Gefitinib efficacy in EGFR mutated Non Small Cell Lung Cancer (NSCLC) patients based on type of mutation: a study from the Galician Lung Cancer Group.

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Background

Screening for Epidermal Growth Factor Receptor (EGFR) mutation is a key molecular test for management of lung cancer. Patients who respond well to an EGFR inhibitor harbor certain mutations in the EGFR exons 18, 19 or 21. An additional mutation in EGFR exon 20 is known to be responsible for acquired resistance to this therapy.

Methods

We conducted an analysis of Galician advanced lung cancer patients who were tested positive for EGFR kinase domain mutations determination and were treated with gefitinib. Frequency and type of EGFR mutations and the clinical response in our area were explored. The aim is to analyse the pattern of response, toxicity, progression free survival and overall survival based on the type of EGFR mutation.

Results

Forty-six patients with EGFR mutations were collected, 36 women and 10 men. The median age was 67 years (43-86). Majority of the patients in the study had PS 0-1 (93%) and adenocarcinoma (96%) in the pathological study. The most frequent sites of metastasis were lymph nodes (59%), bones (33%), lung (33%) and pleura (33%). The median duration of treatment was 6 months. Progression disease was the most frequent reason of discontinuation of gefitinib; in 9 patients was discontinued because of toxicity. Ten patients were switched to cytotoxic chemotherapy and 10 patients continued with erlotinib.

Twenty patients were detected to be positive for mutation in exon 19, 4 patients in exon 20 and 20 patients in exon 21. The L858R point mutation in exon 21 was observed in 14 patients and the L833F point mutation in the same exon was observed in 1 patient.

Thirty-five patients were included in the response analysis. The response ratio to gefitinib was 57%. Depending on the type of mutation, the response in exon 19 mutation patients was 64%, in exon 20 patients was 0% and in exon 21 patients was 60%.

Rash or acne was the most frequent toxicity (48%), only 2% was grade 3-4. Diarrhea and dysnea were the main toxicities grade 3-4 (9% both), without statistical differences based on type of mutation (p=0.78).

Progression free survival (PFS) of patients with EGFR mutations was 6 months. Patients with mutation in exon 19 had 9 months compared to 6.4 months for patients with exon 21 mutation, presenting a statistically significance difference (p=0.002).

Overall survival (OS) was 17 months for EGFR mutations patients (19 months for exon 19 mutation patients and 14 months for exon 21 mutation patients; p=0.119).

Conclusion

Pacients in our area with exon 19 EGFR kinase domain mutations treated with gefitinib have higher PFS compare to exon 21 EGFR kinase domain mutations. Exon 20 mutation in our patients is responsible for resistance to gefitinib.