

# Dr. Ben Wiese views on Actinic Keratosis & non-melanoma Skin Cancer | The Chronical of Skin & Allergy

## Actinic keratosis and non-melanoma skin Ca

by John Evans  
Senior Editor, *The Chronicle*

Ongoing research into new therapeutic approaches to non-melanoma skin cancers (NMSCs) and actinic keratoses (AKs) could mean that coming years will see improved outcomes for patients who develop these conditions. However, public education and better equipping general practitioners to support prevention and earlier detection could have a more considerable overall impact. Several experts shared these ideas with THE CHRONICLE OF SKIN & ALLERGY.

### SCC and BCC treatments in development

There is ongoing research into sonic hedgehog inhibitors for treating basal cell carcinomas (BCCs), said Dr. David Zloty, Clinical Professor and director of surgical education in the Department of Dermatology and Skin Science at the University of British Columbia in Vancouver. This includes both refining treatment with systemic agents, and exploring topical approaches, he said.

One topical sonic hedgehog inhibitor, patidegib, is currently undergoing clinical trials, Dr. Zloty said. “I am part of that trial, and we are trying to see if a daily topical application of this agent will reduce facial BCC burden in basal cell nevus syndrome patients. Some early small studies and preliminary evidence suggested it probably is effective.”

As the biochemistry on these agents is refined during the next 10 to 20 years, topical hedgehog inhibitors will likely play an impactful role in BCC treatment, he said.

Systemic hedgehog inhibitors are also under study in BCC treatment, Dr. Zloty said, including the oral agent vismodegib. In particular, different dosing regimens are being researched to reduce side effects while maintaining efficacy.

PD-1 inhibitors are being investigated for squamous cell carcinomas (SCCs), he said. One, cemiplimab, was approved in Canada in 2019 to treat locally advanced or metastatic SCCs. While the response rate to cemiplimab is less than 50 per cent, and the complete response rate is only five to 10 per cent, Dr. Zloty said that patients could experience a

noticeable difference even with only a partial response improvement in their quality of life.

More therapeutic agents that work through the same immune pathway as PD-1 inhibitors will likely be developed, Dr. Zloty said, and will probably have positive effects on the treatment of both SCCs and Merkel cell carcinomas. He noted that there has been early research into using PD-1 inhibitors for BCCs in patients who have failed on sonic hedgehog inhibitors.

Different dosing regimens of PD-1 inhibitors are also being explored, he said, noting that even if less-frequent dosing did not impact side-effect profiles, if efficacy can be maintained, it is beneficial to patients to need fewer trips into clinic—especially for patients who travel long distances.

Other potential treatments that Dr. Zloty said are in early research stages include:

- local laser-thermal modulation treatments, where an agent which becomes hot when irradiated with a laser is applied to the surface of a lesion;
- adjuvant radiotherapy for SCCs with perineural involvement;
- intra-lesional injections of the HPV vaccine.

That last approach, because of its relatively benign nature, could be of particular benefit to patients with multiple SCCs, or senior patients with comorbidities that would preclude radiation or surgical treatment, he said. However, there has so far been limited research on this approach, Dr. Zloty said, and it is not clear if it is the HPV vaccine component itself having an effect or only a local immune response to the aluminum adjuvant.

### Actinic keratosis

One area of AK treatment where there is room for improvement is the efficacy of field therapy, said Dr. Marie-Michèle Blouin, a dermatologist in practice at Centre Hospitalier Universitaire de Québec (CHU de Québec), with sub-specializations in Mohs micrographic surgery and skin oncology.

While field therapies have a 70 per cent response rate, rates of reoccurrence are high, she said, so agents that produce longer-lasting results are needed.

Shorter duration of field treatments would also benefit patients, she said, noting she had patients stop topical 5-FU due to the number of days they had to take off work for the treatment.

Dr. Blouin did say she is trying a combination of topical 5-FU in combination with calcipotriol to see if efficacy can be improved while shortening the period of treatment.

Daylight photodynamic therapy (PDT) often does not live up to its promises of equivalent efficacy to in-office PDT in Canada due to less sun and fewer days warm enough for effective treatment, Dr. Blouin said. She noted some research into achieving the greater tolerability of daylight PDT in an office setting.

Another research area that Dr. Blouin said she believes deserves attention is understanding how and why some AKs progress to become cancers.

While not research-related, she said there is room for improvement in AK treatment access, as some field therapy is not covered by public health insurance in Canada.

Technology and non-dermatologist care  
Primary care physicians and other non-dermatolo-

gists will need to play a greater role in NMSC and AK prevention and treatment, as demand for specialists will likely always outstrip supply, said Dr. Ben Wiese. He is a primary care physician in Kelowna, B.C., with a practice that focuses on diagnosing and treating skin cancers.

Dr. Wiese said there is a large role for technological tools to support treatment, but post-treatment tracking and follow-up, and data-sharing between physicians treating NMSCs. He has been using an Australia-based system known as the Skin Cancer Audit & Research Database (SCARD) to audit his own practice and compare it to his peers. This simplifies case management and helps prevent patients from falling through the cracks, he said.

Advances in photography will assist in the diagnosis and monitoring of skin lesions, said Dr. Wiese. He said he expects both full-body photography and digital dermoscopy to become less expensive and more accessible to dermatologists and primary care physicians. However, he did express cautions regarding the growth of interest in mobile apps that claim to diagnose and monitor skin lesions, as inaccurate software could give people a false sense of security and delay a consultation with a physician.

Related to photography, Dr. Zloty noted that there are several technological tools available that can assist in the evaluation of lesion margins. He said that confocal microscopy, high-frequency ultrasound, and impedance path thermography had been used in this way. However, they are now primarily limited to research settings, and their accuracy does not yet exceed that of an experienced physician with practice evaluating margins. These technologies get smaller, less expensive, and more accurate, though Dr. Zloty said he expects them to appear in more ways.

Other technological innovations Dr. Zloty identified which may support NMSC patients in the future include: using fractionated ablative lasers to create surface channels in a lesion to improve absorption of topical agents, and; using gene analysis to stratify patients by risk of metastasis.

### Physician and patient education

Education about AKs, NMSCs, and treatments will continue to be a priority for physicians and the general public, note Drs. Zloty and Wiese. Dr. Zloty said that even when effective treatments become available, they do not always reach patients because of a lack of awareness.

“Part of that is primarily letting practitioners know that advanced and metastatic non-melanoma skin cancers, in some select cases, may now have an effective therapy where that was not available in the past,” Dr. Zloty said.

Greater physician and public education regarding AKs and NMSC would help shorten the time to diagnose and potentially improve outcomes, said Dr. Wiese.

“People walk around with lesions just way too long, not knowing that they are at risk,” he said.

Yet currently, he said, some primary care physicians do not feel confident in their ability to identify cancerous lesions or to stratify patients by risk for purposes of referral to a specialist.

For the general public, efforts to raise awareness of melanoma have been mostly successful, said Dr. Blouin, but public awareness of NMSCs and AKs has lagged.



Dr. Marie-Michèle Blouin