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 ($P = 0.0615$).

DA-COVID-19 Study Group: Dario Francesco D'Urso, Dionisio Silvaggio, Annunziata Dattola, Maddalena Napolitano, Giacomo Dal Bello, Tommaso Bianchelli, Chiara Rovati, Flavia Pigliacelli, Michela Ortoncelli, Katharina Hansel, Alvise Sernicola, Giulia Calabrese, Camilla Loi, Michela Iannone, Federica Veronese, Filomena Russo, Paolo Romita, Greta Tronconi, Francesca Caroppo, Giovanna Tilotta, Maria Esposito, Francesca Raponi, Giulio Gualdi, Giulia Rech, Maria Letizia Musumeci, Steven Paul Nisticò, Alessio Campitiello, Laura Bonzano, Viviana Piras

A.C., L.DN., M.T., and M.G. contributed equally to this work.

A.C. served as advisory board member and consultant receiving fees and speaker's honoraria or has participated in clinical trials for AbbVie, Almirall, Biogen, Fresenius Kabi, Leo Pharma, Eli Lilly, Janssen, Novartis, Pfizer, Sanofi Genzyme, and UCB Pharma. G.F. acted as speaker and consultant for AbbVie and Leo Pharma. G.G. has been principal investigator in clinical trials sponsored by and/or and has received personal fees from AbbVie, Almirall, Amgen, Biogen, Boehringer Ingelheim, Bristol-Meyers Squibb, Celgene, Eli Lilly, Leo Pharma, Novartis, OM Pharma, Pfizer, Regeneron, Samsung, and Sandoz. A.O. has been a scientific consultant/speaker/clinical study investigator for AbbVie, Celgene, Janssen, Leo Pharma, Eli Lilly, MSD, Novartis, Pfizer, Sanofi, Alfasigma, and Almirall. M.T.R. has received personal fee for advisory board meeting from Sanofi, AbbVie, Novartis, and Cantabria. L.B. reports personal fees from speaker and as consultant for AbbVie, Novartis, Janssen-Cilag, Pfizer, UCB, and Leo Pharma, outside the submitted work. L.S. has been principal investigator in clinical trials sponsored by and/or received personal fees from AbbVie, Almirall, Celgene, Eli Lilly, Janssen, Novartis, and Sanofi-Genzyme. G.P. has been principal investigator in clinical trials sponsored by and/or received personal fees from AbbVie, Almirall, Eli Lilly, Leo Pharma, Novartis, and Sanofi. A.P. has served as a speaker and received honoraria from Sanofi-Genzyme for lectures, research grants, and as an advisory board member. C.F. has been speaker for Sanofi and AbbVie. M.C.F. has served on advisory boards, received honoraria for lectures, and research grants from Almirall, AbbVie, Galderma, Leo Pharma, Mylan, Medac Pharma, Celgene, Pierre Fabre, UCB, Eli Lilly, Pfizer, Janssen, Novartis, Sanofi Genzyme, Roche, Sun Pharma, and MSD. F.R. has served on advisory board, received honoraria for lectures and research grants from Novartis, AbbVie, Janssen-Cilag, Eli Lilly, Leo Pharma, and Sanofi-Genzyme. P.A. has received speaker honoraria from Sanofi, AbbVie, Janssen, Celgene, Novartis, and Sandoz. G.M. has been a scientific consultant/clinical study investigator for AbbVie, Eli Lilly, Janssen-Cilag, Leo Pharma, and Novartis. C.P. has been a consultant and held sponsored conferences for AbbVie, Novartis, Pfizer, and Sanofi. I.Z. has been a consultant and/or speaker for Novartis, Celgene, and Amgen. K.P. reports grants and personal fees for advisory board meeting from Almirall, AbbVie, Biogen, Lilly, Celgene, Galderma, Leo Pharma, Novartis, Pierre Fabre, Sanofi, Sandoz, Sun Pharma, and Janssen. S.F. has been principal investigator in clinical trials by AbbVie and Sanofi-Genzyme, has served on advisory board, received honoraria for lectures and research grants from Novartis, Menarini, and Almirall. The remaining authors have no funding or conflicts of interest to declare.

IRB approval status: Approved by the national ethical committee for COVID-19–related studies (Istituto Nazionale per le Malattie Infettive Lazzaro Spallanzani I.R.C.C.S.).

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)	
	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
Time point 2 (visit in remote modality during lockdown)	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)	
	Mean EASI score (±SD)		5.8 (15.1)	5.3 (6.7)	0.91	12.3 (10.0)	0.064
Time point 3 (latest phase of lockdown)	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.

Andrea Chiricozzi, MD
Dermatologia
Dipartimento Scienze Mediche e Chirurgiche
Fondazione Policlinico Universitario A. Gemelli IRCCS
Rome, Italy
Dermatologia
Dipartimento Universitario di Medicina e Chirurgia Traslazionale
Università Cattolica del Sacro Cuore
Rome, Italy
chiricozziandrea@gmail.com

Lucia Di Nardo, PhD
Dermatologia
Dipartimento Universitario di Medicina e Chirurgia Traslazionale
Università Cattolica del Sacro Cuore
Rome, Italy

Marina Talamonti, MD
Marco Galluzzo, MD
Dermatology Unit
Policlinico Tor Vergata
Department of Systems Medicine
Tor Vergata University of Rome
Italy

Clara De Simone, MD
Dermatologia
Dipartimento Scienze Mediche e Chirurgiche
Fondazione Policlinico Universitario A. Gemelli IRCCS
Rome, Italy
Dermatologia
Dipartimento Universitario di Medicina e Chirurgia Traslazionale
Università Cattolica del Sacro Cuore
Rome, Italy

Gabriella Fabbrocini, MD
Section of Dermatology
Department of Clinical Medicine and Surgery
University of Naples Federico II
Naples, Italy

Angelo Valerio Marzano, MD
Dermatology Unit
Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico
Milan, Italy
Department of Pathophysiology and Transplantation
Università degli Studi di Milano
Milan, Italy

Giampiero Girolomoni, MD
Section of Dermatology and Venereology
Department of Medicine
University of Verona
Italy

Annamaria Offidani, MD
Dermatological Clinic
Department of Clinical and Molecular Sciences
Polytechnic University of the Marche Region
Ancona, Italy

Maria Teresa Rossi, MD
Department of Dermatology
ASST Spedali Civili of Brescia
University of Brescia
Italy

Luca Bianchi, MD
Dermatology Unit
Policlinico Tor Vergata
Department of Systems Medicine
Tor Vergata University of Rome
Italy

Antonio Cristaudo, MD
Clinical Dermatology
San Gallicano Dermatological Institute
Rome, Italy

Maria Teresa Fierro, MD
Medical Sciences Department
Dermatologic Clinic
University of Turin
Italy

Luca Stingeni, MD
Dermatology Section
Department of Medicine
University of Perugia
Italy

Giovanni Pellacani, MD
Unit of Dermatology
Department of Clinical Internal
Anesthesiological, and Cardiovascular Sciences
Sapienza University of Rome
Italy

Giuseppe Argenziano, MD
Dermatology Unit
University of Campania Luigi Vanvitelli
Naples, Italy

Annalisa Patrizi, MD
Dermatology UOC
Department of Experimental
Diagnostic and Specialty Medicine
University of Bologna
Italy

Paolo Pigatto, MD
Department of Biomedical
Surgical and Dental Sciences
Clinical Dermatology
IRCCS Galeazzi Orthopaedic Institute
University of Milan
Italy

Marco Romanelli, MD
Department of Dermatology
University of Pisa
Italy

Paola Savoia, MD
Department of Health Sciences
Amedeo Avogadro University of Eastern Piedmont
Novara, Italy

Pietro Rubegni, MD
Dermatology Unit
Department of Medical
Surgical and Neurosciences
University of Siena
Italy

Caterina Foti, MD
Department of Biomedical Science and Human Oncology
Unit of Dermatology
University of Bari
Italy

Nicola Milanesi, MD
Dermatology Clinic
Department of Health Sciences
University of Florence
Italy

Anna Belloni Fortina, MD
Dermatology Unit
Department of Medicine DIMED
University of Padova
Italy

Maria Rita Bongiorno, MD
Section of Dermatology
Department of Health Promotion
Mother and Child Care
Internal Medicine and Medical Specialties
University of Palermo
Italy

Teresa Grieco, MD
Unit of Dermatology
Department of Clinical Internal
Anesthesiological, and Cardiovascular Sciences
Sapienza University of Rome
Italy

Sergio Di Nuzzo, MD
Department of Medicine and Surgery
University of Parma
Italy

Maria Concetta Fargnoli, MD
Dermatology
Department of Biotechnological and Applied Clinical Sciences
University of L'Aquila
Italy

Andrea Carugno, MD
Dermatology Unit
ASST Papa Giovanni XXIII Hospital
Bergamo, Italy

Alberico Motolese, MD
Dermatology Unit
Department of Medical Specialties
Arcispedale Santa Maria Nuova-IRCCS di Reggio Emilia
Italy

Franco Rongioletti, MD
Vita-Salute San Raffaele University and IRCCS San Raffaele Hospital
Milan, Italy
Unit of Dermatology
Department of Medical Sciences and Public Health
University of Cagliari
Italy

Paolo Amerio, MD
Department of Medicine and Aging Science
Dermatologic Clinic
G. D'Annunzio University
Chieti, Italy

Riccardo Balestri, MD
Division of Dermatology
Santa Chiara Hospital
Trento, Italy

Concetta Potenza, MD
Department of Medico-Surgical Sciences and Biotechnologies
Dermatology Unit 'Daniele Innocenzi' Sapienza University of Rome–Polo Pontino
Italy

Giuseppe Micali, MD
Dermatology Clinic
University of Catania
Italy

Cataldo Patruno, MD
Dermatology Unit
Department of Health Sciences
Università Magna Graecia
Catanzaro, Italy

Iris Zalaudek, MD
Department of Dermatology
University of Trieste
Italy

Maurizio Lombardo, MD
Unit of Dermatological Diseases
ASST Sette Laghi
Ospedale di Circolo
Varese
Italy

Claudio Feliciani, MD
Section of Dermatology
Department of Medicine and Surgery

University of Parma
Italy

Flaminia Antonelli, MD
Dermatologia
Dipartimento Scienze Mediche e Chirurgiche
Fondazione Policlinico Universitario A. Gemelli IRCCS
Rome, Italy
Dermatologia
Dipartimento Universitario di Medicina e Chirurgia Traslazionale
Università Cattolica del Sacro Cuore
Rome, Italy

Silvia Mariel Ferrucci, MD
Dermatology Unit
Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico
Milan, Italy

Fabrizio Guarneri, MD
Dermatology
Department of Clinical and Experimental Medicine
University of Messina
Italy

Ketty Peris, MD
Dermatologia
Dipartimento Scienze Mediche e Chirurgiche
Fondazione Policlinico Universitario A. Gemelli IRCCS
Rome, Italy
Dermatologia
Dipartimento Universitario di Medicina e Chirurgia Traslazionale
Università Cattolica del Sacro Cuore
Rome, Italy

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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

Address reprint requests to Natale Schettini, Section of Dermatology and Infectious Diseases, Department of Medical Sciences, University of Ferrara, Azienda Ospedaliera-Universitaria di Ferrara, Via Aldo Moro 8, 44124, Ferrara, Italy. E-mail: natale.schettini@gmail.com.

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