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.

dupilumab. Our small cohort did not demonstrate any association between ICI-BP and cancer outcomes. Based on our data, we recommend prescription of SSA therapy for patients with ≥grade 2 ICI-BP at initial presentation to minimize interruptions of ICI therapy and the need for systemic steroids. Dupilumab has been reported as a promising therapy for BP outside of the cancer setting[4,5] and may have a role in ICI-BP given its success rate in our cohort.

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Conflicts of interest

None disclosed.

REFERENCES

1. Siegel J, Totonchy M, Damsky W, et al. Bullous disorders associated with anti–PD-1 and anti–PD-L1 therapy: a retrospective analysis evaluating the clinical and histopathologic features, frequency, and impact on cancer therapy. *J Am Acad Dermatol*. 2018;79(6):1081-1088. https://doi.org/10.1016/j.jaad.2018.07.008
2. U.S. Department of Health and Human Services. Common terminology criteria for adverse events (CTCAE) v5.0. 2017. Accessed August 25, 2022. https://ctep.cancer.gov/protocoldevelopment/electronic_applications/docs/ctcae_v5_quick_reference_5x7.pdf
3. Joly P, Roujeau JC, Benichou J, et al. A comparison of oral and topical corticosteroids in patients with bullous pemphigoid. *N Engl J Med*. 2002;346(5):321-327. https://doi.org/10.1056/NEJMoa011592
4. Regeneron Pharmaceuticals. A Multicenter, Randomized, Double-Blind, Placebo-Controlled, Parallel Group Study to Evaluate the Efficacy and Safety of Dupilumab in Adult Patients With Bullous Pemphigoid. clinicaltrials.gov. 2021. Accessed August 25, 2022. https://clinicaltrials.gov/ct2/show/NCT04206553?term=dupilumab&cond=bullous+pemphigoid&draw=2&rank=1
5. Abdat R, Waldman RA, de Bedout V, et al. Dupilumab as a novel therapy for bullous pemphigoid: a multicenter case series. *J Am Acad Dermatol*. 2020;83(1):46-52. https://doi.org/10.1016/j.jaad.2020.01.089

https://doi.org/10.1016/j.jaad.2022.08.001

The risk of COVID-19 in patients with psoriasis: A retrospective cohort study

To the Editor: Clinical trials and real-world data generally suggest that biologics do not increase susceptibility to COVID-19.[1] However, it remains unknown whether these therapies may confer a protective effect against contracting COVID-19. Therefore, we sought to assess the risk of COVID-19 infection in patients with psoriasis compared with the general population and in patients receiving systemic and topical therapies. This study used the Symphony Health dataset, a large repository of pharmacy data, inpatient and outpatient medical claims, and remittance data (over 300 million patients, 7 million COVID-19 cases, and payer information: Medicaid/Medicare/commercial/cash).

Patients with at least 2 recorded International Classification of Diseases-10 diagnosis codes for psoriasis (L40.x) (n = 167,027) and controls without International Classification of Diseases-10 codes for psoriasis (n = 1,002,162) were randomly sampled in a 1:6 ratio between May 1, 2019, and January 1, 2020. Two recorded diagnosis codes for psoriasis were required to increase the positive predictive value, a strategy employed by prior studies.[2,3] Each patient was assigned to 1 of 9 mutually exclusive cohorts based on the last prescription dispense (biologic: Tumor necrosis factor [TNF]-α inhibitor, ustekinumab, interleukin [IL] 17 inhibitor, and IL-23 inhibitor; oral: acitretin, cyclosporine, methotrexate, and apremilast cohorts; topical: none of the above medications). Follow-up began on January 1, 2020, and ended with the first occurrence of any of the following: (1) COVID-19 diagnosis code or (2) November 11, 2020 (the end of the study). Vaccination status was unable to be ascertained from the database because Emergency Use Authorization vaccine approved by the Food and

Table I. Cohort characteristics

Demographics	Psoriasis (n = 167,027)	No psoriasis (n = 1,002,162)	Total (n = 1,169,189)
Male No. (%)	77,725 (46.5)	444,472 (44.3)	522,197 (44.7)
Age, mean (SD), y	58.1 (13.6)	57.7 (16.1)	57.7 (15.7)
Race No. (%)			
Caucasian	132,036 (79.1)	748,490 (74.7)	880,526 (75.3)
Hispanic	15,568 (9.3)	90,413 (9.0)	105,981 (9.1)
African American	13,848 (8.3)	130,392 (13.0)	144,240 (12.3)
Asian	2894 (1.7)	17,171 (1.7)	20,065 (1.7)
Other	2681 (1.6)	15,696 (1.6)	18,377 (1.6)
High-risk factors (ICD-10) for COVID-19, No. (%)			
Congestive heart failure	10,354 (6.2)	48,025 (4.8)	58,379 (5.0)
Type 1 diabetes mellitus	37,975 (22.7)	158,987 (15.9)	196,962 (16.9)
Obesity	44,557 (26.7)	145,347 (14.5)	189,904 (16.2)
Chronic obstructive pulmonary disease	16,514 (9.9)	64,145 (6.4)	80,659 (6.9)
Psoriasis treatment cohorts*			
Topical	99,395 (59.5)	NA	NA

Systemic treatments	Oral systemic cohort, n = 31,468 (18.8)	Biologic cohort†, n = 36,164 (21.7)	Total systemic treatments received, n = 67,632
Oral systemics No. (%)			
Methotrexate	21,478 (68.3)	230 (0.6)	21,708 (32.1)
Apremilast	7398 (23.5)	99 (0.3)	7497 (11.1)
Cyclosporine	1573 (5.0)	7 (0.02)	1580 (2.3)
Acitretin	1072 (3.4)	5 (0.01)	1077 (1.6)
Biologics No. (%)			
TNF-α inhibitors			
Adalimumab	0	9553 (26.4)	9553 (14.1)
Infliximab	0	3366 (9.3)	3366 (5.0)
Etanercept	0	4201 (11.6)	4201 (6.2)
Certolizumab	0	1438 (4.0)	1438 (2.1)
IL-12/23 inhibitor			
Ustekinumab	0	5085 (14.1)	5085 (7.5)
IL-17 inhibitors			
Secukinumab	0	6266 (17.3)	6266 (9.3)
Ixekizumab	0	3135 (8.7)	3135 (4.6)
Brodalumab	0	142 (0.4)	142 (0.2)
IL-23 inhibitors			
Guselkumab	0	1687 (4.7)	1687 (2.5)
Risankizumab	0	1021 (2.8)	1021 (1.5)
Tildrakizumab	0	312 (0.9)	312 (0.5)

ICD, International Classification of Diseases; *IL,* interleukin; *NA,* not available; *TNF,* tumor necrosis factor.

Drug Administration did not occur until December 2020.

Demographics were summarized by frequency (percentage) and mean (SD) (Table I). Logistic regression models were constructed with psoriasis status as the independent variable, COVID-19 International Classification of Diseases-10 diagnosis code as the dependent variable, and the following covariates: age, sex, race, congestive heart failure (I50.X), chronic obstructive pulmonary disease (J41/J43/J44), type-2 diabetes mellitus (E11.x/E13.x), and obesity (E66.0-E66.2/E66.8-E66.9/Z68.3-Z68.5).

Psoriasis was associated with 18% higher odds of incident COVID-19 (adjusted odd ratio [aOR], 1.18; 95% CI, 1.13-1.23) compared with controls (Supplementary Fig 1, available via Mendeley at https://data.mendeley.com/datasets/68fht87h68/1). In contrast to data from Northeast Italian cohorts, our results appear to align with recent findings from a global registry-based study suggesting that patients receiving no systemic therapy were estimated to have an increased risk of COVID-19 hospitalization compared with patients on biologics.[4,5] In analyses of psoriasis patients (Fig 1), TNF inhibitor (aOR, 0.87;

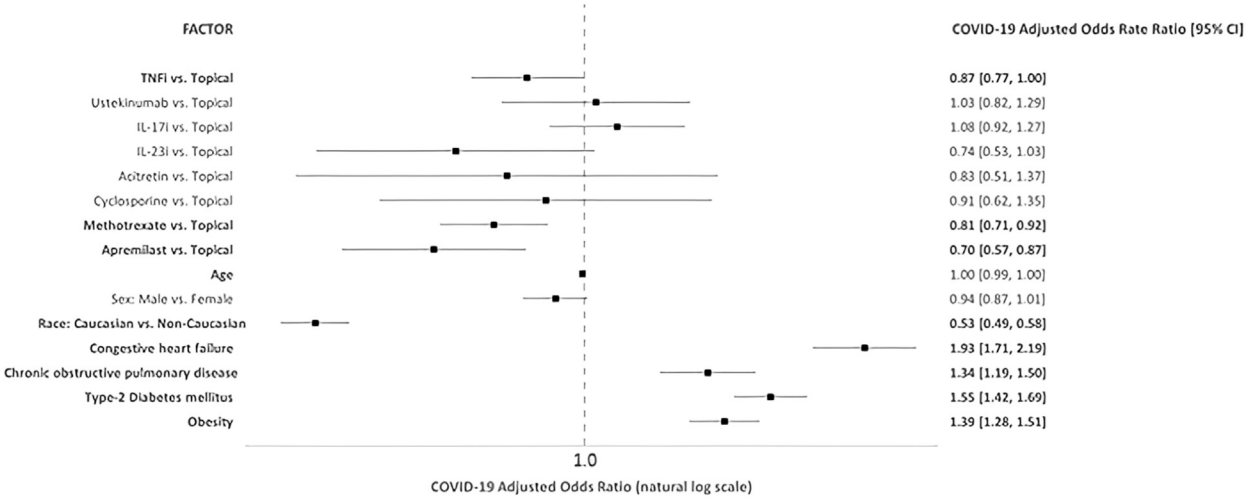

Fig 1. Multivariable logistic regression assessing factors (International Classification of Diseases-10) associated with COVID-19 infection comparing systemic versus topical therapy.* *Multivariable logistic regression models were constructed with COVID-19 as the dependent variable, the treatment cohort as the independent variable with the topical cohort as the reference group. The following covariates were specified in the model: age (linear), sex (male vs female), race (Caucasian vs non-Caucasian), congestive heart failure, chronic obstructive pulmonary disease, type 2 diabetes mellitus, and obesity. Adjusted odds ratios were computed for all treatment comparisons with the topical cohort. *P* value of <.05 was considered significant. *CI*, Confidence interval; *IL*, interleukin; *TNFi*, tumor necrosis factor inhibitor.

95% CI, 0.77-1.00), methotrexate (aOR, 0.81; 95% CI, 0.71-0.92), and apremilast (aOR, 0.70; 95% CI, 0.57-0.87) use had decreased odds of incident COVID-19 compared with patients on topical therapy. Odds ratios remained unchanged after excluding patients on concomitant biologic and oral therapy. Among the limitations, first, we cannot differentiate between the impact of psoriasis severity and systemic therapy on the risk of COVID-19, because disease severity was defined based on treatment history. Second, smoking status and other cardiovascular comorbidities were not adjusted in the logistic regression model. Nonetheless, the protective role exerted by TNF-inhibitor and methotrexate is supported by the mechanistic plausibility of proinflammatory cytokine inhibition, particularly of TNF-α, IL-6, and IL-1. Our findings suggest that these drug classes do not increase the risk of acquiring COVID-19 and, thus, are safe options for continuing psoriasis treatment during the COVID-19 pandemic.

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Conflicts of interest

Dr Wu is or has been an investigator, consultant, or speaker for AbbVie, Almirall, Amgen, Arcutis, Aristea Therapeutics, Boehringer Ingelheim, Bristol-Myers Squibb, Dermavant, Dr Reddy's Laboratories, Eli Lilly, Galderma, Janssen, LEO Pharma, Mindera, Novartis, Regeneron, Sanofi Genzyme, Solius, Sun Pharmaceutical, UCB, Valeant Pharmaceuticals North America LLC, and Zerigo Health. With no relation to the present work, Dr Egeberg has received research funding from Pfizer, Eli Lilly, Novartis, Bristol-Myers Squibb, AbbVie, Janssen Pharmaceuticals, the Danish National Psoriasis Foundation, the Simon Spies Foundation, and the Kgl Hofbundtmager Aage Bang Foundation, and honoraria as a consultant and/or speaker from AbbVie, Almirall, Leo Pharma, Galápagos NV, Sun

Pharmaceuticals, Samsung Bioepis Co, Ltd, Pfizer, Eli Lilly and Company, Novartis, Galderma, Dermavant, UCB, Mylan, Bristol-Myers Squibb, and Janssen Pharmaceuticals. Authors Liu, Thatiparthi, and Martin have no conflicts of interest to declare.

REFERENCES

1. Jones ME, Kohn AH, Pourali SP, et al. The use of biologics during the COVID-19 pandemic. *Dermatol Clin*. 2021;39(4):545-553. https://doi.org/10.1016/j.det.2021.05.010
2. Icen M, Crowson CS, McEvoy MT, Gabriel SE, Maradit Kremers H. Potential misclassification of patients with psoriasis in electronic databases. *J Am Acad Dermatol*. 2008;59(6):981-985. https://doi.org/10.1016/j.jaad.2008.08.034
3. Takeshita J, Gelfand JM, Li P, et al. Psoriasis in the US Medicare population: prevalence, treatment, and factors associated with biologic use. *J Invest Dermatol*. 2015;135(12):2955-2963. https://doi.org/10.1038/jid.2015.296
4. Piaserico S, Gisondi P, Cazzaniga S, Naldi L. Lack of evidence for an increased risk of severe COVID-19 in psoriasis patients on biologics: a cohort study from Northeast Italy. *Am J Clin Dermatol*. 2020;21(5):749-751. https://doi.org/10.1007/s40257-020-00552-w
5. 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

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Value of permanent pathology for debulk and Mohs specimens during Mohs micrographic surgery for cutaneous squamous cell carcinoma: A retrospective cohort study

To the Editor: Certain cutaneous squamous cell carcinoma (cSCC) characteristics such as deep invasion, large caliber perineural invasion (PNI), and poor differentiation increase the risk for metastasis and local recurrence.[1] The American Joint Committee on Cancer-8 and Brigham and Women's Hospital staging systems prognosticate tumors to guide management of cSCC.

Preoperative biopsies of cSCC often only sample a small portion of a lesion; therefore, staging systems based on biopsies can be inaccurate. The tumor may demonstrate aggressive features intraoperatively during Mohs micrographic surgery (MMS). While MMS examines 100% of a tumor's margin, the central portion ("debulk") is not routinely evaluated for additional pathologic features. Notably, it is standard to analyze the debulk of melanomas treated with Mohs with permanent sections for accurate staging.[2-4] To assess for additional high-risk features in cSCC when there is concern for upstaging such as with larger tumors, incomplete biopsies and/or when a lesion is in a higher risk (eg, immunosuppressed) patient, the authors send Mohs debulks and at times thawed Mohs sections for permanent pathology when there is concern for high-risk pathology. This single-institution retrospective cohort study evaluates the frequency of tumor upstaging with the addition of debulk analysis.

Mohs case logs identified cSCC cases between 2015 and 2020; cases were included if tissue was sent for permanent pathology. Patient and tumor characteristics were extracted from the electronic medical record. Statistical analysis was done using χ^2 and Fisher tests.

Of 3900 cSCCs treated, 78 (2.0%) tumors were submitted for debulk analysis (Supplementary Table I, available via Mendeley at https://doi.org/10.17632/g7xcsd33kb.1). Of these, a total of 47 (60%) were upstaged (Supplementary Table II, available via Mendeley at https://doi.org/10.17632/g7xcsd33kb.1). 29 of 47 (62%) were upstaged by MMS, but not on debulk analysis, and 14/47 (30%) were upstaged by debulk analysis, but not MMS frozen sections. Four of 47 (9%) were upstaged on both MMS section and debulk analysis. Therefore, debulk analysis may reveal upstaging 18% of the time (14 out of 78 tumors) independent of MMS sections. Upstaged tumors were more likely to have large caliber PNI ($P < .001$). Patients with upstaged tumors were significantly more likely to be referred for adjuvant radiation ($P = .012$). Only these factors were significantly associated with upstaging. This study supports the use of permanent pathology analysis for select high-risk lesions treated with MMS for accurate staging and to guide management. Further prospective studies are needed to define when debulks should be sent in cSCC for staging.

A recent study evaluating debulk analysis showed that 1.4% and 2% of tumors were upstaged according to the Brigham and Women's Hospital and American Joint Committee on Cancer-8 staging systems, respectively.[5] Our study found a larger percentage of upstaged lesions, potentially because more patients were transplant recipients (24% vs 14.7%), the lesions were larger (64.5% $\geq$ 2 cm vs 15.7%), and there is higher ultraviolet exposure in our location. While the utility of debulk analysis has been demonstrated and is considered standard in melanoma,[2,3] there are no uniform guidelines for evaluating the central portion of cSCC. In select suspected high-risk cases or lesions that intraoperatively prove to be high risk, permanent section pathology should be considered for appropriate staging. Given advances in immunotherapies, accurate staging may optimize patient outcomes.

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