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What is the value of flow cytometry in assessing for minimal residual disease in MM?

Welcome to *Managing Myeloma*. My name is Ola Landgren, and I am Chief of the Myeloma Service at Memorial Sloan Kettering Cancer Center in New York City.

I am frequently asked, "What is the relative value of multicolor flow cytometry in an assessment for minimal residual disease in multiple myeloma compared to allele-specific PCR?" These are very technical questions. Let me briefly describe what multicolor flow cytometry is. It is a way to label cells from the bone marrow, and as you may know, there is no one way of defining an abnormal plasma cell, which is what we refer to as a myeloma cell. So, we need a panel of different antibodies, and the whole setting of the sample needs to be gated in a flow cytometry machine. This is exactly how people have been working to advance the field, to make flow cytometry a tool for minimal residual disease, trying to figure out which antibodies to use and how to gate. The strengths of the flow cytometry approach is that we do all have flow cytometry machines in hospitals, and these antibodies are commercially available. The weakness is exactly the same thing: although we have all these machines and all these antibodies are available, unfortunately people have not fully agreed how to use them, how to gate, and which antibodies should be used, etc. So, I think part of the work that has been done in more recent times, which is ongoing, is harmonization and standardization, and this will really help to make flow cytometry an important tool for MRD testing in myeloma.

When it comes to allele-specific PCR, this is a molecular test that can be used in order to trace evidence of the disease in patients. The problem is that, when using PCR primers you need to sequence the patient first, and then, when you have the sequence figured out, you can use PCR primers, and follow the patient's samples for MRD status. The problem then is that every patient needs to be sequenced so that you know exactly what primers to use. Another approach could be to use what is called a consensus primer, a combination of primers. So, you use these consensus primers and you run that same consensus panel on every patient you see in clinic. A problem with this approach is that, unfortunately, not every patient will be captured by these primers. The strength of this technology, overall, is that it is probably more sensitive than flow cytometry, and its weakness is all of these practical things that I have been discussing: that you could sequence each and every patient, but that becomes very technically cumbersome and expensive. Or you could use consensus primers, but you could miss as many as 30% of patients. So, although the technology is more sensitive, in reality, you may miss some patients.

Now, there are newer technologies, which I mentioned during my presentation, including the VDJ sequencing technology that is available, in which you sequence every VDJ sequence that is available in each and every patient and you follow them. I think there are new molecular technologies that are going to become the new way of doing MRD testing, but we are not yet there, they are not commercially available, and we cannot use them easily.

In summary, flow cytometry and the standardized protocols that have been proposed by the International Myeloma Working Group would be my preference right now. But moving into the future, I do think that the next generation sequencing-based technologies will be more stable, they will not be dependent on the person who runs it under individual labs, and they will be very reproducible. What we need is to have access to these new next-generation sequencing technologies in every lab around the world. Then, we will have very sensitive technologies that can be run everywhere on a day-to-day basis.

With this, I would like to thank you so much for viewing this activity. For additional resources, please view the other educational activities on *ManagingMyeloma.com*. Thank you very much.