Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

therapy during the COVID-19 outbreak. *Dermatol Ther*. 2020;33(4):e13680.
3. Marzano AV, Moltrasio C, Genovese G, et al. Hidradenitis suppurativa and adalimumab in the COVID-19 era. *Eur J Dermatol*. 2020;30(6):748-749.
4. Galan JL, Silvente C, Gonzalez M, et al. Experience in patients with hidradenitis suppurativa and COVID-19 symptoms. *J Am Acad Dermatol*. 2020;83(4):e309-e311.
5. Lima XT, Cueva MA, Alora MB. COVID-19 in patients with hidradenitis suppurativa. *Br J Dermatol*. 2021;184(1):182-184.

https://doi.org/10.1016/j.jaad.2021.09.016

Immunosuppressive biologics did not increase the risk of COVID-19 or subsequent mortality: A retrospective matched cohort study from Massachusetts

To the Editor: The COVID-19 pandemic raised concerns about the management of patients with immune-mediated inflammatory diseases treated with immunosuppressive biologics. A third of patients with psoriasis who discontinued their medications had disease progression.[1] As population-level analyses of this patient group remain limited, we compared the incidence of COVID-19 and subsequent mortality in a large cohort of patients prescribed biologics and matched controls.

We identified all patients aged 18 years and older with at least 1 prescription for a biologic from July 1, 2019 to February 29, 2020 in the Massachusetts General Brigham Enterprise Data Warehouse. The primary and secondary outcomes for this study were risk of COVID-19 and subsequent mortality, respectively. A multivariable logistic regression was used on matched data to calculate the odds ratio (OR) for COVID-19 diagnosis between the 2 groups, adjusting for age, sex, race, Charlson Comorbidity Index severity grade, median income, and local infection rates. A multivariable Poisson regression was used to compare all-cause mortality among patients diagnosed with COVID-19, adjusting for age, sex, Charlson Comorbidity Index severity grade, median income, and local infection rates. Detailed methods and sensitivity analyses are included in the Supplemental Materials (available via Mendeley at https://data.mendeley.com/datasets/w4478kftkk/1).

We identified 7361 patients who received biologics and 74,910 matched controls. Patient baseline characteristics are presented in Table I. Tumor necrosis factor inhibitors (adalimumab [28.4%], infliximab [15.6%], and etanercept [11.9%]), CD20-directed antibody (rituximab [15.6%]), and interleukin-4A inhibitor (dupilumab [8.6%]) were the most frequently prescribed biologics. Rheumatoid arthritis (27.5%), psoriasis (27.3%), psoriatic arthritis (16.2%), Crohn's disease (24.9%), and ulcerative colitis (18.9%) were the most common indications for biologics in our study.

Overall, biologics were not associated with COVID-19 (OR, 0.88; 95% confidence interval [CI], 0.71-1.09; $P = .25$), adjusting for demographics, comorbidity burden, and local infection rates (Table II). Patients treated with tumor necrosis factor inhibitors were less likely to be diagnosed with SARS-CoV-2 infection compared to matched controls (OR, 0.69; 95% CI, 0.48-0.98; $P = .04$). Similarly, those treated with dupilumab had lower odds of diagnosis (OR, 0.38; 95% CI, 0.12-1.18), although this difference was not statistically significant ($P = .10$). Mortality rates were also similar between the 2 groups after adjusting for demographics, comorbidity burden, and local infection rates (OR, 1.13; 95% CI, 0.57-2.76; $P = .57$).

Despite the ongoing vaccination efforts, COVID-19 remains a top health concern. The major finding of our study is that biologics did not increase the risk of a positive COVID-19 diagnosis, which is consistent with published literature.[2-4] Additionally, distinct biologics classes are known to cause varying susceptibilities to other viral infections. In our study, tumor necrosis factor inhibitors were associated with lower odds of COVID-19 diagnosis, consistent with reports of this class of biologics being associated with less-severe disease among large cohorts of patients.[2,4] Furthermore, we did not identify an association between biologics and mortality.

Our results must be considered in light of the real-world data it is based upon, because these patients may have altered their behavior to decrease their risk of infection, as has been reported in surveys of patients with inflammatory bowel disease and rheumatic diseases.[5] Dermatologists and patients should prioritize the well-established risk factors for COVID-19 when making decisions to continue therapy.

The authors thank Stacey Duey and Celina Li of the Research Patient Data Registry for their help with access to patient chart data and Bernard Rosner of Harvard Medical School for his valuable guidance in the study design and analysis.

Vartan Pahalyants, MD, MBA,[a,b] William S. Murphy, MD, MBA,[a] Nikolai Klebanov, MD,[a] Chenyue Lu, MBI,[a] Nicholas Theodosakis, MD,[a] R. Monina Klevens, DDS,[c] Hossein Estir, PhD,[d,e] Evelyn Lilly, MD,[a] Maryam Asgari, MD,[a] and Yevgeniy R. Semenov, MD, MA[a]

From the Department of Dermatology,[a] Laboratory of Computer Science,[d] and Department of

Table I. Demographics and clinical characteristics of patients on biologics and matched controls

Demographic or clinical variable	Biologic group N = 7361	Matched controls N = 74,910	*P* value
Age group (years), N (%)			>.99
18-44	2783 (37.8%)	28,321 (37.8%)	
45-64	2838 (38.6%)	28,881 (38.6%)	
65-74	1135 (15.4%)	11,550 (15.4%)	
≥75	605 (8.2%)	6157 (8.2%)	
Sex, female, N (%)	4124 (56.0%)	41,968 (56.0%)	>.99
Race and ethnicity, N (%)			>.99
White non-Hispanic	6223 (84.5%)	63,329 (84.5%)	
Asian or Pacific Islander non-Hispanic	263 (3.6%)	2676 (3.6%)	
Black non-Hispanic	332 (4.5%)	3379 (4.5%)	
Other non-Hispanic	139 (1.9%)	1415 (1.9%)	
Hispanic	223 (3.0%)	2269 (3.0%)	
Unknown	181 (2.5%)	1842 (2.5%)	
Charlson comorbidity index grade, N (%)			>.99
Mild (1-2)	4050 (55.0%)	41,215 (55.0%)	
Moderate (3-4)	1591 (21.6%)	16,191 (21.6%)	
Severe (≥5)	1720 (23.4%)	17,504 (23.4%)	
Medical comorbidity, N (%)			
Hypertension	2147 (29.2%)	21,561 (28.8%)	.49
Congestive heart failure	355 (4.8%)	4867 (6.5%)	**<.001**
Diabetes	818 (11.1%)	11,234 (15.0%)	**<.001**
Chronic pulmonary disease	933 (12.7%)	10,738 (14.3%)	**<.001**
Other pulmonary disease	1529 (20.8%)	17,546 (23.4%)	**<.001**
Renal disease	561 (7.6%)	5797 (7.7%)	.72
Liver disease	1156 (15.7%)	11,821 (15.8%)	.86
Hematologic cancer	593 (8.1%)	3043 (4.1%)	**<.001**
Solid organ cancer, not metastatic	1270 (17.3%)	15,949 (21.3%)	**<.001**
Solid organ cancer, metastatic	145 (2.0%)	3592 (4.8%)	**<.001**
Indication			
Asthma	1428 (19.4%)	13,162 (17.6%)	**<.001**
Atopic dermatitis	2022 (27.5%)	15,112 (20.2%)	**<.001**
Chronic lymphocytic leukemia	65 (0.9%)	263 (0.4%)	**<.001**
Non-Hodgkin lymphoma	483 (6.7%)	1421 (1.9%)	**<.001**
Giant cell arteritis	186 (2.5%)	159 (0.2%)	**<.001**
Granulomatosis with polyangiitis	104 (1.4%)	105 (0.1%)	**<.001**
Microscopic polyangiitis	20 (0.3%)	6 (0.01%)	**<.001**
Systemic lupus erythematosus	233 (3.2%)	521 (0.7%)	**<.001**
Pemphigus	32 (0.4%)	59 (0.1%)	**<.001**
Hidradenitis suppurativa	166 (2.3%)	387 (0.5%)	**<.001**
Psoriasis	2012 (27.3%)	3054 (4.1%)	**<.001**
Psoriatic arthritis	1192 (16.2%)	369 (0.5%)	**<.001**
Rheumatoid arthritis	2027 (27.5%)	1930 (2.6%)	**<.001**
Ankylosing spondylitis	452 (6.1%)	183 (0.2%)	**<.001**
Uveitis	211 (2.9%)	594 (0.8%)	**<.001**
Crohn's disease	1829 (24.9%)	515 (0.7%)	**<.001**
Ulcerative colitis	1388 (18.9%)	1094 (1.5%)	**<.001**
COVID-19 positive, N (%)	87 (1.2%)	1063 (1.4%)	.10
Died, N (% of COVID-19–positive patients)	7 (8.0%)	71 (6.7%)	.79
COVID-19 town or county positivity rate per 100 mean (SD)	1.4 (0.9)	1.6 (1.1)	**<.001**
	N = 7317	N = 74,389	
Median income in $1000s mean (SD)	82.0 (29.2)	79.7 (29.2)	**<.001**

P values <0.05 appear in bold.

Table II. Multivariable logistic regression of the risk of COVID-19 infection and subsequent mortality for patients treated with immunosuppressive biologics

Variable	OR	95% CI	*P* value
Risk of infection for all immunosuppressive biologics			
Biologic use	0.88	0.71-1.09	.25
Age group (years)			
18-44	ref*	ref*	ref*
45-64	0.92	0.79-1.07	.28
65-74	0.67	0.53-0.85	**.001**
≥75	1.22	0.96-1.56	.11
Sex, female	0.95	0.85-1.07	.43
Race and ethnicity			
White non-Hispanic	ref*	ref*	ref*
Asian or Pacific Islander non-Hispanic	0.36	0.21-0.62	**<.001**
Black non-Hispanic	2.10	1.73-2.56	**<.001**
Other non-Hispanic	1.36	1.04-1.79	**.02**
Hispanic	1.39	0.99-1.94	.06
Unknown	0.28	0.13-0.58	**.001**
CCI grade			
Mild (1-2)	ref*	ref*	ref*
Moderate (3-4)	1.32	1.11-1.56	**<.01**
Severe (≥5)	1.88	1.56-2.26	**<.001**
COVID-19 town or county positivity rate	1.24	1.19-1.29	**<.001**
Median income in $1,000s	0.98	0.95-1.00	.06
Risk of infection by immunosuppressive biologic class			
Class			
B-cell activating factor inhibitor	0	0.00-Inf	**.98**
CD20-directed cytolytic antibody	1.16	0.73-1.83	**.53**
Integrin receptor antagonist	1.27	0.61-2.68	**.52**
Interleukin-1 receptor antagonist	2.23	0.31-15.82	**.42**
Interleukin-4A receptor antagonist	0.38	0.12-1.18	**.10**
Interleukin-6 receptor antagonist	1.35	0.60-3.02	**.47**
Interleukin-12/23 receptor antagonist	0.88	0.33-2.34	**.79**
Interleukin-17A receptor antagonist	1.75	0.83-3.69	**.14**
Interleukin-23 antagonist	1.60	0.23-11.40	**.64**
Selective T-cell costimulation modulator	1.63	0.61-4.36	**.33**
Tumor necrosis factor inhibitor	0.69	0.48-0.98	**.04**
Risk of subsequent all-cause mortality for all immunosuppressive biologics			
Biologic use	1.13	0.57-2.76	**.57**
Age	1.06	1.04-1.09	**<.001**
Sex, female	0.53	0.34-0.83	**<.01**
CCI grade			
Mild (1-2)	ref*	ref*	ref*
Moderate (3-4)	2.12	0.69-6.51	.19
Severe (≥5)	2.96	0.99-8.86	.05
Median income in $1000s	0.90	0.80-1.00	.06
COVID-19 town or county positivity rate	0.93	0.78-1.11	.45

CCI, Charlson Comorbidity Index; *OR*, odds ratio; *ref*, reference.
*Reference variable.
P values <0.05 appear in bold.

Medicine, Massachusetts General Hospital, Boston[e]; Department of Medicine, Brigham and Women's Hospital, Boston, Massachusetts[b]; and Massachusetts Department of Public Health, Bureau of Infectious Disease and Laboratory Sciences, Boston.[c]

Drs Pahalyants and Murphy are cofirst authors.

IRB approval status: Approved by the institutional review boards of Mass General Brigham (Protocol 2020P001191) and Massachusetts Department of Public Health (Protocol 1606024-2).

Funding sources: None.

Correspondence and reprint requests to: Yevgeniy R. Semenov MD, MA, Department of Dermatology, Massachusetts General Hospital, 40 Blossom Street, Bartlett Hall 6R, Room 626, Boston, MA 02114

E-mail: ysemenov@mgh.harvard.edu

Conflicts of interest

None disclosed.

REFERENCES

1. Burlando M, Carmisciano L, Cozzani E, Parodi A. A survey of psoriasis patients on biologics during COVID-19: a single centre experience. *J Dermatolog Treat*. May 25, 2020. https://doi.org/10.1080/09546634.2020.1770165
2. Mahil SK, Dand N, Mason KJ, et al. Factors associated with adverse COVID-19 outcomes in patients with psoriasis—insights from a global registry-based study. *J Allergy Clin Immunol*. 2021;147(1):60-71. https://doi.org/10.1016/j.jaci.2020.10.007
3. Strangfeld A, Schäfer M, Gianfrancesco MA, et al. Factors associated with COVID-19-related death in people with rheumatic diseases: results from the COVID-19 Global Rheumatology Alliance physician-reported registry. *Ann Rheum Dis*. 2021;80(7):930-942. https://doi.org/10.1136/annrheumdis-2020-219498
4. Gianfrancesco M, Yazdany J, Robinson PC. Epidemiology and outcomes of novel coronavirus 2019 in patients with immune-mediated inflammatory diseases. *Curr Opin Rheumatol*. 2020;32(5):434-440. https://doi.org/10.1097/BOR.0000000000000725
5. Hooijberg F, Boekel L, Vogelzang EH, et al. Patients with rheumatic diseases adhere to COVID-19 isolation measures more strictly than the general population. *Lancet Rheumatol*. 2020;2(10):e583-e585. https://doi.org/10.1016/S2665-9913(20)30286-1

https://doi.org/10.1016/j.jaad.2021.08.065