NSCLC, metastatic

1241P Afatinib efficacy and cerebrospinal fluid concentration in NSCLC patients with EGFR mutation developing leptomeningeal carcinomatosis


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Background: Afatinib (AFA) is an effective treatment in advanced non-small-cell lung cancer (NSCLC) patients harboring epidermal growth factor receptor (EGFR) mutation. However, there are few reports about the cerebrospinal fluid (CSF) penetration rate and the efficacy for treatment of central nervous system (CNS) metastasis. Therefore, we conducted a study to evaluate the CSF penetration rate and efficacy of AFA in NSCLC patients harboring EGFR mutation with leptomeningeal carcinomatosis (LC).

Methods: Eligibility criteria included performance status (PS) 0-3, aged 20 years or older, pathologically proven NSCLC, harboring EGFR mutation, with LC, adequate organ function, and written informed consent. Patients received AFA (40mg/body every day). We analyzed the blood and CSF level of AFA before administering AFA on the eighth day. The primary endpoint was the CSF penetration rate. Secondary endpoints included objective response rate (ORR), progression-free survival (PFS), overall survival (OS), and safety profile.

Results: A total of 11 patients were enrolled. And we could analyze the blood level in 10 patients and the CSF level in 8 patients. Median patient age was 66 years. All patients were adenocarcinoma. In EGFR mutation status, 5 patients had exon 19 deletion, 3 had L858R and 3 had minor (exon18) mutation. There were 3 patients of PS2 and 4 patients were PS3. Almost all patients received AFA after third-line or further line chemotherapy. The median blood level was the 88.2 (range: 30.4-373) ng/ml, the median CSF level was 1.4 (range: 0.39-2.85) ng/ml and the median CSF penetration rate was 1.65 (range: 0.1-9.25) %. The ORR was 27.3%. Median OS was 3.8 (95%CI: 1.1-13.1) months and median PFS was 2.0 (95%CI: 0.6-5.8) months. Hematological toxicity was mild; however diarrhea and skin toxicities were relatively strong, especially in patients with poor PS.

Conclusions: The median CSF penetration rate of AFA was higher than the rate in previous reports; however the rate was lower compared with that of erlotinib in the prior reports. The efficacy for LC was moderate. And we have to take care of diarrhea and skin toxicities, especially in the patients with poor PS.

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