Table 1
The Characteristics of the Cohort

Patient no.	Age/sex, y	Mastocytosis	SARS-CoV-2 vaccines			Premedication	Any vaccine reaction
			First dose	Second dose	Third dose		
1	26/M	Indolent systemic	Sinovac	Sinovac	—	No	No
2	50/F	Aggressive systemic	Sinovac	Sinovac	BioNTech	Intravenous 45.5 mg pheniramine and 16 mg methylprednisolone 1 h before each dose	No
3	47/F	Indolent systemic	Sinovac	Sinovac	—	No	No
4	46/F	Aggressive systemic	Sinovac	BioNTech	BioNTech	No	No
5	54/M	Indolent systemic	Sinovac	Sinovac	Sinovac	No	No
6	28/F	Cutaneous	Sinovac	Sinovac	—	Oral 22.7 mg pheniramine and 40 mg methylprednisolone 1 h before each dose	Swelling of the throat, cough, and shortness of breath 2 min after each dose

Abbreviations: F, female; M, male; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

after BioNTech vaccines. Furthermore, although there were only 3 patients vaccinated with BioNTech in our study, all of them could be safely vaccinated. Four patients did not receive premedication and did not experience any reaction.

Limitations of this study are primarily the small sample size and that patients had only received BioNTech and Sinovac vaccines. Despite the COVID-19 pandemic continuing at full speed, the introduction of new vaccines will enrich current knowledge with new data that will emerge in large populations with mastocytosis. Further studies are needed to ensure the safety of COVID-19 vaccines, however. The strength of the study was that it provides information to literature about possible reaction risk for the Sinovac vaccine. The findings of the current study suggest that most patients with mastocytosis can be safely vaccinated, even those with an allergy or anaphylaxis history. Our results point that the COVID-19 vaccines seem to be safe, and patients should be encouraged to get vaccinated. The role of premedication in preventing vaccine reactions was not supported by the data in this study.

Gülseren Tuncay, MD*
Ozge Can Bostan, MD
Ebru Damadoglu, MD

Gül Karakaya, MD
Ali Fuat Kalyoncu, MD
Division of Allergy and Clinical Immunology, Faculty of Medicine
Hacettepe University
Ankara, Turkey
seren_tuncay@hotmail.com

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The impact of dupilumab treatment on severe acute respiratory syndrome coronavirus 2-coronavirus disease 2019 antibody responses in patients with atopic dermatitis

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Immunomodulatory therapies are typically used to treat patients with moderate-to-severe atopic dermatitis (AD). Thus, it is critical to understand their effects on coronavirus disease 2019 (COVID-19) outcomes. We recently reported that patients with AD on dupilumab were more likely to be asymptomatic or have milder COVID-19 symptoms.[1] However, the impact of dupilumab and systemic immunosuppressants on severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)/COVID-19 antibody levels in patients with AD remains unknown. We, thus, evaluated immunoglobulin (Ig)G antibody levels in unvaccinated patients with COVID-19 infection and after messenger RNA (mRNA) vaccination.

As part of a prospective registry related to COVID-19 in the Department of Dermatology at the Icahn School of Medicine at Mount Sinai, we collected serum samples from patients before vaccination and after mRNA vaccination between June 8, 2020 and October 14, 2021. Patients were enrolled under institutional review board

−approved consent, and the study was conducted according to the Declaration of Helsinki. Inclusion criteria included being older than 12 years of age with a diagnosis of moderate-to-severe AD, defined as currently or previously on systemic therapy (including dupilumab, phototherapy, or oral immunomodulatory medications), or as candidates for systemic therapy. On the basis of reported COVID-19 −related symptoms, each patient was given a COVID-19 symptom severity score from 0 to 2: 0 being "asymptomatic"; 1 being "mild disease" (no fever, no dyspnea, resolving in <7 days, resembling a common cold); and 2 being "moderate disease" (some fever, cough, or other lower respiratory symptoms, resolving at home in 7-14 days).

As we aimed to compare the effects of dupilumab treatment on antibody responses, we only included samples from patients on dupilumab for at least 2 months at the time of sample collection (to ensure enough time and treatment had passed to allow effects of dupilumab to manifest). Patients with positive IgG antibodies lacking vaccination were defined as COVID-19−infected. The SARS-CoV-2 IgG antibody levels were measured using the Mount Sinai Laboratory COVID-19 enzyme-linked immunosorbent assay IgG antibody test, which received emergency use authorization from the Food and Drug Administration (https://www.fda.gov/media/137029/download) but was used for research purposes in this study. Antibody levels were categorized into 4 groups on the basis of the Mount Sinai Laboratory predefined levels: negative (<5 arbitrary unit [AU]/mL), weak (5-15 AU/mL), moderate (16-39 AU/mL), and strong (≥40 AU/mL).

There were 3 treatment groups compared: (1) limited (topical therapy or no active treatment); (2) systemics (broad-acting treatments, namely: Janus kinase [JAK] inhibitors, prednisone, phototherapy); and (3) dupilumab. Antibody group proportions were compared using a 2-sided Fisher test, and $\log_{10}$ antibody level comparison was performed using multivariate linear regression models. Spearman correlations were used to determine whether the postvaccine antibody rate decreases over time.

A total of 54 serum samples (dupilumab, n = 23; systemics, n = 8; limited, n = 23) were collected from different patients before vaccination and 180 samples (dupilumab, n = 101; systemics, n = 15; limited, n = 64) were collected from 180 individuals at least 14 days after the second mRNA vaccine dose (either Pfizer or Moderna) and were included in the analysis. Systemics before vaccination included JAK inhibitors (n = 4), prednisone (n = 2), and phototherapy (n = 2) and after vaccination included JAK inhibitors (n = 9), prednisone (n = 1), and phototherapy (n = 5). No significant differences were observed in terms of age, sex, or race among the 3 treatment groups before vaccination (age: P = .07; sex: P = .10; race: P = .18) or after vaccination

(age: P = .26; sex: P = .08; race: P = .45). Among the 54 COVID-19 −positive samples prevaccination, decreased symptom severity was associated with lower IgG antibody levels across all treatments, consistent with studies associating more severe COVID-19 with greater SARS-CoV-2 IgG antibody levels.[1−5] Asymptomatic patients and those with mild COVID-19 symptoms exhibited lower antibody titers than those with moderate symptoms (52.5 ± 20.3 vs 96.2 ± 36.1 [mean ± SE]; P = .03). Dupilumab-treated patients with AD had significantly lower antibody levels than those on systemics when comparing both the proportions of weak vs moderate/strong groups (8/23 for dupilumab vs 1/8 for systemics; P = .01) and age-adjusted quantitative antibody levels (29.0 ± 35.7 vs 170.5 ± 54.9 [mean ± SE]; P = .01). A trend toward lower levels was also observed in dupilumab-treated patients vs limited group (8/23 for dupilumab vs 4/23 for limited group for weak vs moderate/strong proportion comparison; P = .09).

To assess if lower antibody levels were caused by treatment-based modulation of antibody production or from differential responses to the SARS-CoV-2 virus itself, we then assessed antibody levels after mRNA vaccination. Overall, we found similar rate decreases in antibody levels over time among treatment groups (Fig 1). Correspondingly, no differences were observed among groups regarding antibody level groups (weak/moderate/strong). Furthermore, using a linear regression model adjusted for age and time after vaccination, we detected no significant differences in antibody concentrations among any treatment groups (P > .18).

Overall, this study found that patients had significantly lower antibody levels after COVID-19 infection when treated with dupilumab vs systemic therapies (P = .01), and lower levels (approaching significance, P = .09) compared with patients receiving limited/no therapy, paralleling our previous finding that dupilumab-treated patients were more likely to have milder symptoms COVID-19 symptoms compared with patients on broad-acting treatments and also those receiving limited/no treatment.[1] However, there were no differences in antibody levels among treatment groups after mRNA vaccination. This suggests that dupilumab does not impair antibody responses, but rather reduces COVID-19 symptom severity and downstream IgG levels. The limitations of this study include unknown COVID-19 infection dates (often because of lack of symptoms and, therefore, testing), the smaller number of systemic patients that tested positive to COVID-19 matching our practice prescribing tendencies, and the lack of a control group without AD. Further studies to characterize T cell components of COVID-19 immune responses with different immunomodulatory treatments are needed. Taken together with our previous publication reporting ameliorated COVID-
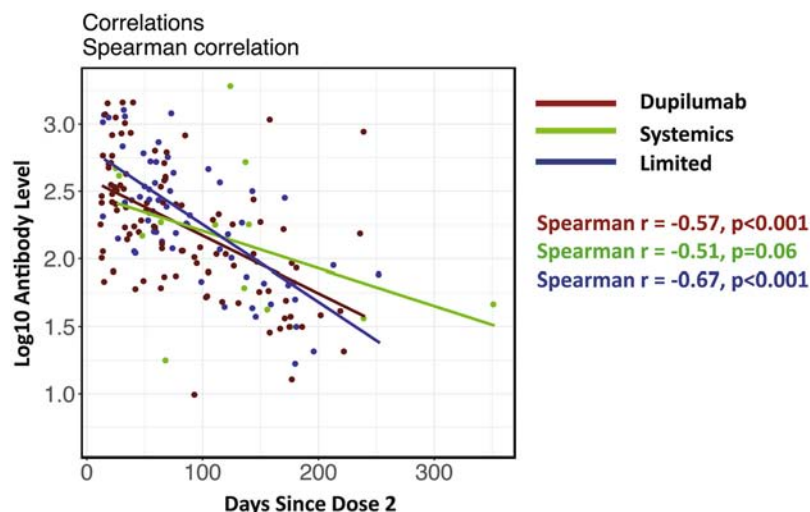

Figure 1. Spearman correlation between $\log_{10}$ antibody levels and days since the second vaccine dose in each treatment group.

19 symptoms with dupilumab treatment in AD, these results provide reassurance that specific T$_H$2-targeting in patients with AD does not affect antibody levels after mRNA vaccination and supports continuing dupilumab treatment during the COVID-19 pandemic irrespective of vaccination status.

Benjamin Ungar, MD*
Leore Lavin, MS*
Alexandra K. Golant, MD*
Alyssa Gontzes, BS*
Eden David, BS*
Yeriel D. Estrada, BS*
Giselle K. Singer, BS*
Ana B. Pavel, PhD*,†
Emma Guttman-Yassky, MD, PhD*
* *Department of Dermatology and Laboratory of Inflammatory Skin Diseases*
Icahn School of Medicine at Mount Sinai
New York, New York

† *Department of Biomedical Engineering*
The University of Mississippi
University Mississippi
eguttman@rockefeller.edu

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