***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***

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

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Dear Editor,

As the COVID-19 pandemic persists, dermatologists continue to balance the desire to achieve effective hidradenitis suppurativa (HS) control through biologic therapy with the risk it may pose during active COVID-19 infection in the context of comorbidities associated with severe COVID-19 infection.[1] This study expands upon previous findings[1] with 188 additional cases reported over 10 more months to the Global Hidradenitis Suppurativa COVID-19 Registry from April 5, 2020 to December 9, 2021. Registry entries were submitted by health care providers (HCPs) and patients (or their caregivers, in the case of children or those too ill or without capacity to complete the survey). Eligible cases had 1) an HCP-confirmed diagnosis of HS and 2) an HCP-confirmed diagnosis of COVID-19 based on a positive test or symptom screening questions. Data were compared based on the type of HS treatment used prior to COVID-19 diagnosis: biologic vs nonbiologic. Nonbiologic treatments included systemic antibiotics, anti-androgenic agents, and disease-modifying anti-rheumatic drugs. Additionally, data from patients who continued biologic therapy through their COVID-19 diagnosis were compared to those who discontinued biologic therapy upon their COVID-19 diagnosis. Statistical comparisons were performed using Fisher’s exact or Pearson χ2 tests. Multivariable logistic regression adjusted for age, sex, cardiovascular disease, pulmonary disease, diabetes, obesity, and tobacco smoking was used to determine whether biologic use predicted COVID-19 outcomes.

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

Among self-reported cases, there was no difference in odds of hospitalization (biologic: 22.86% (8/35); nonbiologic: 17.56% (36/205), adjusted odds ratio (aOR) 0.93, 95% CI 0.36-2.40, *P*=0.89) or required respiratory support (biologic: 31.43% (11/35); nonbiologic: 24.88% (51/205), aOR 0.99, 95% CI 0.42-2.29, *P*=0.97) based on biologic use. No differences were observed in COVID-19 treatments (*P*>0.2 for all) or COVID-19 duration (biologic: mean [standard deviation] 21.70 [12.31] days; nonbiologic: 23.45 [26.22] days, *P*=0.13) between groups. Patients treated with biologics more frequently reported HS exacerbations with COVID-19 infection (biologic: 51.43% (18/35); nonbiologic: 25.37% (52/205), *P*<0.01). Subgroup analysis revealed no association between disease severity and HS exacerbation during COVID-19 infection among patients using biologics (mild: 19.0% (11/58); moderate-to-severe: 32.4% (59/182), *P*=0.07). Furthermore, biologic therapy was associated with HS exacerbation during COVID-19 infection among patients with moderate-to-severe HS (biologic: 54.8% (17/31); nonbiologic: 26.5% (40/151), *P*<0.01). No other differences in COVID-19 complications were observed between groups (*P*>0.1 for all). One case each of sepsis and myocardial infarction were reported in patients not treated with biologics. No cases of stroke or death were reported. There were no differences in hospitalization rates (*P*=0.61), respiratory support requirement (*P*=0.20), or complication rates (*P*>0.05 for all)—including HS flares (*P*=0.30), between those who remained on versus discontinued biologics upon COVID-19 diagnosis.

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

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

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

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

Considering the prolonged duration of the pandemic, our findings from the largest international cohort of HS patients with COVID-19 infection offer meaningful support to 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

|  |  |  |
| --- | --- | --- |
|  | Patient/Caregiver-reported cases | Health care provider-reported cases |
| Characteristics | 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.