NSCLC, metastatic

A PHASE II TRIAL OF GEFTINIB IN COMBINATION WITH BEVACIZUMAB AS FIRST-LINE THERAPY FOR ADVANCED NON-SMALL-CELL LUNG CANCER WITH ACTIVATING EGFR GENE MUTATIONS: OLCSG 1001


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Aim: Epidermal growth factor receptor (EGFR) tyrosine kinase inhibitors (TKIs) such as gefitinib, erlotinib or afatinib are essential drugs for the treatment of advanced non-small cell lung cancer (NSCLC) with activating EGFR gene mutations. However, disease progression inevitably occurs around 10-12 months after EGFR-TKI treatment. Bevacizumab (Bmab) enhances the effect of cytotoxic chemotherapy with advanced NSCLC while it remains unknown whether Bmab enhances the effect of EGFR-TKIs on EGFR mutant NSCLC. We conducted a phase II trial to investigate the efficacy and safety of gefitinib when combined with Bmab as a first-line therapy in patients with advanced NSCLC harboring EGFR gene mutations.

Methods: In this trial, 42 patients with PS 0 to 2 received daily gefitinib (250mg/body) and Bmab (15mg/kg, every 3 weeks). The primary endpoint was 1-year progression-free survival (PFS) rate, and the secondary endpoints included response rate, PFS time, overall survival (OS) time and toxicity.

Results: The patients had a median age of 73 (range, 42-86), of whom 40% were male, 75% with PS 0-1, 79% in stage IV, and 21% with postoperative recurrence. As for the activating EGFR gene mutations, 57% of the patients had exon 19 deletion (del), 38% exon 21 point mutations (L858R), 2.5% exon 18 G719A, and 2.5% exon 21 G861Q. At the time of this analysis, 34 pts (81%) had dropped out of the protocol treatment, wherein 10 out of 42 pts (24%) discontinued it because of adverse events (AEs). The 1-year PFS rate was 56.7% (95% confidence interval: 39.9-70.5%), which did not meet the primary endpoint. The median PFS time (month) was 14.4 with a significant difference between those of exon 19 del (18.0) and L858R (9.4, p = 0.006). The objective response rate and disease control rate were 73.8% and 97.6%, respectively. The median OS was not yet reached. The severe AEs included grade 3 liver dysfunction (19%), hypertension (17%), acneiform (14%), proteinuria (7%), intracranial hemorrhage (3%), and grade 4 perforation of the digestive tract (3%), but no treatment-related death.

Conclusions: Gefitinib in combination with Bmab as a first line therapy seems a favorable and well-tolerated treatment for patients with advanced NSCLC with activating EGFR gene mutations, especially for those with exon 19 del mutations.

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