

CaSMO Recommendations for Prevention and Treatment of Cutaneous Adverse Events Related to Cancer Therapies in Darker Skin Phototypes

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Abstract: The Canadian Skin Management in Oncology (CaSMO) project has expanded its practical recommendations to address cancer therapy-related cutaneous adverse events (CAEs) in patients with diverse skin phototypes, particularly those with darker skin phototypes. This initiative responds to growing awareness of the underrepresentation of non-White populations in cancer research, clinical trials, and dermatologic literature. The guidelines emphasize that CAEs often present differently in individuals with darker skin phototypes, where common clinical signs such as erythema or inflammation may be subtle, atypical, or altogether absent. These diagnostic challenges can lead to delayed recognition, undertreatment, or even misdiagnosis of skin toxicities, increasing the risk of long-term complications such as post-inflammatory hyperpigmentation (PIH) and scarring. Improved clinician awareness of these variations is essential for ensuring timely and equitable management of CAEs across all skin phototypes. The paper presents practical guidance for CAE prevention and management tailored to diverse skin types, including skincare, sun protection, and treatment of pigmentary changes. It also outlines the need for personalized skincare based on individual preferences and physiological differences. The authors advocate for improved clinician education, more inclusive clinical trials, and culturally sensitive care approaches to reduce inequities in oncology dermatology. The article concludes by calling for better representation, research, and resources to support equitable care for patients with skin diversity in Canada.

Keywords: skin of color, cutaneous adverse events, cancer therapy, skin phototypes, skin diversity, cancer disparities

Introduction

The Canadian Skin Management in Oncology (CaSMO) practical recommendation project was developed to improve the quality of life for cancer patients and survivors who experience therapy-related cutaneous adverse events (CAEs).^{1–4} A natural extension of the project was to develop practical guidance for the management of cancer therapy-related CAEs in patients with darker skin phototypes.⁵

Skin tone diversity in dermatology is rapidly gaining awareness, interest, and support.^{6,7} Reporting health inequalities related to skin of color (SoC) in cancer is also growing, both in Canada and internationally. Historically, people with SoC have been underrepresented in research, medical textbooks, and medical education. In cancer research specifically, there is still a gap between SoC patients and Caucasian patients in terms of access to care.⁸

Skin Diversity Can Be Defined in a Multitude of Ways

Skin diversity is prevalent in Canada, with one in four citizens identifying as non-white, and projections indicating that up to 39.9% of the working-age population will belong to visible minority groups by 2036.⁹ Defining skin diversity is



complex and varies across measures such as skin tone, ethnicity, ancestry, and classification systems like the Fitzpatrick phototype classification (FPC).¹⁰ However, FPC alone may not adequately capture the range of skin tones. The term “skin of color” (SoC) is often used to encompass individuals from diverse racial and ethnic backgrounds, but CaSMO recognizes that the SoC population is not uniform, highlighting the need for more nuanced and inclusive approaches in clinical research and care.

Skin diversity is prevalent in Canada. One in four Canadian citizens identify as non-white, defined as persons, other than indigenous people, who are non-white in skin color. According to projections, skin diversity is increasing. By 2036, among the working-age population, between 34.7% and 39.9% are expected to belong to a visible minority group, compared with 19.6% in 2011.¹⁰

Skin diversity can be defined in a multitude of ways: skin tones, Fitzpatrick phototype classification (FPC), race, ethnicity, ancestry, colorimeters or mexameters and more.¹⁰ There is significant heterogeneity in the way diversity is ascertained in clinical trials.¹⁰ Differences between skin tones, self-identified ethnicity, social and cultural identity, family background, and ancestry make it challenging to develop a standardized data collection method. In recently published articles on skin diversity, the term SoC was commonly used, and it identifies individuals of African, Asian, Hispanic/Latino or Pacific Island, American Indian/Native American, Aboriginals, and mixed (multiracial) ancestry. SoC can also refer to populations who identify as other than non-Hispanic White or simply refer to different skin tones. In the context of skin toxicities in cancer treatments it is important to acknowledge that SoC population is not homogeneous.

Cancer Affects All Skin Types, but Epidemiology, Pathophysiology, Diagnosis, Management, and Outcomes May Differ Depending on Skin Phototypes

Cancer is a growing public health issue in Canada, now the leading cause of death, with nearly half of Canadians expected to be diagnosed in their lifetime (Canadian cancer Statistics <https://cancer.ca/en/research/cancer-statistics/canadian-cancer-statistics>). The most common cancers are lung, breast, prostate, and colorectal.¹¹ Cancer incidence, cancer mortality, and the distribution of cancer types in Canada vary by ethnicity and gender.¹² These differences likely reflect differences in cancer risk factors, in the use of screening tests, and in other preventive and treatment interventions. Genetic variations, socioeconomic and cultural factors may explain the susceptibility and/or diagnosis of specific cancers for patients with SoC. In Canada, there is a knowledge gap on cancer incidence, outcome, and mortality according to phototype and there is a need for more data on these possible disparities. Although Canada’s healthcare system aims for equitable access, disparities remain—particularly in cancer care—due to factors like language barriers, health literacy, and cultural perceptions of illness and treatment.

Disparities Exist Between Skin Phototypes for Specific Cancers

Melanoma in people with SoC is underrecognized by both the public and healthcare providers, leading to disparities in diagnosis and outcomes. Although melanoma incidence is lower in SoC populations, mortality rates are higher, often due to delayed diagnosis and differences in clinical presentation.^{6,13} Melanoma in people with SoC frequently develops in sun-protected areas¹⁴ and at a significantly younger age.⁶ People with SoC present with later-stage melanoma, including a primary melanoma with an increased thickness and an increased incidence of ulceration, compared to white people, maybe due to delays in diagnosis or care.^{7,13} There is a need to examine non-sun-exposed areas and specifically assess mucosal surfaces, nails, and palmoplantar areas in individuals with SoC. The mortality rate is higher in SoC patients across all melanoma stages at diagnosis.⁶ There are disparities in access to melanoma treatments; black patients have a longer time to definitive surgery and start immunotherapy than white people.⁶

Breast cancer is the most prevalent cancer in Canadian women of all ethnicities, yet outcomes vary significantly based on ethnic background.¹² Immigrant women in Ontario are more likely to be diagnosed at later stages compared to Canadian-born women, particularly those who have lived in Canada for less than 10 years.¹⁵ Similar disparities affect Black and Hispanic women in both Canada and the US, where they are more often diagnosed with advanced or metastatic disease and have poorer survival rates.^{16–18} African descent women are disproportionately affected by triple-negative breast cancer, an aggressive subtype associated with higher mortality and requiring intensive treatment.¹⁹

Prostate cancer is the most prevalent cancer in Canadian males, independent of ethnicity.¹² While some studies suggest that Black men have a higher risk of developing aggressive prostate cancer at a younger age, a Canadian study did not show increased prostate cancer-specific mortality in this group.^{20,21} In contrast, South Asian and East Asian men had lower rates of prostate cancer-specific mortality compared to other ethnic groups.²¹

In the US, Black individuals face a higher risk of lung cancer.²² For the same low-to-moderate level of smoking (1–20 cigarettes per day), African Americans and Native Hawaiians have a significantly increased risk of lung cancer compared to Whites, Latinos, and Japanese Americans.²² However, this disparity is not observed among heavy smokers, where lung cancer risk is similar across groups.²²

Cutaneous T cell lymphoma (CTCL) has a higher incidence in black individuals than in white, Asian/Pacific Islander, and American Indian/Native Alaskan individuals and they are often diagnosed at a younger age and with more advanced disease.^{6,7} Hypopigmented mycosis fungoides (MF), a subtype of CTCL, is more common in people with SoC and may be mistaken for other hypopigmented conditions like vitiligo.⁷ Black individuals with MF have significantly shorter overall survival (OS) compared to white people, likely due to a combination of biological differences, delayed diagnosis, and systemic social inequities.⁷

Determinants of Health Outcomes in Diverse Populations Include Racism, Discrimination, and Socioeconomic Disadvantages, Among Other Factors

Access to cancer prevention and treatment is hindered for immigrants and visible minorities, due to language barriers, socioeconomic challenges, limited knowledge of the healthcare system, and systemic discrimination.²³ In Canada, SoC and visible minorities are underrepresented in health research, and the lack of disaggregated data contributes to inadequate, one-size-fits-all approaches to healthcare policy and delivery.⁸

Scope of the CaSMO Group and Objectives of This Paper

The CaSMO project aims to improve the quality of life for cancer patients and survivors by offering tools to prevent and manage CAEs. A general management algorithm to reduce the incidence of all CAEs and maintain healthy skin using general measures and skin care,^{24,25} an algorithm to reduce and treat acute radiation dermatitis,¹ an algorithm for the management of hormonal therapy-related CAEs,² and treatment guidelines to treat common CAEs induced by immune checkpoints inhibitors (ICIs)³ and by targeted therapy⁴ were previously published. These publications aim to support healthcare professionals treating oncology patients, including physicians, nurses, pharmacists, and advanced providers. A natural extension of the project was to review the recommendations to prevent and manage CAEs related to cancer therapies and specifically add additional considerations for patients with darker phototypes (III to VI). This article also has the role of highlighting the need for greater inclusivity of patients with skin diversity in cancer clinical trials to develop more knowledge and awareness of cancer outcomes and side effects in different populations.

Management of CAEs According to Skin Diversity: General Principles Awareness of Differences in Skin Reactions to Cancer Treatment in SoC May Be Lacking

CAEs induced by cancer treatments can affect anyone, independent of skin tone. However, CAEs can have different clinical presentations and outcomes in darker skin tone. It may be harder to recognize or differentiate certain skin conditions as well as appreciate erythema in darker skin tones. There is a need for a detailed and thorough skin exam, in all patients but especially for patients with darker phototypes.

On the other hand, some skin conditions such as hypopigmentation and depigmentation are more noticeable in people with SoC and may have a more significant impact.²⁶ Awareness of these differences and understanding them is important for healthcare professionals to provide a more equitable diagnosis and treatment.^{26,27} There is a critical gap in the literature regarding CAEs induced by cancer treatments in SoC, compounded by a general lack of clinical awareness. These guidelines are therefore essential in addressing this unmet need—offering practical, inclusive recommendations to improve detection, management, and outcomes for patients with diverse skin phototypes.

Skincare is a Cornerstone of Managing Cutaneous Reactions to Cancer Treatment

Skincare measures can prevent, reduce severity, and/or manage CAEs induced by cancer treatments and involve three main components: cleansing, moisturizing, and sun protection.²⁵ The skincare regimen should start before the initiation of the cancer treatment. **Box 1** shows general skin cleansing and moisturizing recommendations.

Diversity in skin types, tones, and textures requires diversity in preventive and management approaches. There are ethnic variations in ceramide content, stratum corneum structure, filaggrin mutations, microbiome, and transepidermal water loss.^{28,29} Asians have a weaker epidermal barrier strength and slower recovery from barrier damage.²⁸ Black patients are at higher risk for xerosis, pruritus, and prurigo nodularis.²⁸ People with darker skin have an increased cosmetic impact from xerosis which can have a grey or ashen appearance on the background of dark skin.²⁸ It is often referred to as “ashy skin” in the black community.²⁸ Skincare measures are the cornerstone for the prevention of CAEs independent of skin tones and should be reviewed in detail with patients. Some general moisturizer recommendations are provided in **Box 2**.

Patient Perceptions of Skincare Regimen and Individual Preferences Around Cleansing, Moisturizing, and Sun Protection May Vary and Should Be Recognized; Sensitivity in Discussions About Skincare Recommendations is Important

There are different norms on skin cleansing and moisturization between patients, including cleansing frequency and vehicle formulation preference. Preferences for over-the-counter moisturizing lotions, creams, and ointments may vary. Some patients may have an individual inclination for oil-based ointment. Preferences for the vehicle of prescribed topical treatments may vary as well. People with more coarse hair may prefer oil-based ointment and foams, including for the treatment of conditions involving the scalp.³⁰ Topical therapies should be compatible with hair texture, hairstyle, and frequency of hair washing. There are differences in shampoo practice between patients. Some patients may wash their hair less than once a week. It is recommended to ask each patient about their cleansing, moisturization, and sun protection habits and incorporate patient preferences into recommendations and/or treatments. This approach helps initiate the dialogue and individualize treatments. Individualized treatments will likely improve the patient adherence to the prescribed topicals. Involving family members may be helpful as they may play a role in patient adherence to the skincare regimen.

There is a perception that people with darker skin do not have to use sunscreen. Leaders in photo-dermatology believe that photoprotection counseling is warranted in people with SoC.³¹ Photoprotection differs among skin tones. Lighter toned individuals have a greater propensity to use sunscreen than darker toned.³¹ Sun protection may have additional roles in people with SoC. Post-inflammatory hyperpigmentation (PIH) is a common complication of numerous CAEs

Box 1 Skincare Using Cleansers and Moisturizers

Use gentle cleansers with a near-physiological skin pH (4.0–6.0).
Avoid the use of soap and cleansers with an alkaline pH (> 7), which may excessively remove skin lipids, elevating skin surface pH, and compromise the skin barrier function further.
Apply moisturizers to the entire body daily.
Apply moisturizers liberally and frequently.

Box 2 Criteria for Moisturizers

Skincare formulations should be safe, effective, free of additives, fragrances, perfumes, irritants or sensitizing agents.
Moisturizer effectiveness depends on the formulation, the vehicle, frequency, and compliance of applications.

induced by cancer treatments and is more prevalent in more deeply pigmented skin.^{32,33} UV exposure may exacerbate PIH and photoprotection thus may prevent and/or decrease the intensity of PIH.

There is a lack of strong data supporting a specific sun protection factor (SPF) in people with SoC especially because testing of SPF is done on light-skinned individuals, so it may not be extrapolated to SoC. SPF value on darker skin may be lower than the SPF value studied in lighter skin and stated on the label.³¹ Without strong data, we recommend the use of broad-spectrum sunscreen with SPF 30 or higher (Box 3). Visible light may also exacerbate PIH, which may be mitigated by the application of inorganic filters (eg, titanium dioxide, zinc oxide) or tinted sunscreens combining iron oxide in addition to titanium dioxide or zinc oxide.³⁴ However, non-tinted sunscreen with inorganic filters and larger particle sizes may unnaturally color the skin surface in SoC that may be cosmetically unacceptable.³⁴

People with SoC Have a Greater Risk of Post Inflammatory Hyper-/Hypopigmentation From Cancer Treatments-Associated Inflammatory Dermatoses. As Such, Earlier, More Aggressive, and/or Longer Treatment May Be Required

Individuals with darkly pigmented skin may have increased frequency, severity, and duration of PIH following inflammation or injury to the skin. In the epidermal form of PIH, there is increased melanin production and increased melanin distribution in the epidermal keratinocytes. In the dermal form, there is melanin entering the dermis due to the damage of the basement membrane. Melanin in the dermis is phagocytosed and stays in melanophages for long period of time. PIH can occur after numerous CAEs induced by cancer treatment including radiation dermatitis, drug-induced lichen planus, dermatitis, pruritus with secondary excoriations, prurigo nodularis, psoriasis, morbilliform exanthema, papulopustular eruptions, and many others. Specifically with bleomycin, a chemotherapy agent, there is a risk of flagellate erythema leading to prolonged flagellate hyperpigmentation for months after the acute adverse event. PIH can be a significant cosmetic concern for patients. To prevent PIH, there is a need for early diagnosis and early and aggressive treatment of inflammatory CAEs induced by cancer treatments. Protection against UV and visible light also has a major role in preventing and decreasing the severity of PIH.³⁶

Postinflammatory hypopigmentation may be more noticeable in people with darker skin tone due to the contrast between the natural skin tone and the hypopigmented area. Psoriasis, dermatitis, and sarcoidosis induced by ICIs are just some examples of dermatoses that can lead to postinflammatory hypopigmentation. Aggressive treatment of these CAEs may prevent the occurrence or reduce the severity and duration of postinflammatory hypopigmentation.

Topical steroids (TCS) are commonly used to manage numerous CAEs induced by cancer treatments. However, they can induce local patchy hypopigmentation and people with SoC may be more affected by this side effect.³⁷ However, this

Box 3 Sun Protection

Sunscreens are one part of a complete program for sun protection that includes protective clothing, shade, and sun avoidance.
Sunscreens may prevent photodamage and can be classified as UVB filters, UVA filters, or physical blockers.
Sun protection factor (SPF)* refers to UVB radiation, and broad spectrum refers to the sunscreen's UVA radiation protection capacity.
Apply daily sunscreen of SPF 30 or higher, especially for sun exposed areas, 15 minutes before sun exposure and every 2 hours after that if rigorous activity, sweating or wetness.
Special populations that are at higher risk for sun-induced toxicities and neoplasms are advised to avoid sun exposure by using UVA and UVB protection as well as sun-protective clothing.
The recommended amount of sunscreen needed for one application to an adult is 2 mg/cm ² or about 35 g to cover an adult in a swimsuit. ³⁵

Notes: *Studied in humans with skin phototype I or II.

Abbreviations: UVB, ultraviolet B; UVA, ultraviolet A; mg, milligram, g, gram; cm², square centimeter.

side effect remains infrequent, and many underlying inflammatory conditions treated with TCS may be the cause of postinflammatory hypopigmentation rather than the TCS. Early and aggressive treatment of CAEs may prevent postinflammatory hyperpigmentation and hypopigmentation, so the CaSMO group believes it is better to use TCS to manage CAEs instead of avoiding them. Once the inflammatory component of the CAE is managed or decreased, transitioning to a steroid-sparing topical, such as a topical calcineurin inhibitor or phosphodiesterase-4 inhibitor, may help with further reduction or prevention of PIH.

Management of CAEs to Specific Treatments

The Clinical Presentation and Severity of Acute Radiation Dermatitis May Be Underestimated in Patients with Darker Skin Tone

Acute radiation dermatitis (RD) is the most common CAE induced by radiation therapy. Black patients are less likely to be diagnosed with grade 2 or 3 acute RD.³² However, SoC have an increased risk of late grade 2 or 3 hyperpigmentation.³² This may suggest that acute RD is underdiagnosed in SoC individuals because of the difficulty in identifying erythema, which is the earliest finding. There is a need for better description and more illustrations in textbooks of erythema in deeply pigmented skin.

Diversity in Skin Tones May Change the Dermatologic Sequelae of Radiation Treatment

There is poor data on radiation therapy and CAEs in people with SoC. In general, SoC individuals have an increased risk of postinflammatory hypopigmentation and hyperpigmentation, which can be the result of an acute RD. The prevention and early diagnosis and treatment of acute RD in addition to photoprotection are the cornerstone for preventing these pigmentary adverse events (Table 1). Radiation treatments may also lead to late dyspigmentation without prior noticeable acute RD. Pigmentary changes can last after the end of the radiation and may be a source of significant distress. Patients should be educated on sun avoidance and sun protection measures before starting radiation treatments (Box 3).

Severe acute RD can lead to erosions and ulcerations. Ulcers and erosions usually heal by secondary intention and may lead to a scar. People with SoC have an increased risk of hypertrophic or keloidal scars. The early recognition and treatment of acute RD can prevent or reduce the risk of hypertrophic or keloidal scars and reduce the evolution to a more advanced stage. It is mandatory to check the radiation field frequently during the radiation treatments and in the following weeks to quickly diagnose this adverse event.

Table 1 RD Treatment According to Presentation

Grade 1: Faint erythema or dry desquamation, possible pain	<ul style="list-style-type: none"> • Cleanse the skin and use a moisturizer. • Avoid sun exposure and use sunscreen. • For dry desquamation start or continue with low to mid potency TCS to decrease progression and severity of itching, burning and irritation.
Grade 2: Moderate to brisk erythema; Patchy moist desquamation mostly confined to skin folds and creases; Moderate edema, pain	<ul style="list-style-type: none"> • Check adherence to grade 1 treatment. • Use saline compresses for cooling. • Continue TCS in the surrounding area of moist desquamation
Grade 3: Moist desquamation in areas other than skin folds and creases; Bleeding induced by minor trauma or abrasion, severe pain	<ul style="list-style-type: none"> • Check adherence to grade 2 treatment. • Discontinue sunscreen on irradiated area until the reaction is over. • Use saline compresses on the areas with moist desquamation. • Continue TCS in the surrounding area of moist desquamation • Use wound dressing for bullae and erosions and select the type of dressing according to the wound bed condition and the exudate production. • Consider putting radiation treatment on hold.

Abbreviation: TCS, Topical Corticosteroids.

Rosacea Following Hormonal Cancer Therapy May Occur, and Treatment May Need to Be More Aggressive in People with SoC

Breast cancer and prostate cancer are the most diagnosed cancers in females and males in Canada. Hormonal therapies are often given in these two cancers. Hormonal treatments for breast cancer include aromatase inhibitors (AIs), selective estrogen receptor modulators (SERMs), selective estrogen receptor degraders (SERDs), and high-dose hormones. Hormonal treatments for prostate cancer include luteinizing hormone-releasing hormone (LHRH) agonists, LHRH antagonists, androgen receptor blockers, and androgen synthesis inhibitors. All these hormonal treatments, except androgen synthesis inhibitors, can lead to hot flashes and flushing. Rosacea has historically been divided into four subtypes: erythematotelangiectatic (ETT), papulopustular (PP), phymatous, and ocular. Hormonal therapies can lead to ETT rosacea. Rosacea is more common in lighter skin tones but can occur in any skin tone. Diagnosing this condition may be more challenging in people with SoC because it may be hard to detect flushing, erythema, and telangiectasia. Rosacea is often an unrecognized disorder in people with SoC. To help diagnose rosacea in SoC, it may be helpful to ask the patient's self-reported symptoms including erythema, flushing, and a recurrent warm, burning, or stinging sensation involving the face.³⁸ Unrecognized and untreated rosacea can lead to PIH.³⁸ Psychosocial impact should not be underestimated.

Treatment of rosacea varies according to the subtype and severity (Table 2). Sun protection has a major role in preventing and decreasing severity of rosacea. Patients also need to avoid triggers such as alcohol intake and spicy food. To treat erythema and telangiectasia, patients can use topical brimonidine or oxymetazoline. Other topical rosacea treatments such as metronidazole, azelaic acid, and ivermectin are more effective at managing PP rosacea but still may have some benefit for ETT rosacea. Vascular laser and intense pulsed light (IPL) can manage ETT rosacea; however, these treatments have a slight risk of burns and hyperpigmentation in SoC individuals.³⁸ People must seek treatments with healthcare professionals specialized in light-based therapies and with a special interest and expertise in SoC. These specialists will be able to counsel about the best device and parameters to use to decrease the risk of complications. Patients who present with PP rosacea can use topical metronidazole, topical ivermectin, benzoyl peroxide, and oral tetracyclines. For severe or refractory cases, isotretinoin can be used. Early and aggressive treatment of rosacea may prevent PIH in people with darker skin tone.

Table 2 Treatment for Rosacea

	Type of Rosaces	Medication, Formulation, and Dosage
First-line treatment	PP, EPP	Metronidazole gel, cream, or lotion 0.75%/BID, Gel 1%/QD
	PP, EPP	Azelaic acid gel 15%/QD or BID
	EPP	Brimonidine gel 0.33%/QD
	PP	Ivermectin cream 1%/QD
Second-line treatment	PP	Sulfacetamide/ sulfur cream 10%/5%: QD or BID
	PP	Benzoyl peroxide gel 5%/ QD or BID
	PP	Erythromycin gel 2%/ BID
	PP	Clindamycin gel 1%/BID
	PP	Doxycycline oral: either 40mg/QD modified release or 100 mg/OD
Third-line	PP	Oral isotretinoin

Abbreviations: PP, Papulopustular; EPP, Erythematotelangiectatic and Papulopustular; QD, once daily; BID, twice daily.

For Hirsutism Induced by Cancer Treatment, Specific Hair Removal Modalities May Not Be Appropriate for All Skin Types

Hirsutism can be induced by hormonal treatments prescribed for breast cancer and can be managed with different treatment options (table 3). However, some treatments may not be safe in people with SoC. Waxing and plucking may induce local trauma, leading to postinflammatory dyspigmentation. Shaving and plucking can lead to pseudofolliculitis in people with curly hair. People with tightly curled hair have an increased risk of pseudofolliculitis and this condition can involve any shaved or plucked area. Electrolysis is effective regardless of skin tone. However, this technique can also lead to PIH. Laser hair removal uses a wavelength targeting the melanin in hairs (chromophore). Laser hair removal in SoC is more challenging because epidermal melanin competes with the follicular melanin target. Complications are more prevalent in SoC patients and include epidermal and dermal burns, hyperpigmentation, hypopigmentation, and depigmentation. The long-pulsed Nd:YAG laser is the safest in darker skin. Skin cooling is essential for the safety of laser in people with darker skin tone. Patients may seek laser hair removal under the care of a specialized dermatologist and a spot test may be done before treating the whole area.

Papulopustular/Acneiform Eruptions are More Likely to Lead to Post Inflammatory Erythema or Hyperpigmentation in People with SoC and Should Be Treated Early and Aggressively

Treating acne vulgaris in SoC patients comes with the challenge of preventing or minimizing PIH or acne pigmented macules (APM).³⁹ Epidermal growth factor receptor (EGFR) inhibitors, mammalian target of Rapamycin (mTOR) inhibitors, and MEK inhibitors are cancer targeted therapies and they commonly induce a papulopustular eruption, also known as an acneiform eruption. Similar to acne vulgaris, papulopustular eruption induced by targeted therapy comes with a high risk of PIH or APM in SoC. For acne vulgaris, the impact of PIH/APM is sometimes even more significant than the impact of acne itself because of the cosmetic appearance and the persistence.³⁹ We can extrapolate these data and make the hypothesis that PIH/APM following the papulopustular eruption has an important impact on cancer patients. Early and aggressive treatments must be prescribed to prevent PIH (Box 4).

As discussed in a previous CaSMO paper, topical retinoids are not part of the treatment guidelines for papulopustular eruption and must be avoided. It is even more important to avoid them in SoC people because of the risk of secondary irritation leading to PIH.

SoC individuals have more glucose-6-phosphate dehydrogenase (G6PD) deficiency, leading to an increased risk of hemolytic anemia with the use of dapsone. Topical dapsone (Aczone) is part of the treatment lines to manage papulopustular eruption. A study evaluated topical dapsone 5% gel twice daily in patients with known G6PD deficiency and acne vulgaris and there was no clinical or laboratory evidence of hemolytic anemia.⁴⁰ Authors concluded that topical dapsone was a safe treatment for patients with G6PD deficiency.⁴⁰

Systemic tetracyclines are a main part of the algorithm to prevent and treat papulopustular eruption. However, they come with a risk of secondary hyperpigmentation, especially with minocycline and especially in people with SoC. In

Table 3 Treatments for Hirsutism

	Treatment	Effectiveness
Local therapies	Plucking, waxing, electrolysis	For mild hair growth (grade 1)
	Laser hair removal	For more severe hair growth (grade 2)
	Eflornithine topical cream BID	For more severe hair growth (grade 2)
Systemic treatment	Spironolactone, 50 to 200 mg/QD ^a	For more severe hair growth (grade 2)

Notes: ^aShould be discussed with the oncologist due to the potential risk of hormonal stimulation in patients with hormone-positive breast cancer.

Abbreviations: QD, once daily; BID, twice daily.

Box 4 Prevention and Treatment Recommendations for Targeted Therapy-Induced Papulopustular Eruption

<p>General principles and prevention</p> <ul style="list-style-type: none"> • Gentle skin care using a fragrance-free cleanser close to skin pH (pH 5.5) • Emollient at least once a day (twice a day is preferable) • Photoprotection (sunscreen with SPF 50+ and other methods)^a • Consider topical hydrocortisone 1% • Consider oral antibiotics in tetracycline class^b (if contraindicated: erythromycin, clarithromycin, or azithromycin) • Consider the combination of an emollient, photoprotection, topical hydrocortisone 1%, and oral antibiotics in tetracycline class^c
<p>First-line treatment</p> <ul style="list-style-type: none"> • Continue preventive measures • Oral antibiotics in tetracycline class (if contraindicated: erythromycin, clarithromycin, or azithromycin) • TCS (low-to-medium potency on face, medium-to-high potency on body) • Avoid topical acne treatments (eg benzoyl peroxide, retinoids, azelaic acid, or alpha-hydroxy acid)
<p>Second-line treatment</p> <ul style="list-style-type: none"> • Bacterial/viral cultures; treat accordingly (including topical and/or systemic antibiotics and antivirals) • Topical dapsone • Low-dose oral isotretinoin
<p>Third-line treatment</p> <ul style="list-style-type: none"> • Systemic steroids • Acitretin • Oral dapsone • Dose reduction or intermittent interruption of targeted therapy

Notes: ^aPhotoprotection must be reinforced if patients are on doxycycline or isotretinoin with the risk of phototoxicity. ^bEither doxycycline 100 once daily to BID, minocycline 50–100 mg BID, or tetracycline 500 mg BID. ^cShould be considered in patients being treated with EGFR inhibitors or MEK inhibitors.

Abbreviation: TCS, Topical Corticosteroids.

a cohort of patients treated with a tetracycline to manage acne vulgaris, Black and Hispanic patients had an increased risk of hyperpigmentation induced by doxycycline and Black patients had an increased risk of hyperpigmentation induced by minocycline compared to lighter skin.⁴¹ The risk was higher with doxycycline compared to minocycline.⁴¹ Doxycycline is also associated with photosensitivity, whereas, minocycline is more commonly associated with blue-grey hyperpigmentation independent of sun exposure. Regardless, sun protection needs to be discussed with patients treated with this molecule. Minocycline is associated with an increased risk of a drug hypersensitivity syndrome as well as lupus-like syndrome and autoimmune hepatitis, occurring even more frequently in Black patients.

Erythema Associated with Skin Reactions of Immunotherapy May Be More Difficult to Detect in People with Darkly Pigmented Skin

ICIs can induce immune-related adverse events, and the skin is the most commonly involved organ. Immune-related CAEs are numerous, the most common ones being xerosis, pruritus, dermatitis, psoriasis, and lichen planus. These inflammatory skin conditions can be more challenging to diagnose in SoC individuals because erythema is an early sign and may be less noticeable in darker skin tone. Patient's self-reported symptoms including pruritus may be helpful in diagnosing these CAEs. There may be a greater need for skin biopsies to better assess the skin condition.

In People with SoC, Earlier Referral to a Dermatologist for Skin Sequelae of Immunotherapy May Be Warranted, Including for the Diagnosis and Management of Immune-Related Depigmentation

Vitiligo-like depigmentation induced by ICIs may have a greater impact in patients with darker skin tone because of the contrast between the natural skin tone and the depigmented area. In patients with advanced or metastatic melanoma

treated with ICIs, vitiligo is a good prognostic sign, associated with a longer progression free survival (PFS) and OS.^{42,43} However, even if vitiligo-like depigmentation is a good sign of treatment response, it may have a severe impact on cosmetic appearance and quality-of-life in patients with darker skin. Untreated immune-related vitiligo is usually permanent despite discontinuation or interruption of ICIs. Treatments include TCS, topical calcineurin inhibitors, topical JAK inhibitors, phototherapy (narrowband UVB) as well as systemic steroids. Camouflage can also be used. Even though depigmentation can be stigmatizing and devastating for self-esteem and quality-of-life, it remains a side effect that is not life threatening. We must acknowledge the impact of this side effect, offer support and treatment options, and encourage patients to stay on the ICIs.

Conclusion

Patients with SoC face distinct challenges in the diagnosis and management of CAEs related to cancer treatment, including a higher risk of complications such as pigmentary alterations. These differences, often underrecognized due to subtle clinical presentations in darker skin tones, contribute to delays in care and long-term psychosocial impact.

This guideline addresses critical gaps in dermatologic oncology by providing guidance for CAE prevention and management tailored to diverse skin types, including skincare, sun protection, and treatment of pigmentary changes. It also outlines the need for personalized skincare based on individual preferences and physiological differences.

Improved education, diverse clinical imagery, and better representation of SoC in clinical trials and research are essential next steps. As efforts continue to advance health equity in cancer care across Canada, integrating skin diversity into oncology practice will be key to improving outcomes for all patients.

Disclosure

Cynthia Fournier reports personal fees from Sanofi, personal fees from Sun Pharmaceuticals, personal fees from La Roche Posay (L'Oreal Canada), personal fees from Vichy (L'Oreal Canada), personal fees from Celltrion Healthcare, personal fees from BioJamp, personal fees from Naos, personal fees from Galderma, personal fees from Arcutis, personal fees from Abbvie, personal fees from Janssen, personal fees from BMS, personal fees from Amgen, personal fees from UCB, personal fees from Novartis, outside the submitted work. Maxwell Sauder reports personal fees from Amgen, personal fees from Abbvie, personal fees from Arcutis, personal fees from Bausch Health, personal fees from Eli Lilly, personal fees from Galderma, personal fees from Incyte Pharma, personal fees from Janssen, personal fees from L'Oreal Canada, personal fees from LEO Pharmaceutical, personal fees from Merck, personal fees from Novartis, personal fees from Pfizer, personal fees from Regeneron, personal fees from Sanofi, personal fees from Sun Pharmaceutical, personal fees from UCB, outside the submitted work. Joel Claveau reports personal fees from L'Oréal Canada, during the conduct of the study; personal fees from L'Oréal, outside the submitted work. Marcus Butler reports grants, personal fees from Merck, personal fees from BMS, grants from Novartis, personal fees from Immunocore, personal fees from Sanofi, personal fees from Regeneron from AstraZeneca, personal fees from Medison, personal fees from Ideaya, personal fees from GlaxoSmithKline, personal fees from Ankyra, personal fees from Pfizer, personal fees from Adaptimmune, personal fees from Iovance, grants from Takara, during the conduct of the study. Tarek Hijal reports personal fees from L'Oreal Canada, during the conduct of the study. Nour Dayeh is an employee of L'Oreal Canada. The authors report no other conflicts of interest in this work.

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