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Fixed Combination Tazarotene and Halobetasol Propionate for Plaque Psoriasis

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ABSTRACT

A novel fixed combination lotion containing the super-potent corticosteroid halobetasol propionate 0.01% and retinoid tazarotene 0.045% (Duobrii™) has recently been introduced and indicated for the treatment of moderate-to-severe plaque psoriasis in adults. Studies have shown that there is synergy between the ingredients and that the product can be safely used intermittently for up to 1 year. Treatment success (i.e., Investigator Global Assessment [IGA] of clear/almost clear [IGA 0/1]) occurred in 58.8% of participants at some point in a 1-year clinical trial. Persistence of treatment success is common after treatment discontinuation. Most treatment-emergent adverse events are application site reactions, mild to moderate in intensity, and occur primarily during the first 12 weeks. Counselling should be considered to optimize treatment outcomes.

Key words: Duobrii, halobetasol, tazarotene, fixed combination, psoriasis, topical, corticosteroid, retinoid

Introduction

The US FDA and Health Canada approved in 2019 and 2020, respectively, a once daily fixed combination lotion containing the super-potent corticosteroid halobetasol propionate (HP) 0.01% and the retinoid tazarotene (TAZ) 0.045% (Duobrii™, HP/TAZ) delivered by polymeric emulsion technology. It is more convenient to apply one topical than two, which may lead to improved adherence. It is supplied in a 100 g aluminum tube for treatment of moderate-to-severe plaque psoriasis in adults.

Unlike other lotions, Duobrii™ does not drip. Duobrii™ improves delivery of HP and TAZ compared to HP 0.05% and TAZ 0.1% creams, increases skin moisturization and decreases transepidermal water loss.[2] Non-medicinal ingredients include carbomer copolymer type B, carbomer homopolymer type A, diethyl sebacate, edetate disodium dihydrate, light mineral oil, methylparaben, propylparaben, purified water, sodium hydroxide, sorbitan monooleate and sorbitol solution 70%.[1] Since retinoids are teratogenic, Duobrii™ should not be used in pregnancy or women who may become pregnant.[1]

Background

Topical therapy is used for all severities of psoriasis, although severe disease is often also treated with systemic therapy. Topical corticosteroids are the mainstay of treatment, however psoriasis quickly recurs when they are discontinued and they may cause atrophy. According to the product monograph of Ultravate® cream and ointment which contain HP 0.05%, they should be applied twice daily or as directed by the patient's physician for a maximum of 50 g/week.[3] The duration of treatment is a maximum of 2 weeks without patient re-evaluation.[3] Since psoriasis is a chronic condition, it is preferable to have a topical product without the requirement for re-evaluation after 2 weeks.

TAZ, the only topical retinoid approved for use in psoriasis, is associated with persistence of improvement after treatment discontinuation, however its use is limited by irritation.[4] TAZ is a synthetic acetylenic retinoid which is a prodrug. Its free-acid active metabolite, tazarotenic acid, binds to the nuclear retinoic acid receptors (RAR) beta (RAR-β), and the predominant subtype gamma (RAR-γ), in the epidermis.[5] In psoriasis, it

ALSO IN THIS ISSUE: **Psoriasis Education Tool for Patient-Physician Decision-Making about Biologics: A Pilot Study** *(page 4)* *and* **Update on Drugs** *(page 12)*

reduces inflammation and keratinocyte hyperproliferation, and normalizes differentiation.[5]

Treatment Rationale for Combination Halobetasol/ Tazarotene Lotion

After 12 weeks of use, once daily TAZ 0.05% and 0.1% creams have comparable efficacy to twice daily fluocinonide 0.05% cream, however the psoriasis recurs more quickly after fluocinonide discontinuation.[4] In an attempt to minimize adverse effects and enhance efficacy, TAZ is usually used with a mid- or high-potency corticosteroid.[6] Concomitant use of mid- to high- potency corticosteroid with TAZ does not compromise the sustained posttreatment improvement seen with TAZ.[7] The rates of burning were less than half as frequent when TAZ was used with the mid-potency corticosteroid mometasone furoate 0.1% cream or high-potency corticosteroid fluocinonide 0.05% cream versus placebo.[7] In a 4-week study, diflorasone diacetate 0.05% ointment reduced epidermal thickness by 43%, however when used in combination with TAZ 0.1% gel, there was only a 28% reduction ($p \leq 0.003$).[8]

Supporting Evidence from Clinical Trials (Table 1)

The fixed combination HP/TAZ lotion is more efficacious than the individual ingredients with a synergistic benefit.[9] In a phase 2 multicenter, randomized, double-blind vehicle-controlled clinical trial, an Investigator Global Assessment (IGA) of clear/ almost clear (IGA 0/1) with at least a 2-grade improvement from baseline at week 8 was seen in 52.5% treated with HP/TAZ, 33.3% with HP ($p=0.033$), 18.6% with TAZ ($p<0.001$), and 9.7% with vehicle ($p<0.001$).[10] At week 2, baseline itching, dryness and burning/stinging also improved, similar to the improvement seen with HP and greater than that seen with TAZ.[11] Four weeks after treatment discontinuation, the improvement associated with HP/TAZ at week 8 was maintained.[12]

Two phase 3 multicenter, randomized, double-blind, vehicle-controlled clinical trials showed that by 2 weeks, HP/TAZ was more efficacious than vehicle. By week 8, 35.8% (study 1) and 45.3% (study 2) achieved IGA 0/1 with at least a 2-grade improvement from baseline.[13]

HP/TAZ may be a treatment option for individuals with skin of color. In a phase 3 clinical trial, a 58-year-old black male with post-inflammatory hyperpigmentation developed hypopigmentation from weeks 2-8, which returned to normal 4 weeks after treatment.[14]

In a 1-year phase 3 open-label long-term clinical trial of 555 adults with psoriasis and an IGA score of 3 (moderate) or 4 (severe) affecting 3-12% body surface area (BSA) at baseline, patients were treated once daily for 8 weeks, then as needed in 4-week intervals if an IGA of 0/1 (treatment success) was not achieved. There was a maximum of 24 weeks continuous treatment at any point in the study. Treatment success was achieved by 57.8% at some point during the study.[15] No retreatment for >4 weeks was required in 55.3%, for >8 weeks in 28.3%, for >12 weeks in 19.5%, and for >16 weeks in 12.4%. Treatment-emergent adverse events (TEAEs) occurred in more than half of participants during the 1-year clinical trial, especially during the first 12 weeks. Most were mild to moderate in intensity. The most common TEAEs were application site dermatitis, pruritus, pain and irritation. Skin atrophy was present in 0.5% at baseline, 1.7% at week 12, 1.4% at week 24 and 0% at week 52. It led to study discontinuation in 1 participant. Striae occurred in 1.1% at baseline, 1.3% at week 12, 0.8% at week 24 and 0.7% at week 52. Folliculitis was present in 0.4% at baseline, 1.5% at week 12, 1.1% at week 24 and 0% at week 52. The discontinuation rate due to TEAEs was 7.5%.

Dosage and Duration

The usual adult dose is a once daily thin coat rubbed in gently to psoriatic plaques until control is achieved.[1] HP/TAZ may

Phase 2[9,11,12]	Week 2	Week 8	Week 12 (4 Weeks off Treatment)
Treatment success†	HP/TAZ: 11.9% HP: 4.8% TAZ: 1.7%	HP/TAZ: 52.5% HP: 33.3% TAZ: 18.6% Vehicle: 9.7%:	HP/TAZ: 38.2% HP: 21.0% TAZ: 12.8% Vehicle: 6.9%
Percent reduction in BSA	HP/TAZ: 11.2% ▼ HP: 6.1% ▼ TAZ: 2.2% ▲	HP/TAZ: 44.1% ▼ HP: N/A TAZ: N/A	HP/TAZ: 44.6% ▼ HP: 10.5% ▲ TAZ: N/A
Phase 3 Pooled Analysis[16]	**N/A**	**Week 8**	**Week 12 (4 Weeks off Treatment)**
Treatment success†	N/A	HP/TAZ: 40.7% Vehicle: 9.9%	HP/TAZ: 33.3% Vehicle: 8.7%
Percent reduction in BSA	N/A	HP/TAZ: 37.6% ▼ Vehicle: 3.1% ▼	If Baseline BSA ≤5 HP/TAZ: 34.5% ▼ Vehicle: 7.3% ▲ If Baseline BSA >5 HP/TAZ: 33.7% ▼ Vehicle: 4.3% ▼

Table 1: Summary of phase 2 and 3 12-week clinical trials with published data

† Treatment success was defined as an Investigator Global Assessment (IGA) score of clear or almost clear (IGA 0/1) with at least a 2-grade improvement from baseline.

BSA, body surface area; HP/TAZ, halobetasol propionate 0.01%-tazoretene 0.045%; HP, halobetasol propionate 0.01%; TAZ, tazarotene 0.045%.

be used less frequently and on and off if redness, peeling or tenderness develop.[1] The maximum weekly amount to be used is 50 g which is one half of a 100 g tube.[1] There is no maximum treatment duration.[1]

Counselling: Practical Tips to Optimize HP/TAZ Treatment and Minimize irritation (Figure 1)

The fixed combination HP/TAZ medication should be applied once daily and rubbed in gently to skin affected with psoriasis, avoiding unaffected skin. It is important to show patients where the psoriasis lesions are and where to apply the medication. Less frequent applications (e.g., one, two, or three times per week) then increasing the frequency as tolerated may be considered, particularly in patients with sensitive skin. A thin coat of the medication should be applied, just enough to cover the psoriasis lesions. It is important to remind patients that more is not better as it can lead to irritation. After bathing, it is important to dry the skin with psoriasis before applying the medication. Failure to do so may result in redness, peeling and/or tenderness. The medication should be allowed to dry before putting on clothes. This prevents inadvertent spread onto unaffected skin. Patients should stop applying the medication when they cannot feel the lesions anymore when their eyes are closed. The medication should not be applied to: (1) sensitive sites such as the face, genitals and anal area; (2) intertriginous areas where two areas of skin touch or rub; (3) sites with erosions, ulcers, or fissures and (4) sites also affected by eczema.[1] One 100 g tube should last at least 2 weeks.

Patients should be warned that sometimes the area around the psoriasis lesions can get irritated with redness, dryness, peeling and tenderness. If patients experience irritation, they should apply moisturizer either all over or just around lesions before applying the HP/TAZ medication and/or reduce the frequency of application of the HP/TAZ medication to every 2nd or 3rd days until it settles.

Application tips for Duobrii™ lotion

- Apply a thin coat of medication once daily, to psoriasis lesions, avoiding unaffected skin.
- Less frequent initial application (e.g. 1, 2, or 3 times per week), increasing the frequency as tolerated, may be considered if you are sensitive.
- After bathing, completely dry your psoriasis lesions before applying the medication.
- Let the medication dry before dressing.
- Sometimes the area around the lesions can become irritated with redness, dryness, and peeling. If this happens,
  - Before applying the medication, moisturize either all over or just around the lesion and/or
  - Reduce the frequency of application of the medication to every 2-3 days until it settles.
- Stop applying the medication when you cannot feel the lesions anymore with your eyes closed.
- **DO NOT use if you are pregnant or may become pregnant.**
- **DO NOT apply to**
  (1) sensitive sites such as the face, genitals and anal area,
  (2) intertriginous areas where two skin areas touch or rub,
  (3) sites with erosions, ulcers, or fissures, and
  (4) sites affected with eczema.
- One tube should last at least 2 weeks.

Figure 1: Application tips for HP/TAZ lotion

Conclusions

The once daily fixed combination HP/TAZ lotion is convenient and provides synergistic benefit that is rapid and sustained for moderate-to-severe psoriasis. Intermittent treatment over 1 year when the IGA is not clear/almost clear is safe and maintains efficacy supporting long-term use of HP/TAZ. The atrophic potential of HP is minimized with TAZ and the irritancy potential of TAZ is minimized with HP. Counselling with application tips should be considered for all patients.

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Psoriasis Education Tool for Patient-Physician Decision-Making About Biologics: A Pilot Study

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ABSTRACT

Although biologics are well-studied, expertise regarding their use is often lacking. Many biologics have been added to the market in recent years with distinctive characteristics. This study was designed to create a tool to assist physicians involved in the care of patients with psoriasis undergoing biologic treatment. We used a quality improvement approach to develop and trial an educational visual aid to deliver comprehensive information about biologics in a convenient manner. As a pilot study, trialing this tool was carried out on a small scale to test the feasibility of both the study design and the visual aid itself, with 8 physician and 8 patients completing questionnaires evaluating the visual aid. From our results, the tool was helpful for improving patient knowledge of biologic treatment and their engagement in clinical decision-making. This visual aid may serve as a central convenient biologic resource for physicians.

Key words: psoriasis, biologics, patient education, shared decision-making

Introduction

Biologics are a class of drugs that are often used to treat moderate to severe psoriasis. Approximately 1 million Canadians are affected by psoriasis and of those, 39.9% are treated with biologics.[1] As new biologics continue to enter the market, understanding the unique characteristics of each drug in this therapeutic class is a complicated endeavor. The authors undertook this study with the primary objective of evaluating the extent to which an educational visual aid of biologics could aid dermatologists in counseling their patients during treatment planning. The biologic handout that was created for this study is the main deliverable which we aim to circulate widely, as a means of encouraging shared decision-making and transparency of pharmaceutical options. Our secondary objective was to identify the factors that physicians consider important in their choice of biologics.

Methods

Our investigation used a pragmatic quality improvement (QI) research approach as it provides a systematic inquiry that generates actionable knowledge aimed at improving the delivery of patient care.[2] This study employed the Model of Improvement, which provided our study with a roadmap for knowledge translation to developed actions, where through an experimentation (Plan-Do Study-Act, PDSA) cycle and practical experience leads to continuous improvement.[3] A PDSA cycle is a systematic approach to planning an intervention, assessing its impact, and proceeding with another cycle of implementation after improvements have been made.[3,4]

With the goal of developing a clinical teaching tool, we consolidated information on biologics available to patients in Canada as of December 2019 (Table 1).

Once consent was obtained from dermatologists and senior dermatology residents, they completed a questionnaire to determine general preferences and reasons for prescribing biologics. Clinicians then used the educational tool to discuss treatment options with their psoriatic patients. After 3 months of use, physicians completed a post-implementation questionnaire. The patients were also provided with an anonymous questionnaire at the end of the visit.

Descriptive statistics were used to understand the characteristics affecting dermatologists' biologic prescribing preference.[5] We used bar graphs to visually determine the factors that dermatologists prioritize when prescribing biologics, as well as the post-implementation data collected from patients about the utility of the visual aid for their involvement in decision-making. Weighted means were calculated for physician biologic preferences at baseline and after 3 months of visual aid use, assigning a score of 5 to each physician's most-preferred treatment, and 1 for the least-preferred. This project was approved by the Research Ethics Board at the University of Alberta (Pro00091432).

Results

Eight dermatologists and residents consented to participate. Of those physicians, 3 completed the post-visual aid questionnaire. Eight patients consented and completed their questionnaire during implementation. All questionnaires were completed

anonymously. The participating physicians prescribed biologics to their patients at baseline, initiating approximately 2-3 patients with this treatment modality per month.

At baseline, the biologics, in order of frequency of prescribing, were: 1) secukinumab, 2) guselkumab, and 3) ustekinumab. The main factors affecting choice of biologic were co-morbidities (n=8, 100%), efficacy (n=7, 87.5%), and contraindications (n=7, 87.5%) (Figure 1). Fifty percent of physicians were familiar with the relative costs of each biologic (n=4), and 75% felt they were not adequately informed about the cost of biologics (n=6).

After 3 months of use, the 'study' portion of the PDSA cycle was initiated with the administration of the post-aid questionnaire to the physicians. Post-implementation, the most popular biologics were 1) guselkumab, 2) risankizumab, and 3) ixekizumab. The physician respondents reported no significant impact of the visual aid on their choice of biologics, although (n=2, 66.5%) found the visual aids slightly useful. One physician commented that the visual aids "helped with listing the adverse effects and to show efficacy, not so much to compare biologics." Patients were asked to complete their questionnaire at the end of physician visual aid use. Generally, patients felt there was no significant impact (n=5, 62.5%) on their choice of biologic. There was a mixed response regarding the frequency that physicians used visual aids during clinic appointments in general (Figure 2). Some participants noted that the decision was still largely made by the physician, regardless of the use of the visual aid for patient education. However, there was a greater proportion of patients who indicated that the visual aids were either somewhat (n=4, 50%) or very (n=3, 37.5%) useful in explaining treatment options to them (Figure 2).

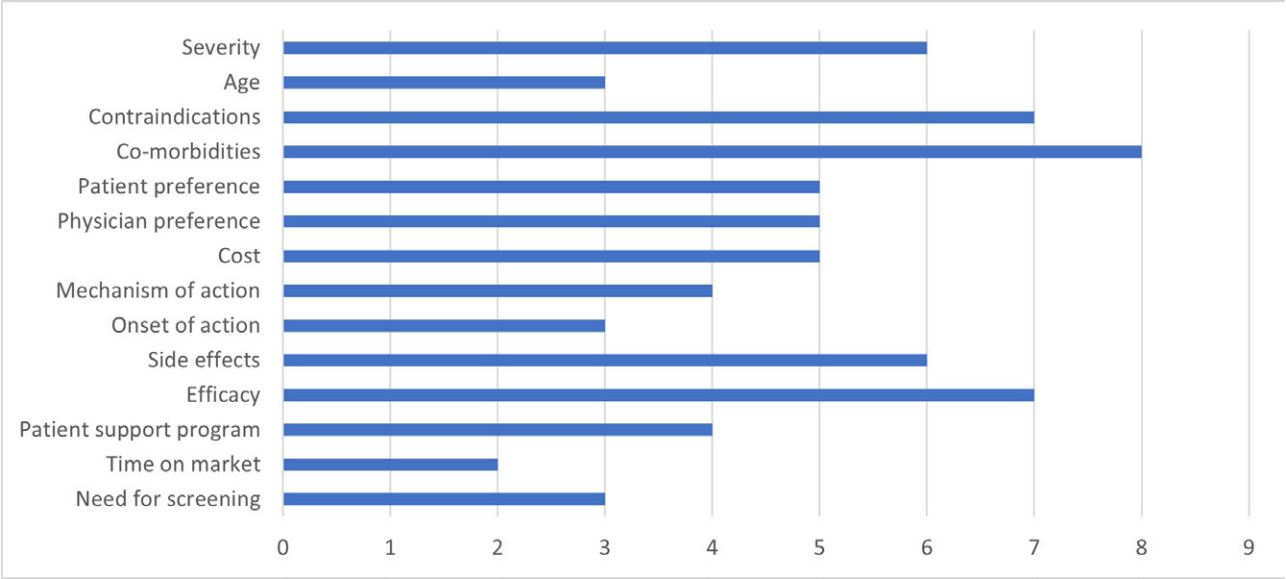

Figure 1: Physician responses to factors affecting dermatologists' choice of biologic

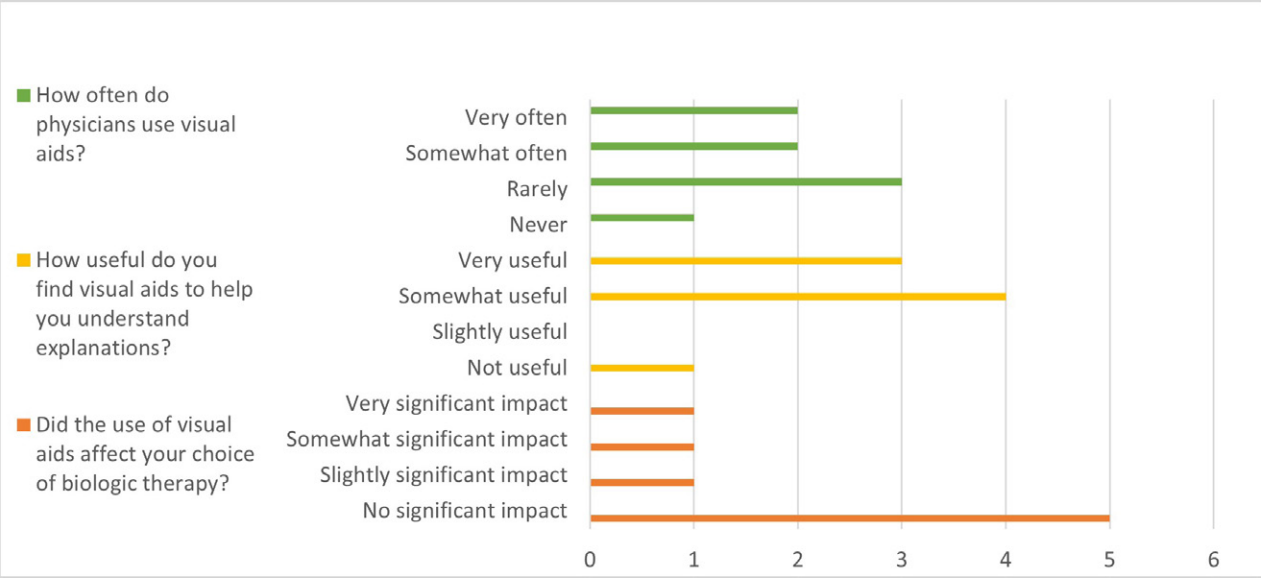

Figure 2: Patient responses to visual aid education use and physician interactions

Biologic	Treatment Indications	Concomitant conditions	Contraindications	Dosing	Annual Cost (First Year)	Side effects	Efficacy (PASI)	Market Date	PSP
Adalimumab (Humira) TNFi	Moderate-severe PsO[8] Nail[9] Scalp[10] Hand and foot[11]	Pregnancy Breastfeeding PsA Crohn's Disease Ulcerative Colitis[8-14]	Active TB or other severe infections Malignancies Hepatitis B Demyelinating disease Heart failure[8]	Every 2 wks (SC)[8]	$21,559[15]	Headache (12%) Skin rash (12%) Infection (>10%) Injection site rxn (20%) Increased liver enzymes (3.5%) URTI (17%) Sinusitis (11%) Cardiac complications (5%)[8]	**75** 46.5% @ 12 wks[8] 70% @ 48 wks[16] **100** 11% @ 12 wks[17]	2004	AbbVie Care
Certolizumab pegol (Cimzia) TNFi	Moderate-severe PsO[18]	Crohn's Disease PsA Pregnancy Breastfeeding[18]	Active TB or other severe infections; heart failure (NYHA Class III/IV)[18]	Every 2 wks (SC)	$19,271[19]	Infection (38%) URTI (18%) UTI (8%) Nasopharyngitis (5%) Headache (5%) Hypertension (5%) Skin rash (9%) Fatigue (3%) Chronic Bronchitis (3%)[18]	**75** 66.7% @ 12 wks[20] 87.1% @ 48 wks[21] **100** 18.8% @ 16 wks[20]	2009	Cimzia Solutions
Etanercept (Enbrel) TNFi	Moderate-severe PsO[22] Nail[9] Scalp[10]	PsA Pregnancy Breastfeeding[12-14,22]	Hypersensitivity to etanercept; patients at risk of sepsis syndrome (e.g., immunocompromised)[22]	Twice weekly for 3 mo, then once weekly (SC)[22]	$25,983[15]	Injection site rxn (15%) Infection (27%) Diarrhea (3%) Skin rash (1%) URTI (17%) Hypersensitivity rxn (1%)[22]	**75** 41.6% @12 wks [22] 61.1% @ 48 wks[23] **100** 5.3% @12 wks[22]	2000	Enliven
Infliximab (Remicade) TNFi	Chronic, severe PsO[24] Nail[9] Scalp[10] Hand and foot[25]	Crohn's Disease PsA Ulcerative Colitis Pregnancy Breastfeeding[12-14,24]	Severe infections (e.g., sepsis, abscesses, tuberculosis, and opportunistic infections); heart failure (NYHA Class III/IV)[24]	Infusion at 0, 2, and 6 2 wks, then every 8 wks thereafter (IV)[24]	$39,080[15]	Headache (17%) Nausea (8%) Increased liver enzymes (4%) Antibody development (59%) Infection (2%) URTI (25%) UTI (2%) Sinusitis (8%) Hypertension (4%) Skin rash (2%) Dyspepsia (2%) Fever (4%)[24]	**75** 80.4% @ wk 1026 60.5% @ week 50[27] **100** 17.8% @ wk 50[28]	2001	BioAdvance
Biosimilar Infliximab (Inflectra) TNFi	Chronic, severe PsO[29]	Crohn's Disease PsA Ulcerative Colitis PsA Ankylosing spondylitis Rheumatoid arthritis[29]	Severe infections (e.g., sepsis, abscesses, TB, and opportunistic infections); heart failure (NYHA Class III/IV) Pregnancy* Breastfeeding*[29]	Infusion at 0, 2, and 6 2 wks, then every 8 wks after (IV)[29]	$21,000[15]	URTI (25%) Pharyngitis (9%) Nausea (8%) Diarrhea (5%) Pruritis (9%) Generalized pain (10%) Headache (17%) Urticartia (4%) Depression (4%) Hypertension (4%)[29]	Not available	2014	enCompass
Brodalumab (Siliq) IL-17i	Moderate-severe[30]	PsA Hepatitis B/C Pregnancy Breastfeeding[30]	Crohn Disease Hypersensitivity to brodalumab[30]	Weekly for 3 wks, then every 2 wks (SC)[30]	$18,060[15]	Infection (25.4%) Fatigue (2.6%) Tinea infection (1.0%) Diarrhea (2.2%) Local site rxn (1.5%) Oropharyngeal pain (2.1%) Headache (4.3%) Arthralgia (4.7%)[30]	**75** 85.1% @12 wks[31] 93.3% @ 48 wks[32] **100** 36.7% @12 wks[31]	2017	Siliq Solutions

Ixekizumab (Taltz) IL-17i	Moderate-severe[33] Genital[34]	PsA Hepatitis B/C[33]	Hypersensitivity to ixekizumab Pregnancy*[13]	Every 2 wks until week 12, then every 4 wks (SC)[33]	$25,823[15]	URTI (10.2%) Injection site rxn(25.3%) Nausea (2.2%) Oral thrush (1.8%) Neutropenia (0.3%) Conjuctivitis (1.3%) Rhinitis (1.8%)[33]	**75** 84% @12 wks[33] 95% @ 52 wks[16] **100** 35.0% @12 wks[16]	2016	LillyPlus
Secukinumab (Cosentyx) IL-17i	Moderate-severe[35] Nail[36] Hand and foot[36]	PsA Hepatitis B/C Pregnancy Breastfeeding[35]	Hypersensitivity to secukinumab IBD (caution) Tuberculosis (caution) Chronic infection (caution)[35]	Loading dose weekly for 4 wks, followed by dose every 4 wks (SC)[35]	$26,320[15]	Infection (28.7%) Diarrhea (4.1%) Nasopharyngitis (11.4%) URTI (2.5%) Pharyngitis (1.2%)[35]	**75** 91.0% @12 wks[37] **90** 74.9% @ 52 wks[38] **100** 39% @12 wks[37]	2015	XPOSE
Guselkumab (Tremfya) IL-23	Moderate to severe[39] Scalp[40] Nail[40] Hands and feet[40]	PsA (phase II RCT) Breastfeeding[40]	Hypersensitivity Active infection Untreated hepatitis B History of lymphoreticular malignancy HIV Pregnancy*[39]	Once at wks 0 and 4, then every 8 wks thereafter (SC)[39]	$21,418[15]	Infection (23%) URTI (14.3%) Headache (4.6%) Injection site rxn (4.5%) Arthralgia (2.7%) Increased liver enzymes (2.6%) Diarrhea (1.6%) Tinea (1.1%)[39]	**75** 86.3 @ 16 wks[41] 87.8 @ 48 wks[41] **100** 34.1 @ 16 wks[41]	2017	CarePath
Ustekinumab (Stelara) IL-12/23i	Moderate to severe[42] Nail[9] Scalp[10]	PsA Crohn's Disease Pregnancy Breastfeeding[42]	Active infection Untreated hepatitis B History of lymphoreticular malignancy Hypersensitivity HIV[42]	Once at 0 and 4 wks, then every 12 wks thereafter (SC or IV)[42]	$22,966[15]	Nasopharyngitis (9.8%) URTI (6.3%) Headache (5%) Fatigue (3%) Dizziness (2%) Depression (1%) Skin carcinoma (2%) Injection site rxn (1-5%)[42]	**75** 66-76% @12 wks[37] 89% @ 52 wks[43] **100** 53.4% @12 wks[37]	2008	CarePath
Risankizumab (Skyrizi) IL-23a	Moderate to severe[44]	Crohn's Disease (Phase II RCT)[14]	Hypersensitivity Pregnancy*[44]	Once at wks 0 and 4, then every 12 wks thereafter (SC)[44]	$24,675[15]	Antibody development (24%) Infection (22.1%) URTI (13.0%) Headache (3.5%) Fatigue (2.5%) Injection site rxn (1.5%)[44]	**75** 88% @ 12 wks[43] 92% @ 52 wks[44] **100** 48% @ 12 wks[43]	2019	AbbVie
Apremilast (Otezla) PDE-4i	Moderate to severe[45] Nail[46] Scalp[46]	PsA	Hypersensitivity Pregnancy Breastfeeding[45]	Daily (PO)[45]	$14,287[15]	Diarrhea (17.8%) Nausea (16.6%) URTI (8.4%) Nasopharyngitis (7.3%) Headache (5.8%) Fatigue (3.0%) Depression (1.4%) Weight loss (1.4%) Vomiting (3.7%) Dyspepsia (3.0%) Abdominal pain (2.0%)[45]	**75** 28.7% @ 16 wks[47] 61.0% @ 52 wks (of those who met PASI 75 at wk 32)48 **100** 3.4% @ 16 wks[47]	2014	ezStart

Table 1: Original visual aid describing characteristics of 11 biologics and 1 small molecule phosphodiesterase 4 inhibitor (i.e., apremilast)

General monitoring for TNFa-i, IL12/23i, IL17i[49]

Baseline screening
CBCd, Complete metabolic profile, Hep B and C serology
TB test +/- CXR if TB positive

Ongoing monitoring
Specific assessment for infections (e.g., tuberculosis, histoplasmosis)
Screening for skin cancer
Yearly testing for latent TB in high risk patients
Infliximab - liver function tests every 3 mos after initiation and if normal then every 6-12 mos
*Use of the biologic has not been studied in pregnant women/the effect on human pregnancy/breastfeeding is unknown.

Biologic	Other Compatible Conditions	Contraindications	Dosing	Approx. Cost (First Year)	Common Adverse Reactions (>10%)	Efficacy – Primary Outcome and Long term Outcome[a]	Market Date	PSP
Adalimumab (Humira) TNFi	Pregnancy Breastfeeding PsA Crohn's/UC[8-14]	Active TB or other severe infections Malignancies Hepatitis B Demyelinating disease Heart Failure[b,8]	Every 2 wks (SC)8	$21,559[15]	Injection site rxn Headache Skin rash Antibody Development URTI/Other infections8	**PASI 75 @ Week 16:** 71-79% **Loss of Adequate Responsed @ Week 52:** 5%8	2004	AbbVie Care
Certolizumab pegol (Cimzia) TNFi	Crohn's Disease PsA Pregnancy Breastfeeding[18]	Active TB or other severe infections Heart failure18	Every 2 wks (SC)18	$19,271[19]	Headache Nausea Antibody development URTI/Other infections18	**PASI 75 @ Week 16:** 75-80% **% of PASI 75 responders maintained until Week 48:** 89-98%21	2009	Cimzia Solutions
Etanercept (Enbrel) TNFi	PsA Pregnancy Breastfeeding[12-14,22]	Hypersensitivity to etanercept Patients at risk of sepsis syndrome22	Twice weekly for 3 mos, then once weekly (SC)22	$25,983[15]	Injection site rxn Headache Skin rash URTI/Other infections22	**PASI 75 @ Week 12:** 47-49% **PASI 75 @ Week 96:** 51%22	2000	Enliven
Infliximab (Remicade) TNFi	Crohn's/UC PsA Pregnancy Breastfeeding[12-14,24]	Severe infections[c] Heart failure24	IV Infusion at 0, 2, and 6 wks, then every 8 wks after24	$30,080[49]	Infusion rxn Headache Antibody development Gastrointestinal symptoms URTI/Other infections24	**PASI 75 @ Week 10:** 75-80% **PASI 75 @ Week 50:** 55-61%24	2001	BioAdvance
Biosimilar Infliximab (Inflectra) TNFi	Crohn's/UC PsA/AS/RA[29]	Severe infections Heart failure Pregnancy Breastfeeding[29]	IV Infusion at 0, 2, and 6 wks, then every 8 wks after29	$21,000[15]	Infusion rxn Headache Antibody development Gastrointestinal symptoms URTI/Other infections[29]	**Not reported (refer to infliximab)29**	2014	enCompass
Brodalumab (Siliq) IL-17i	PsA Hepatitis B/C Pregnancy Breastfeeding[30]	Crohn Disease Hypersensitivity to brodalumab30	Weekly for 3 wks, then every 2 wks (SC)30	$18,060[15]	URTI/Other infections30	sPGA 0/1 @ Week 12: 76-80% % of sPGA responders maintained until Week 52: 79-83%30	2017	Siliq Solutions
Ixekizumab (Taltz) IL-17i	PsA Hepatitis B/C[33]	Hypersensitivity to ixekizumab Pregnancy[13]	Every two wks until week 12, then every 4 wks (SC)33	$25,823[15]	URTI Injection site rxn332	sPGA 0/1 @ Week 12: 73-83% % of sPGA responders maintained until Week 60: 75%16	2016	LillyPlus
Secukinumab (Cosentyx) IL-17i	PsA Hepatitis B/C Pregnancy Breastfeeding35	Hypersensitivity to secukinumab IBD Tb Chronic Infection35	Loading dose weekly for 4 wks, then every 4 wks after (SC)35	$26,320[15]	URTI/Other infections35	PASI 75 @ Week 12: 75-87% % of PASI 75 responders maintained until Week 52: 81-84%37	2015	XPOSE
Guselkumab (Tremfya) IL-23i	PsA (phase II RCT) Breastfeeding40	Hypersensitivity to guselkumab Active infection Untreated hepatitis B Hx of lymphoreticular malignancy HIV Pregnancy39	Once at wks 0 and 4, then every 8 wks after (SC)39	$21,418[15]	URTI/Other infections39	PASI 90 @ Week 16: 70-73% % of PASI 90 responders maintained until Week 48: 89%39	2017	CarePath
Ustekinumab (Stelara) IL-12/23i	PsA Crohn's Disease Pregnancy Breastfeeding42	Active infection Untreated hep B Hx of lymphoreticular malignancy Hypersensitivity HIV42	Once at 0 and 4 wks, then every 12 wks after (SC/IV)42	$22,966[15]	Antibody development URTI/Other infections42	PASI 75 @ Week 12: 67% % of PASI 75 responders maintained until Week 52: 89%42	2008	CarePath
Risankizumab (Skyrizi) IL-23i	Crohn's Disease (Phase II RCT)44	Hypersensitivity Pregnancy44	Once at wks 0 and 4, then every 12 wks after (SC)44	$24,675[15]	Antibody development URTI/Other infections44	sPGA 0/1 at Week 16: 84-88% sPGA 0/1 @ Week 52: 87%44	2019	AbbVie

Table 2: Revised visual aid describing characteristics of 12 biologics approved by Health Canada between 2000-2019

General monitoring for TNFa-i, IL12/23i, IL17i[49]
Baseline screening CBCd, Complete metabolic profile, Hep B and C serology TB test +/- CXR if TB positive
Ongoing monitoring Specific assessment for infections (e.g., tuberculosis, histoplasmosis) Screening for skin cancer Yearly testing for latent TB in high risk patients Infliximab - liver function tests every 3 mos after initiation and if normal then every 6-12 mos

a - Primary outcome considered as proportion of patients at study's defined primary outcome, maintenance considered as long term (>24 weeks) change to primary outcome or as defined by study
b - Heart Failure as per NYHA Class III/IV
c - Severe infections (e.g., sepsis, abscesses, tuberculosis, and opportunistic infections)
d - Loss of Adequate Response defined as Psoriasis Area and Severity Index (PASI) score after week 33 that resulted in less than 50% reduction relative to week-0 baseline score and at least a 6-point increase in PASI score relative to week-33 PASI score

Abbreviations used – AS, ankylosing spondylitis; CXR, chest x-ray; hx, history; IV, intravenous; mos, months; PsA, psoriatic arthritis; PsO, psoriasis; PASI, Psoriasis Area and Severity Index; sPGA 0/1, static Physician Global Assessment of clear or almost clear; RA, rheumatoid arthritis; rxn, reaction; SC, subcutaneous; TB, tuberculosis; UC, ulcerative colitis; URTI, upper respiratory tract infection; wks, weeks

Discussion

The purpose of this quality improvement project was to advance patient education by using a visual aid. The results of the pre- and post-implementation questionnaires suggest that the visual aid is best suited to informing patients. The visual aid itself had minimal impact on therapeutic decision-making.

For future iterations of a PDSA cycle, we simplified the visual aid (Table 2). Terminology was changed to improve clarity; the list of adverse reactions was reduced to common adverse reactions (frequency greater than 10%) and efficacy reported as two figures (primary outcome and maintenance outcome). In future studies, it would be prudent to consider patient education in the dynamic of the patient-physician relationship. Some studies have noted that patients feel their role is to simply accept decisions made by physicians.[6,7] Shared decision-making has been shown to be inhibited by patient feelings, as they may be uncomfortable to raise concerns.[4,6,7] Additionally, as patients may feel ill-equipped to be involved in care decisions, physician expertise is perceived as most important.[7] As opposed to highly detailed product monographs, a visual aid may allow patients to glean details with a glance. Therefore, incorporating patient education through visual aids has the potential to promote increased dialogue with their care provider, thereby encouraging adherence and satisfaction with their care plan.

A major limitation of this investigation was the small sample sizes, as it is difficult to estimate the true impact on larger populations. In particular, the poor reuptake by physicians post-implementation greatly limits our ability to judge how the visual aid would be used on a longer timescale. While physicians may initially be open to using the tool, an important consideration would be to know whether the visual aid added benefit to physicians' clinic encounters sufficiently in order to continue use on a routine basis. In future trials, rather than providing anonymous surveys, we plan to conduct focus groups to allow for improved follow-up as well as open discussion about the tool's utility. Overall, the visual aid was appreciated by physicians as an educational aid tool that helped to facilitate conversations, therefore, there is merit in further developing and studying its benefits in the clinic setting. Similarly, patients noted that the visual aid was helpful for better understanding the selected treatment. General feedback from physicians were that the visual aid appeared content dense due to the high amount of information provided. For future iterations of a PDSA cycle, we plan on simplifying the visual aid for patients, while maintaining the key components of indication, adverse events, efficacy, and contraindications.

Conclusion

Counseling patients to start biologics is a complex task. As medicine is moving towards empowering patients, presenting a large amount of information about biologics may be intimidating to them. Our study suggests that the use of a visual aid may help patients better retain information during counseling and reduce anxiety and uncertainty when starting biologic treatment. This visual aid may also be useful for dermatologists, wherein the consolidated information will allow them to compare biologic options, in addition to promoting open communication with patients about treatment options. Developing tools to facilitate patient satisfaction in an otherwise daunting clinical experience may contribute to better patient outcomes.

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Erratum

In the article "Hair removal practices: a literature review" by Kang CN, Shah M, Lynde C, and Fleming P. *Skin Therapy Lett.* 2021 Sep-Oct;26(5):7-11, electrolysis is noted as the only permanent method of hair removal and that lasers are a temporary hair removal practice (Abstract, page 9 in the paragraph under Lasers, page 10 in the paragraph under Electrolysis, Table 1 under Lasers Permanency, and Conclusion). However, laser hair removal can in fact be permanent in some individuals especially with longer treatments, as noted in a recent article by Altunel CT, Kartal SP. Reconceptualizing the permanence of alexandrite laser hair removal results: a long-term follow-up study. *J Cosmet Laser Ther.* 2020 Nov 16;22(6-8):271-4. doi: 10.1080/14764172.2021.1936067. Epub 2021 Jun 5. PMID: 34096438. Table 1 also states that lasers are "effective for thin vellus hairs, and white, grey, or red hairs" under Advantages but this should state lasers are "ineffective for thin vellus hairs, and white, grey, or red hairs" under Disadvantages, as stated on page 9 in the paragraph under Lasers.

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Update on Drugs & Devices

Name/Company	Approval Dates/Comments
Difelikefalin for IV use *Korsuva*™ Vifor Pharma Cara Therapeutics	In August 2021, the US FDA approved this first-in-class, selective peripheral kappa opioid receptor agonist for the treatment of moderate-to-severe pruritus associated with chronic kidney disease (CKD-aP) in adults undergoing hemodialysis. An oral formulation of difelikefalin is also in development for pruritus associated with atopic dermatitis.
Topical MEK inhibitor *NFX-179* NFlextion Therapeutics	In August 2021, the FDA granted Orphan Drug designation for NFX-179 for the treatment of cutaneous neurofibromatosis type 1 (NF1). NFX-179 is a topical, first-in-class, "soft" (metabolically labile) mitogen-activated protein kinase kinase (MEK) inhibitor that is currently being investigated in Phase 2 clinical trials for cutaneous NF1.
Maralixibat oral solution *Livmarli*™ Mirum Pharmaceuticals	FDA approval was granted in September 2021 for maralixibat (a minimally absorbed ileal bile acid transporter inhibitor) as the first and only approved medication to treat cholestatic pruritus in patients with Alagille Syndrome aged ≥1 year.
Ruxolitinib cream 1.5% *Opzelura*™ Incyte	The FDA approved this first-in-class, selective, topical Janus kinase (JAK) 1/JAK2 inhibitor in September 2021 for the short-term and noncontinuous chronic treatment of mild to moderate atopic dermatitis (AD) in nonimmunocompromised patients ≥12 years of age whose disease is not adequately controlled with topical prescription therapies, or when those therapies are not advisable. The approval was based on data from TRuE-AD1 and TRuE-AD2 trials, which demonstrated significantly clearer skin and itch reduction in patients using ruxolitinib 1.5% cream. Additionally, significantly more patients treated with ruxolitinib cream achieved Investigator's Global Assessment (IGA) Treatment Success (IGA-TS; primary endpoint) at week 8 (defined as an IGA score of 0 [clear] or 1 [almost clear] with at least a 2-point improvement from baseline): 53.8% in TRuE-AD1 and 51.3% in TRuE-AD2, compared with nonmedicated treatment (15.1% in TRuE-AD1, 7.6% in TRuE-AD2; P<0.0001). Opzelura™ carries a class-wide boxed warning for serious infections, mortality, cancer, major adverse cardiovascular events, and thrombosis, which is based on data from the oral JAK inhibitor tofacitinib in rheumatoid arthritis. This drug is also being developed for vitiligo.
Ruxolitinib tablets *Jakafi*® Incyte	In September 2021, the FDA approved oral ruxolitinib for chronic graft-versus-host disease (GVHD) after failure of 1 or 2 lines of systemic therapy in patients ages ≥12 years of age. This marks the fourth FDA-approved indication for Jakafi®.
Avacopan capsules *Tavneos*™ ChemoCentryx	FDA approved avacopan in October 2021 as an add-on treatment to standard therapy including glucocorticoids for adults with severe active anti-neutrophil cytoplasmic autoantibody (ANCA)-associated vasculitis. This orally administered selective complement 5a receptor inhibitor is indicated for granulomatosis with polyangiitis and microscopic polyangiitis, which are the 2 main forms of ANCA vasculitis.