Managing Myeloma

**Should I be concerned about second primary malignancies when prescribing maintenance therapy with lenalidomide?**

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Welcome to *Managing Myeloma*, I'm Dr. Sarah Holstein. Today I'd like to briefly review whether or not clinicians should be concerned about second primary malignancies when prescribing maintenance therapy with lenalidomide. I'll be specifically talking about maintenance therapy in the post-transplant setting with lenalidomide. Early on when the first several randomized studies began to present their results showing profound benefits with progression-free survival with lenalidomide maintenance after transplant, they also began to report a disturbing signal that patients who were receiving lenalidomide had an increased risk of second primary malignancies or SPMs. We now have long-term follow up for many of these studies, and although they do show significant both PFS and OS benefit, there truly is a signal that there is an increased risk of SPMs with lenalidomide. However, it's important to understand that there are several risk factors that are associated. One, just having a plasma cell neoplasm regardless of whether or not you have any therapy has been shown to be associated with an increased risk of hematological SPMs. In addition, it's been known for quite some time that high-dose melphalan in the context of autologous stem cell transplant is also associated with an increased risk of hematological SPMs, particularly myelodysplastic syndrome and AML. What we've seen though with the lenalidomide maintenance studies is that the risk is even higher with lenalidomide maintenance. Not only are we seeing the risk of MDS and AML that we saw with high-dose melphalan transplant, but we also are seeing a signal that a small number of patients are being diagnosed with B-cell ALL. In addition, there also seems to be a small, but real, increased risk of solid tumor malignancies. However, it's important to put this in context into the benefit of maintenance therapy, particularly with respect to preventing progression of their myeloma and death from their myeloma.

What I always counsel patients and also other providers about is that a) it is important to understand that this risk exists, but b) it's also important to understand the relative risk of the SPM as opposed to the relative benefit of not progressing from myeloma or dying from myeloma. Understanding the magnitude of these risks is very important. For that reason, I do think that the benefit versus risk is in the favor of benefit for lenalidomide maintenance, but I always counsel patients that this risk exists. It is for that reason that I strongly recommend that patients who are lenalidomide maintenance undergo monthly CBCs and, in particular, if there is a sudden change in their blood counts, there should be a really low threshold for having the patient undergo a bone marrow biopsy to make

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sure that a new process isn't developing in their bone marrow. From a solid tumor perspective, there really hasn't been one particular malignancy which has been shown to be associated with lenalidomide maintenance, and so in this context I really recommend that patients undergo age-appropriate cancer screening.

To summarize, I do think that there is an increased risk of SPMs with lenalidomide maintenance, but we have to put this into the context of the benefit that patients receive with respect to both progression-free and overall survival. Thank you for viewing this activity.

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