

Dermatology Letter

Biologic therapy is not associated with increased COVID-19 severity in patients with hidradenitis suppurativa: Updated findings from the Global Hidradenitis Suppurativa COVID-19 Registry

Jazzmin C. Williams,¹ Raed Alhusayen,² Sandra Guilbault,³ Nancy K. Hills,⁴ John R. Ingram,⁵ Margaret V. Kudlinski,¹ Michelle A. Lowes,⁶ Angelo V. Marzano,^{7,8} Maia Paul,¹ Bente Villumsen,⁹ Christine A. Yannuzzi,¹⁰ Haley B. Naik¹

¹Department of Dermatology, University of California San Francisco, San Francisco, CA, U.S.A.; ²Dermatology Division, Department of Medicine, Sunnybrook Research Institute, University of Toronto, Toronto, ON, Canada.; ³Hope for HS, Troy, MI, U.S.A.; ⁴Department of Neurology, Epidemiology and Biostatistics, University of California San Francisco, San Francisco, CA, U.S.A.; ⁵Division of Infection and Immunity, Department of Dermatology & Academic Wound Healing, Cardiff University, Cardiff, U.K.; ⁶The Rockefeller University, New York, NY, U.S.A.; ⁷Dermatology Unit, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy.; ⁸Department of Pathophysiology and Transplantation, Università degli Studi di Milano, Milan, Italy.; ⁹Patientforeningen HS Danmark, Copenhagen, Denmark; ¹⁰HS Warriors, Port Richey, FL, U.S.A.

Short Title: Updated findings from the Global Hidradenitis Suppurativa COVID-19 Registry

Corresponding Author:

Haley B. Naik, MD, MHSc
Associate Professor of Dermatology
University of California, San Francisco
2340 Sutter Street, S429
San Francisco, CA 94143-0808 USA
Mail Code 0808
Phone: +1 415 514 9769
Email: haley.naik@ucsf.edu

Key Message: HS patients on biologics have similar COVID-19 outcomes to those on nonbiologic therapy.

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1 Dear Editor,

2

3 As the COVID-19 pandemic persists, dermatologists continue to balance the desire to achieve
4 effective hidradenitis suppurativa (HS) control through biologic therapy with the risk it may
5 pose during active COVID-19 infection in the context of comorbidities associated with severe
6 COVID-19 infection.[1] This study expands upon previous findings[1] with 188 additional
7 cases reported over 10 more months to the Global Hidradenitis Suppurativa COVID-19
8 Registry from April 5, 2020 to December 9, 2021. Registry entries were submitted by health
9 care providers (HCPs) and patients (or their caregivers, in the case of children or those too ill
10 or without capacity to complete the survey). Eligible cases had 1) an HCP-confirmed
11 diagnosis of HS and 2) an HCP-confirmed diagnosis of COVID-19 based on a positive test or
12 symptom screening questions. Data were compared based on the type of HS treatment used
13 prior to COVID-19 diagnosis: biologic vs nonbiologic. Nonbiologic treatments included
14 systemic antibiotics, anti-androgenic agents, and disease-modifying anti-rheumatic drugs.
15 Additionally, data from patients who continued biologic therapy through their COVID-19
16 diagnosis were compared to those who discontinued biologic therapy upon their COVID-19
17 diagnosis. Statistical comparisons were performed using Fisher's exact or Pearson χ^2 tests.
18 Multivariable logistic regression adjusted for age, sex, cardiovascular disease, pulmonary
19 disease, diabetes, obesity, and tobacco smoking was used to determine whether biologic use
20 predicted COVID-19 outcomes.

21

22 311 self-reported and 113 HCP-reported cases were submitted to the registry. Of the self-
23 reported cases, we excluded 58 without confirmed COVID-19 diagnosis and 6 without an HS
24 diagnosis. We excluded 48 incomplete HCP-reported cases. 240 self-reported (median age:
25 33.5 years, IQR: 27-42 years, range: 13-72 years) and 65/113 HCP-reported (median age: 33
26 years, IQR: 27-42 years, range: 16-65 years) were included in the study. Additional patient
27 characteristics are described in **Table 1**. Tumor necrosis factor-inhibitors were the most
28 frequently reported biologic (self-reported: 33/35, 94.29%; HCP-reported: 31/36, 86.11%).
29 Systemic antibiotics were the most frequently reported nonbiologic (self-reported: 34.1%
30 (70/205); HCP-reported: 79.3% (23/29)).

31

32 Among self-reported cases, there was no difference in odds of hospitalization (biologic:
33 22.86% (8/35); nonbiologic: 17.56% (36/205), adjusted odds ratio (aOR) 0.93, 95% CI 0.36-

34 2.40, $P=0.89$) or required respiratory support (biologic: 31.43% (11/35); nonbiologic: 24.88%
35 (51/205), aOR 0.99, 95% CI 0.42-2.29, $P=0.97$) based on biologic use. No differences were
36 observed in COVID-19 treatments ($P>0.2$ for all) or COVID-19 duration (biologic: mean
37 [standard deviation] 21.70 [12.31] days; nonbiologic: 23.45 [26.22] days, $P=0.13$) between
38 groups. Patients treated with biologics more frequently reported HS exacerbations with
39 COVID-19 infection (biologic: 51.43% (18/35); nonbiologic: 25.37% (52/205), $P<0.01$).
40 Subgroup analysis revealed no association between disease severity and HS exacerbation
41 during COVID-19 infection among patients using biologics (mild: 19.0% (11/58); moderate-
42 to-severe: 32.4% (59/182), $P=0.07$). Furthermore, biologic therapy was associated with HS
43 exacerbation during COVID-19 infection among patients with moderate-to-severe HS
44 (biologic: 54.8% (17/31); nonbiologic: 26.5% (40/151), $P<0.01$). No other differences in
45 COVID-19 complications were observed between groups ($P>0.1$ for all). One case each of
46 sepsis and myocardial infarction were reported in patients not treated with biologics. No
47 cases of stroke or death were reported. There were no differences in hospitalization rates
48 ($P=0.61$), respiratory support requirement ($P=0.20$), or complication rates ($P>0.05$ for all)—
49 including HS flares ($P=0.30$), between those who remained on versus discontinued biologics
50 upon COVID-19 diagnosis.

51
52 Among HCP-reported cases, 90.0% (54/60) had mild or asymptomatic COVID-19 infection,
53 and no association was found between COVID-19 severity and use of biologic therapy (aOR
54 3.08, 95% CI 0.26-36.6, $P=0.37$). No differences in COVID-19 complication rates ($P=0.55$)
55 or treatment type were observed ($P=0.48$). Like self-reported cases, there was no association
56 between COVID-19 severity and continued use or discontinuation of biologic therapy with
57 COVID-19 infection ($P=0.63$).

58
59 Here, we report the most recent data from the Global Hidradenitis Suppurativa COVID-19
60 Registry, which further demonstrate that HS patients on biologics do not have higher odds of
61 hospitalization or required respiratory support compared to those on nonbiologic therapies.
62 Although previous studies of smaller HS cohorts have reported similar findings,[1,2] the
63 findings from this report, which includes 126 cases (105 self/caregiver-reported and 21 HCP-
64 reported) that were reported after the introduction of COVID-19 vaccines, are notable given
65 that anti-TNF therapy is associated with faster declines in COVID-19 vaccine-induced
66 neutralizing antibodies in patients with chronic inflammatory diseases.[3]

67

68 Despite growing evidence that biologic use does not increase risk of severe COVID-19
69 outcomes, patients with immune-mediated diseases frequently experience interruptions in
70 biologic treatment. In this study, 17/35 patients on biologics reported discontinuing therapy
71 upon COVID-19 diagnosis. Similarly, a global registry of 374 psoriasis patients with
72 confirmed or suspected COVID-19 reported biologic discontinuation in 51.2% of patients.[4]
73 Yet, an analysis of claims data from IBM[®] MarketScan[®] Research Databases showed that of
74 787 patients with COVID-19 and comorbid immune-mediated conditions treated with
75 immunomodulating therapy, patients who did not experience interruptions in
76 immunomodulator therapy had lower odds of hospitalization compared to patients with
77 interrupted therapy (aOR 0.31, 95% [0.12-0.80], $P=0.02$).[5]

78

79 Limitations of this study include small sample size, recall bias, and non-response bias. Our
80 study population is notable for the underrepresentation of Black patients, a group known to
81 be disproportionately affected by both HS[6] and COVID-19.[7] For example, one study of
82 7,361 patients treated with biologics and 74,910 matched controls showed that Black patients
83 on biologics had greater risk of COVID-19 infection compared to White patients on biologics
84 (aOR 2.10, 95% CI [1.73-2.56], $P<0.001$).[8] Thus our findings may not be generalizable to
85 groups with high social and structural risk for increased COVID19 infection.[7]

86

87 Considering the prolonged duration of the pandemic, our findings from the largest
88 international cohort of HS patients with COVID-19 infection offer meaningful support to
89 continue biologic therapy for HS patients.

Statements

Conflict of Interest Statement

Dr Alhusayen has received fees for participating in advisory boards for AbbVie, Janssen, and Novartis; has received consulting fees from Sandoz, Merck, and Boehringer Ingelheim; and is a board member of the Canadian Hidradenitis Suppurativa Foundation. Author Ingram has received fees for participating in advisory boards for Viela Bio and Kymera Therapeutics; consulting fees from UCB Pharma, Novartis, ChemoCentryx, and Boehringer Ingelheim; editorial honorarium as BJD Editor-in-Chief; royalties as chapter author for UpToDate; and

co-copyright holder for the HiSQOL, HS Patient Global Assessment, HS Investigator Global Assessment. He received travel expenses and a speaker's honorarium from UCB Pharma. His department receives income from copyright of the Dermatology Life Quality Instrument (DLQI) and related instruments. Dr Lowes has received fees for participating in advisory boards for AbbVie, Janssen, Viela Bio and consulting fees from Incyte, BSN, XBiotech, Kymera, and Almirall and is the Vice President of the US Hidradenitis Suppurativa Foundation. Author Guilbault has received compensation for patient advisory board from Boehringer Ingelheim and is a board member of the US HS Foundation and Hope for HS. Author Villumsen has received consulting fees from Boehringer Ingelheim, UCB and Novartis and is the President of Patientforeningen HS Danmark and co-copyright holder for the HiSQOL, HS Patient Global Assessment, HS Investigator Global Assessment. Dr Naik has received grant support from AbbVie, consulting fees from 23andme, advisory board fees from Invitrogen Biovitrum; has served as an investigator for Pfizer; and is a board member of the US Hidradenitis Suppurativa Foundation. Dr Marzano and Authors Williams, Kudlinski, Paul, and Yannuzzi have no conflicts of interest to declare.

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Author Contributions

J.C.W. led manuscript writing, review, and editing, and supported formal analysis. R.A., J.R.I., M.A.L., A.V.M., and B.V. contributed a supporting role in study conceptualization, data curation, methodology, and manuscript review and editing. S.G. and C.Y. contributed a supporting role in study conceptualization, data curation, and methodology. N.H. led formal analysis. M.V.K. supported formal analysis and led data curation and project administration. M.P. supported data curation and project administration. H.B.N. led study conceptualization, methodology, funding acquisition, investigation, resources, and supervision, and supported data curation, formal analysis, project administration, and manuscript review and editing.

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Table 1 Patient Characteristics

Characteristics	Patient/Caregiver-reported cases			Health care provider-reported cases		
	Biologic	No Biologic	All	Biologic	No Biologic	All
Number	35	205	240	36	29	65
Age, y (median, IQR)	38 (32-46)	34 (26-41)	35 (27-42)	34 (25-42)	36 (28-42)	35 (27-42)
Female sex, n (%)	32 (91.4)	186 (90.7)	218 (90.8)	21 (58.3)	19 (67.9)	40 (62.5)
Race/ethnicity, n (%)						
White	22 (62.9)	146 (71.2)	168 (70.0)	16 (44.4)	11 (37.9)	27 (41.5)
Black, African	4 (11.4)	2 (1.0)	6 (2.5)	2 (5.6)	6 (20.7)	8 (12.3)
Black, Afro-Caribbean	0 (0.0)	3 (1.46)	3 (1.25)	1 (2.8)	1 (3.5)	2 (3.1)
Black, African American	2 (5.7)	6 (2.9)	8 (3.3)	6 (16.7)	1 (3.5)	7 (10.8)
Asian	0 (0.0)	2 (1.0)	2 (0.8)	3 (8.3)	1 (3.5)	4 (6.2)
Hispanic	3 (8.6)	21 (10.2)	24 (10.0)	3 (8.3)	1 (3.5)	4 (6.2)
Mixed race	4 (11.4)	17 (8.3)	21 (8.75)	0 (0.0)	2 (6.9)	2 (3.1)
Other	0 (0.0)	8 (3.9)	8 (3.3)	5 (13.9)	6 (20.7)	11 (16.9)
Country, n (%)						
United States	32 (91.43)	107 (52.2)	139 (57.9)	16 (44.4)	9 (31.0)	25 (38.5)
United Kingdom	1 (2.9)	16 (7.8)	17 (7.1)	5 (13.9)	4 (13.8)	9 (13.9)
Brazil	0 (0.0)	29 (14.2)	29 (12.1)	1 (2.8)	2 (6.9)	3 (4.6)
Sweden	0 (0.0)	16 (7.8)	16 (7.8)	–	–	–
Argentina	0 (0.0)	13 (6.3)	13 (5.4)	1 (2.8)	0 (0.0)	1 (1.5)
France	–	–	–	1 (2.8)	10 (34.5)	11 (16.9)
Italy	0 (0.0)	1 (0.5)	1 (0.4)	5 (13.9)	1 (3.5)	6 (9.2)
Other	2	23	25*	7 (19.4)	3 (10.3)	10 (15.4) [†]
Comorbidities, n (%)						
Obesity	25 (71.4)	127 (62.0)	152 (63.3)	12 (33.3)	9 (31.0)	21 (32.3)
Diabetes	4 (11.4)	11 (5.4)	15 (6.3)	5 (13.9)	2 (6.9)	7 (10.8)
Pulmonary disease	13 (37.1)	41 (20.0)	54 (22.5)	2 (5.6)	2 (6.9)	4 (6.2)
Tobacco smoking	5 (14.3)	34 (16.6)	9 (16.3)	–	–	–
CV disease	1 (2.9)	5 (2.4)	6 (2.5)	2 (5.6)	0 (0.0)	2 (3.1)
Hurley stage, n (%)						
Hurley 1	–	–	–	3 (8.6)	5 (17.2)	8 (12.5)
Hurley 2	–	–	–	14 (40.0)	11 (37.9)	25 (39.1)
Hurley 3	–	–	–	18 (51.4)	12 (41.4%)	30 (46.9)
Unknown	–	–	–	0 (0.0)	1 (3.5%)	1 (1.6%)

CV, Cardiovascular; IQR, interquartile range.

* Other category includes 1-5 cases each from Austria, Belgium, Canada, Czech Republic, Denmark, Germany, Ireland, Peru, Saudi Arabia, and Spain.

† Other category includes 1-5 cases each from Canada, Czech Republic, India, Israel, and Saudi Arabia.