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LETTER TO THE EDITOR

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

KEY WORDS

Non-small-cell lung cancer, erlotinib, gefitinib, EGFR mutation

The Editor
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Re. Karam I, Melosky B. Response to second-line erlotinib in an *EGFR* mutation-negative patient with non-small-cell lung cancer: make no assumptions. *Curr Oncol* 2012;19:(COMP: add page range once known**).**

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 [1] 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 [2]. 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) [3–6], 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 TKI 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 [7] and OPTIMAL [8], 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 Hofmann–La Roche and AstraZeneca Pharmaceuticals for participation on advisory boards.

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REFERENCES

1. Kosaka T, Yamaki E, Mogi A, Kuwano H. Mechanisms of resistance to EGFR TKIs and development of a new generation of drugs in non-small-cell lung cancer. *J Biomed Biotechnol* 2011;2011:165214.
2. Waltman BA, Dias–Santagata D, Cosper AK, *et al.* SNAPshot multigene assay to detect mechanisms of acquired resistance to EGFR tyrosine kinase inhibitors (TKIs) [abstract 7554]. *J Clin Oncol* 2010;28:. [Available online at: http://www.asco.org/ASCOv2/Meetings/Abstracts?&vmview=abst_detail_view&confID=74&abstractID=43365; cited December 8, 2011]
3. Kim ES, Hirsh V, Mok T, *et al.* Gefitinib versus docetaxel in previously treated non-small-cell lung cancer (INTEREST): a randomised phase III trial. *Lancet* 2008;372:1809–18.
4. Maruyama R, Nishiwaki Y, Tamura T, *et al.* Phase III study, V-15-32, of gefitinib versus docetaxel in previously treated Japanese patients with non-small-cell lung cancer. *J Clin Oncol* 2008;26:4244–52.
5. Lee DH, Park K, Kim JH, *et al.* Randomized phase III trial of gefitinib versus docetaxel in non-small cell lung cancer patients who have previously received platinum-based chemotherapy. *Clin Cancer Res* 2010;16:1307–14.
6. Vamvakas L, Agelaki S, Kentepozidis, *et al.* Pemetrexed (MTA) compared with erlotinib (ERL) in pretreated patients with advanced non-small cell lung cancer (NSCLC): results of a randomized phase III Hellenic Oncology Research Group trial [abstract 7519]. *J Clin Oncol* 2010;28:. [Available online at: http://www.asco.org/ASCOv2/Meetings/Abstracts?&vmview=abst_detail_view&confID=74&abstractID=43881; cited December 8, 2011]
7. Rosell R, Gervais R, Vergnenegre A, *et al.* Erlotinib versus chemotherapy (CT) in advanced non-small cell lung cancer (NSCLC) patients (p) with epidermal growth factor receptor (EGFR) mutations: interim results of the European Erlotinib Versus Chemotherapy (EURTAC) phase III randomized trial [abstract 7503]. *J Clin Oncol* 2011;29:. [Available online at: http://www.asco.org/ASCOv2/Meetings/Abstracts?&vmview=abst_detail_view&confID=102&abstractID=78285; cited December 8, 2011]
8. Zhou C, Wu YL, Chen G, *et al.* Efficacy results from the randomized phase III OPTIMAL (CTONG 0802) study comparing first-line erlotinib versus carboplatin plus gemcitabine in Chinese advanced non-small cell lung cancer patients with *EGFR* activating mutations [abstract LBA13]. *Ann Oncol* 2010;21(suppl 8):.