Oral Retinoid May Ease Painful Skin Reactions to Anticancer Therapy

— Preliminary data on acitretin therapy are promising

by Michal Ruprecht, Editorial Intern, MedPage Today
May 11, 2022

Last Updated May 13, 2022

Acitretin (Soriatane) may improve outcomes for cancer patients with multikinase inhibitor (MKI)-mediated hand-foot skin reaction (HFSR), according to a small retrospective study.

Of eight MKI users who developed HFSR, seven saw symptom improvement after acitretin initiation. Seven thus continued their anticancer treatment -- two of them able to resume full-dose therapy.

Seven individuals continued daily acitretin treatment until MKI discontinuation or death, whereas one person stopped treatment due to worsened preexisting mucosal xerosis/epistaxis, reported Nicole LeBoeuf, MD, MPH, of Dana-Farber/Brigham and Women's Cancer Center in Boston, and colleagues

"The HFSR necessitated MKI dose reduction for all patients, despite imaging-confirmed tumor responses on initial restaging in six of eight patients," wrote LeBoeuf and coauthors. "Ultimately, acitretin facilitated MKI continuation or dose re-escalation in nearly all cases."

"Thus, acitretin may uncouple HFSR from its potential negative effect on MKI dosing/delivery," they wrote in their report, published in *JAMA Dermatology*

HFSR is a hyperkeratotic toxic effect that can be painful in moderate and severe cases, limiting activities of daily living. Up to 70% of cancer patients treated with MKIs are thought to experience HFSR, explained LeBoeuf and colleagues, adding that the side effect is most frequent with regorafenib (Stivarga), sorafenib (Nexavar), sunitinib (Sutent), and cabozantinib (Cometriq).

Acitretin is a systemic retinoid approved for psoriasis treatment that has also been used off-label to manage diverse hyperkeratotic disorders like palmoplantar keratodermas, Darier disease, and ichthyoses, according to the authors.

Jennifer Huang, MD, of Harvard University in Boston, told *MedPage Today* that HFSR is "very common" among patients on MKI therapy. She noted that the condition is difficult to treat due to ineffective and expensive treatment regimens.

"This paper shows both safety and efficacy in the use of low dose acitretin in a small group of patients, and provides an alternative to topical therapy for some patients," explained Huang, who was not involved in the study.

She added that the drug should not be used in patients who are thinking of pregnancy or those with liver issues.

The authors noted that the case of nonsevere mucosal xerosis/epistaxis was consistent with acitretin's known adverse event profile, which also includes hyperlipidemia, hepatotoxicity, and teratogenicity.

For their analysis, the investigators used patient data collected from 2000 to 2021 from the Mass General Brigham/Dana-Farber Cancer Institute. The eight individuals included had a median age of 56 years.

HFSR grading and diagnosis were verified by two dermatologists. The skin condition appeared on average 17.1 days after MKI initiation. The majority of patients started with a 10-mg dose of acitretin and three participants later raised their dose to either 20 mg, 25 mg, or alternating doses of 10/25 mg.

Before beginning acitretin, all of the participants had tried using urea cream to treat their HFSR without success, while some also used high-potency corticosteroid ointments.

About 28 days into treatment, the median toxic effects grade decreased from moderate-severe to mild (from 2.5 to 1 according to the CTCAEv5.0 palmoplantar erythrodysesthesia syndrome guidelines).

LeBoeuf's group suggested that the mechanism linking MKI use and HFSR may be related to tissue angiogenesis inhibition and dysregulated skin repair.

"Acitretin may oppose this off-target effect in keratinocytes by activating retinoic acid nuclear receptor isoforms that control cellular differentiation, promoting antikeratinization, antiproliferative, and anti-inflammatory effects," according to the researchers.

A major limitation of the study was the small cohort from a single center. The retrospective, observational study left room for selection bias.

Despite these constraints, the authors argued that their results support "future investigations of oral retinoids in the management of this frequently dose-limiting skin toxic effect of MKI therapy."

Michal Ruprecht is a medical student based in Michigan. He is a former reporting intern for MedPage Today. Follow

---

Disclosures

LeBoeuf disclosed receiving personal fees from Bayer, Seattle Genetics, Sanofi, Silverback Therapeutics, and SynOx Therapeutics.

Primary Source

JAMA Dermatology

Source Reference: *Said JT, et al "Outcomes of acitretin treatment for refractory multikinase inhibitor-induced hand-foot skin reaction"JAMA Dermatol 2022; DOI: 10.1001/jamadermatol.2022.1425.*

0 Comments

Recommended For You

Quizzes

Make the Diagnosis: First He Had a Sore Throat. Now This. What's Up?

Dermatology

Nonsteroidal Topical OK'd for Atopic Dermatitis

Dermatology

Parents Lose Sleep to Kids' Eczema

Oncology

Cosibelimab OK'd for Cutaneous Squamous Cell Carcinoma

Dermatology

FDA Approves New IL-31 Drug for Eczema

Dermatology

Could Psoriasis Treatment Be This Simple?

Medical News From Around the Web

CBS NEWS

When a teen's medication stopped working, he decided to try a surgery that could stop his episodes for good

USA TODAY

The popular weight-loss drug Zepbound can now be used to treat sleep apnea

CNN

FDA approves weight-loss drug Zepbound for obstructive sleep apnea | CNN

NPR

FDA approves weight loss drug Zepbound to treat obstructive sleep apnea

CIRCULATION

Activation of Imprinted Gene PW1 Promotes Cardiac Fibrosis After Ischemic Injury.

JOURNAL OF CLINICAL ONCOLOGY

Long-Term Follow-Up and Overall Survival in NRG258, a Randomized Phase III Trial of Chemoradiation Versus Chemotherapy for Locally Advanced Endometrial Carcinoma.