# Cutaneous reactions to chemotherapeutic drugs and targeted therapies for cancer

## Part II. Targeted therapies

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1. Reading of the CME Information (delineated below)
2. Reading of the Source Article
3. Achievement of a 70% or higher on the online Case-based Post Test
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After completing this learning activity, participants should be able to identify the mechanism of action of targeted chemotherapeutic drugs, recognize cutaneous reactions caused by targeted chemotherapeutic drugs, and plan the appropriate management of cutaneous reactions.

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Targeted drugs are increasingly being used for cancer management. They are designed to block specific cancer cell processes, and are often better tolerated than conventional chemotherapeutic drugs. Cutaneous reactions, however, are not uncommon, because some target molecules are also present in the skin. Tyrosine kinase inhibitors can cause edema and macular rash, whereas *p*apulopustular rash, paronychia, *r*egulatory changes in hair, *i*tching, and *d*ryness caused by *e*pidermal growth factor receptor inhibitors (PRIDE) syndrome can be seen in patients treated with these drugs. Vismodegib may result in muscle spasms and alopecia. Multiple rashes can be seen with bortezomib, while sunitinib and sorafenib cause hand–foot skin reactions. New melanoma therapies, such as ipilimumab, cause immune-related adverse events of dermatitis and pruritus, while BRAF inhibitors can produce exanthematous rash and lead to an increased risk of squamous cell carcinoma. Dermatologists should be aware of these new therapies and their cutaneous reactions to be able to provide appropriate care and management for cancer patients. (J Am Acad Dermatol 2014;71:217.e1-11.)

***Key words:*** cancer therapy; chemotherapy; cutaneous reactions; drug hypersensitivity; rash; target drugs.

Targeted therapy blocks the growth and spread of cancer by inhibiting specific molecules involved in tumor pathogenesis. Unlike conventional chemotherapeutic drugs, which act at the cellular level to treat tumors, targeted drugs are theoretically more effective and less harmful to normal cells because specific molecular mechanisms are involved (Table I).[1] Cutaneous reactions to these therapies, however, are not uncommon, because some target molecules (ie, endothelial growth factor receptor [EGFR] and vascular EGFR [VEGFR]) are also present in the skin.[2] Knowledge of these target drugs and their characteristic patterns of skin reaction is essential for providing proper treatment and care for cancer patients.

*Abbreviations used:*

| | |
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| EGFR: | epidermal growth factor receptor |
| EGFRI: | epidermal growth factor receptor inhibitor |
| HFSR: | hand–foot skin reaction |
| IRAE: | immune-related adverse event |
| MAPK: | mitogen-activated protein kinase |
| PDGFR: | platelet-derived growth factor receptor |
| PRIDE: | papulopustular rash, paronychia, regulatory hair changes, itching, and dryness caused by epidermal growth factor receptor inhibitors |
| VEGFR: | vascular endothelial growth factor receptor |

## SIGNAL TRANSDUCTION INHIBITORS

### Key points

- **Tyrosine kinase inhibitors for chronic myeloid leukemia may cause edema, hypopigmentation, and a generalized skin rash**
- **Epidermal growth factor receptor inhibitors can cause papulopustular rash, paronychia, regulatory hair changes, itching, and dryness syndrome**
- **Vismodegib, which targets the hedgehog pathway in basal cell carcinoma, may produce muscle spasms, alopecia, and dysgeusia**

### Imatinib, dasatinib, and nilotinib

Imatinib was the first molecule drug developed to inhibit the tyrosine kinases *bcr-abl* in chronic myeloid leukemia, *c-kit* in rare gastrointestinal stromal tumors, and several platelet-derived growth factor receptors (PDGFRs) in other malignancies.[3,4] Dasatinib and nilotinib are second-generation tyrosine kinase inhibitors that were developed to treat resistant chronic myeloid leukemia cases with acquired *bcr-abl* mutations.[4] All are taken orally once or twice daily. Between 7% and 88.9% of patients taking imatinib experience cutaneous reactions[4,5]; 35% of patients taking dasatinib and 10% to 28% of patients taking nilotinib also have cutaneous reactions.[4]

**Edema.** Superficial edema is distinct to imatinib, and primarily presents as periorbital edema causing epiphora, conjunctivochalasis, and chemosis.[3,4] Edema may also occur in the extremities and occasionally as central fluid retention.[4,5] Dasatinib causes pleural effusions in 30% of patients, while nilotinib rarely induces peripheral edema or pleural effusion.[6,7] It has been postulated that the inhibition

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