

Clinical practice

Therapeutic year in review

2017



More choice gives clinicians options for the treatment of non-responders

■ Guselkumab for psoriasis, dupilumab for AD and rupatadine for urticaria among significant approvals

by LOUISE GAGNON,
Correspondent, The Chronicle

Innovations in genetics to treat an orphan condition, the arrival of non-steroidal, topical options to treat atopic dermatitis (AD), and the introduction of a new biologic agent to treat moderate to severe psoriasis in Canada are some of the highlights in the practice of dermatology in 2017, say Canadian key opinion leaders in the specialty.

“Patients are excited about the arrival of a biologic like guselkumab [for psoriasis],” said Dr. Anatoli Freiman, a dermatologist and co-founder of Toronto Dermatology Centre in Toronto. “There is good efficacy and safety.” Guselkumab was approved for use in Canada in late November.

Toronto dermatologist Dr. Benjamin Barankin, also a co-founder of Toronto Dermatology Centre, says guselkumab’s selectivity of action makes it attractive as a treatment choice. “It is an inhibitor of interleukin-23 [IL-23],” noted Dr. Barankin. “We are familiar with the IL-12/IL-23 pathways through our experience with ustekinumab. The PASI [psoriasis area severity index] scores are very impressive.”

Dupilumab, a biologic to treat moderate-to-severe AD, was approved for use in Canada in early December. Crisaborole ointment, an inhibitor of phosphodiesterase-4 and a topical treatment for mild-to-moderate AD, became available for prescription, is expected to be available in the near future in Canada. Phosphodiesterase-4 has been shown to promote signs and symptoms of AD, so its inhibition has proven to be an effective pathway for treatment.

Advance in treatment of EB

Rare skin conditions such as epidermolysis bullosa (EB) are difficult to treat, but a breakthrough was reported this year in which a seven-year-old boy was treated with sheets of epidermis grown with gene therapy. The success of this case represents the great potential for gene therapy in other dermatologic conditions that are hard to treat, according to Dr. Mariusz Sapijaszko, clinical professor at the University of Alberta in Edmonton.

“There are many orphan diseases

for which there is very little other than supportive measures that we can offer our patients,” Dr. Sapijaszko said. “For many of these orphan diseases, corticosteroids become a go-to-treatment.

“With researchers connecting more and more around the globe, there are more opportunities for immunology approaches, which will pave the way

for novel treatments for some of these orphan conditions,” he predicted.

Dr. Sandy Skotnicki, a dermatologist in Toronto, observed that the gene therapy case in treating EB is illustrative of a trend that will become more popular in the future. “The model will become more common, and it is really an example of personalized medicine,” said Dr. Skotnicki, agreeing that genetics and immunology will have more significant roles in dermatology, and likely medicine overall, with the passing of time.

The quality of life of those with skin conditions has been increasingly recognized as an important measurement.

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Dr. Anatoli
Freiman



Dr. Benjamin
Barankin



Dr. Mariusz
Sapijaszko



Dr. Sandy
Skotnicki

Other relevant warnings and precautions:

- May increase the risk of infection and should be used with caution in patients with clinically important chronic or active infection.
- Tuberculosis (TB): Should not be given to patients with active TB. Evaluate for TB infection prior to initiating treatment. Initiate treatment of latent TB infection prior to administering Taltz. Consider anti-TB therapy in patients with a history of latent or active TB and in whom an adequate course of treatment cannot be confirmed. Monitor patients closely for signs and symptoms of active TB during and after treatment with Taltz.
- Serious hypersensitivity reactions, including anaphylaxis, angioedema and urticaria, have been reported in Taltz-treated patients in clinical trials.
- Caution should be exercised in patients with inflammatory bowel disease, including Crohn's disease and ulcerative colitis; monitor patients who have inflammatory bowel disease.
- Prior to initiating therapy, consider completion of all age appropriate immunizations; patients treated with Taltz should not receive live vaccines.
- No clinical studies have been conducted in pregnant women to establish safety during pregnancy.
- Caution should be exercised when administered to nursing women.
- No data are available on the effect of Taltz on human fertility.
- Safety and effectiveness in patients <18 years of age have not been evaluated.
- There is insufficient data to determine whether patients ≥65 years of age respond differently from younger patients.

For more information:

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† UNCOVER-2: 12-week, multicenter, randomized, double-blind, placebo-controlled, active-comparator study with 48 week follow-up for patients who achieved sPGA (0,1) (responders). Patients were randomized to Taltz 80 mg Q2W subcutaneously (n=351; initial dose 160 mg), Taltz 80 mg Q4W subcutaneously (n=347; initial dose 160 mg), etanercept 50 mg twice-weekly subcutaneously (n=358), or placebo subcutaneously (n=168). After 12 weeks, responders were re-randomized to Taltz 80 mg Q4W or Taltz 80 mg Q12W. Co-primary endpoints were the proportion of patients who achieved at least a 75% reduction in PASI score (PASI 75) from baseline to Week 12 and the proportion of patients with an sPGA (0,1) (clear or minimal) with at least a 2-point improvement from baseline.

‡ UNCOVER-1: 12-week, multicenter, randomized, double-blind, placebo-controlled study with 48-week follow-up for patients who achieved sPGA (0,1) (responders). Patients were randomized to Taltz 80 mg Q2W subcutaneously (n=433; initial dose 160 mg), Taltz 80 mg Q4W subcutaneously (n=432; initial dose 160 mg), or placebo subcutaneously (n=431). Weeks 12-60, responders were randomized to Taltz 80 mg Q4W (n=229); Taltz 80 mg Q12W (n=227), or placebo (n=226). Co-primary endpoints were the proportion of patients who achieved at least a 75% reduction in PASI score (PASI 75) from baseline to week 12 and the proportion of patients with an sPGA (0,1) (clear or minimal) with at least a 2-point improvement from baseline.

References: 1. Taltz Product Monograph. Eli Lilly Canada Inc., March 9, 2017.

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Therapeutic year in review

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Many patients with hidradenitis suppurativa (HS) find its impact on their life to be debilitating. Canadian investigators have developed an instrument, the HS-QoL, to measure the effect that the disease has on quality of life (*J Cutan Med Surg* 2017 Oct 1:1203475417736281).

“HS is a condition that has a tremendous impact on quality of life,” said Dr. Barankin. “It’s a great idea to have a quality-of-life [instrument] that has been validated, especially for research purposes.”

Currently, the biologic adalimumab is the only approved treatment for moderate-to-severe HS, but Dr. Barankin pointed to preliminary data published earlier this year which suggested apremilast could offer efficacy in the management of HS. A case series of nine patients with moderate-to-severe HS suggested improvements in the condition itself, decreased pain, and improved quality of life with apremilast (*J Am Acad Dermatol* 2017; 76:1189–1191).

News about hair loss

In cosmetic dermatology, the evidence for using platelet-rich plasma (PRP) for hair restoration has been mounting, particularly for the treatment of a common form of hair loss. “For people with androgenetic alopecia and alopecia areata, it is a good option,” said Dr. Skotnicki. “It is something nice to have in your toolbox.”

In a recent study of 50 male subjects where PRP was compared to placebo, it was found there was an improvement in hair density, quality and thickness with PRP injections. No major side effects were seen with PRP and overall patient satisfaction was high (*J Cutan Aesthet Surg* 2017; 10:86–89).

Rosacea

Ivermectin has been well-received as a therapy to treat rosacea, with its target being demodex mites. A systematic review published in the fall of this year looked at infestation of demodex mites in rosacea and found not only that patients with rosacea had significantly higher prevalence and degrees of demodex mite infestation than subjects without rosacea, but that demodex mites play a role in both erythematotelangiectatic rosacea and papulopustular rosacea (*J Am Acad Dermatol* 2017; 77:441–447).

“We have more experience with combination therapy. Many patients are happy with the combination of slow-release doxycycline and topical ivermectin,” said Dr. Freiman. “This approach works on the anti-inflammatory level and has anti-demodex action as well.”

Pruritus

Results from animal studies have identified IL-31 as critical in the development of pruritus, a condition that affects numerous disease states (*Acta Derm Venereol* 2017; 97:922–927).

“Itch is associated with conditions like atopic dermatitis and psoriasis but itch also is associated with the use of some medications and with kidney impairment,” noted Dr. Barankin. “IL-31 is being targeted to address itch.”

Acne

Acne fulminans is a presentation of acne that can have far-reaching systemic effects with patients experiencing symptoms like fever and joint pain. A consensus panel released guidelines this year outlining the treatment course for acne fulminans, noted Dr. Sapijaszko (*J Am Acad Dermatol* 2017; 77:109–117).

“Acne fulminans can have an abrupt onset,” he said. “Prompt treatment with oral corticosteroids should be initiated, and isotretinoin should be gradually introduced. The situation usually resolves [with proper treatment] so that there is no permanent damage.”

Urticaria

In pediatric dermatology, rupatadine became available for prescription in 2017 in Canada to treat chronic spontaneous urticaria.

“It is a nice addition to our armamentarium,” says Dr. Barankin, noting the banana flavour of the oral solution makes it more palatable for young children. “It does not taste medicinal, and it’s a non-sedating option.”

Non-proprietary and brand names of therapies: *guselkumab (Tremfya, Janssen); dupilumab (Dupixent, Sanofi Genzyme); crisaborole (not approved in Canada); adalimumab (Humira, AbbVie); apremilast (Otezla, Celgene); subantimicrobial dose modified release doxycycline 40 mg (Aprilon, Galderma); ivermectin 1% cream (Rosiver, Galderma); isotretinoin lidose (Epuris, Cipher); rupatadine (Rupall, Pediapharm).*

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