Skin Therapy Letter ©
January 2024 Supplement
EDITOR: DR. RICHARD THOMAS

Real-World Insights from Atopic Dermatitis Patients Treated with Abrocitinib

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Disclosures and Acknowledgment: The authors conducted the real-world series, supported by an educational grant from Pfizer Canada. The authors acknowledge and thank Sophie Guénin, MSc, for her assistance in preparing this manuscript.

ABSTRACT

Background: Atopic dermatitis (AD) is a heterogeneous disease characterised by epidermal barrier dysfunction and immune dysregulation. It commonly presents with pruritus and eczematous lesions that significantly impact quality of life. Abrocitinib is a JAK inhibitor approved for treatment of refractory, moderate-to-severe AD in patients 12 years and older.

Objectives: This real-world case series intends to illustrate a variety of moderate-to-severe AD patient cases to help guide discussions around abrocitinib and describe its treatment strategies used by experts in the field.

Methods: Expert panel members were recruited from across Canada to discuss varying clinical AD phenotypes seen in their clinic. Guided by literature, the panel shared their opinions and insights to provide a holistic view of the overarching question, "Which patients are good abrocitinib candidates?"

Results: The panel reported on ten real-world patient cases that detailed the use of abrocitinib in biologic naïve patients, refractory AD patients, complex medical patients, and those with differing treatment goals. Cases aim to demonstrate the broad use of abrocitinib in patients with AD, offering a learning point with each real-world case.

Conclusions: Each presented real-world case reflects the panel's clinical experience. Panel members concluded that abrocitinib is a fast-acting, safe, and efficacious therapy for a wide variety of AD patients with differing disease severities and comorbidities. Treatment with abrocitinib may cause transient nausea that frequently resolves by taking it with food. Overall, patients are highly satisfied with the treatment.

Key words: atopic dermatitis, real-world cases, JAK inhibitor, abrocitinib

Introduction

Atopic dermatitis (AD) is a heterogeneous, chronic inflammatory skin disease characterized by epidermal barrier breakdown, immune dysregulation, and significantly reduced quality of life (QoL).[1] Approximately 3.5% of the total Canadian population and 25.4% of the pediatric Canadian population is affected with AD.[1,2] This relapsing condition may present as dry, erythematous, sensitive skin or pruritic, excoriated, eczematous, and painful patches with weeping erosions and prurigo nodules.[1] About one-third of AD patients are affected by atopic comorbidities such as asthma, food allergy, and hay fever.[3]

Patients with AD report impaired quality of life that limits their daily lives and social interactions.[3] Pruritus is reported as the most burdensome symptom of AD, with 95% of patients reporting itch as the most important indicator of treatment response.[4] Other burdensome symptoms included excessive dryness, scaling, inflamed skin, skin pain, and sleep disturbance.[4] Impaired barrier function in AD is largely attributed to filaggrin dysfunction.[5] Meanwhile, immune dysregulation in AD largely stems from T-helper (Th)2 cell cytokines, interleukin (IL)-4 and IL-13, in its acute phase and Th1 skewing in chronic disease.[6] IL-22 and IL-17-producing T cells have also been implicated in the pathogenesis of AD.[6]

Systemic Treatment for Moderate-to-Severe AD

The consensus-based European guidelines for the treatment of AD recommend proactive therapy with topical calcineurin inhibitor (TCI) or topical glucocorticosteroids (TCS) for moderate AD along with narrow band (nb) UVB phototherapy, psychosomatic counseling, and climate therapy.[6] For severe AD, the guidelines recommend hospitalization in specific cases, systemic immunosuppression with cyclosporine, short-course oral glucocorticosteroids, methotrexate, azathioprine, or mycophenolate mofetil.[7] Biologic monoclonal antibody therapies such as dupilumab are also recommended for severe AD patients.[7]

Dupilumab is an anti-IL-4-receptor α monoclonal antibody that inhibits the signaling of both IL-4 and IL-13.[6] Since the guidelines were published in 2018, an additional monoclonal antibody therapy, tralokinumab, an IL-13 inhibitor, has been approved for AD treatment in Canada, as well as two janus kinase inhibitors (JAK) inhibitors (JAKi): abrocitinib and upadacitinib.[6]

Newer topicals such as the topical PDE4 inhibitor, crisaborole, has also been recently introduced for AD treatment, and ruxolitinib, a topical JAK inhibitor, not yet available in Canada.[6,7]

Abrocitinib & JAK Inhibitors (JAKis)

JAKis are a new class of systemic treatments for AD that function by blocking downstream cytokine inflammatory signaling.[6] Abrocitinib and upadacitinib are once daily, oral JAK1 inhibitors that block IL-4 and IL-13, cytokines involved in the pathogenesis of AD, downstream.[8,9] Abrocitinib is available in three doses: 50 mg, 100 mg, and 200 mg, and is approved for moderate-to-severe AD patients aged 12 and older.[9] In pivotal trials JADE MONO-1 and JADE-MONO-2, abrocitinib demonstrated significant pruritus reduction within two weeks.[10,11] In a phase 3 comparative clinical trial, JADE-COMPARE, abrocitinib 200 mg demonstrated greater IGA response and itch response at endpoint than dupilumab.[12] As with all JAK inhibitors, abrocitinib has inherited a black box warning for thrombosis, major adverse cardiovascular events (MACE), and malignancy. Despite this, clinical trial safety analysis at 48 weeks of both the 100 mg and 200 mg abrocitinib dosage groups showed only 0% to 0.3% incidence of the following: nonmelanoma skin cancer (NMSC), malignancy, MACE, or VTEs.[13]

Upadacitinib is approved for the treatment of AD, rheumatoid arthritis, psoriatic arthritis, ulcerative colitis, Crohn's disease, ankylosing spondylitis, and non-radiographic axial spondylarthritis.[9] In refractory moderate-to-severe AD, upadacitinib is approved in Canada for ages 12 and up with two dosing options: 15 mg and 30 mg; recommendations suggest initiating treatment at 15 mg prior to titrating up to 30 mg.[14]

As more treatments become available, it will be important for clinicians to partner with patients in a treat-to-target (TTT) paradigm to identify the optimal AD treatment for each patient.[15]

Methods

Aim of the Project

This real-world case series illustrates a variety of patients with moderate-to-severe AD treated with abrocitinib. The cases outline the TTT paradigm and demonstrate patient-provider partnerships that highlight patient priorities and ideal treatment options. Expert panelists' thought processes, reasoning, and rationales are detailed in the following patient cases to serve as a guide for licensed providers who treat patients with AD.

Steps in the Process

The project was conducted in the following five steps: 1) project definition and expert panel selection 2) data collection and preparation of patient cases, 3) patient case discussion and selection for publication 4) literature review to support selected cases 5) drafting, review, and finalization of the manuscript.

Role of the Panel

The panel consisted of 10 dermatologists practicing in Canada who commonly care for patients with AD. Panelists were chosen from 3 provinces in Canada to capture geographical and provincial differences in dermatological practice. During the Dermatology Update conference on April 30th, 2023, in Vancouver, panelists met to report on and discuss clinical cases of AD patients who were suitable candidates for abrocitinib treatment.

The panel used the following template to gather insight through a case-based approach:

a) Initial Steps in Treatment
   i) Prevention and Education
   ii) Patient-Focused Treatment StrategiesTreatment Options
b) Treatment Options
c) Special Considerations
d) Advantages of Abrocitinib for these Cases

Panelists were asked to select two patient cases from their clinical practice to share and discuss. In the second half of the meeting, panelists examined and collaborated to select ten real-world cases for inclusion in the publication. Panel members agreed that real-world cases should focus on common AD scenarios encountered in the clinic. The publication was prepared and reviewed by the panel.

Experience Gathering and Atopic Dermatitis Outcome Measures

Suggested information and outcome measures to present included patient demographics, concomitant medications, comorbidities and Investigators' Global Assessment (IGA) score, Eczema Area and Severity Index (EASI), Peak Pruritus Numerical Rating Scale (PP-NRS), and patient-reported Dermatology Life Quality Index (DLQI) at weeks 0, 2, and 4 (+/- 5 days) of abrocitinib treatment (Appendix 1). Panelists were also requested to report patient compliance, treatment satisfaction, and any adverse events experienced.

Results

Selected Real-World Cases

The panel selected ten cases to demonstrate the real-world use of abrocitinib in a diverse group of patients with varying skin concerns, past treatment failures, severity, and comorbidities. The findings reflect real-world clinical use of oral abrocitinib and patient treatment outcomes.

Case 1: The recalcitrant, severe AD patient with intense pruritus

A 31-year-old Caucasian, Fitzpatrick Skin Type (FST) 1, female struggling with severe, recalcitrant AD for the past 18 years presented with reported worsening anxiety, avoidance of social activities, and sleep interruption due to debilitating pruritus. Intense pruritus led to diffuse excoriations and multiple skin infections. Her EASI was 22, and DLQI 20. Over the years, the patient had tried TCS, TCI, crisaborole, nbUVB phototherapy, and systemic therapies: prednisone, methotrexate, and intramuscular triamcinolone injection. She had developed striae on her abdomen and arms from frequent TCS use and continued to suffer from intractable itch. The patient started dupilumab but discontinued it after three months due to repeated flu-like symptoms and nasopharyngitis. Having failed first, second-, and third-line therapies for AD, the patient was started on abrocitinib, 200 mg daily. The rationale for beginning abrocitinib at the higher dose was the failure of previous treatment and the patient's primary complaint of incessant itch. Within eight weeks, she saw rapid improvement; her EASI was 8 and DLQI 4. At week 16, her EASI was 2 and DLQI 0. When asked about her experience, the patient reported that abrocitinib had "life-changing" effects after only one month of treatment. No adverse events occurred, and the patient was reduced to 100 mg abrocitinib daily without exacerbation.

Learning point: Abrocitinib is a fast-acting, effective, and safe treatment option for patients with longstanding, recalcitrant AD. It may be an option for patients who have failed many prior therapies. Abrocitinib therapy can improve patients' QoL and reduce the need for TCS and other adjunct therapies, thereby sparing patients from the undesirable adverse effects of these treatments.

Case 2. The biologic-naïve patient

Since early childhood, a 55-year-old Caucasian (FST1) salesman with hypertension, hypercholesterolemia, and prediabetes had suffered from severe AD that affected extensive parts of his head, neck, trunk, and extremities. Since starting amlodipine and rosuvastatin for his comorbid conditions, the patient reported worsening xerosis and diffuse erythema.

While biologic naïve, he had previously tried various moisturizers, TCS, TCI, phototherapy, and oral antihistamines with only modest benefit. Despite the multimodal treatment approach, the patient continued to have frequent visits to the Emergency for infections and exacerbations. His condition greatly impacted his work and social interactions as well as his psychological and sexual health. Given his frequent business travel, busy family life, and needle aversion, the patient expressed interest in a convenient, effective treatment that would improve his worsening xerosis and eliminate the requirement for additional therapies. For these reasons, the patient was started on 100 mg abrocitinib. Within two weeks, the patient's IGA score reduced from 3 to 2, EASI score from 4 to 2 and PP-NRS score from 8 to 3. Two weeks later, the patient saw continued improvement with an IGA score of 1, EASI score of 1, and PP-NRS score of 2. Rapid reduction in itch made the patient extremely satisfied with abrocitinib monotherapy. He did not experience any adverse events and was "thrilled" with his outcome. The patient remains on abrocitinib 100 mg with the option to increase to 200 mg, if necessary.

Learning point: JAKi is an option for biologic-naïve patients for whom self-injection does not correspond to their lifestyle. Patients who travel frequently or lead busy lifestyles may have difficulty transporting subcutaneous injections that must be stored in cool temperatures or having the proper setting to self-inject. Further, some patients are needle-phobic and would prefer an effective, oral treatment option.

Case 3. The patient with post-inflammatory hyperpigmentation

A 29-year-old Southeast Asian (FST4) female presented with sensitive skin, longstanding AD and significant post-inflammatory hyperpigmentation (PIH) around her eyes and on her arms. She had been treated with multiple courses of prednisone with a good response but would predictably flare 2-4 weeks after steroid discontinuation. Having suffered from AD since infancy, she reported the post-inflammatory hyperpigmentation from AD as her most bothersome symptom. Previous treatments included TCS, TCI, and crisaborole. She saw a slight improvement in her skin and pruritus with topical therapy in conjunction with oral antihistamines. Despite mild improvement, she was still desperate for a long-term, effective solution. Her primary care physician had recently made her aware of abrocitinib and encouraged her to seek evaluation by a dermatologist. As a young, single female without any plans for pregnancy in the near future, the patient was a good candidate for abrocitinib and was started on abrocitinib 100 mg. Her IGA was 3 at baseline, EASI score was 4, and PP-NRS score was 8. By week 4, her IGA, EASI, and PP-NRS scores were all 1, and

she felt happy and hopeful that PIH marks would continue to fade with time. No compliance issues or adverse reactions were reported.

Learning point: Patients with skin of colour are at increased risk for PIH. Consistent AD treatment with abrocitinib and control of AD, results in PIH improvement and improved mood and QoL. It also reduces inappropriate, long-term use of oral corticosteroids. In females of childbearing age, it is also important to inquire about pregnancy and/or contraceptive use. Pregnancy is a contraindication for abrocitinib use. It should be recognized that contraceptive use may lead to low risk of VTE. Family planning should be discussed with all patients of childbearing potential who are contemplating treatment with abrocitinib.

Case 4. The atopic patient with barriers to treatment access

A 22-year-old (FST2) male with lifelong AD and comorbid atopic diseases (hay fever, asthma, and urticaria) presented with worsening pruritus. Physical exam revealed symmetric, generalized excoriated red, scaly patches with significant lichenification on his bilateral extremities, face, scalp, and back. Working as a dishwasher, the patient reported wearing gloves most of the day to protect his skin from irritating soaps or dryness. Despite his precautions, his skin began impacting his ability to work. He reported skin burning, discomfort, unbearable itch, and skin pain, which frequently disrupted his sleep. At presentation, while on methotrexate, his EASI was 23, IGA score 4, and DLQI 18, with 31% of his body surface area (BSA) affected by AD (Figure 1A [back – face]). Throughout his lifetime, the patient had tried lifestyle modifications such as fragrance-free, hypoallergenic detergent, gentle cleansers, moisturizer application every 2 hours as well as TCS, TCI, calcipotriol gels, oral antihistamines, systemic corticosteroids, and 1-year of methotrexate. Given the severity of the patient's AD and worsening QoL, the plan was to begin biologic monoclonal antibody therapy. Unfortunately, the patient could not gain access to dupilumab or tralokinumab through his insurance, compassionate drug program, or patient assistance programs. Fortunately, the patient was able to access 100 mg abrocitinib and was thus started on this oral therapy in lieu of biologic therapy. The 100 mg dose was chosen since the patient and his mother were risk-averse and wished to try the 100 mg dose first, increasing to 200 mg only if the 100 mg dose was not sufficient. Two weeks prior to starting abrocitinib, the patient was given his first shingles vaccine. At his 11-week follow-up visit, the patient reported no skin pain and minimal itch with only slight residual erythema on his face (EASI 1.1, IGA 1) (Figure 1B [face – back]). He reported that he could sleep through the night and was able to stop using topical therapies and antihistamines. Of note, the patient experienced mild initial nausea and abdominal pain that abated within the first few weeks of treatment. He had his second shingles vaccine after commencing abrocinitib treatment.

Learning point: Abrocitinib is readily accessible to some patients who are unable to gain coverage for monoclonal antibody therapies such as dupilumab and tralokinumab. While addressing itch, abrocitinib also effectively targets skin pain. It is important to consider shingles vaccination prior to abrocitinib start. The second dose of the vaccine can be given 1-6 months later.[16] Nausea may also be an important adverse effect to discuss with patients. Nausea is frequently transient and can be improved by taking abrocitinib with food.

Figure 1: 22-year-old male with severe AD
(Photos courtesy of Lyn Guenther MD, FRCPC)

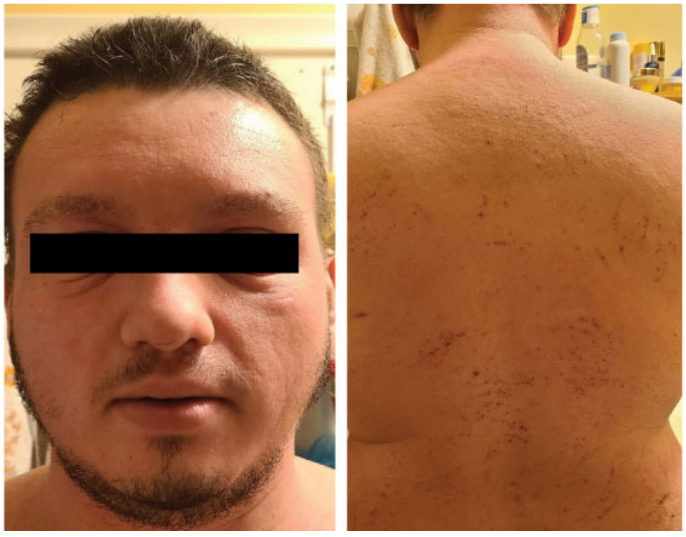

Figure 1A: Xerosis, excoriations, and eczematous lesions over face and back with appreciable Dennie-Morgan lines, prior to abrocitinib treatment.

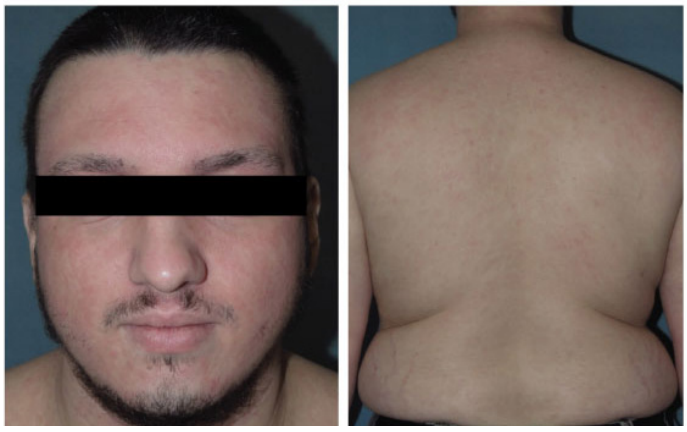

Figure 1B: Significant improvement in AD lesions after 11 weeks on daily 100 mg abrocitinib therapy.

Case 5. The complex medical patient with persistent AD-related pruritus

The retired aerospace worker, two-time widower, and former smoker the 63-year-old man, has atopic triad and comorbid anxiety, depression, hyperlipidemia, hypertension, and a history of stroke. He presented with persistent AD, severe pruritus, and atopic keratoconjunctivitis (AKC). His concomitant medications included: citalopram, atorvastatin, ezetimibe, perindopril, and clopidogrel. Despite his other conditions, the patient was most concerned with his pruritus as it had prevented him from sleeping, exercising, socializing, dating, and working. He had only slept through the night three times in the past year. Embarrassed by his skin, he has not been in a swimming pool for over ten years. His EASI was 50, DLQI 26, IGA 4, PP-NRS 10, and BSA 49% (Figure 2A [face – back – legs]).

Having tried numerous moisturizers, TCS, 12 years of nbUVB phototherapy, antihistamines (up to 4 times approved dosing), and multiple cycles of prednisone, he continued to suffer from his skin condition. He was enrolled in a lebrikizumab clinical trial, which helped his AD and pruritus but did not clear his face and neck. However, during the clinical trial, he suffered a non-treatment-related posterior cerebral artery infarct, which has deterred him from future biologic use. The patient redeveloped generalized erythema, lichenification, and scaling off the biologic.

The rationale for starting abrocitinib stemmed from numerous conversations with the patient, during which he highlighted his preference for QoL over mere survival. He was desperately seeking to sleep through the night and regain control of his life. Use of immunosuppressants such as methotrexate and cyclosporine were contraindicated in this patient due to his heavy alcohol use and hypertension, respectively. Given his AKC, dupilumab, and tralokinumab were eliminated as options to reduce the risk of worsening his ocular involvement. The lower perceived rates of MACE and VTE events with abrocitinib compared to upadacitinib led to the patient being started on abrocitinib. Two weeks prior to starting abrocitinib, he received his first dose of the shingles vaccine. The decision was made to start at 50 mg of abrocitinib to mitigate any potential risk for drug interactions or adverse cardiovascular events. He reported that during his first week on abrocitinib, he was able to sleep itch-free every night and noticed smoother skin texture. After one month of monitoring without any adverse events nor appreciable changes in blood values, the patient was increased to 100 mg abrocitinib. After two weeks on 100 mg abrocitinib, the patient's EASI was reduced to 6.4, DLQI to 6, IGA to 2, PP-NRS to 1.5, and BSA to 10% (Figure 2B [face – back – legs]). The patient remains on 100 mg of abrocitinib with good control of AD, itch, and good tolerability.

Learning point: Assessment of risks and benefits with a patient remains an important consideration in the TTT paradigm for AD treatment. While extra precautions must be considered in a complex medical patient, their complexity does not preclude

Figure 2: 63-year-old medically complex male with anxiety, depression, hyperlipidemia, hypertension, and a history of stroke
(Photos courtesy of Lyn Guenther MD, FRCPC)

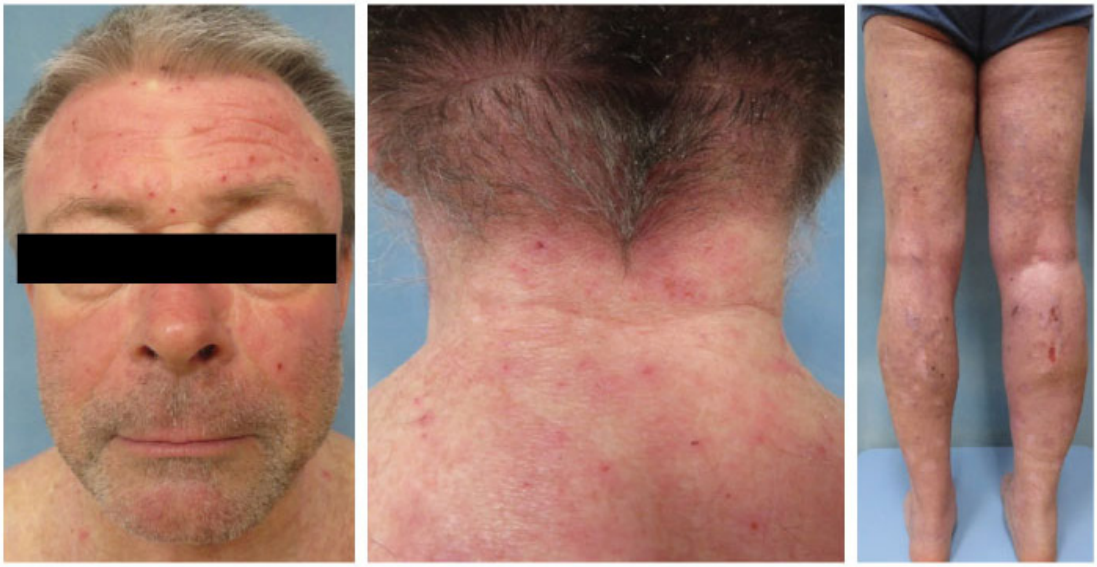

Figure 2A: Before abrocitinib

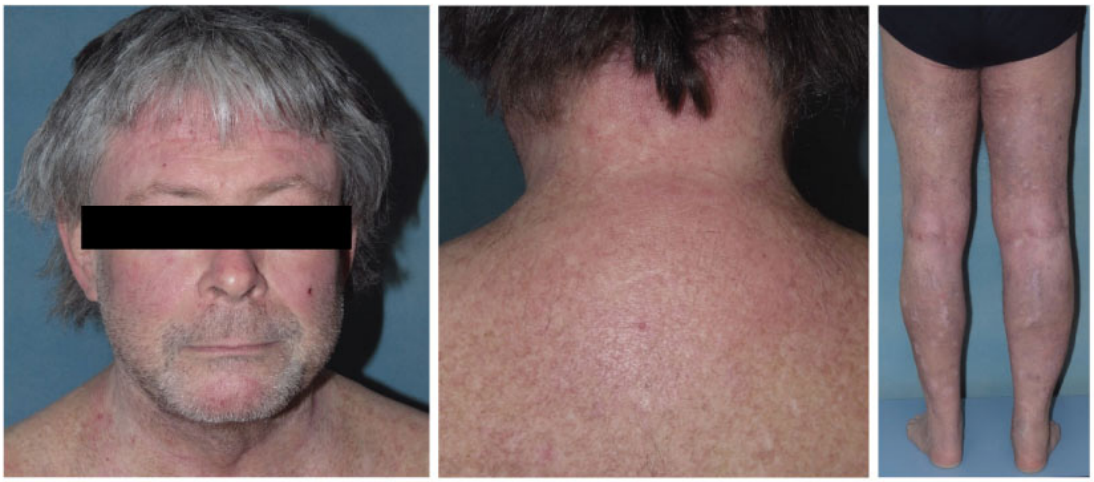

Figure 2B: After six weeks of abrocitinib therapy (50 mg x 4 weeks, followed by 100 mg x 2 weeks)

them from abrocitinib therapy. Titration of the abrocitinib dose, starting at 50 mg, may also help minimize any potential risk while simultaneously allowing patients to benefit from treatment.

Case 6. The busy professional biologic naïve patient needing a fast-acting therapy

A 38-year-old lawyer of Asian (FST4) descent presented to the clinic in search of a rapid solution for his AD. He had no significant past medical history other than lifelong AD. At presentation, his DLQI was 28, EASI was 50, and IGA was 4 (Figure 3A [face – legs]). He had only previously tried betamethasone 0.1% cream and prednisone with mild, transient improvement after each therapy. Despite being naïve to systemic therapies beyond prednisone, he wanted a quick, easy solution to his skin condition that would not impact his busy schedule and allow him to enter conference rooms with confidence. Understanding the patient's aggressive treatment goals, the provider started him on 200 mg of abrocitinib with concomitant use of tacrolimus ointment 0.1% twice daily, as needed. Four weeks later, the patient returned with 90% skin clearance, including complete clearance on his face and only post-inflammatory erythema remaining on his extremities (Figure 3B face – legs]. At his 6-month follow-up, he had clear skin (Figure 3C [legs]). While he was given the option to reduce to the 100 mg dose, the patient has been reluctant to decrease the dosage given his rapid, lasting response to the current abrocitinib 200 mg regimen.

Learning point: The 200 mg dose of abrocitinib may be an optimal first-choice therapy for select patients. The JAKi allows for fast results, and the ease of a once-daily pill makes it an ideal option for working professionals with hectic lives. The 100 mg and 200 mg abrocitinib dosing options also allow patients to choose how aggressively they would like to treat their AD while relying on their provider to help them weigh the risks and benefits.

Case 7. The dupilumab failure AD patient

A 62-year-old (FST3) male with generalized AD since adolescence was initiated on 100 mg of abrocitinib therapy. Having struggled most of his adult life with daily TCS and emollient regimens, the patient was frustrated as his AD had a determinantal impact on his daily activity, social life, sports participation, and sleep. He had previously tried one year of dupilumab treatment with an inadequate response. Prior to starting abrocitinib, his EASI was 12, IGA 3, and PP-NRS 8. After two weeks on abrocitinib, the patient had an EASI of 3.2, IGA 1, and PP-NRS of 1. Despite reporting nausea from therapy, he expressed 8 out of 10 satisfaction, given his dramatic skin response. At his 4-week follow-up, the patient had an EASI of 2.1, IGA 1, and PP-NRS of 1, with resolution of his nausea and no further adverse events.

Learning Point: Abrocitinib is an ideal step-up therapy for patients who have an inadequate response to dupilumab. The differing mechanisms of action of abrocitinib and dupilumab make the trial of abrocitinib worthwhile in a patient who may have failed IL-4 receptor blockade. Nausea, when and if it occurs, often resolves spontaneously.

Figure 3: 38-year-old biologic naïve male
(Photos courtesy of Andrei Metelitsa MD, FRCPC)

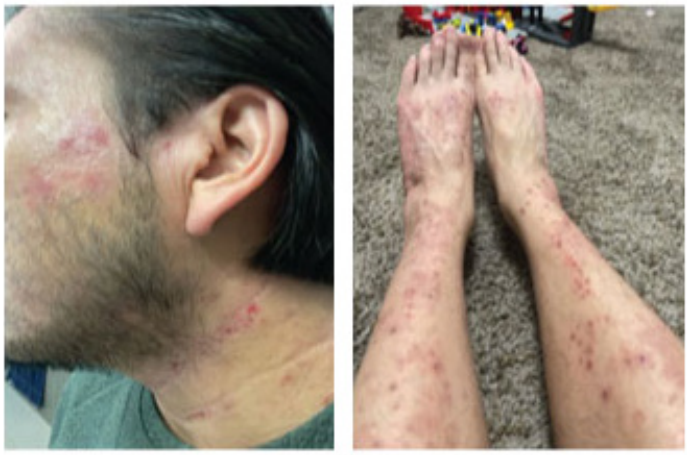

Figure 3A. Eczematous lesions on face and legs before abrocitinib

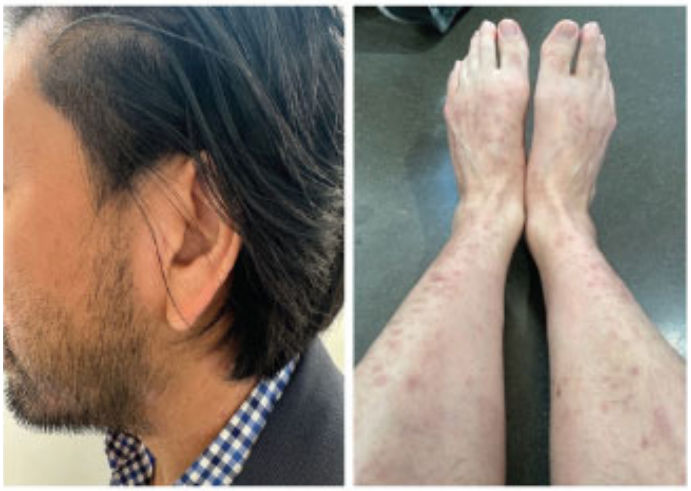

Figure 3B. After four weeks of 200 mg abrocitinib therapy

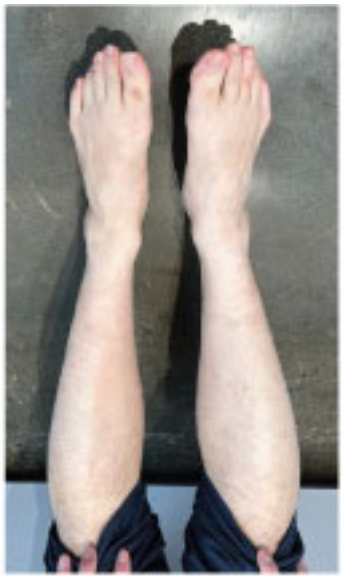

Figure 3C. After six months of 200 mg abrocitinib therapy

Case 8. The patient intolerant to dupilumab

Struggling with AD since childhood, a 47-year-old female (FST4) with mild asthma and severe AD presented after 16 months of dupilumab therapy. While dupilumab was effective for the first year, her skin failed to maintain its initial response. She had also developed persistent conjunctivitis secondary to dupilumab use. AD covered her trunk, face, and proximal extremities and often caused her to miss work and avoid romantic and social relationships. She struggled to sleep through the night without scratching. In the past, she had tried topical tacrolimus and clobetasol without any lasting improvements. The rationale for starting 100 mg abrocitinib was intolerance and failure to maintain response to dupilumab. On Day 0, her EASI was 35, IGA 4, and PP-NRS score 8. Upon starting abrocitinib treatment, the patient reported mild nausea that improved when the tablet was taken with food. By week 4, the nausea had resolved, and the patient had an EASI of 16, IGA of 2, and PP-NRS of 3. She reported feeling more confident in her skin, with reduced pruritus and improved sleep and quality of life. Without experiencing any other side effects, the patient remains on 100 mg of abrocitinib and is highly satisfied with the treatment.

Learning Point: The side effect profile for abrocitinib does not include conjunctivitis or any other ocular effects, making it ideal for patients sensitive to the adverse reaction of dupilumab or tralokinumab or patients with comorbid ocular conditions. Lastly, nausea is a common adverse effect of abrocitinib therapy that usually resolves with time and may be mitigated by taking the medication with food.

Case 9. The patient with adult-onset AD

The 49-year-old (FST2) male presented with a 4-year history of adult-onset AD. He had a remote history of alcohol-induced pancreatitis but no other comorbidities. Expressing high levels of frustration with his inadequate sleep and intractable itch, the patient wanted rapid control of his pruritic skin. He had tried TCS, TCI, and cyclosporine without sustained skin improvement, and he experienced deterioration of his kidney function from cyclosporine. His EASI was 25, IGA 4, and PP-NRS score 9. The rationale for starting abrocitinib was that the patient was desperate for rapid control. While upadacitinib was considered for rapid pruritus relief, the patient's history of alcoholism made abrocitinib a safer option as it does not require monitoring of liver function tests. After four weeks of abrocitinib 100 mg daily use, the patient no longer required use of TCS and had an EASI of 1.2, IGA of 2 and PP-NRS of 4. He was extremely satisfied with treatment and tolerated the treatment without any adverse events.

Learning Point: Immunosuppressants such as cyclosporine and methotrexate have long been used to treat AD, although Health Canada does not approve them for treating AD. In addition, these immunosuppressants are often associated with kidney toxicity (cyclosporine), liver and bone marrow toxicity (methotrexate) as well as malignancy (both medications). Thus, long-term use of these immunosuppressants is not appropriate for long-term use in AD patients. In addition, the increasing availability of efficacious, safe, and targeted treatments for AD makes the use of broad immunosuppressants inappropriate.

Case 10. The AD patient switching from another JAK inhibitor

The 21-year-old (FST4) male university student presented with severe AD involving his torso and limbs. His AD first presented in childhood. He had a positive family history of atopic disease. Having tried TCS, crisaborole, and a 2-year course of methotrexate without improvement, the patient was started on upadacitinib. While the upadacitinib helped to significantly clear his skin, he developed acneiform lesions on his face which led to treatment cessation. His AD returned upon upadacitinib cessation (EASI 24, IGA 4, and BSA 30%). A healthy young man, the patient was offered to start at the higher 200 mg dose of abrocitinib, which should allow for faster control of his AD and a quicker return time to being more productive at school. At his 4-week follow-up, the patient had an EASI of 1.2, IGA of 2, and BSA of 3%, with the most considerable improvement on his face and neck. The patient reported mild nausea a few hours after taking abrocitinib; however, the nausea abated when he started taking it with food. Interestingly, he did not experience acne on abrocitinib.

Learning Point: Abrocitinib is a good treatment option for patients who had adverse reactions to another JAKi. There is a low risk of acne as an adverse reaction to abrocitinib versus upadacitinib. Thus, if a patient develops acne on one JAKi, it does not preclude them from trying abrocitinib.

Discussion

Real-world cases provide highly impactful insight into patient and provider experience with a new treatment. Without a cure, the AD treatment goal is aimed at reducing symptoms to a level that has minimal or no impact on patient QoL. In the patient cases discussed above, all patients had previously tried and failed topical therapies such as TCS, TCI, and various emollients and moisturizers. While some had tried systemic therapies, a few were naïve to systemic AD therapies prior to starting abrocitinib. Each patient discussed had a complete or near complete response by week 4 of abrocitinib therapy and reported significant satisfaction with treatment. This real-world case discussion provides invaluable insight into abrocitinib use in a diverse population of Canadian patients suffering from moderate-to-severe AD.

Biologic Naïve Patients

The 2018 consensus-based European guidelines for the treatment of adult AD only recommend the use of dupilumab in severe AD.[6] While JAKi's were not yet approved when these guidelines were released, clinical experience suggests that many practices do not recommend JAKi until a patient has failed all other standard therapies, such as dupilumab and other immunosuppressants. However, panel members discussed five cases of biologic-naïve patients with safe, efficacious, and accessible treatment with abrocitinib. The patients' successful treatment with abrocitinib as a second-line therapy after topicals suggests that requiring a patient to cycle through a biologic prior to a JAKi may be unnecessary. Biologic naïve patients reported being "thrilled" and "very satisfied" with abrocitinib oral dosing that provided rapid itch relief and improvement in QoL.

Dupilumab Failed/Intolerant Patients

Another recurring rationale for initiating a patient on abrocitinib therapy was previous inadequate response or intolerance to dupilumab treatment. Three patients presented had previously been on dupilumab and stopped either due to inefficacy, failure to maintain response, or secondary conjunctivitis. Switching to abrocitinib after prior dupilumab therapy had no effect on the JAKi's efficacy. Each patient saw near complete response to abrocitinib on either 100 mg and 200 mg dosing approaches. Failure to maintain response to dupilumab may stem from the monoclonal antibody's ability to trigger the development of anti-drug antibodies (ADA).[17] Some reports show a 7.61% ADA incidence in dupilumab studies, which may be higher in sporadic dupilumab injectors.[18] Abrocitinib, a small-molecule JAK inhibitor, does not trigger the production of ADAs, which may contribute to greater maintenance of initial response.[18] In one-year clinical trials, JADE EXTEND for abrocitinib and LIBERTY AD CHRONOS for dupilumab, 60.5% of patients on abrocitinib 200 mg exhibited an IGA 0/1 at week 48 while only 40% of patients on dupilumab 300 mg weekly and 36% of patients on dupilumab 300 mg biweekly exhibited an IGA score of 0/1 at week 52.[19,20]

Jumping JAKi's and Adverse Reactions

To date, two systemic JAKi's, upadacitinib and abrocitinib, are indicated in Canada for AD treatment. The most common adverse reactions to abrocitinib include nasopharyngitis, nausea, headache, herpes simplex, increase in blood creatinine phosphokinase, dizziness, urinary tract infection, fatigue, acne, and vomiting. Acne occurred in 4.7% of patients on 200 mg abrocitinib and 1.6% of patients on 100 mg abrocitinib in placebo-controlled trials.[8] While upadacitinib shares many similar adverse reactions to abrocitinib, 16% of patients on 30 mg and 10% on 15 mg of upadacitinib developed acne during placebo-controlled clinical trials.[14] Case 10 illustrates that patients who develop acne on upadacitinib may not have this adverse event on abrocitinib.

In the real-world cases presented, nausea was the most common adverse event experienced by four patients in the series. The nausea was reported to subside over time or when counseled to take abrocitinib with food. Reactivation of the varicella-zoster virus (VZV) has also been reported in approximately 1% of abrocitinib-treated patients.[13] The panel suggests shingles vaccination in conjunction with JAKi use. Two presented cases reported that first dose shingles vaccination occurred two weeks prior to abrocitinib start.

Dosing Approach

Abrocitinib is unique in that it offers three potential dosing strategies: 50 mg, 100 mg, and 200 mg.[8] Depending on preference, patients and providers may choose to start at a higher dose and titrate down or start at a lower dose and titrate up. Considering patient factors, disease factors, and concomitant medications, providers should work with their patients to choose the best dosing strategy for them.

Abrocitinib is predominately metabolized by CYP2C19 (~53%) and CYP2C9 (~30%); thus, co-administration of abrocitinib with a strong CYP2C19 and CYP2C9 inhibitor is not recommended and may increase the risk of adverse reaction to abrocitinib.[8] Case 5 had a history of cerebral infarct and anxiety treated with CYP2C19 inhibitor, clopidogrel, and CYP2C19 substrate, citalopram, respectively. Despite his complex medical history, because of the impact of his severe AD on his QoL and sleep (he only slept three nights/year pre-abrocitinib), he was initiated on 50 mg of abrocitinib to assess safety. He tolerated the regimen without any adverse reactions. The 50 mg abrocitinib allows for further dose titration in patients with poor renal function or who are poor CYP2C19 metabolizers.

While extra caution must be taken, the panel agreed that patients with complex medical histories should not be excluded as potential candidates for abrocitinib without first evaluating the risks and benefits and having a thorough discussion with these patients.

Future Directions

The panel agreed that patient testimonials are highly impactful and educational. Patients are often enthusiastic about sharing their experiences. In the future, it will be important to direct discussions toward more complex AD cases to help healthcare providers choose appropriate dosing strategies and treatment regimens with the proper precautions. Further investigation into AD-associated PIH in individuals with sensitive skin may also help elucidate therapy plans for all skin types. Lastly, one panel member suggested further training of other medical specialties outside of dermatology in order to earlier recognize and appropriately treat AD patients. In particular, emergency medicine (EM) practitioners come in frequent contact with AD patients suffering from recurrent infections or exacerbations. Educating EM providers may allow for faster AD treatment and reduced patient suffering.

Conclusion

The real-world cases presented reflect the expert panel's clinical experience with abrocitinib for the treatment of patients with moderate-to-severe AD. The panel's cumulative insight suggests that abrocitinib is a safe, effective, and rapid-acting AD therapy that may be used in all Fitzpatrick skin types and disease stages. Through a multi-option dosing approach, abrocitinib fosters a TTT paradigm that allows patients and providers to form successful, individualized AD treatment plans.

Limitations

The presented cases represent real-world experience with abrocitinib. All outcome measures were reported from providers in the clinic and reflect real-life data rather than data from a controlled, clinical trial environment. Actual experience with abrocitinib may differ with each patient and/or provider. Our expert panel included general dermatologists and did not include specialized pediatric dermatologists. Thus, this discussion does not provide real-world experience in a pediatric setting. Off-label use of abrocitinib is up to the discretion of treating healthcare providers.

Appendix 1

Eczema Area and Severity Index (EASI)

EASI measures extent of body surface area involvement and clinical characteristics of disease.[21] The scale assesses four body parts in the following categories: (a) erythema, (b) induration/papulation, (c) excoriation, and (d) lichenification.[21] EASI scores may range from 0 to 72 with higher scores representing more severe disease.[21]

Investigators' Global Assessment (IGA)

IGA is a 6-point static scale that allows investigators to assess overall disease severity.[21] Symptoms such as xerosis, excoriations, erythema, weeping, papulation, and crusting may help inform investigators' scores.[21] Scores range from 0 (clear) to 5 (very severe disease).[21]

Peak Pruritus Numerical Rating Scale (PP-NRS)

The PP-NRS was developed to evaluate worst itch intensity for adults with moderate-to-severe AD.[22] It is a single-item question that asks patients to rate their itch at the worst moment during the past 24 hours on scale from 0 to 10, with 0 being "no itch" and 10 being the "worst itch imaginable".[22] A clinically meaningful response is defined as 4-point change from baseline PP-NRS score.[22]

Dermatology Life Quality Index (DLQI)

The DLQI is a 10-item questionnaire with high sensitivity, internal consistency, and reliability.[21] It inquires patients about how their skin condition affects their daily life, work, and social interactions.[21] DLQI scores range from 0 to 30 with higher scores indicating worse quality of life (QoL).[21]

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