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An insight into the protective role of biologics in COVID-19 infections: a single-centre case series

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There is an ongoing concern regarding patients on biological therapy and their increased susceptibility to severe COVID-19 infection. The British Association of Dermatologist's guidance on continued care of the clinically extremely vulnerable, last updated in November 2020, advised that those on immunosuppressive therapies (including biologics) have a 'sufficient to significantly increased risk of infection' and were therefore recommended to shield and are now considered for primary third booster vaccines in light of this risk. This advice is evidenced based on the poor outcome this cohort of patients experienced during the pandemic. However, there have been minimal studies performed to evaluate the risk patients on biologics have when compared with the wider population. The authors believe this is an important topic to address as it may provide a consensus into risk stratification for this cohort of patients. The clinical characteristics of 15 patients under dermatology care on biologics and COVID-19-positive (confirmed by polymerase chain reaction) were reviewed retrospectively between November 2020 and March 2021. A 20-item tool was used to collect quantitative data. This encompassed demographics, skin disease, biologic, hospitalization, intensive care admission, the severity of disease (as determined by oxygen therapy, imaging and symptoms), and the presence of long COVID. Patients included ranged in age from 37 to 75 years; 12 were white, one was Asian and one was South-East Asian, with one unknown. Patients were on a range of biologics including tralokinumab (n = 1), dupilumab (n = 1), ustekinumab (n = 3), adalimumab (n = 5), risankizumab (n = 2) and secukinumab (n = 3). The majority of patients included had multiple comorbidities (73%), of which 21% had a respiratory condition. Approximately a third of patients required hospitalization (33%) and oxygen (29%). However, none required intensive care or noninvasive ventilation, and the chest X-ray findings from all participants were clear, illustrating no scarring or evidence of long-COVID clinical changes. This study has shown that exposure to biologics did not appear to increase the susceptibility of patients to COVID-19. Although being a significant comorbid group, outcomes following infection with COVID-19 were good and did not seem to affect the clinical outcomes or mortality in this cohort. This suggests that biologics for dermatological conditions could be used continuously during the COVID-19 pandemic. However, larger multicentre case series assessing the treatment efficacy of biologics vs. nonbiological therapy in those with skin disease and COVID-19 infection is warranted.

BI25

Eruptive keratoacanthomas in association with leflunomide and adalimumab treatment for psoriatic arthritis: an insight into cancer prevention?

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Leflunomide is frequently used in the treatment of rheumatoid arthritis and psoriatic arthritis. We report a rare case of eruptive keratoacanthomas associated with leflunomide and discuss the relevance of the case to recent research on leflunomide as an anticancer therapy (Mao C, Liu X, Zhang Y *et al*. DHODH-mediated ferroptosis defence is a targetable vulnerability in cancer. *Nature* 2021; **593**: 586–90; Hosseini M, Dousset L, Michon P *et al*. UVB-induced DHODH upregulation, which is driven by STAT3, is a promising target for chemoprevention and combination therapy of photocarcinogenesis. *Oncogenesis* 2019; **8**: 52). A 76-year-old Irish woman presented with a 5-year history of a pruritic nodular eruption. The nodules were nontender and self-resolved after several weeks. The eruption started a few months after starting leflunomide for treatment of psoriatic arthritis. Adalimumab was added 2 years later. She had four siblings: one brother had colorectal cancer and one sister had breast cancer. There was no other past medical or family history. On examination there were multiple excoriated nodules on a background of > 100 atrophic scars and photodamage on the limbs and upper torso. Six nodules were subsequently excised and histologically diagnosed as keratoacanthomas or well-differentiated cutaneous squamous cell carcinoma. No mismatch repair deficiency was identified on immunohistochemistry. Leflunomide and adalimumab were changed to apremilast and no further lesions occurred at 9 months. There have been two reports of eruptive keratoacanthomas in association with leflunomide and no reports for adalimumab. In previous cases, both patients were female and keratoacanthomas occurred over a 2-year period. Leflunomide inhibits dihydroorotate dehydrogenase (DHODH), a key enzyme in the *de novo* pyrimidine synthesis pathway that is upregulated in several types of cancer. Initially, DHODH was thought to benefit cancer cells through maintaining a nucleotide pool for cell proliferation and repair of DNA damage (Hosseini *et al*.). More recently, DHODH has been shown to protect cells against ferroptosis, an iron-dependent form of regulated cell death (Mao *et al*.). Inhibition of DHODH *in vitro* and in ultraviolet B-irradiated mice prevents tumour formation (Mao *et al*.; Hosseini *et al*.). Irradiated leflunomide-treated mice instead develop hyperkeratotic skin lesions (Hosseini *et al*.). While our patient developed > 100 keratoacanthomas and some well-differentiated cSCCs, she did not develop moderately or poorly differentiated cSCCs. However, the rarity of the association suggests other contributing factors, which may include other enzymes involved in ferroptosis (Mao *et al*.) or a predisposing genetic mutation. In conclusion, our case provides a serendipitous insight into the effects of DHODH inhibition in human skin, and further research on leflunomide in skin cancer oncogenesis would be valuable.