Managing Myeloma

What is the significance of minimal residual disease (MRD) as a surrogate marker in myeloma?

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Now, when you think about MRD status in myeloma, there are three main goals for using MRD testing in myeloma. The simplest thing is as a prognostic factor. This is amply evident from all the meta-analysis and all the phase 3 trials that have been done in the past. If you get to be MRD negative with a given treatment, you will do better than the patients who don't get to be MRD negative at the same time point. And this is probably a reflection of how deep or how few myeloma cells are left behind, and the time it takes for this clone to grow back up.

The second use of the MRD status is as a surrogate endpoint. As we know that the survival in patients with multiple myeloma has significantly improved over the years. Now, we are looking at median PFS close to 8 to 10 years, and that makes it very difficult to do clinical trials in this patient population when we are looking at endpoints for PFS and overall survival. Again, given that myeloma, there's only like 32,000 patients with myeloma diagnosed each year in the US, there's only so many patients who go on clinical trials.

There has been a lot of interest in trying to identify surrogate markers that can be assessed much earlier, which will then translate into a much longer-term outcome like PFS or overall survival. The MRD testing appears to fit the bill there, with all these meta-analyses demonstrating a clear relationship between the MRD status and the progression-free survival and overall survival. There's an ongoing effort to put together the data that exists in order to allow regulatory agencies, or for the regulatory agencies to allow us to do clinical trials with MRD negativity as an endpoint.

The third potential use is what has been the biggest challenge. We know that MRD negativity is a good prognostic factor, but what we don't know is if somebody is MRD positive after a given treatment or a given set of treatments, giving a different treatment or intensifying treatment to try and get that person to be MRD negative, will that affect or improve their outcome? Similarly, on the other end of the spectrum, if somebody is already MRD negative with, let's say a year or two years of therapy, can we potentially decrease or discontinue the therapy, thus improving their overall quality of life and also decreasing the cost of care?

There are no prospective data from the clinical trials to guide us. There are clinical trials that are currently ongoing, that are specifically asking this question. So, between these trials, I think we will be able to get some answers to the question: can we use MRD negativity as an actionable tool in the clinic, to decide how we approach treatments for patients with myeloma?