

## Research

# Options for Tx of AKs continue to expand

■ General trend toward using both field and spot treatments may lead to improved results

by LOUISE GAGNON,  
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**T**he potential availability of topical ingenol disoxate and a new photosensitizer for photodynamic therapy (PDT) are advances in the management of actinic keratoses (AKs) that Canadian dermatologists can look forward to in the future.

“Ingenol disoxate is in early phase trials now,” explained Dr. Sonya Cook, a dermatologist in Toronto and co-director of Compass Dermatology. “It is more chemically stable than ingenol mebutate, so it will not need to be refrigerated.”

One of the limitations of ingenol mebutate is that the compound has to be kept refrigerated in order to maintain its clinical efficacy, explained Dr. Cook. “If a patient does not show improvement in their actinic keratoses, following the treatment with ingenol mebutate, you wonder if the medication may have been less effective due to lack of refrigeration,” said Dr. Cook.

## Field therapies considered

Research published in 2016 concluded that *in vitro* and *in vivo* pharmacological properties driving ingenol mebutate efficacy are preserved or improved in ingenol disoxate (*Dermatol*

*Ther (Heidelb)* 2016 Dec; 6(4):599–626).

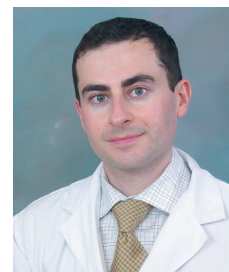
While cryotherapy is used to treat individual AKs, there is a recognition that field therapies should be initiated either in combination or as part of a sequence of treatments, pointed out Dr. Benjamin Barankin, a Toronto dermatologist and



Dr. Sonya Cook



Dr. Mark Lupin



Dr. Benjamin Barankin



Dr. Charles Lynde

co-founder of the Toronto Dermatology Centre.

“If patients develop repeated AKs, they really should be considered for field therapy,” said Dr. Barankin. “There can be field cancerization that is not just about the appearance of individual spots. If the individual spots are treated, months later there can be AKs devel-

oping in an adjacent area. If there are large areas where AKs are recurring, then liquid nitrogen on its own [is simply insufficient].”

Still, Dr. Barankin noted that at-home, spot treatments such as the new salicylic acid and 5-fluorouracil (5-FU) combination with a brush applicator for the face and scalp has a role in the management of single AKs, particularly when they are hyperkeratotic.

A review of data published last year suggested low dose 5-FU with the keratolytic salicylic acid added is effective and well-tolerated for mild-to-moderate hyperkeratotic AKs (*J Cutan Med Sur* 2016 Jul 21).

“Patients like it [5-FU with salicylic acid] because it goes on clear, so they can discretely treat AKs,” said Dr. Mark Lupin, a dermatologist and clinical instructor in the Department of Dermatology and Skin Science in the Faculty of Medicine at the University of British Columbia in Victoria, B.C. “They can manage little spots by themselves.”

A follow-up appointment is needed after 12 weeks of application of 5-FU combined with salicylic acid to ensure

the AK has been effectively treated, Dr. Lupin said in an interview with THE CHRONICLE OF SKIN & ALLERGY.

“When you are treating more thickly scaled AKs, and you can’t see the base of the AK, it is important to follow up to see the result after 12 weeks,” said Dr. Lupin.

More than one treatment can be used to ensure clearance of AKs, Dr. Lupin pointed out.

“There is a general trend to using both field and spot treatments. You might combine, for example, photodynamic therapy and cryotherapy.”

## Combined approaches may be the most efficacious

A recent study of 131 patients supports the effectiveness of combining treatments for AKs: eight weeks after treatment, patients who were treated with a formulation that combined 5% 5-FU and 0.005% calcipotriol experienced a mean 87.8% decrease in the number of AKs on the face compared with a mean 26.3% reduction of the controls treated with 5-FU alone. Patients applied the treatments twice daily for four days.

“Field therapy is the gold standard and includes treatments like 5-FU, imiquimod, and ingenol mebutate,” said Dr. Charles Lynde, Director of the Lynde Institute for Dermatology in Markham,

Ont. and associate professor, Department of Medicine, University of Toronto in Toronto.

Data published last year demonstrated imiquimod was well-tolerated and effective in clearing AKs, both clinical and subclinical, in patients with Fitzpatrick Skin Types I through IV (*J Drugs Dermatol* 2016 Mar; 15(3):285–289).

## PDT an option to consider

Conventional PDT and daylight PDT can both be employed to clear AKs. Recent research points to comparable clinical outcomes with either form of PDT in preventing AKs in patients who exhibited actinic field damage (*J Eur Acad Dermatol Venereol* 2017 Feb 21).

“From the beginning of May to the beginning of October, daylight PDT is a reasonable option in Canada,” said Dr. Barankin, noting an advantage of daylight PDT is that it is a less painful treatment than conventional PDT. A meta-analysis of available evidence on daylight PDT found patients reported significantly less pain with daylight PDT ( $p < 0.001$ ) (*Actas Dermosifiliogr* 2017 Jan 4).

An emerging photosensitizer is BF-200 ALA, a nanoemulsion formulation containing 10% aminolaevulinic acid hydrochloride, that has been studied when using the BF-RhodoLED lamp.

When compared to placebo, it was found to be significantly superior in lesion complete clearance, although treatment-emergent adverse events were experienced by all patients exposed to the novel photosensitizer and 69% of patients in the placebo group (*Br J Dermatol* 2016 Oct; 175(4):696–705).

## Non-proprietary and brand names of therapies:

*ingenol mebutate (LEO Pharma); ingenol disoxate (not licensed in Canada); salicylic acid and 5-FU (Actikerall, Cipher); PDT (Metvix, Galderma); imiquimod 3.75% (Zyclara, Valeant); 5% 5-FU and 0.005% calcipotriol (not licensed in Canada); BF-200 ALA (not licensed in Canada).*

## TCA peels: Outcomes improved with technique

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which is why he worked to develop a technique to improve outcomes with the peels.

“The most common indication for my type of peel is people who have spots on their face and their skin [quality] is not nice enough,” Dr. Fanous said. These are patients in the age range of 20 to 50 years who have sun damage other than wrinkles, uneven pigmentation, large pores and similar complaints.

“Nothing beats a peel as the simplest, most efficient technique to give a better look to all the skin of the face in one sitting,” said Dr. Fanous. Laser procedures are expensive, and it can be challenging to achieve a homogenous result across an entire face using them, he said.

## Standardized approach includes evaluation, application

To ensure minimal adverse events to accompany those good results, Dr. Fanous developed a standardized approach to patient evaluation, skin classification, and application of the acid, all steps to improve control over the depth of the peel.

When Dr. Fanous performed these types of acid peels

earlier in his career, he found that using Fitzpatrick skin type was a limited predictor of outcomes. Light-skinned patients with family backgrounds from northern Asia, in spite of whitish skin, react like darker-skinned patients from southern Asia to the acid peel, developing redness and discoloured spots.

He found that the region of the world the patient’s ancestors came from was a better predictor of skin response to the acid.

The newly published peel technique starts by assessing a patient’s skin type according to a genitico-racial skin classification Dr. Fanous previously published in *The Canadian Journal of Plastic Surgery* (Spring 2011; 19(1)), which is available in open-access at <http://owlyleUKu30eQmmD>. A specific acid concentration is then selected based on that assessment and whether a light, medium, or strong peel is required for the patient’s skin. Finally, the acid is applied in a standardized ‘strip’ pattern over the face to ensure uniform coverage and exposure time.

“It used to be that what counted was the concentration,” said Dr. Fanous. “People would say that 30 per cent

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