
From the Editor

The summary of first-line therapy for the relatively uncommon set of genomic alterations of the *ALK* gene in non-small cell lung cancer (NSCLC) provided in this issue of the *American Journal of Hematology/Oncology*[®] by Wakelee et al demonstrates the clear and steady progress in genomically personalized cancer therapy. The initial presenta-



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tion of the dramatic activity of crizotinib in *ALK*-rearranged lung cancer at the ASCO 2010 Plenary Session ushered in a new era of effective treatments for rare subsets of common cancers.¹ It is also notable that this presentation came only 3 years after the initial discovery of the *EML4-ALK* fusion gene as a driver of lung cancer.² Since this time, it is remarkable that for a rare cancer subtype there are now 4 approved agents for this genomic aberration, a necessary development because escape pathways invariably develop to most targeted agents. Some of these newer drugs will be shifted to when they should best be used—alectinib was approved in 2015 for second-line treatment of *ALK*-positive lung cancer after progression on crizotinib, but with the recent demonstration of

significant activity in untreated patients, and just-published (online) positive findings of the ALEX trial showing superior progression-free survival with alectinib compared with crizotinib, it is now expected to be approved as frontline therapy.³ And an added bonus is less toxicity and fewer central nervous system progression events seen with alectinib. It is encouraging that although these drugs are not curative, they are being rapidly developed and optimized in terms of sequence of use.

A case report by Raez and Rolfo also in this issue presents an interesting case of another mutation, T790M, that drives resistance in NSCLC to the first-line *EGFR* mutation-targeting drugs erlotinib and gefitinib. In this case, the use of liquid biopsy was able to show this evolutionary genomic change after a tumor biopsy failed to do so. Although there are no standards regarding multiple repeat biopsies, and the costs for doing this may prove untenable, we clearly need improvements in diagnostic sensitivity and several new technologies are attempting to do just that. In this case report, a response was seen to osimertinib, which is approved specifically for T790M mutation-associated NSCLC in second-line therapy. The FLAURA trial results recently released showed that osimertinib outperformed erlotinib or gefitinib as first-line therapy for *EGFR*-mutant NSCLC—so more shuffling is likely to ensue.⁴ And the beat goes on....

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