The Practical Oncologist

How should secondary malignancies that arise during vemurafenib therapy be managed?

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Hello. I am Keith Flaherty, a medical oncologist specializing in melanoma, based at the Massachusetts General Hospital Cancer Center in Boston Massachusetts. One of the participants raised a question, what can be done to reduce the risk of secondary malignancies with the use of vemurafenib?

This question relates to the observation in all of the clinical trials conducted with vemurafenib that patients who received this therapy can have non-melanoma skin lesions appear generally relatively early in the course of their treatment, within one, two, or three months. These are patients who have a fairly extensive sun exposure history, but what can be noted is that squamous cell carcinomas and lesions that look very similar to squamous cell carcinomas, referred to as keratoacanthomas, can erupt as either individual lesions or occasionally multiply early in the course of treatment. These are generally asymptomatic or painless lesions, but when they appear in the course of vemurafenib treatment, the practice in clinical trials was to remove them and to obtain histologic diagnosis. And it was found that the lesions typically represented either keratoacanthomas or well-differentiated squamous cell carcinomas. Standard practice now that the vemurafenib is an available therapy has been to excise these lesions and continue patients on therapy without either interruption or dose modification.

It is unknown at this time whether other types of malignancies could arise in the setting of vemurafenib therapy. A fairly careful mechanistic analysis seems to explain why these skin lesions appear and would not necessarily raise concern about other secondary malignancies. In terms of avoiding these, generally speaking for patients who have an extensive sun exposure history, the damage has already been done in terms of the precursor lesions that might have formed and are acted upon by the therapy and there is not a preventative strategy necessarily. There are ongoing clinical trials that are evaluating the concomitant use of preventative therapy in addition to vemurafenib as the BRAF inhibitor backbone, but obviously, results are needed from those studies to understand whether any of those approaches will move forward. So, for now, it is a matter of close surveillance and removal of lesions as they appear, but generally speaking is not a cause for interruption or cessation of therapy.