Afatinib shows clinical benefit for lung cancer patients with brain metastases

25 January 2016

Non-small cell lung cancer (NSCLC) patients with common epidermal growth factor (EGFR) mutations and brain metastases showed improved progression-free survival (PFS) and response from the EGFR tyrosine kinase inhibitor (TKI) afatinib compared to standard platinum doublet chemotherapy.

More than 25% of patients with advanced NSCLC experience progression to the brain from their primary lung cancer and this number increases to 44-63% for those NSCLC tumors driven by EGFR mutations. Prognosis is poor and typically ranges for 1-5 months for those with brain metastases. EGFR TKIs are highly effective therapies for advanced NSCLC driven by EGFR mutations, especially the common mutations, exon 19 deletions and L858R point mutations. Even though there are a number of EGFR TKIs approved for first-line therapy of EGFR mutation positive NSCLC, there is a scarcity of prospective data for EGFR TKIs in patients with brain metastases.

An international group of investigators evaluated afatinib vs. standard platinum doublet therapy for previously untreated stage IIIB/IV adenocarcinoma patients with confirmed EGFR mutations in two randomized, open-label, phase III clinical trials. LUX-Lung 3 was conducted globally with cisplatin/pemetrexed as the chemotherapy comparator and LUX-Lung 6 was performed in China, South Korea, and Thailand with cisplatin and gemcitabine. Patients with clinically asymptomatic and controlled brain metastases were eligible for inclusion in either study. The primary endpoint was PFS and the key secondary endpoints were overall survival (OS), objective response rate (ORR), and patient-reported outcomes.

The overall results from both clinical trials have been published previously and showed that afatinib demonstrated significantly improved PFS, ORR, and patient-reported outcomes compared with platinum-based chemotherapy. Also, afatinib demonstrated, for the first time with an EGFR TKI, improved OS in patients harboring EGFR Del19 mutations, the most common EGFR aberration in NSCLC patients.

In the current analyses published in the *Journal of Thoracic Oncology*, the official journal of the International Association for the Study of Lung Cancer (IASLC), a total of 35 out of 345 (10.1%) randomized patients in LUX-Lung 3 and 46 out of 364 (12.6%) in LUX-Lung 6 had brain metastases present at baseline and the common (Del19 and L858R) EGFR mutations. Pooling the results from both trials together, afatinib, compared to chemotherapy, significantly improved PFS in patients with brain metastases (8.2 vs. 5.4 months; HR, 0.50; p=0.0297) and ORR was remarkably higher with afatinib (73% vs. 25%). The adverse events profile for afatinib in patients with brain metastases was similar to those without brain metastases, with no unexpected safety findings.

The authors commented that, "Given the apparent efficacy of afatinib, it is interesting to speculate how TKIs could potentially become incorporated into current standard treatment regimens for patients with brain metastases. It is possible, for example, that treatment with a first-line TKI in patients with asymptomatic brain metastases could delay the requirement for whole brain radio therapy (WBRT), thereby delaying or preventing exposure to the side effects of cranial irradiation."

More information: *Journal of Thoracic Oncology*, www.jto.org/article/S1556-0864(15)00220-8/abstract

Provided by International Association for the Study of Lung Cancer