Randomized phase II trial of osimertinib with or without local consolidation therapy (LCT) for patients with EGFR-mutant metastatic NSCLC (NORTHSTAR)


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**Background:** Osimertinib has been shown to be superior to erlotinib or gefitinib in previously untreated patients with EGFR mutant (exon 19 deletion/L858R) NSCLC. Osimertinib is approved for the treatment of patients with metastatic T790M+ NSCLC who have disease progression after EGFR-TKI therapy. The majority of EGFR mutant NSCLC patients who are treated with a TKI ultimately acquire resistance, including those treated with osimertinib. We have recently completed a phase 2 randomized clinical trial demonstrating that patients with oligometastatic NSCLC treated with aggressive local consolidation therapy (surgery or radiation) have improved progression-free survival compared to those patients treated with systemic therapy alone (Gomez et al., Lancet Oncol, 2016). A retrospective review of EGFR-mutant subset of patients enrolled in the trial suggests that EGFR-mutant patients may derive greater benefit from this approach. Thus, two premises underlie the current randomized trial: 1) osimertinib is standard of care for treatment of primary and TKI resistant EGFR-mutant metastatic NSCLC, and 2) the majority of patients treated with osimertinib ultimately become resistant, and LCT has been found to improve outcomes compared to systemic therapy alone.

**Trial design:** A phase 2 randomized, multicenter, study to evaluate the efficacy of osimertinib with or without LCT for patients with EGFR-mutant metastatic NSCLC. Eligible patients include 1) Previously untreated patients with EGFR-mutant NSCLC (L858R or exon 19 deletion) or 2) NSCLC patients with acquired EGFR T790M that was acquired following progression on first or second generation TKI, this subset of patients must have not received prior third generation TKI. Patients who don’t have disease progression after 6-12 weeks of induction osimertinib will be randomized 1:1 to osimertinib continuation or to osimertinib continuation with LCT Primary end point is progression free survival Exploratory biomarkers associated with resistance to osimertinib will be evaluated in tumor tissue and plasma collected at baseline and progression. 140 patients will be enrolled in 5 centers in North America.

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