Post hoc Analysis of Clinical Activity of Quizartinib in Patients with Prior TKIs

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I'm Mark Levis. I am here in Chicago at the ASCO meeting and I am talking about a poster that we are going to present tomorrow morning at the poster session. The poster addresses an issue that is emerging in the field of AML, and it is emerging because of some very recent important developments. Last year, the RATIFY trial results led to the approval of the drug midostaurin for the treatment of newly diagnosed FLT3 mutated AML patients; and much more recently the results of the QuANTUM-R trial, a randomized trial of quizartinib in the relapsed/refractory AML setting, have just been publicized and will be presented at the EHA meeting later this month. Finally, Astellas, the sponsor for a drug called gilteritinib, another potent selective FLT3 inhibitor, has filed for approval of that drug, presumably on the basis of a positive phase 3 study. Therefore, I predict within the next 12 months, we will have three drugs approved for the treatment of FLT3 mutated AML. In that setting a new issue arises, namely that of resistance.

If a patient has been treated with one FLT3 inhibitor and progresses, will they respond to another one? We have attempted to begin addressing this issue by looking at a large dataset of patients treated with quizartinib. This is data derived from technically three trials comprising over 300 FLT3 ITD mutated patients treated with varying doses of quizartinib. Amongst those greater than 300 patients on these studies, we came up with 38 patients who had received prior treatment with other FLT3 inhibitors, mostly sorafenib which is available as off-label* for the treatment of this disease, but a few were treated with midostaurin. The idea was to see whether the response rate in these 38 patients was the same as the response rates in the so-called TKI naïve population. The heads-up comparison was that as expected, the response rates were lower, but not greatly lower; they went from 53% to 33%, which is an important finding because that is still a pretty meaningful response. It is kind of what we expect, and I suspect that is what we are going to see for the other FLT3 inhibitors as well.

The other important point to raise about these patients, for those who did respond, is that you want to know if the response helped them. A responder should do well; a responder should have a survival benefit compared to a non-responder. In fact, we did see that if you had been exposed to a prior FLT3 inhibitor and you got quizartinib and responded, your survival was better than patients who did not respond; the responses appeared to be in the same category of clinical benefit. The two major findings were: there is a meaningful response rate when you use quizartinib in a patient who has already had a FLT3 inhibitor; and two, that response

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appears to be associated with a survival benefit, at least in this nonrandomized setting compared to non-responders. Thank you.

*Sorafenib is not approved by the FDA for use in patients with acute myeloid leukemia

Abstract:

Levis M, Smith C, Ishizuka K, et al. Post hoc exploratory analysis of two phase 2 trials of quizartinib monotherapy in patients (pts) with FLT3-ITD–mutated (mu) relapsed/refractory (R/R) AML with or without prior 1st-generation FLT3 tyrosine kinase inhibitors (TKI) treatment. ASCO 2018. Abstract 7017.
https://meetinglibrary.asco.org/record/162108/abstract

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