Nature Reviews Clinical Oncology | Published online 5 Dec 2017; doi:10.1038/nrclinonc.2017.192

LUNG CANCER

Osimertinib strengthens the frontline

The first-generation and second-generation EGFR inhibitors erlotinib, gefitinib, and afatinib are effective in stalling the progression of *EGFR*-mutant non-small-cell lung cancer (NSCLC); however, drug resistance and disease progression are inevitable. Osimertinib, a third-generation inhibitor, can subsequently delay disease progression in patients with the predominant $EGFR^{T790M}$ resistance mutation. An obvious question, now addressed in the ongoing phase III FLAURA trial, is whether first-line osimertinib would result in better disease control and improve patient outcomes.

In FLAURA, 556 patients with untreated, advanced-stage *EGFR*-mutant NSCLC received either osimertinib or standard-of-care (SoC) treatment with erlotinib or gefitinib; response rates were similarly high in both arms (80% versus 76%), but the median progression-free survival duration was 18.9 months versus 10.2 months. "Osimertinib therapy resulted in a 54% reduction in the risk of disease progression or death compared with the present SoC, and also exerted better activity against brain metastases," adds corresponding author Suresh Ramalingam. The range of toxicities was similar in both treatment arms, but the frequency of grade ≥3 events was lower with osimertinib (34% versus 45%).

"In light of the FLAURA data, sequencing of a first- or second-generation agent followed by osimertinib, as second-line therapy, is not likely to be a viable strategy to maximize patient outcomes," Ramalingam opines. "Our results will lead to a new treatment paradigm for *EGFR*-mutated NSCLC: osimertinib will now be the preferred frontline treatment," he concludes. Importantly, crossover of patients from the SoC arm to receive osimertinib upon $EGFR^{T790M}$-mediated resistance is allowed in FLAURA; thus, the overall survival data will provide insights into the relative benefits of upfront versus sequenced treatment with osimertinib. Promisingly, in an interim analysis (at 25% maturity), 18-month overall survival was 83% with osimertinib versus 71% with SoC treatment. Mature survival data are eagerly awaited.

David Killock

ORIGINAL ARTICLE Soria, J.-C. *et al.* Osimertinib in untreated *EGFR*-mutated advanced non-small-cell lung cancer. *N. Engl. J. Med.* http://dx.doi.org/10.1056/NEJMoa1713137 (2017)