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The effect of biologic therapy for immune-mediated inflammatory diseases on clinical outcomes of COVID-19 in the greater Houston area: A retrospective chart review

To the Editor: Scrutiny of biologic use has increased in light of the COVID-19 pandemic. The American Academy of Dermatology and other professional organizations currently recommend the discontinuation of biologics in COVID-19+ patients.\textsuperscript{1} We performed a retrospective chart review to evaluate whether patients on biologics for immune-mediated inflammatory diseases in the greater Houston area (GHA) were more likely to test positive and have worse outcomes (hospitalization and death).

Demographic and clinical data were analyzed from patients receiving immunomodulatory biologics for immune-mediated inflammatory diseases between November 1, 2019, and November 15, 2020. Charts of patients with confirmed COVID-19 were examined for hospitalization, ICU admission, mechanical ventilation, and death, and compared to those from the GHA. GHA population and demographic data were obtained through the Census Bureau.\textsuperscript{2} Numbers of confirmed COVID-19\textsuperscript{1} cases, hospitalizations, and deaths for the GHA were obtained on November 15, 2020, through the Texas Medical Center Coronavirus Dashboard.\textsuperscript{3}

In total, 7,398,408 unique patient records were analyzed from the combined records of the Harris Health System, University of Texas Physicians, Memorial Hermann Health System, and MD Anderson Cancer Center. Of these patients, 4820 were taking 5131 biologic medications (Table I). TNF-\(\alpha\) inhibitors were the most common biologic used (3087). Patients on anti-CD20 medications had the highest rates of COVID-19 positivity (2.7%) and hospitalization (1.7%). Out of 4820 patients on biologics, 73 (1.5%) tested positive for COVID-19. Among these 73 patients, 16 (21.9%) were hospitalized and 3 (4.1%) died. Hospitalized patients were older and more likely to be taking anti-CD20 biologics (31.25%) compared to the ambulatory group (5.3%) (Supplementary Table I, available via Mendeley at https://doi.org/10.17632/kbzx8hbvggl1).

Our study cohort had a significantly greater proportion of female, White, and obese patients compared to the GHA (\(P < .0001\)) (Table II). The COVID-19 positivity rate in our study cohort (1.5%) was significantly lower (\(P < .0001\)) than to the positivity rate in the GHA (3.4%). In patients who were confirmed COVID-19\textsuperscript{1}, the study cohort (21.9%) had a significantly higher hospitalization rate (\(P = .045\)) compared to the GHA (12.0%). There was no significant difference in the death rate between the study cohort and the GHA.

Anti-CD20 was the only drug category with statistically significantly increased risks of COVID-19 infection and hospitalization (Supplementary Table II). There were no statistically significant changes in COVID-19 susceptibility based on race or gender. However, obese patients were found to be significantly more susceptible to COVID-19 compared to patients with normal or low BMIs.

Our study adds to the body of evidence that patients on biologics are not at increased risk of contracting COVID-19 or having worse outcomes, except for those on rituximab (which has been

### Table I. Outcomes by drug class

| Drug Class | Abatacept (N = 245) | Anti-CD 20 (N = 293) | IL-4, -13 inhibition (N = 217) | IL-12, -23 inhibition (N = 220) | IL-17 inhibition (N = 542) | IL-23 inhibition (N = 53) | Other (vedolizumab, tocilizumab) (N = 473) | TNF-\(\alpha\) inhibition (N = 3087) |
|------------|---------------------|----------------------|-------------------------------|-------------------------------|----------------------------|----------------------------|---------------------------------|-------------------------------|
| COVID \^\textsubscript{1} | 241 (98.4%) | 285 (97.3%) | 215 (99.1%) | 216 (98.2%) | 535 (98.7%) | 53 (100%) | 470 (99.2%) | 3042 (98.5%) |
| COVID \^\textsubscript{1} or not tested | 4 (1.6%) | 8 (2.7%) | 2 (0.9%) | 4 (1.8%) | 7 (1.3%) | 0 (0%) | 4 (0.8%) | 45 (1.5%) |
| Hospitalization | | | | | | | | |
| Yes | 1 (0.4%) | 5 (1.7%) | 0 (0%) | 4 (1.8%) | 7 (1.3%) | 0 (0%) | 1 (0.2%) | 9 (0.3%) |
| No | 3 (1.2%) | 3 (1.0%) | 2 (0.9%) | 4 (1.8%) | 7 (1.3%) | 0 (0%) | 3 (0.6%) | 36 (1.2%) |
| ICU level care or mechanical ventilation | | | | | | | | |
| Yes | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | 2 (0.1%) |
| No | 1 (0.4%) | 5 (1.7%) | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | 1 (0.2%) | 7 (0.2%) |
| Death | | | | | | | | |
| Yes | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | 3 (0.1%) |
| No | 4 (1.6%) | 8 (2.7%) | 2 (0.9%) | 4 (1.8%) | 7 (1.3%) | 0 (0%) | 4 (0.8%) | 42 (1.4%) |

\textit{ICU}, intensive care unit; IL, interleukin; TNF, tumor necrosis factor.
shown to increase the hospitalization rate). In fact, our results suggest that patients on biologics have a lower rate of COVID-19 positivity than the GHA population, suggesting a possible protective effect. Furthermore, biologics have been shown to decrease hospital admission rates among patients with COVID-19, possibly by attenuating cytokine storms. Although our analysis was limited in sample size, our population size was comparable to or larger than those in most available studies. Emerging data, including our findings, and the availability of effective vaccines behoove us to reconsider the guidelines reflecting the relative safety of biologics.

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Kevin P. Lee, BS,a Misha V. Koshelev, MD, PhD,b D3CODE Team,c and Omar Pacha, MDd

From the University of Texas at Houston McGovern Medical School, Houston, Texas; the Department of Dermatology, University of Texas Health Science Center at Houston, Houston, Texas; the Data-Driven Determinants for COVID-19 Oncology Discovery Effort (D3CODE) Team, University of Texas, MD Anderson Cancer Center, Houston, Texas; and the Department of Dermatology, MD Anderson Cancer Center, Houston, Texas.

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Correspondence to: Omar Pacha, MD, Department of Dermatology, MD Anderson Cancer Center, 1515 Holcombe, Unit 1452, Houston, TX 77030

E-mail: opacha@mdanderson.org

Conflicts of interest
None disclosed.

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Table II. Comparison of the study cohort to the greater Houston area

| Variable            | Category                  | Cohort counts | Cohort proportion | GHA count | GHA proportion | tstat | P value | Difference between cohort and GHA proportions | 95% CI lower | 95% CI upper |
|---------------------|---------------------------|---------------|-------------------|-----------|----------------|-------|---------|---------------------------------------------|--------------|--------------|
| Population          | Population                | 4820          | 0.015             | 7,168,679 | 0.001          |       |         |                                             |              |              |
| Age                 | Median age                | 52            | 0.667             | 35.63     |                |       |         |                                             |              |              |
| Gender              | Female                    | 3216          | 0.677             | 3,467,102 | 0.557          | -2.19 | 0.03    | 0.134                                      | -0.144       | -0.157       |
| Gender              | Male                      | 1604          | 0.333             | 3,417,036 | 0.443          | -1.53 | 0.12    | 0.222                                      | -0.202       | -0.180       |
| Race                | Hispanic or Latino        | 862           | 0.194             | 2,652,411 | 0.356          | -1.53 | 0.123   | 0.000                                      |                 |              |
| Race                | White or Caucasian        | 2218          | 0.460             | 2,580,724 | 0.360          | -0.99 | 0.323   | 0.171                                      | 0.086        | 0.114        |
| Race                | African American          | 701           | 0.145             | 1,218,675 | 0.170          | -1.37 | 0.172   | 0.222                                      | -0.025       | -0.015       |
| Race                | Other                     | 941           | 0.195             | 716,868   | 0.100          | -1.00 | 0.317   | 0.095                                      | 0.084        | 0.106        |
| BMI                 | Normal or overweight      | 1395          | 0.289             | 2,172,110 | 0.303          | -2.08 | 0.038   | -0.014                                     | -0.026       | -0.001       |
| BMI                 | Obese                     | 2122          | 0.440             | 2,910,484 | 0.406          | -1.67 | 0.097   | 0.020                                      | 0.040        |              |
| Positivity rate     | COVID                      | 73            | 0.015             | 241,186   | 0.034          | -10.51| 0.000   | -0.018                                     | -0.022       | -0.015       |
| Positivity rate     | COVID or not tested       | 4747          | 0.985             | 6,927,493 | 0.966          | 10.51| 0.000   | 0.018                                      | 0.015        | 0.022        |
| Hospitalization     | Hospitalized              | 16            | 0.219             | 28,911    | 0.120          | 2.04  | 0.045   | 0.099                                      | 0.002        | 0.197        |
| Hospitalization     | Not hospitalized           | 57            | 0.781             | 212,275   | 0.880          | -2.04 | 0.045   | -0.099                                     | -0.197       | -0.002       |
| Fatality rate       | Deceased                  | 3             | 0.041             | 2686      | 0.011          | 2.04  | 0.045   | 0.030                                      | -0.017       | 0.077        |
| Fatality rate       | Not deceased              | 70            | 0.959             | 238,500   | 0.989          | -1.28 | 0.205   | -0.030                                     | -0.077       | 0.017        |

BMI, Body mass index; GHA, greater Houston area.
Psoriasis flares and rebound phenomenon following exposure and withdrawal of systemic steroids: A systematic review and meta-analysis

To the Editor: It is believed that systemic steroids should be avoided in psoriasis due to the possibility of a rebound pustular flare. However, 1 study has shown that systemic steroids were prescribed during 3% of psoriasis visits, primarily by dermatologists. In this review, we evaluate the proportion of patients with psoriasis with cutaneous flares during tapering/cessation of systemic steroids and the proportion in whom tapering/cessation of systemic steroids was attributed as a cause of flare.

The search was conducted using MEDLINE, Embase, Scopus, Cochrane Central Register of Controlled Trials, and LILACS databases from inception to July 11, 2021, and reported with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines. The protocol was registered in PROSPERO (CRD42021279568).

Randomized case-control, cross-sectional, and cohort studies reporting cutaneous outcomes following systemic steroids (oral, intravenous, subcutaneous, intramuscular, and intra-articular) were included. Data were independently screened and extracted by 2 authors and were resolved by a third author.

Twenty-five articles were included from 6606 unique citations (Supplementary Files 1 and 2, available via Mendeley at https://data.mendeley.com/datasets/4dydwh73f7/2). There were 2 study types. The first included prospective and retrospective cohorts exposed to systemic steroids and longitudinally followed for flares after tapering/cessation. The second comprised case series in which psoriatic flares were analyzed for triggering factors, including systemic steroids.

In the first group comprising 9 studies (2 exclusive to generalized pustular psoriasis [GPP]) with 853 patients, worsening of skin lesions on tapering/cessation of systemic steroids was reported in 114 of 703 instances. One patient had an erythrodermic flare of psoriasis, but the causal nature was unconfirmed, as the steroids were prescribed for worsening rashes.3 There were no documented flares, intensive care admissions, or deaths attributable to systemic steroid tapering/cessation, although recurrences were reported in “more aggravated” forms that may represent rebound flares (Supplementary Table I, available via Mendeley at https://data.mendeley.com/datasets/4dydwh73f7/2).

The second group comprised 16 studies (11 exclusive to GPP) reporting psoriatic flares in 897 patients. The proportion of flares attributed by the clinician to systemic steroids ranged from 0 to 44% (Supplementary Table II, available via Mendeley at https://data.mendeley.com/datasets/4dydwh73f7/2), with a pooled proportion of 16.0% (95% confidence interval, 7.1%-25.0%) in patients with GPP and 10.8% (95% confidence interval, 4.6%-17.0%) in patients with psoriasis (not limited to GPP subtype) (Supplementary File 3, available via Mendeley at https://data.mendeley.com/datasets/4dydwh73f7/2).

This review found low rates of rebound flare after tapering/cessation of steroids, although recurrences of lesions were common. However, systemic steroids were retrospectively attributed as a trigger for psoriatic flares in 15%. A survey of dermatologists and rheumatologists found that 47% had observed at least 1 psoriasis flare following treatment with oral steroids. The reasons for the discrepancies include attribution bias and difficulty differentiating an expected recurrence of the dermatosis from a true rebound phenomenon. Finally, the risk of flares may differ depending on the underlying disease (eg, higher risk in patients with GPP).

The limitations of this study include the lack of standardized definitions for psoriasis flares and overall low quality and high heterogeneity of the included studies. Nevertheless, this highlights the lack of evidence supporting the commonly propagated belief regarding the rebound phenomenon after systemic steroids in psoriasis and the need for higher quality studies to assess the true risk of rebound and pustular flares.

Valencia Long, MRCP, Yik Weng Yew, PhD, Nisha Suyien Chandran, MRCP, and Ellie Ci-En Choi, MRCP

From the Division of Dermatology, Department of Medicine, National University Healthcare System, Singapore; and Medical Department, National Skin Centre, Singapore.

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