How to manage skin toxicity related to EGFR-inhibitors?

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EGFR-targeted therapies (monoclonal antibodies such as cetuximab and panitumumab and tyrosine kinase inhibitors like erlotinib and gefitinib) are responsible for a unique spectrum of mechanism-based, class-specific side effects associated with the skin. Besides the well-known acneiform eruption, skin toxicity consists of xerosis (leading to eczema and fissures), paronychia, hair changes, telangiectasia, hyperpigmentation and mucosal changes.

Dermatologic treatment is supportive and aims at maintaining quality of life while continuing EGFR inhibitor therapy. Treatment recommendations are mainly based on personal experience, as randomized controlled trials are very sparse.

Sun protection and measures to maintain skin hydration (use of bath/shower oil, lukewarm water, emollients) are advised for all patients. Most cases of acneiform eruption are well controlled by topical metronidazole and oral minocycline at a dose of 100 mg qd. For severe reactions, the minocycline dose is doubled and saline compresses are very valuable. For superinfection with *Staphylococcus aureus*, oral cefuroxim axetil can be added for a short term. It is still a matter of debate whether oral tetracyclines should be given in a prophylactic or reactive way. Two studies demonstrated that prophylactic use of oral minocycline or other tetracyclines decreased the severity of EGFR-inhibitor-induced acneiform eruption. Very recently the STEPP-study (Skin Toxicity Evaluation Protocol with Panitumumab) compared prophylactic versus reactive treatment with a combination of sunscreen, emollients, a weak topical steroid and doxycycline 100 mg bid. In the prophylactic skin treatment group, grade 2 or higher skin toxicities were not only significantly reduced but the time to their first appearance was significantly delayed as well. Do these findings advocate immediate introduction of prophylactic treatment of EGFR-inhibitor-related skin toxicity? Probably, some caution is justified until further research can corroborate these data and assess the contribution of each constituent of the skin treatment protocol used.

Emollients and topical steroids can be administered for skin dryness or eczema. Paronychia is the most difficult side effect to treat, but antiseptic soaks and a corticosteroid paste can alleviate symptoms to some degree.
In conclusion, the vast majority of patients experiencing EGFR-inhibitor-induced skin toxicity are easily managed without dose adjustment or interruption of the EGFR-inhibitor, despite the absence of solid evidence-based guidelines.
Key references


First detailed dermatological description of the skin effects of an EGFR-inhibitor (cetuximab).


Evidence that prophylactic tetracycline decreases the severity of EGFR-inhibitor-induced acneiform eruption.


Review exploring the pathophysiology behind EGFR-inhibitor-induced skin toxicities.


Recommendations on treatment of EGFR-inhibitor skin toxicity by an American expert panel.


Study showing superiority of a prophylactic over reactive skin treatment protocol (doxycycline + weak topical steroids + sunscreen + emollients) to decrease skin toxicity in panitumumab-treated patients.


Comprehensive review on skin toxicity of EGFR inhibitors.
Recommendations on treatment of EGFR-inhibitor skin toxicity by a European expert panel.

Practical recommendations on the treatment of EGFR-inhibitor-related skin toxicity.

Well-conducted study demonstrating the effectiveness of prophylactic minocycline in preventing acneiform eruption during cetuximab treatment.