READERS OPINION

Epidermal growth factor receptor mutation frequency and non-small cell lung cancer management: implication for treatment choices

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Dear Editor,

I read the recent article by Bacchi *et al.* in a recent issue of your esteemed journal with great interest (1). The article is highly thought provoking. Over the past few years, new data have emerged that reveal the emerging role of epidermal growth factor (EGF) and its receptor (EGFR) in the personalization of non-small cell lung cancer (NSCLC) treatment.

Currently, EGFR tyrosine kinase inhibitors (TKIs), such as erlotinib and gefitinib, have been demonstrated to be effective in prolonging progression-free survival (PFS) and overall survival (OS) in patients with advanced NSCLC and *EGFR* mutations in exon 19 and 21 (2). In 2009, Rosell *et al.* reported *EGFR* mutations in 16.6% of lung cancer patients in a Spanish study (3). In that study, the median PFS and median OS were 14 months and 27 months, respectively (3). A Japanese study conducted by Tanaka *et al.* confirmed that *EGFR* mutations are more frequent in the adenocarcinoma histological type and in light smokers (4). In Tanaka's study, the overall frequency of *EGFR* mutations was 31% (4). Kosaka *et al*. conducted a study in Japan in 397 patients with lung adenocarcinoma who underwent potentially curative pulmonary resection (5). They found that 196 patients (49%) had *EGFR* mutations. Of these, 83 mutations were exon 19 deletions (42%), and 92 were L858R (47%). The study (5) showed that patients with *EGFR* mutations survived longer than those without mutations ($p = 0.0046$). There was no difference in the overall survival between patients with an exon 19 deletion and those with L858R ($p = 0.41$) (5).

In the Brazilian study conducted by Bacchi *et al*., the *EGFR* mutation frequency was 30.4% (1). In that study, 169 of 207 patients (81%) had adenocarcinoma, and 38 of 207 (18.35%) patients had a non-adenocarcinoma histology. Of the 207 patients, 120 (57.97%) were male. *EGFR* mutations were more prevalent in the adenocarcinoma histological type and in non-smokers than in non-adenocarcinoma histological types and smokers, respectively. The Brazilian study did not show differences between Asian and non-Asian patients regarding the *EGFR* mutation frequencies. That study has a patient selection bias. Despite the authors' assertion that the study sample represents all five Brazilian geographic regions, not all of the NSCLC patients had the opportunity for *EGFR* mutation assessment in their origin centers. The data were obtained from the laboratory files, and this may be a source of bias. Among the 63 patients with an *EGFR* mutation, 57 (90.04%) patients presented with an adenocarcinoma histological type. In previous studies, the rate of *EGFR* mutation in the adenocarcinoma histological type was 49% (5). The gender distribution in this study is another point of controversy. In the Brazilian study, the proportion of male patients was 57.97% (120/207), which was less than 75%, the previously published proportion of male patients (2-4). Differences in histology and gender distribution may lead to an unexpectedly higher frequency of *EGFR* mutation in the Brazilian population (30.4%) than has been reported in other publications (16.6–16.9%) (3,6) because the adenocarcinoma histological type predominates in this patient selection (1-3). As in any retrospective study, several potential sources of bias cannot be ruled out, and the reader should take this into consideration when reading the manuscript. Despite these limitations, this study is important to characterize the frequencies of *EGFR* mutations among different populations and improve the systemic treatment selection for patients with advanced NSCLC.

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