The Practical Oncologist

How is pharmacologic management and sequencing handled in advanced melanoma?

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Hello. I am Keith Flaherty, a medical oncologist specializing in melanoma and based at the Massachusetts General Hospital Cancer Center in Boston Massachusetts. A participant raised a question, how do I sequence ipilimumab and vemurafenib in advanced melanoma?

This is a critical question that arises now that both of these agents are FDA-approved for the treatment of advanced or metastatic melanoma, and both of them are specifically approved as first-line or later line of therapy. We have evidence from phase 3, as well as phase 2 clinical trials with both agents that they can act effectively not only as first line treatments, but also as salvage therapies and when thinking through the sequence of therapies, of course one has to first recognize that the vemurafenib is a only a relevant treatment for patients who have an activating BRAF mutation, approximately 50% of advanced melanoma patients. For those who do not have an activating BRAF mutation, ipilimumab represents the only newly approved drug for those patients and the current evidence would support its use as first-line treatment.

For patients who have an activating BRAF mutation on the other hand, both options are available and without head-to-head data yet comparing these therapies and helping to sort out which is the optimal first therapy versus which is the optimal second-line or salvage therapy, one has to consider a couple of points that were reviewed during the course of the presentation. For patients with symptomatic bulky metastatic disease, vemurafenib represents an excellent palliative therapy with short-term tumor control. Ipilimumab on the other hand does not offer a high likelihood of early treatment response, and while some patients with bulky disease can respond, it is fairly clear from the evidence that they are somewhat less prone to respond than those who have smaller volume asymptomatic disease. For those with small volume asymptomatic disease, many currently consider ipilimumab to be the optimal first-line therapy, reserving vemurafenib then as the second-line or salvage therapy for those who do not respond to that treatment. And so, for those patients, it is recommended that they be watched closely, and if there is evidence of disease progression following induction therapy with ipilimumab, then at that point, vemurafenib therapy be considered.