Effectiveness and safety of dupilumab for the treatment of atopic dermatitis in a real-life French multicenter adult cohort

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Background: Dupilumab is the first biologic available to treat atopic dermatitis (AD). Its effectiveness and safety were demonstrated in clinical trials.

Objective: We sought to assess the effectiveness and safety of dupilumab in adults with AD in a real-life French multicenter retrospective cohort.

Methods: We included patients treated during March 2017-April 2018. Efficacy outcomes, including Scoring Atopic Dermatitis (SCORAD) and Eczema Area and Severity Index (EASI) scores, were collected at baseline and 3 months when available. Adverse events (AEs) were recorded at follow-up.

Results: We included 241 patients. The median ± interquartile range (IQR) follow-up time was 3.8 ± 3.7 months. A ≥75% improvement in SCORAD was achieved in 27 of 163 (16.6%) patients, and a ≥75% improvement in EASI was achieved in 40 of 82 (48.8%) patients. The median SCORAD and EASI

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scores at 3 months were significantly lower than those at baseline (SCORAD ± IQR, 25 ± 21 vs 56 ± 27.4, $P < 10^{-9}$ and EASI ± IQR, 4.1 ± 6.8 vs 17.9 ± 15.4, $P < 10^{-9}$, respectively). Conjunctivitis was reported in 84 of 241 (38.2%) patients. The proportion with eosinophilia (>500 cells/mm^3) during follow-up (57%) was higher than that at baseline (33.7%) (n = 172, $P < 10^{-6}$). Dupilumab was stopped in 42 cases; 27 patients stopped because of AEs.

Limitations: No control group, missing data.

Conclusion: This real-life study demonstrated a similar dupilumab effectiveness as that seen in clinical trials, but it also revealed a higher frequency of conjunctivitis and eosinophilia. (J Am Acad Dermatol 2019;81:143-51.)

Key words: adults; atopic dermatitis; biotherapy; conjunctivitis; dupilumab; eosinophilia.

Atopic dermatitis (AD), a chronic inflammatory disease affecting 2%-5% of adults,[1] can have a major impact on quality of life. For moderate-to-severe AD, the efficiency of topical therapy is often limited, and conventional systemic treatments (eg, cyclosporine) that carry significant long-term use risks might be required for treatment. Dupilumab, a monoclonal antibody directed against the alpha subunit of the interleukin 4 receptor, is the first biologic that became available for the treatment of inadequately controlled moderate-to-severe AD in adults. The data available regarding efficacy and safety are from clinical trials[2-4] and, therefore, represent a select population that does not necessarily reflect prescribing conditions in daily practice. This study was designed to assess the effectiveness and tolerance of dupilumab in adult patients with AD in a real-life French multicenter retrospective cohort.

CAPSULE SUMMARY

- Few data are available with regard to the effectiveness and safety of dupilumab in real-life conditions.
- This study confirmed the effectiveness of dupilumab in daily practice but demonstrated a higher frequency of conjunctivitis and eosinophilia compared with clinical trial results.

METHODS

Study design and population

In this study, we evaluated data collected from a French multicenter retrospective cohort conducted by the Groupe de Recherche sur l'Eczéma Atopique. Consecutive patients >18 years old evaluated by members of the Groupe de Recherche sur l'Eczéma Atopique during March 2017-April 2018 given AD diagnoses according to the revised Hanifin and Rajka criteria[5] were eligible for this study. The patients received dupilumab for moderate-to-severe

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Conflicts of interest: Dr Jachiet, Prof Bouaziz, Dr Lasek, Dr Du-Thanh, Dr Raison-Peyron, Dr Tetart, Dr Duval-Modeste, Prof Misery, Prof Richard, Dr Barete, and Prof Seneschal received personal fees from Sanofi Genzyme. Dr Reguiai received personal fees from Leo-Pharma, AbbVie Inc, and Sanofi Genzyme. Dr Nosbaum received research grants and personal fees from Sanofi Genzyme. Dr Morice received personal fees from Sanofi Genzyme, Novartis, and Janssen. Dr Soria received personal fees from Sanofi Genzyme and Novartis. Prof Lacour received personal fees from Sanofi Genzyme and personal fees and research grants from Regenron, United States. Prof Barbarot received personal fees from Sanofi Genzyme, Leo Pharma, Janssen, AbbVie, Bioderma, and Pierre Fabres. Prof Staumont-Sallé received personal fees from Sanofi Genzyme. Dr Faiz, Dr Giovannelli, Ms Podevin, Dr Ferrier le Bouëdec, Prof Aubin, Prof Dompmartin, Dr Droitcourt, Dr Arnault, Dr Delaunay, Dr Mahé, Dr Schoeffler, Dr Begon, Dr Walter-Lepage, Dr Dillies, Dr Rappelle-Duruy, Dr Bellon, Dr Beneton, and Dr Valois have no conflicts of interest to disclose.

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Abbreviations used:

AD:	atopic dermatitis
AE:	adverse event
DLQI:	Dermatology Life Quality Index
EASI:	Eczema Area and Severity Index
EASI50:	EASI score improvement of at least 50%
EASI75:	EASI score improvement of at least 75%
IQR:	interquartile range
SCORAD:	Scoring Atopic Dermatitis
SCORAD50:	SCORAD score improvement of at least 50%
SCORAD75:	SCORAD score improvement of at least 75%

AD due to inefficiency, loss of efficiency, or contraindication of a previous systemic agent according to the French Early Access Program set up during this period.

This study was approved by the organization Commission Nationale de l'Informatique et des Libertés (no. DEC16-355). Patients' nonopposition for the use of their deidentified records was obtained for this noninterventional study, according to French legislation.

Data collection

A questionnaire was completed by clinicians using the medical charts. Baseline characteristics were demographic variables, comorbidities, AD form, previous treatments, date of introduction, and dose of dupilumab. Three validated scores, the Scoring Atopic Dermatitis (SCORAD), Eczema Area and Severity Index (EASI), and Dermatology Life Quality Index (DLQI),[6-8] and the blood eosinophil count were recorded at baseline and follow-up. In addition, adverse events (AEs) were collected. Last, we evaluated the discontinuation of dupilumab at the end of follow-up and collected the reasons for stopping treatment.

Outcomes

SCORAD, EASI, and DLQI at 3 months were defined by using a conservative approach, the highest score recorded after 2, 3, or 4 months of treatment, to increase the number of patients with available outcomes because the follow-up time was not standardized among the different centers. The primary outcome was defined as SCORAD at 3 months compared with baseline. The secondary outcomes were defined in the same way for the EASI and DLQI scores. Other outcomes for effectiveness were the median percent change of SCORAD and EASI between baseline and 3 months, the mean change of DLQI, and the proportion of patients with improvements of SCORAD or EASI scores of at least 50% (SCORAD50, EASI50) or 75% (SCORAD75, EASI75). AD flares were defined as AD exacerbations according to the investigators' opinion. Eosinophilia and hypereosinophilia were defined as a blood eosinophil count >500 cells/mm^3 and >1500 cells/mm^3, respectively. Eosinophilia at follow-up (assessed or evaluated with or by at least 1 dosage of blood eosinophils within 6 months of follow-up) was compared with baseline. AEs were defined as occurrences of any untoward medical condition during the treatment period.

Statistical analyses

Characteristics of patients with and without an assessment of outcomes were compared by using Student *t* tests, Wilcoxon tests (in cases of nonnormality) for quantitative variables, and Fisher's exact tests for qualitative variables. The comparison between the SCORAD, EASI, or DLQI scores from baseline to 3 months was performed by using Wilcoxon's matched pairs tests. A sensitivity analysis was performed by excluding the patients treated with concomitant systemic treatments for AD. The comparison between the proportions of patients with eosinophilia at baseline and follow-up was performed by using the McNemar test. We reported the number (percentage) of patients with AEs, as well as the reasons they stopped treatment with dupilumab. Because the follow-up was not the same for all patients, we evaluated maintenance of dupilumab during the follow-up using the Kaplan–Meier method. All statistical analyses were performed with R version 3.3.3 by using the Hmisc and survival packages. The threshold for statistical significance was set at $P < .05$.

RESULTS

Baseline characteristics

The study population included 241 patients from 29 hospital centers with a median ± interquartile range (IQR) follow-up time of 3.8 ± 3.7 months (Table I). The median ± IQR scores at baseline were 54 ± 26.8 for SCORAD, 18.3 ± 15 for EASI, and 14 ± 10.8 for DLQI. The SCORAD score was assessed at baseline and 3 months in 163 (67.6%) patients. Complete data was available from 82 (34%) patients for EASI and 85 (35.3%) patients for DLQI.

Dupilumab effectiveness

The median ± IQR SCORAD score for patients at 3 months was significantly lower than that at baseline (25 ± 21 vs 56 ± 27.4, $P < 10^{-9}$), corresponding to a median ± IQR percent change of −52.5% ± 44% (Table II; Fig 1). The median ± IQR EASI and DLQI

Table I. Baseline characteristics of whole population and comparison of patients with and without a SCORAD score assessment at baseline and 3 months

Characteristic	Patients (patients with SCORAD assessed), n	Whole population, n = 241	SCORAD score assessed at baseline and 3 months		
			Yes, n = 163	No, n = 78	*P* value
Demographics					
Follow-up, months, median (IQR)	241 (78)	3.8 ± 3.7	4.3 ± 3.9	3.3 ± 3.6	<.001
Age, years, median (IQR)	241 (78)	37 ± 22	36 ± 23	38 ± 19.5	.27
Male sex	240 (162)	144 (60)	98 (60.5)	46 (59)	.89
Body mass index, kg/m^2	197 (53)	24.4 ± 4.7	24.5 ± 4.6	24.2 ± 5.2	.71
Education level, years of full-time education					.56
<9	178 (132)	1 (0.6)	1 (0.8)	0 (0)	
9	178 (132)	14 (7.9)	9 (6.8)	5 (10.9)	
<11	178 (132)	27 (15.2)	21 (15.9)	6 (13)	
12	178 (132)	46 (25.8)	31 (23.5)	15 (32.6)	
>12	178 (132)	90 (50.6)	70 (53)	20 (43.5)	
Smoking status					.11
Current smoker	204 (145)	64 (31.4)	40 (27.6)	24 (40.7)	
Former smoker	204 (145)	38 (18.6)	26 (17.9)	12 (20.3)	
Never smoker	204 (145)	102 (50)	79 (54.5)	23 (39)	
Alcohol use, >0 g/day	195 (141)	11 (5.6)	8 (5.7)	3 (5.6)	>.99
Atopic dermatitis factors					
Diagnosis					.54
Infant	237 (160)	81 (34.2)	59 (36.9)	22 (28.6)	
Child	237 (160)	118 (49.8)	78 (48.8)	40 (52)	
Teenager	237 (160)	18 (7.6)	11 (6.9)	7 (9.1)	
Adult	237 (160)	20 (8.4)	12 (7.5)	8 (10.4)	
Localization					
Diffuse	230 (157)	207 (90)	144 (91.7)	63 (86.3)	.24
Head and neck	225 (155)	18 (8)	11 (7.1)	7 (10)	.44
Scores at baseline, median (IQR)					
SCORAD	211 (48)	54 ± 26.8	56 ± 27.4	48.5 ± 29.3	.017
EASI	100 (19)	18.3 ± 15	18.2 ± 15.3	20 ± 11.4	.32
DLQI	122 (19)	14 ± 10.8	14 ± 10.5	14 ± 8.5	.30
History of treatments for atopic dermatitis					
Topical treatments					
Topical corticosteroids	235 (159)	232 (98.7)	157 (98.7)	75 (98.7)	>.99
Topical tacrolimus	218 (150)	179 (82.1)	120 (80)	59 (86.8)	.26
Emollients	237 (160)	236 (99.6)	159 (99.4)	77 (100)	>.99
Systemic treatments					
Number of lines	241 (78)	2.9 ± 1.4	2.8 ± 1.4	3.2 ± 1.5	.050
Phototherapy	236 (158)	154 (65.3)	98 (62)	56 (71.8)	.15
Cyclosporine	239 (162)	179 (74.9)	115 (71)	64 (83.1)	.06
Methotrexate	232 (157)	125 (53.9)	84 (53.5)	41 (54.7)	.89
Azathioprine	219 (148)	24 (11)	14 (9.5)	10 (14.1)	.36
Other systemic treatment*	221 (152)	75 (33.9)	48 (31.6)	27 (39.1)	.29
Medical history					
Atopy					
Allergic asthma	235 (159)	155 (66)	103 (64.8)	52 (68.4)	.66
Allergic rhinitis	226 (157)	129 (57.1)	98 (62.4)	31 (44.9)	.019
Allergic conjunctivitis	225 (158)	101 (44.9)	74 (46.8)	27 (40.3)	.38
Food allergy	224 (155)	58 (25.9)	41 (26.5)	17 (24.6)	.87
Eosinophilia, >500 cells/mm^3	218 (150)	88 (40.4)	63 (42)	25 (36.8)	.55
Viral infections					
HSV recurrent infection	198 (142)	26 (13.1)	19 (13.4)	7 (12.5)	>.99
Disseminated HSV infection	223 (156)	14 (6.3)	9 (5.8)	5 (7.5)	.76
Varicella	159 (116)	30 (18.9)	23 (19.8)	7 (16.3)	.82
Herpes zoster	204 (143)	11 (5.4)	8 (5.6)	3 (4.9)	>.99

Quantitative variables are expressed as mean ± standard deviation and compared with Student *t* tests, or median ± interquartile range and compared with Wilcoxon tests in case of non-normality. Qualitative variables are expressed as n (%) and compared with Fisher's exact tests.

DLQI, Dermatology Life Quality Index; *EASI*, Eczema Area and Severity Index; *HSV*, herpes simplex virus; *IQR*, interquartile range; *SCORAD*, Scoring Atopic Dermatitis.

*Other systemic treatments: systemic corticosteroids (n = 20), mycophenolate-mofetil (n = 17), retinoids (n = 16), omalizumab (n = 12), polyvalent immunoglobulins (n = 5), antifungals (n = 3), tetracyclines (n = 3), thalidomide (n = 2), tumor necrosis factor α inhibitors (n = 2), lebrikizumab (n = 2), extracorporal photopheresis (n = 2), apremilast (n = 1), dapsone (n = 1), and montelukast (n = 1).

Table II. Efficacy outcomes at 3 months

Outcome	N (% of the whole population)	Baseline	Month 3	*P* value*
SCORAD, median ± IQR	163 (67.6)	56 ± 27.4	25 ± 21	$<10^{-9}$
EASI, median ± IQR	82 (34.0)	17.9 ± 15.4	4.1 ± 6.8	$<10^{-9}$
DLQI, median ± IQR	85 (35.3)	13 ± 11	4 ± 8	$<10^{-9}$
Median percent change ± IQR in SCORAD	163 (67.6)		−52.5 ± 44	
Median percent change ± IQR in EASI	82 (34.0)		−71.3 ± 41.3	
Mean change ± SE in DLQI	85 (35.3)		−7.3 ± 0.8	
SCORAD50, n (%)	163 (67.6)		86 (52.8)	
SCORAD75, n (%)	163 (67.6)		27 (16.6)	
EASI50, n (%)	82 (34.0)		59 (72)	
EASI75, n (%)	82 (34.0)		40 (48.8)	

Outcomes are a comparison between baseline and follow-up at 3 months.
DLQI, Dermatology Life Quality Index; *EASI*, Eczema Area and Severity Index; *EASI50*, EASI score improvement of at least 50%; *EASI75*, EASI score improvement of at least 75%; *HSV*, herpes simplex virus; *IQR*, interquartile rangen; *SCORAD*, Scoring Atopic Dermatitis; *SCORAD50*, SCORAD score improvement of at least 50%; *SCORAD75*, SCORAD score improvement of at least 75%; *SE*, standard error.
*Compared with Wilcoxon's matched pairs tests. The median percent change ± IQR was defined as the median of the percentage of change in SCORAD (or EASI) from baseline to 3 months calculated for each patient. The mean change ± SE was defined as the mean of the difference in DLQI from baseline to 3 months calculated for each patient.

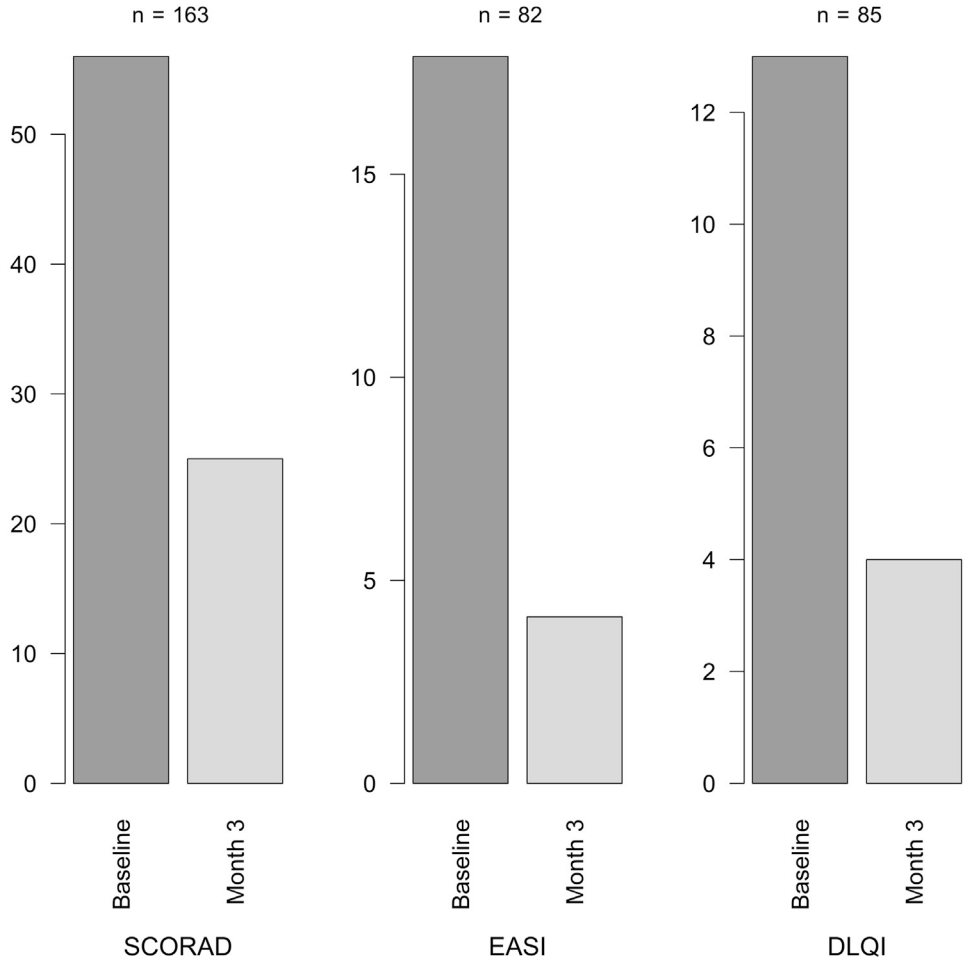

Fig 1. SCORAD, EASI, and DLQI scores at baseline and month 3. *DLQI*, Dermatology Life Quality Index; *EASI*, Eczema Area and Severity Index; *SCORAD*, Scoring Atopic Dermatitis.

scores at 3 months were significantly lower than those at baseline (EASI 4.1 ± 6.8 vs 17.9 ± 15.4, $P < 10^{-9}$ and DLQI 4 ± 8 vs 13 ± 11, $P < 10^{-9}$, respectively). A total of 188 (79%) patients were concomitantly treated with topical corticosteroids. The results were similar when we excluded the 12 patients treated with concomitant systemic treatments (data not shown).

At 3 months, 86 of 163 (52.8%) patients had achieved SCORAD50 and 27 (16.6%) SCORAD75, while 59 of 82 (72%) patients had achieved EASI50 and 40 (48.8%) EASI75 (Table II). Patients who achieved SCORAD50 at 3 months had a higher SCORAD ± IQR at baseline than their counterparts (62 ± 24 vs 48 ± 22.8, $P < .001$) and a lower proportion of topical corticosteroid (TCS) use concomitantly with dupilumab (69.4% vs 87%, $P < .008$).

AD flares

While being treated with dupilumab, 75 (31.1%) patients experienced at least 1 event considered as an AD flare by the investigator. A total of 106 flares were recorded. For cases in which data on severity of flares was available (96/106), 20 (20.8%) flares were described as severe exacerbation of AD. The first exacerbation occurred at a median ± IQR of 2.3 ± 1.5 months after dupilumab introduction. The management of flares was mainly accomplished (89.4%) by the use of topical treatments (emollients, TCS, or tacrolimus). In 1 patient, concomitant treatment with methotrexate was initiated.

Dupilumab safety

At least 1 AE was reported in 171 of 241 (71%) patients (Table III). Of 220 patients, 107 (48.6%) had a noninfectious ophthalmologic AE, including 84 (38.2%) cases of conjunctivitis. Among the 84 patients with conjunctivitis diagnosed by the investigator, 39 were referred to an ophthalmologist who made the diagnosis of conjunctivitis in 32 (82.1%) patients. The development of conjunctivitis was associated with a medical history of allergic conjunctivitis (57.3 in patients who have developed conjunctivitis vs 35.7% in patients who have not developed conjunctivitis, $P < .003$).

In total, 6 of 208 (2.9%) patients, including 1 patient with herpes simplex virus keratoconjunctivitis, developed eye infection.

Of the 177 patients who had at least 1 blood eosinophil count within 6 months of follow-up, 100 (56.5%) had blood eosinophilia. Among cases with available data (172/177), the proportion of patients who had eosinophilia at follow-up (57%) was significantly higher than the proportion at baseline (33.7%, $P < 10^{-6}$). The result of the blood eosinophil count in the follow-up was unknown for 6 patients. Of the 94 patients with eosinophilia, 28 (29.8%) had hypereosinophilia (>1500 cells/mm^3); the maximum eosinophil count was 7800 cells/mm^3. Eosinophilia at follow-up was associated with eosinophilia at baseline (64.2% in patients who have

Table III. Adverse events

Adverse event	N	Patients, n (%)
At least 1 adverse event	241	171 (71)
Noninfectious ophthalmologic	220	107 (48.6)
Conjunctivitis		84 (38.2)
Ocular pruritus		52 (23.6)
Blepharitis		31 (14.1)
Xerophthalmia		27 (12.3)
Keratitis		14 (6.4)
Infectious ophthalmologic	208	6 (2.9)
Conjunctivitis		4 (1.9)
Keratitis		2 (<1)
Hordeolum		1 (<1)
Eosinophilia, cells/mm^3		
>500*	177	100 (56.5)
500-1000	94	44 (46.8)
1000-1500		22 (23.4)
>1500		28 (29.8)
Injection-site reaction	229	21 (9.2)
HSV infection of eye	209	11 (5.3)
HSV disseminated infection		1 (<1)
At least 1 other reported	241	60 (24.9)
Asthenia		7 (2.9)
Headache		7 (2.9)
Diarrhea		4 (1.7)
Other cutaneous†		20 (8.2)
Other infectious‡		12 (4.9)
Other§		24

HSV, Herpes simplex virus.

*Patients with at least 1 episode of eosinophilia within 6 months of follow-up.

†Other cutaneous adverse events includes folliculitis, perioral dermatitis, acne (n = 4; 1.7%); maculopapular rash (n = 3; 1.2%); flush (n = 3; 1.2%); bacterial cutaneous infection (impetigo, erysipelas, folliculitis; n = 3; 1.2%); urticaria and angioedema (n = 2; <1%); alopecia (n = 2; <1%); erythema nodosum (n = 1); photosensitivity (n = 1); and primary cutaneous CD30$^+$ lymphoma (n = 1).

‡Other infectious adverse events includes human papillomavirus infection (n = 4; 1.7%), upper respiratory tract infection (n = 3; 1.2%), urinary tract infection (n = 3; 1.2%), and digestive infection (cholecystitis, sigmoiditis; n = 2; <1%).

§Other adverse events includes nausea (n = 3; 1.2%), lymphadenopathy (n = 3; 1.2%), exacerbations asthma and chronic obstructive pulmonary disease (n = 3; 1.2%), depressive syndrome (n = 3; 1.2%), chills (n = 2; <1%), epigastric pain (n = 2; <1%), weight loss (n = 1), weight gain (n = 1), dizziness (n = 1), edema of the lower limbs (n = 1), rectal bleeding (n = 1), pudendal neuralgia (n = 1), adrenal insufficiency (n = 1), and monocytosis (n = 1).

presented eosinophilia at follow-up vs 13.5% in patients who have not presented eosinophilia at follow-up, $P < 10^{-9}$), asthma (81.4% vs 49.3%, $P < .001$), allergic rhinitis (67.8% vs 50%, $P = .025$), and food allergy (29.7% vs 16%, $P = .044$). No clinical impact was reported.

Primary cutaneous $CD30^+$ lymphoma was diagnosed in 1 patient treated with dupilumab for 3 months. However, a relationship between exposure to dupilumab and development of lymphoma was not established.

Discontinuation of dupilumab

The proportion of patients still treated with dupilumab at 3 and 6 months was 95.6% (92.9:98.5) and 79.7% (73.2:86.8), respectively. The reasons for stopping dupilumab treatment in 42 patients are summarized in Table IV.

Table IV. Discontinuation of dupilumab at the end of the follow-up period

Reason for discontinuation	n (%)
Adverse event	27 (11.3)
Noninfectious ophthalmologic	10 (4.2)
Persistent hypereosinophilia, >1500 cells/mm^3	5 (2.1)
Other*	12 (5)
Inefficiency	9 (3.8)
Wish of patient	8 (3.4)
Constraint of visits	3 (1.3)
Constraint of injections	2 (<1)
Another reason	3 (1.3)
Temporary contraindication	6 (2.5)
Pregnancy	2 (<1)
Risk of infection before surgery	4 (1.7)
Improvement of atopic dermatitis	2 (<1)

Information concerning dupilumab discontinuation was not available for 3 patients. Five patients had 2 reasons for stopping dupilumab, 1 patient had 3 reasons, and 1 had 4 reasons.
*Other adverse events includes maculopapular rash (n = 2), extension of molluscum contagiosum, urinary tract infection revealing pelvic fistula, alopecia, lymphadenopathies, exacerbation of chronic obstructive pulmonary disease, exacerbation of asthma, primary $CD30^+$ cutaneous lymphoma, lower limbs edema, nausea and diarrhea, and hepatic cytolysis.

DISCUSSION

This observational study demonstrates the effectiveness of dupilumab in real-life conditions and provides safety data during the first 6 months of exposure to dupilumab.

The strengths of this real-life study are that patients were not selected (as they are in clinical trials) and they represented a large sample of the total population treated with dupilumab in France (estimated at 530 patients in April 2018). However, our study also has some limitations, the main one being the absence of a control group. Other factors, such as the natural evolution of the disease and regression toward the average, might have had an impact on outcomes of efficacy and safety. Another important limit was the retrospective study design, which resulted in a substantial amount of missing data concerning outcomes, leading us to use the maximum score at 2-4 months as the outcome definition to increase the number of patients with available outcomes. However, the median ± IQR SCORAD according to this definition (25 ± 21, n = 163) was similar to the median ± IQR SCORAD calculated exclusively at 3 months (25.7 ± 22, n = 117), suggesting a limited measurement bias. In addition, with regard to efficacy, the characteristics of patients with and without available scores were similar, suggesting that the selection bias of patients was limited. Moreover, this real-life study was conducted to evaluate the efficiency of dupilumab in patients who concomitantly use TCS. Concerning safety outcomes, we might have underestimated the proportion of AEs. Moreover, the definition of AEs as flares and conjunctivitis were subject to investigator assessment and not standardized. Last, we were not able to assess the evolution of blood eosinophil count because only a single cell count was available for most of the patients.

Characteristics of our 241 patients were similar to those of patients included in clinical trials in terms of age, sex ratio, disease duration, atopic comorbidities, and severity.[2-4] Before dupilumab, our patients may have received more previous systemic treatments (median of ~3 previous lines), including cyclosporine, as in the LIBERTY AD CAFÉ study,[4] or methotrexate.[9]

Our study confirmed the effectiveness of dupilumab in real-life conditions; results were similar to those obtained in clinical trials. The median percent changes in SCORAD and EASI at 3 months were −52.5% and −71.3%, respectively, in our study, and the least-squares mean percent change at week 16 was −57.7% and −72.3% in the SOLO1 trial, −51.1% and −67.1% in the SOLO2 trial, −62.1% and −76.7% in the CHRONOS trail, and −62.4% and −79.8% in the CAFÉ trial. EASI75 was achieved at 3 months in 48.8% of our patients, while EASI75 was achieved at week 16 in 51% of patients in the SOLO1 trial, 44% in the SOLO2 trial, 69% in the CHRONOS trial, and 62.6% in the CAFÉ trial.[2-4]

For 12 patients, dupilumab was administered with another systemic agent during the follow-up (mainly cyclosporine or methotrexate). For most of these

patients, this concomitant treatment corresponded to an overlap between the systemic agent previously prescribed and the introduction of dupilumab, to keep the disease controlled before obtaining good efficacy with dupilumab. The sensitivity analysis performed after exclusion of these patients led to similar efficacy results. Results from the CHRONOS trial suggested that dupilumab efficacy was higher when combined with TCS.[3] In our population, 79% received concomitant treatment with TCS. The patients who did not achieve SCORAD50 at 3 months used slightly more TCS concomitantly with dupilumab than those who reached SCORAD50, suggesting the need for TCS to control the disease in our study.

Compared with the results from clinical trials, we observed a particularly high rate of conjunctivitis with dupilumab. Indeed, this AE was reported in 38.2% of our patients versus 8% of patients receiving dupilumab in a meta-analysis of these trials.[10] When the patient was referred to the ophthalmologist, the diagnosis of conjunctivitis was confirmed in >80%, suggesting a slight overestimation of this proportion. Most of the conjunctivitis was not viral or bacterial and remained of unknown cause. This AE seems to be specific to AD, considering it was not observed in patients involved in trials assessing dupilumab in conjunction with asthma[11,12] and nasal polyposis.[13] The occurrence or recurrence of conjunctivitis with dupilumab treatment was significantly associated with a medical history of atopic conjunctivitis in our study; this AE was also associated with other atopic comorbidities and with AD severity in a series of 12 patients.[14] The semiology and pathophysiology of dupilumab-induced eye disorders remain unknown, and future studies are needed to better explain the mechanism and the specificity of this AE. In our study, several therapeutics were prescribed, from artificial tears to cyclosporine eye drops, without available data concerning their effectiveness. No severe complications were reported by our investigators; however, ophthalmologic AEs often have an effect on quality of life and can lead to treatment discontinuation.

The other AE of interest in our study was eosinophilia. Indeed, we observed a higher proportion of patients with eosinophilia at follow-up compared with baseline, as well as the occurrence of hypereosinophilia in 23 patients. This AE appeared more frequently in our study than in the AD trials. Indeed, the clinical trials showed transient eosinophilia in <2% of patients.[2,3] In trials assessing dupilumab in asthma, a transient increase in blood eosinophils was mostly reported in patients with preexisting eosinophilia at baseline.[11,12] In our study, eosinophilia with dupilumab was also associated with a history of eosinophilia, asthma, and allergic rhinitis. None of our patients presented clinical signs of organ involvement due to eosinophil infiltration. However, our investigators decided to stop dupilumab for 5 patients because of persistent hypereosinophilia without another etiology. The mechanisms underlying dupilumab-induced hypereosinophilia remain unknown. Some researchers have hypothesized that dupilumab blocks the migration of eosinophils into tissue by inhibiting the interleukin 4– and interleukin 13–mediated production of eotaxins and vascular cell adhesion molecule but not eosinophil production in bone marrow.[15] Further investigations are necessary to assess whether this dupilumab-increased eosinophilia might have a clinical impact or not.

In conclusion, this real-life study of dupilumab in the treatment of AD in adults showed similar effectiveness as clinical trials, but this study also showed a higher frequency of conjunctivitis and eosinophilia that threatened the continuation of treatment.

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