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[Translated article] Tralokinumab in Atopic Dermatitis: Real-Life Data from a Spanish Tertiary Referral Center

Tralokinumab en dermatitis atópica: datos de práctica clínica en un hospital de tercer nivel en España

To the Editor,

Atopic dermatitis (AD) is a chronic skin disease characterized by outbreaks of pruritic eczematous lesions involving an impaired quality of life for the patient[1,2] The origin of AD is multifactorial, with its pathogenesis involving immune dysregulation characterized by an increased cutaneous Th2 lymphocyte response, leading to elevated levels of interleukins (IL): IL-4, IL-5, IL-13, IL-25, and IL-31.[3]

Up until the appearance of biological therapies with dupilumab—the first monoclonal antibody against IL-4/IL-13—in 2007 the management of moderate-to-severe AD posed a therapeutic challenge due to the lack of effective drugs with a good long-term safety profile.[1,2] Since then, other targeted therapies have been approved, among them, tralokinumab (2021), a monoclonal antibody directed against IL-13 that prevents its interaction with the IL-13Rα1/IL-4Rα receptor.[3–5] The aim of this study was to evaluate the safety and efficacy profile of tralokinumab in the management of moderate-to-severe AD.

We conducted a descriptive, retrospective study of all patients with cyclosporine-refractory moderate-to-severe AD treated with tralokinumab (1 subcutaneous injection of 600 mg followed by 300 mg every 2 weeks) for, at least, 16 weeks from June 2022 through February 2023 at a Spanish tertiary referral center. Data were collected from the patients' electronic health records, including sex, age, dosage, treatment duration, and previous treatments. Effectiveness was evaluated using the SCORing Atopic Dermatitis (SCORAD) and Validated Investigator Global Assessment for Atopic Dermatitis (vIGA-ADTM) scales at baseline, and on weeks 16 and 24.[6,7]

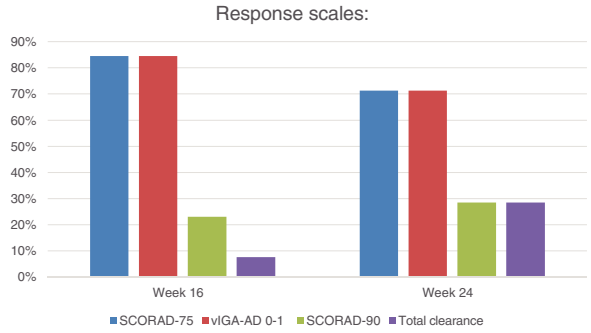

Figure 1 Evaluation of effectiveness using the SCORAD scale after 16 and 24 wees on therapy showing the percentage of patients who achieved the target responses.

The main outcome variables of the study were the proportion of patients who achieved responses between 0 and 1 on the vIGA-AD scale (vIGA-AD 0-1) 16 and 24 weeks after treatment, and a reduction of, at least, 75% from baseline in the SCORAD scale (SCORAD-75). Secondary variables included a reduction of, at least, 90% from baseline in the SCORAD scale (SCORAD-90), and ''total clearance of the disease'' or SCORAD of 0 between such weeks. Finally, drug safety was evaluated by collecting all adverse effects (AE) and their suspensions.

A total of 14 patients were included, whose sociodemographic characteristics and previous therapies are shown in Table 1. The median baseline scores were SCORAD-56 (range, 21-72) and vIGA-AD 4 (range, 1-4). The median treatment duration was 24 weeks (range, 16-32). All patients were evaluated on week 16. However, at the time of the study, only half of the patients had completed a sufficient treatment period including evaluation on week 24 (7/13; 53.8%). One patient was excluded due to death unrelated to the studied disease.

Regarding the main variables, on week 16, 11 patients (11/13; 84.6%) achieved a vIGA-AD 0-1 response, and SCORAD-75 (figure 1). On week 24, 5 of 7 evaluated patients (5/7; 71.4%) achieved a vIGA-AD 0-1 response and SCORAD-75. Regarding secondary variables, 3 patients achieved SCORAD-90 on week 16 (3/13; 23.1%) while 2 patients did so on week 24 (2/7; 28.6%). One (1/13; 7.7%) and 2 patients

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Table 1 Results of the analyzed cohort and results observed in the pivotal clinical trials ECZTRA 1, ECZTRA 2, and ECZTRA 3.

	Analyzed cohort		
Total	14		
Women, n (%)	8 (57.1)		
Median and age range (years)	29 (18-85)		
Previous therapies. n (%)			
Topical corticoids	14 (100)		
Oral corticoids	14 (100)		
Oral antihistamines	14 (100)		
Oral cyclosporine	11 (78.6)		
Dupilumab	3 (21.4)		
Upadacitinib	2 (14.2)		
Baseline severity score, median (range)			
Baseline SCORAD	56 (21-72)		
vIGA-AD	4 (1-4)		
Patients studied, n (%)	13 (92.9)		
Reasons for exclusion from the study, n (%)			
Death unrelated to treatment	1 (7.1)		
Evaluation of the treatment's efficacy, n (%)	Week 16 (n = 13)	Week 24 (n = 7)	
SCORAD-75	11 (84.6)	5 (71.4)	
SCORAD-90	3 (23.1)	2 (28.6)	
vIGA-AD 0-1	11 (84.6)	5 (71.4)	
Total clearance	1 (7.7)	2 (28.6)	
Adverse events. n (%)			
Xerophthalmia and ocular pruritus	5 (38.4)		
Injection-site reaction	2 (13.4)		
Drug discontinuation, n (%)	3 (23.1)		
Lack of evidence	2 (15.4)		
Adverse events	1 (7.7)		
Results seen in clinical trials, %	ECZTRA 1	ECZTRA 2	ECZTRA 3
vIGA-AD 0-1 on week 16	15.8	22.2	21.4
Adverse events	76.4	66	67.9

(2/7; 28.6%) achieved total clearance on weeks 16 and 24, respectively. Three patients (3/13; 23.1%) discontinued tralokinumab, 2 of them (2/13; 15.4%) due to inefficacy after a median 7-month therapeutic regimen (range, 5-9), and 1 (1/13; 7.7%) due to an injection-site reaction.

Half of the patients (7/13; 53.8%) experienced some AEs, mostly of mild. Five patients (5/13; 38.4%) reported xerophthalmia and conjunctivitis, which well tolerated with symptomatic measures, while 2 (2/13; 13.4%) had an injection site-related AE.

Tralokinumab proved safe and effective to treat moderate-to-severe AD in clinical trials (ECZTRA 1, ECZTRA 2, ECZTRA 3).[8,9] There are few long-term studies of its use in the routine clinical practice (Table 2), whose results are comparable to those observed in our study.[5–7] Most patients responded within 16 weeks, maintaining response until week 24. Only 15% had to stop tralokinumab due to inefficacy. Tolerance was adequate, and half experienced mainly mild ocular AEs, which were treated symptomatically. Only 1 case required treatment discontinuation following an injection site-related AE.

The added value of this study is the need to have data available on tralokinumab in the routine management of moderate-to-severe AD, being the second largest study ever conducted in Spain with the longest evaluated response period, assessing patients up to 24 weeks after starting treatment.[10] The limitations of our study lie in its small sample size. Future studies should evaluate the response of tralokinumab in the routine clinical practice with larger populations and longer follow-ups.

Table 2 Safety and efficacy visualized in real-life experience studies of tralokinumab for moderate-to-severe atopic dermatitis published to this date.

Study	N	Mean efficacy			Safety
		Baseline	1st assessment	2nd assessment	
Pezzolo and Naldi[a]	12	Mean (range) EASI 27.58 (20-35) PP-NRS 8.42 (7-10) S-NRS 7 (3-10)	*Week 12:* EASI 4.67 (0-13) -> 80% mean reduction EASI 75: 100% PP-NRS 2.92 (0-5) -> 60% mean reduction S-NRS 1.92 (0-5) -> 70% mean reduction	Not assessed	No AEs reported
Moennig and Traidl[b]	1	EASI 9.4 SCORAD 34.5 DLQI 34 IGA 4	*Week 12:* EASI 3.5 (65% reduction) SCORAD 15.8 DLQI 16 IGA 2	*Week 38:* EASI 2.3 (75.5% reduction) SCORAD 15 DLQI 3 IGA 2	AD exacerbation after COVID-19 vaccine on week 18 No changes after COVID-19 infection
Schlösser et al.[c]	37	Median (IQR) IGA 2 (1-4) Responders: 2 (1-4) Nonresponders: 3 (2-4) PP-NRS 6 (1-10) Responders: 5 (1-8) Nonresponders 7 (4-10)	*Last visit (between weeks 12 and 24)* IGA 2 (1-4) Responders: IGA 2 (1-3) Nonresponders IGA 2 (2-4) PP-NRS 5 (3-10) Responders: PP-NRS 2 (0-8) Nonresponders PP-NRS 8 (3-10)	Collected all the data together as 'last medical record of last visit.' all of them between weeks 16 and 24.	Conjunctivitis, 24%, controlled with symptomatic treatment Hair loss, 5% Scalp dermatitis, 3% Injection-site reaction, 2.35% → suspension Monoarthritis, 2.35% → suspension Anterior blepharitis, 2.35% → suspension Suspensión due to inefficacy, 32.4% Suspensión due to AEs, 8.10%
De Greef et al.[d]	21	Median (± IQR) EASI 71.6 (± 15.9) SCORAD 58.9 (± 21.8) DLQI 12 (± 10) PP-NRS 8 (± 1)	*Week 16:* Median (± IQR) EASI 1.8 (± 6.1) -> −85% median reduction (± 19.2) EASI 50: 76.2% EASI 75: 66.7% EASI 90: 28.6% EASI 75 patients without additional therapy: 52% SCORAD 25.1 (± 18.8) -> −64.7% median reduction (± 37.3) SCORAD 50: 47.6% SCORAD 75: 23.8% SCORAD 90: 0% DLQI 2 (± 9) -> n −75% (± 73.3) median reductio PP-NRS 3 (± 4) -> −57.1% (± 50) median reduction	Not assessed	At least 1 AE, 52.4% Eczema flare-ups, 23.8% Injection-site reaction, 19% Drug discontinuation, 19%: 9.5% ineffectiveness and 9.5% injection-site reactions Conjunctivitis, 0% Severe AEs, 0%

Table 2 (*Continued*)

Study	N	Mean efficacy			Safety
		Baseline	1st assessment	2nd assessment	
Gargiulo et al.[e]	10	Median (± IQR)	*Week 16:*	Not assessed	No severe AE 10% nasopharyngitis
		EASI 20 (± 8)	Median (± IQR) EASI 3.1 (± 3.35) EASI 50: 100% EASI 75: 70%		No discontinuations due to AE
		PP-NRS 9 (± 1.5)	PP-NRS 4.5 (± 3) -> reduction in ≥ 4 points: 70%		
		S-NRS 7 (± 1.1)	S-NRS 2 (± 4) -> reduction in ≥ 4 points: 50%		
		ADCT 16 (± 2.75)	ADCT 5.5 (± 2) -> reduction to a score ≤ 7: 80%		
		IGA ≥ 3: 100%	IGA 0/1: 30%		
Pezzolo et al.[f]	107	Mean EASI 24	*Week 32:*	*Week 52:*	Injection-site reaction, 2.9%
			Mean EASI 1.6 -> 93.4% mean reduction EASI 50: 100% EASI 75: 95.1% EASI 90: 73.8%	Media EASI 1.1-> 95.5% mean reduction EASI 50: 100% EASI 75: 95.4% EASI 90: 95.4%	Psoriasis, 1.2% (suspension) Conjunctivitis, 1.7% and temporary suspension, 0.6% Herpes virus, 0.6% Erythroderma, 0.6% Ineffectiveness and suspension, 1.17% Suspension due to improvement, 0.6% Suspension due to pregnancy, 0.6%
		PP-NRS 7.7	PP-NRS 1.6 -> 79.2% mean reduction	PP-NRS 1.3 -> 83.1% mean reduction	
		S-NRS 6.1	S-NRS 0.7 -> 88.5% mean reduction	S-NRS 0.8 -> 86.8% mean reduction	
		DLQI 13.2	DLQI 2.4 -> 81.8% mean reduction	DLQI 1.5 -> 88.6% mean reduction	
Pezzolo et al.[g]	17	Prurigo nodularis-like phenotype	Prurigo nodularis-like phenotype	Prurigo nodularis-like phenotype	Mild conjunctivitis, 12% Local injection-site reaction
		Mean (range)	*Week 12:*		Localized rash
		EASI 27.2 (16-45)	EASI 50: 100% EASI 75: 100%	*Week 32:* EASI 1.7 EASI 50: 100% EASI 75: 100% EASI 90: 100%	Mild herpetic stomatitis
		IGA 3.7 (3-4)	IGA 0/1: 47%	IGA 0/1 70%	
		PP-NRS 9.8 (8-10)	60% mean reduction	95% mean reduction	
		S-NRS 8.9 (6-10)	85% mean reduction	95% mean reduction	
		DLQI 16.3 (14-24)	70% mean reduction	85% mean reduction	

Table 2 (*Continued*)

Study	N	Mean efficacy			Safety
		Baseline	1st assessment	2nd assessment	
García Castro et al.[h]	15	Mean (range) EASI 22 (1-45) Unknown basal IgA Unknown basal PP-NRS	*Week 16:* EASI 75: 60% EASI 90: 27% EASI 100: 6.67% IGA 0/1: 33% PP-NRS improvement in, at least, 4 points: 33%	Not assessed	Mild dry eye, 7% Blepharoconjunctivitis, 7%
Pereyra-Rodríguez et al.[i]	85	Mean (± SD) EASI 25.4 (± 8.1) Biologic therapy-naïve patients: EASI 24.6 Non-biologic therapy-naïve patients: EASI 27.2 SCORAD 55.8 (± 13.3) DLQI 15.8 (± 5.4) PP-NRS 8.1 (± 1.8) IGA 4: 55% of the patients	*Week 16:* Mean (± SD) EASI 7.5 (± 6.9) -> 70% mean reduction EASI 50: 82% EASI 75: 58% EASI 90: 21% Biologic therapy-naïve patients: EASI 6.3 EASI 75: 67% Non-biologic therapy-naïve patients: EASI 10.2 EASI 75: 41% SCORAD 20.0 (± 14.78) -> 64% mean reduction DLQI −64% mean reduction PP-NRS 3.5 (± 2.4) -> 57% mean reduction IGA 0/1: 19%	Not assessed	Conjunctivitis, 6% → 1.17% discontinued treatment Red face, 6% Worsening of AD lesions 4% Local injection-site reaction, 2.35% Depression/anxiety, 2.35% Arthralgia, 1.17% Corneal herpes, 1.17% Menstrual pain, 1.17% Upper respiratory tract infection, 1.17% Syncopal episodes, 1.17%
De Greef et al.[j]	14	*Study on adolescents* Median (± IQR) EASI 24.3 (± 8.4) PP-NRS 8.0 (± 2.0)	*Study on adolescents* *Week 12-16* EASI 50: 71.4% EASI 75: 28.6% PP-NRS improved in, at least, 4 points: 42.8%	Not assessed	Flares of atopic dermatitis, 50% Injection-site reaction, 14.3% → cause for discontinuation in 6.66% 6.66% discontinued due to inefficacy
Current study	14	Mean (range) SCORAD 56 (21-72)	*Week 16:* SCORAD 75: 84.6% SCORAD 90: 23.1%	*Week 24:* SCORAD 75: 71.4% SCORAD 90: 28.6%	Xerophthalmia and ocular pruritus, 38.4% Injection-site reaction 13.4% (7.7% reason for drug discontinuation) Lack of efficacy and discontinuation, 14.5%

Table 2 (*Continued*)

Study	N	Mean efficacy			Safety
		Baseline	1st assessment	2nd assessment	
		IGA 4 4 (1-4) Total clearance 0%	IGA 0/1 84.6% Total clearance 7.7%	IGA 0/1 71.4% Total clearance 28.6%	

The above are the different real-world studies of tralokinumab available after conducting a bibliographic search on PubMed using the criteria ''Tralokinumab'' and ''Real life'' or ''Clinical practice.'' Real-world studies whose main objectives were to assess dupilumab-related conjunctivitis after switching to tralokinumab were not included. The objectives of each study, patient characteristics, and mode of evaluation differ, complicating comparisons among them. However, similar efficacy can be seen in all of them, with a good safety profile for tralokinumab to treat moderate-to-severe AD.

ADCT, Atopic Dermatitis Control Tool; AE, adverse event; DLQI, Dermatology Life Quality Index; EASI, Eczema Area and Severity Index; IGA, Investigator's Global Assessment; IQR, interquartile range; PP-NRS, Peak Pruritus Numerical Rating Scale; S-NRS, Sleep-Numerical Rating Scale; SCORAD, SCORing Atopic Dermatitis; SD, standard deviation.

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Conflicts of interest

None declared.

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