

among patients. These data are in contrast to those of other series, which reported an increase in the percentage of non attendees.<sup>5</sup>

We consider that keeping our ED service open not only allowed diagnosis of acute conditions, but also allowed the incidental diagnosis of melanomas or other tumours. This would not have been possible with teleconsultation, as pointed out by other authors.<sup>4</sup>

There are some limitations to this study: it was a single-centre study, with data collected retrospectively and was with a previous time series. However, the data reveal changes in healthcare provision and in the usage patterns of healthcare resources as a result of the pandemic. It would be interesting to know why those patients required urgent attention, and if these trends will continue over time or return to pre-pandemic levels.

In conclusion, we found that ED consultations remain important during the pandemic period. The observed data are consistent with those reported for the first wave of the virus in other parts of the world.

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## COVID-19 vaccines do not trigger psoriasis flares in patients with psoriasis treated with apremilast

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Dear Editor,

Although COVID-19 vaccination is strongly recommended for patients with psoriasis (PsO) by several dermatological societies worldwide, only one recently published Italian case series has reported the safe and effective role of the vaccine in this patient subset. Notably, the vaccine information highlights that there are limited data about the vaccine in immunosuppressed patients and that vaccination should be performed in agreement with the vaccinator.<sup>1</sup> Furthermore, PsO itself is not considered an immunosuppressive status, but some antipsoriatic, effective and safe drugs are codified as immunosuppressants. Thus, patients with moderate to severe PsO undergoing targeted therapies [e.g. interleukin (IL)-17 inhibitor (i), IL-12/23i, IL-23i and tumour necrosis factor- $\alpha$ ], small molecule therapy (apremilast, dimethyl fumarate) and conventional therapies (methotrexate, ciclosporin) are considered immunosuppressed by the World Health Organization.<sup>2</sup> Among the systemic antipsoriatic treatments, only acitretin is not considered an immunosuppressant (Table 1).

Apremilast, a phosphodiesterase (PDE)-4 inhibitor, displays immunomodulatory effects on both keratinocytes and immune cells, decreasing cutaneous hyperplasia and mitigating the proinflammatory microenvironment. Notably, apremilast is orally delivered and well-tolerated in young patients, needlephobics and patients with other circumstances that represent a relative contraindication for biologics (e.g. neoplasia or HIV).<sup>2</sup> For some patients with PsO, the COVID-19 pandemic has affected adherence,<sup>3</sup> anti-vaccination opinions<sup>4</sup> and lifestyle,<sup>4</sup> complicating the monitoring of chronic immunosuppressive therapy. There are no data on interactions between apremilast and COVID-19 vaccines to guide physician daily practice during the ongoing pandemic. We report three patients with PsO under apremilast who also received COVID-19 vaccination.

Patient 1 was a 48-year-old man with PsO and psoriatic arthritis (PsA). Following nonresponse to ixekizumab or etanercept, the patient was commenced on apremilast, achieving stable remission, which was maintained for 8 months. He experienced flares of both his PsO and PsA during asymptomatic COVID-19, which resolved spontaneously 10 days after COVID-19 remission. Six months after this infection, he received both doses of the Pfizer mRNA BNT162b2 vaccine without experiencing any PsO flare.

Patient 2, a 76-year-old man with PsO, had been taking apremilast since 2017 with a stable residual Psoriasis Area Severity Index (PASI) of 3. After the first dose of the Astra-Zeneca-Oxford vaccine AZD1222 he experienced fever

**Table 1** The Anatomical Therapeutic Chemical Classification System for the main systemic antipsoriatic drugs published by the World Health Organization Collaborating Centre for Drug Statistics<sup>a</sup> Methodology.

Systemic drug	ATC five-levels code					IS
	I <sup>b</sup>	II <sup>c</sup>	III <sup>d</sup>	IV <sup>e</sup>	V <sup>f</sup>	
Conventional therapies						
Methotrexate	L	04	A	X	03	Yes
Ciclosporin	L	04	A	D	01	Yes
Acitretin	D	05	B	B	02	Not
Small molecules						
Apremilast	L	04	A	A	32	Yes
DMF	L	04	A	X	03	Yes
Biologics						
Etanercept <sup>g</sup>	L	04	A	B	01	Yes
Infliximab <sup>g</sup>	L	04	A	B	02	Yes
Certolizumab	L	04	A	B	05	Yes
Adalimumab <sup>g</sup>	L	04	A	B	04	Yes
Ustekinumab	L	04	A	C	05	Yes
Secukinumab	L	04	A	C	10	Yes
Ixekizumab	L	04	A	C	13	Yes
Brodalumab	L	04	A	C	12	Yes
Guselkumab	L	04	A	C	16	Yes
Tildrakizumab	L	04	A	C	17	Yes
Risankizumab	L	04	A	C	18	Yes

ATC, Anatomical Therapeutic Chemical Classification System; DMF, dimethyl fumarate; IS, immunosuppressant. <sup>a</sup>[https://www.whocc.no/atc\\_ddd\\_index/](https://www.whocc.no/atc_ddd_index/); <sup>b</sup>one letter that indicates the anatomical main group among the 14 codified; <sup>c</sup>two digits that indicate the therapeutic subgroup; <sup>d</sup>one letter that indicates the therapeutic/pharmacological subgroup; <sup>e</sup>one letter that indicates the chemical/therapeutic/pharmacological subgroup; <sup>f</sup>two digits that indicate the chemical substance; <sup>g</sup>includes its biosimilars.

(38.5 °C) and myalgia for 3 days, whereas the second dose was not complicated by any adverse effects (AEs). On both occasions he did not experience any PsO flare.

Patient 3 was a 36-year-old woman with plaque PsO (PASI 3) and concurrent pustular PsO (Palmoplantar Psoriasis Area and Severity Index 2.3), who had been stably treated with apremilast and narrowband UVB for 3 years. She received the Pfizer mRNA-BNT162b2 vaccine without any AEs or PsO flare.

All four patients developed IgG antibodies to the SARS-CoV-2 S1 receptor binding domain, suggesting that apremilast does not interfere with the acquisition of SARS-CoV-2 immunity. Furthermore, none of the COVID-19 vaccines, both mRNA-based and viral vector-based, did not trigger PsO or PsA flares in any of these three patients treated with apremilast. Interestingly, real-life data have also highlighted the potential protective effect against SARS-CoV-2 in this patient subset,<sup>5,6</sup> while at the same time warning about the possible apremilast-related gastrointestinal and taste AEs, which may be misinterpreted as suggestive of COVID-19.<sup>7-9</sup>

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### Intravenous immunoglobulins: an eye opener on the successful treatment of severe adult-onset paraprotein-associated xanthogranulomatosis

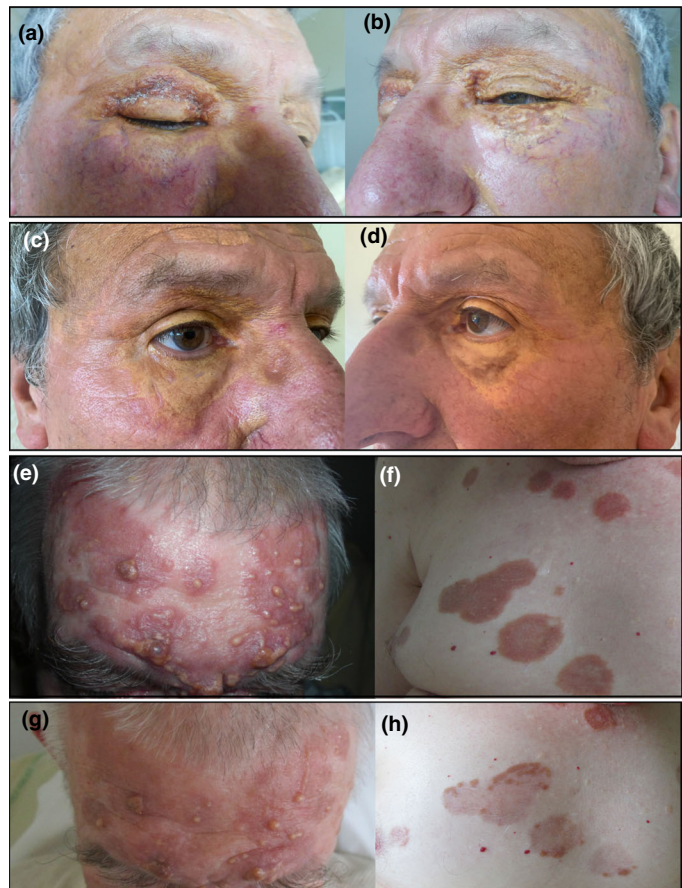
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Dear Editor,

Xanthogranulomatosis (XG) is a granulomatous dermatitis presenting as multiple xanthogranulomas. It is a common non-Langerhans histiocytosis that is mainly observed in children (juvenile XG) and usually regresses over time. By contrast, adult XG, which was first described in 1963, is characterized by persistent lesions, which can be severe, painful and sometimes disfiguring.<sup>1</sup> Adult XG is often associated with haematological disorders, including monoclonal gammopathies of

undetermined significance (MGUS).<sup>2,3</sup> To date, there are no guidelines for the treatment of XG. We report two cases of adult XG successfully treated with intravenous immunoglobulin (IVIG) therapy.

Patient 1 was a 64-year-old man, who presented with a 4-year history of progressively growing lesions over his eyelids, trunk and arms. Eleven years previously, he had been diagnosed with MGUS [IgG lambda peak 20.5 g/L (normal range 8–13.5 g/L; 3% plasma cells on bone marrow aspirate (normal range 2–3%)]. Skin biopsy was consistent with xanthogranuloma. The patient was initially treated with intralesional steroids (one injection of triamcinolone 40 mg/mL), three sessions of CO<sub>2</sub> laser and methotrexate 15 mg/week for 7 months with no improvement. The periorbital lesions continued to worsen, leading to ptosis (Fig. 1a,b). Treatment with IVIG 2 g/kg/month was then started, with a dramatic improvement in the periorbital plaques noted shortly after the first infusion (Fig. 1c,d), resulting in near-complete resolution. At the most recent follow-up (2 years after he first presented to us), a total of 12 cycles had been completed; the improvement was maintained and the M-spike level (the IgG peak) remained unchanged.



**Figure 1** (a–h) Clinical pictures of Patients 1 and 2 before and after intravenous immunoglobulin (IVIG) treatment. (a–d) Patient 1: (a) large infiltrated periorbital plaques leading to complete ptosis of the right eyelid; (b) large infiltrated periorbital plaques leading to partial ptosis of the left eyelid; (c,d) dramatic improvement after 10 cycles of IVIG. (e–h) Patient 2: (e) large infiltrated plaques and firm yellowish nodules over the forehead; (f) infiltrated plaques over the torso; (g,h) improvement after nine cycles of IVIG, with the lesions becoming progressively less infiltrated.