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 ORIGINAL ARTICLE

The ABCs of JAKis: A Clinician's Guide to Safety and Monitoring of the Systemic JAK Inhibitors

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ABSTRACT

Janus Kinase Inhibitors (JAKis) have recently emerged in the arsenal of tools to treat dermatological conditions. However, there are some concerns regarding these treatments due to their boxed warning. Here we discuss the safe and effective use of JAKs for the treatment of a wide variety of dermatologic conditions. We will also discuss monitoring guidelines.

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INTRODUCTION

Since the release of the first US Food and Drug Administration (FDA)-approved targeted biologic agent in 2017, several years have elapsed since a new systemic therapy has been approved for atopic dermatitis (AD). Now, however, Janus Kinase Inhibitors (JAKis) have arrived and opened an entirely new therapeutic approach to patients with refractory AD. JAKis have previously been utilized to treat other chronic inflammatory disorders such as rheumatoid arthritis, psoriatic arthritis, juvenile idiopathic arthritis, axial spondyloarthritis, ulcerative colitis, and now atopic dermatitis and alopecia areata.[1] There are three JAKis that have been approved by the FDA in 2021 and 2022 for the treatment of AD. Upadacitinib and abrocitinib are oral medications that are approved for moderate-to-severe atopic dermatitis,[2] and ruxolitinib is a topical that is approved for mild-to-moderate AD, as well as non-segmental vitiligo. Baricitinib is another oral JAK inhibitor that has recently been approved for the treatment of severe alopecia areata and is approved for AD outside of the US.[3] Tofacitinib is another JAK inhibitor that is new to dermatology and has been approved for symptomatic psoriatic arthritis.[4]

The inflammatory pathway of JAK is interlinked with signal transducers and activators of transcription (STAT), to constitute the JAK-STAT pathway. When a cytokine binds to a receptor, JAK phosphorylates the receptor chains. This allows STAT to bind the phosphorylated site and dimerize along with the phosphate molecule. These STAT dimers move to the nucleus and activate gene transcription.[5] This pathway is not only relevant for dermatology, but for immune and hematopoietic function. Though inhibition of this pathway is the mechanism for these medications, genetic loss of function of JAK3 causes severe immunodeficiency syndrome.[6] Gain of function mutations can cause the JAKs to act as oncogenes in malignancies such as T cell lymphoma[7], thus a healthy balance of this proliferative pathway is necessary.

Many sporadic autoimmune and autoinflammatory conditions rely on this JAK-STAT pathway for the pathogenesis of disease, thus JAK inhibitors have been developed to treat these autoimmune conditions.[8] This mechanism differs from the biologic drugs, which often are monoclonal antibodies targeted against only one or two specific cytokines, such as IL-13. These pathways are closely intertwined, however, as IL-4, IL-13, IL-31, and other interleukins and cytokines signal via JAK1, JAK2, and JAK3. Inhibition of JAK1/2 leads to decreased IFNγ with decreased production of Th1 cells. Inhibition of JAK1/3 leads to decreased IL-2, IL-4, and IL-9 with decreased production of Th2 cells and JAK2 inhibition decreases IL-5.[9] Legacy immunosuppressive medications such as systemic corticosteroids or cyclosporine have a broad immunomodulatory effect, touching many areas of the immune system and beyond. On the other hand, biologics in this space are extremely targeted, affecting only one or two specific cytokines. The JAK inhibitor class sits between these two extremes.

As the JAK-STAT system is involved in many functions beyond inflammation such as hematopoiesis, tissue repair, and adipogenesis, gross modulation of this pathway may not be desired. Thus, selective JAKis have been developed that preferentially target the JAK members that are most relevant to the desired therapeutic effect. In AD, JAK 1 is involved in the

signaling of several key cytokines including IL-4, IL-13, and IL-31, while JAK 3 signaling plays a role in lymphocyte development and function. Focusing on these appears to improve the risk/benefit profile for the treatment of AD by minimizing off-target effects and reducing potential side effects that may be associated with the broader inhibition of the JAK-STAT pathway.

JAK inhibitors can work very rapidly, within hours to days for dermatologic diseases.[10] Because they are small molecules, they can be administered orally and topically, unlike biologic agents which tend to require injection, an important consideration in some cases. With rapid action targeting a broader portion of the inflammatory process, these medications are a welcome addition to the treatment armamentarium. The purpose of this review is to condense and highlight the safety and tolerability findings in the literature and help identify key points for clinicians when discussing these medications with their patients in terms of safety, tolerability, and monitoring.

Tolerability

Though safety and tolerability are often conflated, there are several tolerability issues specifically with JAK inhibitors that can be seen as distinct from safety, not directly endangering the patient. These include acne related to JAKis (sometimes referred to as "JAKne"), headache, cough, folliculitis, nausea, abdominal pain, increased fatigue, weight gain, and myalgia. In the literature, many of these tolerability issues are noted as adverse events but are often categorized along with safety concerns.

In regards to acne caused by JAKis, in a study with 60 patients prescribed baricitinib and upadacitinib for moderate-to-severe AD, 8 of the patients experienced acne at an incidence rate of 13.3%.[11] In a prior 16-week double-blind placebo-controlled study of 901 patients, 10% of patients with upadacitinib 15 mg and 14% with upadacitinib 30 mg reported acne, compared with 2% with placebo.[12] Additionally Silverberg et al saw in their study of 391 patients with AD that daily use of 100 mg and 200 mg abrocitinib resulted in 1.3% and 5.8% incidence rates of acne vs 0% in patients receiving a placebo. This suggests a dose-dependent relationship similar to that noted with the use of upadacitinib.[13] In the treatment of alopecia areata, acne occurred in 16/270 patients (5.7%) with 4 mg baricitinib, 10/183 patients (5.5%) with 2 mg baricitinib, and 1/189 patients (0.5%) with placebo in their first trial. In their second trial, it occurred in 11/233 patients (4.7%), 9/155 patients (5.8%), and 3/154 patients (1.9%), respectively.[14] In the treatment of vitiligo, application site acne was reported in up to 13/228 (5.9%) in the ruxolitinib-treated group compared with 2/115 (1.7%) in placebo. Additionally, some of these patients experienced pruritus at the site at rates of 12/228 (5.4%) and 2/115 (1.7%), respectively.[15] Finally, in the treatment of psoriasis, acne occurred in 15/531 (2.8%) in deucravacitinib compared with no events in placebo.[16]

In treating these side effects of JAKne, many experts view the management as no different than managing acne in general. Patients with prior acne are often at the greatest risk for exacerbation, though it is very unlikely to be a limiting factor for treatment with JAKis.[17]

In the treatment of AD, headaches were the most common neurologic side effect. It was reported in 12/156 (8%) in abrocitinib 100 mg, 15/154 (10%) in 200 mg, and 2/77 (3%) in placebo groups. 100 mg dosing did not report a difference from placebo; however, 200 mg dosing was associated with a higher incidence of headaches than placebo.[18] Another study found headaches were relatively short lived with a mean duration of 4 days in the abrocitinib 100 mg group and 3 days in the 200 mg group.[19] In the treatment of alopecia areata, Headaches occurred in 4.4–9% of patients on baricitinib compared with 4.8–6.5% in placebo.[14] With the treatment of vitiligo, Headaches occurred in 6/221 (2.7%) and 11/228 (4.8%) compared with 2/109 (1.8%) and 4/115 (3.5%) in placebo.[20]

Among tolerability issues, gastrointestinal discomfort of nausea was seen in 9% of patients on abrocitinib 100 mg and 20% in abrocitinib 200 mg, compared to 3% in placebo for the treatment of AD.[19] A later meta-analysis of four clinical trials of abrocitinib found that the doses of 100 mg and 200 mg were associated with increased nausea than placebo as well.[18] 9.1% of patients on 200 mg of abrocitinib experienced diarrhea as well. Upadacitinib 15 mg was seen to cause nausea in 2.4% of the patients and 7.1% with the dose of 30 mg compared to 2.5% in placebo. Additionally, diarrhea was seen in less than 7% of patients on upadacitinib.[21] In the treatment of psoriasis, Deucravacitinib caused nausea and diarrhea at a rate of 2.1% and 3.9%, respectively. This was similar to the placebo rates in their study of 2.4% and 3.6%.[16]

Some less common issues among systemic JAKis are hyperseborrhea at 1.2%, folliculitis at 0.9%, weight gain at 0.7%, fatigue at 0.7%, and allergy symptoms at 0.6%.[22] With topical JAKis the most common adverse effects were scalp irritation at 11.2%, folliculitis at 1.2%.[22]

Safety

The FDA recently placed a black box warning on this class of medications due to safety concerns based largely on data from studies investigating tofacitinib in patients with rheumatoid arthritis.[4] The study, comprising patients 50 years of age and older with a cardiovascular disease risk factor at baseline and concurrent administration of methotrexate, found that tofacitinib exposure was associated with a higher incidence of cancer and major adverse cardiovascular events (MACE) compared to TNF-inhibitors. The FDA came to the conclusion that tofacitinib carries a higher risk of MACE, blood clots, cancer (such as lymphomas, lung cancer), and death than TNF-inhibitors. This

conclusion led to a mandate from the FDA for a boxed warning on tofacitinib and all other JAKis due to similar mechanisms despite the differences in molecular targeting and selectivity. While the safety profiles of each of these medications differ, the boxed warning appears on all of these agents as a result of these studies, including the topical formulation of ruxolitinib. Systemic absorption of these medications is known to be decreased when utilized topically compared to oral medications.[23] When maximally used, the topical 1.5% formulation of ruxolitinib was found to have a mean steady-state plasma concentration below the half-maximal inhibitory concentration of Janus kinase-mediated myelosuppression.[24]

Importantly, dermatologists have utilized medications with boxed warnings for many years. With decades of experience and thorough knowledge of treatment options for patients, the boxed warnings should alert both patients and healthcare providers to clinical circumstances in which the risk may outweigh the benefits of a drug. These warnings are not to be seen as a label to avoid the medications, but instead to consider them carefully. In an analysis of JAKis safety done in 2022, Elmariah noted the low absolute risk of major adverse events compared to each other and TNF-α inhibitors.[25] Bunick et al compared this risk of adverse events including malignancy, MACE, and venous thromboembolism to systemic usage of methotrexate, cyclosporine, and corticosteroids. They found that, specifically for malignancy rates, upadacitinib (15 mg) and abrocitinib (15 mg and 30 mg) exhibited the lowest rates at 0.2 events per 100 patient-years (/100PY). Upadacitinib (30 mg) had 0.5 events per 100 patient years while methotrexate and cyclosporine were 0.5 and 0.6, respectively in the rates of malignancy. In contrast, they noted that systemic corticosteroids showed the highest malignancy risk at 4.3 events per 100 patient-years.[3]

Of note, the overall incidence rate of all malignancies excluding cutaneous basal and squamous cell carcinoma, in the United States was 0.55 events per 100 patient-years in 2020.[26] When comparing the treatments in the context of nonmelanoma skin cancer, the rates were similarly low for upadacitinib and abrocitinib: upadactinib had a rate of 0.4 and abrocitinib had a rate of 0.6/100PY, while methotrexate and cyclosporine were found to be 0.3 and 0.5, respectively. Once again systemic corticosteroids were found to have a higher rate of nonmelanoma skin cancer at a rate of 3.9 per 100 patient years.

When comparing rates of MACE, upadacitinib had the lowest rate between 0.0 and 0.1 events per 100 patient-years, followed by abrocitinib at 0.2 events. Comparatively, methotrexate had a rate of 0.5, cyclosporine with a rate of 2.8 events, and corticosteroids with 7.6 events per 100 patient years–an order of magnitude greater than the JAKis. Finally, when comparing venous thromboembolism all of the JAKis had low rates between 0 and 0.4 events compared to methotrexate having a rate of 0.5 events per 100 patient years.3 Despite these relatively low rates of serious adverse events, JAKis have a boxed warning along with methotrexate. Interestingly, corticosteroids have no such warning or label despite having higher rates of malignancy and MACE.

JAK inhibitors may lessen the immune response, potentially leading to decreased defense against pathogens. The most frequently reported (>5% of patients) infections include upper respiratory tract infections and nasopharyngitis. The rate of upper respiratory tract infections in pooled analysis of four phase 3 trials on abrocitinib and upadacitinib for AD, did not find a statistical difference between the abrocitinib-treated groups and placebo.[18] The rates themselves within various trials were between 7–9% and 6–13%, compared with 4–5% and 4–7% in placebo.[13,19] In the same studies, nasopharyngitis was up to 15% and 12% for abrocitinib and upadacitinib groups compared to 6-10% and 5-6% with placebo. In patients receiving topical ruoxlitinib, infections were much less common at less than 3%.[10] For alopecia areata, baricitinib-treated patients had upper respiratory infections at similar rates of a placebo, 4.97.7% versus 5.3–7.3%.[14] Nasopharyngitis was seen at a rate of 7.5% compared to 4.5%-6.6%. Of note, urinary tract infection rates were increased in the two groups at 4.7% with 2 mg and 7.7% with 4 mg of baricitinib in contrast with the placebo group at 1.3%. In the treatment of vitiligo, nasopharyngitis was noted in 4.1% and 4.4% of ruxolitinib patients compared to 3.7% and 0.9% in placebo.[20] Finally, with the treatment of psoriasis with decravacitinib, upper respiratory tract infection, and nasopharyngitis were seen at a rate of 6.3% compared to 3.6% and 4.2% in placebo groups.[16]

Other serious concerns that should be screened for prior to initiation of JAKis include hepatitis B reactivation, disseminated tuberculosis, gastrointestinal perforation, and drug-induced reactions. However, many of these adverse safety events are noted in specific patient populations that often differ from the majority of dermatologic patients. JAKis may provide a safer alternative therapy to mitigate the long-term side effects of other therapies such as corticosteroids. Holistic consideration of each patient's care along with shared decision making is critical.

Patient Selection and Contraindications

With JAKis reducing the immune response in patients, clinicians should be well aware of the patient's comorbid conditions. Specifically, in patients who are HIV positive, pregnant, hepatitis positive, have tuberculosis, or are immunocompromised, JAKis should be avoided. The majority of noted infectious events related to JAKis are seen with tofacitinib, due to its usage beginning in 2012. However, this JAKis is not commonly used in dermatology as it is mainly for the treatment of psoriatic arthritis. Additionally, in October of 2022, the European Medicines Agency announced recommendations to minimize

the serious side effects of JAKis for chronic inflammatory disorders. These guidelines recommend against the following patient populations: "those aged 65 years or above, those at increased risk of major cardiovascular problems (such as heart attack or stroke), those who smoke or have done so for a long time in the past and those at increased risk of cancer".[27] These guidelines were suggested with chronic inflammatory disorders in mind and not necessarily dermatology, so clinicians should use their judgment in specific situations.

The Japanese dermatological association outlined specific exclusion criteria for the use of oral JAKis in the treatment of AD. Patients between 12 and 65 years of age should weigh more than 30 kg. They recommend against use in pregnant and lactating individuals. Those with a Hepatitis B viral load ≥ 20 IU/mL (1.3 LogIU/mL) should also not use JAKis. In cases with a lower viral load, they recommend monitoring every 1 to 3 months in addition to transaminases. With active tuberculosis, they also recommend against the usage of JAKis. In the case of latent tuberculosis, they recommend tuberculosis chemoprophylaxis (isoniazid) at least three weeks before starting JAKis and chemoprophylaxis for 6 to 9 months while administering JAKis. Additionally, they recommend against live virus vaccination during treatment with JAKis, and live virus vaccines should be administered 30 days prior to starting JAKis. In patients with renal dysfunction, they recommend specific dosing of baricitinib and abrocitinib depending on creatinine clearance. In cases of lymphopenia, neutropenia, and thrombocytopenia JAKis are contraindicated. Finally, Patients with a prior history of cancer should be monitored on a case-by-case basis.[28,29]

Monitoring

Patients should be monitored for concerning symptoms and lab abnormalities. However, specific guidelines for each treatment are still relatively vague and many off-label uses for JAKis are still being investigated.[30] The international multidisciplinary Task Force of experts on JAK inhibitors in inflammatory diseases recommends the following before treatment[31]:

Before treatment:

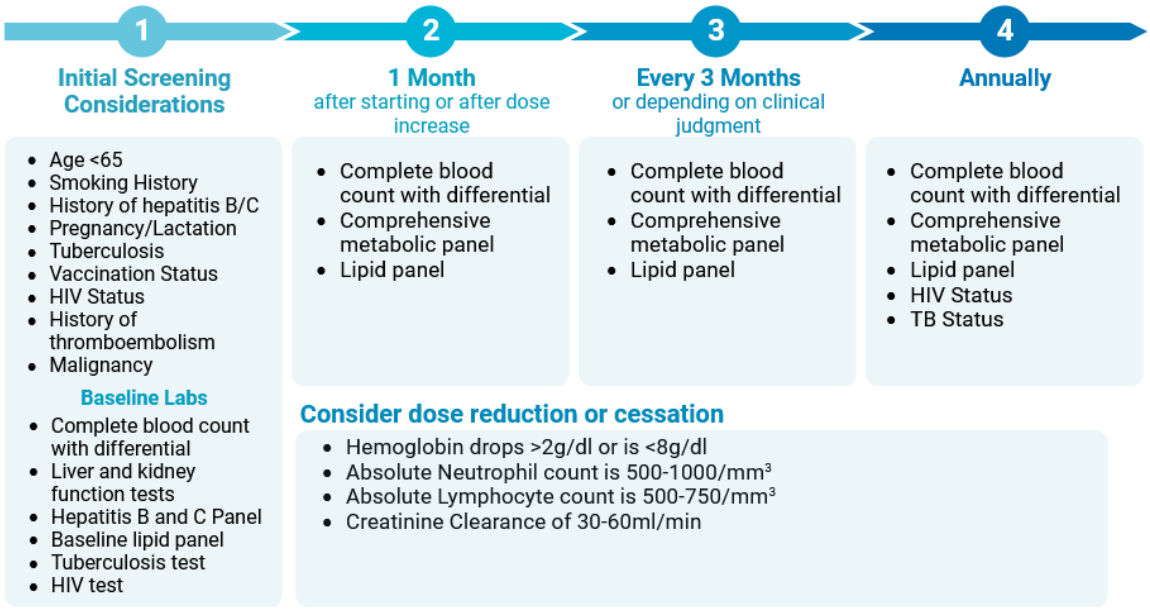
- Complete medical history
- Chest X-ray
- Baseline skin cancer check
- Complete blood exam (hemogram, liver enzymes, renal function, lipid levels, and serologies for HBV and HIV)
- Screening for tuberculosis
- Vaccination status check

During treatment:

- Regular skin examinations
- Periodic blood exams (1st and 3rd months, then periodically such as every 3 months)
- Pneumococcal and influenza vaccinations
- Herpes zoster virus vaccine in case of a positive serology

In practice, clinicians monitor for changes in infectious symptoms and rapid weight changes, and collect routine labs. In specific cases as mentioned above, clinicians may collect additional labs tailored to each patient's case and prior medical history. A sample monitoring schedule is included in Figure 1.

FIGURE 1. Possible laboratory monitoring approach.



CONCLUSION

JAKis have emerged as part of the dermatology toolbox, with impressive efficacy and a favorable safety and tolerability profile. With recent off-label usage being studied as well in over 35 different dermatological conditions, JAKis may be a solution for many difficult dermatological conditions.[30] JAKis are powerful, transformative medications that unfortunately have some rare concerns to be discussed with patients and monitored closely. Given the rarity of these safety concerns, however, with shared decision-making and careful monitoring, JAKis can be used with confidence for the appropriate patient.

DISCLOSURES

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REFERENCES

1. Spinelli FR, Meylan F, O'Shea JJ, Gadina M. JAK inhibitors: ten years after. *Eur J Immunol.* 2021;51(7):1615-1627.
2. Simpson EL, Papp KA, Blauvelt A, et al. Efficacy and safety of upadacitinib in patients with moderate to severe atopic dermatitis: analysis of follow-up data from the measure up 1 and measure up 2 randomized clinical trials. *JAMA Dermatol.* 2022;158(4):404-413.
3. Daniele S, Bunick C. JAK inhibitor safety compared to traditional systemic immunosuppressive therapies. *J Drugs Dermatol.* 2022;21(12):1298-1303.
4. Ytterberg SR, Bhatt DL, Mikuls TR, et al. Cardiovascular and cancer risk with tofacitinib in rheumatoid arthritis. *N Engl J Med.* 2022;386(4):316-326.
5. Damsky W, King BA. JAK inhibitors in dermatology: The promise of a new drug class. *J Am Acad Dermatol.* 2017;76(4):736-744.
6. Macchi P, Villa A, Giliani S, et al. Mutations of Jak-3 gene in patients with autosomal severe combined immune deficiency (SCID). *Nature.* 1995;377(6544):65-68.
7. Damsky WE, Choi J. Genetics of cutaneous t cell lymphoma: from bench to bedside. *Curr Treat Options Oncol.* 2016;17(7):33.
8. Clark JD, Flanagan ME, Telliez JB. Discovery and development of Janus kinase (JAK) inhibitors for inflammatory diseases. *J Med Chem.* 2014;57(12):5023-5038.
9. Samuel C, Cornman H, Kambala A, Kwatra SG. A Review on the safety of using Jak inhibitors in dermatology: clinical and laboratory monitoring. *Dermatol Ther.* 2023;13(3):729-749.
10. Papp K, Szepietowski JC, Kircik L, et al. Efficacy and safety of ruxolitinib cream for the treatment of atopic dermatitis: Results from 2 phase 3, randomized, double-blind studies. *J Am Acad Dermatol.* 2021;85(4):863-872.
11. Lee SD, Ahn HJ, Shin MK. A case series of acne following Janus kinase inhibitors in patients with atopic dermatitis. *JAAD Case Rep.* 2022;30:11-16.
12. Reich K, Teixeira HD, de Bruin-Weller M, et al. Safety and efficacy of upadacitinib in combination with topical corticosteroids in adolescents and adults with moderate-to-severe atopic dermatitis (AD Up): results from a randomised, double-blind, placebo-controlled, phase 3 trial. *Lancet.* 2021;397(10290):2169-2181.
13. Silverberg JI, Simpson EL, Thyssen JP, et al. Efficacy and safety of abrocitinib in patients with moderate-to-severe atopic dermatitis: a randomized clinical trial. *JAMA Dermatol.* 2020;156(8):863-873.
14. King B, Ohyama M, Kwon O, et al. Two phase 3 trials of baricitinib for alopecia areata. *N Engl J Med.* 2022;386(18):1687-1699.
15. Rosmarin D, Pandya AG, Lebwohl M, et al. Ruxolitinib cream for treatment of vitiligo: a randomised, controlled, phase 2 trial. *Lancet.* 2020;396(10244):110-120.
16. Armstrong AW, Gooderham M, Warren RB, et al. Deucravacitinib versus placebo and apremilast in moderate to severe plaque psoriasis: Efficacy and safety results from the 52-week, randomized, double-blinded, placebo-controlled phase 3 POETYK PSO-1 trial. *J Am Acad Dermatol.* 2023;88(1):29-39.
17. JAKne is on the horizon. Available at: https://www.aad.org/dw/dw-insights-and-inquiries/archive/2022/jakne-is-on-the-horizon. Accessed August 9, 2023.
18. Fadlalmola HA, Albadrani MS, Elhusein AM, et al. Effectiveness and safety of abrocitinib in patients with moderate-to-severe atopic dermatitis: a systematic review and meta-analysis of randomized clinical trials. *Dermatol Res Pract.* 2021;2021:8382761.
19. Simpson EL, Sinclair R, Forman S, et al. Efficacy and safety of abrocitinib in adults and adolescents with moderate-to-severe atopic dermatitis (JADE MONO-1): a multicentre, double-blind, randomised, placebo-controlled, phase 3 trial. *Lancet.* 2020;396(10246):255-266.
20. Rosmarin D, Passeron T, Pandya AG, et al. Two phase 3, randomized, controlled trials of ruxolitinib cream for vitiligo. N Engl J Med. 2022;387(16):1445-1455.
21. Chang PH, Huang SF, Chang PS, Yu Y. Safety considerations of systemic Janus kinase inhibitors in atopic dermatitis applications. *J Dermatol.* 2021;48(11):1631-1639.
22. Papierzewska M, Waśkiel-Burnat A, Rudnicka L. Safety of janus kinase inhibitors in patients with alopecia areata: a systematic review. *Clin Drug Investig.* 2023;43(5):325-334.
23. Scoviak M. How to explain JAK inhibitor warnings to patients. *Dermatol. Times.* 2022;43:18-18.
24. Bissonnette R, Call RS, Raoof T, et al. A maximum-use trial of ruxolitinib cream in adolescents and adults with atopic dermatitis. *Am J Clin Dermatol.* 2022;23(3):355-364.
25. Elmariah SB, Smith JS, Merola JF. JAK in the [black] box: a dermatology perspective on systemic JAK inhibitor safety. *Am J Clin Dermatol.* 2022;23(4):427-431.
26. Islami F, Siegel RL, Jemal A. The changing landscape of cancer in the USA - opportunities for advancing prevention and treatment. *Nat Rev Clin Oncol.* 2020;17(10):631-649.
27. European Medicines Agency. Meeting highlights from the Pharmacovigilance Risk Assessment Committee (PRAC) 24-27 October 2022. Available at: https://www.ema.europa.eu/en/news/meeting-highlights-pharmacovigilance-risk-assessment-committee-prac-24-27-october-2022. Accessed September 21, 2023.
28. Saeki H, Akiyama M, Abe M, et al. English version of Japanese guidance for the use of oral Janus kinase (JAK) inhibitors in the treatments of atopic dermatitis. *J Dermatol.* 2023;50(1):e1-e19.
29. Miot HA, Criado PR, de Castro CCS, et al. JAK-STAT pathway inhibitors in dermatology. *An Bras Dermatol.* 2023;98(5):656-677.
30. Corbella-Bagot L, Riquelme-McLoughlin C, Morgado-Carrasco D. Long-term safety profile and off-label use of JAK inhibitors in dermatological disorders. *Actas Dermosifiliogr.* doi:10.1016/j.ad.2023.08.002
31. Nash P, Kerschbaumer A, Dörner T, et al. Points to consider for the treatment of immune-mediated inflammatory diseases with Janus kinase inhibitors: a consensus statement. *Ann Rheum Dis.* 2021;80(1):71-87.

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