

## A review of nail findings associated with COVID-19 infection

According to recent data, up to 20% of patients with COVID-19 have cutaneous manifestations. Nails can also develop abnormalities during and after infection. In this article, we review the nail findings observed in patients with COVID-19.

We reviewed the PubMed and Embase databases to identify all articles up to May 2021 that have described nail findings in association with COVID-19.

A total of 70 studies were reviewed including 61 studies on chilblain-like lesions, which are one of the most widely identified cutaneous findings associated with the COVID-19 pandemic.

Nine studies described specific nail findings (Table 1). Three of these findings [Beau lines,<sup>1</sup> transverse leukonychia,<sup>1,2</sup> and onychomadesis (Figure 1a)] are commonly seen with other systemic disease, including viral infection, and are likely the consequence of high fever and/or severe illness. One finding, paronychia, was seen in association with chilblain-like lesions,<sup>3</sup> and three nail findings (the red half-moon sign<sup>4,5</sup> (Figure 1d), the transverse orange discoloration<sup>6</sup> and the diffuse red-white nail bed discoloration<sup>7</sup>) are novel and potentially related to the microvascular injury due to COVID-19. Of note, an orange-brownish discoloration of the nail in a transverse pattern, the most similar finding to date, has been described in patients with Kawasaki disease, which shares a similar inflammatory response component to COVID-19.

COVID-19's effects on the nail blood vessels were documented by Navarro *et al.* in 12 pediatric patients with COVID-19-related chilblains, described in Table 1.<sup>8</sup> At dermoscopy of the nail fold and hyponychium, they found a red background with globules, indicative of vascular damage.

We also documented dilated and tortuous capillaries at dermoscopy in a patient with transverse leukonychia after COVID-19 infection (Figure 1c).

The presence of microvascular abnormalities was confirmed by a capillaroscopy study of the nails of 82 patients, enrolled during hospitalization for COVID-19 (28), or shortly after discharge.<sup>9</sup> Using nail video capillaroscopy (NVC), the authors observed microvascular abnormalities in all patients, which are described in detail in Table 1. Findings varied between acutely ill and discharged patients, providing visual evidence of a vascular pathogenic component to COVID-19 infection.

Chilblain-like lesions are a commonly reported manifestation involving the digits. They are also known as 'COVID toes,' even

though they can also affect fingers, and they present as erythematous, purpuric, papules and macules on the dorsal phalanges, nail folds and digital pulps (Figure 1b). Chilblain-like lesions are predominantly found in children and adolescents. Nail findings have been reported in association with chilblain-like lesions. In a prospective study conducted by Docampo-Simon *et al.*, two patients with chilblain-like lesions also presented with paronychia.<sup>3</sup> A causative link between COVID-19 and chilblains has not been firmly established despite an increase in the prevalence of these lesions during the pandemic.

Studies suggest that this well-known manifestation of COVID-19 infection may be the consequence of an exacerbated INF- $\alpha$  response. Very few patients presenting with chilblain-like lesions have other symptoms of COVID-19 infection, and only a few test positive for the infection when presenting with the lesions. It has been suggested that the overproduction of INF- $\alpha$ , which is produced at declining rates with age, may lead to rapid control of viral infection, thereby protecting younger patients from more severe disease and resulting in lower rates of positive nasopharyngeal swabs. The study by Hubiche *et al.*<sup>10</sup> also demonstrates that an increase in INF- $\alpha$  in patients with chilblain-like lesions could help young patients clear the virus rapidly. Other nail findings described in patients with chilblains include periungual erythema, peeling around the nail, nail fold telangiectasia and erythematous macules around the distal nail folds.

Our review of the literature did not reveal an association of nail disease with poor outcome for patients.

### Acknowledgements

The patients in this manuscript have given written informed consent to the publication of their case details.

### Conflicts of interest

Dr. Tosti acts as a consultant for DS Laboratories, Monat Global, Almirall, Tirthy Madison, Eli Lilly, Leo Pharmaceuticals, Bristol Myers Squibb and P&G. Dr. Morrison and Edward Haderler have nothing to disclose.

### Funding sources

None.

E. Haderler,\*  B.W. Morrison, A. Tosti

Dr. Phillip Frost Department of Dermatology and Cutaneous Surgery, University of Miami Miller School of Medicine, Miami, FL, USA

\*Correspondence: E. Haderler. E-mail: ehaderler@med.miami.edu

This paper has not been previously published or posted and is not under consideration elsewhere.

**Table 1** Nail findings described during the COVID-19 pandemic, including studies documenting nail findings associated with COVID-19 infection and studies describing nail involvement in patients with chilblain-like lesions

Nail finding Study title	Author, month, year, country	Patient characteristics	COVID-19 disease course/associated symptoms and treatment	Onset of nail symptoms and resolution	Detailed description of cutaneous and nail findings	Time to nail symptom resolution	Additional Comments
Studies documenting nail findings associated with COVID-19							
Beau lines and leukonychia	Ide, November, 2020, Japan	68 years old, male	18-day hospital stay, received hydroxychloroquine 400 mg/day for 7 days, methylprednisolone 0.5 mg/kg/day for 5 days.	1.5 months after diagnosis of COVID-19	White horizontal nail striae and sunken nails clinically defined as leukonychia and Beau lines	Unknown	
<i>Beau's Lines and Leukonychia in a COVID-19 Patient</i> Case report							
Beau lines	Alobaida, September, 2020, Canada*	45 years old, male	Presented with diarrhea, fever, shortness of breath. Symptoms lasted 10 days and no hospital admission was required.	3.5 months after diagnosis of COVID-19	Horizontal grooves over fingernails and toenails, most noticeably over his great toenails bilaterally, with a horizontal groove 5 mm from the proximal nailfold, clinically defined as Beau lines	Unknown	Toenail growth (approximately 1.62 mm per month) used to link distance of Beau lines from proximal nailfold to time of COVID-19 infection
<i>Beau lines associated with COVID-19</i> Case report							
Transverse leukonychia	Fernandez-Nieto, November, 2020, Spain	47 years old, male	Admitted to hospital with mild COVID-19 bilateral pneumonia, treated with lopinavir/ritonavir 100mg/400mg BID for 10 days with good response and no need for oxygen. Labs notable for mild lymphopenia (830 cells/ $\mu$ L, range 1000–4500 cells/ $\mu$ L) and slight elevation of D-dimer (1330 ng/mL, range 0–500 ng/mL).	5 days after diagnosis of COVID-19	Transverse, non-blanchable white lines on all fingernails, which progressively migrated with the growth of the nail and persisted at time of visit, clinically defined as Mees' lines, or transverse leukonychia.	Unknown	
<i>Transverse leukonychia (Mees' lines) nail alterations in a COVID-19 patient</i> Case report							
Onychomadesis	Senturk, November, 2020, Turkey*	47 years old, female	Patient was hospitalized and received hydroxychloroquine, azithromycin, oseltamivir, and ceftriaxone.	3 months after hospitalization for COVID-19	Finger and toenails were detached, and new healthy nails were growing from the proximal matrix, clinically defined as onychomadesis	Unknown	Patient had pre-existing hypertension and diabetes mellitus, continued these medications during hospital course
<i>Onychomadesis following COVID-19 infection: Is there a relationship?</i> Case report							

**Table 1** Continued

Nail finding Study title	Author, month, year, country	Patient characteristics	COVID-19 disease course/associated symptoms and treatment	Onset of nail symptoms and resolution	Detailed description of cutaneous and nail findings	Time to nail symptom resolution	Additional Comments
Orange discoloration in transverse pattern <i>Transverse orange nail lesions following SARS-CoV-2 infection</i> Case report	Tammaro, December, 2020, Italy	89 years old, female	Patient presented with cough and asthenia. A nasal PCR was negative for COVID-19. 16 weeks later the patient presented with orange nail discolorations. A blood test was positive for IgG against SARS-CoV-2 and ferropenic anemia. She also developed sarcopenia at this time	16 weeks after initial symptoms	Orange discolorations at the end of nail beds, following the shape of the lunula	Unchanged one month following the discovery of the nail discolorations	
Convex red half-moon <i>The red half-moon nail sign: a novel manifestation of coronavirus infection</i> Case report	Neri, November, 2020, Italy	60 years old, female	Patient presented with history of fever (>38 degrees Celsius) and cough. 7 days after these symptoms the patient had dyspnea associated with anosmia and ageusia. The patient had a normal chest x-ray, but chest CT showed bilateral ground-glass opacities, leading to a diagnosis of bilateral interstitial pneumonia. Diagnosis was confirmed by nasal PCR swab. Patient was hospitalized, therapy included hydroxychloroquine, lopinavir/ritonavir, ceftriaxone, heparin, and oxygen. Patient experienced complete remission of respiratory symptoms 10 days after treatment.	2 weeks after initial onset of symptoms of COVID-19	Distally convex half-moon shaped red band surrounding the distal margin of the lunula appeared on all nails, denied associated symptoms and no other skin manifestations. One month follow up, bands still present and wider.	Ongoing at follow up one month after initial presentation	
Convex red half-moon <i>COVID-19 and nail manifestation: be on the lookout for the red half-moon nail sign</i> Case report	Méndez-Flores, August, 2020, Mexico	37 years old, female	Patient presented with anosmia, dry cough, persistent fever, relatively normal O2 saturation (>92%), positive nasal swab PCR confirmed SARS-CoV-2 infection. Managed at home, no oxygen therapy required.	2 days after initial onset of symptoms of COVID-19	Red-violet bands in the nail bed, above the nail lunula	1 week after initial presentation	

Table 1 Continued

Nail finding Study title	Author, month, year, country	Patient characteristics	COVID-19 disease course/associated symptoms and treatment	Onset of nail symptoms and resolution	Detailed description of cutaneous and nail findings	Time to nail symptom resolution	Additional Comments
Red-white nailbed discoloration Heterogenous red-white discoloration of the nail bed and distal onycholysis in a patient with COVID-19	Demir, May, 2021, Turkey	23 years old, male	Patient presented with history of fever, sore throat and joint pain, four months prior to onset of nail discoloration.	4 months after initial onset of symptoms of COVID-19	Heterogenous red-white discoloration in all nails; two round onycholytic areas surrounded by erythema in the distal part of the second nail on the left hand	Unknown	
<b>Case report</b> Nailfold video capillaroscopy (NVC) findings in patients with coronavirus disease 2019 Nailfold capillaroscopy findings in patients with coronavirus 2019: Broadening the spectrum of COVID-19 microvascular involvement Prospective observational study	Natalello, January, 2021, Italy	82 patients (mean age 58.8 ± 13.2 years, 68.3% male)	Patients were affected by COVID-19 pneumonia, diagnosed by laboratory test (nasopharyngeal PCR) and suggestive chest imaging. (n, %): (11, 13.4%) smoked, (25, 30.5%) had hypertension, (9, 11%) had diabetes, (4, 4.9%) had rheumatic disease, (50, 61%) had a BMI > 25kg/m <sup>2</sup> , (8, 9.8%) had acral symptoms, (47, 57.3%) required oxygen therapy, (5, 6.1%) were admitted to the ICU, (21, 25.6%) received Anti-IL6R therapy, (39, 47.5%) received enoxaparin therapy, (8, 9.8%) had PTE or DVT. 28 patients enrolled during hospitalization, 54 enrolled after discharge.	Duration from onset of symptoms was 37.3 ± 23.1 days	Abnormalities classifiable as non-specific patterns in 53 patients (64.6%). Findings: Precapillary edema (80.5%), enlarged capillaries (61%), sludge flow (53.7%), meandering capillaries and reduced capillary density (50%). Acute COVID-19 patients, compared to recovered patients, showed higher prevalence of hemosiderin deposits as a result of micro-hemorrhages (p = .027), micro-thrombosis (p < 0.016), sludge flow (p = 0.001) and precapillary edema (p < 0.001). Recovered patients showed higher prevalence of enlarged capillaries (p < 0.001), loss of capillaries (p = 0.002), meandering capillaries (p < 0.001), and empty dermal papillae.	Unknown	
Studies describing nail involvement with chilblains-like manifestations of COVID-19 Subungual erythema Two cases of COVID-19 presenting with a clinical picture resembling chilblains: first report from the Middle East Case series	Alarmithan, May, 2020, Kuwait*	27-year-old female and 35-year-old female	PCR positive in both patients, patients had reported recent travel to UK. No additional information provided on disease course or treatment	Unknown	Red-purple papules on the dorsal aspect of the fingers on both hands; patient 2 had diffuse erythema in the subungual area of her right thumb	Unknown	

**Table 1** Continued

Nail finding Study title	Author, month, year, country	Patient characteristics	COVID-19 disease course/associated symptoms and treatment	Onset of nail symptoms and resolution	Detailed description of cutaneous and nail findings	Time to nail symptom resolution	Additional Comments
Periungual erythema <i>Chilblains in children in the setting of COVID-19 pandemic Retrospective case series</i>	Andina, May, 2020, Spain*	22 patients (13 male, 9 female); median age: 12 (range: 6–17)	Respiratory symptoms (cough or rhinorrhea) (9, 41%), GI symptoms (abdominal pain or diarrhea) (2, 9%), shortness of breath 0, fever 0. Household contact with proba- ble case of COVID-19 12 (55%), confirmed case of COVID-19 1 (4%). PCR positive in 1, negative in 18.	Duration of lesions before consultation ranged from 1 to 28 days (median 7 days).	Feet affected in all 22 cases: acrally located, erythematous- violaceous or purpuric macules on the toes and lateral aspects of the feet and heels. The <b>tips and periungual or distal subungual areas of the toes</b> were commonly involved. <b>3 patients showed similar lesions on fingers, located predominantly on periungual areas.</b>	Lesions showed marked improvement or almost complete resolution 3–5 weeks after onset.	
					Dermoscopy recorded in 10 patients: signs observed included erythema, dilated capillaries, ischemic areas, purpuric dots, and hyperpigmentation. Pruritus (9, 41%), and mild pain (7, 32%) present in some cases. Skin biopsy obtained in 6 patients, all showed similar results: superfi- cial and deep angiocentric and eccentric lymphocytic infiltrate, papillary dermal edema, vacuolar degeneration of the basal layer and lymphocytic exocytosis to the epi- dermis and acrosyria. Features of lymphocytic vasculopathy seen in all cases.		

Table 1 Continued

Nail finding Study title	Author, month, year, country	Patient characteristics	COVID-19 disease course/associated symptoms and treatment	Onset of nail symptoms and resolution	Detailed description of cutaneous and nail findings	Time to nail symptom resolution	Additional Comments
Erythematous macules around the distal nailfolds <i>Clustered cases of acral perniois: Clini- cal features, histopathology, and relationship to COVID-19 Case series</i>	Cordoro, May, 2020, United States*	6 patients (age range: 12–17 years; 5 male, 1 female)	2 siblings from one family reported rhinorrhea, congestion, sore throat, and subjective fevers 1 week prior to onset of skin lesions; none of the patients had cough, shortness of breath, or changes in smell or taste. All 6 patients had contact with adults who had mild, transient upper respiratory infection symptoms 1–2 weeks prior to the onset of skin lesions. None had known contact with con- firmed COVID-19 cases.	1 week after presentation of other COVID-19 systemic symptoms and or contact with adults who had mild upper respiratory infection symptoms	Nearly all described lesions as itchy and few reported tenderness in context of swelling. Red violaceous macules and dusky, purpuric plaques scattered on the mid and distal aspects of toes. More severely affected digits were edematous with overlying superficial bullae and focal hemorrhagic crust. None of the digits appeared ischemic or necrotic. Several patients had scattered petechial and purpuric macules on the heels, soles, and distal aspect of the dorsal feet and a predominant distribution along the lateral foot, <b>a few had subtle erythematous macules around the distal nailfolds</b> . Half had livedo reticularis involving the flexor surfaces of the forearms, dorsal hands, and dorsal feet. 2 biopsies: superficial and deep lymphocytic infiltrate that also abuts junctional zone, where vac- uolar change and purpura noted. Hemorrhagic parakeratosis found in stratum corneum. Dermal infil- trate was tightly perivascular and also perieccrine and intramural lymphocytes ("lymphocytic vasculi- tis") present in thin muscular walls of small vessels. No evidence of thrombosis in vessels. Immunoflu- orescence negative for immunore- actant deposition in all cases	Unknown	All PCR negative. COVID-19 IgM- and IgG negative.

Table 1 Continued

Nail finding Study title	Author, month, year, country	Patient characteristics	COVID-19 disease course/associated symptoms and treatment	Onset of nail symptoms and resolution	Detailed description of cutaneous and nail findings	Time to nail symptom resolution	Additional Comments
Paronychia <i>Are chilblain-like acral lesions really indicative of COVID- 19? A prospective study and literature review Prospective study</i>	Docampo-Simon, September, 2020, Spain	58 patients (median age: 14, range 3 months–85 years), male 29 (50%), female 29 (50%).	Experienced COVID symptoms: Yes (11, 21.2%), No 41 (78.8%). Exposure or contact with con- firmed case 12 (21.8%), sus- pected case 7 (12.1%), none 36 (65.5%). PCR positive in 1 (1.7%)	Time from development of lesions to PCR test: median 12 days, range: 1–28 days; time from COVID- 19 symptoms to development of lesions (n = 11), median 7 days (0–42 days)	Hands (9, 15.5%), feet (36, 62.1%), hands and feet (13, 22.4%). Symptoms: pain (17, 32.1%), pruritus (20, 37.7%), pain and pruritus (5, 8.6%), asymptomatic (11, 20.8%). Morphology: chilblain-like (42, 72.4%), purpuric (3, 5.2%), macu- lopapular (3, 5.2%), vesiculobul- lous (3, 5.2%), eczematous (3, 5.3%), <b>paronychia (2, 3.4%)</b> , ulcer (1, 1.7%), desquamation (1, 1.7%).	Unknown	
Periungual erythema <i>Histological findings in chilblain lupus-like COVID lesions: in search of an answer to understand their aetiology Case report</i>	Rodriguez-Villa Lario, October 2020, Spain*	17-year-old male	Caregiver to patient convalescing from COVID pneumonia	2 days of evolution	<b>Periungual erythema in second and third finger toe</b> ; 2 days of evolution Punch biopsy showed marked hydropic degeneration of the basal layer, isolates of necrotic ker- atinocyte. In papillary and reticular dermis, a moderate lymphocyte infiltration around the vessels as sleeves. The endothelium was conspicuously predominant without visualizing fibrinoid necrosis. Dense pericyclic infiltration. Posi- tive CD123 around vessels and sweat glands.	Unknown	Blood analysis revealed elevation of IgA. PCR negative. Serologies showed positive IgG, negative IgM.



Table 1 Continued

Nail finding Study title	Author, month, year, country	Patient characteristics	COVID-19 disease course/associated symptoms and treatment	Onset of nail symptoms and resolution	Detailed description of cutaneous and nail findings	Time to nail symptom resolution	Additional Comments
Periungual erythema and onychomadesis <i>Are SARS-CoV-2 IgA antibodies in paediatric patients with chilblain-like lesions indicative of COVID- 19 asymptomatic or paucisymptomatic infection?</i> <i>Prospective study</i>	Diociaiuti, January, 2021, Italy*	30 patients (all adolescents)	17 patients (group A), belonged to previous published series (2 lost to follow up), underwent second serology testing for SARS-CoV-2. Group B consisted of 13 new patients who underwent PCR and serology.	Fever, headache, sore throat, 1 month before (1 patient); fever, 2 months before (1 patient); sore throat, fever, diarrhea, 1.5 months before (1 patient); fever cough, 2 months before (1 patient); flu-like symptoms, 1 month before (2 patients); asthenia, headache, 1 month before (1 patient); asymptomatic with positive PCR, 1 month before (1 patient); negative (20 patients)	Group B: 3 patients reported flu- like symptoms 3–4 weeks before skin lesion, 1 patient developed chilblain after proving positive to SARS-CoV-2; other patients presented cutaneous manifestations 2–8 weeks before screening visit. All patients presented with swel- ling, erythematous-violaceous-pur- puric macules, pustules and crusts on the toes, in some cases the heels, lateral foot aspect and soles Group A: <b>4 patients had residual periungual toe erythema</b> , 4 pre- sented with <b>toenail onychomade- sis at follow-up visit (5–7 weeks after first consultation)</b> Serology specific for S1-specific IgA and IgG in 30 patients showed 16 positive (53.3%), IgG detectable in 5 (16.6%).	Unknown	
Peeling around the nails <i>What are COVID toes? A case study</i> <i>Case report</i>	Beuscher, December, 2020, United States* female	45-year-old female	March 12 2020: Patient presented with diarrhea, dry cough, sore throat, eye irritation, swollen lymph nodes, abdominal pain, intermittent hypoxia as low as 84, chest pain during deep inhalation, altered sense of smell	7 days after altered sensations (neuropathic-type symptoms) in her feet	April 19: Presented with hot and itchy and tingling toes and <b>peeling around the nails.</b>	Symptoms ongoing after 21 days	COVID test negative 21 days after symptom onset
Nail fold telangiectasia <i>COVID-19 associ- ated chilblain-like lesions in an asymp- tomatic doctor</i> <i>Case report</i>	Hadjieconomou, July 2020, United Kingdom*	Woman, no age provided	No other symptoms described.	Cutaneous symptoms started 2 days before COVID-19 diagnosed in her partner.	2-week history of burning, itching of her fingers and toes, with erythematous and purple papules. Erosion present on her fingers, and <b>nail fold telangiectasia</b> was seen.	Unknown	



**Table 1** *Continued*

<b>Nail finding Study title</b>	<b>Author, month, year, country</b>	<b>Patient characteristics</b>	<b>COVID-19 disease course/associated symptoms and treatment</b>	<b>Onset of nail symptoms and resolution</b>	<b>Detailed description of cutaneous and nail findings</b>	<b>Time to nail symptom resolution</b>	<b>Additional Comments</b>
<p>Dermoscopy features of nails in patients with chilblains</p> <p><i>Dermoscopy features of COVID-19 related chilblains in children and adolescents</i></p> <p><i>Prospective study</i></p>	<p>Navarro, December, 2020, Spain</p>	<p>12 patients (children and adolescents)</p>	<p>No other symptoms described.</p>	<p>Unknown</p>	<p>Background area present in all cases; predominant color was red in 18 pictures, brown in 11, purple in 10, grey in 2; most pictures (31) contained areas of other colors within the areas whereas in 10 (24.4%) there was only one homogenous color present; globules seen in 38 (92.7%) and prominent in 32, mild in 6; reticule observed in 12 images (29.3%); other features found were splinter hemorrhages in nails (3 image), dilated capillaries in nail folds with loss of polarity (2 images) and subcorneal hemorrhagic dots (1 image).</p>	<p>Unknown</p>	<p>41 dermoscopy pictures obtained from 12 patients. Three main dermoscopic features described: a background area, globules, and reticule. Background area is the predominant background color in the lesion (ranging from red, purple, brown to grey); globules are round oval structures of red to purple color; the network reticule is a mesh of grey-brown interconnected lines usually located peripherally with in the background macule.</p>

\*Not included in the references as only 10 references are allowed as per the letter format.



**Figure 1** (a) Onychomadesis involving all toenails. This picture was taken 4 months after the patient was hospitalized for 30 days, including 10 days in ICU, because of severe COVID-19 infection. (b) Chilblain-like lesions, located distally on the fingers around the nail folds (Courtesy of Dr. Maria Pia De Padova, Bologna, Italy). (c) Nail plate dermoscopy showing leukonychia and dilated and tortuous capillaries. This picture was taken 3 months after patient had a mild COVID-19 infection. FotoFinder<sup>®</sup> 50X. (d) Red discoloration of the nail arranged in a convex half-moon shape, located distally on the lunula. In this patient, this was associated with orange discoloration of the distal nail plate. All fingernails were affected. This picture was taken 2 months after the patient had COVID-19 infection not requiring hospitalization.

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DOI: 10.1111/jdv.17448

## Low incidence rate of respiratory and viral infections over 5 years of treatment with tildrakizumab in patients with moderate-to-severe psoriasis: pooled analysis from reSURFACE 1 and reSURFACE 2 phase 3 trials

## Editor

In the context of the current coronavirus disease 2019 (COVID-19) pandemic, there is no direct evidence to support any preferred biologic therapy for psoriasis. However, known safety profile of different classes of biologic therapies as well as individual risk factors for infections must be considered.<sup>1</sup> Here, we

report incidence rates of respiratory or viral infections through 5 years among patients with moderate-to-severe plaque psoriasis who were treated with the interleukin (IL)-23p19 inhibitor tildrakizumab from reSURFACE 1 and reSURFACE 2 phase III trials.<sup>2,3</sup>

Adult patients with moderate-to-severe plaque psoriasis from two double-blinded, randomized, 244/256-week (reSURFACE 2/1), placebo-controlled trials were included. Detailed methodology and patient characteristics have been previously described.<sup>2</sup> Safety data over 244/256 weeks were pooled across trials and treatments (tildrakizumab 100 mg or 200 mg) for the all-patients-as-treated population. Data pools for the treatment initiation period (up to week 16) versus treatment follow-up (from week 16 up to week 244/256), and data pools for the placebo-controlled period (up to week 12) were also analysed. Predefined Medical Dictionary for Regulatory Activities preferred terms related to respiratory or viral infections were included. Exposure-adjusted incidence rates (EAIRs) are reported.

Overall, 872 patients on tildrakizumab 100 mg and 928 patients on tildrakizumab 200 mg were analysed. Baseline characteristics have been published previously and were similar across treatment groups.<sup>2</sup> In the 5-year period, the total exposure to tildrakizumab 100 mg and tildrakizumab 200 mg was 2688 and 2754 PYs, respectively. The most common respiratory infections were upper respiratory tract infection (3.8 and 4.6 patients with event per 100 patient-years [PYs] with tildrakizumab 100 mg and 200 mg respectively) and influenza (2.4 and 3.1 per 100 PYs of exposure to tildrakizumab 100 mg or 200 mg), none of them fulfilling the regulatory definition of a serious adverse event. Few patients had non-fatal serious respiratory or viral infections during the 5-year follow-up period (Table 1). During treatment initiation, EAIRs for respiratory or viral infections (any preferred term) with tildrakizumab 100 mg and 200 mg (18.2/100 PYs and 26.2/100 PYs respectively) were higher than EAIRs during treatment follow-up, 10.5/100 PYs and 11.4/100 PYs, respectively. In the placebo-controlled period, EAIRs of respiratory or viral infections were comparable for tildrakizumab 100 mg (21.0/100 PYs), tildrakizumab 200 mg (31.0/100 PYs) and placebo (34.0/100 PYs).

The current analysis demonstrates that both tildrakizumab 100 mg and 200 mg have a favourable long-term safety profile with low exposure-adjusted rates of respiratory or viral infections up to 5 years. The occurrence of respiratory or viral infections did not follow a dose-related trend. Respiratory viral infections are the most common cause of infection among the general population with the majority of individuals presenting multiple infections per year.<sup>4</sup> Thus, our results would be comparable with general population and would also be in line with prior data stating that targeting IL-23 does not increase the risk for infections or induce a more severe course of them in patients with psoriasis under treatment with an IL-23 inhibitor.<sup>5,6</sup> Moreover, it has been reported that patients with COVID-19 have