The Practical Oncologist

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What other emerging therapies are there for advanced melanoma?

Hello. I am Keith Flaherty, a medical oncologist specializing in melanoma and based at the Massachusetts General Hospital Cancer Center in Boston Massachusetts. One of the participants raised a question, what other emerging therapies are there for advanced melanoma?

Well, beyond vemurafenib and ipilimumab, the recently FDA-approved treatments, there are therapies that are similar to each of those that are currently in clinical trials and showing promise for the treatment of advanced or metastatic melanoma. Specifically, analogous to the vemurafenib, there is another BRAF inhibitor referred to currently as dabrafenib, formerly known as GSK2118436, that has shown promising evidence in the same patient population in which vemurafenib works. Its comparative advantages are currently unknown, although it does have a somewhat different side-effect profile, which may offer an advantage for some patients, and there is emerging evidence that this agent has significant activity for brain metastases that have been otherwise untreated, and since brain metastases are quite common in melanoma, this is certainly an agent that might end up finding a place, particularly for patients with active brain involvement.

MEK inhibitors that target the downstream molecule from BRAF have also shown promise in BRAF mutated melanoma, and one of those agents has been through phase 2 and now phase 3 clinical trial. Based on the available results from a phase 2 clinical trial, this is a therapy that seems to be highly active, has a different side-effect profile for BRAF inhibitor therapy, and maybe a therapy that could either be used in the future as a sequential therapy or potentially in combination with the BRAF inhibitors. And there is an ongoing clinical trial, preliminary results of which appear fairly promising.

In the immune therapy category, beyond ipilimumab, there are other agents that have a similar mechanism of targeting specific molecules on the surface of the immune effector cells that are capable of recognizing and destroying melanoma cells, and the most promising of these agents is one that targets the PD-1 antigen on T-cells. Like ipilimumab, PD-1 is a negative regulator of T-cell function and blocking it with an antibody activates T-cells. And this antibody that I am referring to, MDX-1106, is one

of now several antibodies in clinical trials, but this one has data that has emerged from a phase 1 clinical trial in which a large number of melanoma patients were included where tumor regressions were observed quite frequently and fairly durable, at least to the extent that follow-up is available at the time that those data were presented. So more clinical trials certainly will be needed and more follow-up to establish whether this is another therapy that could join the melanoma treatment armamentarium, but it is certainly capturing some attention in the melanoma field.