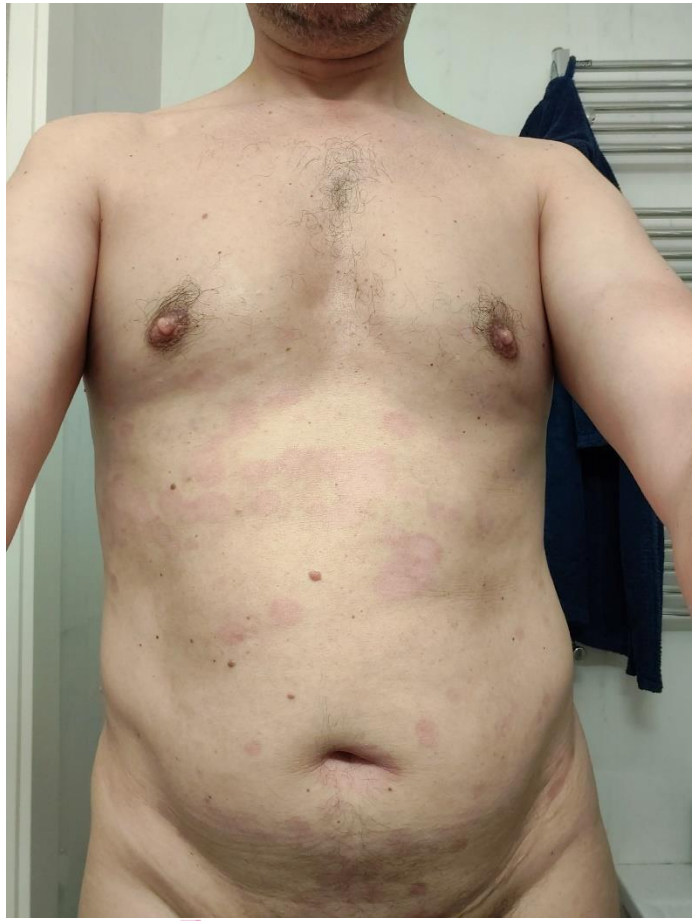

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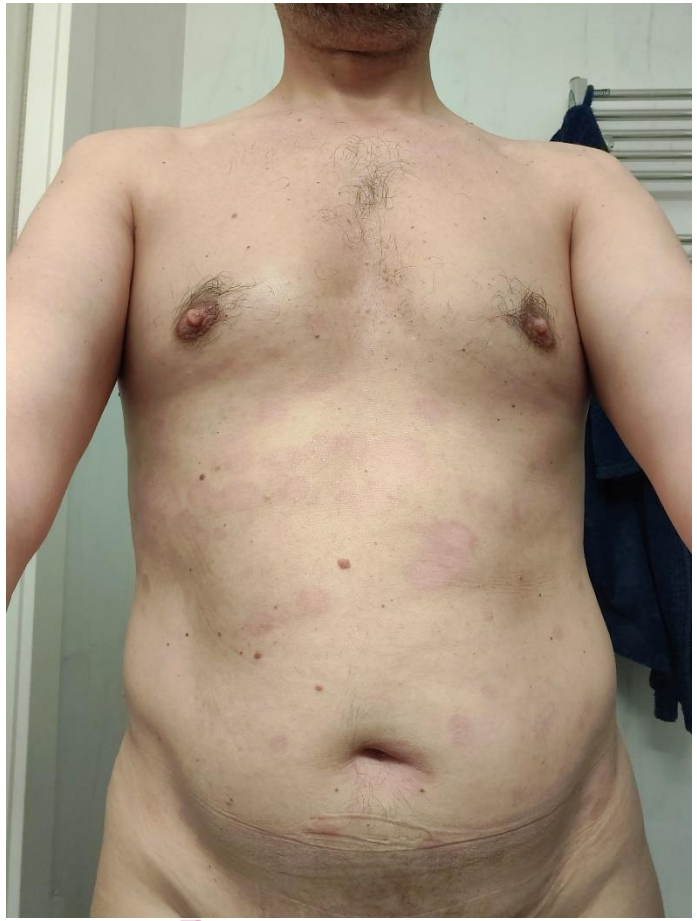

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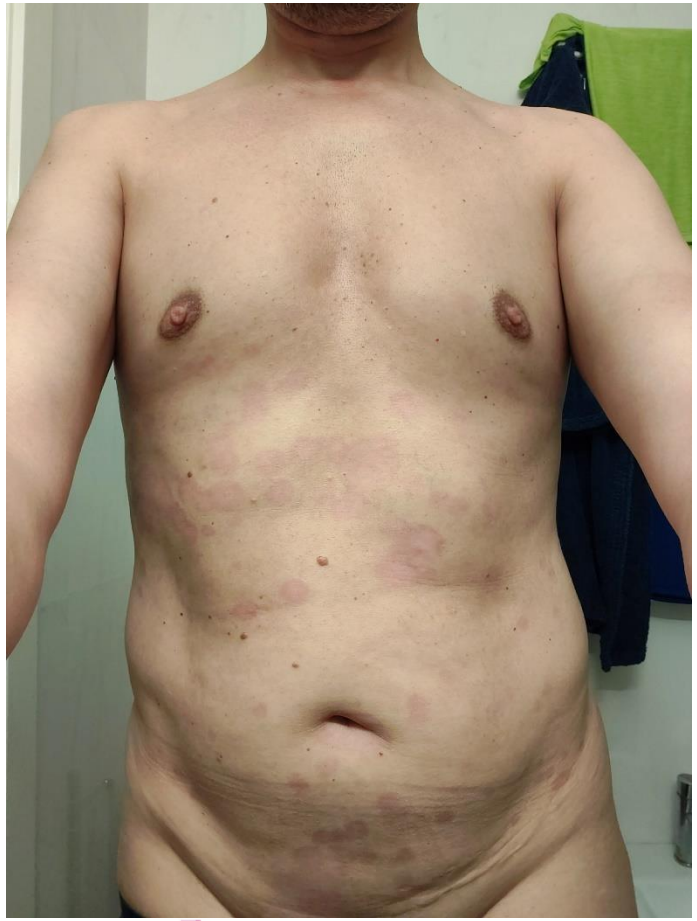

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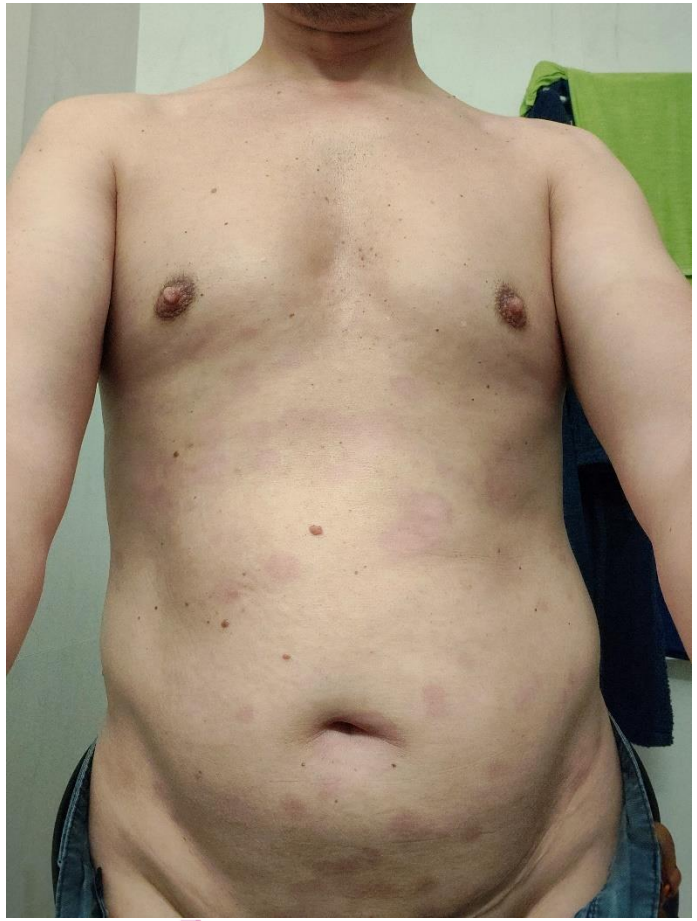

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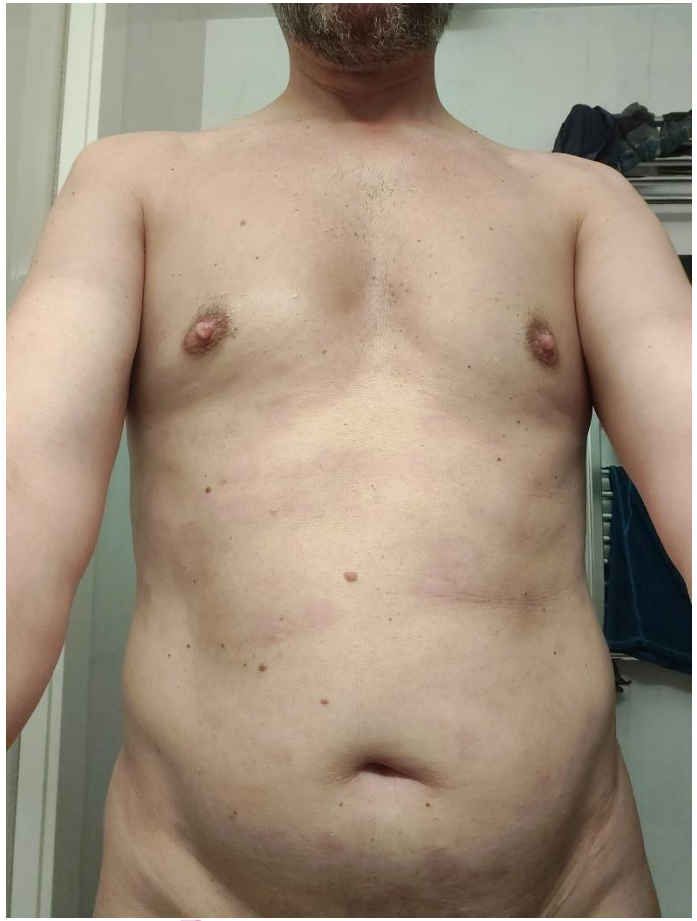

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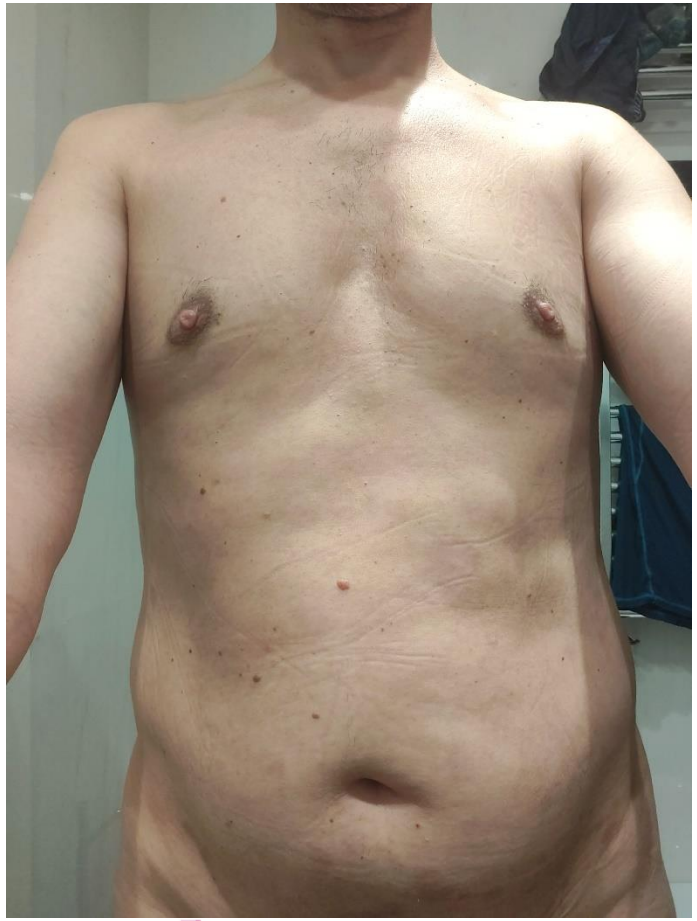
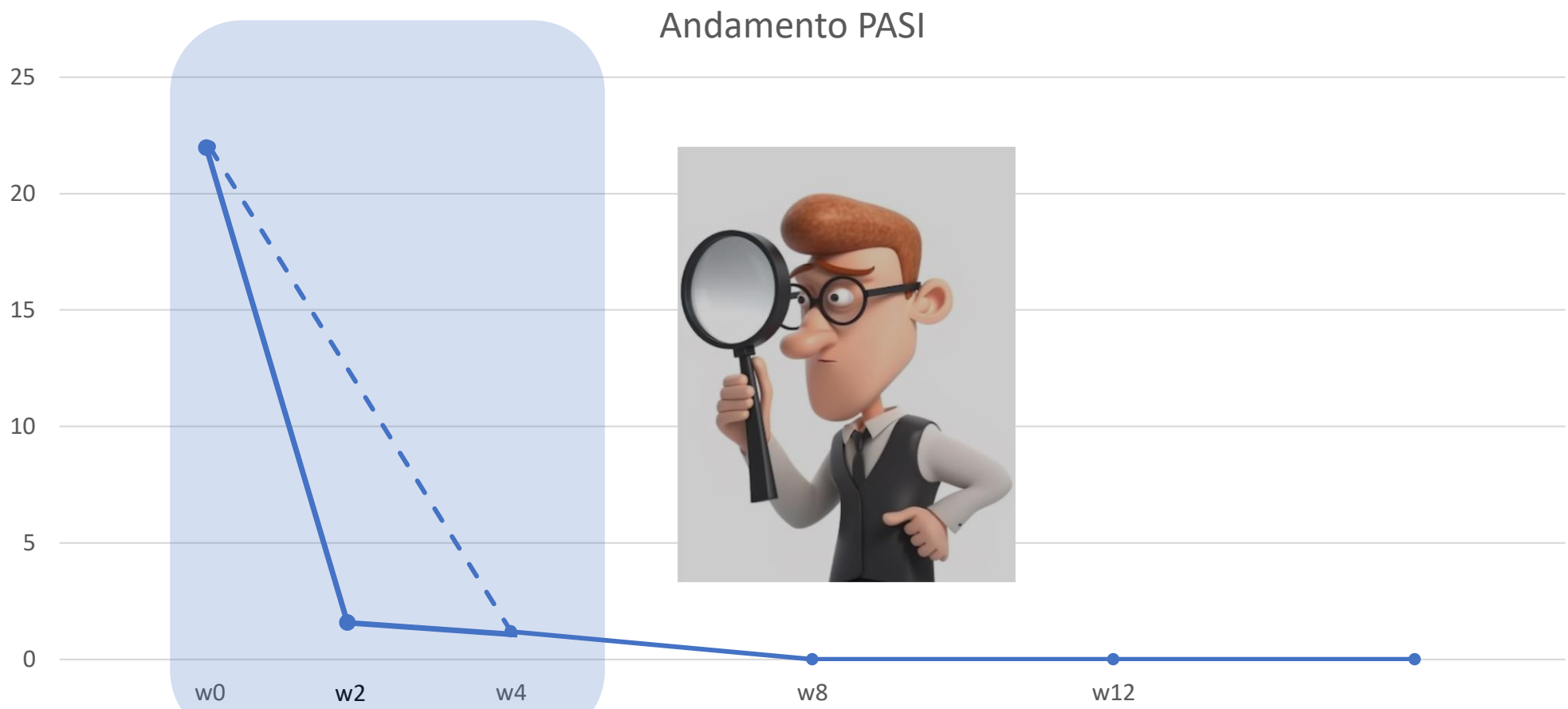
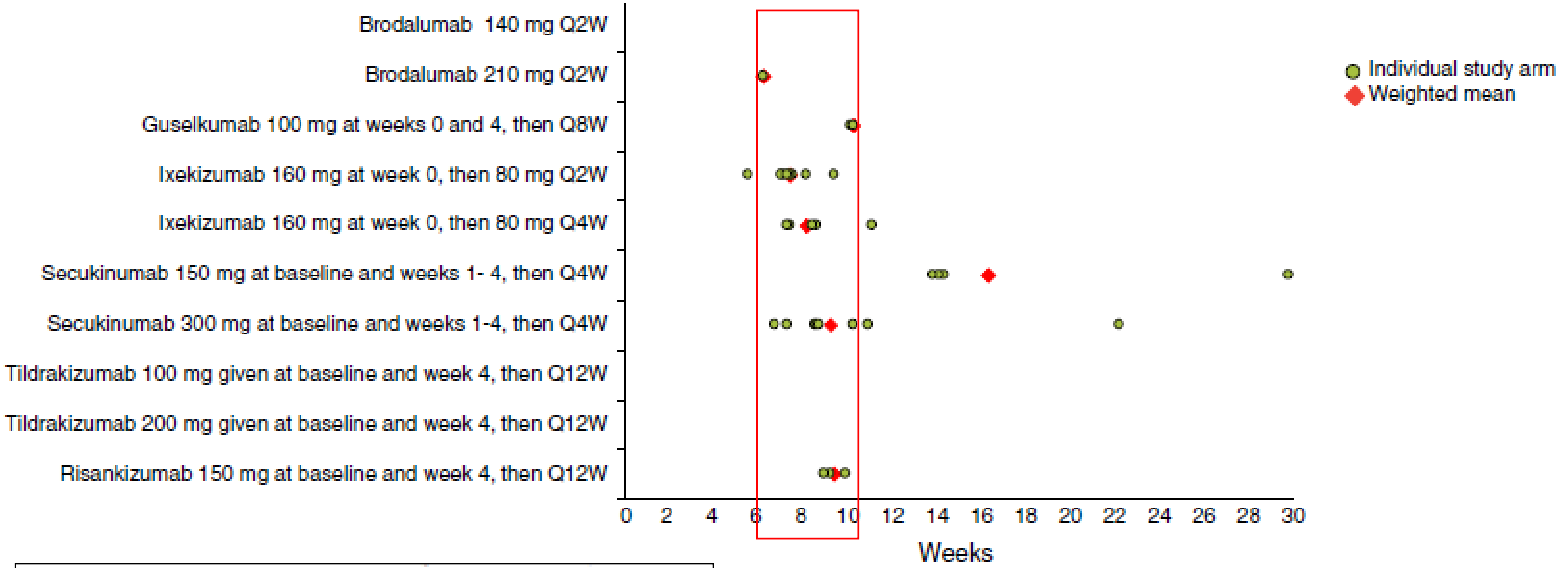


Caso 3 - Alessandro



Systematic review on rapidity of onset of action for interleukin-17 and interleukin-23 inhibitors for psoriasis



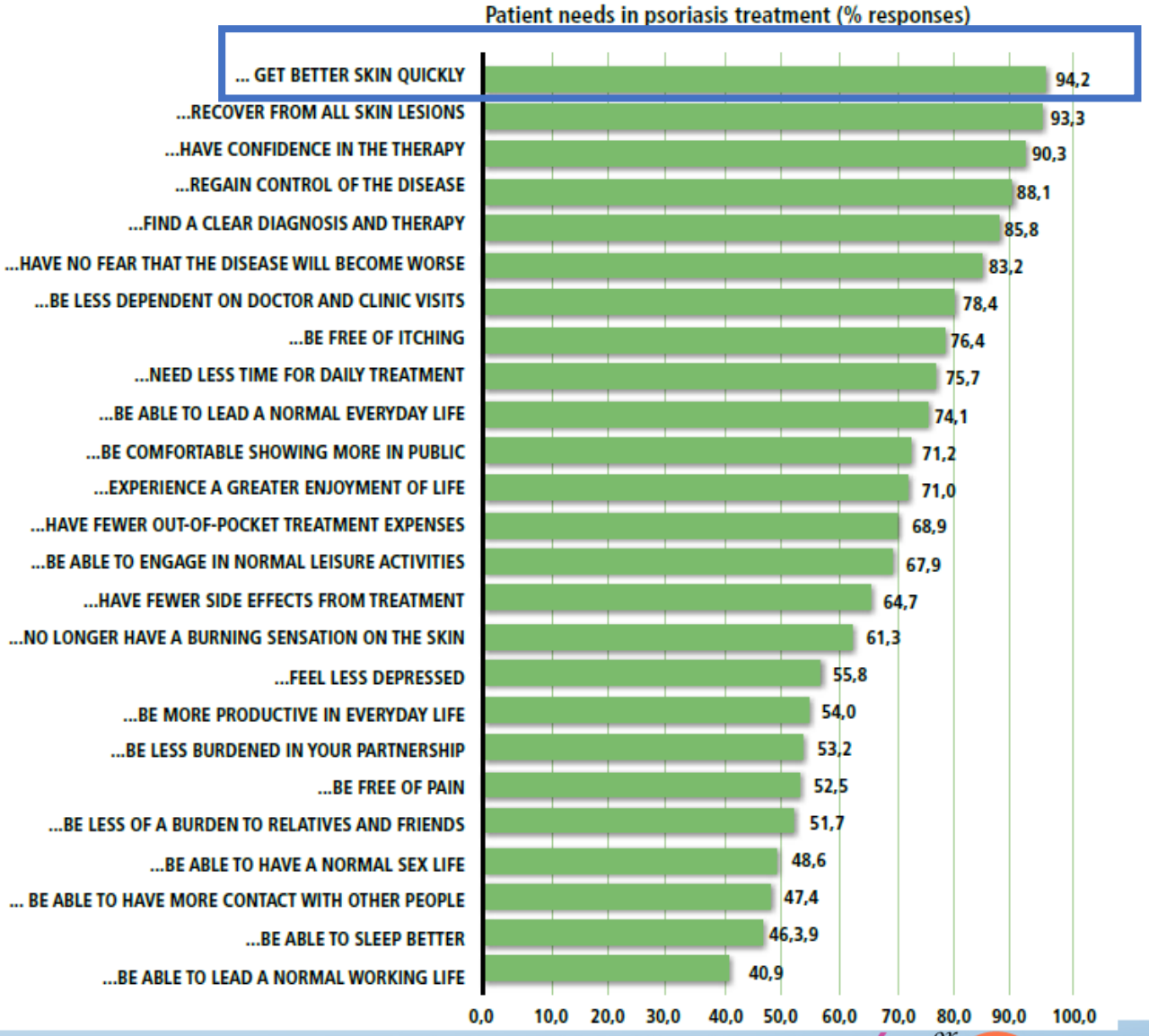
Time until 50% of patients achieve PASI90

JEADV 2020, 34, 39–46

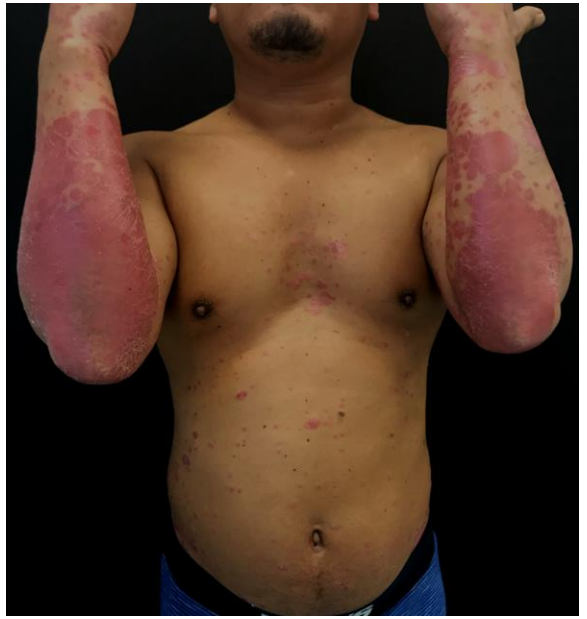
Il punto di vista del paziente

Global report on
PSORIASIS

World Health Organization



La terapia della psoriasi?



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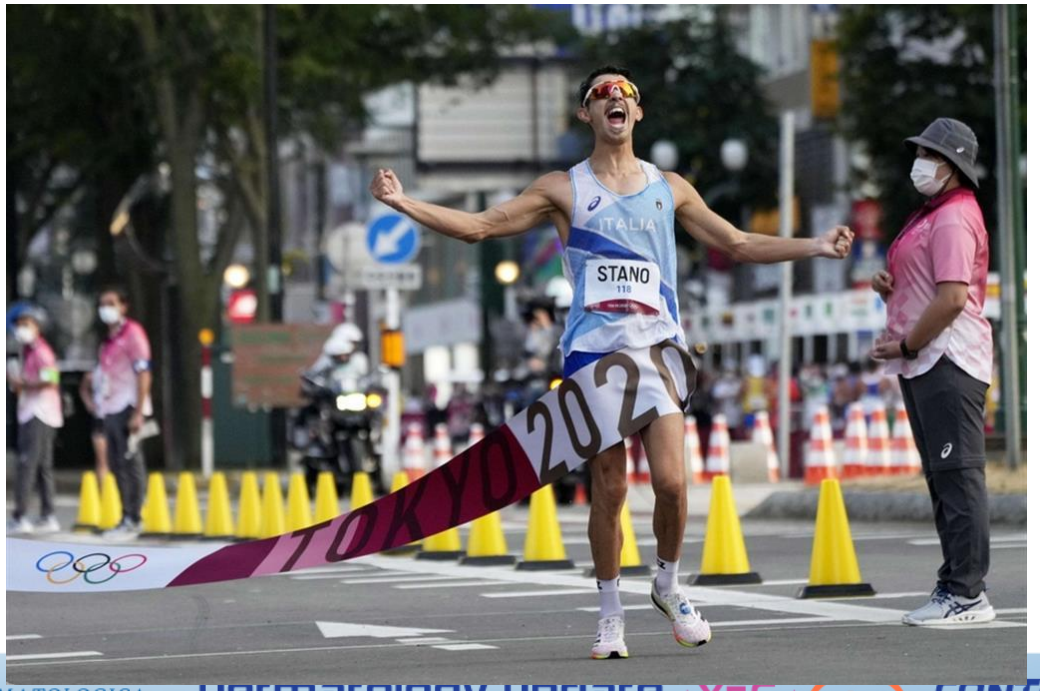


Psoriasi

- Definizione: Malattia infiammatoria della cute con **decorso cronico-recidivante**, nella quale fasi di esacerbazione si alternano a fasi di remissione di durata variabile.

Database con >1000 pazienti affetti da psoriasi

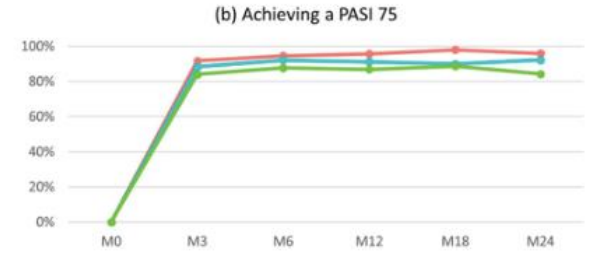
Durata media di malattia: 22,4 anni

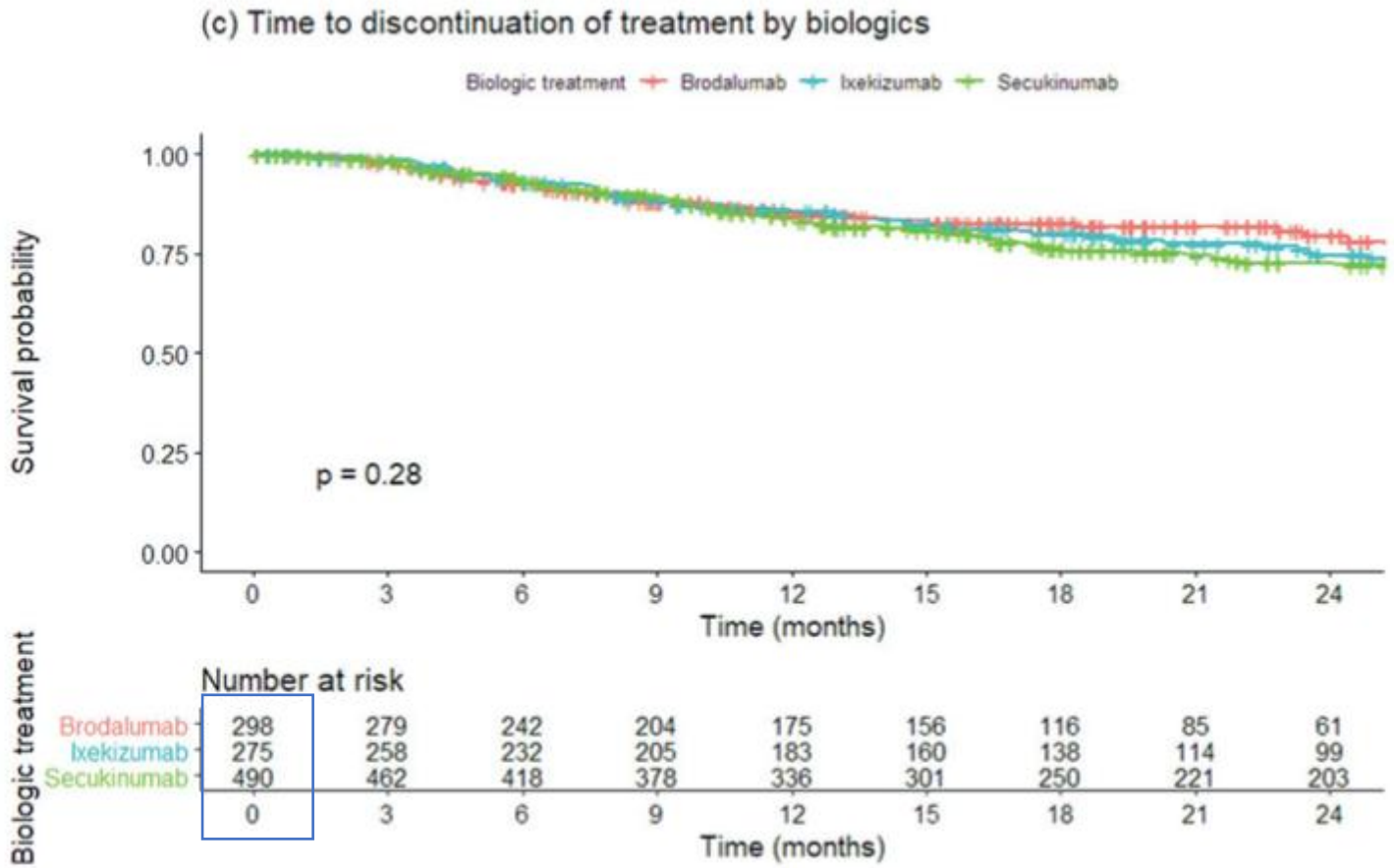
Journal of Dermatological Treatment

ISSN: (Print) (Online) Journal homepage: https://www.tandfonline.com/loi/ijdt20

Efficacy, safety, and drug survival of patients with psoriasis treated with IL-17 inhibitors – brodalumab, ixekizumab, and secukinumab: real-world data from the Czech Republic BIOREP registry

Martina Kojanova, Jan Hugo, Barbora Velackova, Petra Cetkovska, Jorga Fialova, Tomas Dolezal, Martin Tichy & Spyridon Gkalpakiotison behalf of the BIOREP study group





- La risposta alla terapia con brodalumab è sostenuta anche nel lungo termine con tassi di risposta PASI 100 marcatamente superiori rispetto a secukinumab ed ixekizumab
- Drug survival del farmaco in linea con gli altri farmaci anti-IL-17

EXPERT OPINION ON BIOLOGICAL THERAPY
2023, VOL. 23, NO. 4, 365–370
https://doi.org/10.1080/14712598.2023.2193288

Taylor & Francis
Taylor & Francis Group

ORIGINAL RESEARCH

Real-life experience with ixekizumab in plaque psoriasis: a multi-center, retrospective, 3-year study

Giacomo Caldarola [a,b], A Chiricozzi [a,b], M Megna [c], P Dapavo[d], A Giunta[e], M Burlando[f], P Malagoli[g], V Dini[h], M Mariani [i], G Fabbrocini [c], P Quaglino[d], L Bianchi [e], A Parodi[f], K Peris [a,b] and C De Simone[a,b]

[a]Section of Dermatology, Dipartimento Universitario di Medicina e Chirurgia Traslazionale, Università Cattolica del Sacro Cuore, Rome, Italy; [b]Dermatology Unit, Dipartimento di Scienze Mediche e Chirurgiche, Fondazione Policlinico Universitario A. Gemelli IRCCS, Rome, Italy; [c]Department of Clinical Medicine and Surgery, University of Naples Federico II, Naples, Italy; [d]Department of Biomedical Science and Human Oncology, Second Dermatologic Clinic, University of Turin, Turin, Italy; [e]Department of Dermatology, University of Rome Tor Vergata, Rome, Italy; [f]Section of Dermatology, Di.S.Sal. Department of Health Science, San Martino Polyclinic Hospital, University of Genoa, Genoa, Italy; [g]Dermatology Unit, Azienda Ospedaliera San Donato Milanese, Milan, Italy; [h]Dermatology Unit, Department of Clinical and Experimental Medicine, University of Pisa, Pisa, Italy; [i]Section of Hygiene, University Department of Health Sciences and Public Health, Rome, Italy

306 pazienti

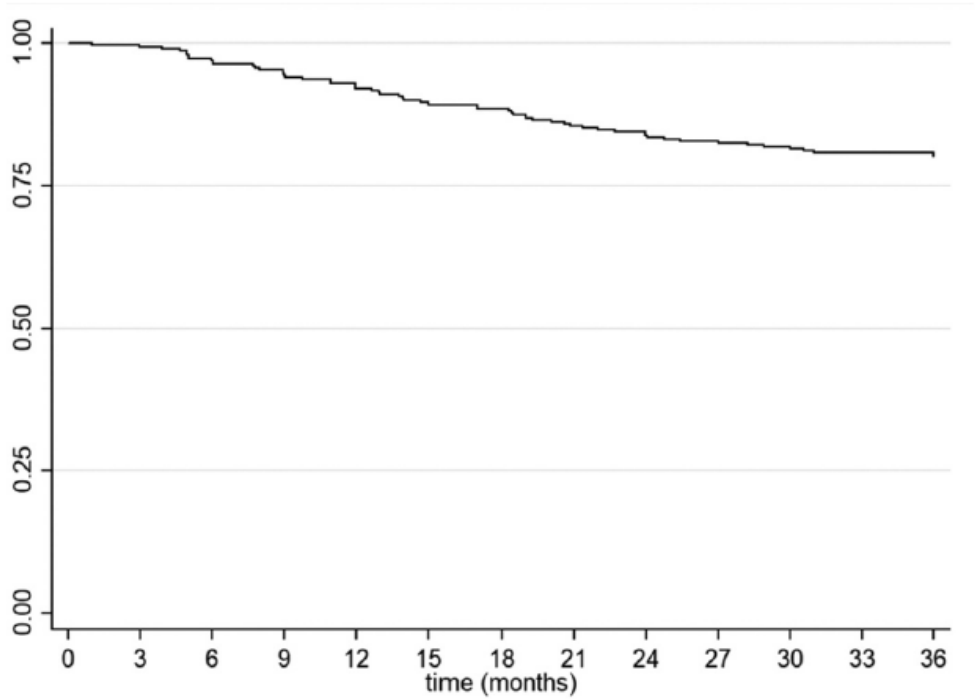


Figure 1. Kaplan Meier survival curve for any cause of ixekizumab discontinuation.

Table 4. Cox regression analysis evaluating predictive factors of drug survival for any reason of discontinuation.

Characteristics		HR (95% CI)	p-value
Age		1,01 (0,99–1,03)	0,348
Gender	Male	Ref	0,641
	Female	0,88 (0,52–1,50)	
BMI		1,03 (0,99–1,08)	0,175
Arthropathy	No	Ref	0,807
	Yes	1,07 (0,63–1,81)	
PASI at baseline		1,00 (0,97–1,03)	0,999
Previous biological drug	No	Ref	0,056
	Yes	1,72 (0,99–2,99)	

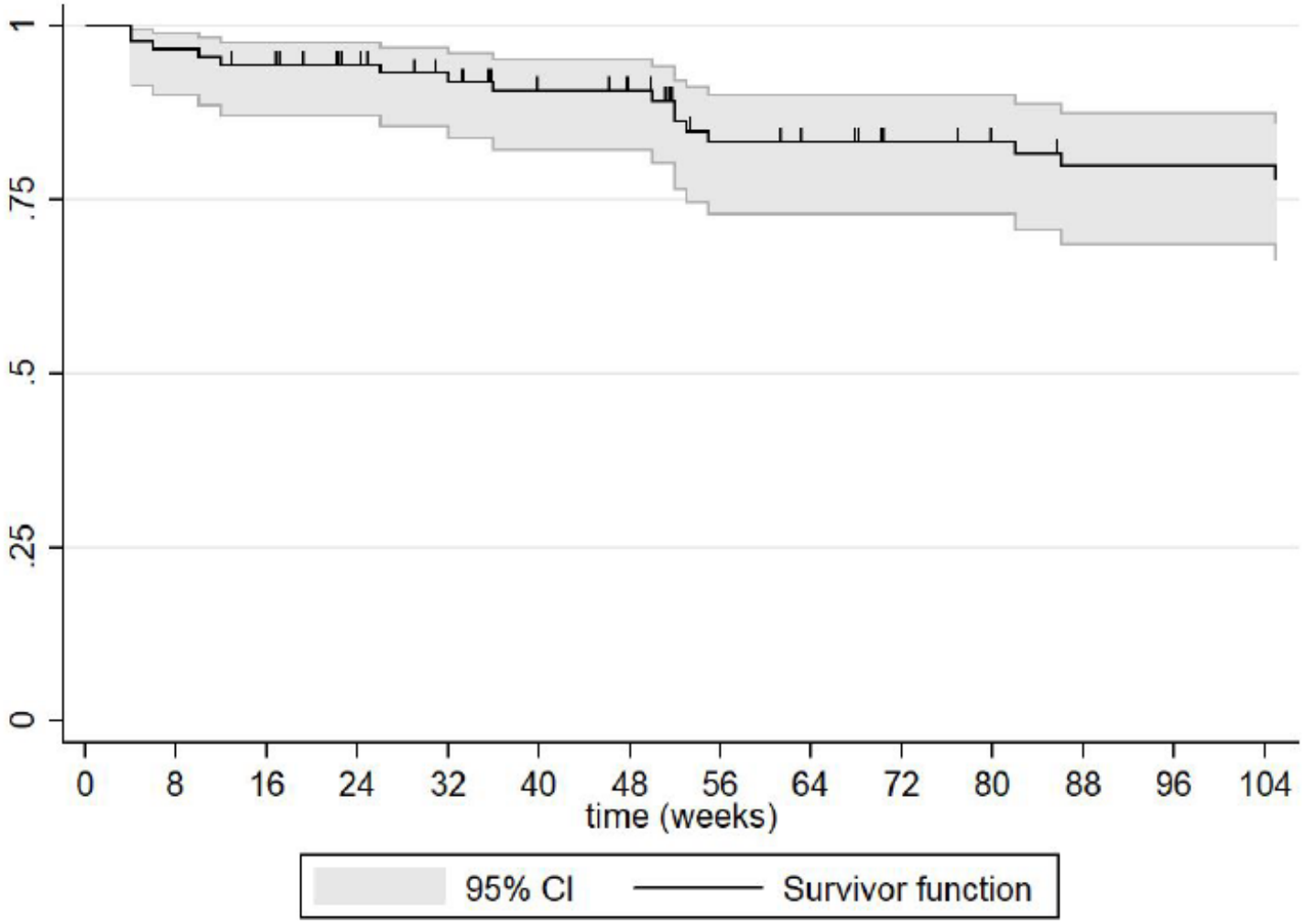
Abbreviations: BMI: body mass index; HR: hazard ratio; CI: confidence interval; Ref: reference value.

Table 3. Survival fraction for any reason of ixekizumab discontinuation (expressed in % CI95% inf and sup).

Reasons of discontinuation	1 year	2 years	3 years
All reasons	92.11 (88.46–94.64)	83.85 (79.20–87.54)	80.19 (75.23–84.25)
Ineffectiveness	95.60 (92.54–97.42)	93.13 (89.56–95.52)	92.37 (88.64–94.91)
Adverse events	96.35 (93.51–97.96)	90.04(85.97–92.97)	86.82(82.33–90.23)

Submitted paper

Long-Term Effectiveness of Brodalumab for the Treatment of Moderate-to-Severe Psoriasis: A Real-Life Multi-Center Study up to 3 Years in Lazio region, Italy



90 pazienti

- In detail, after 52 and 104 weeks, 86.32% and 78.09% of patients, respectively, were still receiving brodalumab.
- These results demonstrated a favorable drug survival rate, with a significant proportion of patients remaining on the treatment throughout the observation period.

Caso 4 - Paola

F, 56 aa

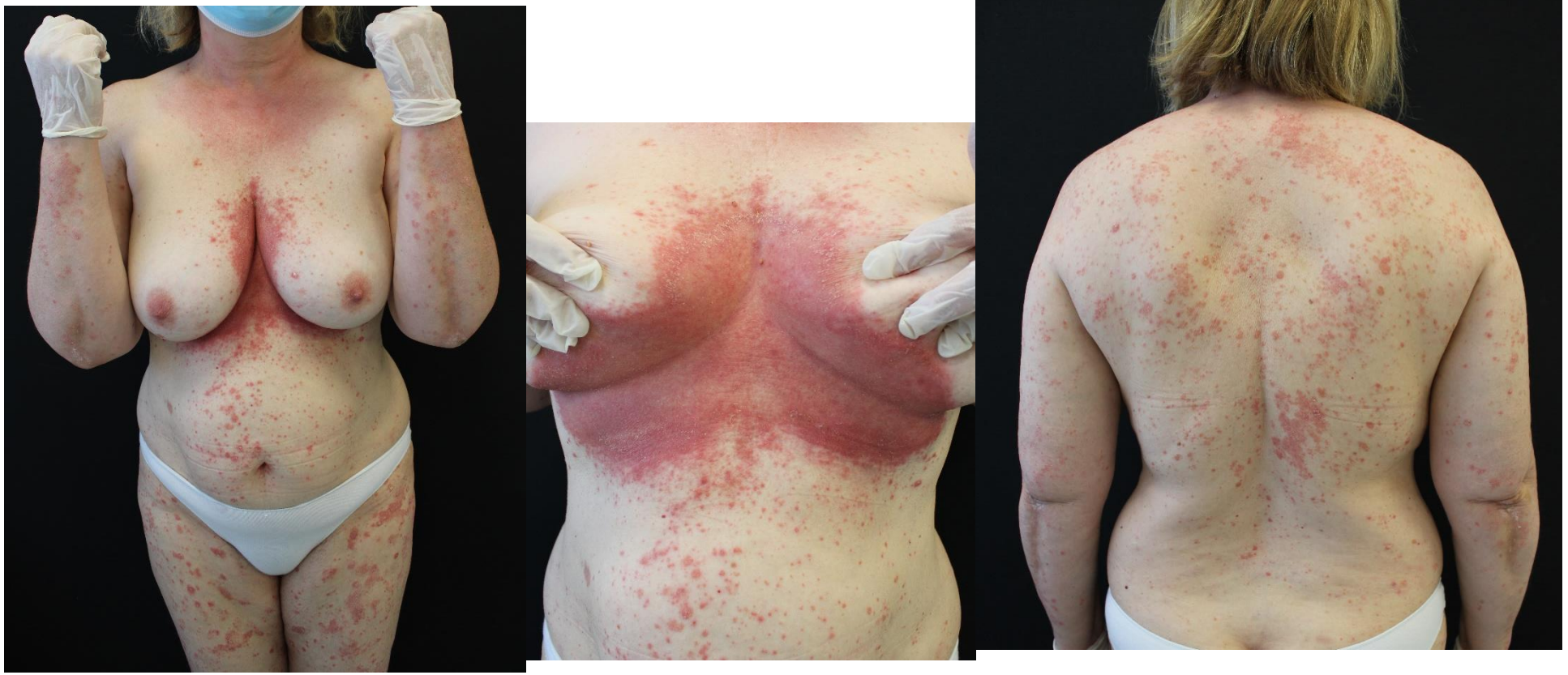
Comorbidità

- nessuna

Precedenti terapie

- 2 cicli di ciclosporina con rapide recidive alla sospensione del farmaco
- un ciclo di MTX sospeso a settembre 2019 per scarso beneficio.

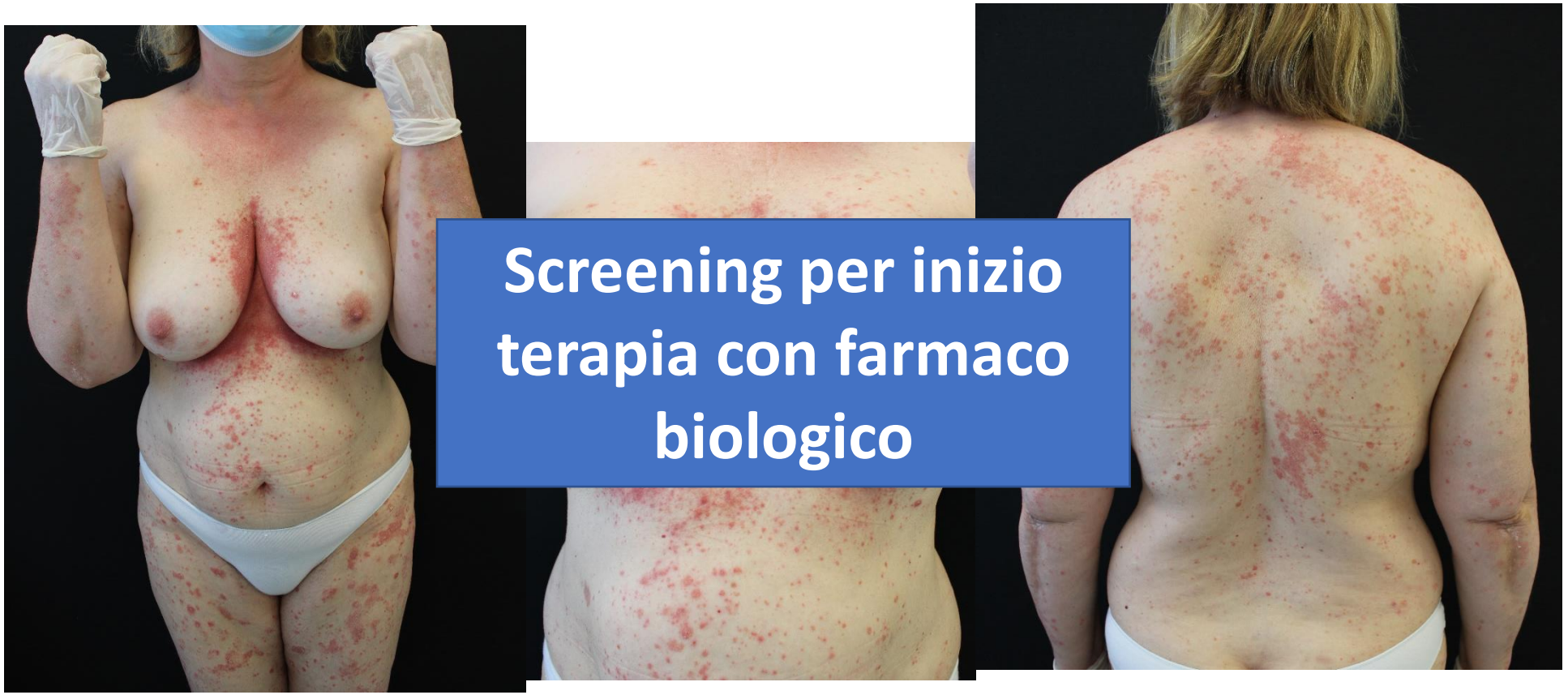
Caso 4 - Paola



PASI = 20

DLQI = 21

Caso 4 - Paola

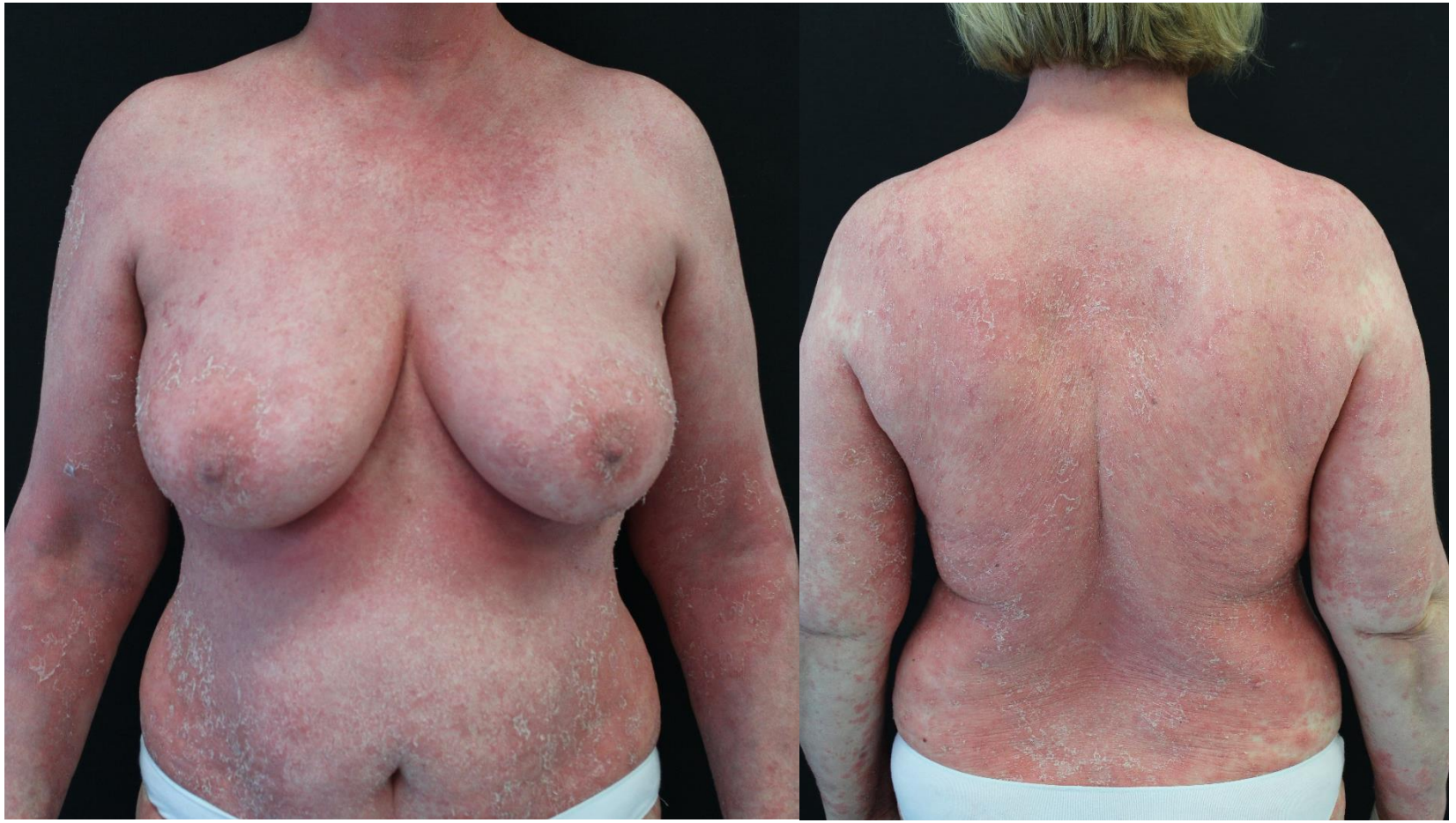


Screening per inizio terapia con farmaco biologico

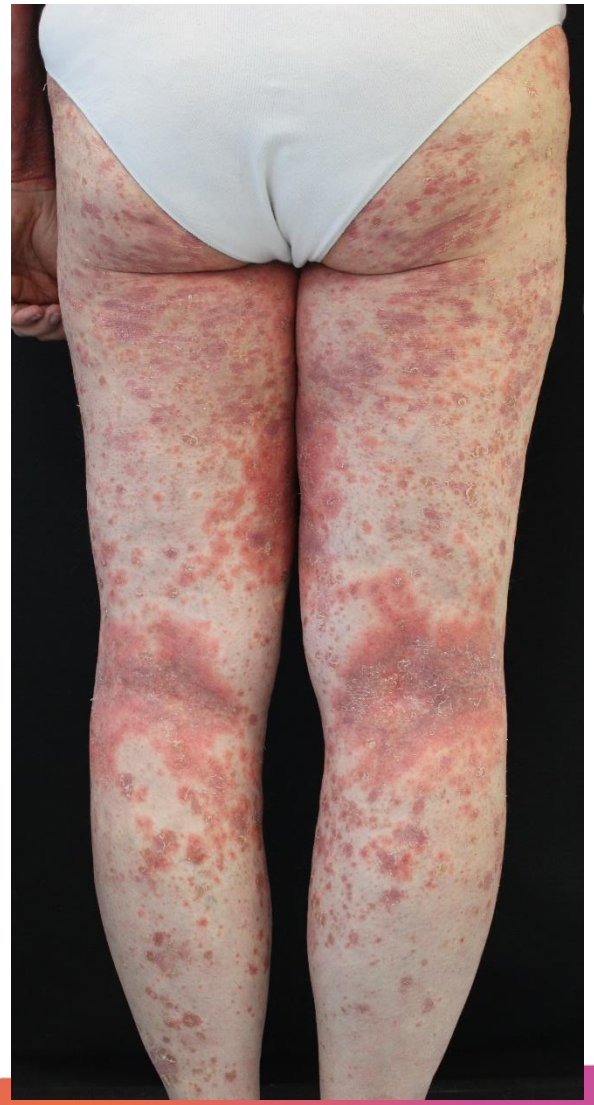
PASI = 20

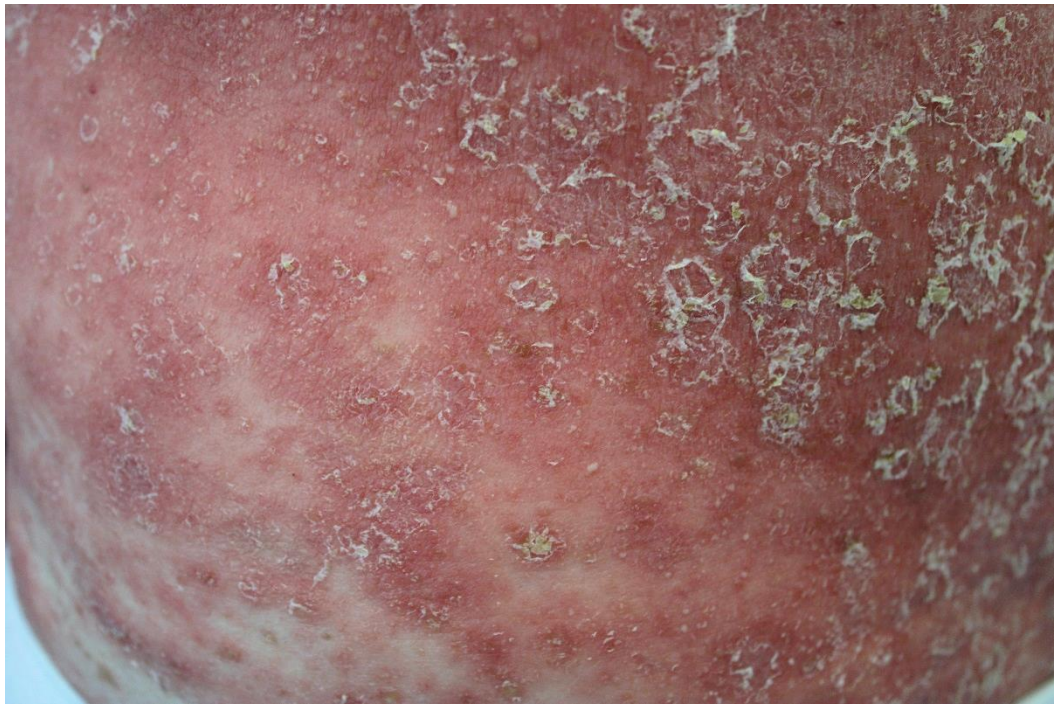
DLQI = 21

Caso 4 - Paola

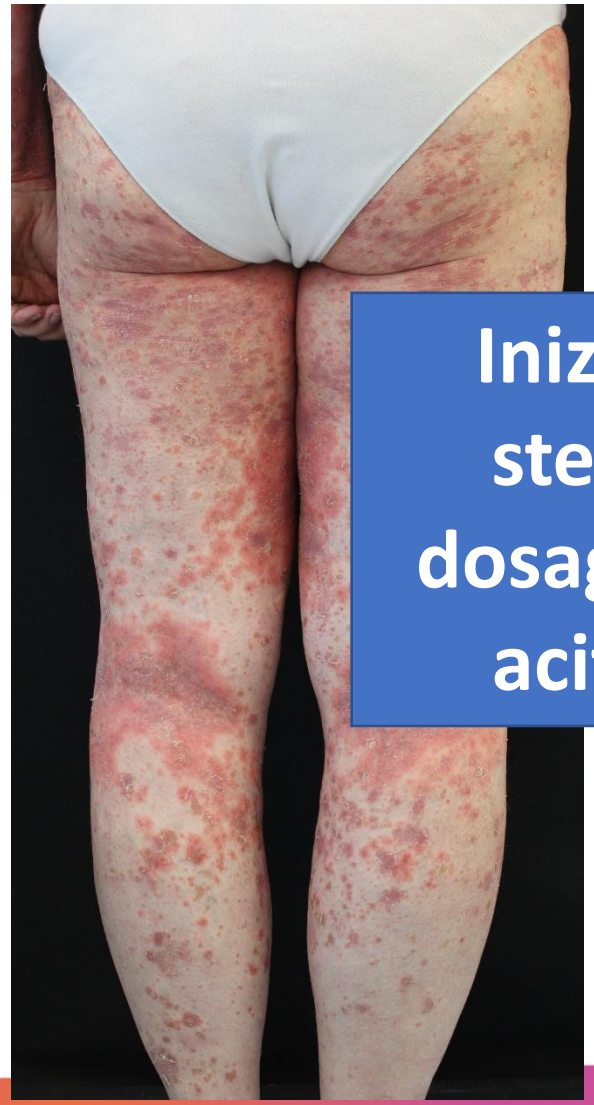


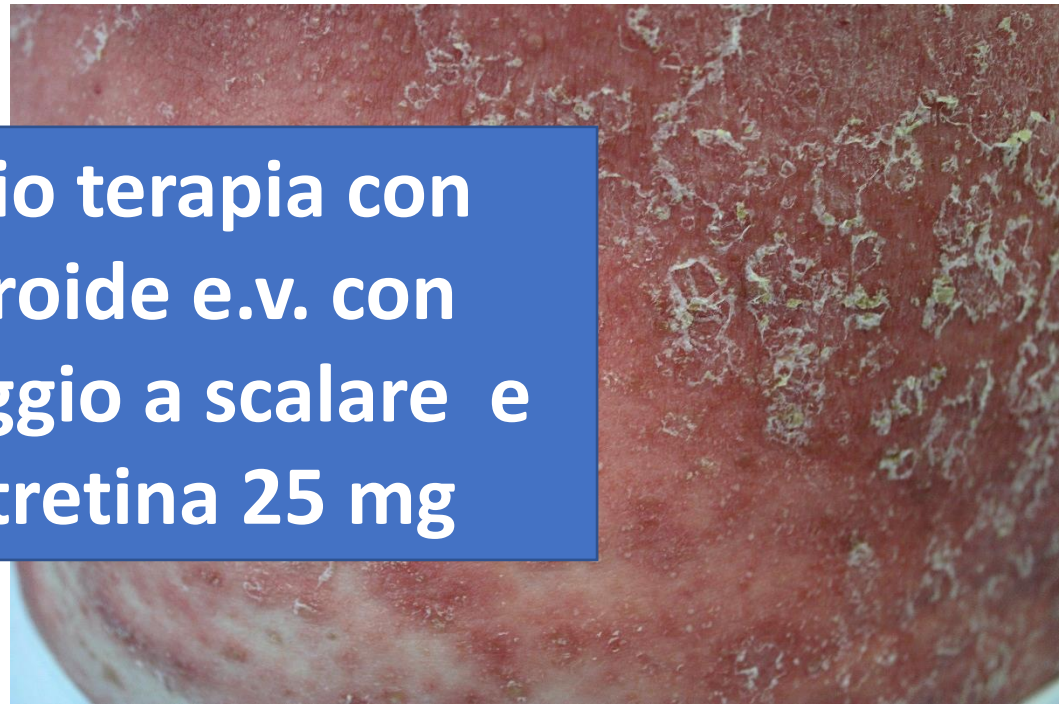
Caso 4 - Paola





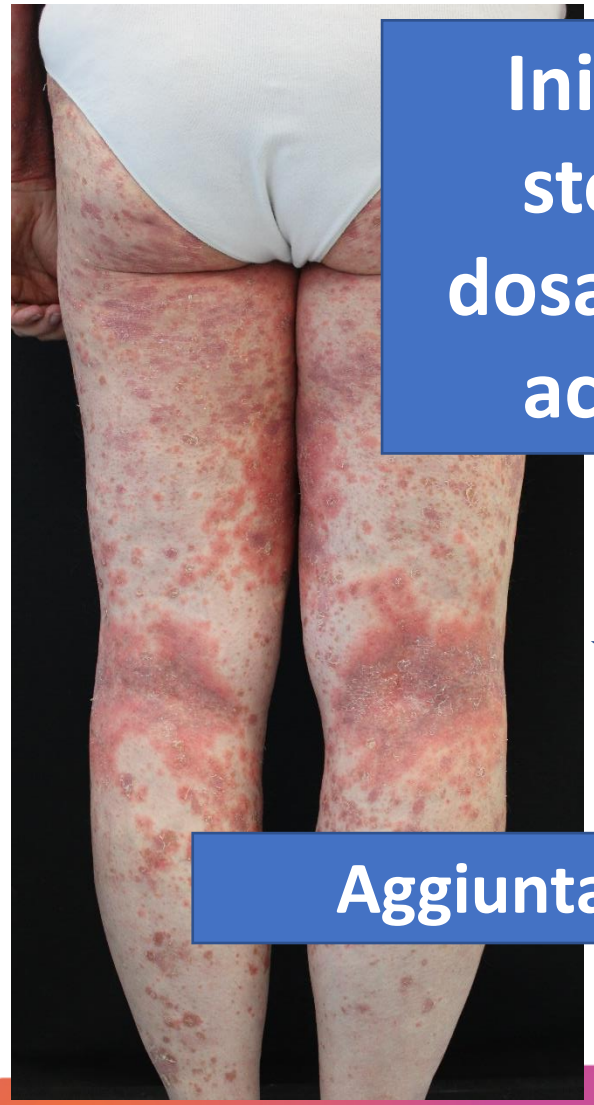
Caso 4 - Paola





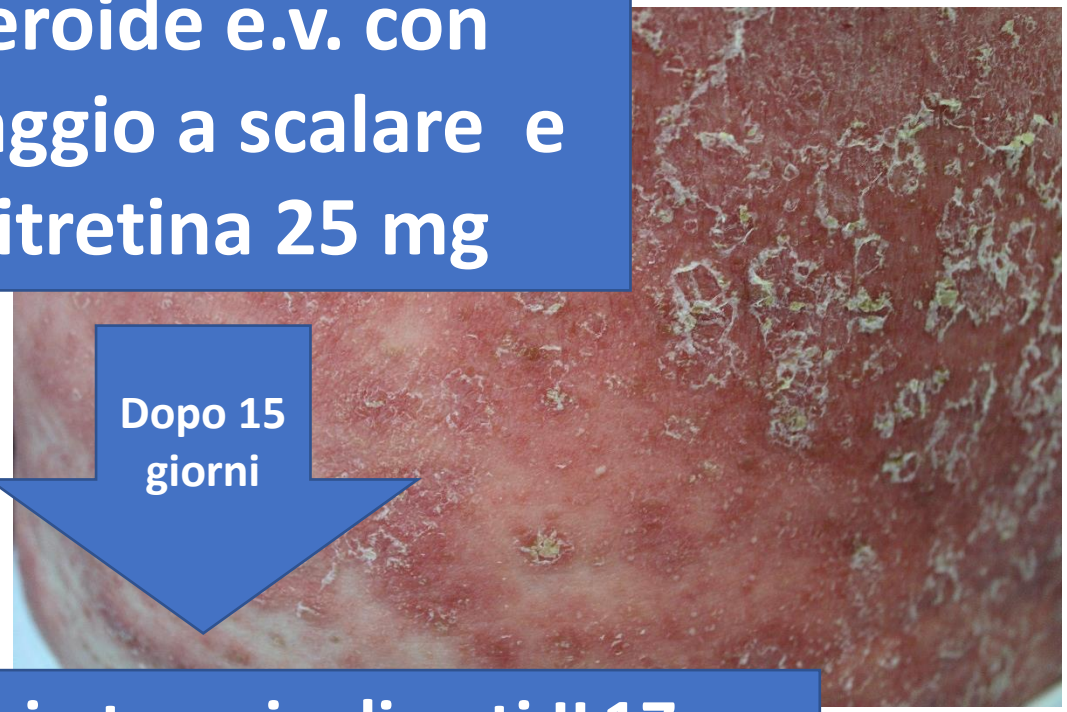
Inizio terapia con steroide e.v. con dosaggio a scalare e acitretina 25 mg

Caso 4 - Paola



Inizio terapia con steroide e.v. con dosaggio a scalare e acitretina 25 mg

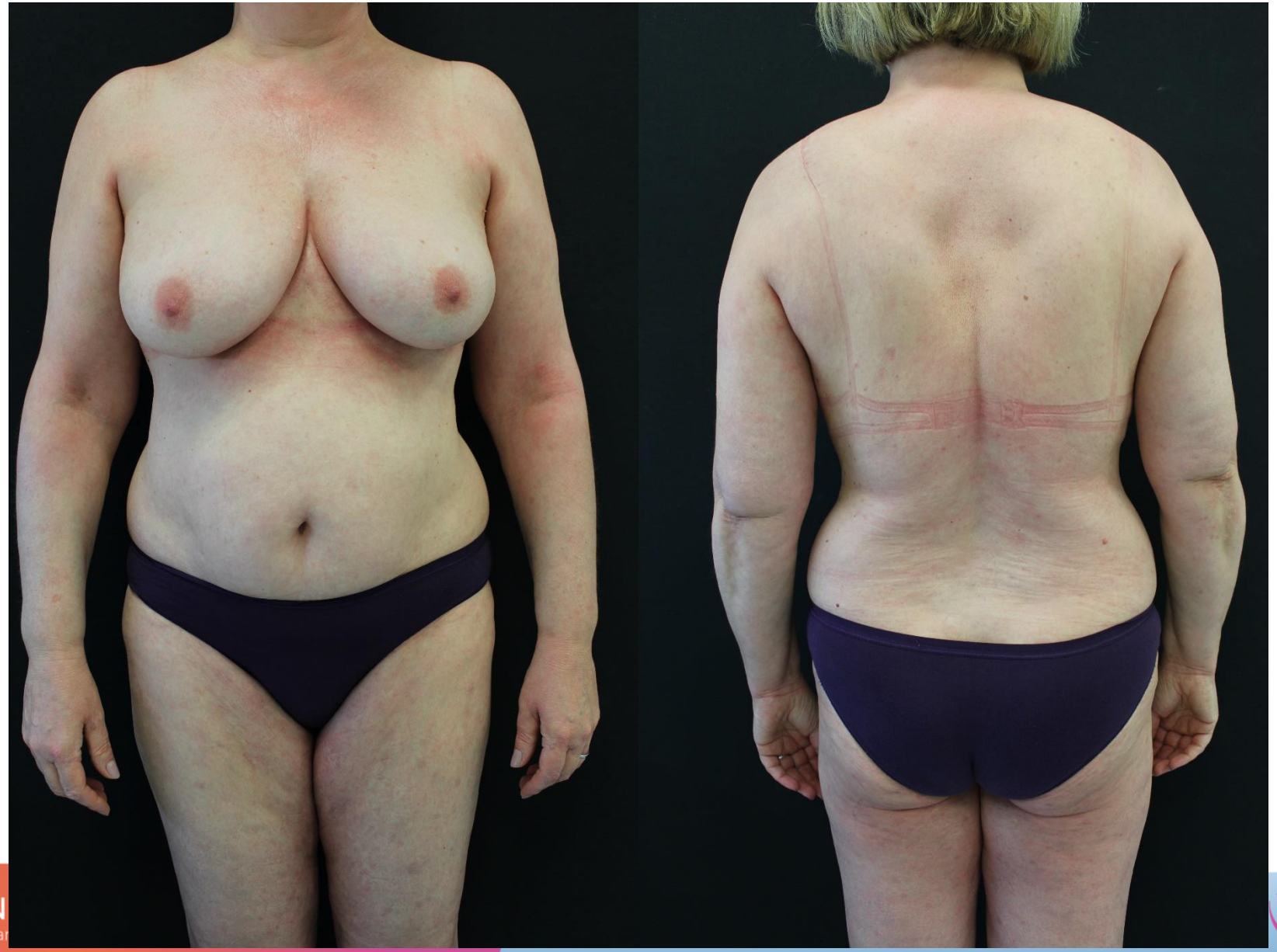
Dopo 15 giorni



Aggiunta in terapia di anti IL17

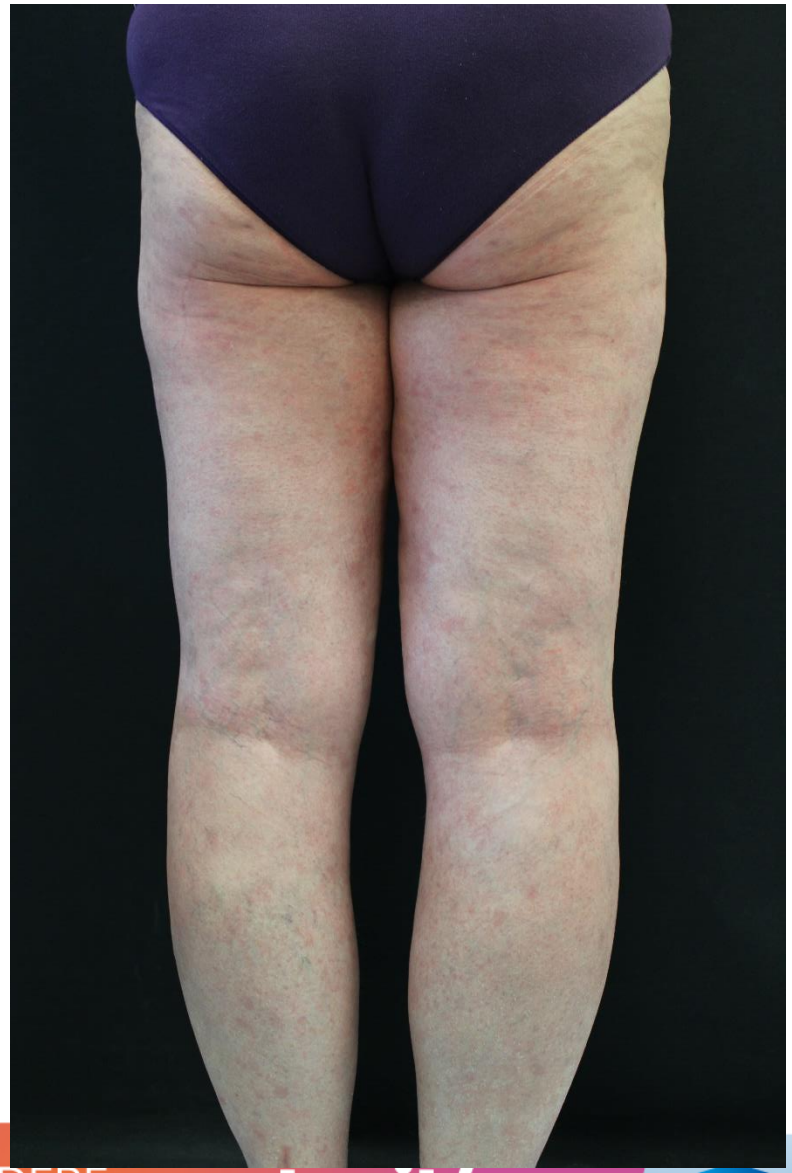
Caso 4 - Paola

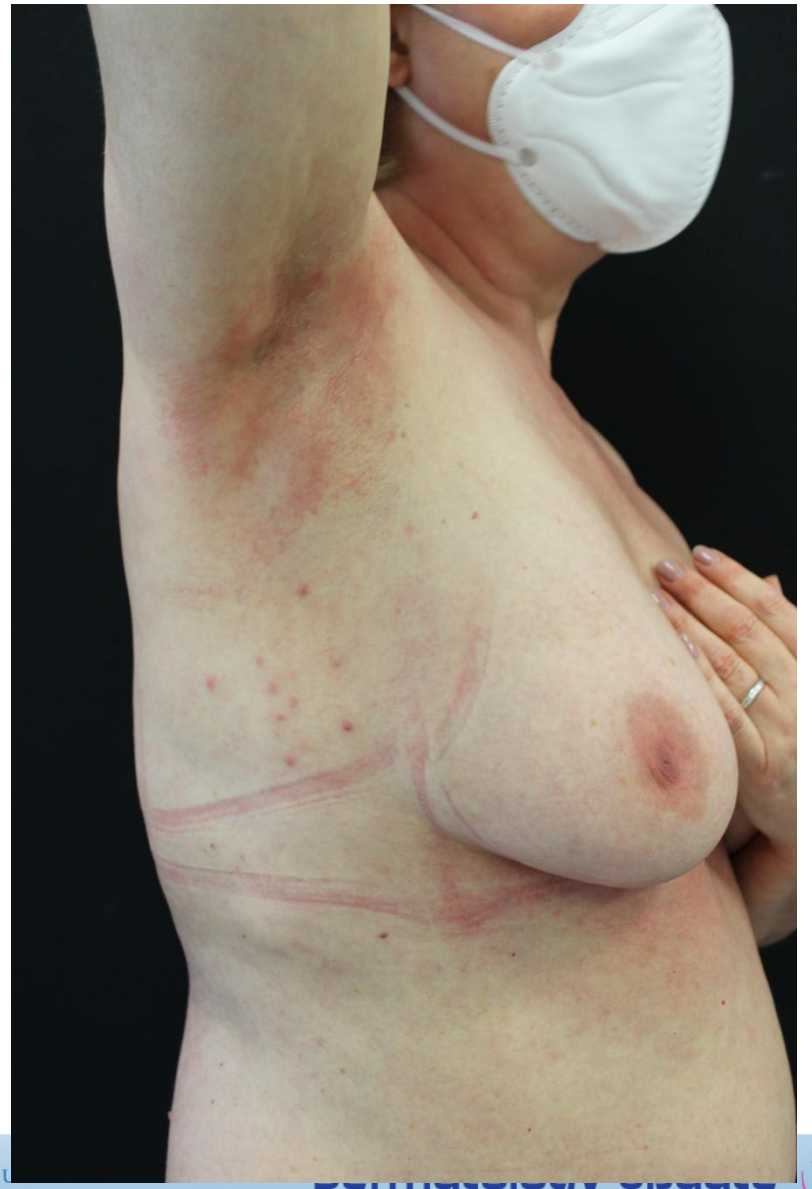
Week 4



Caso 4 - Paola

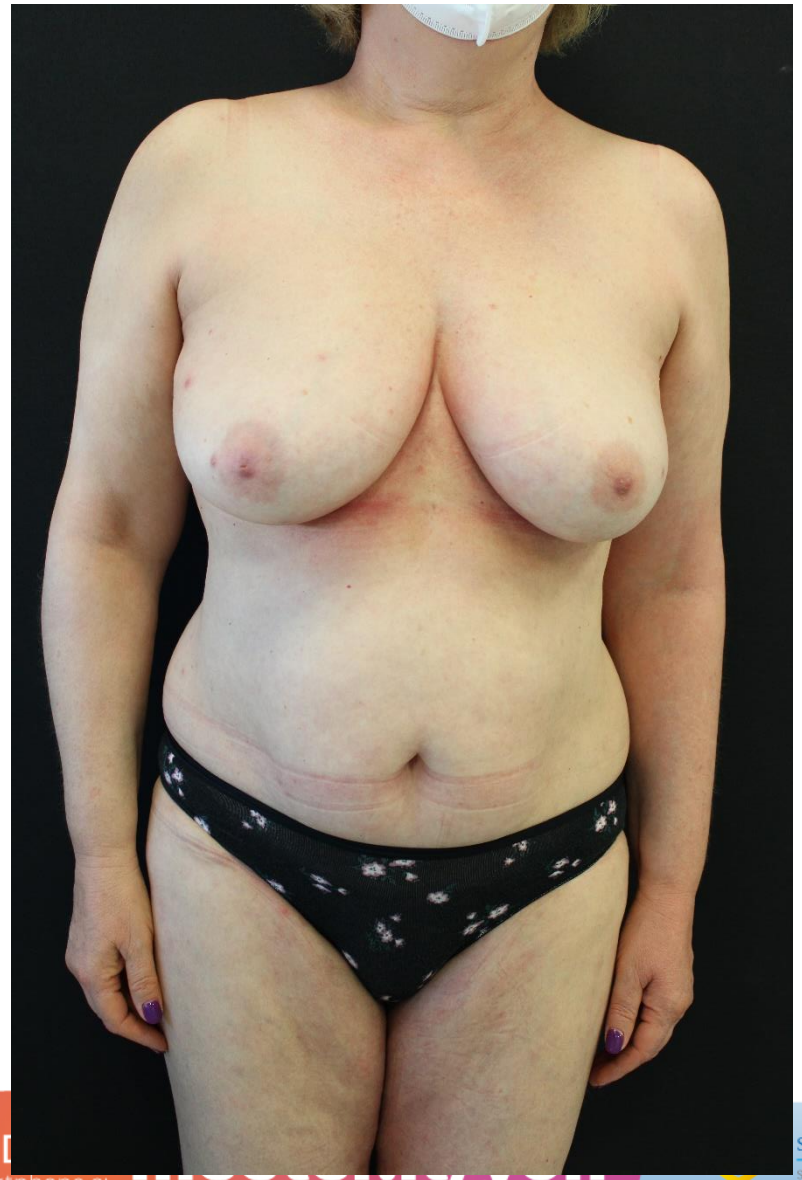
Week 4

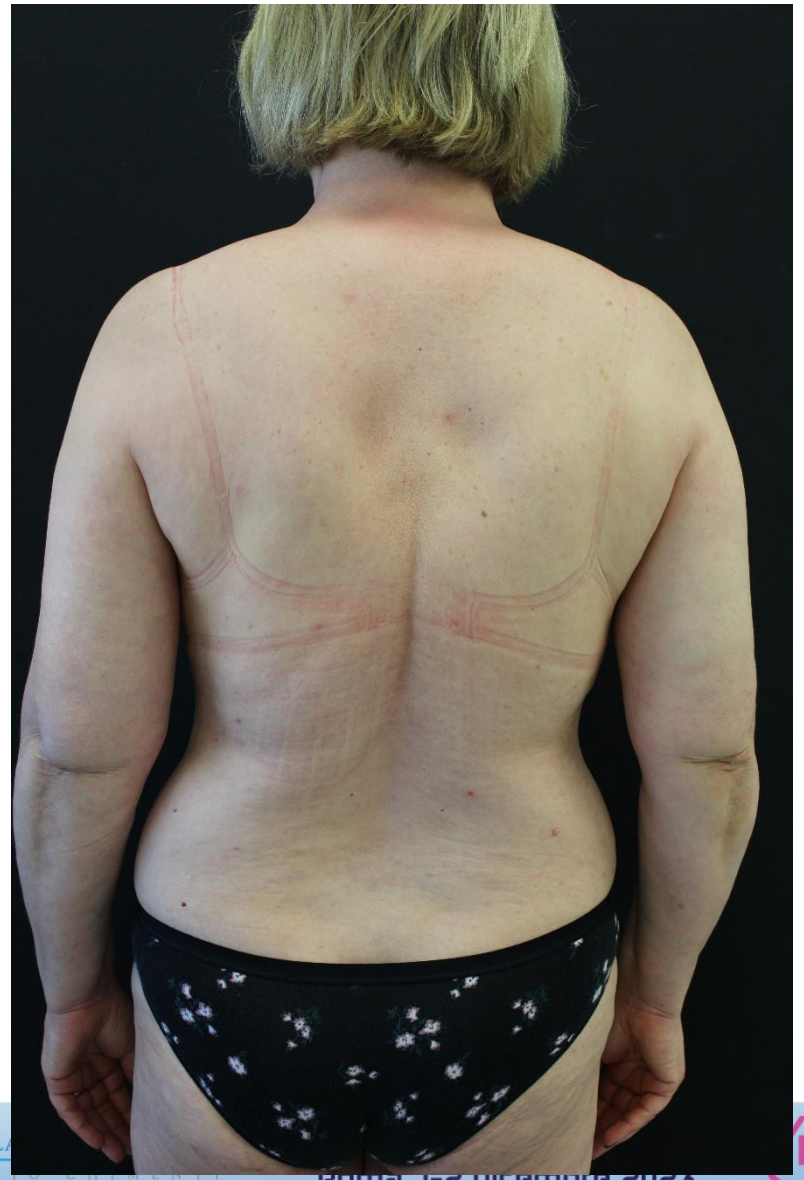




Caso 4 - Paola

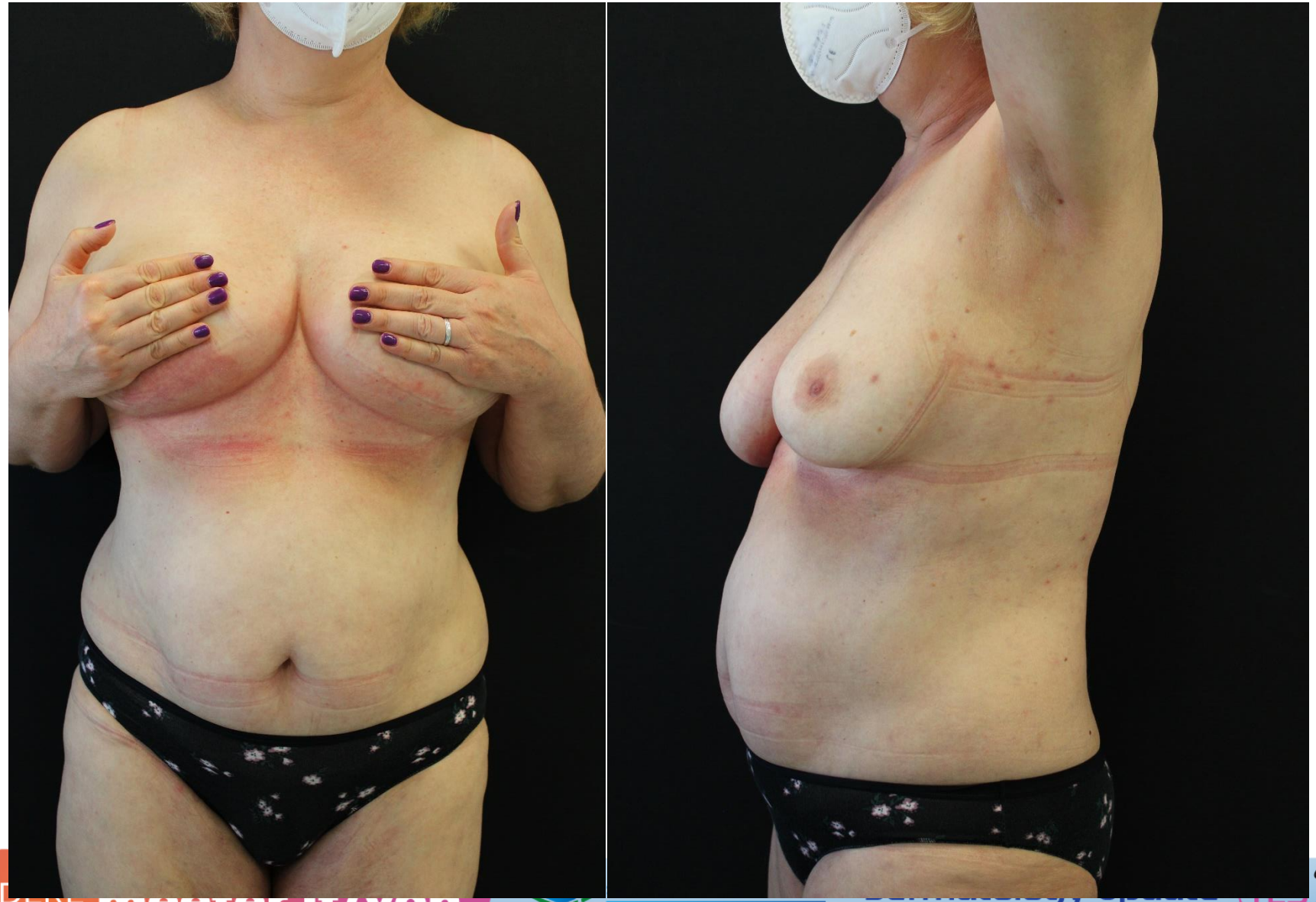
Week 12



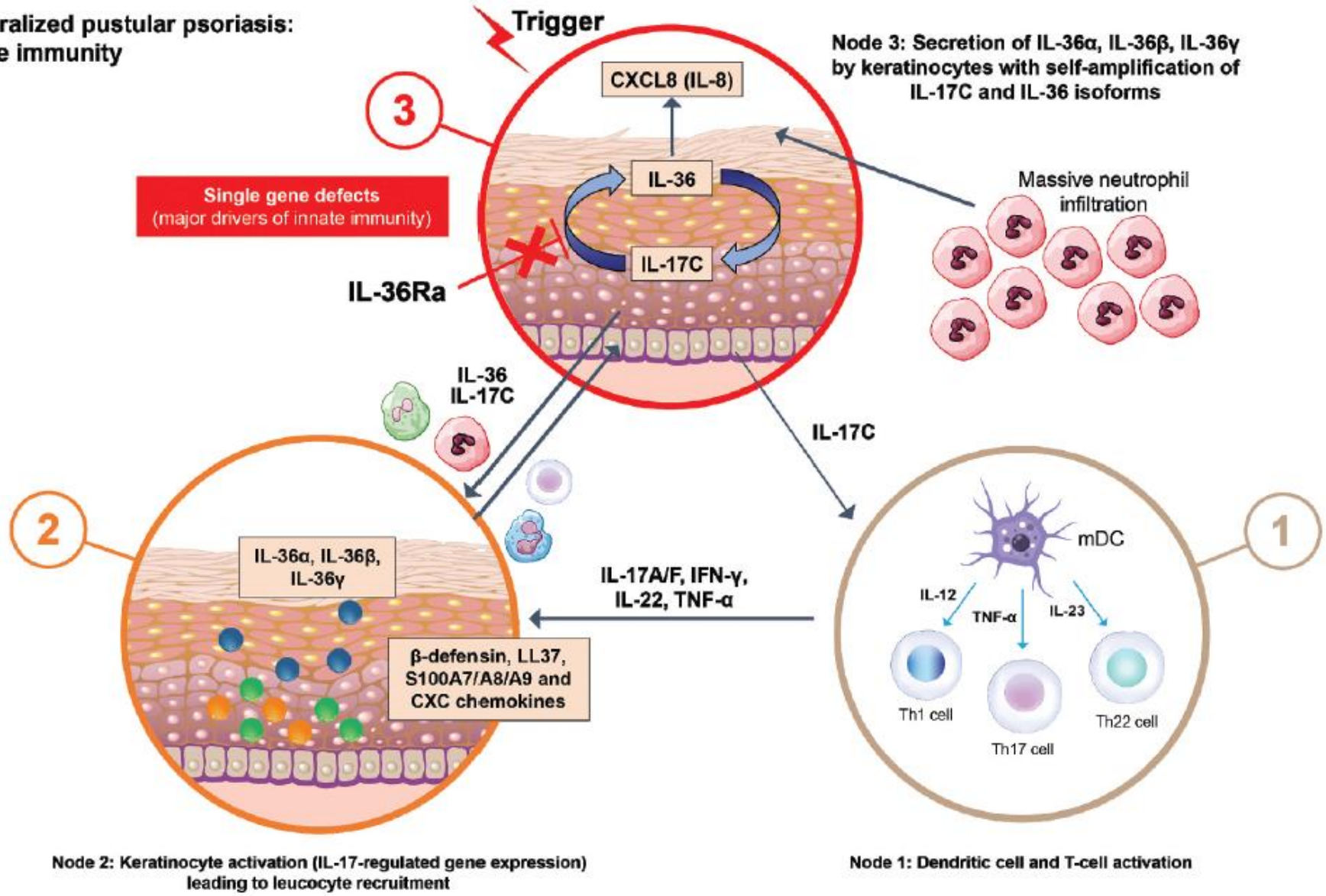


Caso 4 - Paola

Week 12



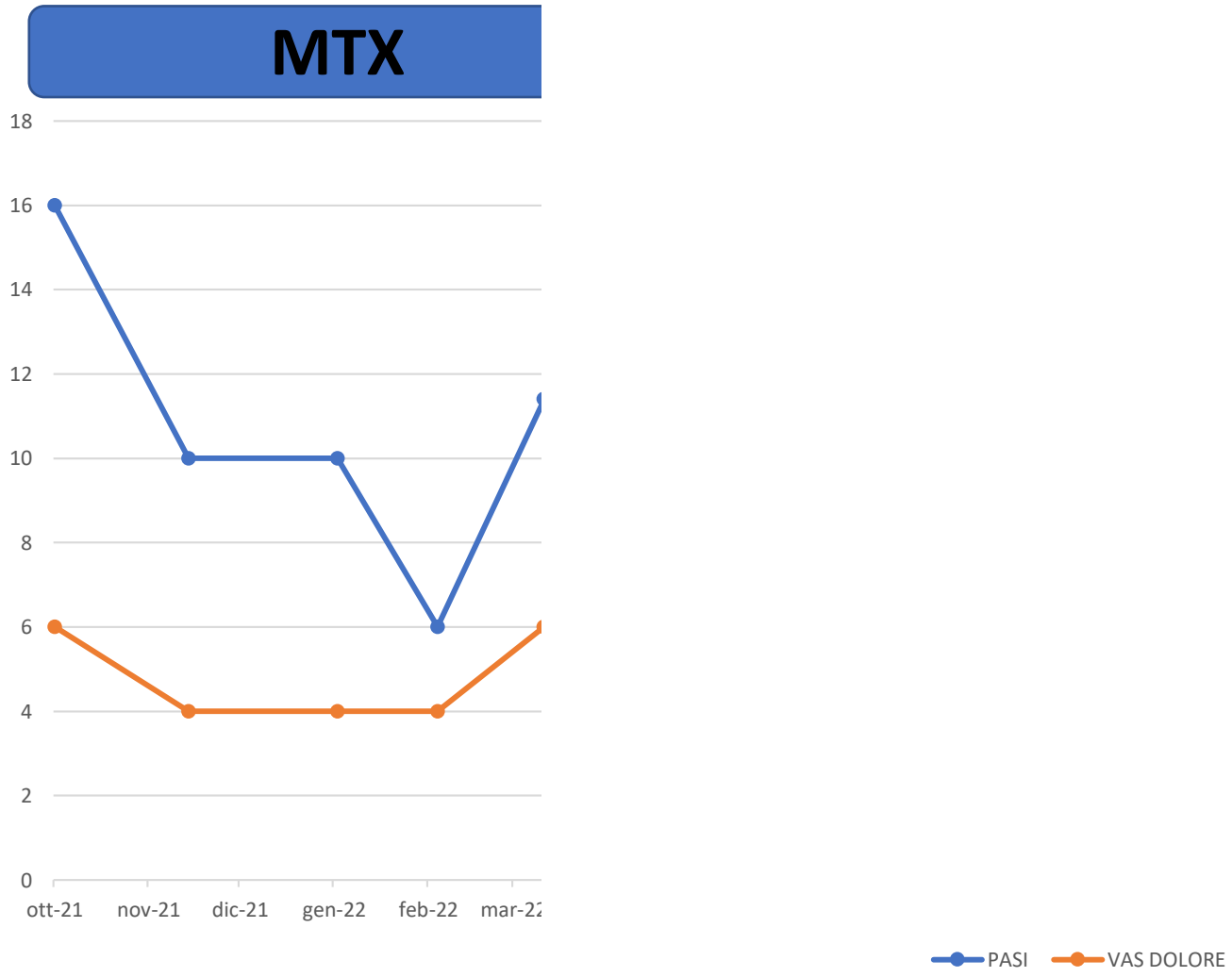
Generalized pustular psoriasis:
Innate immunity



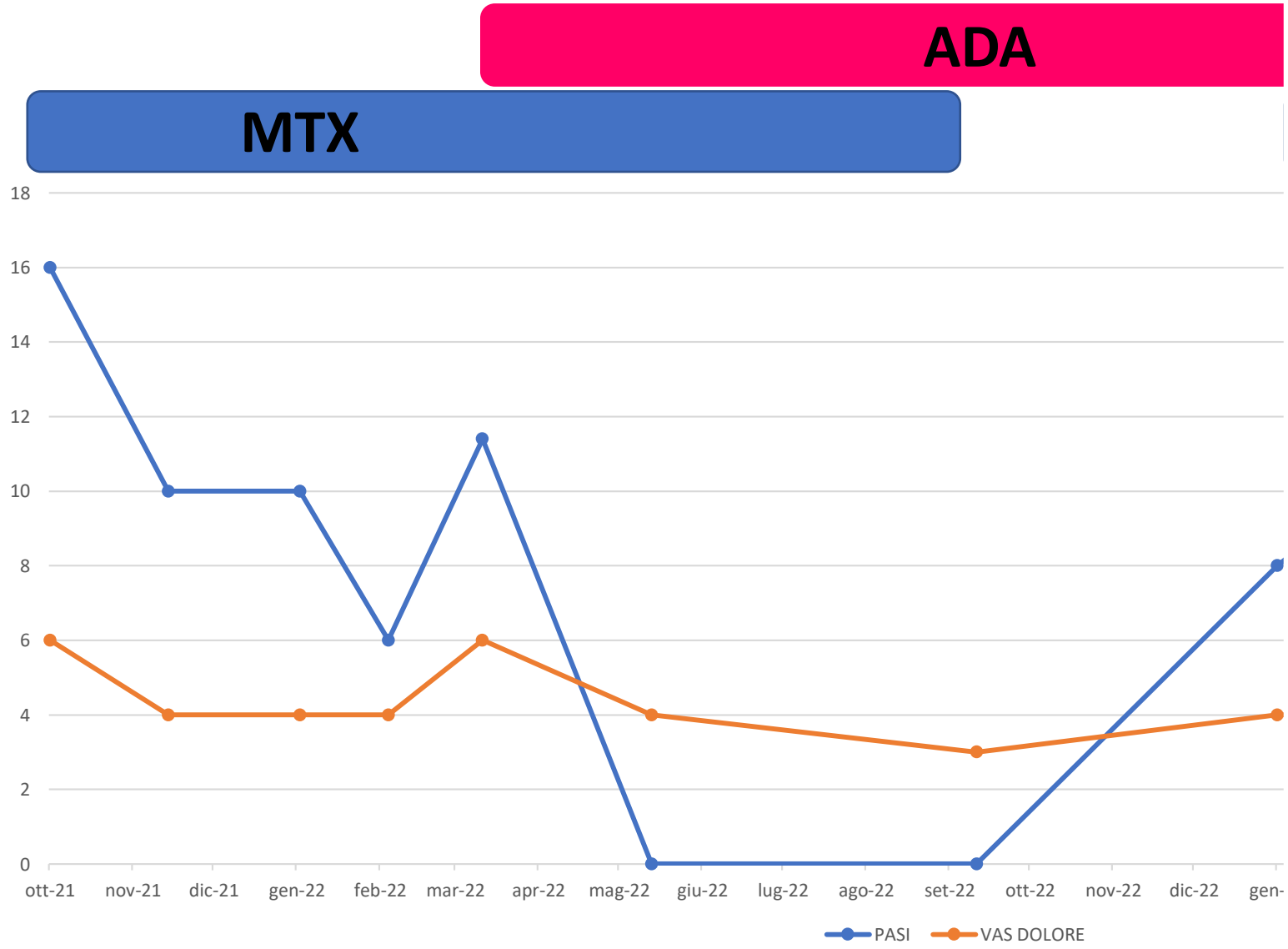
Caso 5 - Mirela

- 50 anni
- BMI 27,8
- In anamnesi, morbo di Basedow ed emorragia subaracnoidea nel 2021.
- Paziente affetta da psoriasi in placche e artrite psoriasica dal 2010

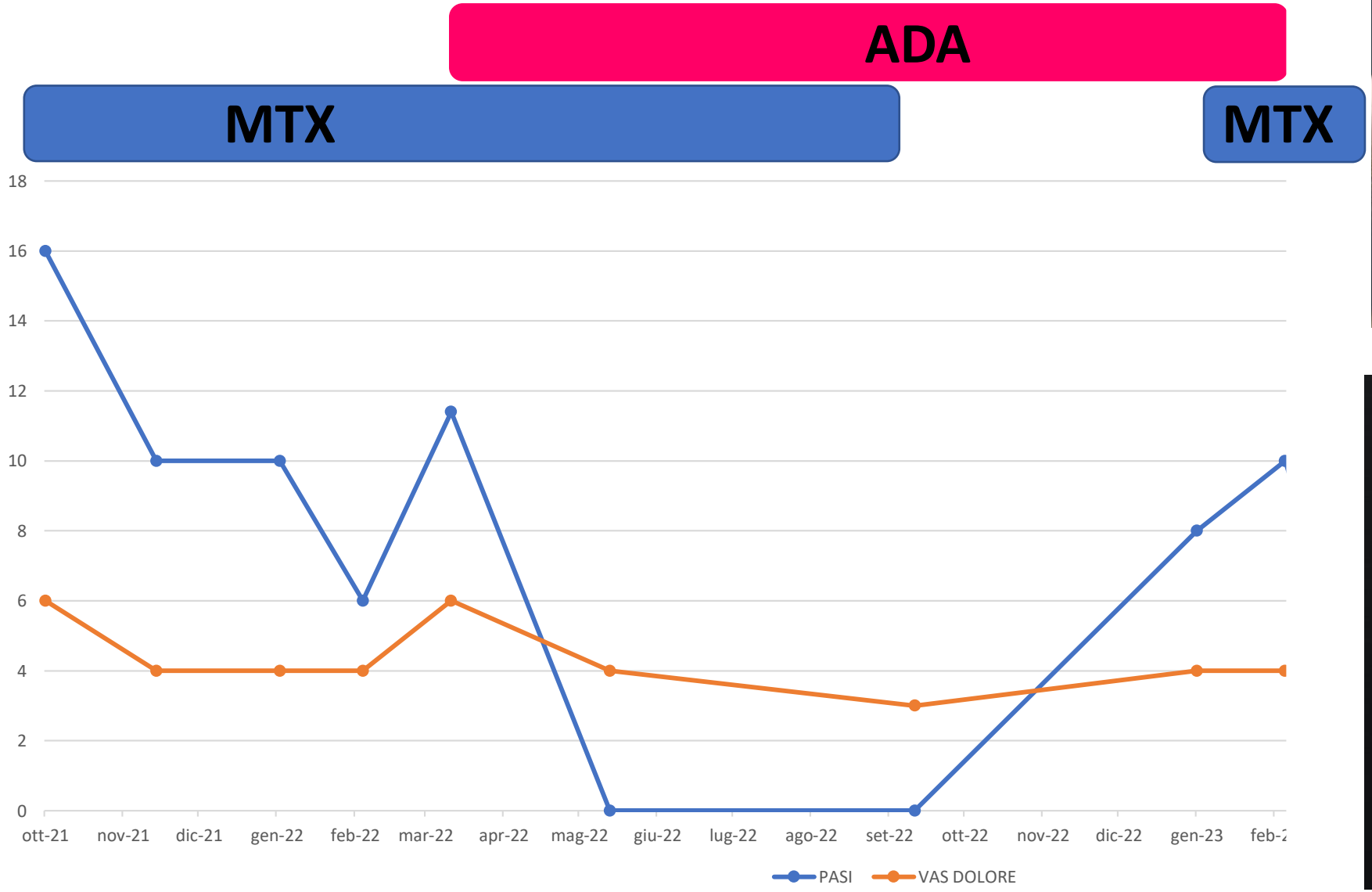
Caso 5 - Mirela

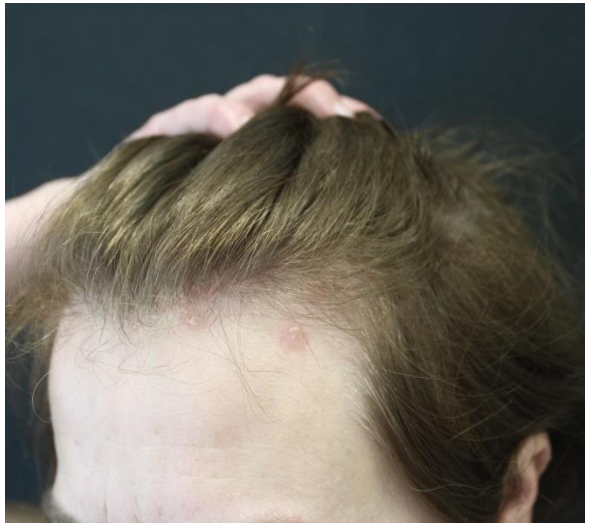


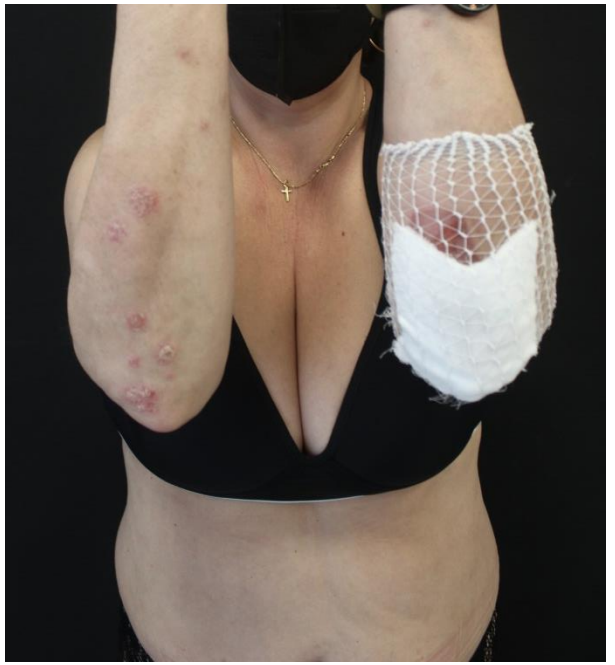
Caso 5 - Mirela



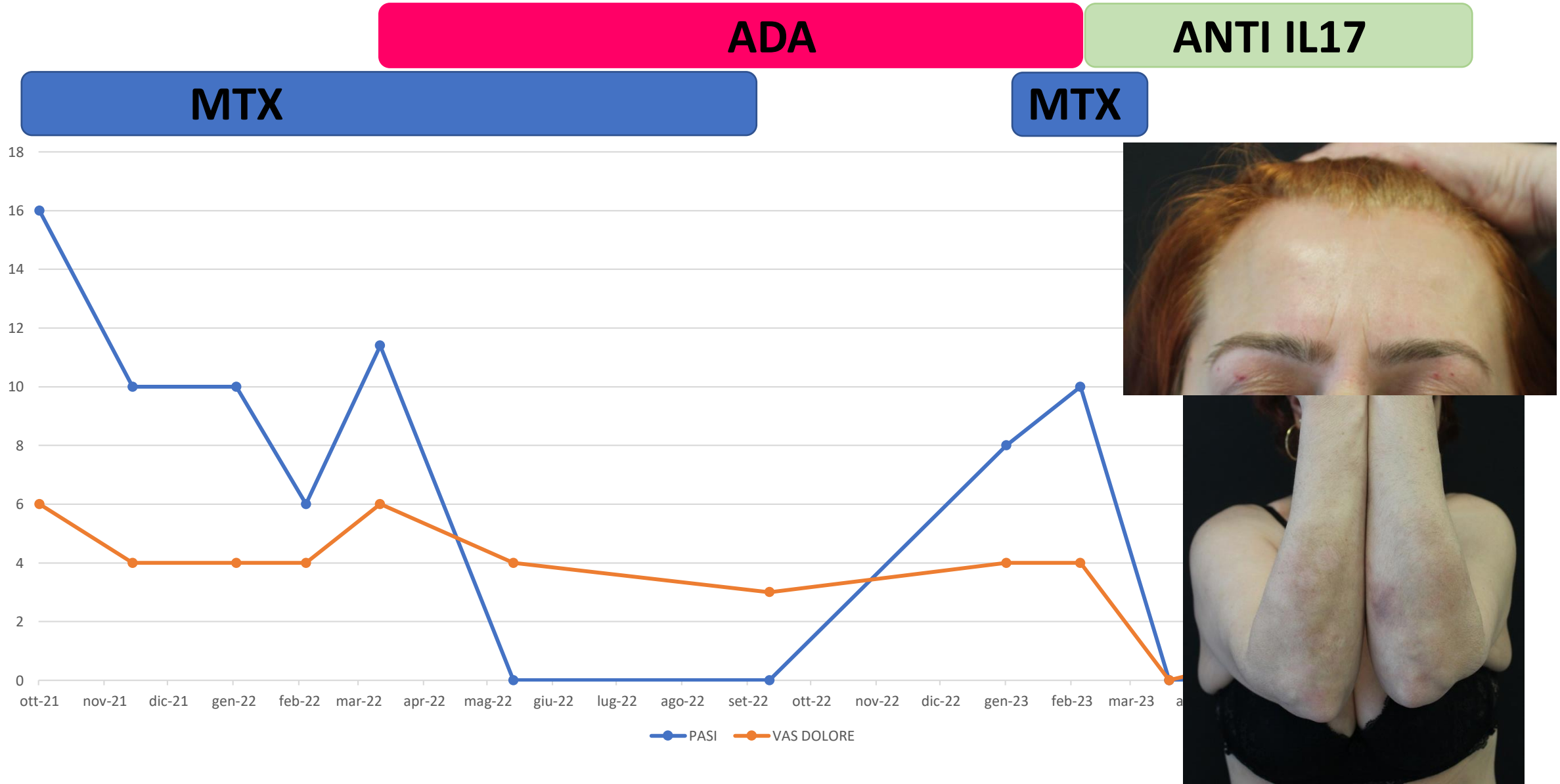
Caso 5 - Mirela







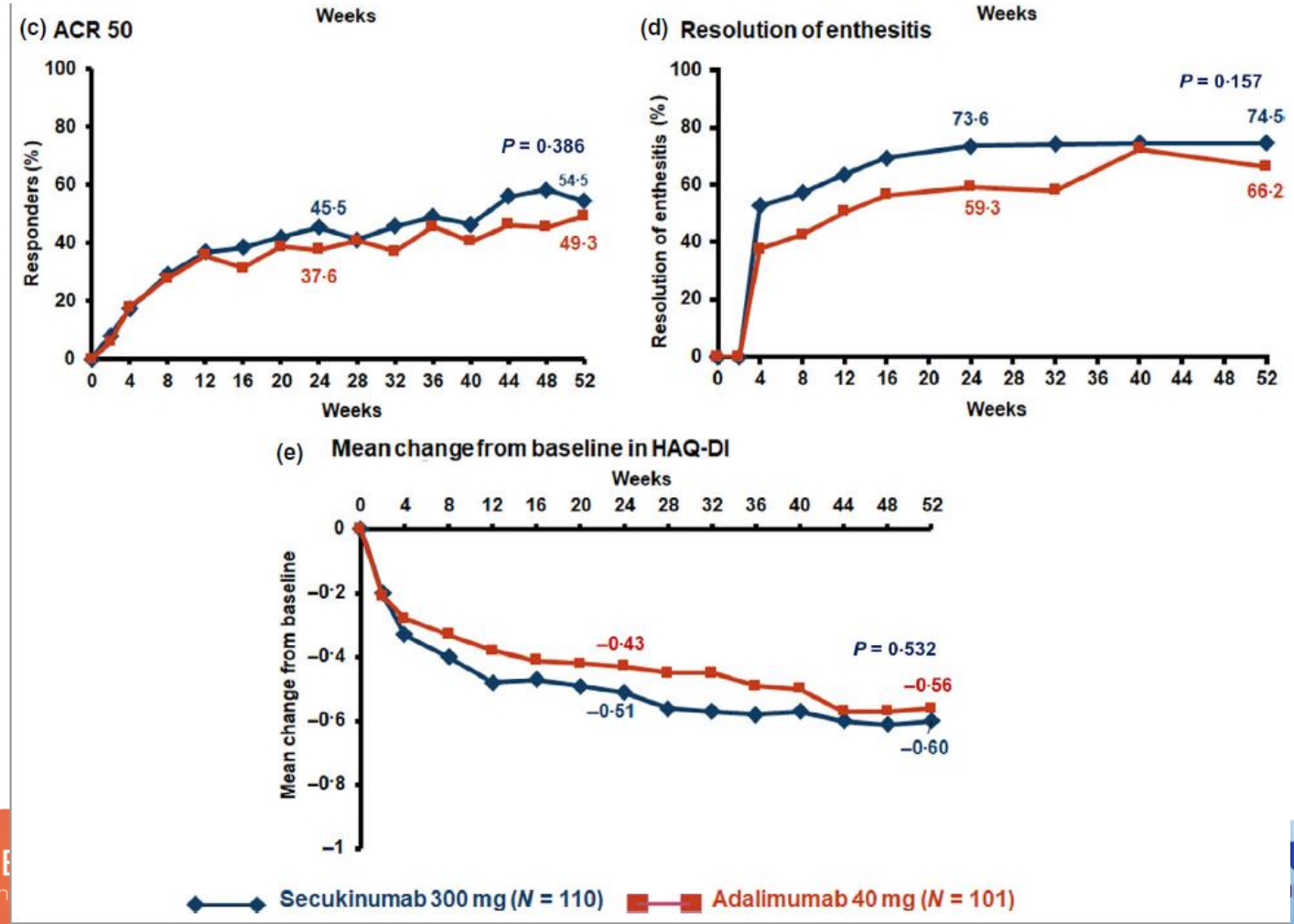
Caso 5 - Mirela



BJD
British Journal of Dermatology

Efficacy of secukinumab and adalimumab in patients with psoriatic arthritis and concomitant moderate-to-severe plaque psoriasis: results from EXCEED, a randomized, double-blind head-to-head monotherapy study

A.B. Gottlieb,[1] J.F. Merola,[2] K. Reich,[3] F. Behrens,[4] P. Nash,[5] C.E.M. Griffiths,[6] W. Bao,[7] P. Pellet,[8] L. Pricop[7] and I.B. McInnes[9]



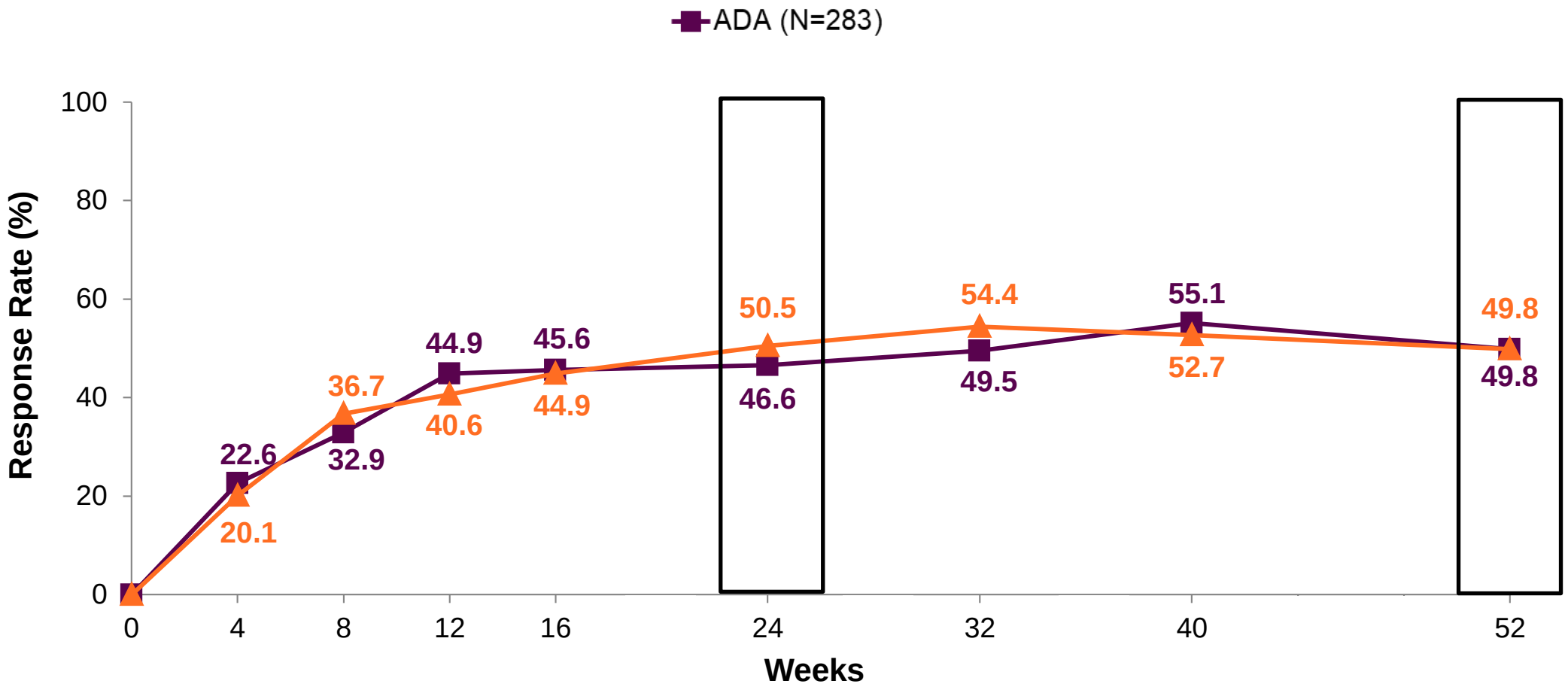
Multicenter, Randomized, Open-Label, Parallel-Group Study Evaluating the Efficacy and Safety of Ixekizumab Versus Adalimumab in Patients With Psoriatic Arthritis Who Are Biologic Disease-Modifying Antirheumatic Drug-Naïve: Final Results by Week 52

Josef S. Smolen[1], Philip Mease[2], Hasan Tahir[3], Hendrik Schulze-Koops[4], Inmaculada de la Torre[5], Lingnan Li[5], Maja Hojnik[5], Christophe Sapin[5], Masato Okada[6], Roberto Caporali[7], Jordi Gratacos[8], Philippe Goupille[9], Soyi Liu-Leage[5], Sreekumar Pillai[5], Peter Nash[10]

[1]Medical University of Vienna, Vienna, Austria; [2]Swedish Medical Center/Providence St. Joseph Health and University of Washington, Seattle, WA, United States of America; [3]Royal Free London NHS Trust, London, United Kingdom; [4]Division of Rheumatology and Clinical Immunology, Department of Internal Medicine IV, Ludwig Maximilians University of Munich, Munich, Germany; [5]Eli Lilly and Company, Indianapolis, IN, United States of America; [6]St. Luke's International Hospital, Tokyo, Japan; [7]Department of Clinical Sciences and Community Health, University of Milan, G. Pini Hospital, Milan, Italy; [8]Rheumatology Department, Hospital de Sabadell, Institut Universitari Parc Taulí, Universitat Autònoma de Barcelona, Sabadell, Barcelona, Spain; [9]Department of Rheumatology and CIC-INSERM 1415, Tours University Hospital; EA 7501, University of Tours, Tours, France; [10]School of Medicine, Griffith University, Brisbane, QLD, Australia.

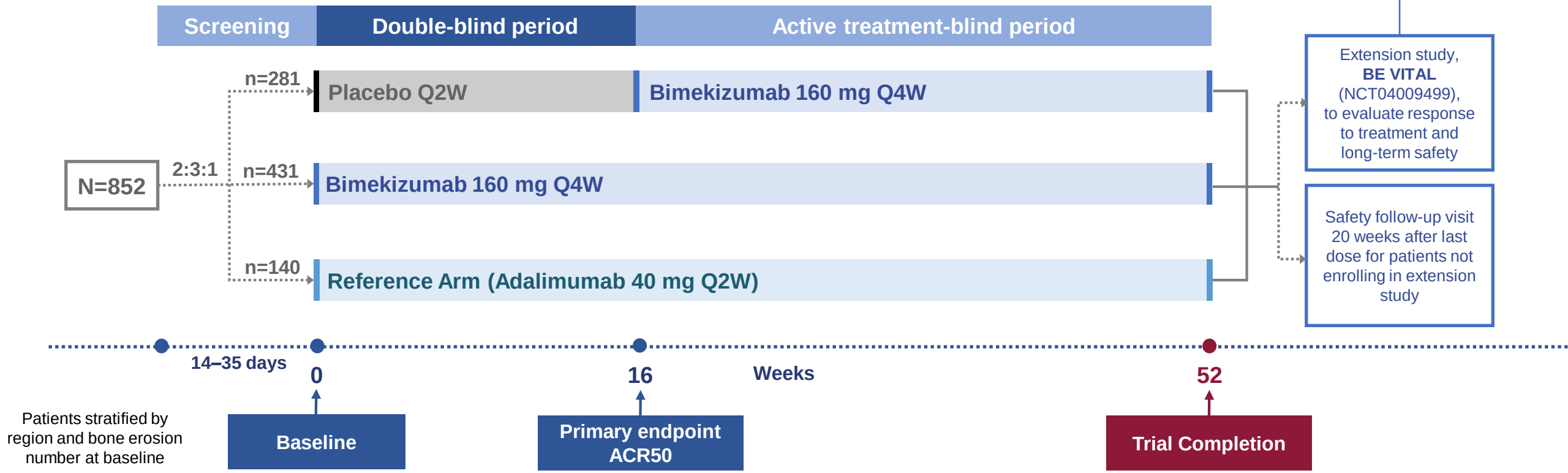
Smolen JS, et al. *Ann Rheum Dis.* 2020; doi:10.1136/annrheumdis-2020-217372 (Ahead of print).

ACR50 Response by Treatment Week, NRI ITT Population (SPIRIT-H2H)



Smolen JS, et al. *Ann Rheum Dis.* 2020; doi:10.1136/annrheumdis-2020-217372 (Ahead of print).

BE OPTIMAL Study Design



Key inclusion criteria

- ≥18 years of age with adult-onset PsA fulfilling CASPAR criteria with a duration of ≥6 months
- TJC ≥3/68 and SJC ≥3/66
- ≥1 active psoriatic lesions and/or a documented history of PSO

Key exclusion criteria

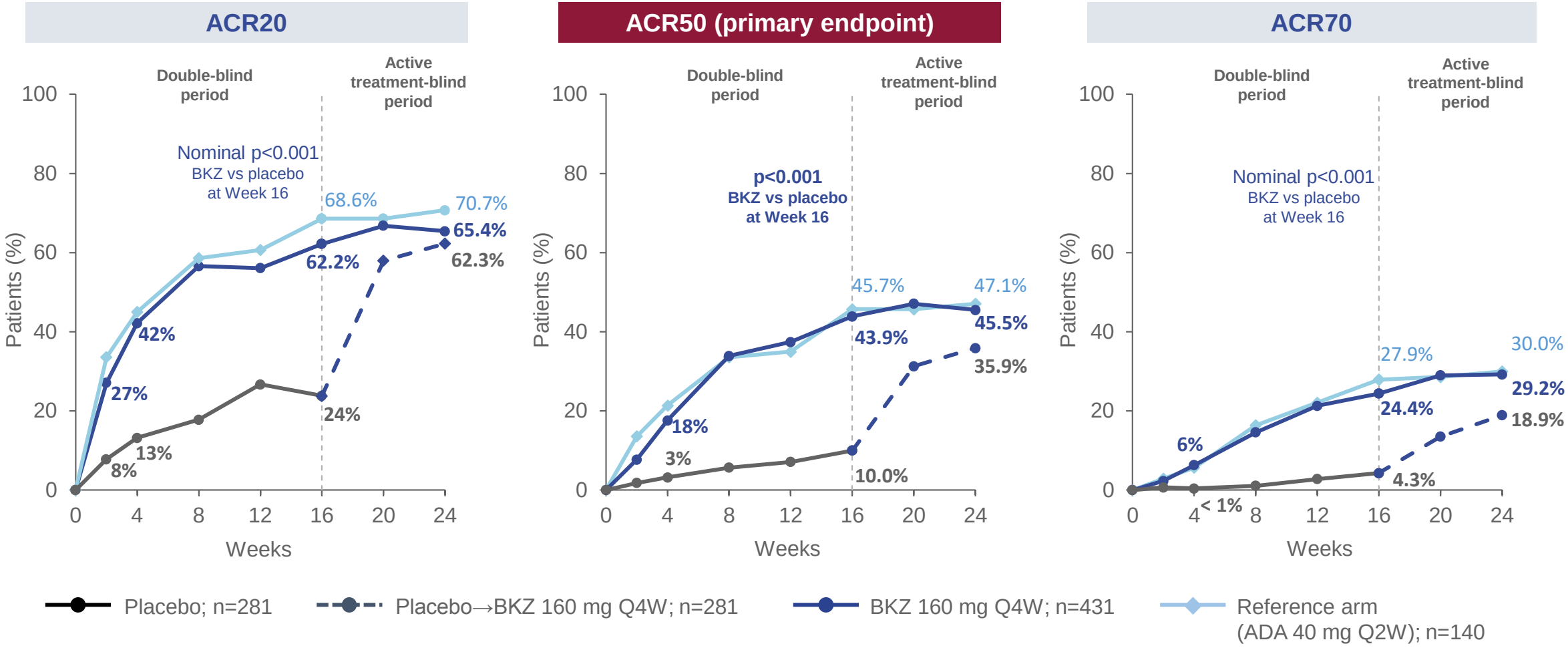
- Current or prior exposure to any biologics for treatment of PsA or PSO
- Active, symptomatic IBD at baseline or screening (prior history was not an exclusion criterion)

McInnes IB, et al., Lancet 2023;401:25-37

BKZ-treated patients were eligible to receive rescue therapy from Week 16 at the discretion of the investigator, while continuing to receive BKZ. ACR: American College of Rheumatology response criteria; BKZ: bimekizumab; CASPAR: Classification Criteria for Psoriatic Arthritis; IBD: inflammatory bowel disease; PsA: psoriatic arthritis; PSO: psoriasis; Q2W: every 2 weeks; Q4W: every 4 weeks; SJC: swollen joint count; TJC: tender joint count.

Efficacy: ACR Response Criteria to Week 24 (NRI)

BKZ demonstrated improvements vs placebo in achievement of ACR response criteria at Week 16



- Randomised set. p values BKZ vs placebo were obtained from logistic regression with treatment, bone erosion at baseline and region as factors. Nominal p values were not adjusted for multiplicity. The study was not powered for statistical comparisons of adalimumab to bimekizumab or adalimumab to placebo. ACR20/50/70: ≥20/50/70% improvement in American College of Rheumatology criteria; ADA: adalimumab; McInnes IB, et al., Lancet 2023;401:25-37
- BKZ: bimekizumab; NRI: non-responder imputation; Q2W: every 2 weeks; Q4W: every 4 weeks.

Table 1 Biologic therapy algorithm for selecting a psoriasis treatment in individuals with comorbidities or in special populations, based on a review of the current literature

Biologic therapy	Psoriatic arthritis	Multiple sclerosis	Congestive heart failure	Inflammatory bowel disease[a]	Hepatitis B	Latent tuberculosis[b]	Pediatric psoriasis	Childbearing and nursing potential[c]	NMSC and lymphoma	COVID-19
TNF inhibitors										
Adalimumab	First line	Avoid	Avoid[d]	First line (CD and UC)	Third line	Second line	Fourth line (EU: age > 4)	Third line	Third line (NMSC) Avoid (lymphoma)	Second line
Etanercept	First line	Avoid	Avoid[d]	Fourth line	Third line	Second line	Third line (age > 4)	Third line	Third line (NMSC) Avoid (lymphoma)	Second line
Infliximab	First line	Avoid	Avoid[d]	First line (CD and UC)	Third line	Second line	NA	Third line	Third line (NMSC) Avoid (lymphoma)	Second line
Certolizumab pegol	First line	Avoid	Avoid[d]	Second line (CD)	Third line	Second line	NA	First line	Third line (NMSC) Avoid (lymphoma)	Second line
IL-17 inhibitors										
Ixekizumab	First line	First line	First line	Avoid	First line	First line	Second line (age > 6)	Fourth line	Second line	Third line
Secukinumab	First line	First line	First line	Avoid	First line	First line	NA	Second line	Second line	Third line
Brodalumab	NA	First line	First line	Avoid	First line	First line	NA	Fourth line	Second line	Third line
IL-12/23 inhibitors										
Ustekinumab	Third line	Second line	First line	Second line (CD)	Third line	Second line	First line (age > 6)	Second line	First line	First line
IL-23 inhibitors										
Guselkumab	Second line	Third line	First line	Third line	Second line	First line	NA	Fourth line	Second line	First line
Tildrakizumab	NA	Third line	First line	Third line	Second line	First line	NA	Fourth line	Second line	First line
Risankizumab	NA	Third line	First line	Third line	Second line	First line	NA	Fourth line	Second line	First line

CD Crohn's disease, *COVID-19* coronavirus disease 2019, *EU* Europe, *IL* interleukin, *LTBI* latent tuberculosis infection, *NA* not applicable, *NMSC* nonmelanoma skin cancer, *NYHA* New York Heart Association, *TNF* tumor necrosis factor, *UC* ulcerative colitis

Thatiparthi A, Martin A, Liu J, Egeberg A, Wu JJ. Biologic Treatment Algorithms for Moderate-to-Severe Psoriasis with Comorbid Conditions and Special Populations: A Review. Am J Clin Dermatol. 2021 Apr 16:1–18.

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Take home message

I farmaci anti IL17 hanno dimostrato negli studi registrativi e nella real life:

- elevati tassi di efficacia (in tutte le forme di psoriasi)
- rapidità d’azione e lunga durata
- sicurezza

thank you
danke
謝謝
ngiyabonga
teşekkür ederim
gracias
merci
obrigado
dziękuję
bedankt
go raibh maith agat
mochchakkeram
sukriya
kop khun krap
terima kasih
grazie
arigatô
dakujem
спасибо
рахмат
Баярлалаа
감사합니다
ありがとう
ευχαριστώ
мерси
хвала
dank je
tapadh leat
maururu
hvala
sağolun
takk
tack
mersi
barka
welalin
spas
kia ora
faafetai lava
vinaka
спасибі
blagodaram
misaotra
matondo
paldies
grazzi
mahalo
kiitos
dankie
nanni
nandri
dhanyavad
köszönöm
akun
dankon
aciú
bayarlalaa
gràcie
enkosi
asante
manana
obrigada
tenki
murakoze
chokrane
djiere dieuf
tau
дякую
mamnun
chnorakaloutioun
gratias ago
gràcies
sulpáy
taiku
sobodi
děkuji
mèsi
didi madloba
najis tuke
kam sah hamnida
rahmat
tanemirt
rahmet
diolch
dhanyavadagalu
shukriya
mercé
trugarez
xièxie
তোমাকে ধন্যবাদ