CNS Activity of First-Line Osimertinib in *EGFR*-Mutant Advanced NSCLC

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Key Points

- CNS progression–free survival was improved with osimertinib vs standard tyrosine kinase inhibitor treatment.
- Response rates were 66% vs 43% among patients with measurable or nonmeasurable CNS lesions.

In a subgroup analysis of the phase III FLAURA trial reported in the *Journal of Clinical Oncology*, Reungwetwattana et al found evidence of greater central nervous system (CNS) activity of osimertinib (Tagrisso) vs standard EGFR tyrosine kinase inhibitors in patients with previously untreated advanced *EGFR*-mutant non–small cell lung cancer (NSCLC). The FLAURA trial supported the recent approval of osimertinib in this setting.

Study Details

In the trial, 556 patients with *EGFR* mutation (exon 19 deletion or L858R) were randomly assigned to receive osimertinib or a standard EGFR tyrosine kinase inhibitor (gefitinib [Iressa] or erlotinib [Tarceva]) as first-line therapy. Osimertinib was associated with significantly prolonged progression-free survival. Brain scans were not mandated unless clinically indicated.

The current analysis includes 61 osimertinib recipients and 67 standard tyrosine kinase inhibitor recipients, with measureable or nonmeasurable CNS lesions among 200 patients with baseline brain scans, including 22 and 19 with ≥ 1 measureable lesion.

The primary outcome measure was CNS progression–free survival assessed by blinded independent central neuroradiologic review.

CNS Activity

Median CNS progression–free survival among patients with measurable or nonmeasurable CNS lesions was not reached in the osimertinib group (95% confidence interval [CI] = 16.5 months–not calculable) vs 13.9 months (95% CI = 8.3 months–not calculable) in the standard EGFR tyrosine kinase inhibitor group (hazard ratio = 0.48, *P* = .014; nominally significant due to hierarchical testing in the full trial). CNS progression–free survival was 87% vs 71% at 6 months, 77% vs 56% at 12 months, and 58% vs 40% at 18 months. CNS objective response rates were 91% vs 68% in patients with ≥ 1 measurable CNS lesion (odds ratio [OR] = 4.6, *P* = .066) and 66% vs 43% among patients with measurable or nonmeasurable CNS lesions (OR = 2.5, *P* = .011).

The investigators concluded, "Osimertinib has CNS efficacy in patients with untreated *EGFR*-mutated non–small cell lung cancer. These results suggest a reduced risk of CNS progression with osimertinib vs standard EGFR tyrosine kinase inhibitors."

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