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Letter to the Editor

Efficacy of Dupilumab in Concomitant Atopic Dermatitis and Chronic Rhinosinusitis With Nasal Polyps: A Preliminary Study

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To the Editor,

The IgG4 monoclonal antibody dupilumab targets the interleukin-4 receptor alpha chain (IL-4Rα), thus inhibiting the biological effects of the cytokines IL-4 and IL-13 essential for the Th2 response.[1-3] We performed a prospective observational real-life study to evaluate the efficacy of dupilumab in patients with chronic rhinosinusitis with nasal polyps (CRSwNP) associated with moderate-to-severe atopic dermatitis (msAD).

A task force of the Italian Society of Allergy, Asthma and Clinical Immunology was involved in this observational, prospective study from September 2018 to October 2019. Adult patients with concomitant CRSwNP and msAD (Eczema Area Severity Index[4] score ≥ 24) were enrolled.

At screening, patients must have a bilateral endoscopic nasal polyp score (NPS)[5] of at least one of the following symptoms and exhibit at least two of the following symptoms: nasal congestion or obstruction and either loss of smell or nasal discharge (anterior or posterior).

The study protocol was approved by the Ethical Committee of Naples University Hospital Italy (IRB No. 161/19). Informed consent was obtained from all patients.

All patients were treated with a 600-mg loading dose and subsequent biweekly 300-mg injections of dupilumab for 16 weeks. Patients were asked to discontinue systemic immunosuppressants and to maintain their pretreatment therapy for the management of CRSwNP before starting dupilumab treatment.

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Disclosure

There are no financial or other issues that might lead to conflict of interest.

Table 1. Change in outcome measures between baseline and 16 weeks for AD patients with CRSwNP treated with dupilumab (n = 9)

Outcome	Baseline	Week 16	*P* value*
Bilateral NPS (scale 0–8)	2.8 ± 1.2	1.9 ± 1.2	< 0.05
SNOT-22 score (scale 0–110)	30.2 ± 17.2	15.8 ± 8.7	< 0.05
Nasal congestion or obstruction score (scale 0–3)	2.6 ± 0.7	1.0 ± 0.7	< 0.05
Loss-of-smell score (scale 0–3)	1.6 ± 1.0	0.2 ± 0.4	< 0.05
Rhinosinusitis disease severity (visual analog scale 0–10 cm)	7.5 ± 1.3	2.8 ± 1.0	< 0.05
RCSS score (scale 10–50)	34.4 ± 7.8	21.2 ± 4.1	< 0.05
RQLQ score (scale 0–6)	1.9 ± 1.1	1.3 ± 0.9	> 0.05
EASI (range 0–72)	40.4 ± 14.0	4.9 ± 1.6	< 0.05
SCORAD (range 0–103)	74.4 ± 14.8	29.6 ± 8.6	< 0.05
IGA (scale 0–4)	3.8 ± 0.4	2.4 ± 1.1	< 0.05
Peak pruritus NRS (range 0–10)	8.7 ± 1.0	2.6 ± 1.3	< 0.05
Peak sleep NRS (range 0–10)	7.8 ± 2.3	0.8 ± 1.3	< 0.05
DLQI (range 0–30)	19.1 ± 8.5	3.7 ± 2.1	< 0.05
IGA score of 0/1 and reduction ≥ 2 points		4 (44.1)	
EASI75		9 (100.0)	
Total IgE (kU/L)	9,116.2 ± 12,628.1	5,200.8 ± 5,286.9	> 0.05
Eosinophils (cells/mm^3)	577.1 ± 340.6	595.7 ± 552.1	> 0.05

Values are presented as mean ± standard deviation or number (%).
AD, atopic dermatitis; CRSwNP, chronic rhinosinusitis with nasal polyps; DLQI, Dermatology Life Quality Index; EASI, Eczema Area and Severity Index; EASI75, Eczema Area and Severity Index score improvement of at least 75%; IGA, Investigator's Global Assessment; NPS, Nasal Polyp Score; NRS, Numerical Rating Scale; RCSS, Rhinitis Control Scoring System; RQLQ, Rhinitis Quality of Life Questionnaire; SCORAD, SCORing Atopic Dermatitis; SNOT-22, 22-item Sino-Nasal Outcome Test; IgE, immunoglobulin E.
*Data were compared with Wilcoxon test for paired data. Statistical significance at a level of $P < 0.05$.

Patients were assessed for medical history, demographics, adverse events, and efficacy outcomes at baseline and every 4 weeks (weeks 4–16). AD and CRSwNP were evaluated using a series of variables as well as ear, nose and throat examinations during dupilumab therapy (**Table 1**).

The coprimary endpoints were changes from baseline in both endoscopic NPS and 22-item Sino-Nasal Outcome Test (SNOT-22)[1] scores in week 16.

Patient data were compared using the Wilcoxon test for paired data. All statistical analyses were performed with SPSS version 20 (IBM, Armonk, NY, USA). The threshold for statistical significance was set at $P < 0.05$.

Nine patients (5 females and 4 males, mean age 41.3 ± 10.5 years) with msAD and CRSwNP were included in the study. All patients had previously received systemic corticosteroids or sinonasal surgery (22.2%).

Table 1 shows the results for each efficacy parameter used for AD and CRSwNP. The endoscopic NPS and SNOT-22 scores significantly diminished from baseline in week 16 ($P < 0.05$), 6 of 9 patients (66.7%) achieving at least a 1-point improvement in NPS in week 16. Such outcomes, although confirmation by trials is warranted, suggest the possibility to treat the 2 different disorders with a single therapy, with favorable effects especially in the cost-effectiveness aspect. Actually, a study analyzing cost-utility of dupilumab for AD by using the appropriate cost-effectiveness parameters, such as quality-adjusted life years and incremental cost-effectiveness ratio (ICER), found that the treatment was more cost-effective in patients with severe AD, but even in patients with moderate AD the ICER remained below the upper range.[6] No pharmacoeconomic analysis on dupilumab for CRSwNP is available.[7] However, considering the cost-effectiveness demonstrated for AD treatment, it is reasonable to hypothesize that a single

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treatment in patients with the 2 different pathologies could be further profitable. This must be confirmed by cost-effectiveness studies with a larger patient population.

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