Adjuvant osimertinib therapy in patients with resected EGFR-mutated (EGFRm) stage IB–IIIA non-small cell lung cancer (NSCLC): updated ADAURA results

Background: Osimertinib is a third-generation epidermal growth factor receptor- tyrosine kinase inhibitor (EGFR-TKI) that potently and selectively inhibits EGFR-TKI sensitising and EGFR T790M resistance mutations. It has efficacy in EGFR-mutated (EGFRm) non-small cell lung cancer (NSCLC), including in central nervous system (CNS) metastases. In the Phase III ADAURA (NCT02511106) primary analysis adjuvant osimertinib showed a significant and clinically meaningful disease-free survival (DFS) benefit vs placebo (PBO) in patients with completely resected EGFRm (ex19del/L858R) NSCLC, ± adjuvant chemotherapy: stage II?IIIA DFS hazard ratio (HR), 0.17; 99.06% confidence interval (CI), 0.11, 0.26; p<0.0001; stage IB?IIIA DFS HR, 0.20; 99.12% CI 0.14, 0.30; p<0.0001. We report updated exploratory analyses of DFS and recurrence patterns after 2 years added follow up.

Methods: Eligible patients (aged ?18 years [?20 in Japan/Taiwan], World Health Organisation performance status 0/1, completely resected EGFRm stage IB?IIIA [American Joint Committee on Cancer 7th edition] NSCLC; adjuvant chemotherapy allowed) were randomized 1:1 to osimertinib 80 mg once daily or PBO for up to 3 years. Primary endpoint: investigator-assessed DFS in stage II?IIIA. Secondary endpoints: DFS in stage IB?IIIA, overall survival and safety. Patterns of recurrence and CNS DFS were pre-specified exploratory endpoints. Data cut-off: 11 April 2022.

Results: Globally, 682 patients were randomized; osimertinib n=339, PBO n=343. In this updated analysis, in patients with stage II?IIIA disease DFS HR was 0.23 (95% CI 0.18, 0.30; 242/470 events; 51% maturity); 3 year DFS rate was 84% with osimertinib vs 34% with PBO. In the overall population (stage IB?IIIA) DFS HR was 0.27 (95% CI 0.21, 0.34; 305/682 events); 3 year DFS rate was 85% with osimertinib vs 44% with PBO. In the osimertinib arm, fewer patients experienced local/regional and distant recurrence vs PBO. CNS DFS HR was 0.24 (95% CI 0.14, 0.42; 63/470 events) in stage II?IIIA. The long-term safety profile remains consistent with the known profile of osimertinib.

Conclusions: With 2 years further follow-up, a continued DFS benefit was sustained with osimertinib vs PBO, consistent with the primary analysis. These mature data reinforce adjuvant osimertinib as standard of care for patients with EGFRm stage IB–IIIA NSCLC after complete tumour resection and adjuvant chemotherapy, when indicated. (ENCORE)

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