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ORIGINAL ARTICLE

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US Cutaneous Oncodermatology Management (USCOM): A Practical Algorithm

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ABSTRACT

Background: An increasing number of patients survive or are living with cancer. Anticancer treatments frequently have cutaneous adverse events (cAEs) that may severely impact patients' quality of life and interrupt anticancer treatment. The US Cutaneous Oncodermatology Management (USCOM) project aims to improve cancer patients' and survivors' quality of life by offering tools for preventing and managing cAEs.

Methods: An algorithm was designed to reduce the incidence of cAEs, treat cAEs, and maintain healthy skin using general measures and over-the-counter agents to support all healthcare providers treating oncology patients, including physicians, nurses, pharmacists, and advanced providers. The panel used a modified Delphi approach, developed, discussed, and reached a consensus on statements and an evidence-based algorithm.

Results: The USCOM algorithm includes education on cAEs for patients and clinicians supporting prevention, treatment, and maintenance using skincare measures before, during, and after cancer treatment. A skincare regimen including hygiene, moisturization, and sun protection products should be safe and effective in helping to minimize cAEs and improving skin conditions such as erythema, xerosis, pruritus, and photosensitivity. The number and quality of studies evaluating skincare formulations and regimens for cAEs are increasing, but the evidence on the benefits of specific formulations is still scarce.

Conclusions: The algorithm focuses on general measures and skincare to prevent or reduce the severity of cAEs. Increased awareness of cAEs by the multidisciplinary team treating and guiding the cancer patient throughout their care may improve patient outcomes.

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BACKGROUND

According to the National Program of Cancer Registries and the North American Association of Central Cancer Registries in the United States (US) in 2019, the estimated number of new cancer cases was 1,762,450.[1] In 2019, the five most commonly diagnosed cancer types in the US for men were prostate cancer, lung and bronchus cancer, colorectum cancer, and urinary bladder cancer. For women, excluding basal and squamous cell skin cancers, common types were breast cancer, colorectal cancer, lung cancer, uterine cancer, and melanoma.[1-4] Increasingly, patients are diagnosed early, and the quality of cancer treatment has improved. Therefore, now more than ever, Americans are living with or surviving cancer.[1-4] As a result, increasing numbers of patients are living with cutaneous toxicities or sequelae of cancer or cancer treatments.[5]

When targeting cancer, various options are available depending on the type, the stage of the disease, and patient-related factors. Treatments may include surgery, radiation, transplantation, chemotherapy, targeted therapy, immunotherapy, hormonal therapy, or combinations of these.[5] Cutaneous adverse events (cAEs) from anticancer treatments occur frequently and are reported as one of the most impactful side effects of cancer treatment.[6,7] These cAEs are often visible and, as a consequence, alter the patients' self-image, leaving their disease exposed.[6,7] Additionally, cAEs related to cancer

treatment do not get medical attention needed to prevent their occurrence or provide early and effective treatment.[8,9] As a result, cutaneous toxicities may be disabling or disfiguring, cause pruritus or pain, alter tactile exchange, impede interpersonal relationships, severely affect the quality of life,[6,7] and may lead to reduction or discontinuation of anticancer treatment, affecting clinical outcomes.[8-12]

A preemptive skincare regimen has been shown to improve patients' quality of life and skin conditions.[7,8] In a study of 95 patients receiving panitumumab-containing therapy, 48 received pre-emptive skincare and 47 received reactive. The incidence of severe skin toxicities in the pre-emptive skincare group had reduced by 50% compared to the reactive skincare group.[7] Moreover, dermatology consultation has led to a reduced interruption of oncology treatment.[9]

A multidisciplinary oncology treatment team should educate on prevention, treatment, and maintenance using OTC skincare as part of their cancer patients' comprehensive care before cancer treatment starts.[12] An algorithm was designed to reduce the incidence of cAEs, treat cAEs, and maintain healthy skin using general measures and OTC agents to support all healthcare providers treating oncology patients, including physicians, nurses, pharmacists, and advanced providers. The clinical algorithm would be feasible to implement by non-dermatologists. It aims to support clinicians working with oncology patients throughout the entire continuum of care to achieve optimal outcomes, improving patients' quality of life.

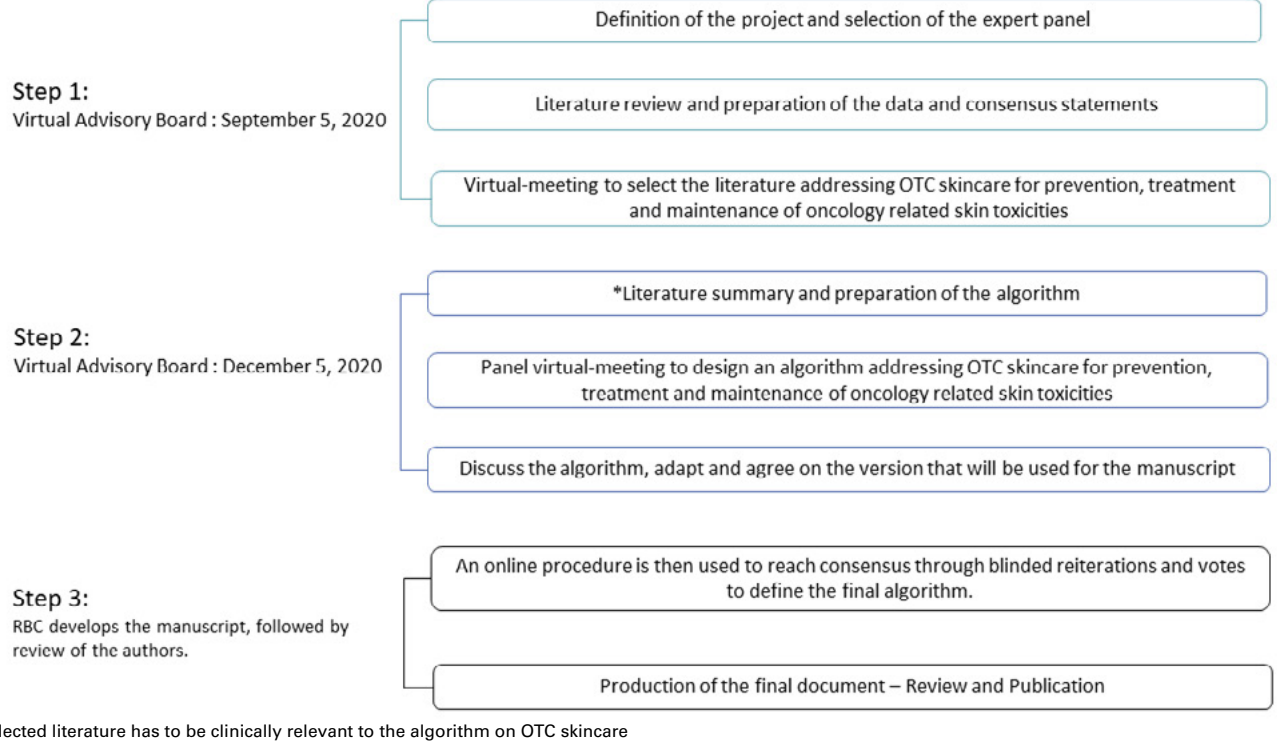
SCOPE

The US Cutaneous Oncodermatology Management (USCOM) project initiated by La-Roche Posay aims to improve cancer patients' and survivors' quality of life by offering tools for preventing and managing cAEs. The USCOM panel of clinicians who treat cAEs developed, discussed, and reached a consensus on statements and an evidence-based algorithm. The algorithm focuses on prevention measures and skincare for cAEs using a skincare regimen, including hygiene, moisturization, sun protection, and camouflage products. The algorithm aims to improve patient outcomes and seeks to determine the best approach for oncology skin care programs for all stakeholders in the US health care setting. These include medical oncologists, radiation oncologists, family practice/internal medicine physicians, dermatologists, oncology nurses, advanced practice providers (APPs), nurse practitioners (NPs), physician assistants (PAs), and pharmacists.

METHODS

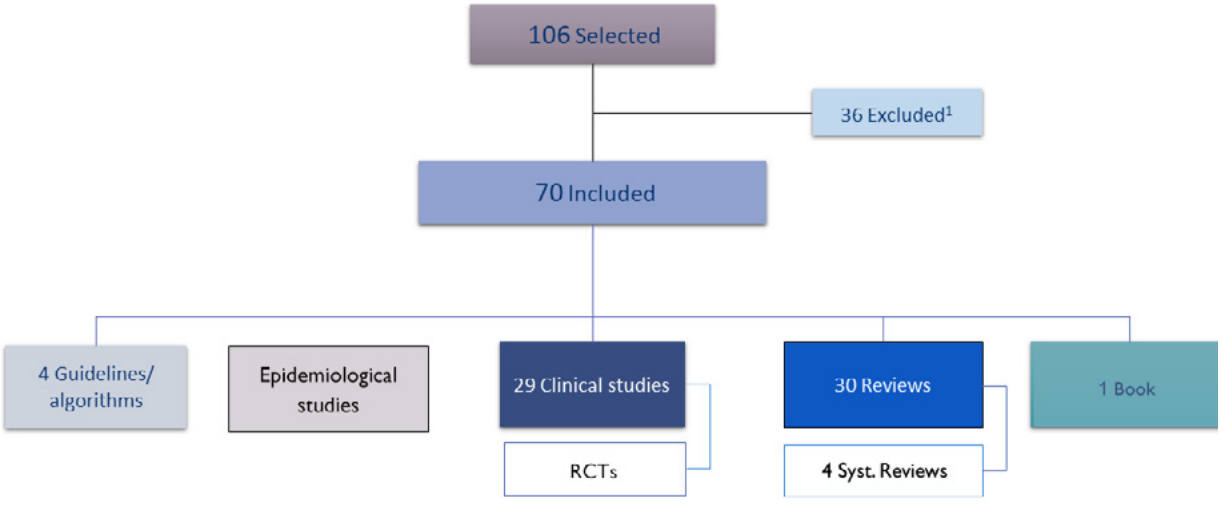
For the statements and the USCOM algorithm's development, the panel used a modified Delphi approach following the AGREE II instrument.[13,14] The modified Delphi method is a communication technique for interactive decision-making for medical projects.[14] The method was adapted from face-to-face meetings to a virtual meeting to discuss the outcome of

FIGURE 1. The process.



*The selected literature has to be clinically relevant to the algorithm on OTC skincare

FIGURE 2. Literature search results.



1. Excluded were: Duplications; In case of an update on a review article, the latest version was used; Poor quality.
2. RCT= randomized controlled trial, Systematic (Syst.)

literature searches and reach a consensus on the statements and algorithm based on the selected literature. The virtual discussion was followed by virtual follow-up, replacing the use of a questionnaire.[14] The process entailed preparing the project, selecting the panel, and conducting systematic literature searches followed by three steps (Figure 1).

Step 1: Virtual panel meeting on September 5, 2020 to review the results of the systematic literature review addressing OTC skincare for prevention, treatment, and maintenance of cAEs and to discuss and adopt statements using evidence coupled with the panels' experience and opinion.

Step 2: Virtual panel meeting on December 5, 2020 to develop, review, and reach consensus on the algorithm.

Step 3: Online process to fine-tune the statements and the algorithm and to prepare and review the publication.

Literature Review

The literature review included guidelines, consensus papers, and publications on the management of cAEs, and clinical and other research studies published in the English language from January 2010 to August 2020. Excluded were articles with no original data (unless a review article was deemed relevant), not dealing with skincare for prevention and treatment of oncology-related cAEs, and publication language other than English.

A dermatologist and a physician-scientist conducted the searches on August 25 and 26, 2020 on PubMed and Google Scholar as a secondary source of the English-language literature using the terms:

Skincare regimens prevent and treat cutaneous toxicities associated with radiation treatment, chemotherapy, targeted therapy, immunotherapy, hormonal treatment, prevention, management, maintenance of cutaneous toxicities, and health-related quality of life. Adjunctive skincare, OTC skincare, staff and patient education, communication strategies, adherence, concordance, efficacy, safety, tolerability, and skin irritation.

The results of the searches were evaluated independently by two reviewers who resolved discrepancies by discussion. The searches yielded one hundred and six publications. After excluding duplicates (n = 36) and articles deemed not relevant for the statements and algorithm (other subjects, low quality, a small number, case studies), 70 papers remained. Thirty were review articles including four systematic reviews, four guidelines/algorithms, five epidemiology studies, one book, one definitions article, and twenty-nine clinical studies (Figure 2).

The literature search results were evaluated independently by two reviewers who graded the clinical publications for study type and quality (randomized controlled trial [RCT) of high quality = A, B, or C) and assigned a level of evidence (level 1 to level 4) using the pre-established criteria (Table 1).[15]

Twenty clinical publications addressed cAEs impacting the quality of life, dermatologic consultation, or skincare, providing important information to support the statements and the USCOM practical algorithm on prevention, treatment, and maintenance using OTC skincare. Most were graded C-3 (n = 13); there were four C-2, and three articles graded B-2 (Table 2).

Consensus Statements

The reviewers drafted statements based on the selected

FIGURE 3. Algorithm for cancer-treatment related cAEs. For grading and risk, see details given in Table 4.

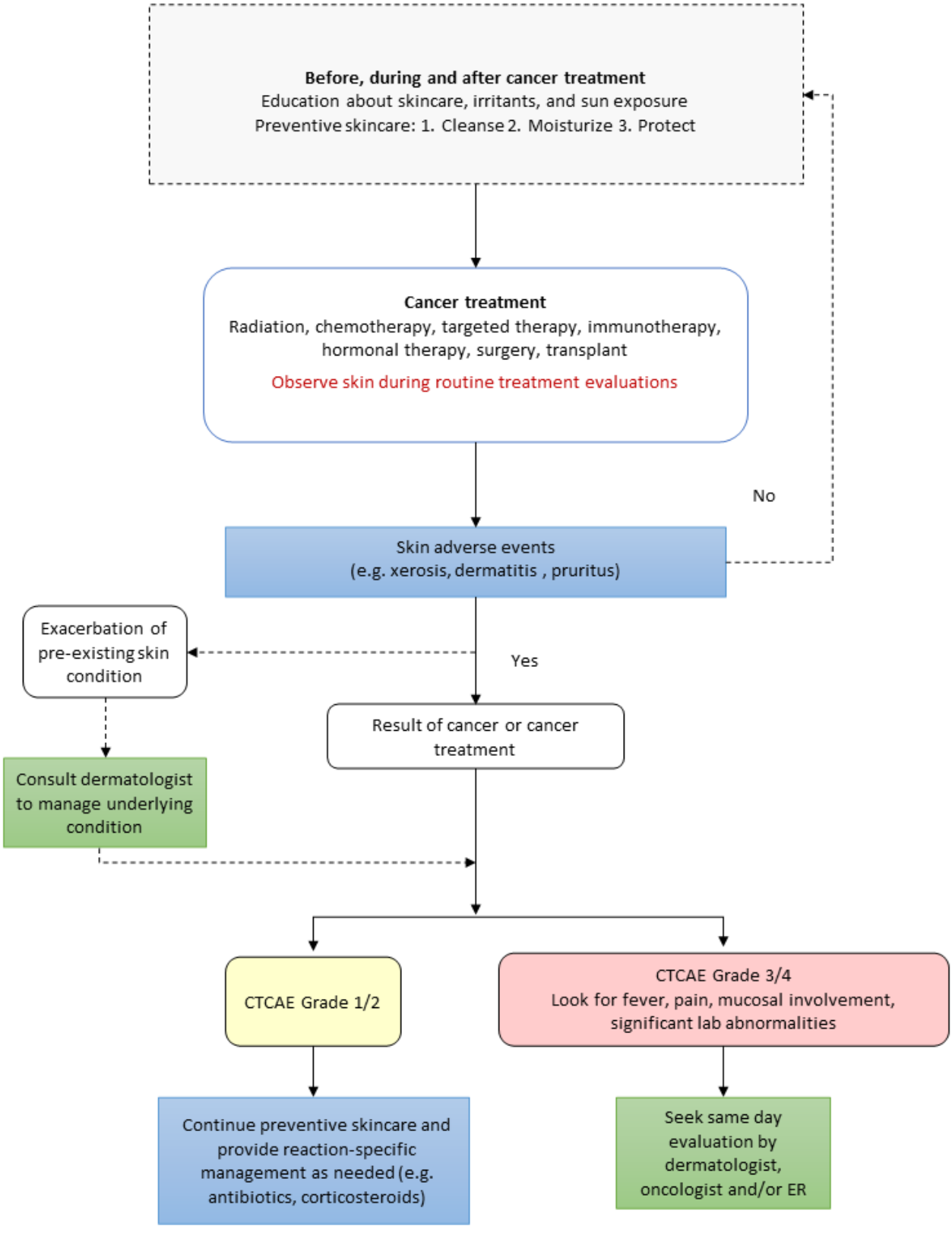


TABLE 1.

Grading and Rating of the Evidence[13]

Grade	Details	Rating	Details
A	RCT, high-quality double-blind trial (eg, sample-size calculation, flow chart of patient inclusion, intention-to-treat analysis, sufficient sample size)	1	Further research is unlikely to change confidence in the estimate of effect (ie, at least two grade A trials are available, and their results are mostly consistent with results of additional grade B or grade C studies)
B	RCT of lesser quality (eg, only single-blind; limited sample size, but with at least 15 patients per study arm)	2	Further research is likely to have a significant effect on confidence in the estimate of effect and may change the estimate (ie, at least three grade B trials are available, and their results are mostly consistent with any additional grade C trials)
C	Comparative trial with severe methodologic limitations (eg, not blinded, very small sample size, no randomization)	3	Further research is very likely to have an important effect on confidence in the estimate of effect and is likely to change the estimate (ie, conflicting evidence or limited number of trials, mostly grade B or grade C)
		4	Any estimate of effect is very uncertain (ie, little or no systematic experimental evidence; trials extremely limited in number and/or quality)

Randomized controlled trial (RCT)

TABLE 2.

Clinical Study Type and Level of Evidence

Clinical Study Type	Level of Evidence	Reference
Cross-sectional study on the impact of skin problems on QoL in patients with cancer treatment	C-3	Lee et al, 2018[6]
Open-label randomized trial on evaluating the impact of a pre-emptive skin treatment regimen on skin toxicities and QoL in patients with metastatic colorectal cancer	B-2	Lacouture ME et al, 2010[7]
Cross-sectional survey on the influence of oncodermatology interventions on patient QoL	C-3	Aizman L et al, 2020[8]
Retrospective cohort on dermatology consultation reducing interruption of oncologic management among hospitalized patients with cAEs	C-3	Chen ST et al, 2020[9]
Retrospective study on outpatient dermatology consultations impact on oncology patients with acute cAEs	C-3	Barrios DM et al, 2020[10]
Retrospective cohort study on cancer treatment interruption and diagnostic concordance between referring clinicians and dermatologists	C-3	Barrios DM et al, 2017[11]
Clinical evaluation of a comprehensive skin toxicity program for patients treated with EGFRi	C-3	Yu Z et al, 2020[17]
Qualitative analysis of acute skin toxicity among breast cancer radiotherapy patients	C-3	Schnur JB et al, 2011[19]
A clinicoepidemiological study of cAEs of chemotherapy in cancer patients	C-2	Biswal SG et al, 2018[23]
A phase II study on pre-emptive skin toxicity treatment for EGFRi evaluating efficacy of skin moisturizers and lymecycline.	C-3	Grande R et al, 2013[26]
Clinical study on targeted therapy-induced facial skin cAEs and the impact on QoL in cancer patients	C-2	Yagasaki K et al, 2018[39]
Assessment of QoL and treatment outcomes of patients with persistent postchemo-therapy alopecia	C-2	Freites-Martinez A et al, 2019[40]
Cohort on early use of steroids affects immune cells and impairs immunotherapy efficacy	C-3	Della Corte CM et al, 2019[42]
Clinical evaluation of supportive and barrier protective skin care products in the daily prevention and treatment of cutaneous toxicity during radiotherapy for breast cancer	C-2	Berger A et al, 2018[46]
Randomized cross-over study on the advantage of a proactive, barrier-protective, supportive skin care in patients with breast cancer on chemotherapy	B-2	Wohlrab J et al, 2011[47]
Evaluation of supportive and barrier-protective skin care products in the daily prevention and treatment of cutaneous toxicity during systemic chemotherapy	C-3	Lüftner D et al, 2018[48]
Outcomes study on embedding dermatologic care within oncology practices	C-3	Sauder MB et al, 2021[50]
Clinical study assessing the validity of clinician advice that patients avoid the use of topical agents before daily radiotherapy treatments	C-2	Baumann BC et al, 2018[54]
Quantitative study on unanticipated toxicities from anticancer therapies: survivors' perspectives	C-3	Cole C et al, 2015[58]
Retrospective survey on the benefits of a multidisciplinary toxicity team for cancer immunotherapy-related cAEs	C-3	Zurfley F et al, 2017[61]

Quality of life (QoL), Cutaneous adverse events (cAEs), EGFR inhibitors (EGFRi)

literature before the meeting. During the virtual meeting, the panel selected and fine-tuned six consensus statements from the draft list of twenty and further added three statements and revised them online after the meeting. Through blinded reiterations and votes, the USCOM panel defined the final statements. The panels' consensus, established as an 80% agreement, was obtained.

Development of the Algorithm

A concept algorithm based on the literature selected before the virtual conference was discussed and adopted using clinical evidence coupled with the panel's expert opinion and experience. An online procedure was then used to reach consensus through blinded reiterations and votes to define the final algorithm.

A clinical algorithm's function is to standardize and support medical decision-making, such as regulating the selection and use of treatment regimens.[13] The best algorithms have inputs and outputs, precisely defined specific steps, and uniquely defined results that depend on the preceding steps used to solve a problem.[16] For the development of the USCOM algorithm, the mnemonic RECUR (Reliable, Efficient, Clear instructions, Understandable, Remember easily) was used.[16]

The current algorithm focuses on preventing and managing cAEs that can benefit from skincare measures and has the following sections: Measures before, during, and after cancer treatment. Assessment includes evaluating the type and severity of the cAEs and describes the action to be taken (Figure 3).

Cancer-Treatment-Related cAEs

Statement 1: *Dermatologic toxicities associated with cancer treatment are common.*

Over the past decade, 5-year cancer survival rates have improved, especially for prostate and breast cancer.[1] Earlier cancer diagnosis, more effective treatments, and enhanced prevention measures, such as anti-smoking measures, have contributed to more cancer patients surviving and living with cancer.[1] Many of these patients suffer from disabling cAEs, which are frequently inadequately managed without the appropriate use of personal hygiene products and skincare.[12,18]

The current review and algorithm focus on a skincare regimen that prevents or reduces the severity of cAEs, treatment, and maintenance. For that reason, it gives only a summary of the cancer treatments and cAEs.

Depending on the type of cancer and cancer treatment, various cAEs may occur.[5] Radiation therapy causes non-specific DNA damage that is limited to the area that received radiation. The damage is dependent on the target volume, dose, and radiation schedule and may affect one to four patients.[20] Acute radiation dermatitis (ARD) may occur during radiation treatment, and subacute radiation dermatitis can persist months after treatment.[19-22]

Mild ARD presents with dry desquamation, mild erythema, and pruritus. Moderate ARD presents with moderate erythema, patchy moist desquamation in skin folds and creases, bleeding induced by minor trauma, and pruritus. Severe conditions show moist desquamation, spontaneous bleeding, severe pain, and even ulceration.[19-22]

Chronic radiation dermatitis ranges from persistent mild to severe pigmentary alteration, atrophy, necrosis, and telangiectasia.[21]

Chemotherapy aims to disrupt the cell cycle's specific phases in actively dividing cancer cells, causing significant effects while on treatment.[23] The cAEs can be non-specific or agent-specific, and sequelae of therapy/metabolites can occur on uninvolved organs.[23] Chemotherapy can be associated with reversible or permanent alopecia, hand and foot syndrome (HFS), nail changes (onycholysis, pigmentary alteration, brittle nails), and phototoxicity.[23] HFS presents with erythema and tenderness, with or without blisters with a surrounded rim of erythema. Painful and thickened lesions can occur and are more pronounced in areas with increased pressure and friction.

Targeted therapies inhibit specific molecules involving tumor pathogenesis.[24-27] Targeted therapy-related cAEs include papulopustular reactions, reversible alopecia hyperkeratosis (keratosis-pilaris like changes, keratoderma), nail changes (onycholysis, pigmentary alteration, brittle nails), paronychia (± pyogenic granulomas), phototoxicity, trichomegaly, and hirsutism.[18,24-28]

Immunotherapy aims to activate the host immune mechanisms by blocking immune-suppressing pathways. cAEs may occur at any time during and after treatment. These cAEs include pruritus, xerosis, lichenoid reactions, psoriasiform reactions, eczematoid eruptions, vitiligo, bullous diseases, etc.[27-36]

Hormonal therapy, for instance, treating breast and prostate cancer, may cause flushing, xerosis, vulvovaginal dryness, atrophy, alopecia, or pigmentary alterations.[37,38]

The panel developed an overview of the treatments and related cAEs, including a glossary to help identify frequently occurring cAEs relevant to the current algorithm.

Impact of Cutaneous Toxicities on the Patients' Quality of Life

Statement 2: *Acute and chronic skin reactions can significantly*

impact the quality of life and disrupt cancer treatment.

Many studies are available on cAEs; however, more robust studies are needed on prevention, treatment, and maintenance using skincare.[5-12,17-20,22,25,29,39] cAEs negatively affect functional and emotional domains relating to QoL in cancer patients. Moreover, multiple negative experiences due to cAEs may increase psychological distress and avoidance of personal relationships, leading to social isolation.[6-8,39]

Patients reported that cAEs significantly limit their daily activities and are an essential contributor to a reduced QoL.[6-8,39] Women noted alopecia as the most traumatic adverse event of various systemic cancer treatments.[18,23,24,40]

Although clinicians acknowledged the importance of achieving a sufficient balance between cancer-treatment efficacy and cAEs to maintain an optimal QoL in cancer survivors, the research available on the prevention and treatment using an effective skincare regimen for these cAEs is limited.[6-12, 39]

Cutaneous AEs Impact Cancer Treatment

Statement 3: *Disabling skin reactions is a significant problem for many patients and their treating physicians.*

Cytotoxic and targeted cancer treatments that impede cancer cells' proliferation also affect rapidly proliferating organ systems. The most commonly documented cAEs include papulopustular rash, xerosis, pruritus, nail changes, chemotherapy-induced alopecia, and hand-foot syndrome/skin reaction.[8] The probability of cancer patients to develop cAEs with cytotoxic and targeted cancer treatments significantly impact wellness and treatment adherence.[5-12,18,28-40] Persistent cAEs may be disabling, and over 50% of cancer patients treated with selected agents may experience an interruption in therapy secondary to these toxicities.[10,11] It is important to have a dermatologist on the multidisciplinary oncology team to enable accurate diagnosis and treatment of the cAEs, allowing the continuation of cancer treatment that historically would have been discontinued.[8,39,41]

When reviewing inpatient records from 2011–2018, Chen et al (2019) selected 33 cases with confirmed cAEs due to immunotherapy with similar severity grading.[9] Systemic steroids used to manage these cAEs decreased the cancer-treatment effect of immunotherapy https://pubmed.ncbi.nlm.nih.gov/31856311/.[42] Involving a dermatologist in the treatment of cAEs, the retrospective study showed that patients were less likely to receive systemic steroids (18% vs 55%) and less likely to have cancer treatment disrupted or discontinued (0 vs 36%).[9] Another study by Barrios et al (2017) demonstrated that 50% of patients who received cytostatic and targeted therapy experienced an interruption in treatment due to cAEs.[11]

Skincare Benefits for cAEs

Statement 4: *When acute cutaneous reactions develop, effective skincare should be reinforced to reduce further complications and assist in managing toxicities.*

Currently, cutaneous toxicity programs are being established, aiming to promote dermatologic health in cancer patients.[39] A multidisciplinary team, including dermatologists, can improve oncology patients' care.[8-10,12] Attention for prevention and early and correct diagnosis ruling out life-threatening cAEs can improve adherence to cancer treatment and, therefore, outcomes.[8-10,12]

A multidisciplinary panel of clinicians treating oncology patients recommended that, ideally, dermatologic services should be readily available for patients undergoing cancer treatments.[12] The service should include urgent access to a dermatologist to identify and assist in managing life-threatening cAEs.[12] Moreover, when acute cAEs develop, an effective skincare regimen should be put in place immediately to prevent further deterioration of the condition and improve patient comfort and quality of life.[12,39,44,45] Although studies have demonstrated that dermatological care resulted in improved patient-reported QoL and cancer treatment outcomes, the influence of skincare on cancer treatment adherence is yet to be elucidated.[8]

Statement 5: *Supportive care and appropriate skincare continue to be mainstays of prevention and treatment for acute and chronic dermatologic toxicities.*

The number and quality of studies evaluating skincare formulations and regimens for various cancer-treatment-related cAEs increase, but the evidence on the benefits of specific formulations is still scarce. Currently, most available studies include patients with ARD. Rosenthal et al (2019) reviewed the efficacy of topical agents for ARD and found formulations containing aloe vera, chamomile, ascorbic acid, pantothenic acid, dexpanthenol, and trolamine to lack benefits.[22] They further showed that formulations containing hyaluronic acid, epidermal growth factor, granulocyte-macrophage colony-stimulating factor, and topical corticosteroids have potential benefits.[22] The review did not consider those topical agents that have ingredients known as soothing to be beneficial, such as niacinamide, panthenol, squalene, glycerin, shea butter, and allantoin.[47]

Lüftner et al (2018) conducted a multicenter prospective observational open-label study to evaluate the use of a 12-product kit for fifty patients receiving chemotherapy who received skincare kits before starting their cancer treatment with instructions to use the skincare throughout the treatment phase.[48] The study indicated skincare benefits, helping to

BOX 1.

Information and Patient Education
• Establish proactive contact with the patient from the start of the treatment. • Allow patients to verbalize their symptoms. • Encourage frequent communication, develop a rapport and trust, and ensure open communication between the patient and the team. • Have a detailed discussion with the patient, treating physician and nurse, or other team members explaining the treatment protocol, cAEs, hospital visits, diagnostic tests, management of cAEs, prophylactic, and preventative measures. • Provide detailed patient education on the skin changes that may occur before starting the cancer treatment. • Give patients contact information and explain who to contact, when, and why. • Explain to the patients that they should always report their skin changes, regardless of severity. • Reinforce that prevention and early treatment of cAEs lead to better cancer-treatment outcomes and quality of life. • Explain the condition and rationale for applying cleansers, moisturizers, and sunscreen to prevent, treat, and maintain cAEs. Demonstrate the application process. • Provide instruction sheets or digital information and websites for later home reference and education.

minimize cAEs and improving the skin condition such as edema, erythema, dryness, desquamation, pigmentation disorders, and cracks.[48]

Education on Prevention Measures

Statement 6: *Early education and skincare use may have benefits for quality of life and prevention of severe skin sequelae for cancer patients and survivors.*

The USCOM panel agrees that early education of patients on their cancer treatment-related cAEs and prevention measures using skincare is an important step in building a therapeutic relationship with the patient enabling their active participation in the cancer treatment plan.[8,12,20] Before starting the cancer treatment, a detailed discussion between the patient, treating physician and nurse, or other multidisciplinary oncology team members should address the treatment protocol, potential side effects, hospital visits, diagnostic tests, and management of cAEs, and preventative measures (Box 1: Information and education).[12] The discussion should be supported by written or digital material to allow the patient to clarify and process the information (Box 2: Resources).[12] This session's outcome should be: 1) The patient expresses an understanding of the treatment and potential cAEs and how to access the relevant information. 2) The patient understands how and when to contact an oncology team member. 3) The patient has been educated on prevention measures and skincare suitable for their individual needs.

BOX 2.

Resources

Title	Type	Function	Reference
Glossary	Review	A brief overview of cAEs	Sauder M et al. *Skin Ther Letter* 2021;S(3):1-10.[50]
AAD Dermatology World. https://oncodermlabs.com/pages/health-guides	Information leaflet	A quick reference to the various cancer treatments, cAEs, and approaches.	Ruth C. *The Dermatology World*, December 2019
MSKCC Dermatologic Health	Website	Introduction to cAEs	https://www.mskcc.org/cancer-care/diagnosis-treatment/symptom-management/dermatologic-health-during-after-treatment
ASCO Cancer net	Website	Cancer physicians and oncology professionals provide information for cancer patients, their families and caregivers	https://www.cancer.net/coping-with-cancer/physical-emotional-and-social-effects-cancer/managing-physical-side-effects/skin-reactions-targeted-therapy-and-immunotherapy
Information about cancer and its treatment	--	--	https://www.cancer.gov/about-cancer/treatment/side-effects/skin-nail-changes

American Academy of Dermatology Association (AAD); American Society of Clinical Oncology (ASCO)

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