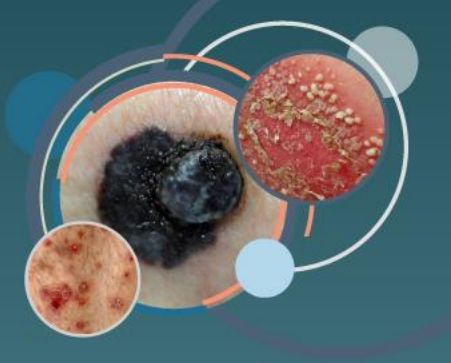
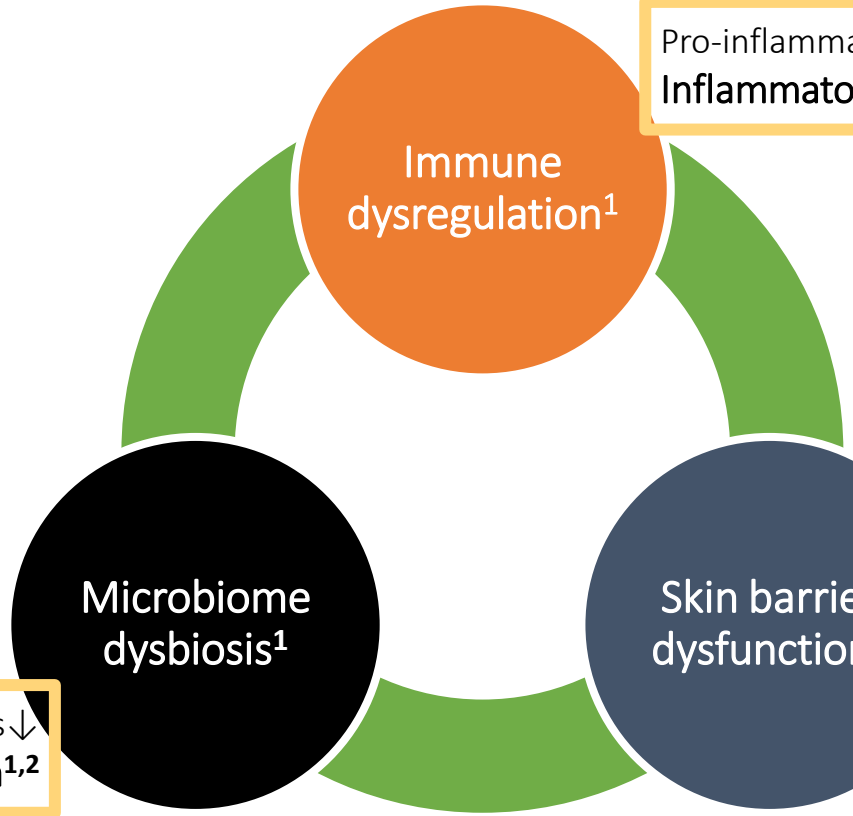
SCUOLA DERMATOLOGICA
SERGIO CHIMENTI
ROMA 17-18 Maggio 2024
Roma Eventi - Piazza di Spagna - Via Alibert 5A, 00187 Roma
1° INCONTRO 2024
YES or NO CONTEST
Dermatology Update



Anna Paola Lugli

Tralokinumab: casistica clinica in dermatite atopica moderata-severa

IL-13 nella dermatite atopica



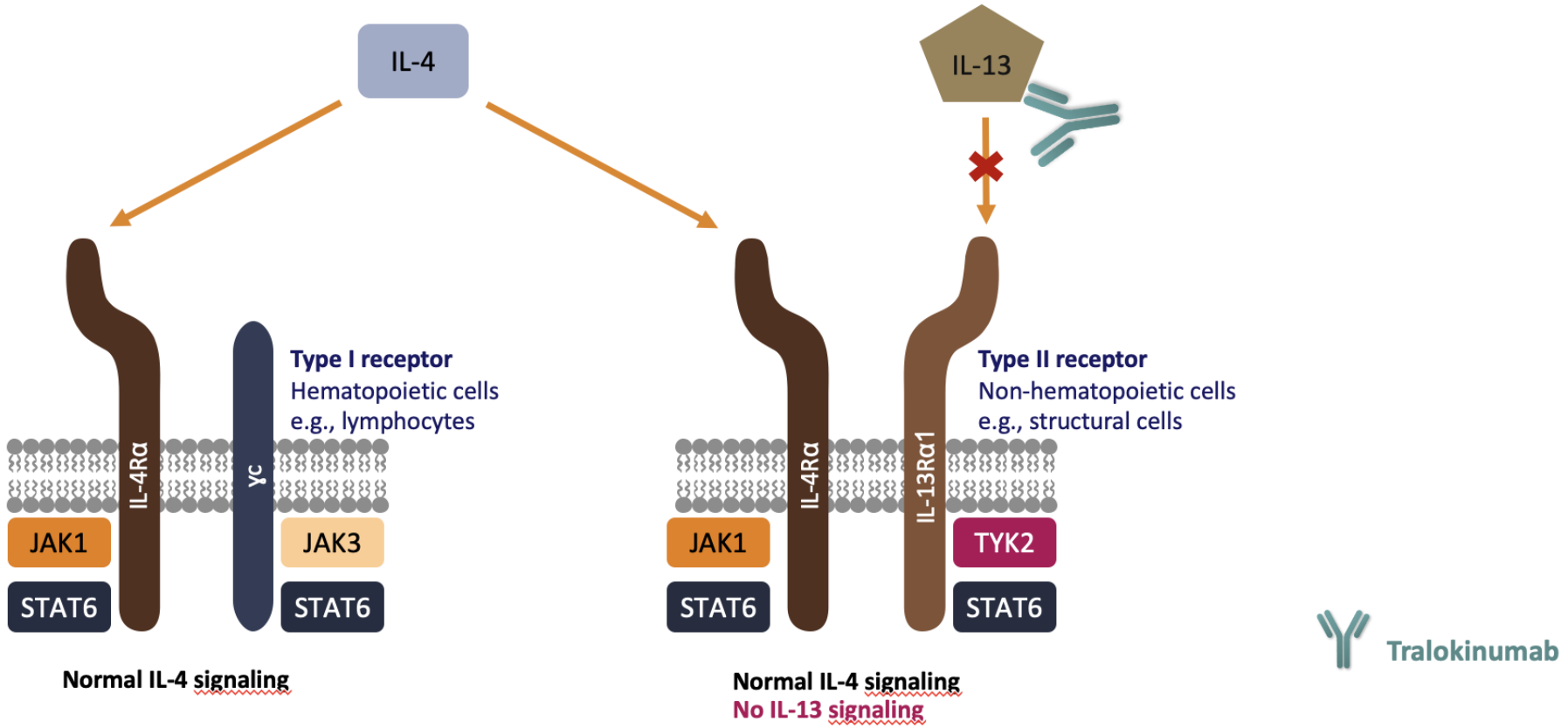
Pro-inflammatory chemokines and cytokines↑
Inflammatory response↑[1,2]

Antimicrobial peptides↓
Increased *S. aureus* colonization[1,2]

Skin barrier proteins and lipids↓
Further disrupted skin barrier[1,2]

1. Bieber T. Allergy 2020;75:54–62;
2. Sugita K, et al. Ann Allergy Asthma Immunol 2020;125:517–527.

Tralokinumab



Approvazione EMA	Giugno 2021
Approvazione AIFA	Determina AIFA n. 537/2022 del 26 luglio 2022, Pubblicata in GU n 181 del **04 agosto 2022.**
Indicazioni	Dermatite Atopica da moderata a severa nei pazienti adulti candidati a terapia sistemica Dermatite Atopica moderata severa pazienti di età superiore ai 12 anni [1]
Posologia	La dose raccomandata di tralokinumab per i pazienti adulti è una dose iniziale di 600 mg seguita da 300 mg somministrata ogni due settimane come iniezione sottocutanea [2]
Principali studi clinici	
ECZTRA 1 e 2	Valutazione dell'efficacia e la sicurezza di tralokinumab in monoterapia verso placebo in pazienti adulti affetti da dermatite atopica moderata severa
ECZTRA 3	Valutazione l'efficacia e la sicurezza di tralokinumab in associazione a TCS verso placebo in pazienti adulti affetti da dermatite atopica moderata severa
ECZTEND	Studio on going a lungo termine in open label che ha l'obiettivo di valutare la sicurezza e l'efficacia di tralokinumab fino a 5 anni
ECZTRA 6	Valutazione dell'efficacia e sicurezza di tralokinumab in monoterapia nei pazienti adolescenti affetti da dermatite atopica moderata grave

1. Approvazione EMA ottobre 2022 in fase di richiesta di rimborso in Italia
2. A discrezione del medico, è possibile prendere in considerazione una somministrazione ogni quattro settimane per i pazienti con una pelle guarita o quasi guarita dopo 16 settimane di trattamento. La probabilità di mantenere la pelle guarita o quasi guarita può essere inferiore con il dosaggio ogni quattro settimane

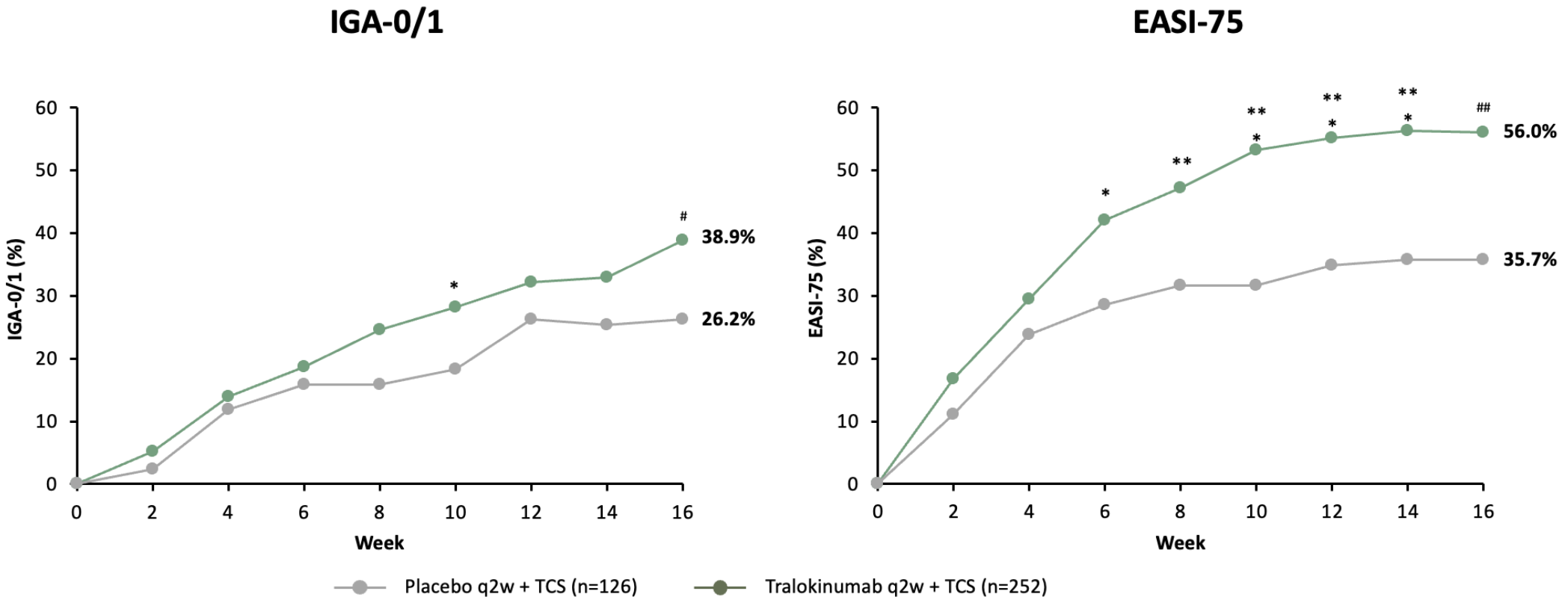
CLINICAL TRIAL

BJD
British Journal of Dermatology

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

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

More patients achieved IGA-0/1 and EASI-75 with tralokinumab + TCS versus placebo + TCS at week 16



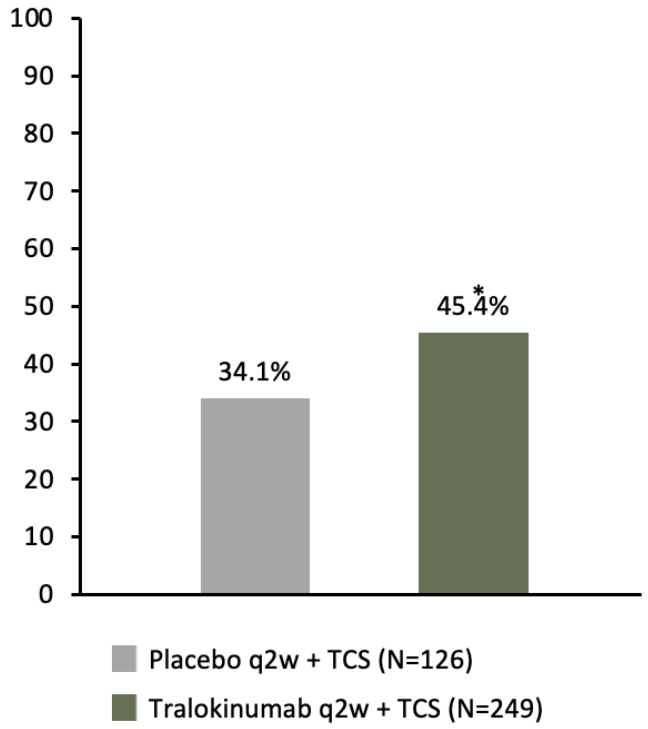
Tralokinumab plus topical corticosteroids for the treatment of moderate-to-severe atopic dermatitis: results from the double-blind, randomized, multicentre, placebo-controlled phase III ECZTRA 3 trial
I.J. Silverberg, BJD 2021

Composite estimand (primary analysis): patients who received rescue medication considered nonresponders; Patients with missing data imputed as nonresponders.

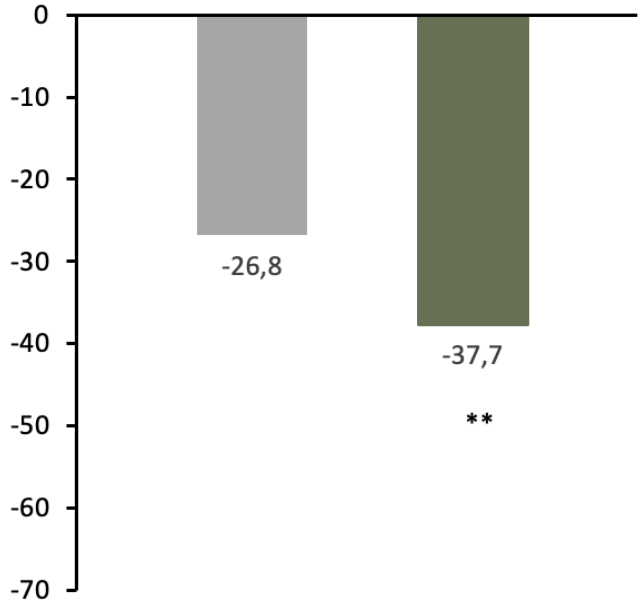
*p<0.05 versus placebo + TCS; **p<0.01 versus placebo + TCS; ***p<0.001 versus placebo + TCS. Model-based treatment difference: #p<0.05 versus placebo + TCS; ##p<0.001 versus placebo + TCS.

Tralokinumab + TCS significantly improved all secondary endpoints at week 16 versus placebo + TCS

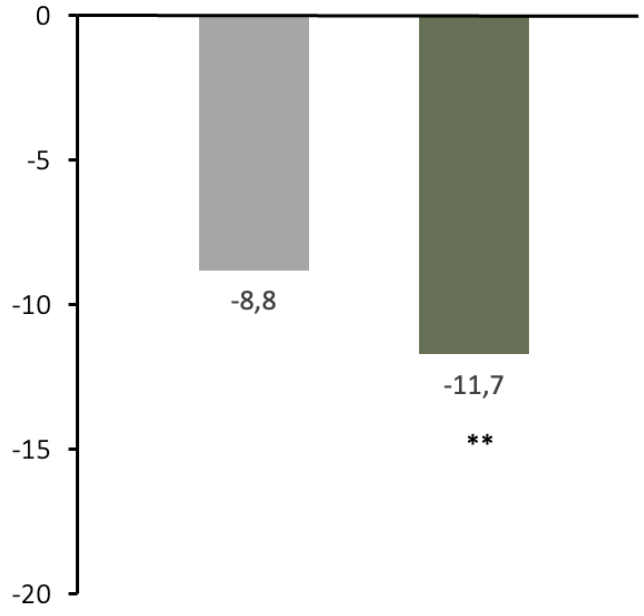
% of patients with a reduction in worst daily pruritus NRS (weekly average) ≥4 at week 16[b]



Adjusted mean change from baseline in SCORAD at week 16[a]



Adjusted mean change from baseline in DLQI at week 16[a]



Placebo q2w + TCS (N=126)
Tralokinumab q2w + TCS (N=249)

Placebo q2w + TCS (N=126)
Tralokinumab q2w + TCS (N=252)

Placebo q2w + TCS (N=126)
Tralokinumab q2w + TCS (N=252)

*p=0.037 versus placebo q2w + TCS; **p<0.001 versus placebo q2w + TCS.

Tralokinumab plus topical corticosteroids for the treatment of moderate-to-severe atopic dermatitis: results from the double-blind, randomized, multicentre, placebo-controlled phase III ECZTRA 3 trial
I.J. Silverberg BJD 2021

CLINICAL TRIAL

BJD
British Journal of Dermatology

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

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

The 15 most frequent AEs by preferred term in the initial treatment period for the AD pool

	Tralokinumab		Placebo	
	adj. %	adj. R	adj. %	adj. R
Dermatitis atopic	15.4	68.0	26.2	139.7
Viral upper respiratory tract infection	15.7	65.1	12.2	53.5
Upper respiratory tract infection	5.6	20.8	4.8	18.5
Conjunctivitis	5.4	21.0	1.9	6.9
Headache	4.6	21.6	3.9	19.6
Injection site reaction	3.5	22.9	0.3	4.0
Pruritus	2.6	10.6	3.0	13.1
Skin infection	1.1	4.0	2.5	9.0
Injection site pain	2.3	13.4	1.7	11.8
Conjunctivitis allergic	2.0	7.1	1.1	4.3
Nausea	1.0	4.2	1.9	7.3
Dermatitis infected	0.5	1.6	1.8	8.8
Asthma	1.5	6.5	1.8	6.4
Diarrhoea	1.8	6.8	1.6	6.1
Influenza	1.3	4.5	1.7	6.1

- The most frequently occurring AEs by preferred term[a] in ≥5% of patients for tralokinumab and placebo were atopic dermatitis, viral upper respiratory tract infection, upper respiratory tract infection and conjunctivitis
- Nearly two-thirds of the events related to upper respiratory tract infections were reported as common cold with tralokinumab (64%) and placebo (65%)

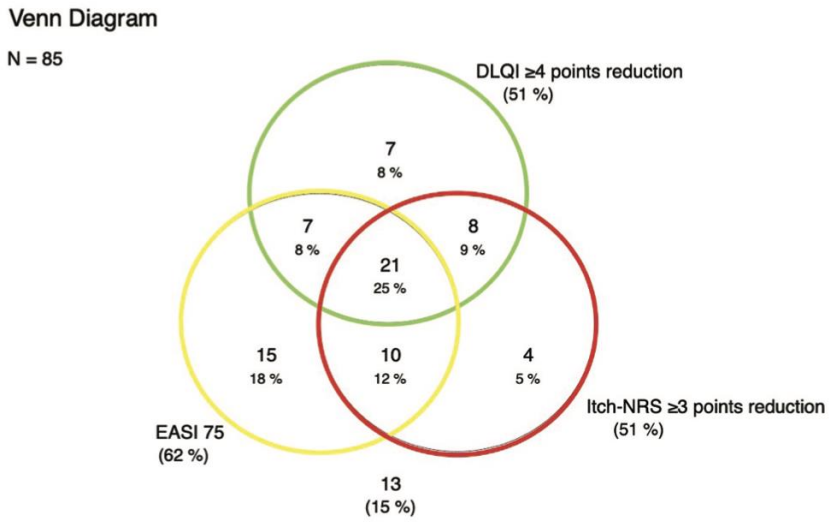
Current treatment goals are achieved by the majority of patients with atopic dermatitis treated with tralokinumab: results from a multicentric, multinational, retrospective, cohort study

A Chiricozzi, SM Ferrucci, L Di Nardo, N Gori, A Balato, M Ortoncelli, M Maurelli, M Galluzzo, M Munera Campos, T Seremet, G Caldarola, C De Simone, E Ippoliti, T Torres, S Gkalpakiotis, C Conrad, JM Carrascosa, L Bianchi, G Argenziano, S Ribero, G Girolomoni, AV Marzano, K Peris & MEDaCoTRA Study Group ...show less

Received 25 Sep 2023, Accepted 05 Dec 2023, Published online: 18 Dec 2023

- **About one third of patients (31%) achieved all therapeutic endpoints commonly used in the trial setting, i.e. EASI50, itch NRS ≥3-point reduction, DLQI ≥ 4 points reduction at week 16.**
- **Specifically, an EASI50 response was largely achieved by 86% of patients, while both DLQI ≥ 4-point and itch-NRS ≥3 points reductions were obtained by half of patients**

A total of 194 adult patients were included in this study. A significant improvement in physician-assessed disease severity was detected at each follow-up visit as compared with baseline and similar trend was observed for patient-reported outcomes and quality of life.
No meaningful difference in effectiveness was found when considering patient age (<65 versus ≥65 years), neither dissecting patient cohort in dupilumab-naive vs dupilumab-treated subjects.
Among tralokinumab-treated patients, 88% achieved at least one currently identified real-world therapeutic goal at week 16



DOI: 10.1111/jdv.19929

JEADV JOURNAL OF THE EUROPEAN ACADEMY OF DERMATOLOGY & VENEREOLOGY

LETTER TO THE EDITOR

Successful response to tralokinumab in patients unresponsive, intolerant or with contraindications to dupilumab and JAK inhibitors: A case series

TABLE 1 Mean values of EASI, DLQI, ITCH-NRS and SLEEP-NRS and % of patients reaching IGA0/1 and EASI 50, 75 and 90 at each time point.

	Baseline	Week 4	Week 16	Week 32
Patients achieving EASI 50 response, % (*n*)	–	65 (11/17)	80 (8/10)	75 (3/4)
Patients achieving EASI 75 response, % (*n*)	–	35.3 (6/17)	50 (5/10)	50 (2/4)
Patients achieving EASI 90 response, % (*n*)	–	5.8 (1/17)	20 (2/10)	50 (2/4)
Patients achieving ≥4-point improvement in Itch NRS, % (*n*)	–	35.3 (6/17)	40 (4/10)	50 (2/4)
Mean EASI score ± SD*	23.1 ± 11.8	9.8 ± 9.6	7.2 ± 10.0	4.8 ± 4.9
Mean Itch-NRS ± SD*	7.7 ± 2.7	5.0 ± 3.3	3.3 ± 3.4	3.0 ± 2.1
Mean Sleep-NRS ± SD*	6.1 ± 3.4	2.8 ± 2.4	3.1 ± 3.1	4.0 ± 3.2
Mean DLQI score ± SD*	11.6 ± 7.5	7.25 ± 3.9	4.5 ± 3.2	3.0 ± 3.2

*$p < 0.001$ for each time point versus baseline.

Abbreviations: DLQI, Dermatology Life Quality Index; EASI, Eczema Activity Severity Index; NRS, Numeric Rating Scale; SD, standard deviation.

Caso clinico 1

Uomo, 73 anni

Insorgenza DA di grado severo confermata istologicamente all'età di 65 anni

Comorbidità atopiche: nessuna

Comorbidità generali: infarto del miocardio acuto nel 2021, glaucoma bilaterale

Anamnesi farmacologica: cardioaspirina 100 mg/die, clopidogrel 75 mg/die, atorvastatina 40 mg/die, bisoprololo 1,25 mg/die, zofenopril 30 mg/die

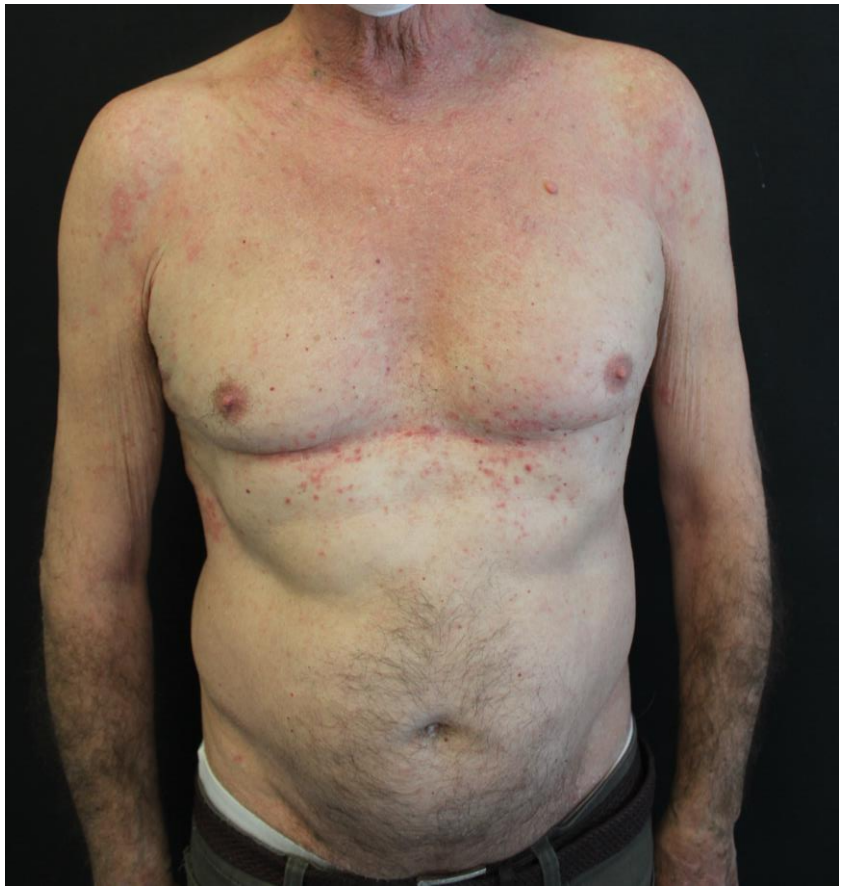
Pregresse terapie per DA:

- Ciclosporina interrotta dopo 2 mesi per riscontro di IA
- Metotrexate sospeso per inefficacia primaria
- Dupilumab interrotto dopo 6 mesi per inefficacia secondaria
- Upadacitnib interrotto per IMA
- Corticosteroidi sospesi per riscontro di glaucoma bilaterale

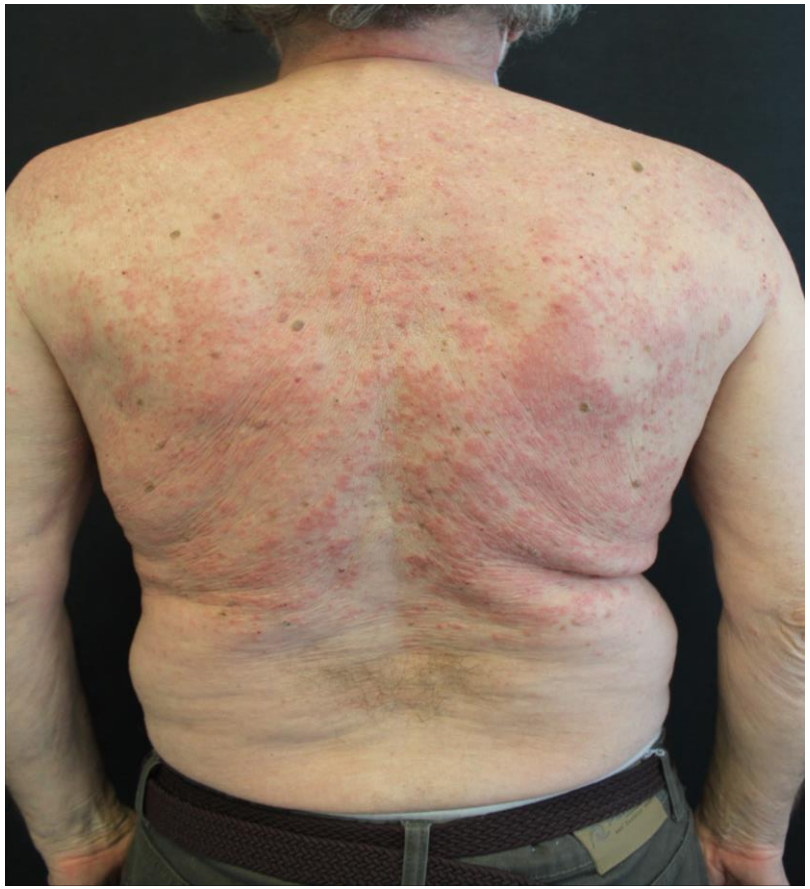
Scelta trattamento

✓ **Tralokinumab 600 mg al baseline seguito da 300 mg ogni 2 settimane**

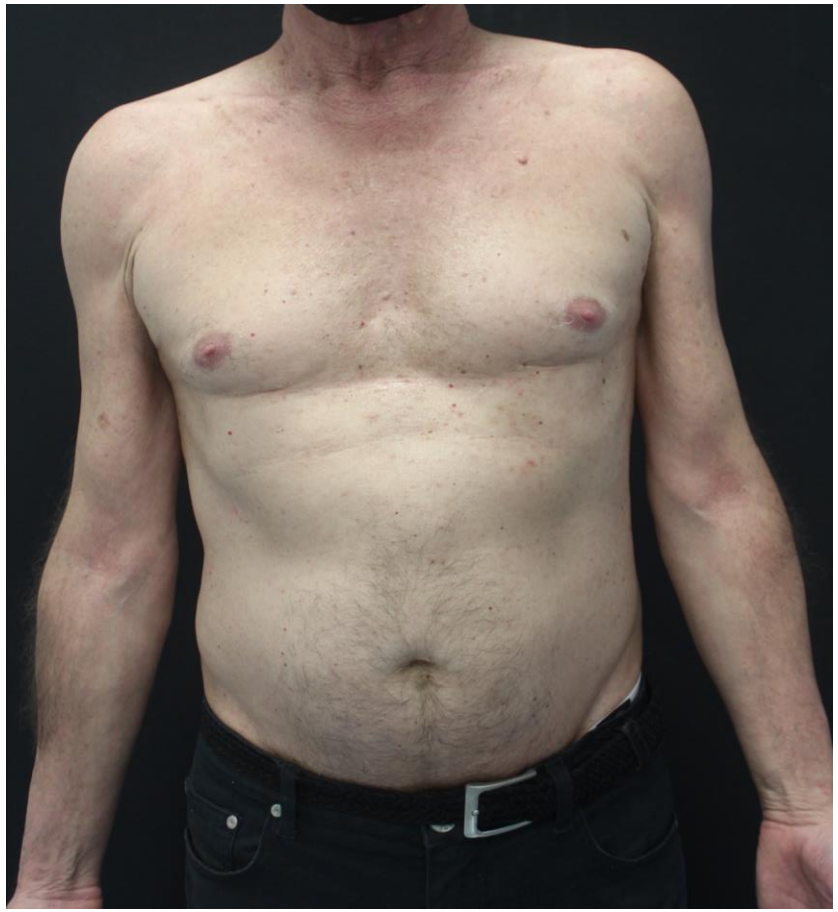
Week 0



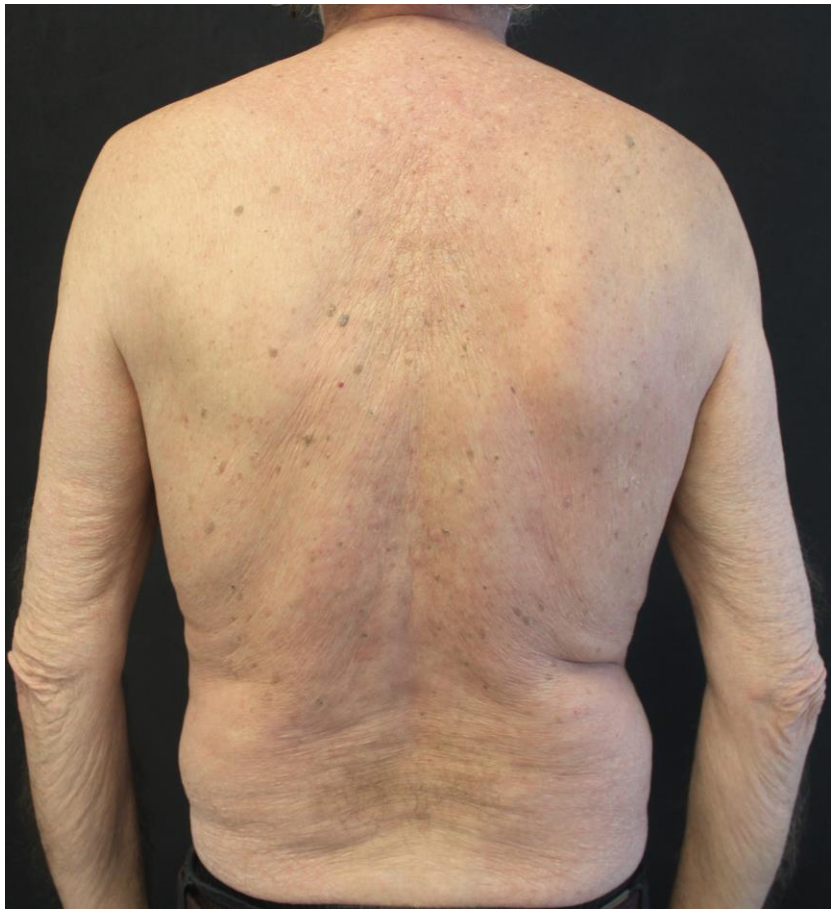
EASI 29
NRS prurito 9/10
NRS sonno 8/10
DLQI 5



Week 16



EASI 10
NRS prurito 4/10
NRS sonno 3/10
DLQI 0



Caso clinico 2

Donna, 75 anni

Esordio di eczema atopico nel febbraio 2022 confermato istologicamente

Comorbidità atopiche: nessuna

Comorbidità generali: ipertensione essenziale, diabete mellito tipo II

Anamnesi farmacologica: telmisartan 20 mg/die, metformina 500 mg/die, Amlodipina 5 mg/die

Pregresse terapie per DA:

- Corticosteroidi locali
- Corticosteroidi sistemici
- Dupilumab interrotto dopo 3 mesi per inefficacia secondaria

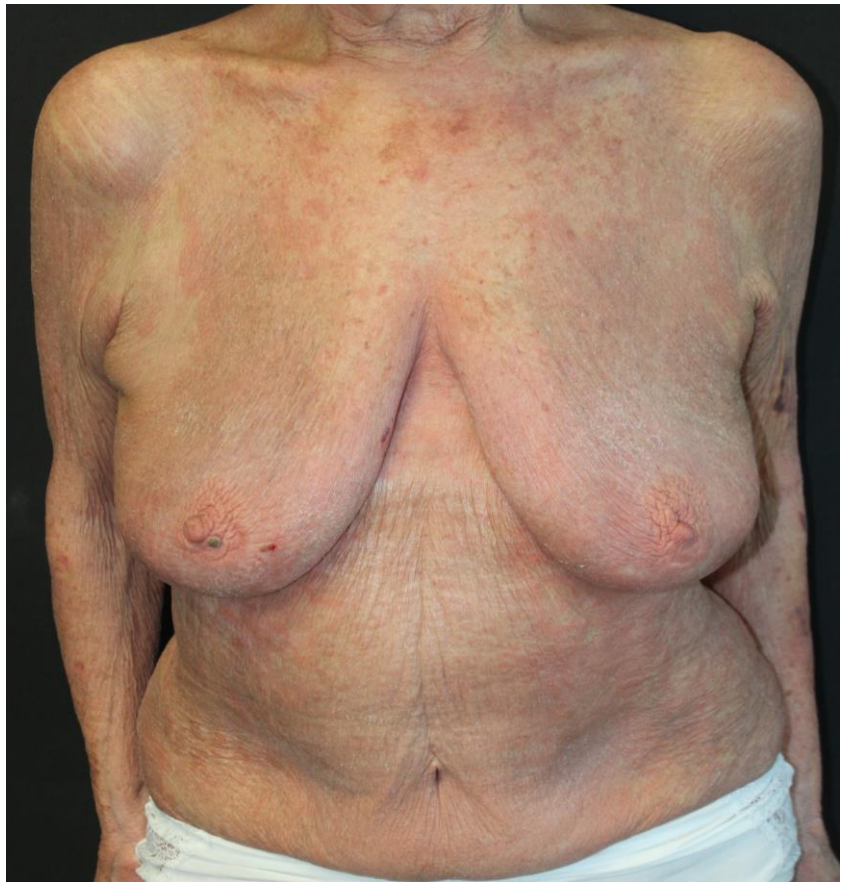
Scelta trattamento

✓ **Tralokinumab 600 mg al baseline seguito da 300 mg ogni 2 settimane**

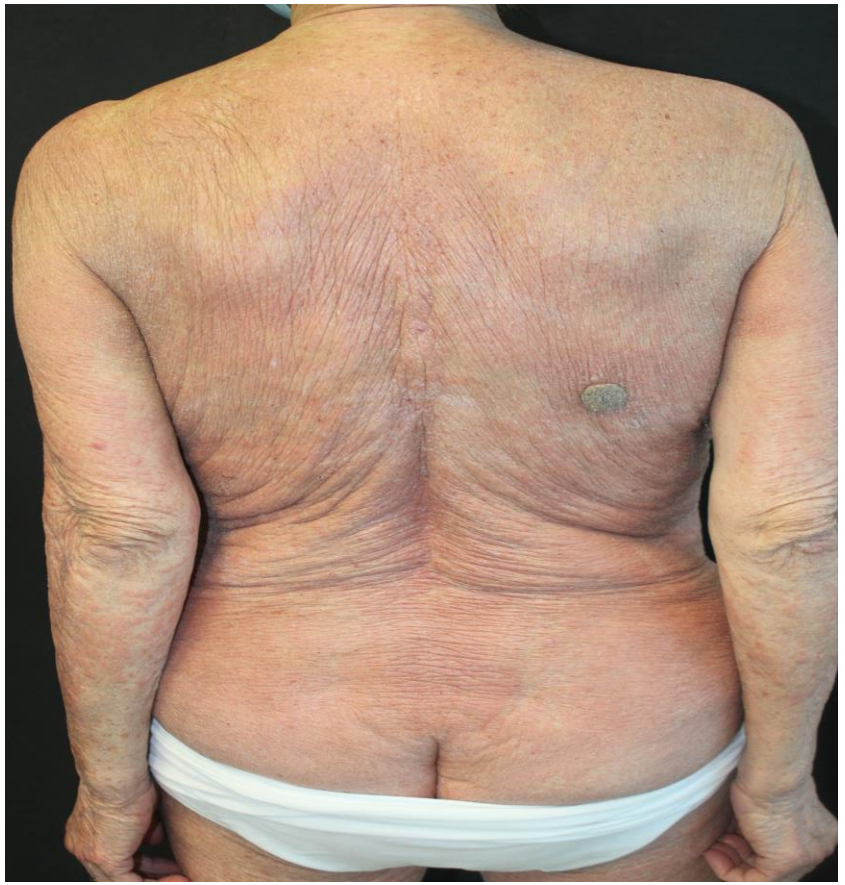
+

✓ **Methotrexate s.c al dosaggio di 7,5 mg a settimana**

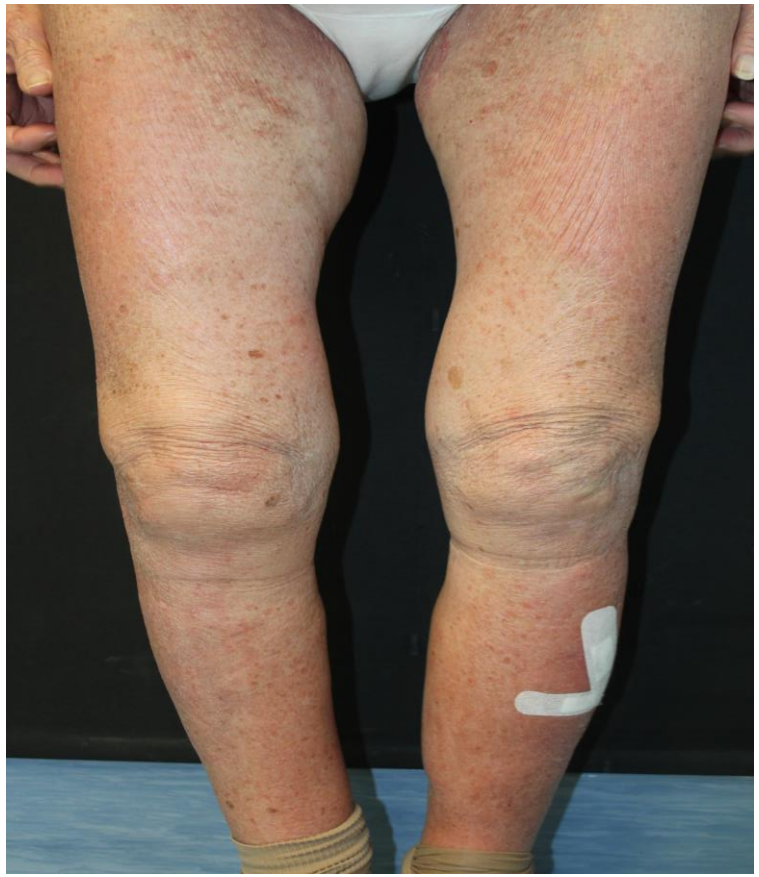
Week 0

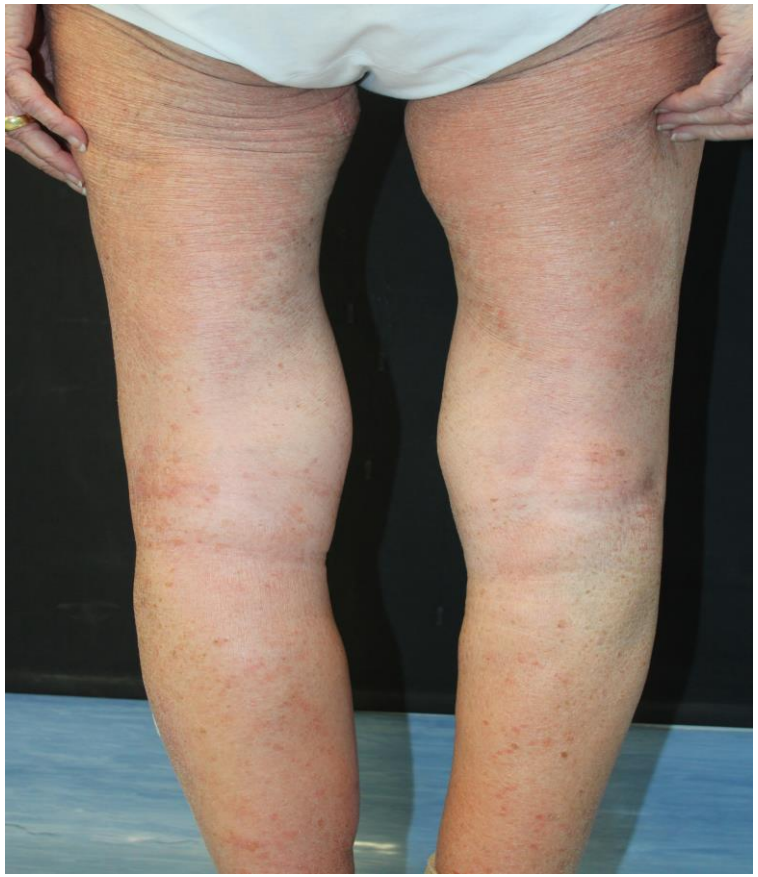


EASI 48
NRS prurito 9/10
NRS sonno 8/10
DLQI 22

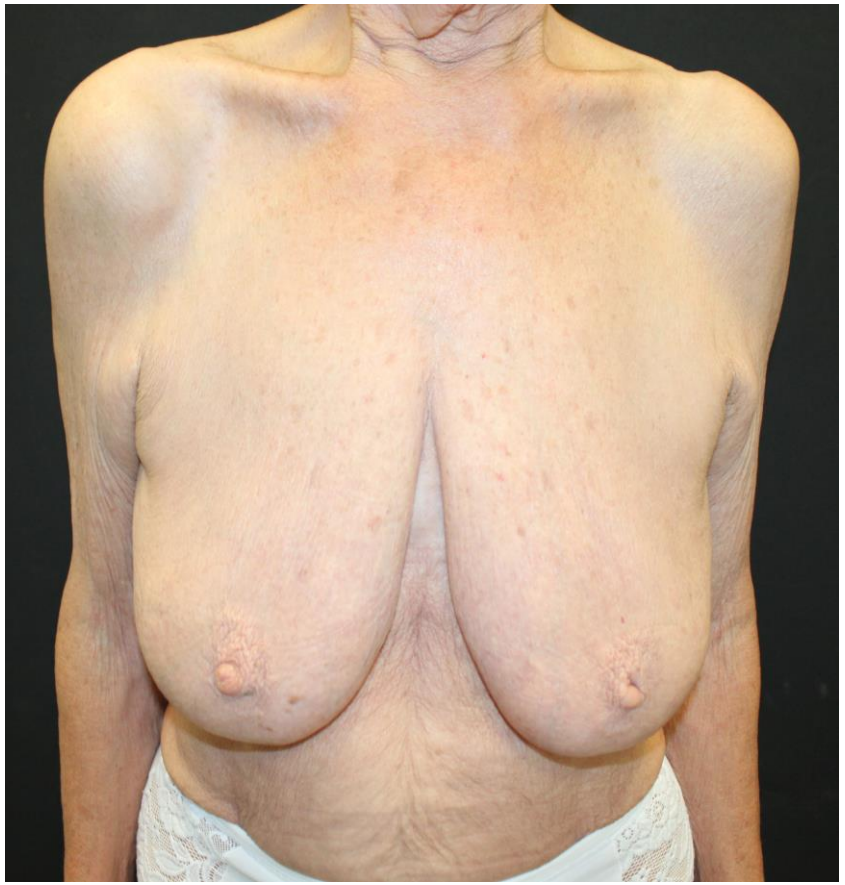


Week 0

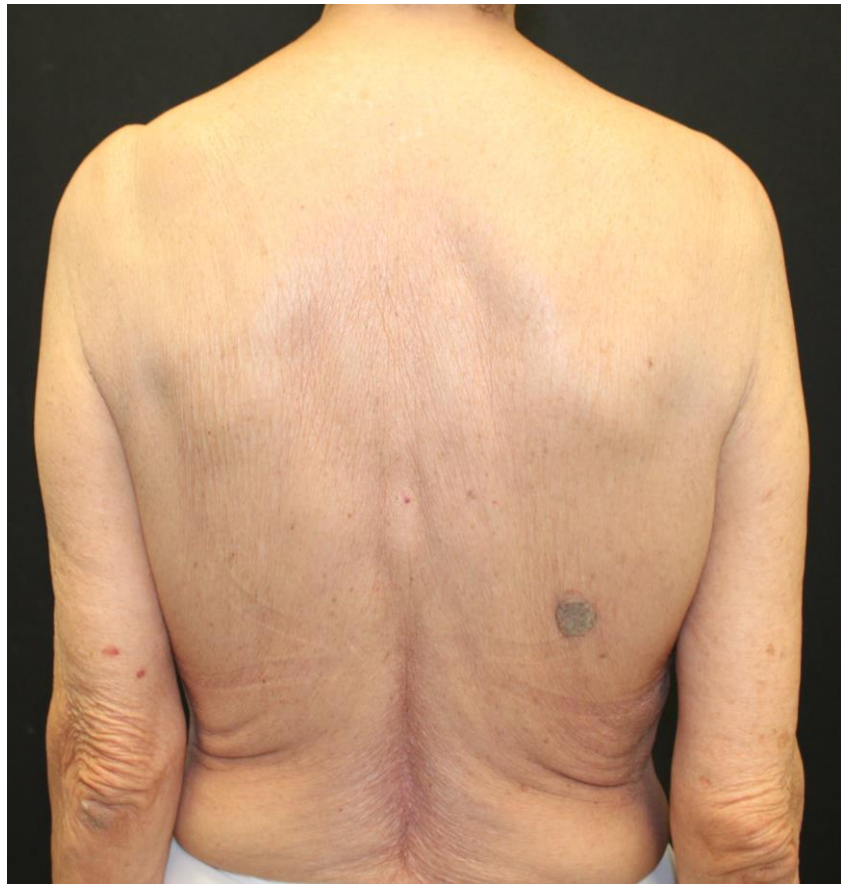




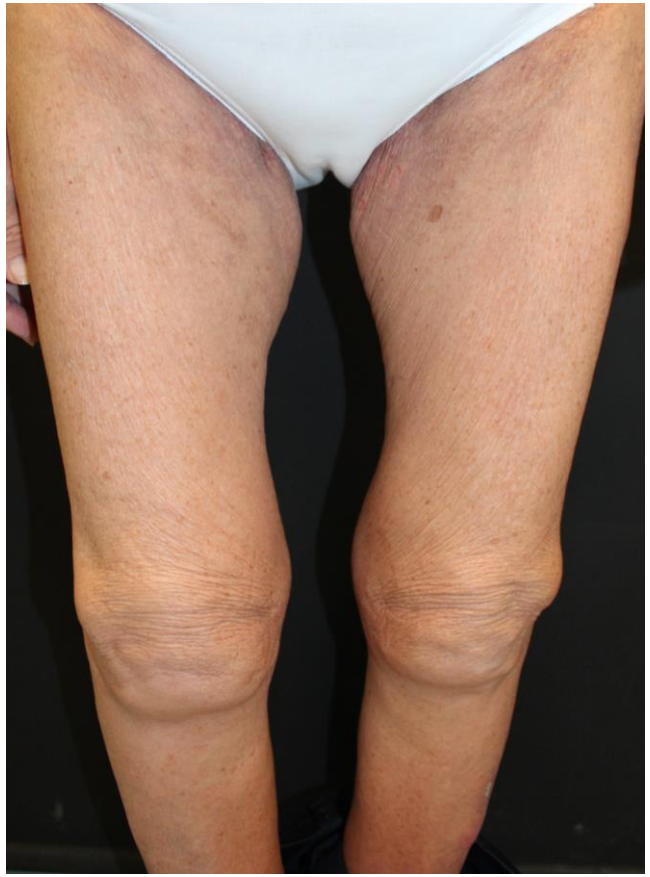
Week 16

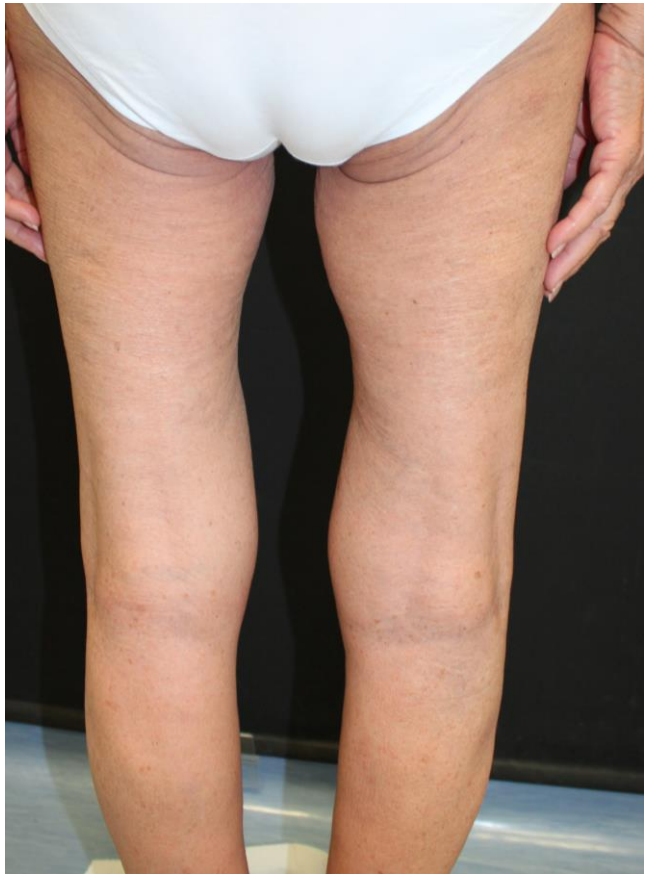


EASI 3
NRS prurito 3/10
NRS sonno 3/10
DLQI 1



Week 16





2. Tralokinumab è un anticorpo Murino contro la interleuchina IL-13?

1. **Sì**
2. **No**

3. Tralokinumab è approvato per il trattamento della dermatite atopica moderata-severa dai 12 anni di età?

1. **Sì**
2. **No**

4. Tralokinumab ha ricevuto approvazione EMA nel 2021?

1. **Sì**
2. **No**