NSCLC: Molecular Targeted Therapy

P3-060
Survival benefit of EGFR gene mutations and gene amplification in advanced NSCLC patients treated with erlotinib by the Korean Cancer Study Group (KCSG)

Ahn, Myung-Ju 1 Ahn, Jin Seok 1 Cho, Jae Yong 2 Ki, Chang-Seok 1 Kim, Heung-Tae 1 Kim, Sang We 5 Lee, Jong Seok 2 Park, Keunchil 1 Park, Se Hoon 1 Shin, Sang Won 4
1 Samsung Medical Center, Seoul, Korea 1 Yonsei University College of Medicine, Yongdong Severance Hospital, Seoul, Korea 1 Department of Laboratory Medicine & Genetics, Samsung Medical Center, Seoul, Korea 4 Research Institute and Hospital, National Cancer Center, Goyang, Seoul, Korea 5 Division of Oncology, Department of Internal Medicine, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea 6 Seoul National University Bundang, Seoul, Korea 7 Gachun Medical School Gil Medical Center, Seoul, Korea 8 Korea University Medical Center, Anam Hospital, Seoul, Korea

Purpose: Mutations in epidermal growth factor receptor (EGFR) are considered as a strong predictive marker for the response to EGFR tyrosine-kinase inhibitors (TKIs) in non-small cell lung cancer (NSCLC) patients. This study by Korean Cancer Study Group (KCSG) was conducted to determine the clinical implications of EGFR gene mutation, increased gene copy number and protein over-expression in Korean patients with advanced NSCLC who were treated with erlotinib.

Patients and Methods: A total of 120 patients received erlotinib (TARCEVA®) at a dose of 150mg daily between January 2005 and February 2006. Ninety-two tissue samples obtained from these patients were analyzed for EGFR mutation (exon 18-21) and K-ras mutation, with EGFR mutations compared to wild type (58.3% vs 16.2%, p=0.0001). With 14.5 month of median follow-up duration, time to progression (TTP) and overall survival (OS) were significantly longer in patients with mutations than those without mutations (p=0.003, p=0.042). Increased EGFR gene copy number was found in 40.9% (36/88) of the PCR samples. Patients with increased gene copy number achieved higher rate of response to erlotinib (38.9% vs 17.3%, p=0.023). Also patients with high gene copy number showed longer TTP (p<0.0001) and OS (p=0.022). Forty-six out of 75 patients (72%) positively expressed the EGFR protein, although there was no relationship between the EGFR expression and the response to erlotinib, TTP or OS.

Conclusions: Our findings indicate that both EGFR mutation and EGFR gene amplification were shown to be important predictive markers not only for achieving clinical response to erlotinib but also for the prolongation of overall survival in Korean patients with advanced NSCLC.

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Erlotinib as single agent in elderly patients (p) with advanced or metastatic NSCLC

Alberola, Vicente 1 Gallego, Oscar 2 López Vivanco, Guillermo 3 Mesía, Carlos 4 Oramas, Juan 5 Trigo, José Manuel 6 Virizuela, Juan Antonio 7 Camps, Carlos 8 Amador, María Luz 9 Massuti, Bartomeu 10 1 Hospital Universitario Arnau de Vilanova, Valencia, Spain 2 Hospital de la Santa Creu i Sant Pau, Barcelona, Spain 3 Hospital de Cruces, Barakaldo, Spain 4 Hospital del Mar, Barcelona, Spain 5 Hospital Universitario de Canarias, Tenerife, Spain 6 Hospital Universitario Virgen de la Victoria, Málaga, Spain 7 Hospital Universitario Virgen Macarena, Sevilla, Spain 8 Hospital General Universitario de Valencia, Valencia, Spain 9 Roche Farma, Madrid, Spain 10 Hospital General Universitario de Alicante, Alicante, Spain

Background: Erlotinib is the first orally available selective EGFR tyrosine-kinase inhibitor that improves survival in 2nd and 3rd line therapy for NSCLC. More than 50% of newly patients diagnosed with NSCLC are over the age of 65 and 30-40% over the age of 70. Several studies suggested an increased risk of toxicity in patients >70 years when treated with chemotherapy due to reduced organ function and the presence of comorbidities. Single agent treatment is considered an option of choice in this subset of patients. We have evaluated the efficacy of Erlotinib in elderly patients (≥70 yrs) with advanced or metastatic NSCLC.

Methods: The TargeT trial was an open-label multicenter study carried out in 103 Spanish institutions. Elderly patients (70 and older) included in this trial were eligible for this analysis. All patients had confirmed advanced or metastatic NSCLC, PS 0-2 and adequate organ function, and had received prior chemotherapy or not. Patients were treated with Erlotinib 150 mg/day po until disease progression or withdrawal.

Results: From April 2004 to March 2006, 1,796 patients (p) were included in the TargeT trial. By the time of this analysis, data from 570 p (≥ 70 years old) were available. Demographics: males 73.9%; median age: 75 yrs. [range 70-95]; stage IV: 76.1%; PS 0-1: 72.1%; histology: adenocarcinoma 51.4%, SCC 26.7%, LCC 15.6%, other 6.3%. Current/ever smokers 73.0%; 1st/2nd/3rd or further: 46.7%/36.3%/17.0%.

In the evaluable population for response (302 p) 23.8% reached partial response and 2 p complete response (0.7%). Of interest, both complete responses were detected in p treated with Erlotinib in the first line setting. Control disease rate was 67.6%. In the univariate analysis RR was significantly higher among women (51.5%; p=0.0001), non-smokers (51.0%; p=0.0001), adenocarcinomas (31.8%; p=0.003) and those treated with Erlotinib in the first line setting (30.7% vs. 18.4%; p=0.01).

In the ITT population, median time to progression (TTP) was 5.4 months [95% CI 4.5-6.5] and median survival was 6.2 months [95% CI 5.2-7.1]. In the univariate analysis, predictive factors for longer survival benefit of EGFR gene mutations and gene amplification in advanced NSCLC patients treated with erlotinib by the Korean Cancer Study Group (KCSG)