

# Afatinib Therapy

## Practical management of adverse events with an oral agent for non-small cell lung cancer treatment

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**BACKGROUND:** Afatinib is an oral, irreversible ErbB family blocker indicated for first-line treatment of metastatic non-small cell lung cancer (NSCLC) in patients with non-resistant epidermal growth factor receptor (EGFR) mutations. Afatinib is also approved for the treatment of metastatic squamous NSCLC following progression on platinum-based chemotherapy. Common afatinib-associated toxicities include gastrointestinal and dermatologic events, which can be dose limiting.

**OBJECTIVES:** In this review, the authors describe clinical trial experiences with afatinib, as well as best practices and practical approaches to the management of afatinib-associated adverse events in EGFR mutation-positive NSCLC.

**METHODS:** Safety and tolerability data from phase 3 trials of afatinib were reviewed, together with real-life experiences from the authors' clinical practices.

**FINDINGS:** Patient education, combined with early assessment and effective management of afatinib-related adverse events as well as dose-reduction strategies, allows patients to continue treatment and maximize the clinical benefits of afatinib.

### KEYWORDS

afatinib; non-small cell lung cancer; adverse events; dose reduction

### DIGITAL OBJECT IDENTIFIER

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**ONCOLOGY TREATMENTS ARE DESIGNED TO PROVIDE SAFETY** while achieving maximum efficacy. In the era of targeted therapies, patients often continue treatment for extended durations. Chronic treatment may cause different toxicities than those reported in clinical trials and, because tolerability varies among patients, dose optimization schemas can help to balance long-term clinical benefit with safety (Dy & Adjei, 2013). Oncology nurses and other advanced oncology practitioners are instrumental in achieving optimal clinical outcomes through patient education, early assessment, and management of potential adverse events (AEs); strategies include supportive care and dose interruption or modifications.

Non-small cell lung cancer (NSCLC) remains the leading cause of cancer mortality worldwide (World Health Organization, 2018). The mutated form of the epidermal growth factor receptor (EGFR) is the best characterized oncogenic driver in NSCLC. Activating mutations have been reported in 10%–50% of cases; most commonly exon 19 deletions (del19) (60%) and exon 21 (L858R) substitutions (35%), where leucine is replaced by arginine at position 858 (Chan & Hughes, 2015). Targeted therapies to inhibit mutant EGFR include tyrosine kinase inhibitors (TKIs) such as gefitinib, erlotinib, osimertinib, and afatinib. Afatinib (Gilotrif®) is an oral, irreversible inhibitor of EGFR and all other members of the ErbB family of tyrosine kinases (HER2 [ErbB2], HER3 [ErbB3], and HER4 [ErbB4]). Afatinib is indicated for the first-line treatment of metastatic NSCLC in patients whose disease harbors non-resistant EGFR mutations, including additional mutations other than del19 and L858R, as identified by a U.S. Food and Drug Administration-approved test (Boehringer Ingelheim, 2018). Afatinib is also approved in Europe for EGFR TKI-naïve adult patients with locally advanced/metastatic NSCLC with activating EGFR mutation(s), including less common mutations in exon 18 (G719X) and exon 21 (L861Q) (Boehringer Ingelheim, 2017). Phase 3 afatinib trials showed improved efficacy versus traditional gold-standard chemotherapy, and a manageable safety profile in patients with advanced EGFR mutation-positive NSCLC (Sequist et al., 2013; Wu, Zhou, et al., 2014). A similar safety profile was observed with afatinib in patients with squamous cell carcinoma (SCC) of the lung (Soria et al., 2015). The safety profile of afatinib is similar to that of first-generation EGFR-targeted therapies and primarily includes gastrointestinal and dermatologic AEs (Park et al., 2016; Sequist et al., 2013; Soria et al., 2015; Wu, Zhou, et al., 2014). These AEs can be bothersome to the patient; education,