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MRD Testing to Guide Treatment Considerations in CLL

Announcer:
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Dr. Munir:
Hi, this is CME on ReachMD, and I'm Dr. Talha Munir. Today, I'll break down the importance of MRD [measurable residual disease] testing in the management of CLL.

So the most important question is what is minimal residual disease, or now as we say that as measurable residual disease? This is primarily the fraction of disease that is left after a treatment for CLL, especially used in therapies with fixed-duration approach, such as chemoimmunotherapy in the past and in the fixed-duration therapies as well. It has been utilized to define duration of therapy as well, but it does give us an idea what is the residual disease left in a CLL patient in CLL treatment.

Where MRD monitoring becomes into play is really with fixed-duration therapy. And the fixed-duration therapy allows us to stop treatment in our patients, following which MRD has got a prognostic role. So we know now from the data from multiple trials that patients who became MRD negative after a combination of BCL-2 inhibitor and anti-CD20 antibody, the MRD retains its prognostic role. So patients who were MRD negative at the end of the treatment have better progression-free survival and actually overall survival as compared to the patients who had measurable residual disease as positive. And this is looking like to be at the level of 1 CLL cell detected in 10,000 leukocytes. So even at that level of measurable residual disease, the progression-free survival and overall survival was important. This highlights the fact that getting patients into deeper remission is important as for short-term endpoints, measurable residual disease becomes very important.

In some of the trials, the measurable residual disease has been used to guide therapy and duration of therapy, but those trials are being updated, and essentially, we will know whether guiding therapy using MRD will lead to improvement in progression-free survival and overall survival for these patients. However, for some other fixed-duration combination therapies, the results of minimal residual disease or measurable residual disease are a bit more not clear at the moment. For example, patients receiving fixed-duration therapy with a BTK inhibitor and BCL-2 inhibitor, the mutated IGHV patients still continue to benefit whether they are measurable residual disease positive or negative at the end of the treatment. Whereas the unmuted IGHV patients are definitely showing a difference in outcomes in terms of the MRD response.

In terms of which test to use, the most commonly used test is flow cytometry because it's easy to use and it is very well recognized in multiple centers, and people are able to utilize this in their normal practice. Whereas other more specific tests such as next-generation sequencing or qPCR utility is less frequent in normal day practice. Whereas in clinical trials, it is a very normal practice to actually look at all of these questions. In terms of the MRD-guided therapy, FLAIR trial has shown that the MRD-guided therapy could be quite useful in patients with unmutated IGHV CLL. And in those patients, when you guide therapy based on MRD, the short-term progression-free survival and overall survival looks extremely good and much better than chemoimmunotherapy.

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So in future we will be able to tell which patients we should be using fixed-duration therapy or MRD-guided approach.

And hopefully that was brief but hopefully a useful overview. My time is up, and thanks for listening.

Announcer:
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