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 ORIGINAL ARTICLE

NECOM 5: Algorithm for the Treatment and Supportive Management of Targeted Therapy-Related Cutaneous Adverse Events

Ada Girnita MD PhD IFAAD FEADV,[a] Peter Bjerring MD DMSc FEADV,[b] Gabriela Lladó Grove MD PhD,[c] Samsa Kauppi MD,[d] Anneke Andriessen PhD,[e] Charles Lynde MD FRCPC,[f] Andreas Stensvold MD PhD[g]

[a]Skin Cancer Center Karolinska University Hospital Stockholm, Sweden

[b]Department of Dermatology, Aalborg University Hospital, Denmark

[c]Department of Dermatology, Copenhagen University Hospital, Denmark

[d]Private Practice, Terveystalo and Epilaser Oy, Finland

[e]Radboud UMC; Nijmegen and Andriessen Consultants, Malden, The Netherlands

[f]Diplomate, American Board of Dermatology; Fellow, Royal College of Physicians and Surgeons of Canada; Associate Professor, Department of Medicine University of Toronto, Toronto, ON, Canada; Lynderm Research, Markham, ON, Canada

[g]Director of Medical Strategy and Development, Østfold Hospital Trust, Norway

ABSTRACT

Background: The cancer burden in the Nordic European countries remains substantial, but new treatment approaches, such as targeted therapy, have increased the survival of cancer patients. During and following cancer treatment regimens, however, patients' quality of life may be severely affected by sequelae, including cutaneous adverse events (cAEs). Overall, practical clinical tools for the management of cAEs in cancer patients and survivors have been lacking.

Methods: The Nordic European Cutaneous Oncodermatology Management (NECOM) project addresses cAEs in cancer patients, aiming to identify specific challenges and develop practical algorithms for their management. NECOM 1 and 2 provided an overview of cAEs and general recommendations for prevention and appropriate skin care regimens. NECOM 3 and 4 explored cAEs related to radiation therapy and immunotherapy, respectively. This NECOM 5 develops a practical algorithm for preventing and treating targeted therapy-related cAEs (TTcAEs).

Results: The NECOM panel discussed the findings of a systematic review of cAEs associated with targeted cancer therapy. The panel reached a consensus on a practical algorithm for TTcAEs, considering the current evidence, expert opinion, and clinical settings in the Nordic countries. The algorithm included general prevention and skin care recommendations, followed by specific advice for addressing the most common TTcAEs (papulopustular eruption, pruritus, hand-foot skin reaction, and paronychia).

Conclusions: Targeted therapy-related cAEs may negatively affect cancer patients and survivors. The NECOM panel provides a practical algorithm for preventing and managing TTcAEs to improve cancer patient outcomes and quality of life.

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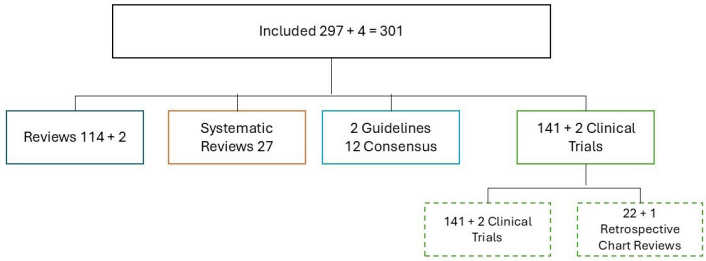
INTRODUCTION

In 2024, an estimated >200,000 new cases of cancer will be diagnosed in Nordic Europeans. Apart from non-melanoma skin cancer, the 4 most commonly diagnosed cancers are prostate, breast, lung, and colorectal cancer, accounting for about half of all cancer diagnoses.[1-3]

Although cancer incidences seemingly continue to rise, ongoing advancements in cancer therapy have simultaneously contributed to improved survival. Nordic survival studies from the past decades have shown clear trends of improved 1- and 5-year survival across different cancer types. Between 2018 and 2022, the relative 5-year cancer survival percentage of males and females in the Nordic countries was between 70 to 78% and 73 to 76%, respectively.[1] In anticipation of longer life spans with earlier diagnosis and improved treatment approaches, more patients will come upon a cancer diagnosis and treatment in their lifetime. Thus, as more Nordic Europeans are living with or surviving cancer, more patients will be affected by adverse events (AEs) or sequelae to their cancer and treatment. Prevention, identification, and management of adverse events are important for patient quality of life (QoL) during and after cancer treatment, as some treatments may present substantial adverse events that negatively affect the patient's daily activities and adherence to treatment regimens.[4-5]

Cutaneous adverse events (cAEs) are a common but rather overlooked negative effect of several cancer therapies that need addressing. The negative impact of cAEs has been reported to be substantial and, in up to 67% of patients, worse than anticipated or even unanticipated altogether. Both treatment adherence and satisfaction may be negatively affected by cAEs due to substantial impact on the patient's appearance, physical or emotional well-being, and body image.[4-5] Targeted cancer therapy comprises a palette of novel, effective treatment approaches, and a concise update on the specific cutaneous side effects described in the literature has been lacking.[6-9]

FIGURE 1. Flowchart of literature search.



The Nordic European Cutaneous Oncodermatology Management (NECOM) project develops tools to prevent and treat cancer therapy-related cutaneous adverse events (cAEs). The NECOM panelists are global experts in onco-dermatology committed to patient-centric and evidence-based skin care for oncological patients.[4-5,10-11] Through a joint evaluation of the current literature and an expert meeting; the NECOM panelists aim to reach a consensus on targeted therapy-related cAEs to develop a practical algorithm for specific prevention and management.

NECOM Project Update

The NECOM project entails a series of scientific papers based on literature reviews and expert consensus. The first 2 NECOM papers presented various cAEs and skincare regimens involving cleansing, hydration, and photoprotection for preventing and managing cAEs.[4-5] The NECOM 3 and 4 practical algorithms focused on preventing and treating acute radia-tion dermatitis,[10] and cutaneous immunotherapy-related adverse events,[11] respectively.

This paper represents NECOM 5, a practical algorithm to prevent and manage cutaneous targeted therapy-related adverse events (TTcAEs) for improving cancer patients' QoL and outcomes.

Overall, the NECOM project aims to develop an evidence-based algorithm for improving the patient journey during and after treatment, reducing and treating cAEs, and promoting the healing of affected skin areas with prescription medication and skincare. The target audience is dermatologists, oncologists, and a broad range of HCPs, including nurses, physician assistants, general practitioners, and pharmacists.

METHODS

A selected group of multidisciplinary panelists within oncodermatology used the AGREE II instrument and a modified Delphi method[12-13] to develop the practical algorithm for treating TTcAEs.

On March 6, 2024, the NECOM panelists discussed the outcome of a literature review in a face-to-face meeting. Drawing from the review's gathered evidence on the TTcAEs spectrum and the panel's collective expertise, a practical algorithm was developed for a systematic approach to TTcAEs management. A subsequent online process allowed for joint refinement of the algorithm and manuscript preparation and review.

Literature Review

A structured literature search was conducted prior to the NECOM 5 meeting to guide the algorithm's development. The search considered clinically relevant material published between January 2010 and 2024, including guidelines, consensus papers, case reports, and review articles on identifying, preventing, and managing TTcAEs. The search was conducted on PubMed and Google Scholar, including the following main search criteria: *cutaneous adverse events* (overall and by specific categories), *targeted therapy* (relevant inhibitors by generic name), and *prevention and treatment* (by relevant categories).

Articles were excluded if they were out of scope or in a non-English language. Three hundred-one (301) publications were deemed suitable for inclusion, comprising 116 reviews, 27 systematic reviews, 3 guidelines, 12 consensus papers, and 143 clinical trials (including 14 case series and 23 retrospective studies). See Figure 1 for the search results flowchart. The clinical evidence of included publications was graded based on pre-defined criteria by 2 independent reviewers who reached a consensus after resolving discrepancies by discussion.

Targeted Therapy-Related Cutaneous Adverse Events

Targeted therapy is a fast-developing treatment approach and represents a shift towards precision medicine in oncology. Currently, numerous targeted therapies have been developed within practically all major cancer fields, and they are often used in combination with other established treatments such as chemotherapy, immunotherapy, radiation, or surgery. The mechanism of action of targeted therapy is on a molecular level, as each particular drug class is designed to target 1 or several specific molecules, proteins, or genetic mutations deemed relevant for the tumorigenesis, growth, and progression of a given cancer type (Table 1). The increased precision can improve efficacy and secure avoidance of some general sequelae seen with other interventions or drugs. However, the targeted molecules often play a part in pathways that are simultaneously necessary for normal function or inhibition of other diseases. As such, targeted therapy can lead to particular adverse events depending on their specific target. Several of these affected pathways involve skin function and may give rise to cAEs. The targeted therapy categories that have been connected to cAEs are extensive and include epidermal growth factor receptor (EGFR) inhibitors, MEK inhibitors, RAF inhibitors, selective vascular endothelial growth factor (VEGF) inhibitors, and platelet-derived growth factor (PDGF) inhibitors, mammalian target of rapamycin (mTOR) inhibitors, and multikinase inhibitors.[14-25] A wide range of cAEs have been described from targeted therapy, including, but not limited to, exanthem and dermatitis, hair- and nail changes, pruritus and xerosis, hand-foot skin reaction, mucosal affection, pigmentary or keratinocyte changes.[26-37]

The Algorithm

A practical algorithm for preventing and managing TTcAEs was developed, drawing on insights from the structured literature review

TABLE 1.

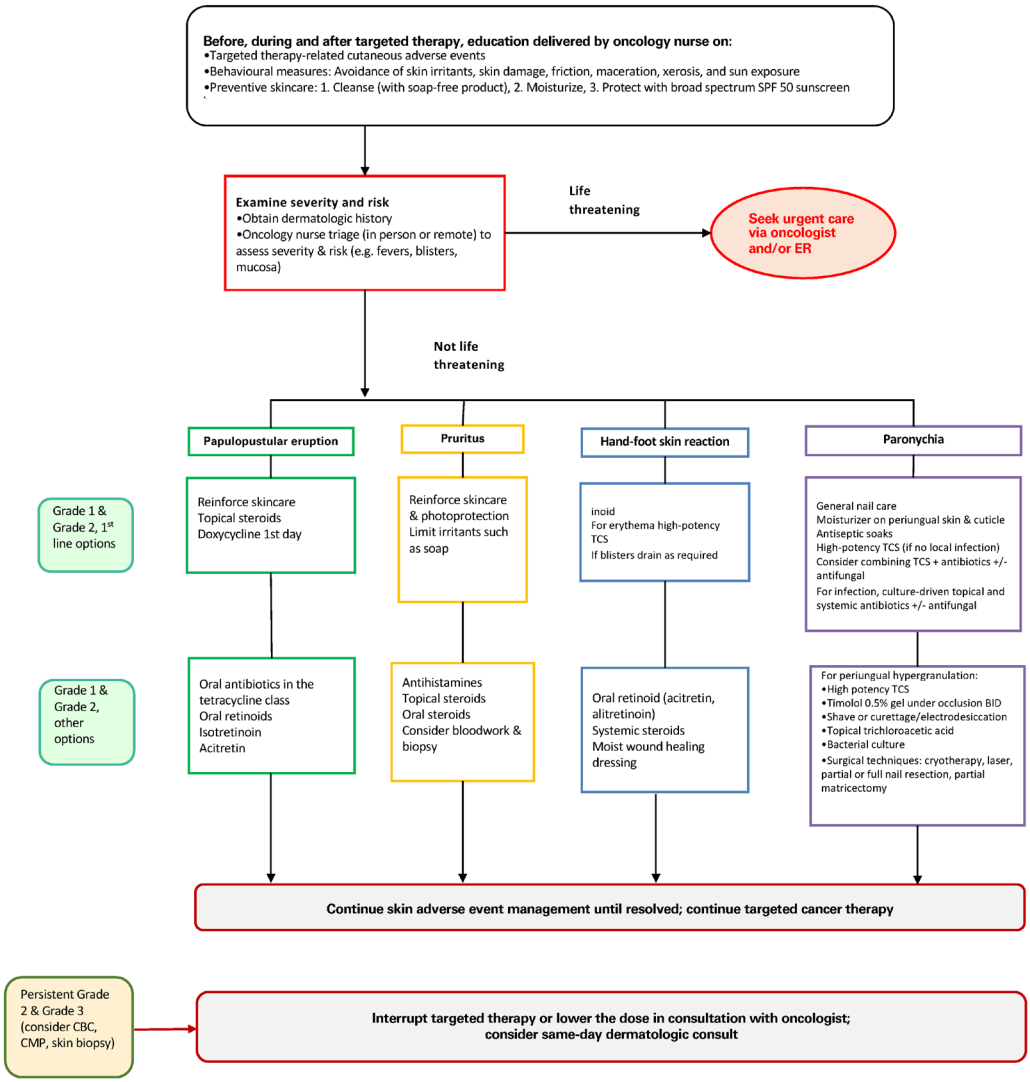
Targeted Therapy Classes, Molecules, and Main Oncological Indications		
Drug Class	**Name**	**Main Oncologic Indications***
Epidermal Growth Factor Receptor (EGFR) inhibitors	Afatinib	NSCLC
	Cetuximab	Head- and neck and colorectal cancer
	Dacomitinib	NSCLC
	Erlotinib	NSCLC and pancreatic cancer
	Gefitinib	NSCLC
	Mobocertinib ^	NSCLC
	Osimertinib	NSCLC
	Panitumumab	Colorectal cancer
Multiple kinase inhibitors	Cabozantinib	RCC, hepatocellular and thyroid cancer
	Canertinib"	(Esophageal squamous cell carcinoma)
	Dasatinib	Ph+ CML and ALL
	Imatinib	Ph+ CML and ALL, gastrointestinal stromal tumor, chron-ic eosinophilic leukemia, myelo-dysplastic/myeloproliferative disease, mastocytosis, dermatofibrosarcoma protuberans
	Lenvatinib	Thyroid, hepatocellular, endometrial cancer and RCC
	Nilotinib	Ph+ CML and ALL
	Pazopanib	RCC and soft tissue sarcoma
	Regorafenib	Colorectal cancer, gastrointestinal stromal tumor, hepatocellular carcinoma, sarcoma
	Sorafenib	RCC, hepatocellular carcinoma, thyroid cancer, AML
	Sunitinib	RCC, gastrointestinal stromal, and pancreatic neuroendocrine tumor
	Vandetanib	Thyroid cancer
Selective VEGF inhibitors	Axitinib	RCC
	Bevacizumab	NSCLC, RCC, colorectal, breast, ovarian and cervical cancer
	Ramucirumab	Gastroesofagial adenocarcinoma
	Ranibizumab	(Ocular vascular tumor)
Mammalian target of Rapamycin (mTOR) inhibitors	Everolimus	RCC, HR+ breast cancer, neuroendocrine tumor
	Sirolimus^	Perivascular epithelioid cell tumor, (lymphangioleiomyomatosis)
	Temsirolimus	RCC
RAF inhibitors	Belvarafenib"	(Solid tumor)
	Dabrafenib	Melanoma, NSCLC and thyroid cancer, solid tumor
	Encorafenib	Melanoma, NSCLC and thyroid cancer, solid tumor
	Vemurafenib	Melanoma, histiocytic neoplasm
MEK inhibitors	Binimetinib	Melanoma, NSCLC
	Cobimetinib	Melanoma, histiocytic neoplasm
	Selumetinib	Plexiform neurofibroma
	Trametinib	Melanoma, NSCLC, and thyroid cancer, glioma
Other	Lapatinib	HER2+ breast cancer
	Neratinib	HER2+ breast cancer
	PDGFR inhibitor	Gastrointestinal stromal tumor, breast and pancreatic cancer
	Pemigatinib (FGFR)	Cholangiocarcinoma and myeloid/lymphoid neoplasms
	Pertuzumab	HER2+ breast cancer

* Oncologic indications for the listed organ target are non-all-encompassing. Each agent has specifically approved indications for subvarieties of each type of cancer-based on biology and/or behavior.
"experimental drug
^not available for all indications in all Nordic countries

TABLE 2.

Preventive Skincare and Xerosis Treatment	
Position	**Treatment**
Prevention	• Regular use of thick emollient • Limited bathing time, avoiding high water temperatures • Gentle skin care with fragrance-free cleanser with pH approximate to skin (pH 5.5) eg, syndet/oily detergents. Minimal usage of cleanser, focused only on axilla, groin, and feet • Avoid irritants such as soap and perfume • Avoid other stress to the skin (mechanical, physical, thermal, chemical, humid, occlusive) • Photoprotection (broad spectrum SPF 50)
1st line	• All the same preventive recommendations • Emollient containing humectants such as urea 5 to 10% or lactic acid or greasy ointment containing petroleum jelly or cholesterol, used minimum twice daily
2nd line	•Topical steroids, especially if coexisting eczema, lichenification, and fissures
3rd line	• Systemic steroids

FIGURE 2. Management of cutaneous adverse events of targeted cancer therapy.



BSA, body surface area; CBC, complete blood count; CMP, comprehensive metabolic panel; TCS, topical corticosteroids

and collective expertise of the NECOM panelists (Figure 2). As with NECOM 3 and 4 algorithms, the proposed algorithm expands on the NECOM 2 algorithm for cancer treatment-related cAEs. Interventions are stepwise based on TTcAE severity and offered alongside grade-based recommendations. Severity grades (1-4 (5)) were based on the Common Terminology Criteria for Adverse Events (CTCAE) (Table 2).[38]

Identifying and managing cAEs to targeted therapy can improve treatment adherence, QoL, and well-being. Although the algorithm was adapted to the Nordic countries, the systematic approach could be a relevant tool for global healthcare providers managing TtcAEs including oncologists, dermatologists, general practitioners (GPs), oncology nurses, advanced practice providers (APPs; nurse practitioners [NPs] and physician assistants [PAs]), and pharmacists.

RESULTS

Based on the structured literature search and the NECOM panel's clinical experience, the following TTcAEs were selected and included in the practical algorithm: hand-foot skin reaction, papulopustular eruption, pruritus and paronychia. Less common cAEs, comprising exanthem, mucositis, and other fissures, were not included in the algorithm but addressed in a separate table.

Hand-Foot Skin Reaction

A skin reaction localized to the palms of the hands and soles of the feet. The exact cause and prevalence remain unknown, but it has been linked to up to a few percent of patients undergoing systemic cancer treatment, particularly targeted therapy. It can present with erythema, edema, painfully dry, hyperkeratotic, or peeling and fissuring skin, and even form bullae and ulcerations. Preventive measures include moisturizer and protection from friction and heat, while medical treatment mainly entails topical corticosteroids, retinoids, or keratinocytes, appropriate medical dressing, and topical analgesics. An incision may be relevant for bullae. In severe cases, oral retinoids or corticosteroids can be used, and adjustment or pausing of the triggering therapy may become necessary (Table 3.1).

Papulopustular Eruption

A skin reaction commonly seen following targeted treatment with EGFR inhibitors typically presents with papules and pustules on the head, neck, and trunk, which may be itching and painful. Skincare with gentle cleansers, moisturizers, and sun protection are the main preventive measures, which may be supplemented by topical antiseptic. Treatment options include topical or oral antibiotics and topical corticosteroids. In severe cases, oral corticosteroids or retinoids may be necessary, or even dose adjustment or interruption of triggering therapy may be required (Table 3.2).

TABLE 3.1.

Cutaneous Adverse Events from Targeted Therapy: Hand-Foot Skin Reaction Management Algorithm	
Position	**Treatment**
Prevention	• Urea 10% • Avoid friction, pressure, hot water and extremes of temperature • Limit traumatic activities inducing stress on extremities such as long walks, running, aerobics, jumping, and heavy carrying without gloves • Wear thick cotton gloves and socks • Wear well-fitted, soft shoes, not too tight to avoid constriction and not too loose to avoid fric-tion. Orthopaedic shoes, orthopaedic shoe inserts, or gel insoles • Prophylactic removal of pre-existing hyperkeratotic lesions, calluses, and corns on hands and feet
1st line	• Same as prevention if not already done by the patient • Topical keratolytic treatment using salicylic acid 3 to 10%, lactic acid 5 to 8%, or urea 10 to 50% • Topical retinoid • High-potency topical with/without occlusion for erythematous and inflammatory lesions • Hydrocolloid dressing for erosion or bullae • Topical analgesics (lidocaine gel, lidocaine 5% patch, EMLA, prilocaine cream or benzocaine gel) twice a day • Cold compresses, cooling packs, or cooling hand and foot baths to manage pain
2nd line	• Incision and drainage if abscess For periungual pyogenic granuloma: • As for paronychia
3rd line	• Oral acitretin 10 to 25 mg daily • Alitretinoin • Systemic steroids • Consider decreasing dose to 50% of the initial dosage or stopping targeted therapy for at least 7 days until it resolves (A). Reintroduction should be done at 50% of the starting dose. • Drug holiday

(A) HFSR is dose-dependent.

TABLE 3.2.

Cutaneous Adverse Events from Targeted Therapy: Papulopustular Eruption Management Algorithm	
Position	**Treatment**
Prevention	• General preventive skin care (Table 2) • Emollient BID • Sun avoidance • Avoid occlusive make-up • Low-potency topical steroids (hydrocortisone 1% or 2.5% cream) for face and trunk BID for the first 6 weeks of treatment • Oral tetracyclines at therapeutic doses from day 1 of EGFRI treatment for at least the first 6 to 8 weeks. • Doxycycline 100 mg BID, minocycline 50 to100 mg BID, tetracycline 500 mg BID. If tetracy-clines are contraindicated, use erythromycin or clarithromycin • Combination: moisturizer, hydrocortisone 1% cream daily, sunscreen, and oral doxycycline 100 mg BID for 6 weeks beginning day -1 (A)
1st line	• Emollient • Photoprotection (broad spectrum SPF 50) • Topical antiseptic wash (triclosan or diluted bleach bath) • Topical low-potency steroid for face and medium-to-high potency steroids for body/scalp • Topical antibiotics (clindamycin lotion or gel, erythromycin, or metronidazole) • Topical dapsone • Topical ketoconazole • Corrective make-up • Avoid typical anti-acne topical treatments (benzoyl peroxide, azelaic acid, alpha-hydroxy acid, or retinoids). • Oral tetracyclines (doxycycline) for severe cases • Isotretinoin for very severe cases
2nd line	• Oral tetracyclines (doxycycline 100 mg BID, minocycline 100 mg BID, tetracycline 500 mg BID) for at least 6 weeks and for a longer period if needed (B) • If tetracyclines are contraindicated, use erythromycin, clarithromycin, azithromycin, TMP-SMX, or cephalexin • If atypical acneiform eruption (C), proceed to bacterial culture and viral (herpectic) swab and cul-ture-driven oral antibiotic or antiviral if proven infection. • Isotretinoin can be used in very severe cases
3rd line	• Low-dose oral isotretinoin (0.2-0.3 mg/kg or 20-30 mg once daily) after discontinuing oral tetra-cycline (D) • Acitretin 25 mg daily • Oral dapsone • Short course of systemic steroids (prednisone or prednisolone up to 0.5 mg/kg/day for 5 to 14 days) with decreasing dosage • Dose reduction of the targeted therapy • Interruption of the targeted therapy. Can restart when back to grade 0 to 1. Restart at 50% of orig-inal dosage

(A) EGFR inhibitors are at higher risk of acneiform eruption than other targeted therapies. We recommend using more aggressive preventive measures for patients receiving EGFR inhibitors. (B) If tetracyclines are used, their photosensitizing activity must be estimated. In regions with high UV index, minocy-cline should be used instead of others because it is less photosensitizing. If the patient has renal insufficiency, doxycy-cline is a safe option. (C) Atypical eruption includes an eruption that is recalcitrant while using appropriate treatment, lasts longer than 8 weeks, starts more than 3 months after the beginning of targeted therapy, is widespread, and involves non seborrheic areas such as the abdomen, buttocks, arms, and legs, or if there are vesicles, yellow crust, discharge, or painful lesions. (D) The use of retinoids is controversial. Some experts think that it is ineffective and could even exacerbate the acneiform eruption. Retinoids may have overlapping side effects with targeted therapy such as xerosis, photosensitivity, and periun-gual pyogenic granuloma. Isotretinoin is superior to acitretin.

TABLE 3.3.

Cutaneous Adverse Events from Targeted Therapy: Pruritus Reaction Management Algorithm	
Position	**Treatment**
Prevention	• Regular use of emollient. Apply emollient within 15 minutes following shower or bath for better absorption and to lock in the moisture present on the skin surface • Limited shower time, avoid hot showers, hot baths, and saunas • Gentle skin care using fragrance-free cleanser with pH approximate to skin (pH 5.5) such as syn-det or oily detergents. Minimal usage of cleanser focused only on axilla, groin, and feet • Avoid irritants such as soap and perfume
1st line	• All the same preventive recommendations • Emollient containing a humectant such as urea or lactic acid • Loose-fit clothing • Cool ambient environment, avoiding heat exposure • Keep fingernails short to avoid scratching and exacerbation of the itch-scratch cycle • Photoprotection • Treat underlying xerosis, asteatosis, eczema, or papulopustular eruption if present • Moderate-to-high potency topical steroids • Topical calcineurin inhibitors (pimecrolimus, tacrolimus) • Cold compresses or wet dressing for cooling effect • Topical lidocaine • Topical capsaicin, menthol, or camphor • Topical pramoxine hydrochloride^ • Topical doxepin 5%^ • Strontium^
2nd line	• 1st generation oral anti-H1 at nighttime and 2nd generation oral anti-H1 at daytime • Oral gabapentinoid (gabapentin, pregabalin)
3rd line	• Oral aprepitant • Oral doxepin • Oral systemic steroids 0.5 to 1 mg/kg for 5 days

^not available in all Nordic countries

TABLE 3.4.

Cutaneous Adverse Events from Targeted Therapy: Paronychia Reaction Management Algorithm	
Position	**Treatment**
Prevention	• Avoid trauma, including aggressive manicures and pedicures, artificial nails, friction, excessive pressure, or biting nails • Gentle nail care (regular trimming once a week for fingernails and once a month for toenails; trim nails after showering). Avoid cutting nails too short, especially at the edges • Apply petroleum jelly to periungual skin and cuticle to create water-proof layer • Cotton gloves beneath plastic or rubber gloves during household or household avoidance • Avoid prolonged contact with water • Wear well-fitted shoes or wide, open-toed shoes • Wear cotton socks • Dry feet carefully before putting on shoes • Correction of nail curvature by a podiatrist if needed
1st line	• Antiseptic soaks to prevent nail fold infection: either dilute bleach or dilute white vinegar soaks • Topical povidone iodine 2% (eyedrop formulation) • Warm soaks • High-potency topical corticosteroids (if no local infection) • Topical calcineurin inhibitor (tacrolimus, pimecrolimus) • Acitretin and alitretinoin • Topical antibiotic (mupirocin, fusidic acid, or gentamycin ophthalmic drops) • Combination of topical steroid and topical antibiotic • Combination of topical steroid, topical antibiotic, and topical antifungal • Oral tetracyclines • If infection, initiate culture-driven topical and systemic antibiotics and antifungals For periungual pyogenic granuloma: • High-potency topical corticosteroids • Topical beta-blockers using timolol 0.5% eyedrop formulation) BID under occlusion • Incision and drainage if abscess
2nd line	For periungual pyogenic granuloma: • Topical trichloroacetic acid • Electrodesiccation • Cryotherapy • Shaving or curettage and electrodessication. • Silver nitrate 1 to 2 a week - can be done by patient if instructed how to (A)^
3rd line	• Surgical approach if medical treatments have failed • Partial matricectomy using phenol • Partial or full nail resection • Laser treatment

(A) Silver nitrate is the most reported treatment to manage periungual pyogenic granuloma in reviews.
^not available in all Nordic countries

Pruritus

An uncomfortable sensation in the skin that prompts a scratching urge. Pruritus can be localized to a specific area or present as more generalized itching ranging from mild to severe. Other skin symptoms such as erythema, edema, and paraes-thesia may accompany the condition, and it can be related to various dermatological and systemic diseases, medicine, and psychological conditions. Preventive measures involve identifying and avoiding triggers as well as providing the skin with optimal conditions in terms of moisture and avoidance of irritants in skincare and clothing. Medical treatment mainly consists of topicals with either corticosteroids, calcineurin inhibitors, local anesthetics, or analgesics, as well as systemic drugs such as antihistamines, gabapentinoids, anti-depressants, or oral corticosteroids and dermatological treatments such as phototherapy (Table 3.3).

Paronychia

Paronychia is an inflammatory, often infectious, condition of nail-adjacent skin. The exact prevalence is not well-documented, but the condition is relatively common in healthy individuals and patients, where it typically presents as acute and chronic, respectively. Clinically, the nail fold will appear erythematous and oedematous, and in the acute form, there may be infection signs, while with the chronic form, the nails often appear thickened and discolored. The main preventive measures are good hygiene, nail care, and avoiding irritants or infectious matters. Friction and trauma are important to avoid. Antiseptics, antifungal treatments, corticosteroids, or calcineurin inhibitors can be utilized topically, depending on the severity and type. In severe cases, systemic treatment with oral antibiotics, corticosteroids, and retinoids can be necessary. In non-responsive cases, there may be a need for procedural or surgical intervention (Table 3.4).

Recommendations for Specific TTcAEs

Recommendations for each main identified TTcAE are presented in a practical algorithm flowchart (Figure 2) and comprehensible tables, presenting specific preventive measures and treatment suggestions by grade severity (Table 3). Finally, recommendations for less common cAEs, specifically exanthem, mucositis, and other fissures, are not included in the algorithm but presented in a separate table by prevention and severity grade (when appropriate) (Table 4).

TABLE 4.

Other Targeted Therapy-Related Cutaneous Adverse Events (Not Addressed in the Algorithm); Exanthem, Mucositis, and Fissures	
Position	**Treatment**
Exanthem	
1st line	• Topical steroids • Oral antihistamines
2nd line	• Check CBC, CMP, skin biopsy and assess for symptoms of systemic capillary leak syndrome (SCAR) • Oral antihistamines • Oral steroids
Mucositis	
Prevention	• Dentist examination before treatment start • Good oral hygiene. Brush teeth after each meal and before bedtime • Mild toothpaste without sodium lauryl sulfate or strong flavors such as mint • Avoid alcohol-containing mouthwash • Avoid trauma due to electric toothbrushes and oral prosthesis • Adequate nutrition free of spicy, salty, citrus-based, and hot foods. Eat soft, moist, non-irritating food that are easy to chew and swallow • Avoid alcohol and tobacco
1st line	• All the same preventive recommendations • Liquid, soft, or normal diet as tolerated • Soft toothbrush such as baby toothbrush • Mouthwash every 1 to 2 hours using physiologic saline, 1 teaspoon table salt in 500 ml water, ¾ of tea-spoon sodium bicarbonate in 500 ml water, or a combination • Rule out HSV and Candida • Analgesia (eg, lidocaine) • Topical steroids (gel, oral rinses) • Oral tacrolimus (ointment, rinse) • Consider specifying the chlorhexidine concentration • Antifungal treatment • Consider biopsy
2nd line	• Check CBC, CMP, skin biopsy, assess for symptoms of SCAR • Oral steroids • If persistent, rule out other etiologies (eg, nutritional deficiencies)
Fissures	
	• Emollient, especially thick ones such as petroleum jelly or zinc oxide ointment and apply cotton socks and gloves for occlusion • Barrier cream • Dilute bleach soaks to reduce infection risk • Liquid skin glue, cyanoacrylate glue • Hydrocolloid dressing • Topical steroid if there is inflammation

General Principles for Treating TTcAEs

Integrating skincare into treatment can improve the patient experience and support adherence to cancer treatment. Recommendations and selection of appropriate skincare products with active ingredients and vehicles are adamant. Finally, patients should be encouraged to adopt a proactive approach to skincare before, during, and after cancer-targeted therapy.

Grading the severity of cAE is important to apply a timely and appropriate strategy for treatment and prevention of devel-opment. Early identification of severe TTcAEs, which may be detected by both cutaneous and non-cutaneous symptoms, including fever, skin pain, epidermal changes, high body surface area involvement, or laboratory abnormalities, is an important step. Regardless of the cutaneous reaction, severe cases should be referred to immediate evaluation by an oncologist and/or dermatologist. Depending on the cAE, it may also include inpatient or even ICU-level care. In case cAEs are very severe or non-manageable based on recommendations and specialized care, the treating oncologist may have to reassess the active treatment regime by interrupting, temporarily or permanently, depending on severity, or reducing the dose.

Overall Skincare Recommendations

Preventive measures for cAEs, including a skincare regimen, should be used throughout and after cancer treatment, comprising appropriate cleansing, moisturizing, and photoprotection. Gentle cleansers should be used, while soaps, surfactants, and detergents should be avoided. The latter, especially those with an alkaline pH (>7), remove skin lipids and elevate skin surface pH, triggering inflammation and lowering the diversity of the skin microbiome. The use of modern moisturizers, containing emollients, humectants, occlusive agents and physiological lipids (ceramides, cholesterol and free fatty acids), can help restore skin barrier integrity and function, including skin elasticity, skin homeostasis, and controlling transepidermal water loss. Sun protection includes sun avoidance measures as well as sunscreen. Photoprotection is particularly important as targeted therapies and some treatments of cAEs themselves increase skin photosensitivity. Any products containing allergens and irritants, such as common preservatives and fragrances, are unsuitable for oncological patients. Finally, according to the NECOM panel, skin care must be tailored to the individual patient and their particular preferences to secure compliance with recommendations.

CONCLUSION

In the light of increasing cancer survival with improved treatment, QoL becomes increasingly crucial for cancer patients and survivors. Targeted therapy-related cAEs, such as papulopustular eruption, pruritus, hand-foot skin reaction, and paronychia, may negatively affect the patient journey. The NECOM panel provides a practical algorithm for preventing and managing TTcAEs with both prescription medication and general skin care to improve cancer patient outcomes and QoL.

DISCLOSURES

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AUTHOR CORRESPONDENCE

Anneke Andriessen PhD

E-mail:..... anneke.a@tiscali.nl