Can Quantitative Measures of T790M Allelic Fraction Predict Survival Outcomes in Patients Receiving Osimertinib? Observations From an Early Access Programme

Aims: Multiple studies have shown conflicting results on the correlation between the EGFR T790M quantitative level and survival outcomes in osimertinib-treated patients. We sought to validate such correlations using data from an osimertinib early access programme (EAP) providing access for metastatic non-small cell lung cancer patients with limited treatment options.

Patients and methods: This observational, multicentre, retrospective analysis included EAP participants who received osimertinib until disease progression, intolerable toxicities or death. Digital droplet polymerase chain reaction-based quantitative plasma genotyping was carried out upon disease progression and data were analysed to explore the relationships between T790M mutant allele fraction (MAF), T790M copy number, MAF ratio and post-osimertinib overall survival. Real-world treatment outcomes and safety were also evaluated.

Results: Data from 156 EAP participants were analysed (median follow-up 37.7 months). The median age was 62 years, 62.2% were women, 79.5% were never-smokers, 60.9% had Eastern Cooperative Oncology Group performance status 0/1. In patients with available plasma data (n = 114), T790M MAF (%) showed no significant relationships with overall survival (hazard ratio 1.02; 95% confidence interval 0.99-1.04) or time to treatment discontinuation (TTD) (hazard ratio 1.01; 95% confidence interval 0.98-1.04). Absolute T790M copy number and T790M to activating EGFR mutation MAF ratio also showed no prognostic value. The investigator-assessed response rate was 42.3% and the disease control rate was 85.5%. The median TTD was 15.8 (95% confidence interval 12.5-18.5) months and the median overall survival was 22.3 (95% confidence interval 18.6-26.1) months.

Conclusion: T790M MAF did not correlate with TTD or overall survival in this EAP cohort but limitations should not be overlooked. Observed survival outcomes and the toxicity profile were consistent with data from other real-world series.