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ORIGINAL ARTICLE

Taiwanese Dermatological Association consensus for the prevention and management of epidermal growth factor receptor tyrosine kinase inhibitor-related skin toxicities

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consensus;
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Abstract *Background/Purpose:* This report describes the 2016 consensus of the Taiwanese Dermatological Association (TDA) regarding the definition, classification, diagnosis, prevention, and management of skin toxicities resulting from treatment with epidermal growth factor receptor (EGFR) tyrosine kinase inhibitors (TKIs). This consensus is distributed to practices throughout Taiwan to provide recommendations for the diagnosis and treatment of such skin

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skin toxicities;
tyrosine kinase inhibitors

toxicities in order to improve the quality of life of patients undergoing EGFR-TKI treatment. The consensus thus serves as an important reference for dermatologists and other interested clinicians, such as oncologists, throughout Taiwan.
Methods: All the consensus contents were voted on by the participating experts, with approval by no less than 75% required for inclusion.
Results: The consensus provides a comprehensive overview of EGFR-TKI skin toxicities, including recent advances in identifying their causes and the processes by which they develop.
Conclusion: All the consensus meeting attendees agreed that there are several major EGFR-TKI-related skin toxicities, including acneiform rash (i.e., papulopustular rash), xeroderma, pruritus, paronychia, stomatitis, mucositis, and hair changes (such as hair loss, slowed hair growth, and trichomegaly). The experts were also generally unanimous in their voting on the specific definitions, onset times, and care suggestions for each of those skin toxicities. Furthermore, the recommended treatment algorithms for the various skin toxicities were ultimately approved by 100% (15/15) of the consensus attendees.
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Introduction

This report provides a detailed description of the development process for the 2016 consensus of the Taiwanese Dermatological Association (TDA) regarding the prevention and management of skin toxicities resulting from treatment with epidermal growth factor receptor (EGFR) tyrosine kinase inhibitors (TKIs) such as afatinib, erlotinib, and gefitinib. Because of the advantages of these EGFR-TKIs over platinum-based chemotherapy in untreated advanced nonsmall cell lung cancer (NSCLC) patients with an activating *EGFR* mutation, including delayed disease progression, higher response rates, lower toxicity, increased tolerability, and improved quality of life, they are currently the standard first-line treatment for such patients.[1–10] However, these drugs may also cause a range of adverse events (AEs), the most common of which consist of cutaneous reactions, such as pruritus, paronychia, xeroderma, and gastrointestinal problems, such as stomatitis/mucositis and diarrhea. Such reactions are usually mild, but they can have strongly deleterious effects on quality of life if they become too severe, resulting in dose modifications or even drug discontinuation, and in consequences that can be highly problematic in light of the fact that effective treatment with EGFR-TKIs is likely to require a minimum of 10 months of continuous administration. As such, the effective management of such gastrointestinal-related and cutaneous AEs, including treatment delays, dose reductions, supportive medications, and prophylactic measures,[11] is of critical importance to the outcomes for NSCLC patients. More specifically, the purpose of such management strategies is to prevent any interruption or termination of the full course of EGFR-TKI treatment due to an intolerable loss in patient quality of life, as the clinical effectiveness of the drugs may be limited or lost due to any such discontinuation.[12,13]

The TDA consensus presented herein focuses primarily on the skin toxicities that may occur as a result of EGFR-TKI treatment. Because EGFR itself plays a key role in numerous physiological processes and biological homeostasis of the skin, including differentiation, wound healing, and epidermal growth, the inhibition of its activity caused by the use of EGFR-TKIs commonly, although not always, results in various skin toxicities, ranging from xeroderma and pruritus to acneiform rash and paronychia.[13,14] The TDA consensus regarding these skin toxicities was based in large part upon several previous reports (please see below for further details). The TDA consensus is distinguished from those earlier reports primarily by its inclusion of a number of amendments made specifically for the sake of clinicians treating EGFR-TKI-related skin toxicities in Taiwan, and the consensus thus serves as an important reference for dermatologists, oncologists, pulmonologists, chest surgeon, and nurses throughout Taiwan.

Methods

Consensus panel

The information in the consensus was agreed upon by a panel of national experts who convened at TDA consensus meetings held on June 18, 2016, with all of the specific aspects of the content requiring approval by at least 75% of the experts in attendance. A total of 15 field experts with extensive experience in the management of EGFR-TKI-related skin toxicities recommended by their respective teaching hospitals in Taiwan and the TDA itself were invited to and attended the TDA consensus meetings held in Taipei, Taiwan. The TDA consensus regarding these skin toxicities was based in a large part upon several previous reports, namely, the "Expert Consensus on the Management of Adverse Events from EGFR Tyrosine Kinase Inhibitors in the UK" by Califano et al., "Dermatologic adverse events associated with afatinib: an oral ErbB family blocker" by Lacouture et al., and "Erlotinib-related skin toxicities: treatment strategies in patients with metastatic non-small cell lung cancer" by Kiyohara et al.[15–17] The aforementioned studies provided the foundations for the consensus that the panel approved in the meeting, although a variety of amendments made specifically for practitioners in Taiwan were also considered. For each of these

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