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Cutaneous side-effects of the potential COVID-19 drugs

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Abstract

COVID-19 disease is a highly contagious and particularly popular problem in all countries. A variety of repurposed drugs and investigational drugs such as remdesivir, chloroquine, hydroxychloroquine, ritonavir, lopinavir, interferon-beta, and other potential drugs have been studied for COVID19 treatment. We reviewed the potential dermatological side-effects of these drugs.

KEYWORDS
COVID-19, dermatology, side-effects, skin

1 | INTRODUCTION

COVID-19 infection has rapidly spread across the world since its identification at the end of 2019. There are still no available evidence-based therapies for this infection.[1] We present the information on potential cutaneous adverse events of anti-COVID-19 drugs on dermatology practice.

2 | ANTIMALARIALS

We use chloroquine and hydroxychloroquine for the treatment of discoid lupus erythematosus and understand its relative safety. Hydroxychloroquine and chloroquine have antiviral activity against COVID-19 in vitro and small-uncontrolled clinical studies with limited and inconclusive results. In COVID-19, a small non-randomized study from France indicated some benefits with serious methodological flaws, and a follow-up study still lacked a control group. However, another very small, randomized study from China in patients with mild to moderate COVID-19 and also a quasi-randomized study from the United States found no difference in the recovery rates.[2,3] Cutaneous adverse events of antimalarials include cutaneous eruptions such as acute generalized exanthematous pustulosis, urticaria, pruritus, dry skin, rashes, flares of psoriasis and exfoliating lesions, Stevens-Johnson-like syndrome, mucocutaneous dyspigmentation, alopecia and bleaching of hair.[4] We also have to do the differential diagnosis of the skin manifestations of COVID-19 infection such as erythematous rash, petechia, urticaria, and vesicles in patients with COVID-19[5] who are using antimalarials.

3 | AZITHROMYCIN

Due to the remarkable pharmacokinetics and efficacy, azithromycin with immunomodulatory and anti-inflammatory properties is well-established as a potent treatment for some skin diseases such as rosacea, psoriasis, and synovitis, acne, pustulosis, hyperostosis, osteitis (SAPHO) syndrome.[6] Combining hydroxychloroquine with the antibiotic azithromycin has also been associated with positive patient outcomes according to the low-powered France study.[7] Whether this results in better clinical outcomes is still being debated. Skin adverse events of azithromycin are cutaneous severe skin reaction associated fever, angioedema, burning in eyes, skin pain, generalized red or purple skin rashes, blistering, skin peeling, toxic pustuloderma, anaphylaxis, DRESS syndrome, cutaneous leukocytoclastic vasculitis, and fixed drug eruptions.[8] These eruptions occur in also COVID infections' findings.

4 | COLCHICINE

Colchicine has been used to treat various dermatologic diseases, some of which are quite seldom, which include Behçet's disease, epidermolysis bullosa acquisita, recurrent oral aphthosis, cutaneous vasculitis, chronic urticaria and Sweet syndrome for its anti-neutrophilic immunomodulatory effect. In the last clinical trial called COLCORONA (Colchicine COVID-19 Trial), colchicine is being used to reduce the inflammatory reaction caused by COVID-19 that can lead to pulmonary involvement, organ failure, and death. It will be used for its anti-inflammatory and anti-cytokine storm effects when treating COVID-19.[9] Skin side-effects of colchicine include diffuse, blanchable, violaceous, morbilliform rash, lichenoid drug eruption, alopecia,

toxic epidermal necrolysis-like reaction, erythema-bullous, and erythema-nodosum-like lesions.[10,11]

5 | REMDESIVIR

Remdesivir shuts down viral replication by inhibiting a key viral enzyme, the RNA polymerase. The drug, which is given intravenously, has been used in hundreds of COVID-19 patients in China, the United States, and Europe as clinical studies. One of the most common adverse events is skin rashes.[12]

6 | OSELTAMIVIR/FAVIPIRAVIR/UMIFENOVIR

These drugs have been approved for the treatment of pandemic influenza A and B treatments. Oseltamivir inhibits the viral neuraminidase and, blocks the release of viral particles from host cells, decreasing the spread in the pulmonary system. Oseltamivir is studied in lots of clinical trials with multiple combinations with chloroquine and favipiravir for COVID-19. Favipiravir is a nucleoside analog that is well-known as a broad-spectrum antiviral drug with a lower side-effects profile.[13] Oseltamivir can cause Stevens-Johnson syndrome/toxic epidermal necrolysis, angioedema allergic, or idiosyncratic cutaneous drug reactions.[14,15] Umifenovir inhibits membrane fusion of the viral envelope and S protein/ACE2 interaction. It is approved for influenza treatment in Russia and China and a randomized-controlled trial of umifenovir is still going on the anti-COVID-19 agent. There are no reports on the skin reaction of umifenovir.[16]

7 | RIBAVIRIN/INTERFERONS

It is a broad antiviral against respiratory viruses such as influenza A and B viruses and parainfluenza 1 virus. Ribavirin, telbivudine, vitamin B12, nicotinamide combinations are proposed for COVID-19 treatment.[9] Dermatological side effects of ribavirin include acneiform eruptions, alopecia, localized scleroderma, maculopapular, and eczematous lesions, skin dryness, pruritus, and rash.[17] Interferon is a broad-spectrum antiviral via interaction with the toll-like receptors and it can inhibit the viral replication. There is an ongoing study to evaluate the efficacy and safety of interferon-α + ribavirin combination.[9] Cutaneous side-effects of interferons are injection site reactions, psoriasis, eczematous drug reactions, alopecia, sarcoidosis, lupus, cutaneous vasculitic lesions, psoriasis, and lichenoid drug reactions. These adverse events are estimated to occur as 13% to 23%.[18,19]

7.1 | Lopinavir/ritanavir and the other antiretrovirals

We use these agents for HIV diseases and they also have anti-coronavirus activity via inhibition of 3-chymotrypsin-like protease. There are mostly case reports and small retrospective non-randomized cohort studies lopinavir and ritonavir as anti-COVID-19 drugs. Although additional randomized controlled trials of these agents are ongoing, the current findings suggest a limited effect for antiretrovirals in COVID-19 treatment. In vitro studies indicated activities of darunavir, protease inhibitors, and integrase strand transfer inhibitors against COVID-19.[20,22] Cutaneous adverse events of antiretroviral drugs include maculopapular drug eruptions, exfoliative erythroderma, Stevens-Johnson syndrome or toxic epidermal necrolysis, severe cutaneous drug reactions, injection site reactions such as cysts, nodules, induration, or scleroderma-like lesions, lichenoid drug eruption, lipodystrophy, annular erythema and photosensitivity, nail, oral mucosa, and skin hyperpigmentations, pruritus, alopecia, paronychia, urticaria, mosquito bite hypersensitivity.[21,23,24]

7.2 | Nitazoxanide

It has broad antiviral and antihelmintic activity with lesser side-effect risks. In vitro studies suggest that nitazoxanide shows anti-COVID19 and immunomodulatory activities.[9] Hair loss, pruritus, and allergic skin reactions such as urticaria, rash, redness are cutaneous skin side-effects.[25]

7.3 | Camostat mesylate/dornase alfa

Camostat mesylate can inhibit host serine protease as the anti-COVID-19 agent. It is an approved drug in Japan for pancreatitis. Rash, itch, yellow discoloration of the skin or conjunctiva, and purpura are the skin effects of this drug.[26] Dornase alfa is a highly purified solution of recombinant human deoxyribonuclease and this drug can reduce mucus viscosity in the lungs and also improve the clearance of secretions. It has no serious side-effects on the skin and phase studies also are still going on as anti-COVID19 agent.[27]

8 | ADJUNCTIVE TREATMENTS

These therapies are steroids, anti-cytokine or immunomodulatory agents, and immunoglobulin therapy.

8.1 | Steroids

Corticosteroids have anti-inflammatory functions and they can suppress the inflammation during COVID-19 associated acute respiratory distress syndrome. Short term (3-5 days) and very low doses (methylprednisolone 1-2 mg/kg/day) are recommended.[9] Skin side-effects of steroids include pruritus, burning, stinging, folliculitis, dryness, acneiform eruptions, skin atrophy, telangiectasia, erythema, edema, fissures, urticaria, disease exacerbation, acne, papulopustular lesions, hirsutism, and stria.[28]

8.2 | Baricitinib and the other Janus kinase inhibitors

Artificial intelligence predicts that Janus kinase (JAK) inhibitors like baricitinib may block viral entry into pneumocytes in COVID-19 infection.[29,30] JAK inhibition also can affect inflammation.[37] Palmoplantar pustulosis-like eruption, allergic skin rashes, *herpes* simplex, and zona zoster infections, melanoma and nonmelanoma skin cancers, urticaria, rash, angioedema are cutaneous side effects of baricitinib and the other JAK inhibitors.[31,38,39]

8.3 | Tocilizumab

COVID-19 can induce the uncontrolled cytokine and chemokine response known as a "cytokine storm," and this condition leads to the over-activation of effector T cells and production of pro-inflammatory cytokines, which in turn lead to acute respiratory distress syndrome associated with increasing plasma leakage, vascular permeability, and disseminated intravascular coagulation. Tocilizumab, a humanized monoclonal antibody against IL-6 receptors, can reverse the cytokine storm as anti-COVID-19 agent.[9] *Skin infection*, pruritus, skin hypersensitivity reactions, *psoriasiform dermatitis* are the cutaneous side-effects of Tocilizumab.[32,33]

8.4 | Anti-IL-1 (Anakinra)

In hyper inflammation during COVID-19 infection, immunosuppression is likely to be beneficial. IL-1 blockade with anakinra in sepsis, showed a significant survival benefit in patients with hyper inflammation, without increased adverse events according to phase 3 randomized controlled trial results.[34] Cutaneous side-effects of anakinra include rash, injection-site reactions, and skin infections such as wound infection, cellulitis.[35,36]

8.5 | Anti-TNF-α biologics

Higher TNF-α levels have been found in patients with COVID-19 and these correlate with disease severity. It has been suggested that anti-TNF-α treatment of COVID-19 may be a potential option, and a randomized, controlled trial of adalimumab has been started.[40] Cutaneous side-effects of anti-TNFs include infusion and injection site reactions, psoriasis and psoriasiform-like lesions, lupus-like syndromes, cutaneous vasculitis, cutaneous infections, eczematous reactions, lichenoid eruptions, granulomatous reactions, cutaneous lymphoma, epithelial skin cancers or melanoma.[39]

8.6 | High-dose intravenous immunoglobulin

High-dose intravenous immunoglobulin (IVIG) collected from recovered Coronavirus-19 patients may protect against COVID-19 and strengthen the immune system of new severe and treatment-resistant patients.[41,42] Skin adverse events of IVIG treatments include anaphylactic reaction, facial vasculitic rash, urticaria, maculopapular rashes, petechiae, eczema, erythema multiforme, and alopecia.[43,44]

8.7 | Checkpoints inhibitors

The inhibition of CD200-CD200R1 and anti-PD agents have positive effects on coronavirus infection, restoring IFN production, and increasing virus clearance. Studies on checkpoint inhibitors are ongoing in CoViD-19 patients.[45] Rash, pruritus, xerosis, alopecia, stomatitis, urticaria, photosensitivity reaction, hyperhidrosis, vitiligo, skin exfoliation, hair color changes, impaired skin wound healing, periungual pyogenic granuloma-like lesions, sarcoidosis-like reactions, granulomatous panniculitis, granuloma annulare, and granulomatous dermatitis are the cutaneous adverse events of checkpoints inhibitors.[46]

9 | DISCUSSION

Skin manifestations of COVID-19 infections include erythematous rash, acute hemorrhagic edema, petechiae, morbilliform rash, chickenpox-like vesicles, livedoid lesions, localized or widespread urticaria confluent erythematous-yellowish papules and plaques may be the most common manifestations in acute severe COVID-19 cases. However, it can be difficult to distinguish the underlying cause of whether viral infection or newly prescribed anti-COVID-medication ([47]). Complete blood count analysis with atypical lymphocytosis, neutrophilia, eosinophilia, higher blood drug, histamine, tryptase and beta-tryptase levels, cutaneous histopathologic examinations with the presence of eosinophils, edema, and inflammation may indicate cutaneous drug eruptions. A good and complete history taking is very vital and helpful for the differential diagnosis.[48] We should obtain the history anti-COVID-19 and other drug exposures including dosage, date started, duration and interruptions in use, initiation of drug use and the onset of reaction, previous adverse cutaneous drug reactions, and type of adverse reaction and previous family or personal history of skin drug eruptions, hypersensitivity syndromes and atopy. Re-exposure to a drug and exacerbation of skin reaction, the improvement after a decrease in drug dosage, or discontinuation of the drug (rechallenge test) are clues for the diagnosis of drug eruptions. In the management of the cutaneous anti-COVID 19 drug eruptions, medium-to-high potency topical corticosteroids generally sufficed, although oral antihistamines and corticosteroids were occasionally needed. In severe cases, we can start at cyclosporin 5 mg/kg/day and IVIG treatments.[48] Early diagnosis of a cutaneous drug eruption allows the clinician the ability to narrow in on a culprit drug and determine whether the medication is safe to continue. A variety of drugs have been identified for COVID19 treatment. However, evaluation of the investigational agents requires adequately powered, randomized, controlled trials with realistic eligibility criteria and appropriate

TABLE 1 Cutaneous side-effects of potential anti-COVID19 drugs

Drugs	Cutaneous side-effects
Chloroquine, hydroxychloroquine, and other antimalarials	Acute generalized exanthematous pustulosis, urticaria, pruritus, dry skin, rashes, flares of psoriasis and exfoliating lesions, Stevens–Johnson-like syndrome, mucocutaneous dyspigmentation, alopecia, and bleaching of hair
Azithromycin	Cutaneous severe skin reaction associated fever, angioedema, burning in eyes, skin pain, generalized red or purple skin rashes, blistering, skin peeling, toxic pustuloderma, anaphylaxis, DRESS syndrome, cutaneous leukocytoclastic vasculitis, and fixed drug eruptions
Colchicine	Diffuse, branchable, violaceous, morbilliform rash, lichenoid drug eruption, alopecia, toxic epidermal necrolysis-like reaction, erythema-bullous and erythema-nodosum-like lesions
Remdesivir	Skin rashes
Oseltamivir/Favipiravir/Umifenovir	Stevens–Johnson syndrome/toxic epidermal necrolysis, angioedema allergic or an idiosyncratic cutaneous drug reactions
Ribavirin	Acneiform eruptions, alopecia, localized scleroderma, maculopapular and eczematous lesions, skin dryness, pruritus, and rash
Interferons	Injection site reactions, psoriasis, eczematous drug reactions, alopecia, sarcoidosis, lupus, cutaneous vasculitic lesions, psoriasis, and lichenoid drug reactions
Lopinavir/Ritanavir and other Antiretrovirals	Maculopapular drug eruptions, exfoliative erythroderma, Stevens-Johnson syndrome or toxic epidermal necrolysis, severe cutaneous drug reactions, injection site reactions such as cysts, nodules, induration, or scleroderma-like lesions, lichenoid drug eruption, lipodystrophy, annular erythema and photosensitivity, nail, oral mucosa, and skin hyperpigmentations, pruritus, alopecia, paronychia, urticaria, mosquito bite hypersensitivity
Nitazoxanide	Hair loss, pruritus, allergic skin reactions; urticaria, rash, redness
Camostat mesylate	Rash, itch, yellow discoloration of the skin or conjunctiva, purpura
Corticosteroids	Transient and mild to moderate pruritus, burning, stinging, folliculitis, dryness, acneiform eruptions, skin atrophy, telangiectasia, erythema, edema, fissures, urticaria, disease exacerbation, acne, papular and pustular lesions, hirsutism and stria
Tocilizumab	*Skin infections*, pruritus, skin hypersensitivity reactions, *psoriasiform dermatitis*
Anakinra	Skin rashes, injection-site reactions and skin infections such as wound infection, cellulitis
Baricitinib and the other JAK inhibitors	Palmoplantar pustulosis-like eruption, herpes zoster, and herpes simplex activations, melanoma and nonmelanoma skin cancers, urticaria, rash, angioedema
Anti-TNF biologics	Infusion and injection site reactions, psoriasis and psoriasiform-like lesions, lupus-like syndromes, cutaneous vasculitis, cutaneous infections, eczematous reactions, lichenoid eruptions, granulomatous reactions, cutaneous lymphoma, epithelial skin cancers or melanoma
IVIG treatments	Anaphylactic reaction, facial vasculitic rash, urticaria, maculopapular rashes, petechiae, eczema, erythema multiforme, and alopecia
Checkpoints inhibitors	Rash, pruritus, xerosis, alopecia, stomatitis, urticaria, photosensitivity reaction, hyperhidrosis, vitiligo, skin exfoliation, hair color changes, impaired skin wound healing, periungual pyogenic granuloma-like lesions, sarcoidosis-like reactions, granulomatous panniculitis, granuloma annulare, and granulomatous dermatitis
Vaccines	Urticaria, scleroderma, maculapapular rashes injection site reactions[49]

stratification of the patients. There are several clinical trials on potential anti-COVID19 therapies such as ivermectin, recombinant human angiotensin-converting enzyme 2 (APN01), natural killer cells, mesenchymal stem cells, SARS-CoV-2-specific neutralizing antibodies, anti-C5a monoclonal antibody, thalidomide, fingolimod (highly potent functional antagonist of S1P1 receptors in the lymph node T cells), Bevacizumab (recombinant humanized VEGF monoclonal antibody), vaccine, mRNA-1273 (encodes the prefusion-stabilized viral spike protein), INO-4800, ChAdOx1 nCoV-19, stabilized subunit vaccines, nanoparticle-based vaccines, pathogen-specific artificial antigen-presenting cells taking place with potential new cutaneous side-effects like others (Table 1).[41] After examining all the treatments, although potentiality effective against COVID-19, we may start them one by one required by the safest and the most effective appropriate drug to minimize the development of the cutaneous drug eruptions and for the easy diagnosis.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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REFERENCES

1. Riou J, Althaus CL. Pattern of early human-to-human transmission of Wuhan 2019 novel coronavirus (2019-nCoV), December 2019 to January 2020. *Euro Surveill*. 2020;25:4.
2. Ying-Hui J, Lin C, Cheng Z-S, et al. A rapid advice guideline for the diagnosis and treatment of 2019 novel coronavirus (2019-nCoV) infected pneumonia (standard version). *Mil Med Res*. 2020;7:4.
3. Joshua B, Daniel K, Freedman R, Le K, Lin X. Clinical outcomes of hydroxichloroquine in hospitalized patients with COVID-19: a quasi-randomized comparative study. *N Eng J med*. 2020;20:882.
4. Salido M, Joven B, D'Cruz DP, Khamashta MA, Hughes GR. Increased cutaneous reactions to hydroxychloroquine (Plaquenil) possibly associated with formulation change: comment on the letter by Alarcón. *Arthritis Rheum*. 2002;246(12):3392-3396.
5. Recalcati S. Cutaneous manifestations in COVID-19: a first perspective. *J Eur Acad Dermatol Venereol*. 2020. https://doi.org/10.1111/jdv.16387.
6. Esther J, van Zuuren ZF, Carter B, van der Linden MMD, Charland L. Cochrane skin group interventions for rosacea. *Cochrane Database Syst Rev*. 2015;4:CD003262.
7. Gautret P, Lagie JC, Parola P, et al. Hydroxychloroquine and azithromycin as a treatment of COVID-19: results of an open-label non-randomized clinical trial. *Int J Antimicrob Agents*. 2020;20:105949.
8. Das A, Sancheti K, Podder I, Das NK. Azithromycin induced bullous fixed drug eruption. *Indian J Pharmacol*. 2016;48(1):83-85.
9. Liu C, Zhou Q, Li Y, et al. Research and development on therapeutic agents and vaccines for COVID-19 and related human coronavirus diseases. *ACS Cent Sci*. 2020;6(3):315-331.
10. Mason SE, Smoller BR, Wilkerson AE. Colchicine intoxication diagnosed in a skin biopsy: a case report. *J Cutan Pathol*. 2006;33(4):309-311.
11. An I, Demir V, Akdeniz S. Lichenoid drug eruption induced by colchicine: case report. *Cut Ocul Toxicol*. 2017;36(2):199-200.
12. Grein J, Ohmagari N, Shin D, Diaz G. Compassionate use of Remdesivir for patients with severe Covid-19. *N Engl J Med*. 2020. https://doi.org/10.1056/NEJMoa2007016.
13. Russell B, Moss C, George G, et al. Associations between immune-suppressive and stimulating drugs and novel COVID-19—a systematic review of current evidence. *E Cancer Med Sci*. 2020;14:1022.
14. Zuo W, Wen LP, Li J, Mei D, Fu Q, Zhang B. Oseltamivir induced Stevens-Johnson syndrome/toxic epidermal necrolysis-case report. *Medicine (Baltimore)*. 2019;98(19):e15553.
15. Kalsi T, Stevenson J, Wade P, Kinirons M. Tongue swelling in association with oseltamivir (Tamiflu). *BMJ Case Rep*. 2011;4:2011.
16. Chen C, Huang J, Yin P. Favipiravir versus Arbidol for COVID-19: a randomized clinical trial. *MedRXiv*. 2020. https://doi.org/10.1101/2020.03.17.20037432.
17. Gupta M, Aggarwal M, Bhari N. Acneiform eruptions: An unusual dermatological side effect of ribavirin. *Dermatol Ther*. 2018;31(5):e12679.
18. Lorcy S, Gaudy-Marqueste C, Botta D, et al. Cutaneous adverse events of telaprevir/peginterferon/ribavirin therapy for chronic hepatitis C: a multicenter prospective cohort study. *Ann Dermatol Venereol*. 2016;143(5):336-346.
19. Bush AE, Hymes SR, Silapunt S. Lichenoid dermatitis from interferon alpha-2a in a patient with metastatic renal cell carcinoma and seronegative HCV. *J Drugs Dermatol*. 2017;16(7):714-716.
20. Kandeel M, Al-Nazawi M. Virtual screening and repurposing of FDA approved drugs against COVID-19 main protease. *Life Sci*. 2020;251:117627.
21. Pistone G, Pistone A, Sorbello D, Viviano E, Bongiorno MR. Cutaneous adverse reactions to highly antiretroviral therapy in HIV-positive patients. *Case Rep Dermatol*. 2014;6(2):145-149.
22. Hoffmann M, Kleine-Weber H, Schroeder S, et al. SARS-CoV-2 cell entry depends on ACE2 and TMPRSS2 and is blocked by a clinically proven protease Inhibitor. *Cell*. 2020;181:271-280.e8. https://doi.org/10.1016/j.cell.2020.02.052.
23. Introcaso CE, Hines JM, Kovarik CL. Cutaneous toxicities of antiretroviral therapy for HIV: part I. lipodystrophy syndrome, nucleoside reverse transcriptase inhibitors, and protease inhibitors. *J Am Acad Dermatol*. 2010;63(4):549-561.
24. Sharma A, Vora R, Modi M, Sharma A, Marfatia Y. Adverse effects of antiretroviral treatment. *Indian J Dermatol Venereol Leprol*. 2008;74(3):234-237.
25. Speich B, Ame SM, Ali SM, et al. Efficacy and safety of nitazoxanide, albendazole, and nitazoxanide-albendazole against Trichuris trichiura infection: a randomized controlled trial. *PLoS Negl Trop Dis*. 2012;6(6):e1685.
26. Reihill JA, Walker B, Hamilton RA, et al. Inhibition of Protease-Epithelial Sodium Channel Signaling Improves Mucociliary Function in Cystic Fibrosis Airways. *Am J Respir Crit Care Med*. 2016;194(6):701-710.
27. Yang C, Montgomery M. Dornase alfa for cystic fibrosis. *Cochrane Database Syst Rev*. 2018;9:CD001127.
28. Spada F, Barnes TM, Greive KA. Comparative safety and efficacy of topical mometasone furoate with other topical corticosteroids. *Australas J Dermatol*. 2018;59(3):e168-e174.
29. Richardson P, Griffin I, Tucker C, et al. Baricitinib as potential treatment for 2019-nCoV acute respiratory disease. *Lancet*. 2020;395:e30-e31.
30. Praveen D, Chowdary PR, Aanandhi MV. Baricitinib- a januase kinase inhibitor- not an ideal option for management of COVID 19. *Int J Antimicrob Agents*. 2020;4:105967.
31. Koumaki D, Koumaki V, Lagoudaki E, Bertsias G. Palmoplantar Pustulosis-like Eruption Induced by Baricitinib for Treatment of Rheumatoid Arthritis. *Eur J Case Rep Intern Med*. 2019;7(1):001383.
32. Markatseli TE, Theodoridou A, Zakalka M, et al. Persistence and adherence during the first six months of tocilizumab treatment among rheumatoid arthritis patients in routine clinical practice in Greece. Results from the single arm REMISSION II study (NCT01649817). *Mediterr J Rheumatol*. 2019;30(3):177-185.
33. Matsushima Y, Hayashi A, Mizutani K, et al. Psoriasiform dermatitis developing during treatment of juvenile idiopathic arthritis with tocilizumab. *Case Rep Dermatol*. 2019;11(3):317-321.
34. Shakoory B, Carcillo JA, Chatham WW, et al. Interleukin-1 receptor blockade is associated with reduced mortality in sepsis patients with features of macrophage activation syndrome: reanalysis of a prior phase iii trial. *Crit Care Med*. 2016;44:275-281.
35. Vastert SJ, Jamilloux Y, Quartier P, et al. Anakinra in children and adults with Still's disease. *Rheumatology (Oxford)*. 2019;58(Suppl 6):vi9-vi22.
36. Kullenberg T, Löfqvist M, Leinonen M, Goldbach-Mansky R, Olivecrona H. Long-term safety profile of anakinra in patients with severe cryopyrin-associated periodic syndromes. *Rheumatology (Oxford)*. 2016;55(8):1499-1506.
37. Peterson D, Damsky W, King B. The use of Janus kinase inhibitors in the time of SARS-CoV-2. *J Am Acad Dermatol*. 2020;9: pii: S0190-9622(20)30522–3.
38. Sonthalia S, Aggarwal P. Oral Tofacitinib: contemporary appraisal of its role in dermatology. *Indian Dermatol Online J*. 2019;10(5):503-518.
39. Sehgal R, Stratman EJ, Cutlan JE. Biologic agent-associated cutaneous adverse events: a single center experience. *Clin Med Res*. 2018;16(1–2):41-46.
40. Tu YF, Chien CS, Yarmishyn AA, Lin YY, et al. A review of SARS-CoV-2 and the ongoing clinical trials. *Int J Mol Sci*. 2020;21(7):E2657.

41. Cao W, Liu X, Bai T, et al. High-dose intravenous immunoglobulin as a therapeutic option for deteriorating patients with coronavirus disease 2019. *Open Forum Infect Dis*. 2020;21(3):7 ofaa102.
42. Jawhara S. Could intravenous immunoglobulin collected from recovered coronavirus patients protect against COVID-19 and strengthen the immune system of new patients?*Int J Mol Sci*. 2020;21(7):2-5.
43. Verma P, Dayal S, Jain VK, Amrani A. Alopecia universalis as a side effect of pegylated interferon α-r combination therapy for hepatitis C: a rare case report. *J Chemother*. 2017;29(6):380-382.
44. Brannagan TH, Nagle KJ, Lange DJ, Rowland LP. Complications of intravenous immune globulin treatment in neurologic disease. *Neurology*. 1996;47:674-677.
45. Vaine CA, Soberman RJ. The CD200-CD200R1 inhibitory signaling pathway: immune regulation and host-pathogen interactions. *Adv Immunol*. 2014;121:191-211.
46. Belum VR, Benhuri B, Postow MA, et al. Characterisation and management of dermatologic adverse events to agents targeting the PD-1 receptor. *Eur J Cancer*. 2016;60:12-25.
47. Estebanez A, Pérez-Santiago L, Silva E, Guillen-Climent S, García-Vázquez A, Ramón MD. Cutaneous manifestations in COVID-19: a new contribution. *J Eur Acad Dermatol Venereol*. 2020. https://doi.org/10.1111/jdv.16474.
48. Perez CE, Dyer JA. Cutaneous Drug Eruptions in Pediatrics-A Primer. *Pediatr Ann*. 2020;49(3):e132-e139.
49. Holdiness MR. Adverse cutaneous reactions to influenza vaccinations and chemotherapy. *Int J Dermatol*. 2001;40(7):427-430.

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