LETTER TO THE EDITOR

Second-line erlotinib in an
EGFR mutation-negative patient
with non-small-cell lung cancer

THE EDITOR

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I agree with the statement in this publication that tyrosine kinase inhibitors (TKIs) against the epidermal growth factor receptor (EGFR) should be considered “for all [non-small-cell lung cancer (NSCLC)] patients in the second-line, third-line, or maintenance setting, including those patients who are EGFR mutation-negative.” But it is vital to remember that not all such patients are eligible for EGFR TKIs. Patients with malabsorption, nausea and vomiting, diarrhea, skin disease (rash), or interstitial lung disease are not good candidates for this treatment.

Mutations other than those on exon 19 or 21, the most frequent mutations of EGFR (as mentioned in the publication), are not routinely tested for. Would exon 18 or other EGFR mutations be positive in this patient? We rarely re-biopsy tumours at the time of disease progression, especially at the time of new metastatic disease after treatment failure. We have learned that mutations of resistance can develop and that metastatic lesions do not necessarily have the same characteristics as the primary tumour. At the time of diagnosis, some tumours are combined small-cell and non-small-cell, but the small-cell component is not detected in the original biopsy. In the re-biopsy specimen, after disease progression, only small-cell tumor may be found. As additional specific targeted agents are developed for each line of treatment, individualized treatment based on new biopsy results will be more appropriate, even though it might be difficult to obtain further specimens or the patient might dislike the idea of re-biopsy.

Currently, EGFR TKIs in wild-type NSCLC tumours—that is, in the second line—demonstrate the same modest efficacy as chemotherapy agents do (response rate, progression-free survival, median overall survival), but the hope is to eventually replace such treatments with more specific, personalized treatments to further increase efficacy.

I agree that EGFR TKIs are the best option for the second-line treatments of wild-type EGFR lung tumors because they are less toxic and more convenient to administer. They can be administered for a longer period of time, even for more than 2 years (which is exceptional for chemotherapy agents), giving patients improved quality of life. In this palliative treatment setting, each line of treatment given to a patient has to be the best available, given the patient’s eligibility. Remember that about 40% of patients are lost to each next-line therapy. Thus, until treatments that are more individualized are available, EGFR TKIs should be available and funded even for wild-type NSCLC tumours treated in the second line.

The authors did not mention the results of erlotinib trials such as EURTAC and OPTIMAL, which compared that agent with platinum doublets in first-line EGFR mutation-positive advanced NSCLC patients, and which further supported EGFR TKIs for first-line treatment in that population.

CONFLICT OF INTEREST DISCLOSURES

VH has received honoraria from Hoffmann-La Roche and AstraZeneca Pharmaceuticals for participation on advisory boards.

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REFERENCES


