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The Role of Skin Care in Oncology Patients

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ABSTRACT

Introduction: As more Canadians are living with or surviving from cancer, an increasing number have cutaneous sequalae of anti-cancer treatments. These cutaneous changes can severely impact quality of life and ultimately treatment outcomes.

Objectives: The consensus paper aims to identify the impact on patients of skin toxicities associated with radiation, chemotherapy, targeted therapy, immunotherapy, and hormonal treatment, as well as evidence-based best practices for skincare to minimize or prevent these changes.

Methods: A literature review explored clinical insights into the role of skin care in cancer- treatment-related skin toxicity. An expert panel of clinicians treating oncology patients convened for a one-day meeting to discuss the literature selected before the meeting, and adopt statements using the expert opinion and experience of the panel. The information is intended for health care providers caring for cancer patients.

Results: Patients frequently report skin toxicities to be unanticipated and much worse than their initial beliefs that may result in treatment reduction, interruption or discontinuation. Strategies to prevent or mitigate skin toxicity aim to reduce inflammation, promote skin healing, improve comfort and quality of life during cancer treatment. While evidence is lacking, a simple skin care regimen focused on a gentle cleanser, a moisturizer, and sunscreen may reduce skin toxicities.

Conclusions: Skin toxicities induced by cancer therapy negatively impact body image, physical, emotional and functional wellbeing, and cancer treatment satisfaction. Management of skin toxicities should focus on the quality of life, psychological wellbeing, improving treatment adherence, and treatment response.

Key words: cancer treatment-related cutaneous toxicities; skincare

Introduction

Excluding skin cancer, the most commonly diagnosed cancer in females is breast cancer, in males, prostate cancer, and lung cancer in both sexes.[1] In 2019, these four cancer-types accounted for over half of all cancer diagnoses (220,400) and cancer deaths (82,100) in Canada.[1] Survival rates are increasing due to a variety of factors, including earlier diagnoses and new classes of more efficacious therapies. With diagnosis and survivorship of cancers both increasing, more Canadians than ever will be living with or have survived cancer.

Cancer treatments may include surgery, radiation, transplantation, traditional chemotherapies, targeted therapies, immunotherapy, or hormonal therapies. The type of treatment is dependant on the specific cancer, stage, and other patients related factors. Despite improved agents used for cancer treatment, adverse cutaneous reactions are common.[2,3] If not managed effectively, these skin toxicities may cause significant discomfort, can be disfiguring, lead to serious morbidities that severely affect the quality of life, and may limit or discontinue anticancer treatment.[3,4] Skin toxicity as a result of cancer treatment is a largely neglected field.[4] The prevention and timely treatment of adverse cutaneous reactions deserve more attention from dermatologists, who should be part of the multidisciplinary oncology treatment team. Skincare products are used widely for inflammatory skin diseases and reported to help restore the dysfunctional epidermal barrier. The application of a proper skincare regime can reduce symptoms associated with dry skin and pruritus.[5-7] The use of gentle cleansers, moisturizers, and sunscreen for cancer-treatment related toxicity have demonstrated a reduced incidence of skin toxicities.[6-12]

Scope

The authors reviewed challenges in addressing skin toxicity issues in oncology patients and to what extent these factors attribute to the patients' quality of life and cancer treatment outcomes. Clinical insights into the best approach for oncology skin care programs for all stakeholders in the Canadian healthcare setting were then further explored to develop expert opinion recommended practices.

Methods

An expert panel of clinicians treating oncology patients convened for a one-day meeting (October 2019; Toronto, ON). Statements, intended for health care providers caring for cancer patients, were developed based on the literature selected before the meeting and were discussed and adopted using evidence coupled with the expert opinion and experience of the panel.

Literature Review

A literature review included guidelines, consensus papers, and publications on the management of oncology treatment-related skin toxicities, clinical and other research studies published in the English language from January 2010 to August 2019.

Excluded were articles with no original data (unless a review article was deemed relevant), not dealing with the management of oncology treatment-related skin toxicity, publication language other than English.

A dermatologist and a physician/scientist conducted the searches on September 16 and 17, 2019 on PubMed and Google Scholar of the English-language literature using the terms:

Cutaneous toxicities associated with radiation treatment, chemotherapy, targeted therapy, immunotherapy, hormonal treatment, prevention, management, maintenance of cutaneous toxicities, health-related quality of life, skincare, dermocosmetics for skin toxicities.

The results of the searches were evaluated independently by two reviewers; discrepancies were resolved by discussion. The searches yielded two-hundred and thirty-six papers, and after exclusion of duplicates, we reviewed one-hundred and forty-two publications. After exclusion of articles that were deemed not to be relevant (other subjects, poor quality, a small number, case studies), forty-nine papers remained. Twenty-eight were review articles, including one guideline, two algorithms, and one systemic literature review. Additionally, eight clinical studies, one book, and thirteen other publications were selected.

Living With Cancer in Canada

The number of Canadians living with cancer has increased since death rates peaked in 1988; mortality has decreased by 35% in males and 20% in females.[1] Reduced mortality rates are likely due to a combination of early detection efforts, increased access to screening for some cancers (for example, breast cancer), and more effective treatments. Moreover, there is an overall decline in the incidence of certain types of cancer because of successful prevention efforts (for example, anti-smoking measures).

When ranking the 1995-2014 five-year survival rates for those with the main four types of cancer, Canada ranks among the highest in the world.[13] More Canadians are living with or surviving from cancer and may have cutaneous changes or sequala of anticancer treatments, impacting their quality of life and/or treatment outcomes.[3,4]

Anticancer Modalities and Associated Skin Toxicities

Radiation Treatment

Approximately 50% of cancer patients receive radiotherapy. Radiotherapy damages the DNA of cancerous cells via ionizing atoms that make up the DNA chain.[14] The development of radiation-induced skin changes is a significant adverse effect of radiation therapy occurring in up to 95% of patients.[15] Radiation dermatitis occurs in up to 87% of breast cancer patients and 90% of head and neck patients and may be aggravated by concurrent anti-cancer therapies.[16] Dermatitis is limited to the area that received the beam and is dependent on the target, dose, and treatment schedule. Radiation dermatitis is categorized as acute, occurring within 1 to 4 weeks of treatment or chronic occurring after four weeks and can develop years after treatment.[16] Cutaneous repercussions of radiotherapy vary considerably in severity, course, and prognosis and can have severe sequelae that impact the quality of life as well as a cancer treatment (Table 1).[15,16]

Chemotherapy

Chemotherapy aims to disrupt specific phases of the cell cycle in actively dividing cancer cells. The adverse effects occur primarily

Acute – ~1 to 4 Weeks	Chronic – Weeks to Years
Mild • Dry desquamation • Moderate erythema • Itch **Severe** • Moist desquamation • Bleeding • Severe pain • Ulceration	• Pigmentary alteration • Telangectasia • Atrophy and fragility • Permanent alopecia • Sweat gland atrophy • Necrosis of soft tissue, cartilage and/or bone • Fibrosis

Table 1: Radiation dermatitis presentations.

while the patient is on treatment, and sequelae of therapy/metabolites can occur on uninvolved organs.[3,15-17]

An observational study that evaluated cutaneous toxicities in a thousand cancer patients undergoing chemotherapy reported that three hundred and eighty-four (38.4%) patients presented with cutaneous adverse reactions.[17] Frequently observed toxicities were anagen effluvium (78.6%), xerosis (4.4%), thrombophlebitis (3.1%), pruritus (2.9%), melanonychia (2.9%), hand-foot syndrome (2.6%), extravasation reactions (1.8%), flagellate dermatosis (1.3%), prurigo nodularis (0.8%), exfoliation (0.5%), ichthyosis (0.5%), papulopustular rash (0.3%), bullous photodermatitis (0.3%), and Sweet's syndrome (0.3%) (Table 2).[17,18] The investigators noted that anagen effluvium was mostly caused by combinations of alkylating agents, handfoot syndrome was mostly due to taxanes (docetaxel), flagellate dermatoses resulted mostly from treatment with antitumor antibiotics (bleomycin), and exfoliation from antimetabolites (methotrexate) therapy.[17]

Targeted Therapy

Targeted therapies are theoretically more effective and less harmful to normal cells than traditional chemotherapy since they act at the molecular level rather than the cellular level of chemotherapy.[18-21] Targeted molecules in chemotherapy have revolutionized the treatment of hematological malignancies and solid tumors of head and neck, breast, lung, liver, kidney or colorectal origin, and melanoma.[21] Examples of these targeted molecules include: BRAF inhibitors (dabrafenib and vemurafenib) and MEK inhibitors (trametinib and cobimetinib), Brc-abl inhibitors (imatinib, dasatinib, nilotinib) and, multikinase inhibitors (sorafenib, sunitinib, sorafenib, etc).[21-26] There are both common and target specific cutaneous reactions to these molecules (Table 3).

Multikinase inhibitors, such as sorafenib, sunitinib, and regorafenib, may cause Hand-Foot Skin Reaction (HFSR).[21-26] HFSR presents with tender hyperkeratotic lesions, with or without blisters, surrounded rim of erythema and thickened, painful lesions are more pronounced on areas with increased pressure and friction.[22] The onset of the reaction is typically between 2 and 24 days with scaling, swelling, redness, then dryness and peeling.

EGFR inhibitors such as erlotinib, cetuximab, and panitumumab, as well as MEK inhibitors, can cause acneiform/papulopustular eruptions.[18, 23] The eruption involves sebaceous areas such as the scalp, face, upper trunk, and occurs in 45-100% of patients.[23] Follicular based papules and pustules become crusted, with no comedones present. Onset is typically at 8-10 days, with a peak at two weeks followed by resolution 8-10 weeks after the end of treatment. [23,24] In past studies, approximately 32% of oncologists will stop the treatment due to rash alone,[23,24] whereas the appearance of the eruption may be a positive prognostic factor.[27]

BRAF related keratinocyte proliferation (KA), neoplasms (SCC), and verrucous keratoses may occur as early as one week after treatment, but on average, it takes 6-12 weeks.[25-29] KA and SCC may occur within a median time of eight weeks (4-31%) when using vemurafenib and when using dabrafenib, it takes up to 16 weeks (6-11%) for adverse skin reactions to appear.[25-28] In general, adverse skin reactions develop in the first six months but may also take over a year to develop.[25-29] With the shift to combination BRAF plus MEK inhibition, there has been a decrease in most cutaneous adverse events.

Immunotherapy

Immunotherapy activates host immune mechanisms to treat cancer. These monoclonal antibodies (moAbs) cut the brakes on the immune system by inhibiting regulatory molecules that inhibit T cell activation.[30-34] Immunotherapy using monoclonal antibodies may be administered as a single agent (anti-CTLA-4 (ipilimumab), anti-PD-1 (pembrolizumab, nivolumab), anti-PD-L1 (atezolizumab, durvalumab, and avelumab)) or a combination (ipilimumab and nivolumab).[30-34]

Skin toxicities can occur at any time throughout the treatment and may continue long after treatment discontinuation. [30-34] Most skin toxicities occur early within the first few weeks of treatment and can impact patient activities of daily living (ADLs), psychological health, and self-image.[4,30-34] The most commonly observed cutaneous immune-related adverse events (irAEs) are 'rash' (24% CTLA-4, 15% anti-PD-1, 40% combo), pruritus (25-35% CTLA-4, 13-22% anti-PD-1, 33% combinations) and vitiligo (~8% of melanoma patients treated with PD-1 and combinations) and is considered a good prognostic indicator of response.[35-39] The fact that most studies state "rash" as most common cutaneous irAE shows the need for dermatologic management. Less common irAEs are vasculitis, sarcoidosis, panniculitis, drug-reaction with eosinophils and systemic symptoms (DRESS), Stevens-Johnson Syndrome or toxic epidermal necrolysis (Table 4).[30]

Hormonal Therapy

Hormonal therapy is frequently applied for breast cancer patients, such as with aromatase inhibitors (anastrozole, exemestane, and letrozole) and selective estrogen receptor modulators (SERMs) (Raloxifene, tamoxifen, and toremifene) (Table 5).[3] These drugs cause reversible alopecia, flushing, and vulvovaginal dryness or atrophy.[30] Dyspareunia and secondary vaginismus are common adverse effects of selective estrogen receptor modulators and aromatase inhibitors.[40] Symptoms of vulvovaginal atrophy are more prevalent in patients taking aromatase inhibitors.[41]

Drug Class	Name	Common Oncologic Indications	Select Skin and Appendageal Reactions
Antimetabolites	5-fluorouracil	Gastrointestinal, breast, pancreatic	Alopecia (reversible and permanent) Hand Foot Syndrome (HFS)/palmoplantar erythrodysesthia (PPE) Nail changes (onycholysis, pigmentary alteration, brittle nails)[18] Phototoxicity
	Capecitabine	Gastrointestinal, breast, pancreatic	
	Gemcitabine	Bladder, pancreatic, ovarian, breast, non-small cell lung	
	Cytarabine	AML, ALL, CML, non-Hodgkin's lymphoma	
	Cladribine	Hairy cell leukemia, CLL	
	Methotrexate	Breast, head and neck, leukemia, lymphoma, lung, osteosarcoma, bladder	
	Hydroxyurea	CML, cervical, polycythemia vera	
	Mercaptopurine	ALL, CML	
Taxanes	Docetaxel	Breast, head and neck, stomach, prostate, non–small-cell lung	Alopecia (reversible and permanent); Periarticular Thenar Erythema and Onycholysis (PATEO); Mucositis; Nail changes (onycholysis, pigmentary alteration, brittle nails); Paronychia (± pyogenic granulomas)[18]
	Paclitaxel	Ovarian, breast, lung, Kaposi sarcoma, cervical, pancreatic	
	Nanoparticle albumin-bound (nab)-paclitaxel	Breast, lung, pancreatic	
Vinca alkaloids	Vincristine	ALL, AML, Hodgkin's disease, neuroblastoma, small cell lung	Oral lesions; Oral ulceration;[18] Alopecia (reversible); Nail changes (Bau lines, leukonychia, Mees lines, Muehrcke lines, onychodermal band, pigmentation)[18]
	Vinblastine	Hodgkin's disease, non-small cell lung, bladder, brain, melanoma, testicular	
Alkylating agents	Cyclophosphamide	Lymphomas, multiple myeloma, leukemia, ovarian, breast, small cell lung, neuroblastoma, sarcoma	Alopecia (reversible and permanent);[18] Facial erythema; Facial urticaria; HFS; Skin pigmentation; Nail changes (Bau lines, leukonychia, Mees lines, Muehrcke lines, onychodermal band, pigmentation)[18]
	Ifosfamide	Testicular, soft tissue sarcoma, osteosarcoma, bladder, small cell lung, cervical, ovarian	
	Melphalan	Multiple myeloma, melanoma, ovarian	
	Dacarbazine	Hodgkin's disease, melanoma	
	Nitrosoureas	Brain	
	Busulfan	Conditioning agent prior to stem cell transplantation	
	Thiotepa	Breast, ovarian, bladder, Hodgkin's disease	

Platinum-based	Cisplatin	Testicular, ovarian, breast, cervical, bladder, head and neck, esophageal, lung, mesothelioma, brain, neuroblastoma	Alopecia (reversible); xerosis; toxic erythema[18]
	Carboplatin	Ovarian, lung	
	Oxaliplatin	Colorectal	
Topoisomerase inhibitors	Topotecan	Ovarian, cervical, lung	Alopecia (reversible); HFS (toxic erythema); Mucositis[18]
	Irinotecan	Colorectal, lung	
	Etoposide	Testicular, lung, lymphoma, leukemia, neuroblastoma, ovarian	
Antibiotics	Bleomycin	Hodgkin's disease, non-Hodgkin's lymphoma, testicular, ovarian, cervical	Nail changes (Bau lines, dystrophy, reduced growth, nail loss, onychodystrophy)[18]
	Actinomycin D	Wilms tumor, rhabdomyosarcoma, Ewing's sarcoma, trophoblastic neoplasm, testicular, ovarian	
Anthracyclines	Doxorubicin	Ovarian, AIDS-related Kaposi sarcoma, multiple myeloma, breast, ALL, AML, Wilms tumor, neuroblastoma, soft tissue and bone sarcomas, bladder, thyroid, gastric, Hodgkin disease, lymphoma, lung	Alopecia (reversible and permanent); HFS/ PPE; Mucositis; Nail changes (onycholysis, pigmentary alteration, brittle nails); Paronychia (± pyogenic granulomas)
	Pegylated liposomal doxorubicin	Ovarian, multiple myeloma, breast, cutaneous T-cell lymphoma, Hodgkin's disease, soft tissue sarcoma, uterine sarcoma	
	Daunorubicin	AML, ALL, CML, Kaposi sarcoma	
	Epirubicin	Breast, ovarian, gastric, lung, lymphomas	

Table 2: Traditional chemotherapies, oncologic indication and selected toxicities.

ALL, acute lymphocytic leukemia; AML, acute myeloid leukemia; CLL, chronic lymphocytic leukemia; CML, chronic myelogenous leukemia.

Adapted from Ferreira MN, et al. Dermatologic conditions in women receiving systemic cancer therapy. Int J Women Dermatol 2019;5(5):285-307. https://doi.org/10.1016/j.ijwd.2019.10.003[3]

Drug Class	Name	Common Oncologic Indications	Select Skin and Appendageal Reactions
EGFR inhibitors/HER1 inhibitors	Cetuximab	Head and neck, colorectal	Papulopustular (acneiform) eruption; Alopecia (reversible); Nail changes (onycholysis, pigmentary alteration, brittle nails); Paronychia (± pyogenic granulomas); Phototoxicity; Trichomegaly, hirsutism
	Panitumumab	Colorectal	
	Erlotinib	Lung, pancreatic	
	Gefitinib	Non-small cell lung	
HER2 inhibitors	Trastuzumab	Breast	Nail changes (onycholysis, pigmentary alteration, brittle nails); Papulopustular (acneiform) eruption; Paronychia (± pyogenic granulomas); Trichomegaly, hirsutism
	Pertuzumab	Breast	
EGFR/HER2 inhibitors	Lapatinib	Breast	Alopecia (reversible); Nail changes (onycholysis, pigmentary alteration, brittle nails); Papulopustular (acneiform) eruption; Papulopustular (acneiform) eruption; Paronychia (± pyogenic granulomas); Phototoxicity; Trichomegaly, hirsutism
	Afatinib	Non-small cell lung	
Bruton's tyrosine kinase inhibitor	Ibrutinib	Mantle cell lymphoma, CLL, Waldenström's macroglobulinemia	Petechiae, purpura and increased bleeding Brittle nails Softening and straightening of hair Pruritus
Multikinase inhibitors	Sorafenib	Renal cell, liver, AML, thyroid	Alopecia (reversible); Hand foot skin reaction (HFSR); Mucocutaneous haemorrhage; Nail changes (onycholysis, pigmentary alteration, brittle nails); Panniculitis; Trichomegaly, hirsutism;
	Sunitinib	Renal cell, GIST	
	Regorafenib	Colorectal, hepatocellular, GIST	
	Pazopanib	Renal cell, soft tissue sarcoma	
	Cabozantinib	Thyroid, renal cell	
	Axitinib	Renal cell	
	Vandetinib	Thyroid	
	Dasatinib	CML, ALL	
	Imatinib	CML, ALL, GIST, hypereosinophilic syndrome, chronic eosinophilic leukemia, systemic mastocytosis, myelodysplastic syndrome	
MEK inhibitors	Trametinib	Melanoma	Nail changes (onycholysis, pigmentary alteration, brittle nails); Papulopustular (acneiform) eruption; Paronychia (± pyogenic granulomas); Trichomegaly, hirsutism;
	Cobimetinib	Melanoma	

B-Raf inhibitors	Dabrafenib	Melanoma, lung	HFSR; Panniculitis; Phototoxicity Keratoacanthoma Keratosis-pilaris like reaction Photosensitivity Morbilliform eruption HFSR
	Vemurafenib	Melanoma, Erdheim-Chester	
mTOR inhibitors	Sirolimus	Lymphangioleiomyomatosis, prevention of transplant rejection	HFSR; Mucositis; Papulopustular (acneiform) eruption; Paronychia (± pyogenic granulomas);
	Everolimus	Renal cell, pancreatic, breast, neuroendocrine, prevention of transplant rejection	
	Temsirolimus	Renal cell	
VEGFR inhibitors	Bevacizumab	Colorectal, lung, renal cell, brain, ovarian	Mucocutaneous hemorrhage
Hedgehog inhibitors	Vismodegib	Basal cell	Alopecia Folliculitis Keratoacanthoma Dermal hypersensitivity
	Sonidegib	Basal cell	

Table 3: Targeted therapies, oncologic indication and selected toxicities.

EGFR, epidermal growth factor receptor; HER, human epidermal growth factor receptor; ALL, acute lymphocytic leukemia; AML, acute myeloid leukemia; CLL, chronic lymphocytic leukemia; CML, chronic myelogenous leukemia; GIST, gastrointestinal stromal tumor; MEK, mitogen-activated protein kinase; BRAF, B-Raf proto-oncogene, serine/threonine kinase; mTOR, mammalian target of rapamycin; VEGFR, vascular endothelial growth factor receptor; HFS, hand-foot syndrome; HFSR, hand-foot skin reaction.

Adapted from Ferreira MN, et al. Dermatologic conditions in women receiving systemic cancer therapy. Int J Women Dermatol 2019;5(5):285-307. https://doi.org/10.1016/j.ijwd.2019.10.003[3]

Skin Toxicity and the Impact on the Quality of Life

Cutaneous adverse events are frequently unanticipated before therapy and severely impact patients' health-related quality of life (HRQL).[42] Almost 70% of patients reported that cutaneous AEs are worse than their initial beliefs before the start of their treatment.[42]

A prospective study measuring the frequency and impact on the quality of life of skin toxicities in women receiving chemotherapy showed that 34% reported the skin AEs as most important during treatment, and they were the most common significant contributor to overall HRQL.[43] Of those who developed skin toxicities, 69% felt significantly limited in their daily activities.[43] Chemotherapy-induced alopecia was rated as the most traumatic side effect in 58% of patients, and 8% of patients would decline chemotherapy because of fear of hair loss.[43]

A single center cross-sectional online survey among fifty-five cancer patients receiving dermatologic care evaluated patients quality of life (adapted questionnaire from the Dermatology Life Quality Index) and patient satisfaction.[44] Patient reported quality of life showed an improvement and dermatologic care resulted in overall satisfied patient outcomes.[44] The influence of dermatologic care on cancer treatment adherence was not clarified.[44]

Prevention and Treatment of Skin Toxicities Using Skincare

For the prevention of skin toxicities, it is recommended to initiate a skincare regime prior to the anticancer treatment.[45-47] Patients should be educated on a daily skincare regime focusing on: hygiene, moisturization, sun protection, and, if applicable, camouflage products.[46-48] The skincare formulations for patients undergoing cancer-therapy should be safe, effective, free of additives, fragrances, perfumes, sensitizing agents, and should have a near physiologic (skin surface) pH.[46-48] Further, the skincare regime should be cosmetically pleasant and easy to use.

According to the panel, the choice of skin care needs to be tailored to the individual patient and may be dependent on the patients' individual preferences. The use of moisturizers can be helpful to restore skin elasticity, sustain skin homeostasis, and control trans-epidermal water loss.[7,15,46-48]

A review of topical agents for the treatment of radiation therapy-related skin toxicities reported no benefits from formulations containing aloe vera, chamomile, ascorbic acid, pantothenic acid, dexpanthenol, and trolamine.[15] However, benefits were shown when using formulations containing hyaluronic acid (HA), epidermal growth factor EGF, granulocyte-macrophage colony-stimulating factor (GM-CSF), topical corticosteroids (TCS) or statins.[15] Topical agents that have common ingredients known as

soothing may be beneficial for the symptoms such as niacinamide, panthenol, squalene, glycerin, and allantoin.[47] Wound healing products and barrier films are widely used, as well, in oncology for cracked skin due to severe dryness.[49,50]

An unpublished multicenter study evaluated the efficacy and tolerability of thermal water containing skincare regime La Roche-Posay (LRP), used for preventing skin toxicity in breast cancer patients undergoing radiotherapy. The regime consisted of two types of cleansers, a moisturizer, a healing baume, and an SPF50+ sunscreen. The two-hundred-fifty-three women with mostly stage I (International Union Against Cancer (UICC) /American Joint Committee on Cancer (AJCC) classification) breast cancer used mainly the cleansers, moisturizer, and healing baume (162 [67%]). Two categories of low and heavy users were defined based on the number of products used (0 to 5) and the frequency at which products were used (Never used = 0; From time to time = 0,5; Often =1; Every day= 2). Those who were heavy users of the skincare regime showed significantly less severe skin toxicities than those with lower use of the skincare regime (Figure 1). There was a statistically significant difference ($p \leq 0.0001$) noted by the investigating physicians between low users and heavy users (Figure 2).

The patient benefit index scores (PBI) [Relevant treatment benefit score PBI ≥ 1, no relevant benefit score PBI ≤ 1] revealed a statistically significant difference between low users and heavy users ($p = 0.095$). For low users: PBI score N = 88) was a mean of 2.7 (SD $\pm$ 1.2), and for the heavy users, the PBI score (N = 143) was a mean of 2.9 (SD $\pm$ 1.1) (Figure 3). The regime was well tolerated and easy to use.

A multicenter prospective observational open-label study evaluated the use of a 12-product kit for patients receiving chemotherapy.[50] Patients received skincare kits before the start of their cancer treatment with instructions to use the skincare throughout the treatment phase. The physicians evaluated the patients' skin condition (edema, erythema, dryness, desquamation, pigmentation disorders, and cracks), and the patients scored the performance of the kit at the end of the study. The study indicated the benefits of skincare, helping to minimize the impact of cutaneous reactions.[50]

Challenges to implementing a skin regimen include: complex regimens, application viewed as a "chore"especially when initiated prophylactically, "wait and see" attitude, socioeconomic status, and cost.

The Role of a Dermatologist as Part of the Multidisciplinary Team

Dermatologists are experts in skin and skin disease. They can improve the care of oncology patients with regards to improving patients' quality of life, treatment outcomes through adherence to anticancer treatment, and rule out life-threatening cutaneous toxicity conditions.[48] The panel recommends that, ideally, dermatologic services be readily available for patients undergoing anticancer treatments. Urgent access is paramount to identify and assist in the management of dangerous or life-threatening cutaneous toxicity and symptoms that are, thankfully, rare. However, almost equally important, is a dermatologists' ability to aid in the improvement of quality of life-related to cutaneous toxicities.[48]

Important to oncologists, an onco-dermatologist or skin toxicities team may be able to preserve anticancer treatment through managing skin toxicities that historically were treated with treatment discontinuation. Chen et al. (2019) reviewed inpatient records from 2011-2018 and selected 33 cases with confirmed cutaneous irAE with similar grading of severity.[48] The use of systemic steroids to manage irAE has been shown to decrease the treatment effect of immunotherapy.[51] In the Chen study, when a dermatologist was involved in the treatment of skin toxicities, patients were less likely to receive systemic steroids (18 versus 55%) and less likely to have the cancer drug discontinued (0 vs. 36%).[48] The multivariable logistic regression showed that a dermatological consult results in a lower risk of disruption of oncologic management.[48]

Conclusion

Cutaneous anticancer toxicities occur at any time during treatment, including well after discontinuation of treatment in the case of radiation and immunotherapy. These toxicities can have a major impact on HRQL.

Patient education, therapeutic relationship, and frequent, open communication between patient and oncology team is essential to treat AEs as early as possible to ensure optimal outcomes. It is necessary to look at the patient holistically and acknowledge the factors involved in their access to resources and willingness to adhere to recommended practices.

A cancer patient's dermatologists/cutaneous toxicities team may improve treatment outcomes, such as reducing the risk of disruption of cancer treatment. Proactively initiating a simple dermocosmetic regime involving hygiene, moisturization, and sun protection is the first step in the prevention or reduction of cutaneous toxicities.

Limitations

As there is a lack of clinical trials on the use of skincare for cancer-treatment related skin toxicities, the recommendations are mainly based on expert opinion.

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Drug Classs	Name	Common Oncologic Indications	Select Skin and Appendageal Reactions
CTLA-4 inhibitors	Ipilimumab	Melanoma, renal cell, colorectal	Non-specific "Maculopapular" rash Pruritus Eczema/spongiosis Lichenoid reactions Psoriasis Pityriasis lichenoides-like Exfoliative Pyoderma gangrenosum Grover's disease Vitiligo Bullous pemphigoid Dermatitis herpetiformis Prurigo nodularis Vasculitis Dermatomyositis Sjögren's syndrome Sarcoidosis Sweet's Syndrome Acneiform rash/papulopustular rosacea Eruptive keratoacanthomas, actinic keratoses and squamous cell carcinoma Erythema nodosum-like panniculitis Radiosensitization Photosensitivity Urticaria Alopecia, alopecia areata, hair repigmentation Sclerodermoid reaction Nail changes Xerostomia
	Tremelimumab	Not FDA approved; orphan drug designation for mesothelioma	
PD-1 inhibitors	Nivolumab	Melanoma, lung, head and neck, Hodgkin's disease, bladder, colorectal, hepatocellular, renal cell	
	Pembrolizumab	Melanoma, lung, head and neck, Hodgkin's disease, primary mediastinal large B-cell lymphoma, bladder, colorectal, gastric, cervical, hepatocellular, Merkel cell, renal cell	
	Cemiplimab	Squamous cell	
PD-L1 inhibitors	Avelumab	Merkel cell, bladder, renal cell	
	Atezolizumab	Bladder, lung, breast	
	Durvalumab	Bladder, lung	

Table 4: Immunotherapies, oncologic indication and selected toxicities

CTLA-4, cytotoxic T-lymphocyte-associated protein 4; PD-1, programmed cell death 1; PD-L1, programmed death–ligand 1.

Adapted from Ferreira MN, et al. Dermatologic conditions in women receiving systemic cancer therapy. *Int J Women Dermatol*. 2019;5(5):285-307. https://doi.org/10.1016/j.ijwd.2019.10.003[3]

Drug Class	Name	Common Oncologic Indications	Select Skin and Appendageal Reactions
Aromatase inhibitors	Anastrozole	Breast	Flushing; Vulvovaginal dryness/atrophy
	Exemestane	Breast	
	Letrozole	Breast	
SERMs	Raloxifene	Breast	Alopecia (reversible); Flushing; Vulvovaginal dryness/atrophy
	Tamoxifen	Breast	
	Toremifene	Breast	

Table 5: Hormonal therapy

SERMs, selective estrogen receptor modulators

Adapted from Ferreira MN, et al. Dermatologic conditions in women receiving systemic cancer therapy. *Int J Women Dermatol.* 2019;5(5):285-307. https://doi.org/10.1016/j.ijwd.2019.10.003[3]

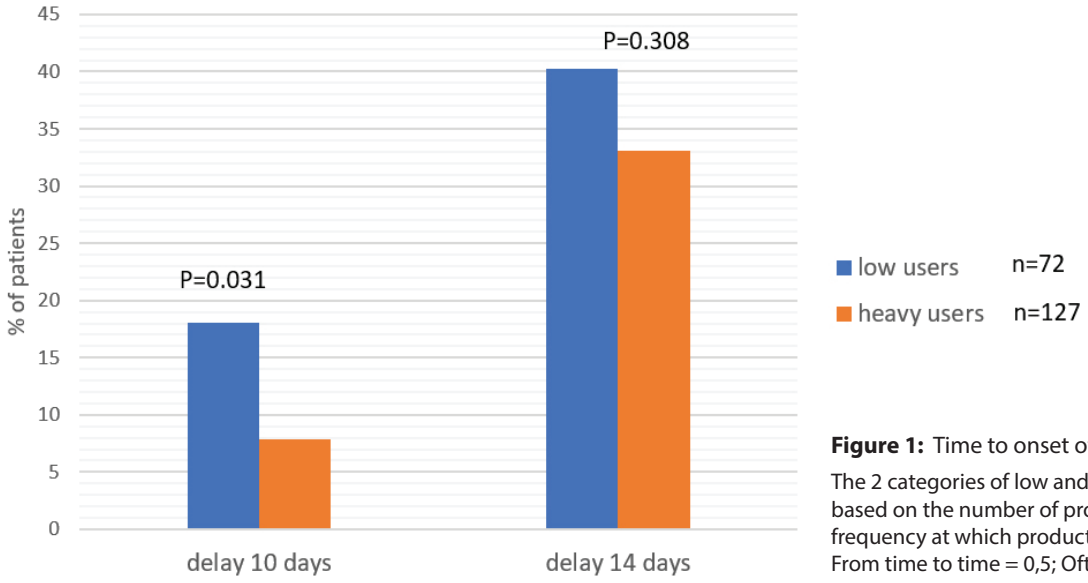


Figure 1: Time to onset of skin reaction

The 2 categories of low and heavy users were defined based on the number of products used (0 to 5) and the frequency at which products were used (Never used = 0; From time to time = 0,5; Often =1; Every day= 2)

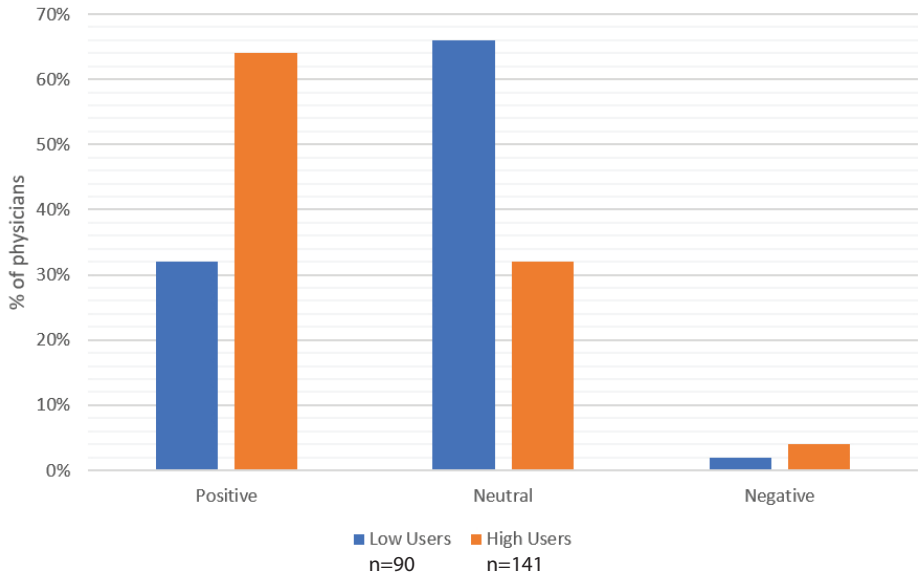
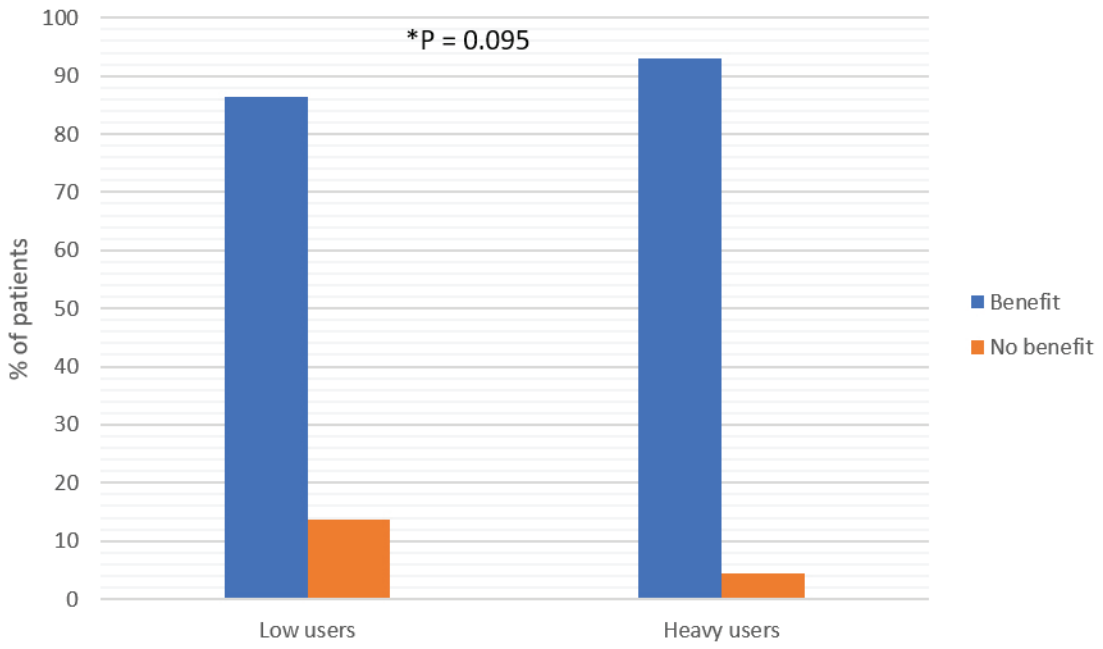


Figure 2: Opinion of investigating physician

The 2 categories of low and heavy users were defined based on the number of products used (0 to 5) and the frequency at which products were used (Never used = 0; From time to time = 0,5; Often =1; Every day= 2)



PBI scores	Low users	Heavy users
	N = 88, Mean (±SD)	N = 143, Mean (±SD)
Reducing social impairements	68, 2.3 (± 1.6)	123, 2.4 (± 1.6)
Reducing psychological impairements	74, 2.6 (± 1.4)	133, 2.7 (± 1.5)
Reducing therapyl impairements	74, 2.5 (± 1.4)	135, 2.8 (± 1.3)
Reducing physical impairements	85, 2.1 (± 1.4)	143, 2.4 (± 1.4)
Reducing confidence in healing	78, 3.0 (± 1.4)	134, 3.0 (± 1.4)
Total PBI score	88, 2.7 (± 1.2)	143, 2.9 (± 1.1)

P-value between low users and heavy users (p = 0.095)

Figure 3: Patient benefit index scores

*Statistically significant difference between low users and heavy users (p = 0.095)

Relevant treatment benefit score PBI ≥ 1, no relevant benefit score PBI ≤1.

Low users: PBI score N = 88) mean 2.7 (± 1.2)

Heavy users: PBI score N = 143) mean 2.9 (± 1.1)

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