Clinical practice

New approvals in 2019

Health Canada approvals—including certolizumab pegol for plaque psoriasis—anticipated by clinicians

by LOUISE GAGNON,
Correspondent, The Chronicle

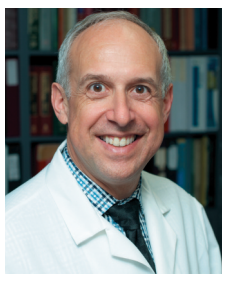
As Canadian dermatologists look forward to new therapeutic developments in 2019, those clinicians contacted by THE CHRONICLE are enthused about the anticipated arrival of a topical lotion to treat plaque psoriasis, the approval of certolizumab to manage psoriasis in their pregnant patients, research into therapies for alopecia areata and vitiligo, and an emerging therapy for axillary hyperhidrosis.

"The combination of halobetasol propionate and tazarotene in one formulation is a very interesting and exciting product," said Toronto dermatologist Dr. Benjamin Barankin, medical director and co-founder ot the Toronto Dermatology Centre. "It is a lotion that is good for scalp application in particular."

The combination product will allow longer duration of use of therapy, noted Dr. Barankin. When these therapies have been used separately to manage plaque psoriasis, they have been limited in duration of use owing to safety concerns. This therapy, however, has demonstrated a proven safety profile.

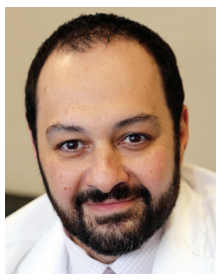
Data from two Phase III, multicenter, randomized, double-blind clinical trials showed the safety and efficacy of the halobetasol/tazarotene combination to treat plaque psoriasis were published in the *Journal of the American Academy of Dermatology.*

Dr. Benjamin Barankin



Dr. Ron Vender

Dr. Catherine Zip



Dr. Sam Hanna

Dr. Danielle Marcoux

Dr. Catherine Zip, a dermatologist at the Dermatology Centre in Calgary and clinical associate professor, University of Calgary, agreed that the availability of the combination product will offer "another option" for scalp psoriasis in particular.

Link between IBD, psoriasis

The link between inflammatory bowel disease (IBD) and psoriasis is recognized as significant, according to Dr. Ron Vender, a dermatologist based in Hamilton, and director of Dermatrials Research Incorporated.

"There is increased understanding that IBD is more common in psoriasis patients than we think and that physicians need to start screening for psoriatic arthritis," said Dr. Vender in an interview with THE CHRONICLE OF SKIN & ALLERGY.

A systematic review and meta-analysis that involved five case-control or cross-sectional studies and four cohort studies showed significant associations between psoriasis and IBD (*JAMA Dermatol* 2018 Dec 1; 154(12): 1417–1423).

Still another new option for psoriasis is particularly suitable for women who are pregnant or contemplating pregnancy, according to Dr. Sam Hanna, a dermatologist and medical director at Dermatology on Bloor in Toronto.

"It [certolizumab pegol] is an anti-TNF [tumour necrosis factor] agent that is pegylated and will not cross the placenta," explained Dr.

Please turn to **Approvals** page **6**→

Approvals ready to make their way to clinics in 2019 include certolizumab pegol for psoriasis, tofacitinib for AA

Continued from page 4

Hanna. "It will be a nice option for women of child-bearing potential who have psoriasis."

Alopecia areata remains a hard-to-treat condition, but oral Janus kinase (JAK) inhibitors are emerging as possible therapies for these conditions, noted Dr. Hanna.

A study that involved 75 patients with alopecia areata who were exposed to tofacitinib and ruxolitinib showed these agents were similarly effective in treating the condition, and both were well-tolerated (*Dermatology* 2018 Dec 19; 1–7).

"There is an unmet need in treating alopecia areata," said Dr. Hanna.

Not only do JAK inhibitors offer promise in treating alopecia areata, but they are offering promise in treating vitiligo, a pigmentary disorder for which few effective therapies are available, added Dr. Hanna.

Psychosocial burden of vitiligo

Not unlike several other dermatologic conditions, vitiligo carries a psychosocial burden for patients, affecting self-esteem and quality of life (*J Drugs Dermatol* 2018; 17(6):688–691).

Some research offers good news for patients with rosacea who are also coffee drinkers and will modify how clinicians counsel their rosacea patients, noted Dr. Barankin.

One study that sought to evaluate the risk of incident rosacea and caffeine intake, including coffee consumption, concluded that limiting caffeine intake is not supported as a way to prevent rosacea (*JAMA Dermatol* 2018; 154(12):1394–1400).

"We often tell our patients with rosacea to avoid caffeine," said Dr. Barankin. "But no association between the risk of rosacea and coffee consumption has been observed."

> *"We often tell our patients with rosacea to avoid caffeine . . . but no association between the risk of rosacea and coffee consumption has been observed."*
> *—Dr. Benjamin Barankin*

According to Dr. Barankin, prescribing patterns may be altered as a result of a conclusion of a study finding that there is an association between hydrochlorothiazide, a diuretic medication used to treat high blood pressure, and an increased risk of Merkel cell carcinoma and malignant adnexal skin tumours (*J Am Acad Dermatol* 2019 Feb; 80(2):460–465.e9).

New therapies for pediatric patients

In pediatric dermatology, therapies such as upadacitinib, which is taken once daily orally, is currently being studied in children for the treatment of atopic dermatitis, noted Dr. Danielle Marcoux, a dermatologist at Sainte Justine Hospital in Montreal and professor of medicine at the University of Montreal.

This research follows the release of data from a Phase 2b dose-ranging study presented in the fall of 2018 at the meeting of the European Academy of Dermatology and Venereology that showed treatment with upadacitinib 7.5 mg, 15 mg or 30 mg resulted in greater improvements in itch and skin lesions, with statistically significant differences observed compared to placebo at week 32.

Another option for patients who have axillary hyperhidrosis is topical glycopyrronium, which has been studied in both adults and children and was approved last year by the U.S. Food and Drug Administration for patients aged nine years and older.

"It appears to work well," noted Dr. Barankin, but noted that there may be some systemic anticholinergic effect produced with the therapy. To date, Canadian approval has not occurred.

Non-proprietary and brand names of therapies: *halobetasol propionate 0.01% and tazarotene 0.045% lotion (not approved in Canada); certolizumab pegol (Cimzia, UCB Canada); tofacitinib (Zeljanz, Pfizer); ruxolitinib (Jakavi, Novartis); upadacitinib (not approved in Canada).*

CLARIFICATION

Two articles in the JOURNAL OF ETHNODERMATOLOGY, published as a supplement to the Dec. 2018 issue of the THE CHRONICLE OF SKIN & ALLERGY (Acne: Increased tolerability, patient compliance with combination topical Tx, page 8 and Post-inflammatory dyspigmentation in patient's with ethnic skin: How to treat it, page 30) incorrectly identified Dr. Monica Li. She is a clinical instructor, Department of Dermatology and Skin Science, University of British Columbia, Vancouver, and a dermatologist at Project Skin MD Clinics.

On page 8, the case involving an 18-year-old male should have read: "After a course of oral isotretinoin, Dr. Li found favourable results in the reduction of his new acne lesions by prescribing a benzoyl peroxide wash along with the topical clindamycin 1.2%/tretinoin 0.025% gel."

Also on page 8, this paragraph should have read as follows: "The combination of tretinoin and clindamycin can be an alternative option for patients who may not be able to tolerate adapalene but are willing to use benzoyl peroxide as part of their skin care management," Dr. Li said.

In the article on page 30, an incorrect concentration of azelaic acid for the treatment of post-inflammatory hyperpigmentation was listed. The correct concentration is 15%.

Research

Single dose of PD-1 inhibitor initiate remission

From the News Resources of The Chronicle via derm.city

A single dose of a PD-1 inhibitor prior to surgery for melanoma may put patients in remission, according to a study published in *Nature Medicine* (Mar. 2019; 25(3):454–461).

Immune responses brought on by this therapy can reach their peak as early as seven days after treatment. Researchers reported that this is much earlier than previous studies have shown.

The largest cohort of patients to be treated with anti-PD-1 drugs before surgery, the participants also completed up to one year of anti-PD-1 therapy after melanoma surgery. Those with complete responses after the initial dose have remained cancer-free for more than two years.

"Knowing so much earlier whether or not patients are responding to PD-1 inhibitors may give us the ability to guide them to the most appropriate therapy with the greatest chance for success," said the lead author Dr. Alexander C. Huang, instructor of hematology-oncology at the University of Pennsylvania Perelman School of Medicine in Philadelphia, in a press release.

A total of 27 patients were treated with one dose of the PD-1 inhibitor pembrolizumab three weeks before undergoing surgery. Eight of the 27 patients (30%) had a complete response or a major response, with less than 10% of the cancer cells remained at the time of their surgery. All eight patients who responded continued to be free of melanoma at a median follow-up time of 25 months.

"It is amazing that we can have greater confidence early on, based on the way patients respond to this treatment before their cancer is surgically removed, that they will do well," said co-senior author Dr. Tara C. Mitchell, an assistant professor of hematology-oncology at the University of Pennsylvania.

Furthermore, in their previous investigations, results showed that anti-PD-1 therapy had a peak immune response in the blood around three weeks. This current study illustrated that tumour cells were already eliminated at that point, meaning the immune response itself must have started at an earlier time. Analysis from additional groups of patients confirmed that hypothesis, with immune responses in the blood peaking as early as seven days.

In addition, investigators isolated patterns in how melanoma develops resistance to PD-1 inhibitors after surgery, which may lead to deeper understanding of how to best treat patients in the future. Researchers identified two causes: tumour mutations—such as B2M or TP53—as well as increased activity of cells that naturally suppress the immune system.

"We have now identified patterns in the way the cancer can adapt to survive, meaning we may be able to guess its next move after PD-1 treatment," said Dr. Huang.

"The longer into treatment we go, the more mutations and resistance mechanisms we find, but identifying the means of resistance early after starting therapy in resected tumours means the resistance mechanisms may be more predictable, which is another benefit of giving this treatment before surgery."