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Response to: Second-line treatment of non-small-cell lung cancer with wild-type *EGFR* status. What is the best approach?

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We thank Drs. Ibrahim Elghissassi, Saber Boutayeb, Hanane Inrhaoun, Hind Mrabti, and Hassan Errihani for their comments on our paper.

The results of our practice review[1] on the use of tyrosine kinase inhibitor (TKI) at a single tertiary centre are not intended to diminish the important findings of prospective trials (DELTA and TAILOR)[2,3]. Yet the popular belief that randomized controlled trials inherently produce "gold standard" results and that all observational studies are inferior or noncontributory does a disservice, in some circumstances, to patient care, clinical investigation, and education of health care professionals. As an example, real-world data can be a useful aid for decision-making; assessing the value of a drug or technology often requires an understanding of its impact on current management in a practical, real-life setting.

We acknowledge that the results from the above-mentioned trials demonstrate that, in patients with wild-type *EGFR,* chemotherapy is superior to erlotinib in the second-line setting in terms of progression-free survival. Unfortunately, little or no benefit in overall survival was observed, which is far from the result that we would like to achieve for our lung cancer patients.

Additionally, it is important to recognize that a better toxicity profile for epidermal growth factor receptor TKI therapy compared with chemotherapy was clearly demonstrated. That finding is not to be minimized, given the palliative nature of both treatments. Our study was not meant to challenge prospective data, but rather to push forward the notion that, in the real-life setting at least, TKI therapy is still an acceptable option for some individuals —particularly when selecting therapy for patients with a poor or borderline performance status.

For the purpose of our analysis, wild-type *EGFR* was defined as negative for the classical mutations at exons 18–21. Mutations were detected by real-time polymerase chain reaction using the standardized U.S. Food and Drug Administration–approved EntroGen kit (Woodland Hills, CA, U.S.A.). The possibility of patients having rare activating mutations cannot be excluded. We agree that that possibility could have led to better progression-free survival in patients treated with TKI compared with patients receiving docetaxel treatment. However, such an analysis was beyond the scope of our study, considering its retrospective nature. Future prospective studies might want to explore that hypothesis.

A very valid point was raised concerning the concept of treatment-free interval as reported by Odabas *et al.*[4] We will consider re-evaluating our published results to determine if that parameter did indeed affect the success rate of second-line treatment in our study population.

Finally, Dr. Elghissassi and colleagues are correct to state that neither docetaxel nor erlotinib are ideal second-line treatments. Fortunately, novel therapies are actively being developed, although they have yet to be integrated into common clinical practice. The major drivers of change will include more comprehensive genetic testing platforms, the identification of additional molecular subtypes of non-small-cell lung cancer, and advances in drug development. As already mentioned, studies evaluating two antiangiogenic drugs, nintedanib and ramucirumab, yielded positive results in this setting. Finally, promising new drugs targeting the immune checkpoint pathways are also being tested. The exciting results emerging from those tests will open tremendous possibilities for future research studies and offer hope that cures can be achieved for at least a subset of patients with advanced non-small-cell lung cancer.

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CONFLICT OF INTEREST DISCLOSURES

We have read and understood *Current Oncology*'s policy on disclosing conflicts of interest, and we declare that we have none.

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