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# Incidence rates of hospitalization and death from COVID-19 in patients with psoriasis receiving biological treatment: A Northern Italy experience



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**Introduction:** Whether biologic therapies enhance the risk of coronavirus 2019 (COVID-19) or affect the disease outcome in patients with chronic plaque psoriasis remains to be ascertained.

**Objective:** We sought to investigate the incidence of hospitalization and death for COVID-19 in a large sample of patients with plaque psoriasis receiving biologic therapies compared with the general population.

**Methods:** This is a retrospective multicenter cohort study including patients with chronic plaque psoriasis (n = 6501) being treated with biologic therapy and regularly followed up at the divisions of dermatology of several main hospitals in the Northern Italian cities of Verona, Padua, Vicenza, Modena, Bologna, Piacenza, Turin, and Milan. Incidence rates of hospitalization and death per 10,000 person-months with exact mid-p 95% CIs and standardized incidence ratios were estimated in the patients with psoriasis and compared with those in the general population in the same geographic areas.

**Results:** The incidence rate of hospitalization for COVID-19 was 11.7 (95% CI, 7.2-18.1) per 10,000 person-months in patients with psoriasis and 14.4 (95% CI, 14.3-14.5) in the general population; the incidence rate of death from COVID-19 was 1.3

(95% CI, 0.2-4.3) and 4.7 (95% CI, 4.6-4.7) in patients with psoriasis and the general population, respectively. The standardized incidence ratio of hospitalization and death in patients with psoriasis compared with those in the general population was 0.94 (95% CI, 0.57-1.45;  $P = .82$ ) and 0.42 (95% CI, 0.07-1.38;  $P = .19$ ), respectively.

**Conclusions:** Our data did not show any adverse impact of biologics on COVID-19 outcome in patients with psoriasis. We would not advise biologic discontinuation in patients on treatment since more than 6 months and not infected with severe acute respiratory syndrome coronavirus 2 to prevent hospitalization and death from COVID-19. (*J Allergy Clin Immunol* 2021;147:558-60.)

**Key words:** Psoriasis, biologics, COVID-19, interstitial pneumonia

## INTRODUCTION

Italy has been deeply affected by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic, particularly in the northern regions.<sup>1</sup> There is substantial concern among physicians regarding an increased risk of coronavirus 2019 (COVID-

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*Abbreviations used*

COVID-19: Coronavirus 2019  
SARS-CoV-2: Severe acute respiratory syndrome coronavirus 2  
SIR: Standardized incidence ratio

19) in patients who are being treated with biologic therapies.<sup>2</sup> However, whether biologics enhance this risk and/or whether the disease course is worsened by the immunosuppressive/immunomodulating treatment remains to be determined. It is debated whether biologics for psoriasis should be interrupted for preventing severe complications of SARS-CoV-2 infection such as interstitial pneumonia. Notably, SARS-CoV-2 infection seems to be most fatal when it triggers a cytokine storm, including TNF- $\alpha$ , IL-6, and IL-17.<sup>3,4</sup> Therefore, biologics are being investigated as treatments for COVID-19.<sup>5</sup>

In this study, we evaluated the incidence of hospitalization and death for COVID-19 in a large sample of patients with plaque psoriasis receiving biologic therapies compared with the general population.

## RESULTS AND DISCUSSION

The characteristics of the studied population are reported in Table 1.<sup>6-9</sup> The prevalence of male sex and comorbidities (obesity, arterial hypertension, and diabetes) was significantly higher in patients with psoriasis than in the general population. We estimated the incidence rate of hospitalization and death for COVID-19 in 6501 patients with plaque psoriasis receiving biologic therapies, corresponding to 15,378.5 patient-months of follow-up, and compared the figures with those obtained from the general adult population of Northern Italy, corresponding to 19,978,806 subjects and 47,260,897.6 patient-months of follow-up. The incidence rate of hospitalization for COVID-19 was 11.7 (95% CI, 7.2-18.1) per 10,000 person-months in patients with psoriasis and 14.4 (95% CI, 14.3-14.5) in the general population; the incidence rate of death from COVID-19 was 1.3 (95% CI, 0.2-4.3) and 4.7 (95% CI, 4.6-4.7) in patients with psoriasis and the general population, respectively. The standardized incidence ratio (SIR) of hospitalization and death in patients with psoriasis compared with the general population was 0.94 (95% CI, 0.57-1.45;  $P = .82$ ) and 0.42 (95% CI, 0.07-1.38;  $P = .19$ ), respectively. We found no significant difference in the rates of hospitalization with the general population when stratifying by age (<65 vs  $\geq$ 65 years) or by class of biologic (Table 1). There were no further deaths for other causes during the study period. We had 1865 of 6501 (ie, 28.7%) patients affected by psoriatic arthritis. Four of 18 hospitalized patients with psoriasis had psoriatic arthritis, whereas none of the dead ones had psoriatic arthritis. All the hospitalized patients fully recovered from the viral infection and then restarted biologic therapy because of psoriasis relapse after a period of time ranging from 6 to 15 weeks from the hospital discharge. They are currently on biologic.

The major finding of our study is that although patients with psoriatic treated by biologics are burdened by higher rates of metabolic and cardiovascular comorbidities, there was no evidence for an increased risk of hospitalization or death from COVID-19 in those patients compared with the general population. Accordingly, some preliminary data on TNF- $\alpha$  inhibitors and IL-12/IL-23 inhibitors in patients with

inflammatory bowel disease showed that these therapies do not worsen the clinical course of COVID-19 compared with sulfasalazine/mesalamine or no treatment.<sup>10</sup> On the contrary, biologics appeared to be associated with a better outcome, even though there were insufficient data to make definite statements.<sup>11</sup> Some systemic complications caused by SARS-CoV-2 infection appear to be associated with excessive inflammatory and cytokine responses.<sup>3</sup> Therefore, treatments that reduce the host inflammatory response, including agents blocking TNF- $\alpha$ , IL-6, or IL-17 pathways, in combination with therapies that have direct antiviral activity, have been proposed, and are currently under investigation for the treatment of COVID-19.<sup>12-14</sup>

We acknowledge the limitations of our study, including the absence of serological or molecular investigations for the diagnosis of SARS-CoV-2 infection in asymptomatic patients with psoriasis. The objective of our study was not to investigate the prevalence of the SARS-CoV-2 infection, but to report the occurrence of hospitalization and death, as indicators of severe outcomes related to COVID-19. Despite a cohort of 6501 patients with psoriasis receiving biologic treatment, we collected relatively few COVID-19 cases, with wide CIs. The low rates in patients treated with biologics are reassuring, especially considering that these patients had a high prevalence of comorbidities that are usually associated with a worse COVID-19 course. Despite the fact that a great effort has been made in retrieving patients with COVID-19, we acknowledge that there is still a possibility that we have missed important cases. However, on the basis of a simulation analysis on our sample size, we estimated that around 3 missed deaths would be required to observe an SIR of 1 and at least 8 deaths for an SIR of more than 2 with  $P$  value less than .05. However, we would have missed at least 11 hospitalized patients to observe an SIR of more than 1.5 with  $P$  value less than .05. Therefore, it is unlikely that we have missed a number of patients needed to completely change our results.

There were no new patients starting biological treatment from February 20 to May 1 in our divisions of dermatology. This is because this time period was overlapping with the lockdown imposed by the Italian government. During that period, public health measures required citizens to stay at home and shield. The clinical dermatological activity was significantly reduced and mostly dedicated to teleconsultation for those patients already on treatment.<sup>15</sup> The access to the hospitals was limited only to symptomatic patients with fever, suspected for SARS-CoV-2 infection. The major strengths of our study are the cohort study design, the focus on Italian regions most affected by the SARS-CoV-2 pandemic, and the completeness of the database. We acknowledge that patients on biologic drugs may have self-isolated more efficiently, thus limiting their own infectious risk. We can rule out that there have been deaths at home that we are not aware of and/or that patients have gone to hospitals outside their catchment area. Our findings are consistent with those of another study that reported that patients with psoriasis on biologics were not at an increased risk of intensive care unit admission or death; conversely, the study found that patients were at a higher risk for testing positive for SARS-CoV-2, to be self-quarantined at home or hospitalized.<sup>16</sup>

The results of our study show that the continuation of biologic therapies during the pandemic does not influence the development of severe complications of the SARS-CoV-2 infection. A prophylactic treatment discontinuation in an attempt

**TABLE I.** Number of patients with chronic plaque psoriasis being treated with biologic therapy or subjects of the general population of Veneto, Lombardy, Emilia Romagna, and Piedmont hospitalized for or died from COVID-19 from February 20 to May 1, 2020

Parameter, n (%)	Patients with psoriasis	General population (18+ y)	SIR (95% CI)	P value*
Number (patient-months)	6,501 (15,378.5)	19,978,806 (47,260,897.6)	—	—
Outcome measure				
Subjects positive for SARS-CoV-2 (IR, 95% CI)	†	144,909 (30.7, 30.5-30.8)	—	—
Hospitalized for COVID-19 (IR, 95% CI)	18 (11.7, 7.2-18.1)	68,099 (14.4, 14.3-14.5)	0.94 (0.57-1.45)	.82
Deaths for COVID-19 (IR, 95% CI)	2 (1.3, 0.2-4.3)	22,013 (4.7, 4.6-4.7)	0.42 (0.07-1.38)	.19
Demography				
Sex: male, n (%)	3,616 (55.6)	9,649,834 (48.3)	—	<.001
Age (y), mean ± SD	53.4 ± 11.0	52.3 ± 20.0	—	<.001
<65, n (%)	5,071 (78.0)	14,403,251 (72.1)	0.68 (0.30-1.35)‡	.31
≥65, n (%)	1,430 (22.0)	5,575,555 (27.9)	1.06 (0.56-1.85)‡	.80
Comorbidity, n (%)				
Obesity	1,633 (25.1)	2,081,748 (10.4)	—	<.001
Hypertension	2,012 (30.9)	4,261,658 (21.3)	—	<.001
Diabetes mellitus	854 (13.1)	1,124,563 (5.6)	—	<.001
Psoriatic arthritis	1,865 (28.7)	—	—	—
Biologic therapy, n (%)				
TNF-α inhibitors	2,106 (32.4)	—	1.02 (0.41-2.12)‡	.91
IL-17 inhibitors	2,486 (38.2)	—	0.80 (0.32-1.67)‡	.62
IL-12/IL-23 inhibitors	1,691 (26.0)	—	0.98 (0.36-2.17)‡	1
IL-23 inhibitors	218 (3.3)	—	1.45 (0.07-7.16)‡	.65

IR, Incidence rate × 10,000 person-months.

Data of subjects hospitalized for or died from COVID-19 in the general population are from the Civil Protection Official Repository<sup>6</sup> and from the National Health Institute (ISS).<sup>7</sup> Data of patients with psoriasis hospitalized for or died from COVID-19 are from electronic medical records of the participating hospitals (accessed May 1, 2020).

Data of comorbidities in the general population are from Istituto Nazionale di Statistica multipurpose survey 2019.<sup>8</sup>

\*Exact mid-p test was reported for SIR. Pearson  $\chi^2$  test and 2-sample *t* test were used for the comparison of nominal and continuous variables between groups.

†Asymptomatic individuals were not tested, and so the true number of COVID-19-positive patients is unknown.

‡SIR for COVID-19 hospitalization was reported.

to prevent a negative outcome of COVID-19 may not be required.<sup>17</sup> Larger studies with longer follow-up periods are needed to confirm these findings.

For detailed methods, please see the **Methods** section in this article's Online Repository at [www.jacionline.org](http://www.jacionline.org).

**Key messages: Biologic discontinuation in patients with psoriasis on treatment to prevent hospitalization and death from COVID-19 is not advisable, unless they are infected with SARS-CoV-2.**

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## METHODS

This is a retrospective multicenter cohort study of patients with chronic plaque psoriasis ( $n = 6501$ ) treated with biologic therapy at a large number of hospitals in Northern Italy. Incidence rates of hospitalization or death from COVID-19 were assessed in these patients and compared with data from the general population in the same geographic areas between February 20 and May 1, 2020. Inclusion criteria for patients with psoriasis were as follows: being regularly followed up at the divisions of dermatology of the hospitals of Verona, Padua, Vicenza, Modena, Bologna, Piacenza, Turin, and Milan (Humanitas Hospital, San Donato Hospital, Ca' Granda Ospedale Maggiore Policlinico); being currently treated with a biological agent, including TNF- $\alpha$ , IL-17, IL-12/IL-23, or IL-23 inhibitors; and the minimal length of treatment 6 months. Clinical data, including comorbidities, were obtained by consulting the electronic medical records of each hospital, and/or by directly contacting the patients by visit, phone, or email. In particular, case ascertainment (ie, being hospitalized or dead) was confirmed by contacting, either by phone or by telecommunications application providing video chat and voice (eg, Skype), all the patients with psoriasis included in the study. For study purposes, demographic data and data on comorbidities in the general adult population of the Italian regions of Veneto, Emilia Romagna, Piedmont, and Lombardy were retrieved from the Istituto Nazionale di Statistica census data (and the Istituto Nazionale di Statistica multipurpose survey 2019).<sup>E1,E2</sup> Data on adult COVID-19 confirmed cases, including demographics, hospitalizations, and deaths, were extracted from the civil protection official repository<sup>E3</sup> and from the National Health Institute (Istituto Superiore di Sanità [ISS]).<sup>E4</sup>

### Statistical analysis

For descriptive purposes, data were presented as means with SDs or numbers with percentages for continuous and categorical variables,

respectively. Incidence rates were calculated as the number of observed cases per 10,000 person-months with exact mid-p 95% CIs. For comparison purpose, SIRs were calculated by using indirectly standardized rates from the number of observed events in the study population and the number of expected events derived by applying, to the target population, age-, sex-, and regional-specific rates of the general adult population of the same geographical areas during the same period of time. SIRs were reported along with their exact mid-p 95% CI and  $P$  values. A stratified SIR analysis by age and class of biologic was also performed for COVID-19 hospitalization. Differences in the distribution of demographics and comorbidities between groups were assessed by using Pearson  $\chi^2$  test and 2-sample  $t$  test for nominal and continuous variables, respectively. All tests were considered significant at  $P$  value less than .05. Analyses were carried out with R software v.3.6.2 (R Foundation for Statistical Computing, Vienna, Austria).

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