Patients Withdrawing Dupilumab Monotherapy for COVID-19–Related Reasons Showed Similar Disease Course Compared With Patients Continuing Dupilumab Therapy

To the Editor:

Atopic dermatitis (AD) is a chronic inflammatory skin disease that is treated with phototherapy or systemic therapies when the disease is assessed as moderate-severe and unresponsive to topical therapies.

During COVID-19 pandemic, a few studies described the therapeutic management of AD.[1–3] In Italy, the DA-COVID-19 national registry was created to collect clinical data about the management of moderate-severe AD patients during the lockdown period (starting from February to June 2020). Pandemic-related sanitary restrictions limited the access to hospitals and determined the implementation of regular visits with telemedicine, resulting in a predominant patient-oriented assessment of disease severity.[3] Three time points for data collection were considered.[3]

Herein,[3] we describe AD course after dupilumab withdrawal. The effectiveness of dupilumab in the treatment of moderate-severe AD has been widely characterized in both real-world and clinical trial settings.[4,5] However, there is no evidence about the maintenance of treatment response after withdrawal of dupilumab therapy.

Of 1013 patients treated with dupilumab monotherapy, 75 (7.4%) interrupted therapy, with a mean duration of treatment withdrawal of 106.4 days (±75.83 days). Significant differences between the subgroup of patients continuing and patients withdrawing therapy throughout the study period were detected, highlighting a lower degree of disease severity in patients continuing therapy (data not shown). In particular, patient self-reported AD severity status showed significantly higher scores in patients withdrawing treatment, independent of the cause of interruption, at any time point (Table 1). Thirty-six of 75 patients withdrew therapy because of the risk factors related to COVID-19 disease (age >65 years, metabolic and/or cardiovascular comorbidities), SARS-CoV-2 infection, fear of increased susceptibility to SARS-CoV-2 infection, or close contact with SARS-CoV-2+ subjects.

Changes in mean scores for Eczema Area and Severity Index (EASI), Itch–Numeric Rating Scale (Itch-NRS), and Sleep–Numeric Rating Scale (Sleep-NRS) from time point 3 and time point 1 were not significantly different in the subcohort of patients withdrawing because of SARS-CoV-2–related reasons versus patients continuing dupilumab therapy (Table 1). In this subcohort of patients, mean dupilumab withdrawal period resulted longer intervals (123.2 ± 11.69 days) compared with patients discontinuing dupilumab because of reasons unrelated to SARS-CoV-2 infection (90.03 ± 12.91 days), although this difference was not statistically significant ($P = 0.0615$).

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TABLE 1. AD Course in Patients Withdrawing Dupilumab Monotherapy Because of Reasons Related or Unrelated to SARS-CoV-2 Infection

			Patients Continuing Dupilumab Monotherapy	Patients Withdrawing Dupilumab Monotherapy for SARS-CoV-2+	*P* for Comparison Patients Continuing vs SARS-CoV-2–Related Withdrawing	Patients Withdrawing Dupilumab Monotherapy for Unrelated SARS-CoV2 Causes	*P* for Comparison Patients Continuing vs SARS-CoV-2–Unrelated Withdrawing
No. patients undergoing dupilumab monotherapy, N = 1013			n = 938	n = 36		n = 39	
Time point 1 (initial phase of lockdown)	Mean EASI score (±SD)		5.6 (7.2)	6.0 (7.0)	0.7122	8.0 (8.7)	0.044
	Mean Itch-NRS score (±SD)		2.0 (1.9)	3.0 (2.1)	0.0015	3.4 (2.4)	<0.0001
	Mean Sleep-NRS score (±SD)		1.3 (1.7)	2.2 (2.3)	0.0007	2.3 (2.6)	0.0002
	AD-NRS score (±SD)		1.9 (1.8)	2.7 (2.1)	0.0197	3.1 (2.4)	0.003
	Self-reported AD status	Improved no. pts (%)	262 (28.0)	7 (19.4)	0.0002	7 (17.9)	<0.0001
		Stable no. pts (%)	612 (65.4)	20 (55.6)		17 (43.6)	
		Worsened no. pts (%)	62 (6.6)	9 (25.0)		15 (38.5)	
Time point 2 (visit in remote modality during lockdown)	Mean Itch-NRS score (±SD)		1.7 (1.8)	2.8 (2.6)	0.0307	3.8 (2.8)	<0.0001
	Mean Sleep-NRS score (±SD)		1.1 (1.5)	2.4 (2.6)	0.0096	2.3 (2.8)	0.04
	AD-NRS score (±SD)		1.7 (1.7)	2.9 (2.8)	0.042	3.0 (2.6)	0.006
	Self-reported AD status	Improved no. pts (%)	262 (28.5)	7 (21.2)	<0.0001	10 (27.8)	<0.0001
		Stable no. pts (%)	601 (65.4)	14 (42.4)		16 (44.4)	
		Worsened n. pts (%)	56 (6.1)	12 (36.4)		10 (27.8)	
Time point 3 (latest phase of lockdown)	Mean EASI score (±SD)		5.8 (15.1)	5.3 (6.7)	0.91	12.3 (10.0)	0.064
	Mean Itch-NRS score (±SD)		1.6 (1.7)	2.9 (3.0)	<0.0001	3.7 (3.0)	<0.0001
	Mean Sleep-NRS score (±SD)		0.9 (1.4)	2.0 (2.5)	<0.0001	2.6 (2.9)	<0.0001
	AD-NRS score (±SD)		1.6 (1.7)	2.5 (2.6)	0.074	3.2 (2.8)	0.0006
	Self-reported AD status	Improved no. pts (%)	258 (28.9)	7 (20.0)	<0.0001	11 (33.3)	0.0019
		Stable no. pts (%)	593 (66.3)	17 (48.6)		16 (48.5)	
		Worsened no. pts (%)	43 (4.8)	11 (31.4)		6 (18.2)	
Change in EASI score from time point 1 to time point 3			**−1.6 (5.4)**	**0.6 (5.6)**	**0.147**	**2.3 (9.4)**	**0.003**
Change in Itch-NRS from time point 1 to time point 3			**−0.3 (1.8)**	**0.1 (3.4)**	**0.177**	**0.4 (3.3)**	**0.019**
Change in Sleep-NRS from time point 1 to time point 3			**−0.3 (1.6)**	**−0.2 (3.0)**	**0.758**	**0.4 (3.2)**	**0.013**

Data are reported as means (±SD) or numbers (%).

AD, atopic dermatitis; EASI, Eczema Area and Severity Index; NRS, Numeric Rating Scale; pts, patients; SD, standard deviation.

Of 75 patients, 39 patients withdrew dupilumab therapy because of reasons unrelated to COVID-19 disease, including ineffectiveness, adverse events, patient's decision, and issues with drug supply. In contrast to patients withdrawing therapy because of SARS-CoV-2–related reasons, these patients experienced a significant worsening of AD with greater changes in mean EASI score, Itch-NRS, and Sleep-NRS at time point 3 versus time point 1, compared with patients continuing therapy (Table 1). Thus, this

study provides relevant insights for physicians about the management of AD patients after dupilumab suspension or withdrawal during COVID-19 pandemic, because a 16-week interruption due to SARS-CoV-2–related reasons did not cause a significant relapse or worsening of the disease.

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A Case of Facial Contact Dermatitis Due to E-Cigarette Flavored Liquids

To the Editor:

E-cigarettes are devices that transform liquids into an aerosol through heating, and over the last few years, their use has skyrocketed.

Numerous vaping-associated dermatological conditions have been reported, such as thermal injuries, oral lesions, and contact dermatitis.[1]

We report a case of allergic contact dermatitis (ACD) related to flavorings contained in e-cigarette refill oils.

A 54-year-old nonatopic woman presented with an itchy, eczematous dermatitis of the perioral region that had started 2 months prior (Fig. 1).

The patient's medical history included systemic scleroderma, diagnosed in 1984.

Patch testing was performed with the Società Italiana di Dermatologia Allergologica Professionale e Ambientale baseline series. Patch test chambers (Van der Bend, Brielle, the Netherlands) were applied on the upper part of the patient's back.

The readings on days 2 and 3, according to the Italian guidelines,[2] showed positive reactions to fragrance mix I (sorbitan sesquiolate) 8% (−/+−−), fragrance mix II 14% (++−/++−), hydroxyisohexyl 3-cyclohexene carboxaldehyde 5% (Lyral, +−−/++−), and *Myroxylon pereirae* 25% (−/+−−).

The patient reported the use of some cosmetics and the habit of smoking with an e-cigarette refilled with flavored e-liquids.

Patch tests with the patient's products were carried out (lip balm, face cosmetic cream, surgical mask used during the pandemic) and even the vaping liquids tested as is ("biscuit scent" and "shinobi oil").

The readings were all negative.

We also tested propylene glycol 5% petrolatum, a common allergen related to vaping, which was negative.

A repeated open application test with both the e-cigarette refill oils was negative after 7 days.

The stop-restart test with the e-cigarette refill oils was strongly and repeatedly positive.

Several allergens contained in e-cigarettes can cause ACD (Table 1).

Nickel has been found to be the responsible allergen for hand dermatitis in some cases, because of the repeated contact with

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