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This book is intended for oncology, nursing, and dermatology students, educators, and practitioners. Any of the modalities used against cancer: surgery, radiation, medical therapies, or therapeutic transplants, may have an effect on skin and its appendages, which can not only affect quality of life, health, but may also impact cost and dose intensity of therapy, all of which may affect clinical outcome. Although the focus is mainly on dermatologic adverse events of medical therapy, the effects of radiation, transplants, and surgeries will also be explored, with an emphasis on accurate diagnosis and effective management. In addition, basic dermatologic nomenclature, pathology, and adverse event grading will be included for readers who have not had these as part of their curriculum or training. As dermatologic conditions may appear before or after the diagnosis of cancer, paraneoplastic conditions that may herald an underlying malignancy, as well as late effects of therapy, respectively, are also described herein by leaders in the field.

The skin is the human body’s largest organ, a self-renewing tissue whose functions include thermoregulation, sensation, immunity, fluid and organ preservation, and vitamin D synthesis. These various functions, along with its multiple layers and the formation of appendages, such as hair and nails, allows for a complexity that is nowhere more manifest than in the oncology setting. Contributing authors have a unique expertise in the diagnosis and treatment of dermatologic conditions in people living with cancer. This vast expertise will undoubtedly assist in mitigating the various untoward events that can affect cancer patients and survivors, both physically and psychosocially.

In order to make this book rapidly accessible whenever a patient presents with a dermatologic condition, chapters have principally been divided into the mechanism of action of medical therapies, when appropriate. In addition, cutaneous structures have also been taken into consideration, with a separate chapter for hair, nails, and mucosae. Basic dermatologic procedures and appearance-related interventions have also been included, to expand the therapeutic options that may improve the quality of life and cutaneous health of our patients. The ultimate goal of this book is to help optimize the treatment of cancer, by minimizing the effects of dermatologic conditions on quality of life and maximizing therapeutic consistency.

Acknowledgment

We are very grateful to cancer patients, survivors, and their families, who have generously donated their time, thoughts, and have allowed us to photograph and discuss their symptoms them at a difficult time in their lives. We are privileged to have participated in their care. We are grateful to the support staff who enable us to deliver care to people touched by cancer. And we thank the readers for allowing us to participate in the care and understanding of their patients’ dermatologic conditions.

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1  Dermatology and Oncology
Epidemiology and Burden of Disease

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Introduction

Due to recent advances in cancer therapies, patients are now living longer than ever before. For all diagnosed cancers, the 5-year relative survival has increased from 50% in 1975–1977 to 66% in 1996–2004 [1]. From 1990 to 2003, all-site cancer deaths in the United States decreased by 1% per year and these declines were especially pronounced for some of the most common malignancies including breast, prostate, colorectal, and lung cancers [2]. In the United States in 2009, there were 1,479,350 new cancers expected to be diagnosed [1], of which 52–87% were treated with surgery, 24–35% with chemotherapy, and 47–51% with radiation therapy (based on 2002 data for breast, lung, and colorectal cancers) [3]. Fifty to sixty thousand hematopoietic stem cell transplants are performed worldwide per year [4].

The large number of people being diagnosed with cancer in combination with increased survival rates have led to an increased number of patients living with a history of cancer, estimated to be 11.1 million in 2005 in the United States [1], of which 270,000 are survivors of pediatric cancers [5]. The increased number of patients living with and after cancer has revealed a number of dermatologic issues specific to this population: affecting cutaneous health, causing a financial burden, decreasing health-related quality of life, and impairing consistent drug dosing.

Financial burden

In addition to the psychosocial effects (discussed in Chapter 6), dermatologic AEs also result in a financial cost to patients. Overall costs of treating cancer have increased by 75% from 1995 to 2004 [3]. A portion of this cost can be attributed to supportive dermatologic care. Median medical costs per patient treated for head and neck or nonsmall cell lung cancer with radiochemotherapy are $39,313 per patient with mucositis/pharyngitis and $20,798 per patient without mucositis/pharyngitis [19]. Much of the increased cost was attributed to increased length of hospital stay [19]. For dermatologic AEs in patients treated with EGFRIs or platelet-derived growth factor receptor (PDGFR) and vascular endothelial growth factor receptor (VEGFR) inhibitors, mean cost of treatment for dermatologic toxicities was $2496 per patient [20]. Costs associated with stem cell transplantation can be increased by as much as $28,100 by development of acute graft versus host disease (GVHD) [21]. It is plausible that a prophylactic approach to managing treatment-induced AEs could decrease these associated costs.

Health-related quality of life

All of the described dermatologic toxicities due to cancer treatment can have a significant impact on a patient’s health-related quality of life (HRQL). Patients most frequently report dermatologic AE as carrying a negative impact and of being unanticipated prior to therapy, with 67% of patients reporting that dermatologic AEs are worse than their initial belief [22]. Fifty-eight percent of patients rate chemotherapy-induced alopecia as the most traumatic side effect from their therapy and 8% of patients would decline chemotherapy because of fear of hair loss [23]. In a study of breast cancer patients receiving radiation therapy, the skin

![Figure 1.1](image1.jpg) DermaLogic events in the life of the cancer patient and/or survivor [7]. GVHD, graft versus host disease. Adapted from Agha, 2007 [7].

![Figure 1.2](image2.jpg) Locations of therapy-induced dermatologic toxicities.
changes induced by radiotherapy were found to negatively impact physical well-being, body image, emotional well-being, functional well-being, and treatment satisfaction [24]. Scars resulting from oncologic surgical procedures can lead to psychologic problems in 15% of survivors of childhood cancers [25]. In a prospective study measuring the frequency and impact on quality of life of dermatologic toxicities in women receiving chemotherapy, 34% of women reported dermatologic AEs as most important during treatment and they were the most common significant contributor to overall HRQL [26]. Of those who develop dermatologic AEs, 69% feel significantly limited in their daily activities [26].

**Dosing of chemotherapy**

Perhaps the most imposing challenge offered by dermatologic AE is their ability to result in dose modifications of anticancer therapies. Although the effects of anticancer therapy dose modification on progression-free survival or overall survival have not been evaluated, one can surmise that by reducing dose intensity, clinical outcome will be negatively affected. Studies linking the frequency and severity of dermatologic AEs to a longer median survival underscore the importance of managing dermatologic events, as patients who develop these untoward events are those most likely to benefit from their antineoplastic therapy [27]. Most notably, the papulopustular (acneiform) eruption to the EGFRIs (e.g., erlotinib, cetuximab, and panitumumab) has been shown to correlate with increased progression-free and overall survival in a variety of solid tumors [28,29].

In patients receiving cetuximab for example, up to 11.3% will develop a grade 3 or higher skin rash, necessitating dose reductions [30]. The development of mucositis is shown to lead to a twofold increased risk of chemotherapy dose reduction and limits the ability to give methotrexate for prevention of GVHD to a twofold increased risk of chemotherapy dose reduction and treatment interruptions as recognizing and treating dermatologic toxicities to chemotherapy limits the ability to give methotrexate for prevention of GVHD [30]. The development of mucositis is shown to lead to overall HRQL [26]. Of those who develop dermatologic AEs, 69% feel significantly limited in their daily activities [26].

**Conclusions**

The increasing number of cancer patients and survivors has led to an increased awareness of the HRQL components and treatment-related dermatologic manifestations seen in this patient population. These dermatologic toxicities are diverse and can have an enormous impact on the cutaneous health of patients, overall costs of treatment, healthcare-related quality of life, and consistent anticancer therapy. The recognition of all of these factors has led to a new field within dermatology: supportive oncodermatology, which is focused on the addressing the aforementioned dermatologic issues facing cancer patients and survivors.

**References**

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from the MASCC skin toxicity study group. Supportive Care in Cancer, 18, 509–522.


Appendix 1.1 Anticancer agents and associated adverse events affecting the skin, mucosa, hair, and nails. Based on data from Litt JZ, 2009 [8].

<table>
<thead>
<tr>
<th>Drug</th>
<th>Skin</th>
<th>Mucosal/ENT</th>
<th>Hair</th>
<th>Nails</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Alkylating agents</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Busulfan</td>
<td>Churg–Strauss syndrome, bullous dermatitis, eccrine squamous syringometaplasia, macular erythema (&gt;10%), erythema multiforme (&lt;1%), exanthems, Kaposi sarcoma, pigmentation (1–10%), purpura, urticaria (&gt;10%), vasculitis, xerosis</td>
<td>Cheilitis, dysgeusia, mucositis, pigmentation</td>
<td>Alopecia (&gt;10%)</td>
<td>Pigmentation</td>
</tr>
<tr>
<td>Thiotepa</td>
<td>Allergic reactions (1–10%), angioedema, eccrine squamous syringometaplasia, leukoderma, pigmentation (1–10%), pruritus (1–10%), rash (1–10%), urticaria (3%)</td>
<td>Stomatitis (&lt;1%)</td>
<td>Alopecia (1–10%)</td>
<td></td>
</tr>
<tr>
<td>Mechlorethamine</td>
<td>Acanthosis nigricans, angioedema, bullous dermatitis, cellulitis, cyst, dermatitis, erythema multiforme (&lt;1%), exanthems (&lt;1%), fungal dermatitis, herpes zoster (&gt;10%), pigmentation, pruritus, purpura, squamous cell carcinoma, SJS, urticaria, xerosis</td>
<td>Dysgeusia (1–10%), tinnitus</td>
<td>Alopecia (1–10%)</td>
<td></td>
</tr>
<tr>
<td>Melphalan</td>
<td>Angioedema, eccrine squamous syringometaplasia, edema, exanthem (4%), petechiae, pruritus (1–10%), purpura, rash (1–10%), scleroderma, urticaria, vasculitis (1–10%), vesiculation (1–10%)</td>
<td>Mucositis</td>
<td>Alopecia (1–10%)</td>
<td>Beau lines</td>
</tr>
<tr>
<td>Chlorambucil</td>
<td>Angioedema, edema, exanthem, facial erythema, herpes simplex, herpes zoster, Kaposi sarcoma, lupus erythematosus, necrosis, perianal irritation, photosensitivity, pruritus, psoriasis, purpura, rash (1–10%), Sézary syndrome, SJS, TEN, urticaria</td>
<td>Oral lesions</td>
<td>Alopecia</td>
<td></td>
</tr>
<tr>
<td>Cyclophosphamide</td>
<td>Allergic reaction, angioedema, carcinoma, dermatitis, dermatitis herpetiformis, dermatofibromas, eccrine squamous syringometaplasia, edema, eosinophilic pustular folliculitis, erythema multiforme (&lt;1%), exanthem, facial burning, graft versus host reaction, hand-foot syndrome, herpes zoster, lupus erythematosus, lymphoma, myxedema, neutrophilic eccrine hidradenitis, pemphigus, photo-recall, pigmentation (&lt;1%), pruritus, purpura, scleroderma, SJS, TEN (&lt;1%), urticaria, vasculitis</td>
<td>Gingival pigmentation, mucositis (10%)</td>
<td>Alopecia (universal and severe in one-third)</td>
<td>Beau lines, dystrophy, leukonychia, onychodermal band, pigmentation (&lt;1%)</td>
</tr>
<tr>
<td>Ifosfamide</td>
<td>Allergic reaction (1–10%), dermatitis (1–10%), pigmentation (1–10%)</td>
<td>Oral lesions, sialorrhea (&lt;1%), stomatitis (&lt;1%)</td>
<td>Alopecia (50–100%)</td>
<td>Ridging (1–10%)</td>
</tr>
<tr>
<td>Carmustine</td>
<td>Dermatitis (&lt;1%), eccrine squamous syringometaplasia, erythema, exanthems, telangiectasia, tenderness</td>
<td>Stomatitis (1–10%)</td>
<td>Alopecia (1–10%)</td>
<td></td>
</tr>
<tr>
<td>Streptozocin</td>
<td>Edema, exanthems, pruritus, purpura, TEN</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dacarbazine</td>
<td>Acinic keratoses, angioedema, erythema, exanthems, fixed eruption, photo-recall, photosensitivity (&lt;1%), rash (1–10%), urticaria, vasculitis</td>
<td>Dysgeusia (1–10%), stomatitis (48%)</td>
<td>Alopecia (1–10%)</td>
<td>Pigmentation</td>
</tr>
<tr>
<td>Temozolomide</td>
<td>Allergic reactions, edema, hand-foot syndrome, Kaposi sarcoma, peripheral edema (11%), pruritus (8%), rash (8%)</td>
<td></td>
<td>Alopecia</td>
<td></td>
</tr>
<tr>
<td>Etoposide</td>
<td>Allergic reactions (1–2%), diaphoresis, eccrine squamous syringometaplasia, erythema, erythema multiforme, exanthems, facial edema, hand-foot syndrome, neutrophilic eccrine hidradenitis, photo-recall, pigmentation, pruritus, purpura, rash, SJS, urticaria</td>
<td>Dysgeusia, mucositis (&gt;10%), tinnitus, tongue edema</td>
<td>Alopecia (8–66%)</td>
<td>Beau lines, onychopathy</td>
</tr>
<tr>
<td>BCNU</td>
<td>Dermatitis (&lt;1%), eccrine squamous syringometaplasia, erythema, exanthems, pigmentation, telangiectasia, tenderness</td>
<td>Stomatitis (1–10%)</td>
<td>Alopecia (1–10%)</td>
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<thead>
<tr>
<th>Drug</th>
<th>Skin</th>
<th>Mucosal/ENT</th>
<th>Hair</th>
<th>Nails</th>
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<tbody>
<tr>
<td><strong>Antimetabolites</strong></td>
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<tr>
<td>Methotrexate</td>
<td>Acne, acral erythema, allergic reactions, angiomas, bullous dermatitis, capillaritis, carcinoma, dermatitis, dermatofibromas, eccrine squamous syringometaplasia, edema, eosinophilic pustular folliculitis, erosion of psoriatic plaques, erythema (&gt;10%), erythema multiforme, exanthems (15%), furunculosis, herpes simplex, herpes zoster, lymphadenopathy, lymphoma, melanoma, molluscum contagiosum, necrosis, nodular eruption, non-Hodgkin lymphoma, photo-recall, photosensitivity (5%), pigmentation (1–10%), pruritus (1–5%), purpura, Raynaud phenomenon, SJS, telangiectasia, TEN (&lt;1%), urticaria, vasculitis (&gt;10%)</td>
<td>Aphthous stomatitis, gingivitis (&gt;10%), glossitis (&gt;10%), mucositis</td>
<td>Alopecia (1–6%), pigmented bands</td>
<td>Discoloration, paronychia, pigmentation</td>
</tr>
<tr>
<td>Pemetrexed</td>
<td>Allergic reactions, desquamation (22%), edema, photo-recall, pressure necrosis, pruritus, purpura, rash (42%), vasculitis</td>
<td>Aphthous stomatitis, gingivitis, mucositis (5–17%)</td>
<td>Alopecia (&lt;1%)</td>
<td>Hyponychial dermatitis, nail loss, onychomadesis, paronychia, subungual hyperkeratosis</td>
</tr>
<tr>
<td>Capecitabine</td>
<td>Dermatitis (37%), diaphoresis (0.2%), edema (9%), erythema, exfoliative dermatitis (31–37%), hand-foot syndrome (7–58%), lupus erythematosus, photo-recall (&lt;1%), photosensitivity, pigmentation, pruritus, purpura (0.2%), pyogenic granuloma, ulcerations, vesication, vitiligo, xerosis</td>
<td>Mucositis, oral candidiasis (0.2%), stomatitis (24%)</td>
<td>Alopecia (&lt;1%)</td>
<td></td>
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<tr>
<td>Cytarabine</td>
<td>Allergic reactions (&lt;1%), angioedema (&lt;1%), dermatitis, diaphoresis, edema (&lt;1%), erythema, exanthems, lichenoid eruption, lupus erythematosus, peripheral edema, photosensitivity, purpura, urticaria, vasculitis</td>
<td>Dysgeusia, tinnitus, xerostomia (1–10%)</td>
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<tr>
<td>Gemcitabine</td>
<td>Acral necrosis, allergic reactions (4%), cellulitis, dermatitis, diaphoresis, edema (13%), erysipelas, exanthems, hand-foot syndrome, linear IgA dermatosis, lipodermatosclerosis, livedo reticularis, necrotizing vasculitis, petechiae (16%), photo-recall (&lt;74%), pruritus (13%), pseudolymphoma, rash (30%), Raynaud phenomenon, scleroderma, SJS, TEN</td>
<td>Dysgeusia, mucositis, stomatitis (11%)</td>
<td>Alopecia (15%)</td>
<td></td>
</tr>
<tr>
<td>6-Mercaptopurine</td>
<td>Dermatitis (2%), edema, exanthems (&lt;1%), herpes zoster, lichenoid eruption, lupus erythematosus, melanoma, neoplasms, palmar-plantar erythema, petechiae, photo-recall, photosensitivity, pigmentation (1–10%), pruritus, purpura, TEN, urticaria, vasculitis</td>
<td>Glossitis (&lt;1%), mucositis (1–10%), oral lesions (1–5%), stomatitis (1–10%)</td>
<td>Alopecia</td>
<td>Nail loss</td>
</tr>
<tr>
<td>6-TG</td>
<td>Exanthems, malignancies, palmar erythema, petechiae, photosensitivity (&lt;1%), pruritus, psoriasis, purpura, rash (1–10%)</td>
<td>Stomatitis (1–10%), xerostomia</td>
<td>Alopecia</td>
<td></td>
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<tr>
<td>Fludarabine</td>
<td>Edema (&gt;10%), exanthems, herpes simplex, paraneoplastic pemphigus, petechiae, rash (&gt;10%), squamous cell carcinoma</td>
<td>Dysgeusia (&lt;1%), stomatitis (&gt;10%)</td>
<td>Alopecia</td>
<td></td>
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<tr>
<td>Cladribine</td>
<td>Allergic reactions, diaphoresis (1–10%), edema (6%), eosinophilic cellulitis, erythema (6%), erythrodema, exanthems (27–50%), halogenoderma, herpes, petechiae (8%), pruritus (6%), purpura (10%), rash (27%), SJS, TEN, transient acantholytic dermatosis, urticaria, vasculitis</td>
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<tr>
<td>Drug</td>
<td>Skin</td>
<td>Mucosal/ENT</td>
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<tr>
<td><strong>Topoisomerase-interacting agents</strong></td>
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<tr>
<td>Irinotecan</td>
<td>Allergic reactions (9%), diaphoresis (16%), edema (10.2%), exanthems, hand-foot syndrome, photosensitivity, pigmentation, pruritus, pyogenic granuloma, rash (&lt;21%)</td>
<td>Dygeusia, mucositis (2%), sialorrhoea</td>
<td>Alopecia (13–60.5%)</td>
<td></td>
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<tr>
<td>Topotecan</td>
<td>Allergic reactions, erythema (&lt;1%), fixed eruption, neutrophilic eccrine hidradenitis, purpura (&lt;1%), scleroderma</td>
<td>Mucositis, stomatitis (24%)</td>
<td>Alopecia (59%)</td>
<td>Pigmentation</td>
</tr>
<tr>
<td>Doxorubicin</td>
<td>Actinic keratoses, allergic reactions (&lt;1%), angioedema, cellulitis, dermatitis, dermatitis herpetiformis, diaphoresis, exanthems, exfoliative dermatitis, fixed eruption, hand-foot syndrome, inflammation, intertrigo, keratoderma, necrosis, photo-recall, pigmentation, pruritus, psoriasis, purpura, rash, Raynaud phenomenon, scleroderma, toxic erythema, urticaria (&lt;1%)</td>
<td>Ageusia, mucositis, oral lesions, pigmentation, stomatitis (&gt;10%), tongue pigmentation</td>
<td>Alopecia (&gt;10%)</td>
<td>Beau lines, melanonychia, Muehrcke lines</td>
</tr>
<tr>
<td>Daunorubicin</td>
<td>Angioedema, dermatitis, erythema, exanthems, exfoliative dermatitis, folliculitis, hand-foot syndrome, hypomelanosis, neutrophilic eccrine hidradenitis, pigmentation, pruritus, rash (&lt;1%), urticaria (&lt;1%)</td>
<td>Mucositis</td>
<td>Alopecia (&gt;10%)</td>
<td>Pigmentation</td>
</tr>
<tr>
<td>Idarubicin</td>
<td>Acral erythema, bullous dermatitis, exanthems (&lt;1%), neutrophilic dermatosis, photo-recall, rash (&gt;10%), urticaria (&gt;10%)</td>
<td>Mucositis (50%)</td>
<td>Alopecia (77%)</td>
<td>Pigmentation</td>
</tr>
<tr>
<td>Mitoxantrone</td>
<td>Allergic reactions (&lt;1%), diaphoresis (1–10%), edema (&gt;10%), erythema, fungal dermatitis (&gt;15%), necrosis, petechiae (&gt;10), bluish pigmentation, purpura (&gt;10), rash (&lt;1), ulcerations, urticaria, vitiligo</td>
<td>Alopecia (20–60%)</td>
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<tr>
<td>Dactinomycin</td>
<td>Acne (&gt;10), actinic keratoses, bullous pemphigoid, cellulitis, dermatitis, erythema, erythema multiforme, exanthems, folliculitis, reactivation of keratoses, lichenoid eruption, photo-recall (&gt;10%), pigmentation, pruritus, pustules, TEN, urticaria</td>
<td>Cheilitis, oral lesions, ulcerative stomatitis (&gt;5%)</td>
<td>Alopecia (&gt;10%)</td>
<td></td>
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<tr>
<td>Teniposide</td>
<td>Facial edema, rash, urticaria</td>
<td>Mucositis (3%)</td>
<td>Alopecia (31%)</td>
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<tr>
<td><strong>Epidermal growth factor receptor/Anaplastic lymphoma kinase/Vascular endothelial growth factor inhibitors</strong></td>
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<tr>
<td>Erlotinib</td>
<td>Acne, acute generalized exanthematous pustulosis, erythema (18%), fissures, folliculitis, papulopustular eruption, photosensitivity, pruritus (13%), rash (75%), telangiectasia, xerosis (12%)</td>
<td>Aphthous stomatitis (17%)</td>
<td>Alopecia, eyelash hypertrophy, trichomegaly</td>
<td>Paronychia, pyogenic granulomas</td>
</tr>
<tr>
<td>Gefitinib</td>
<td>Acne (39–52%), acute generalized exanthematous pustulosis, desquamation (39%), erosive pustular dermatosis, exanthems, folliculitis, glucagonoma syndrome, hand-foot syndrome, pigmentation, pruritus, pyoderma gangrenosum, rash (52%), rosacea, scaling, seborrhea, ulcerations, urticaria, xerosis</td>
<td>Epistaxis, oral ulceration, stomatitis</td>
<td>Abnormal texture, alopecia, hypertrophy</td>
<td>Paronychia (6%), pyogenic granulomas, nail changes (17%)</td>
</tr>
<tr>
<td>Cetuximab</td>
<td>Acne (88%), allergic reactions, burning, erythema, exanthems, fissures, folliculitis, papulopustular eruption, peripheral edema (10%), pruritus (10%), rash, transient acantholytic dermatosis, xerosis</td>
<td>Stomatitis (11%)</td>
<td>Alopecia (5%)</td>
<td>Nail changes (16%), paronychia</td>
</tr>
<tr>
<td>Panitumumab</td>
<td>Acne (57%), eczema, erythema (65%), exfoliative dermatitis (25%), fissures (20%), peripheral edema (12%), photosensitivity, pigmentation, pruritus (57), rash (22), telangiectasia, xerosis (10%)</td>
<td>Oral mucositis (6%)</td>
<td>Hair changes</td>
<td>Nail changes, paronychia (25%), pyogenic granulomas</td>
</tr>
<tr>
<td>Crizotinib [33]</td>
<td>Edema (16%)</td>
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<tr>
<td>Ziv-aflibercept [34]</td>
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<td>Stomatitis (20%)</td>
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### Multikinase small molecule tyrosine kinase inhibitors

<table>
<thead>
<tr>
<th>Drug</th>
<th>Skin</th>
<th>Mucosal/ENT</th>
<th>Hair</th>
<th>Nails</th>
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</thead>
<tbody>
<tr>
<td>Imatinib</td>
<td>Acne, acute febrile neutrophilic dermatosis, acute generalized</td>
<td>Oral lichenoid eruption</td>
<td>Follicular mucinosis</td>
<td>Dystrophy, pigmentation</td>
</tr>
<tr>
<td></td>
<td>exanthematous pseudolus, carcinoma, dermatomyositis, eccrine</td>
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<tr>
<td></td>
<td>squamous syringometaepitasis, edema (1–5%), erythema, exanthems,</td>
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<tr>
<td></td>
<td>exfoliative dermatitis, hypomelanosis, lichen planus, mycosis fungoides,</td>
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<td></td>
<td>necrolysis, neutrophilic eccrine hidradenitis, palmar-plantar</td>
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<td></td>
<td>hyperkeratosis, petechiae (1–10%), photosensitivity, pigmentation,</td>
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<td></td>
<td>pityriasis rosea, pruritus (6–10%), psoriasis, rash (32–39%), SJS,</td>
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<td></td>
<td>TEN, urticaria, vasculitis</td>
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<tr>
<td>Dasatinib</td>
<td>Acne, dermatitis, hyperhidrosis, photosensitivity, pigmentation,</td>
<td>Dysgeusia, mucositis (16%)</td>
<td>Alopecia</td>
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<tr>
<td></td>
<td>pruritus (11%), rash (39%), urticaria, xerosis</td>
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<tr>
<td>Nilotinib</td>
<td>Pruritus (17%), rash (22%), xerosis (12%)</td>
<td>Dysgeusia (21–43%),</td>
<td>Alopecia (6%)</td>
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</tr>
<tr>
<td>Sunitinib</td>
<td>Bullous dermatitis, edema, hand-foot syndrome, peripheral edema (17%),</td>
<td>glossodynia (15%),</td>
<td>Alopecia (5–12%),</td>
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<tr>
<td></td>
<td>pigmentation, pyoderma gangrenosum, rash (14–38%), xerosis (17%)</td>
<td>mucositis (29–53%),</td>
<td>pigmentation</td>
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<tr>
<td>Sorafenib</td>
<td>Acne (1–10%), inflammation of actinic keratoses, desquamation</td>
<td>Anguloar stomatitis,</td>
<td>Alopecia (27%)</td>
<td>Splinter hemorrhages</td>
</tr>
<tr>
<td></td>
<td>(40%), eczema (&lt;1%), eruptive facial cysts, erythema (&gt;10%), erythema</td>
<td>cheilitis, dysphagia (1–10%),</td>
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<td></td>
<td>multiforme (&lt;1%), folliculitis (&lt;1%), hand-foot syndrome (30%),</td>
<td>glossodynia (1–10%),</td>
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<tr>
<td></td>
<td>hyperkeratosis, pruritus (19%), rash (40%), seborrheic dermatitis,</td>
<td>mucositis (1–10%),</td>
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<tr>
<td></td>
<td>squamous cell carcinoma, urticaria (&lt;1%), vasculitis, xerosis (11%)</td>
<td>rhinorrhea (&lt;1%), xerostomia</td>
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</tr>
<tr>
<td>Pazopanib</td>
<td>Decubitus ulcer (3%), edema (3%), flushing (3%), hand-foot syndrome</td>
<td>Epistaxis (11%)</td>
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<tr>
<td></td>
<td>(3%), hyperhidrosis (3%), hypopigmentation (3%), pruritus (3%),</td>
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<tr>
<td></td>
<td>xerosis (3%)</td>
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<tr>
<td>Vandetanib</td>
<td>Rash (26%), photosensitivity (16%)</td>
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<tr>
<td>Ponatinib</td>
<td>Rash (32%), acneiform dermatitis (14%), dry skin (14%), erythema</td>
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<td></td>
<td>nodosum (2%), melanoma (1%)</td>
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<tr>
<td>Axitinib</td>
<td>Palmar-plantar erythrodysaesthesia (27%), rash (13%)</td>
<td>Mucosal inflammation (15%),</td>
<td>Alopecia (4%)</td>
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<tr>
<td></td>
<td></td>
<td>stomatitis (15%)</td>
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<tr>
<td>Cabozantinib</td>
<td>Rash (13%), palmar-plantar erythrodysesthesia (30%)</td>
<td>Stomatitis (11%), mucosal</td>
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<tr>
<td></td>
<td></td>
<td>inflammation (21%)</td>
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<tr>
<td>Bosutinib</td>
<td>Rash (20%)</td>
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<tr>
<td>Regorafenib</td>
<td>Hand-foot skin reaction (56%), rash (18%)</td>
<td>Oral mucositis (38%)</td>
<td>Alopecia (24%)</td>
<td></td>
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<tr>
<td>Drug</td>
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<td>Mucosal/ENT</td>
<td>Hair</td>
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<tr>
<td>Paclitaxel</td>
<td>Allergic reactions (15%), angioedema, desquamation (7%), edema (21%), erythema, exanthems (&lt;1%), fixed eruption, folliculitis, hand-foot syndrome, lupus erythematosus, photo-recall (&lt;1%), photosensitivity, pigmentation, pruritus (&lt;1%), purpura, pustules, rash (12%), scleroderma, SJS, urticaria</td>
<td>Mucositis (&gt;10%), oral lesions (3–8%), stomatitis (2–39%)</td>
<td>Alopecia (87–100%), alopecia areata</td>
<td>Nail changes, leukonychia, Mees lines, paronychia, pigmentation (2%), subungual hyperkeratosis, thickening</td>
</tr>
<tr>
<td>Docetaxel</td>
<td>Allergic reactions, angioedema, edema (1–20%), erythema (0.9%), exanthems, fixed eruption, hand-foot syndrome, lupus erythematosus, photo-recall, photosensitivity, pigmentation, pruritus, radiodermatitis, rash (0.9%), scleroderma, seborrheic keratoses, squamous syringometaplasia, SJS, TEN, urticaria, xerosis</td>
<td>Dysgeusia, dysphagia, mucositis, nasal septal perforation, stomatitis (5–42%)</td>
<td>Alopecia (80%)</td>
<td>Beau lines, discoloration, dystrophy, hyponychial dermalitis, nail loss, paronychia, pigmentation, subungual abscess, subungual hemorrhage, subungual hyperkeratosis, transverse superficial loss of nail plate</td>
</tr>
<tr>
<td>Albumin-bound paclitaxel [11]</td>
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<td>Alopecia (86.9%)</td>
</tr>
<tr>
<td>Vincristine</td>
<td>Actinic keratoses, allergic reactions angioedema, dermatitis herpetiformis, edema, erythroderma, exanthems, hand-foot syndrome, pigmentation, pruritus, rash (1–10%), Raynaud phenomenon, urticaria</td>
<td>Dysgeusia (1–10%), oral lesions (1–10%), oral ulceration (1–10%), stomatitis (&lt;1%)</td>
<td>Alopecia (20–70%)</td>
<td>Beau lines, leukonychia, Mees lines, Muehrcke lines, onychodermal band, pigmentation</td>
</tr>
<tr>
<td>Vinblastine</td>
<td>Acne, acral necrosis, angioedema, bullous dermatitis (&lt;1%), cellulitis, dermatitis (1–10%), erythema, erythema multiforme, exanthems, photo-recall, photosensitivity (1–10%), pigmentation, purpura, Raynaud phenomenon (1–10%), ulcerations, urticaria</td>
<td>Dysgeusia (&gt;10%), oral lesions (1–5%), oral vesiculation, ototoxicity, stomatitis (&gt;10%)</td>
<td>Alopecia (&gt;10%), hair changes</td>
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<tr>
<td>Vinorelbine</td>
<td>Angioedema, erythema, hand-foot syndrome, pigmentation, pruritus, rash (&lt;5%), TEN, vasculitis</td>
<td>Dysgeusia (&gt;10%), mucositis, stomatitis (&gt;10%)</td>
<td>Alopecia (12%)</td>
<td></td>
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<tr>
<td>Estramustine</td>
<td>Acne, allergic reactions, angioedema, edema (&gt;10%), exanthems, facial flushing, pigmentation (&lt;1%), pruritus (2%), purpura (3%), rash (1%), urticaria, xerosis (2%)</td>
<td></td>
<td>Alopecia (&lt;1%)</td>
<td></td>
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<tr>
<td>Drug</td>
<td>Skin</td>
<td>Mucosal/ENT</td>
<td>Hair</td>
<td>Nails</td>
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<tr>
<td><strong>Histone deacetylase, proteasome inhibitors, retinoids, and demethylating agents</strong></td>
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<tr>
<td>Vorinostat</td>
<td>Angioedema (9%), exfoliative dermatitis (9%), peripheral edema (13%), pruritus (12%)</td>
<td>Dysgeusia (28%),  xerostomia (16%)</td>
<td>Alopecia (19%)</td>
<td></td>
</tr>
<tr>
<td>Romidepsin [12]</td>
<td>Skin and subcutaneous disorder (4%)</td>
<td>Dry mouth (4%)</td>
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<tr>
<td>Arsenic trioxide</td>
<td>Acral desquamation, carcinoma, bullous dermatitis, dermatitis, dermatofibrosarcoma protuberans, edema, ephelides, erythema, erythema multiforme, erythema nodosum, exanthems, exfoliative dermatitis, fixed eruption, follicular keratosis, herpes simplex, herpes zoster, hyperhidrosis, hyperkeratosis of the palms and soles (40%), hypomelanosis, keratoses, leukomelanosis, lichen planus, livedo reticularis, melanoma, melanosis, Merkel cell carcinoma, morphea, palmar-planter erythema, palmar-planter hyperhidrosis, parapsoriasis, photo-recall, photosensitivity, pityriasis rosea, pruritus, psoriasis, purpura, rash, Raynaud phenomenon, SJS, ulcersations, urticaria, vitiligo, xerosis</td>
<td>Dysgeusia, oral mucosal eruption (8%), oral pigmentation, stomatitis</td>
<td>Alopecia</td>
<td>Leukonychia, Mees lines, pigmentation</td>
</tr>
<tr>
<td>All-trans retinoic acid</td>
<td>Acne (1%), acute febrile neutrophilic dermatosis, bullous dermatitis, burning (10–40%), carcinoma, cellulitis (1–10%), crusting, dermatitis, desquamation (14%), diaphoresis (20%), edema (29%), erythema (1–49%), erythema nodosum, facial edema (1–10%), flaking (23%), hyperkeratosis (78%), hypomelanosis (5%), irritation (5%), pallor (1–10%), palmar-planter desquamation (1–10%), photosensitivity (10%), pigmentation (5%), pruritus (10–40%), pyogenic granuloma, rash (54%), retinoic acid—APL syndrome (25%), scaling (10–40%), shivering (63%), stinging (1–26%), ulcersations (penile), vasculitis, vesiculobullous eruption, xerosis (49–100%)</td>
<td>Cheilitis (10%), gingivitis (&lt;1%), xerostomia (10%)</td>
<td>Alopecia areata (14%)</td>
<td>Alopecia (4–11%)</td>
</tr>
<tr>
<td>Bexarotene</td>
<td>Acne (&lt;10%), allergic granulomatous angitis, bacterial infections (1.2–13.2%), burning, cold extremities, dermatitis, erythema, exanthems (&lt;10%), exfoliative dermatitis (10–28%), facial edema, irritation, necrosis, nodular eruption (&lt;10%), peripheral edema (13.1%), photosensitivity, pruritus (20–30%), pustules, rash (16.7%), stinging, ulcerations (&lt;10%), vasculitis, vesiculobullous eruption (&lt;10%), xerosis</td>
<td>Cheilitis (&lt;10%), gingivitis (&lt;10%), xerostomia (&lt;10%)</td>
<td>Alopecia (4–11%)</td>
<td></td>
</tr>
<tr>
<td><strong>Miscellaneous agents</strong></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>L-Asparaginase</td>
<td>Allergic reactions, angioedema, diaphoresis, edema, exanthems, pruritus (&lt;1%), TEN, urticaria (1–15%)</td>
<td>Aphthous stomatitis (1–10%), oral lesions (26%)</td>
<td>Alopecia</td>
<td></td>
</tr>
<tr>
<td>Bleomycin</td>
<td>Acral necrosis, acral sclerosis, allergic reactions, angioedema, bullous dermatitis (1–5%), calcification, dermatitis, digital gangrene, eccrine squamous syringometaplasia, erythema, erythema gyratum, exanthems, fixed eruption, flagellate erythema/pigmentation, hand-foot syndrome, hyperkeratosis of the palms and soles, intertrigo, neutrophilic eccrine hidradenitis, nodular eruption, palmar nodules, photo-recall, pigmentation (50%), pruritus (&gt;5%), rash, Raynaud phenomenon (&gt;10%), scleroderma, SJS, striae, urticaria, vesiculation, xerosis.</td>
<td>Glositis, oral papillomatosis, oral ulceration, stomatitis (&gt;10%), tongue erosions</td>
<td>Alopecia (50%), graying of the hair</td>
<td>Beau lines, dystrophy, reduced growth, nail loss, onychodystrophy</td>
</tr>
<tr>
<td>Procarbazine</td>
<td>Allergic reactions (&lt;1%), angioedema, dermatitis (&lt;1%), diaphoresis, edema, exanthems (4–9%), exfoliative dermatitis, fixed eruption, herpes zoster, petechiae, photosensitivity, pigmentation (1–10%), pruritus (&lt;1%), purpura, rash, TEN, urticaria (9%)</td>
<td>Oral lesions (1–5%), stomatitis (&gt;10%), xerostomia</td>
<td>Alopecia (1–10%)</td>
<td></td>
</tr>
</tbody>
</table>
## Chapter 1  Epidemiology and Burden of Disease

### Miscellaneous agents

<table>
<thead>
<tr>
<th>Drug</th>
<th>Skin</th>
<th>Mucosal/ENT</th>
<th>Hair</th>
<th>Nails</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thalidomide</td>
<td>Bullous dermatitis (5%), burning, dermatitis, desquamation, diaphoresis, edema, erythema, erythema multiforme, erythema nodosum, erythoderma, exanthems, exfoliative dermatitis, facial erythema, nodular eruption, palmar erythema, pruritus, psoriasis, purpura, pustuloderma, rash (11–50%), SJS, TEN, ulcerations, urticaria (3%), vasculitis, xerosis</td>
<td>Xerostomia</td>
<td>Alopecia</td>
<td>Brittle nails</td>
</tr>
<tr>
<td>Lenalidomide</td>
<td>Acute febrile neutrophilic dermatosis, diaphoresis (8%), erythema (5.4%), peripheral edema (20%), pruritus (42%), rash (36%), xerosis (14%)</td>
<td>Dysgeusia (6%), rhinitis (7%), stomatitis, xerostomia (7%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vemurafenib [41]</td>
<td>Keratoacanthomas (6%), cutaneous squamous cell carcinoma (12%), rash (10%), pruritus (6%)</td>
<td></td>
<td>Alopecia (8%)</td>
<td></td>
</tr>
<tr>
<td>Ingenol mebutate [42]</td>
<td>Erythema (34%), flaking/scaling (29%), crusting (9.2%), erosion/ulceration (1.9%), hypopigmentation/hyperpigmentation (19.8%), scarring (0.6%)</td>
<td></td>
<td></td>
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<tr>
<td>Vismodegib [43,44]</td>
<td>Xerosis</td>
<td>Keratitis (3%), corneal abrasion (3%)</td>
<td>Alopecia (63.8%)</td>
<td></td>
</tr>
<tr>
<td>Everolimus [45]</td>
<td>Acne-like skin lesions (22%), eczema (10%)</td>
<td>Stomatitis (48%), mouth ulceration (19%), aphthous stomatitis (19%)</td>
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</tr>
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</table>

### Biotherapy

<table>
<thead>
<tr>
<th>Drug</th>
<th>Skin</th>
<th>Mucosal/ENT</th>
<th>Hair</th>
<th>Nails</th>
</tr>
</thead>
<tbody>
<tr>
<td>Interferon-a2a</td>
<td>Acne (1%), acral sclerosis, allergic reactions, angioedema, atrophie blanche, Behçet disease, bullous dermatitis, dermatitis, dermatitis herpetiformis, dermatomyositis, diaphoresis (22%), eczema, edema (11%), erythema, erythema nodosum, exanthems, fungal dermatitis (&lt;1%), halo dermatitis, herpes simplex (1%), Kaposi sarcoma, keratoses, lichen myxedematous, lichen planus, lichenoid eruption, linear IgA dermatosis, livedo reticularis, lupus erythematosus, melanoma, necrosis, nodular eruption, pemphigus, photo-reaction, photosensitivity (&lt;1%), pigmentation (&lt;1%), capillaritis, pityriasis versicolor, pruritus (13%), psoriasis, purpura, rash (44%), Raynaud phenomenon, sarcoidosis, scleroderma, seborrheic dermatitis, telangectasia, ulcerations, urticaria (&lt;3%), vasculitis, vitiligo, xerosis (17%)</td>
<td>Ageusia, anosmia, aphthous stomatitis, dysgeusia (25%), oral lichen planus, oral pemphigus, sialodacryoadenitis, stomatitis (1–10%), xerostomia (&gt;10%)</td>
<td>Alopecia (1–10%), alopecia areata, curly hair, hypertrichosis, pigmentation, straight hair</td>
<td></td>
</tr>
<tr>
<td>Interferon-a2b</td>
<td>Allergic granulomatous angiitis, allergic reactions (&lt;1%), angioedema, bullous dermatitis, bullous pemphigoid, dermatitis, desquamation, edema (47%), erythema (41%), erythema multiforme, erythema nodosum, erythoderma, exanthems, exfoliative dermatitis (14%), intertrigo, Kaposi sarcoma, linear IgA dermatosis, necrosis, pemphigus, petechiae (4%), photosensitivity, pruritus (48%), psoriasis, purpura (4%), rash (26%), sarcoidosis, scleroderma, SJS, TEN, urticaria (2%), vasculitis, vitiligo, xerosis (15%)</td>
<td>Aphthous stomatitis, dysgeusia (7%), glossitis, oral mucosal erosion, oral ulceration, stomatitis 93%, xerostomia</td>
<td>Alopecia (&lt;1%)</td>
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(Continued)
### Section 1  Dermatology and Oncology

<table>
<thead>
<tr>
<th>Drug</th>
<th>Skin</th>
<th>Mucosal/ENT</th>
<th>Hair</th>
<th>Nails</th>
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</thead>
<tbody>
<tr>
<td><strong>Monoclonal antibodies</strong></td>
<td></td>
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<tr>
<td>Trastuzumab</td>
<td>Acne (2%), allergic reactions (3%), angioedema (&lt;1%), cellulitis (&lt;1%), diaphoresis, edema (8%), hand-foot syndrome, herpes simplex (2%), herpes zoster (1%), peripheral edema (10%), photosensitivity, rash (18%), ulcerations (1%)</td>
<td>Stomatitis (&lt;1%)</td>
<td>Alopecia</td>
<td>Dystrophy</td>
</tr>
<tr>
<td>Bevacizumab</td>
<td>Exfoliative dermatitis, pigmentation, ulcerations, xerosis, hand-foot syndrome</td>
<td>Dysgeusia, oral ulceration, stomatitis, xerostomia</td>
<td>Alopecia</td>
<td>Changes</td>
</tr>
<tr>
<td>Rituximab</td>
<td>Angioedema (&gt;10%), dermatitis, diaphoresis, exanthems, herpes zoster, Kaposi sarcoma, necrosis, paraneoplastic pemphigus, peripheral edema, pruritus (10%), rash (10%), SJS, TEN, urticaria (10%)</td>
<td>Orogenital ulceration, otitis, perianal ulcerations, rhinitis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alemtuzumab</td>
<td>Abscess, allergic reactions (&lt;1%), angioedema (&lt;1%), bullous dermatitis (&lt;1%), cellulitis (&lt;1%), facial edema (&lt;1%), hematoma (&lt;1%), herpes simplex, herpes zoster, peripheral edema (13%), pruritus, purpura (8%), rash, squamous cell carcinoma (&lt;1%), urticaria</td>
<td>Dysgeusia (&lt;1%), gingivitis (&lt;1%), sinusitis, stomatitis (14%), stomatodynia</td>
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<tr>
<td>Gemtuzumab</td>
<td>Herpes simplex (22%), peripheral edema (21%), petechiae (21%), rash (23%)</td>
<td>Mucositis (4–25%), stomatitis (32%)</td>
<td></td>
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<tr>
<td>Ibritumomab</td>
<td>Allergic reactions (2%), angioedema (5%), bullous dermatitis, diaphoresis (4%), erythema multiforme, exfoliative dermatitis, peripheral edema (8%), petechiae (3%), pruritus (9%), purpura (7%), rash (8%), SJS, TEN, urticaria (4%)</td>
<td>Mucositis</td>
<td>Alopecia</td>
<td></td>
</tr>
<tr>
<td>Tositumomab</td>
<td>Allergic reactions, angioedema, carcinoma, diaphoresis (8%), peripheral edema (9%), pruritus, rash (17%)</td>
<td>Rhinitis (10%)</td>
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<tr>
<td>Ipilimumab</td>
<td>Vitiligo (2.3%), rash (19.1%), pruritus (24%)</td>
<td></td>
<td>Alopecia</td>
<td></td>
</tr>
<tr>
<td>Pertuzumab</td>
<td>Pruritus (6%), dry skin (6%), acneiform rash (13%)</td>
<td>Mucosal inflammation (7%)</td>
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</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Endocrine agents</strong></th>
<th></th>
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</thead>
<tbody>
<tr>
<td>Tamoxifen</td>
<td>Dermatomyositis, diaphoresis, edema (2–6%), exanthems (3%), lupus erythematosus, photo-recall, pruritus, purpura, radiodermatitis, rash (1–10%), sarcoma, urticaria, vasculitis, xerosis (7%)</td>
<td>Dysgeusia, vaginal pruritus, xerostomia (7%)</td>
<td>Alopecia, hirsutism, hypertrichosis, pigmentation</td>
<td></td>
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<tr>
<td>Toremifene</td>
<td>Dermatitis, diaphoresis (20%), edema (5%), pigmentation, pruritus</td>
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<tr>
<td>Raloxifene</td>
<td>Capillaritis, diaphoresis (3.1%), edema, peripheral edema (3–5%), rash (5.5%), vitiligo</td>
<td>Vaginitis (4.3%)</td>
<td></td>
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<tr>
<td>Anastrozole</td>
<td>Angioedema, diaphoresis, erythema multiforme, lupus erythematosus, peripheral edema (10.1%), pruritus (2–5%), rash (7.5%), shivering, SJS, urticaria</td>
<td>Vaginal dryness (1.7%), xerostomia</td>
<td>Alopecia (2–5%)</td>
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<tr>
<td>Letrozole</td>
<td>Diaphoresis (&lt;5%), exanthems (5%), pruritus (2%), psoriasis (5%), rash (1–10%), TEN, vesiculation (5%)</td>
<td></td>
<td>Alopecia (&lt;5%)</td>
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</tr>
<tr>
<td>Exemestane</td>
<td>Diaphoresis (6–12%), edema (7%), hyperhidrosis, peripheral edema (9%), pruritus (2–5%), rash (2–5%)</td>
<td></td>
<td>Alopecia (2–5%)</td>
<td></td>
</tr>
<tr>
<td>Fulvestrant</td>
<td>Diaphoresis (5%), edema (9%), rash (7%)</td>
<td>Vaginitis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Drug</td>
<td>Skin</td>
<td>Mucosal/ENT</td>
<td>Hair</td>
<td>Nails</td>
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<tr>
<td><strong>Endocrine agents</strong></td>
<td></td>
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</tr>
<tr>
<td>Leuprolide</td>
<td>Acne, allergic granulomatous angiitis, dermatitis (5%), dermatitis herpetiformis, diaphoresis, edema (1–10%), exanthems, lupus erythematosus, nodular eruption, photosensitivity, pigmentation (&lt;5%), pruritus (&lt;5%), purpura (&lt;1%), rash (1–10%), stickiness, urticaria, xerosis (&lt;5%)</td>
<td>Dysgeusia (&lt;5%), vaginitis,</td>
<td>Alopecia (&lt;5%), hypertrichosis (&lt;1%)</td>
<td></td>
</tr>
<tr>
<td>Flutamide</td>
<td>Bullous dermatitis, diaphoresis, edema (4%), erythema, exanthems, lupus erythematosus, photosensitivity, rash (3%), TEN, urticaria</td>
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<td></td>
<td></td>
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<tr>
<td>Bicalutamide</td>
<td>Angioedema, carcinoma, diaphoresis (6%), edema (2–5%), exanthems (&lt;1%), herpes zoster, pruritus (2–5%), rash (6%), urticaria, xerosis (2–5%)</td>
<td>Xerostomia</td>
<td>Alopecia</td>
<td></td>
</tr>
<tr>
<td>Nilutamide</td>
<td>Diaphoresis (6%), edema (2%), pruritus (2%), rash (5%), urticaria, xerosis (5%)</td>
<td>Xerostomia (2%)</td>
<td>Alopecia</td>
<td></td>
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<tr>
<td>Fluoxymesterone</td>
<td>Acne (&gt;10%), dermatitis, edema (&gt;10%), exanthems, furunculosis, lichenoid eruption, lupus erythematosus, pruritus, psoriasis, purpura, seborrhea, striae, urticaria</td>
<td>Stomatitis</td>
<td>Alopecia, hirsutism (1–10%)</td>
<td></td>
</tr>
<tr>
<td>Estradiol</td>
<td>Acanthosis nigricans, acne (5%), allergic granulomatous angiitis, angioedema, bullous dermatitis, chloasma (&lt;1%), dermatitis, eczema, edema (&lt;1%), erythema multiforme, erythema nodosum, exanthems, exfoliative dermatitis, fixed eruption (&lt;1%), hyperkeratosis, livedo reticularis, lupus erythematosus, Mucha–Habermann disease, osteoma cutis, papulovesicular eruption, photosensitivity, pigmentation, porphyria cutanea tarda, pruritus, pseudolymphoma, purpura, rash (&lt;1%), Raynaud phenomenon, scleroderma, spider nevi, striae, telangiectasia, urticaria, vasculitis, vesication</td>
<td>Gingival hyperplasia/ hypertrophy, mucosal eruption, pigmentation, vulvovaginal candidiasis</td>
<td>Alopecia (9%), hirsutism (&lt;5%), straight hair</td>
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<tr>
<td>Octreotide</td>
<td>Allergic granulomatous angiitis, allergic reactions, cellulitis (1–4%), diaphoresis, edema (1–10%), exanthems, petechiae (1–4%), pruritus (1–4%), purpura (1–4%), rash (&lt;1%), Raynaud phenomenon (1–4%), urticaria (1–4%)</td>
<td>Vaginitis (1–4%), xerostomia</td>
<td>Alopecia (&lt;1%)</td>
<td></td>
</tr>
<tr>
<td>Megestrol</td>
<td>Acne, acute generalized exanthematous pustulosis, angioedema, dermatitis, diaphoresis (31%), edema, erythema multiforme, erythema nodosum, exanthems, hemorrhage, melasma, pruritus, rash, telangiectasia, urticaria</td>
<td></td>
<td>Alopecia, hirsutism</td>
<td></td>
</tr>
<tr>
<td>Medroxyprogesterone acetate</td>
<td>Acne (1–5%), allergic reactions (&lt;1%), angioedema, chloasma (1–10%), diaphoresis (&lt;31%), edema (&gt;10%), erythema nodosum, exanthems, hemorrhage, Mucha–Habermann disease, photosensitivity, pigmented purpuric eruption, pruritus (1–10%), rash (1–5%), scleroderma (&lt;1%), striae, urticaria, xerosis (&lt;1%)</td>
<td>Bromhidrosis (&lt;1%), vaginitis (1–5%)</td>
<td>Alopecia (1–5%), hirsutism (&lt;1%)</td>
<td></td>
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</tbody>
</table>

(Continued)
## Agents for management of hematologic reactions

<table>
<thead>
<tr>
<th>Drug</th>
<th>Skin</th>
<th>Mucosal/ENT</th>
<th>Hair</th>
<th>Nails</th>
</tr>
</thead>
<tbody>
<tr>
<td>Epoetin Alfa</td>
<td>Acne, angioedema (1–5%), dermatitis, edema (17%), erythoderma, exanthems, lichenoid eruption, photosensitivity, pruritus, rash (1–10%), urticaria</td>
<td>Alopecia, alopecia totalis, hypertrichosis</td>
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<tr>
<td>Darbepoetin</td>
<td>Edema (21%), pruritus (8%), rash (7%), urticaria</td>
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<tr>
<td>Filgastrim</td>
<td>Abscess, acne, acral erythema, acute febrile neutrophilic dermatosis, allergic granulomatous angiitis, allergic reactions (19%), diaphoresis, edema, erythema, erythema nodosum, exanthems (5–63%), exfoliative dermatitis (10%), folliculitis, graft versus host reaction, lichenoid eruption, linear IgA dermatosis, lupus erythematosus, neutrophilic eccrine hidradenitis, palmar-plantar pustulosis, pruritus (1–5%), psoriasis, pyoderma gangrenosum, rash (&lt;40%), urticaria, vasculitis</td>
<td>Dysgeusia, mucositis (40%), stomatitis (&gt;10%)</td>
<td>Alopecia (&gt;10%)</td>
<td></td>
</tr>
<tr>
<td>Sargramostin</td>
<td>Abscess, acne, acral erythema, acute febrile neutrophilic dermatosis, allergic granulomatous angiitis, allergic reactions (19%), diaphoresis, edema, erythema, erythema nodosum, exanthems (5–63%), exfoliative dermatitis (10%), folliculitis, graft versus host reaction, lichenoid eruption, linear IgA dermatosis, lupus erythematosus, neutrophilic eccrine hidradenitis, palmar-plantar pustulosis, pruritus (1–5%), psoriasis, pyoderma gangrenosum, rash (&lt;40%), urticaria, vasculitis</td>
<td>Dysgeusia, mucositis (40%), stomatitis (&gt;10%)</td>
<td>Alopecia (&gt;10%)</td>
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</tr>
<tr>
<td>Pegfilgastrim</td>
<td>Acute febrile neutrophilic dermatosis, allergic reactions (&lt;1%), peripheral edema, pyoderma gangrenosum, rash (&lt;1%), urticaria (&lt;1%)</td>
<td>Dysgeusia, mucositis, stomatitis</td>
<td>Alopecia</td>
<td></td>
</tr>
<tr>
<td>Oprelvekin [13]</td>
<td>Peripheral edema (4%), rash (1%)</td>
<td>Tearing (1%)</td>
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<td>Discoloration</td>
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<tr>
<td>Low molecular weight heparin</td>
<td>Allergic reactions (1–10%), angioedema (&lt;1%), baboon syndrome, burning, dermatitis, erythema, erythema nodosum exanthems, fixed eruption, hemorrhage, livedo reticularis, necrosis, peripheral edema, petechiae, pruritus (&lt;1%), purpura (&gt;10%), rash, scleroderma, toxic dermatitis, TEN, ulcerations, urticaria (&lt;1%), vasculitis</td>
<td>Gingivitis (&gt;10%)</td>
<td>Alopecia</td>
<td></td>
</tr>
<tr>
<td>Warfarin</td>
<td>Abscess, acral purpura, angioedema (&lt;1%), bullous dermatitis, dermatitis, exanthems, exfoliative dermatitis, hematomas, hemorrhage, livedo reticularis, necrosis (&gt;10%), pruritus (&lt;1%), purple toe syndrome, purpuric erythema of the feet and toes (&lt;1%), purpura, rash (&lt;1%), ulcerations, urticaria, vasculitis, vesiculation</td>
<td>Oral ulceration (&lt;1%), tongue hemorrhage</td>
<td>Alopecia (&gt;10%)</td>
<td></td>
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</tbody>
</table>

APL, acute promyelocytic leukemia; Ig, immunoglobulin; SJS, Stevens–Johnson syndrome; TEN, toxic epidermal necrolysis.
The vast array of anticancer treatment modalities including surgical interventions, radiotherapy, stem cell transplantation, conventional cytotoxic chemotherapy, and novel targeted agents has drastically changed the lives of oncology patients throughout the last century. Nevertheless, this remarkable progress in therapeutics has not been devoid of significant systemic adverse events (AEs) affecting hematopoietic, gastrointestinal, and dermatologic organ systems. While the advent of systemic antibiotics and blood transfusions has reduced the high morbidity associated with bone marrow suppression and an altered immune system, AE affecting the skin and its adnexae have not attracted the same attention, and there has been a relative paucity of effective management strategies.

The major shift in chemotherapeutics in the last decade has been driven by the development of “targeted” agents. Although this has resulted in improved patient survival and a lower incidence of acute nonspecific AE, a wide spectrum of dermatologic toxicities affecting the majority of patients has been recognized. Their significant burden on patients’ quality of life (QoL), with impact on consistent administration of anticancer therapy, has heightened the importance of dermatologic health in cancer patients. Subsequent multidisciplinary research efforts have made considerable strides toward elucidating underlying mechanisms, better understanding of impact on QoL, and the development of evidence-based management strategies, leading to the emergence of “supportive oncodermatology” – a discipline dedicated to dermatologic health in cancer patients undergoing therapy, as well as cancer survivors (Figure 2.1).

**Evolution of anticancer therapeutics**

Evidence of cancer identified in Peruvian and Egyptian mummies dates back to approximately 2500 BC. The early treatment approach consisted of tumor eradication with a hot iron [1]. The Ebers papyrus, 1500 BC, contains descriptions of arsenic paste used against ulcerated tumors [2], and surgical removal of breast carcinomas was performed by Celsus in 30 BC to 38 AD [3]. Besides physical destruction, oral remedies were also used, with Pliny the Elder (AD 23–79) utilizing several compounds (e.g., amygdaline or vitamin B17) [4]. An array of chemicals including mercury, lead, iron, potassium, and iodine were utilized by Paracelsus (1493–1541) to treat a spectrum of internal diseases including cancer [5].

Only 2 months after the discovery of X-rays in November 1895 by William Conrad Röntgen, Emil Grubbe, at the time a Chicago medical student, was allegedly the first to utilize radiation to treat breast cancer [6]. The first successful application of radiotherapy for a dermatologic indication (a giant hairy nevus) was performed by Leopold Freund in 1896 [7]. The term “chemotherapy” was coined by the Nobel laureate Paul Ehrlich (1854–1915), with the era of modern chemotherapy emerging in the 1940s when nitrogen mustard, a nonspecific DNA alkylating agent, was shown to induce regression in lymphoma patients [8,9].

As the list of chemotherapy agents continued to expand, it was realized that combining different agents yielded better results. In 1965, a combination of methotrexate, vinca alkaloid (vincristine), 6-mercaptopurine, and prednisone (POMP) was demonstrated to achieve long-term remissions in children with acute lymphocytic leukemia [10]. The addition of 5-fluorouracil to the arsenal of chemotherapeutics in 1957 was a significant step forward in the treatment of solid malignancies [11]. Driven by discoveries of intricate mechanisms responsible for tumorigenesis, an abundance of chemotherapy agents were synthesized and approved in the latter part of the twentieth century, including alkylating agents (busulfan), plant alkaloids (paclitaxel), antitumor antibiotics (doxorubicin), antimetabolites (capecitabine), and topoisomerase inhibitors (irinotecan).
Figure 2.1 Timeline of selected key events and clinical trials in supportive oncodermatology. BMJ, British Medical Journal; EGFR, epidermal growth factor receptor; EGFRI, epidermal growth factor receptor inhibitor; FDA, Food and Drug Administration; HFS, hand-foot syndrome; MASCC, Multinational Association of Supportive Care in Cancer; QOL, quality of life; RCT, randomized controlled trial; SCC, squamous cell carcinoma.