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NorthStar: A phase II randomized study of osimertinib (OSI) with or without local consolidative therapy (LCT) for metastatic EGFR-mutant non-small cell lung cancer (NSCLC)

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Background

Osimertinib is the standard of care for EGFR-mutant metastatic NSCLC. The NorthStar trial assessed whether the addition of LCT improves progression-free survival (PFS) in patients treated with osimertinib.

Methods

Eligible patients had EGFR-mutant metastatic NSCLC and were either TKI-naïve or had acquired T790M without prior exposure to third-generation EGFR TKIs. All patients received osimertinib 80 mg daily for 6–12 weeks, after which those without disease progression were randomized 1:1 to continue osimertinib alone or receive LCT in addition to osimertinib. Stratification factors included line of therapy, number of metastases (≤3 vs >3), response to induction (PR vs SD), and CNS involvement. The primary endpoint was PFS.

Results

A total of 119 patients were randomized (63 to osimertinib alone, 56 to osimertinib+LCT). Most patients in both arms had polymetastatic disease (>3 lesions: 37 patients [59%] osimertinib alone, and 32 patients [57%] osimertinib+LCT). LCT modalities included radiation alone in 59%, surgery in 29%, and combined modalities in 12%. Adverse events of any grade occurred in over 96% of patients in each arm, with grade ≥3 events occurring in approximately 16% of osimertinib-alone patients and 29% in the osimertinib+LCT arm. The most common toxicities were skin disorders (65.1% vs 64.4%), anorexia (19.0% vs 16.9%), and dyspnea (17.5% vs 30.5%). No unexpected adverse events were observed, confirming that the addition of LCT to osimertinib is feasible and safe.

Median PFS was significantly prolonged in the osimertinib+LCT arm at 25.4 months compared to 17.0 months with osimertinib alone, corresponding to a 40% reduction in the risk of progression (HR 0.60, 95% CI 0.40–0.92; p=0.02).

Conclusions

The addition of local consolidative therapy to osimertinib significantly extends progression-free survival in patients with EGFR-mutant metastatic NSCLC, even in the setting of polymetastatic disease. These results support the integration of LCT into the treatment paradigm for appropriately selected patients receiving EGFR-targeted therapy and may inform future standards of care.

Clinical trial identification

NCT04479306.

Legal entity responsible for the study

The authors.

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Disclosure

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