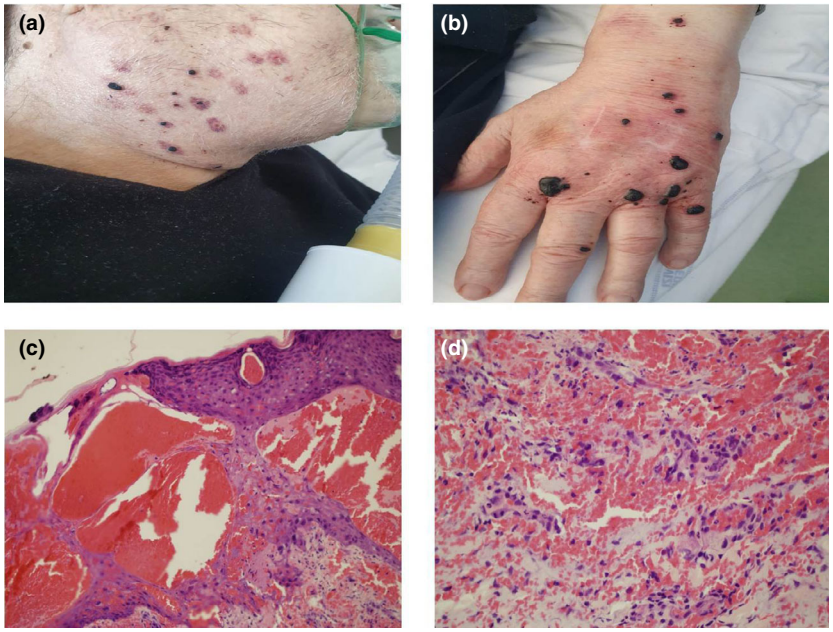

Figure 1 Clinical images of COVID-19-associated cutaneous eruption (a, b). Histopathological images of epidermis and dermis. Haematoxylin and eosin staining, original magnification: 20×, 40× (c, d).

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Conflicts of interest

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Systemic or biologic treatment in psoriasis patients does not increase the risk of a severe form of COVID-19

Dear Editor

Some systemic and biologic psoriasis treatments [SBT] have been associated with an increased risk of infection.[1] To date, more and more data regarding the risk of COVID-19 infection in patients receiving SBT become available.[2-5]

To enrich these data, we evaluated the frequency of severe COVID-19 infections, defined as hospitalization or death, in psoriasis patients receiving SBT, especially during the 4 months following SBT initiation.

From 27 April to 7 May 2020, we conducted a national, multicentre, cross-sectional study during consultations or teleconsultations, including adult psoriasis patients receiving SBT.

The following elements were collected: gender, age, current psoriasis treatment, treatment period (initiation [up to 4 months] or maintenance [from 5th month]), treatment continued or stopped during the pandemic. Moreover, we collected data about comorbidities such as obesity, hypertension and diabetes putting patients at risk of a severe form of COVID-19 infection, and information about a clinically confirmed diagnosis of COVID-19 defined as acute febrile respiratory infection, or sudden onset of headache, myalgia, ageusia, anosmia or asthenia,[6] as well as COVID-19 confirmation by PCR testing and hospitalization.

Overall, data from 1418 patients were included. Patient characteristics are detailed in Table 1. Of the included patients, 300 were receiving methotrexate, 26 cyclosporine, 4 acitretin, 48 apremilast, 25 etanercept, 165 adalimumab, 40 infliximab, 8 certolizumab pegol, 240 ustekinumab, 206 secukinumab, 112 ixekizumab, 38 brodalumab, 146 guselkumab, 25 risankizumab and 35 combination of methotrexate and biologic. In total, 22.4% of patients on systemic therapy and 13.8% on biologics discontinued treatment during the pandemic.

We reported five patients with COVID-19 infection requiring hospitalization: a 27-year-old obese woman with Crohn's disease treated with adalimumab, a 36-year-old man treated with guselkumab, a 53-year-old man treated with methotrexate, and two patients required intensive care: a 71-year-old obese woman treated with methotrexate and etanercept, a 34-year-old obese man treated with ustekinumab. No deaths were reported. In all, 54 patients presented with a possible COVID-19 infection; confirmation by PCR testing was performed for 12 patients. The frequency of cases according to treatment and treatment period is specified in Table 2.

In our study, 0.35% of patients had a severe form of COVID-19 requiring hospitalization, 60% of whom (all in intensive care units) presented with other risk factors for severe infection. Two patients were hospitalized, due to their SBT, considered at the beginning of the pandemic as a risk factor for a severe form of COVID-19 infection.

Our data are consistent with those collected and analysed in Italy: Damiani *et al.* reported 5 hospitalizations out of 1193 patients treated by biologic or small molecules for their psoriasis, and no death was reported.[6] Gisondi *et al.* reported in Northern Italy 4 hospitalizations out of 5206 patients receiving biologic treatment for psoriasis, again no death was reported. There was no over-risk of hospitalization in intensive care and death reported for patients receiving biological psoriasis treatment when compared to the general population.[2] Moreover, biologic treatment using immunosuppressive drugs such as guselkumab, ustekinumab,

Table 1 Patient characteristics

	Overall population		Treatment initiation period		Maintenance treatment period	
	n	%	*n*	%	*n*	%
	1418	100	230	16.22	1188	83.78
Sex						
Men	797	56.29	131	56.96	666	56.16
Women	619	43.71	99	43.04	520	43.84
Missing data	2		0		2	
Treatment						
Systemic	330	23.27	62	26.84	268	40.18
Biologic	1005	70.87	156	67.53	849	127.29
Anti-TNF	238	16.78	14	6.06	224	18.86
Anti-interleukin	767	54.09	142	61.47	625	52.61
Apremilast	48	3.39	10	4.33	38	3.20
Combination of methotrexate and biologic	35	2.47	2	0.87	33	2.78
Risk factor for severe COVID-19 infection						
Diabetes	111	7.83	12	5.15	99	8.32
Obesity (BMI> 30)	245	17.28	27	5.15	218	18.32
HTA	232	16.36	31	13.30	201	16.89
None	920	64.88	163	69.96	757	63.61

Treatment initiation period defined as the 4 months following treatment initiation. Maintenance treatment period defined as starting the 5th month of treatment. Systemic treatment: acitretin, methotrexate, cyclosporine. Anti-TNF: etanercept, adalimumab, infliximab, certolizumab pegol. Anti-interleukin: ustekinumab, secukinumab, ixekizumab, brodalumab, guselkumab, risankizumab.

Table 2 Frequency of COVID-19 infection cases according to treatment and treatment period

	Overall population		Treatment initiation period		Maintenance treatment period	
	n	%	*n*	%	*n*	%
Overall population						
Probable case	54	3.81	6	2.58	48	4.04
Case confirmed by PCR	12	0.85	1	0.43	11	0.93
Case confirmed by PCR and hospitalized	5	0.35	1	0.43	4	0.34
Systemic treatments						
Probable case	17	5.15	2	3.17	15	5.60
Case confirmed by PCR	3	0.91	0	0.00	3	1.12
Case confirmed by PCR and hospitalized	1	0.30	0	0.00	1	0.37
Biologics						
Probable case	33	3.28	3	1.92	30	3.53
Case confirmed by PCR	8	0.80	1	0.64	7	0.82
Case confirmed by PCR and hospitalized	3	0.30	1	0.64	2	0.24
Apremilast						
Probable case	3	6.25	1	10.00	2	5.26
Case confirmed by PCR	0	0.00	0	0.00	0	0.00
Case confirmed by PCR and hospitalized	0	0.00	0	0.00	0	0.00
Combination of methotrexate and biologics						
Probable case	1	2.86	0	0.00	1	3.03
Case confirmed by PCR	1	2.86	0	0.00	1	3.03
Case confirmed by PCR and hospitalized	1	2.86	0	0.00	1	3.03

Probable case defined as acute febrile respiratory infection, or sudden onset of headache, myalgia, ageusia, anosmia or asthenia. Treatment initiation period defined as 4 months following treatment initiation. Maintenance treatment period defined as starting the 5th month of treatment. PCR: polymerase chain reaction.

adalimumab, secukinumab, brodalumab or ixekizumab may even protect against the onset and evolution of COVID-19 infection.[3,4,7]

[Correction added on 28 August 2020, after first online publication: On paragraph 8, the word 'brodalumab' has been added in this version.]

We did not observe a significant difference in the number severe cases of COVID-19, according to whether the patient was in the treatment initiation period (1 out of 230 patients) or in the maintenance period (4 out of 1188 patients), Fisher test $P = 0.58$, OR = 1.29 [95%CI 0.03–13.4].

The absence of a control group and no PCR or serologic confirmations of all probable cases were limitations of this study.

In conclusion, our study provides first data showing that there is no increased incidence of severe COVID-19 in psoriasis patients receiving SBT in the treatment initiation period compared to those in the maintenance period. Results may allow physicians to initiate, on a case-by-case basis, SBT in patients with severe psoriasis in the context of COVID-19 pandemic.

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Catastrophic acute bilateral lower limbs necrosis associated with COVID-19 as a likely consequence of both vasculitis and coagulopathy

Case report

A-83-year-old man was admitted on the 3 of April 2020 for respiratory distress. He had presented with fever the 20th of March. On the 2nd of April, he had an acute pain of both legs associated with discolouration. He was admitted to the emergency room on the following day. His temperature was 38°C, and he was dyspnoeic despite oxygen. He had bilateral and symmetrical well limited black skin on both legs (Fig. 1).

The patient had multiple comorbidities including obesity, type 2 diabetis mellitus, hypertension, mesenteric ischaemia in 2007, distal arteriopathy and ischaemic cardiopathy treated by coronary bypass in 2015. He had the following treatment: acetylsalicylic acid, fluindione, ramipril, bisoprolol, furosemide and prednisolone 7.5 mg per day (for pseudopolyarthritides rhizomelic).

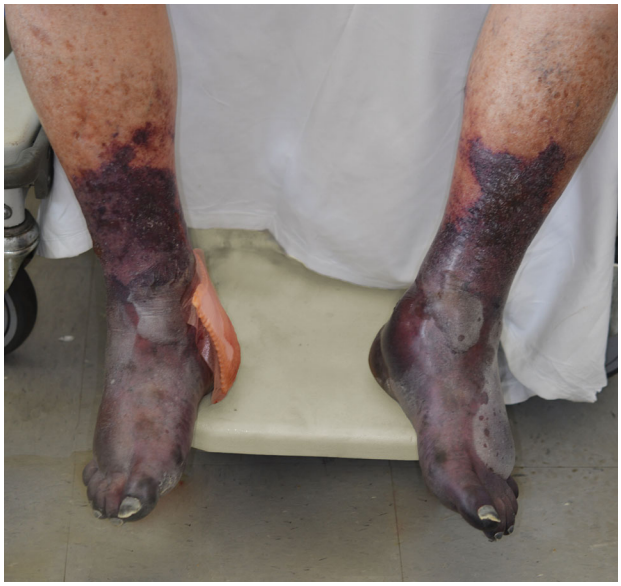

Figure 1 Acute bilateral lower limb necrosis.

Laboratory tests showed a C-reactive protein concentration of 246 mg/L (normal range, <5 mg/L). Complete blood count showed white blood cell count 19 × 10^9/L (normal range, 4–12 × 10^9/L) and neutrophils 16 × 10^9/L (1.5–8.5 × 10^9/L), and a lymphopenia 0.92 × 10^9/L (1–4 × 10^9/L). D-dimer was 7650 ng/L (normal range < 500 ng/L), and platelet count down to 148 × 10^9/L (normal range 150–500 × 10^3/L). Nasal tests for influenza A and B viruses were negative. Bacterial blood cultures were negative. The computed tomography scan presented multiple ground-glass opacities with 80% of the lung affected. There was no sign of pulmonary embolism. The patient was diagnosed with COVID-19 on the basis of positive RT-PCR analysis of sputum.

During the hospitalization, we observed a coagulation degradation with disseminated intravascular coagulation (DIC) with decrease of platelet 100 × 10^9 and a decrease of fibrinogen 0.52 g/L normal range 2–3.93 g/L and DDIMERE 6900 ng/L was also increased normal <500 ng/L. There was no antiphospholipid syndrome (lupus anticoagulant, anticardiolipin and anti-beta2-glycoprotein1 antibodies were negative). His condition worsened and the patient died.

Our patient had a catastrophic acute bilateral legs and foot necrosis during the course of COVID-19 infection. Zhang et al.[1] reported 7 critical COVID-19 patients with acro-ischaemia in a single centre in Wuhan. All had acro-ischaemia presentations including finger/toe cyanosis, skin bulla and dry gangrene. D-dimer, fibrinogen and fibrinogen degradation product were significantly elevated in most patients, and 4 patients were diagnosed with definite DIC. Zang et al.[2] proposed antiphospholipid antibodies as the

