

Dupilumab: short-term effectiveness and security in real clinical practice – A retrospective multicentric study

Dear Editor,

Atopic dermatitis (AD) is a chronic systemic disease that has a multifactorial aetiology, where immune system disorders and epidermal barrier dysfunction are added to the influence of genetic and environmental factors.¹⁻⁴ In AD, Th2 lymphocytes secrete several cytokines, where IL-4/IL-13 plays a key role in the proinflammatory loop, decreasing the expression of structural proteins of the epidermis, and leading to the formation of inflammatory and very pruritic lesions.⁵⁻⁷ Dupilumab is a fully human monoclonal antibody (mAb) targeted against the α -subunit of interleukins 4 and 13 receptors (IL-4R α) that blocks the signalling of both IL-4 and IL-13.⁵ Both IL-4 and IL-13 are highly expressed in acute and chronic epidermal lesions of patients with AD, and their inhibition has been proved effective in adult patients with moderate and severe AD. Dupilumab has been approved by the US and EU regulatory agencies in 2017 for the treatment of moderate to severe atopic dermatitis in adult patients who are candidates for systemic treatment.^{6,7}

The clinical trials SOLO1, SOLO2 and CHRONOS analyse the efficacy and safety data of more than 2100 patients. The first two studies show short-term results (16 weeks) of dupilumab used in monotherapy, and the last one in the medium term (52 weeks), allowing the concomitant use of topical corticosteroids. In these trials, the mean baseline SCORAD was over 65, and dupilumab arms achieved a significant improvement (69.7% vs. baseline SCORAD) at week 52.

In this short report, we present a retrospective multicentric study, in which five hospitals in Andalusia, Spain, have taken part. Data from patients were collected between October 2017 and mid-April 2018. Our objective is to evaluate the safety and effectiveness of dupilumab in patients with moderate to severe AD with at least 12 weeks of treatment follow-up. In the moment of the analysis, 27 adult patients, who were treated following the standard posology (dupilumab 300 mgx2 at week 0 and 300 mg s.c. every 2 weeks), were reviewed. Demographic variables (age, sex, time of evolution of atopic dermatitis) and comorbidities and personal history (nasal polyposis, seasonal rhinitis, extrinsic bronchial asthma, food allergies and conjunctivitis) were collected. Baseline characteristics are shown in Table 1. Severity was assessed by measuring baseline SCORAD and pruritus VAS, and its evolution at weeks 4 and 12. Drug survival was also collected at each cut-off point, as also were adverse effects that led to treatment interruption or intervention.

Table 1 Baseline characteristics of our series

Variable	Value
Age (years)	42.11 (19-64)
Male (gender)	70.37 males (19/27)
Average time of evolution of AD (years)	25.70 years (3-44 ys)
Comorbidities (%)	
Nasal polyposis	14.81%
Conjunctivitis	33.38%
Extrinsic bronchial asthma	37.03%
Allergic rhinitis	55.55%
Food allergies	22.22%
Previous treatments	
Systemic corticosteroids	100%
Oral cyclosporine	96.29%
Phototherapy (UVBBE)	40.74%
Methotrexate	37.03%
Azathioprine	44.44%
MMF	14.80%
Immunoglobulins ivs	29.62%

Table 2 Evolution of SCORAD and VAS pruritus

Severity scores			
	Basal	W4	W12
SCORAD	58.7	20	15.03
VAS pruritus	8.18	3.04	2.4

The efficacy and safety data achieved throughout the treatment period in our series are reflected in Table 2. A significant improvement of SCORAD and pruritus VAS was observed from week 4, with a slower but progressive further improvement at week 12. Three cases of conjunctivitis at week 4 have been described, persisting at week 12. These cases were treated with routine anti-inflammatory eye drops, without suspension of dupilumab treatment. In our series, based on actual clinical practice, the use of topical corticosteroids on demand has been allowed according to the patients criteria. To date, all patients continue under treatment with dupilumab.

The most frequently reported side-effects have been reactions at the site of injection (erythema and oedema) and conjunctivitis, which seems to be a specific adverse effect although its current pathology is unknown. No severe adverse effects have been reported.⁸

The main limitation of our series is the lowest number of patients enrolled, but gives valuable preliminary information about the short-term efficacy and safety of dupilumab in real-world patients. Another limitation is having assessed SCORAD instead (or in addition to) EASI score, which may have allowed us to establish further and deeper comparisons to RCT. It is necessary to continue collecting efficacy and safety data in the medium and long terms, in order to evaluate the survival of the drug and the potential need (if exists) of simultaneous use of systemic therapies.

Author contributions

RRV, JDC, JCAH,LMP,SAL,JJPR: Acquisition of data, Editing. RRV, JJPR: Study concept and Design, Writting, Editing. RRV, JJPR: Design, Critical Review.

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Real-life effectiveness of biological drugs on psoriatic difficult-to-treat body regions: scalp, palmoplantar area and lower limbs

Editor

Psoriasis is a chronic, inflammatory disease, often requiring long-term therapy.¹ Scalp, nails, palms and soles have been

labelled as ‘difficult locations’ of psoriasis. Indeed, they are usually too sensitive to be treated with potent topical products for long periods, frequently necessitating systemic drugs, possibly are more resistant to therapies respect to other body sites and tend to show recurrent disease relapse. All these features increase the psychological burden of disease.^{2–4} To date, knowledge about the use of biological antipsoriatic therapies in the management of difficult-to-treat body regions is fragmentary, lacking in agreement on the best therapeutic modalities and/or universally shared algorithm.^{2–10} Here, we report the results of our perspective real-life study, aimed to evaluate the effect of biological drugs on difficult-to-treat psoriatic areas.

Subjects were enrolled consecutively from patients attending the Psoriasis Care Center of the Outpatient Clinic of the Section of Dermatology, University of Naples Federico II, between March 2017 and January 2018. Inclusion criteria were as follows: (i) adult age (≥ 18 years); (ii) diagnosis of moderate-to-severe plaque psoriasis (with or without psoriatic arthritis) since at least 6 months; (iii) presence of at least one of three difficult psoriatic locations, among scalp, palmoplantar region (non-pustular psoriasis) and lower limbs; besides these, other body areas could also be involved. Patients did not receive any systemic or topical antipsoriatic treatment for at least 3 months before the study onset. Assessment was performed before (t0) and after a course of 12 weeks (t1) of biological therapy, by the use of multiple scores: (i) local indexes of the difficult-to-treat areas [Psoriasis Scalp Severity Index (PSSI), Palmoplantar Pustulosis Psoriasis Area and Severity Index (PPPASI), Lower Limb Psoriasis Area and Severity Index (LLPASI)]; (ii) Psoriasis Area and Severity Index (PASI) referred to the full-body area interested by disease; (iii) body surface areas (BSA); and (iv) Dermatology Life Quality Index (DLQI).

Forty-six patients with psoriasis met the inclusion criteria, and 24 of 46 had psoriatic arthritis. Baseline demographic characteristics and medication history are summarized in Table 1,

Table 1 Baseline demographic characteristics and medication history of 46 enrolled psoriatic patients

Gender, n (%)	
Male	27 (58.7)
Female	19 (41.3)
Mean age, years	49.6
Age range, years	18–78
Previous traditional therapies (acitretin and/or cyclosporine and/or methotrexate), n (%)	34 (73.9)
Biologics-naïve patients, n (%)	30 (65.2)
Previous biological therapies, n (%)	16 (34.8)
anti-TNF- α	14 (87.5)
anti-IL-12/23	2 (12.5)
anti-IL-17	0 (0)

n, number of patients.