ADVANCES IN IBD

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JAK Inhibitor–Associated Acne in IBD: Recognition and Management

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G&H How often does acne develop in inflammatory bowel disease patients treated with Janus kinase inhibitors?

BC Acne is most commonly associated with the Janus kinase (JAK) 1–selective inhibitor upadacitinib (Rinvoq, AbbVie), and the risk appears to be clearly dose-dependent. In clinical trials, acne is reported in approximately 6% to 8% of patients receiving the 45-mg induction dose. However, real-world data suggest substantially higher rates, with acne reported in approximately 16% of patients treated with upadacitinib in a large international multicenter cohort study. Acne occurs predominantly during the higher-dose induction phase—typically 8 weeks in ulcerative colitis (with extension up to 16 weeks in partial responders) and 12 weeks in Crohn's disease—and may persist, although often with reduced severity, following dose reduction. As the dose is decreased, the incidence of acne declines to approximately 4% to 6% with the 30-mg dose and approaches placebo rates of around 2% to 4% with the 15-mg maintenance dose. In contrast, tofacitinib (Xeljanz, Pfizer), which is not JAK1-selective but instead inhibits JAK1 and JAK3 (with some JAK2 activity), is associated with lower rates of acne overall. In the same international cohort, acne was reported in approximately 4% of patients treated with tofacitinib, and rates in clinical trials are generally similar to placebo, at approximately 1% to 2%. Taken together, these data suggest that acne is not a uniform class effect but is more prominent with JAK1-selective inhibition and at higher doses, highlighting the importance of anticipatory counseling and proactive management.

G&H Which of those inflammatory bowel disease patients are at greatest risk of developing acne?

BC JAK inhibitor–associated acne is seen most commonly in younger patients, although it can occur across all age groups. There does not appear to be a consistent sex predilection, and a prior history of acne does not reliably predict risk. The strongest predictors are treatment-related, with acne occurring more frequently at higher doses—particularly during the induction phase—and early after treatment initiation, suggesting that risk is driven more by treatment exposure than by inherent patient factors.

G&H What is the typical clinical presentation of JAK inhibitor–associated acne?

BC In contrast to corticosteroid-induced acne, which is often monomorphic and predominantly comedonal, JAK inhibitor–associated acne typically presents as an inflammatory acneiform eruption. It most commonly involves the face—reported in up to 80% to 90% of cases in real-world cohorts—with less frequent involvement of the chest and back. The predominant lesions are papules and pustules. Comedones may be present but are not dominant, and nodules or cysts are relatively uncommon. These features distinguish JAK inhibitor–associated acne from classic acne vulgaris, which usually has a more mixed lesion profile and greater comedonal involvement. The affected skin is often erythematous and can appear irritated, with some patients describing a sunburn-like appearance or

associated pruritus. Most cases are mild to moderate in severity, although more inflammatory or extensive disease can occur, particularly during higher-dose induction therapy. Overall, JAK inhibitor–associated acne is a predominantly inflammatory acneiform phenotype that differs from both corticosteroid-induced and classic acne vulgaris, and can be disproportionately noticeable and distressing to patients despite often being clinically mild.

> Proactive counseling is essential when initiating JAK inhibitor therapy.

G&H When starting JAK inhibitor therapy, how should patients be counseled about the risk of developing acne?

BC Proactive counseling is essential when initiating JAK inhibitor therapy. Early in my experience, I likely underestimated the impact of acne, and some patients found it sufficiently distressing to consider discontinuing an otherwise highly effective treatment. Patients should be informed upfront that acne is a recognized, dose-dependent adverse effect, most commonly occurring during the higher-dose induction phase and often improving with dose reduction or appropriate treatment. I now routinely provide patients with a simple management plan at initiation, so they feel prepared to address symptoms early if they arise. It is also important to reassure patients that not all individuals develop acne, and for many, the benefits of disease control outweigh this side effect. Setting expectations early and equipping patients with a management strategy are key to maintaining adherence and avoiding unnecessary discontinuation of effective therapy.

G&H If acne develops with JAK inhibitor therapy, how should patients be managed?

BC Management should be proactive and stepwise, with the goal of controlling symptoms while maintaining JAK inhibitor therapy. For mild acne or as prophylaxis in higher-risk patients, a topical retinoid such as adapalene, tretinoin, or trifarotene can be initiated. For more established disease with papulopustular lesions, combination topical therapy is appropriate, most commonly a topical retinoid with either clindamycin or benzoyl peroxide, all of which have comparable efficacy in mild-to-moderate disease.

A key practical point is the use of the sandwich method to improve tolerability. Patients are advised to apply a gentle moisturizer, followed by a pea-sized amount of the active treatment, and then a second layer of moisturizer. These should be applied at night and left on overnight, with the skin gently cleansed in the morning. This approach reduces irritation and allows sustained use, which is critical for adherence. Treatment should be started gradually, typically 2 to 3 times per week, and increased as tolerated to nightly use. Daily sunscreen use is essential, and patients should avoid concurrent use of other potentially irritating topical agents unless advised. In practice, I provide patients with a simple treatment protocol at the time of JAK inhibitor initiation, including a prescription for combination topical therapy to use if acne develops. This allows early intervention and helps patients feel prepared to manage symptoms proactively. Early recognition and prompt topical treatment are key to preventing progression and maintaining adherence.

G&H If topical or combination treatment is not sufficient, what other therapeutic options are available?

BC For patients with more persistent or inflammatory disease, oral antibiotics such as doxycycline (typically 100 mg daily) can be used for 6 to 12 weeks, particularly during higher-dose induction. However, relapse is common once the antibiotics are discontinued, and there is understandable reluctance to use prolonged courses in patients with inflammatory bowel disease (IBD). For this reason, there should be a low threshold for dermatology referral in patients with ongoing or distressing acne.

Dermatology involvement is particularly important for consideration of oral isotretinoin in refractory or more severe cases. Although there were historical concerns regarding isotretinoin use in patients with IBD, current evidence is reassuring, and it is highly effective and generally well tolerated in this setting. Importantly, JAK inhibitor therapy should usually be continued, as acne is manageable with appropriate dermatologic treatment and is rarely a reason to discontinue an otherwise effective therapy.

G&H Could you expand on when these patients should be referred for dermatologic consultation?

BC Referral should be individualized based on severity, patient preference, and response to initial therapy. In many cases, acne develops during the higher-dose induction phase of upadacitinib and may improve with dose reduction or over time, so immediate referral is not always

necessary. However, this needs to be balanced against the impact on the patient, as even a relatively short period of visible acne can be distressing, particularly for younger individuals.

I generally manage mild-to-moderate cases initially with topical or short-course oral therapies, but there should be a low threshold for dermatology referral in patients with persistent, more inflammatory, or distressing acne, or in those who are not responding to first-line treatment. Early referral is also appropriate for patients with a prior history of difficult-to-control acne or those who express significant concern about their skin.

Access to dermatology services varies by region, and in settings where access is limited, gastroenterologists may need to take a more proactive role in management. Ultimately, the goal is to ensure timely escalation of care when needed while supporting patients to remain on effective JAK inhibitor therapy.

G&H If the acne is particularly persistent or severe, should JAK inhibitor therapy be reduced or discontinued?

BC In general, no. Full induction dosing is important to achieve disease control, and reducing therapy prematurely risks treatment failure and disease flare. For this reason, I would not typically reduce or discontinue JAK inhibitor therapy solely because of acne.

In most patients, upadacitinib 30 mg remains the mainstay of maintenance therapy, particularly in those with more severe or treatment-refractory disease. Although lower doses such as 15 mg may be appropriate in selected patients with milder disease, dose reduction is usually guided by disease control rather than the presence of acne.

Instead, acne should be managed with appropriate dermatologic therapies, including topical, oral, and specialist-directed treatments as needed. Patients should be reassured that improvement often occurs with time or dose reduction following induction, and that even more persistent cases can be effectively treated. With appropriate counseling and management, acne is rarely a reason to discontinue an otherwise highly effective therapy and should not compromise optimal IBD treatment.

G&H What further research is needed?

BC The mechanisms underlying JAK inhibitor–associated acne are not yet fully understood. The higher rates observed with JAK1-selective inhibition, particularly with upadacitinib, suggest that JAK1-mediated pathways may play a more direct role compared with less-selective agents such as tofacitinib, although this remains to be clearly defined. There is likely a multifactorial process involving alterations in follicular keratinization, sebaceous gland activity, innate immune signaling, and the skin microbiome.

Emerging data suggest that JAK inhibition may influence epidermal growth factor receptor pathways and shift immune responses toward T-helper 1 and 17 profiles, which could contribute to inflammation and dysbiosis within the skin. In addition, interactions between the JAK-STAT pathway and androgen signaling may influence sebum production. However, these mechanisms remain incompletely understood, and further translational studies are needed to better characterize the pathophysiology.

From a clinical perspective, prospective studies are needed to better define incidence, risk factors, and optimal management strategies in real-world populations. Ultimately, a clearer understanding of the underlying biology may allow for more targeted prevention and treatment approaches. Although attention is often focused on cardiovascular risks with JAK inhibitors, acne is one of the most impactful adverse effects for patients—particularly younger individuals—and, if not anticipated, may affect adherence. With appropriate counseling and proactive management, however, it remains a highly manageable side effect that should not limit the use of these highly effective therapies.

Disclosures

Associate Professor Christensen has received consultant and advisory board fees from AbbVie, Pfizer, and Gilead.

Suggested Reading

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