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Measuring Depth of Remission in Chronic Lymphocytic Leukemia

ReachMD Announcer:

Welcome to ReachMD. The following program, “Measuring Depth of Remission in Chronic Lymphocytic Leukemia” is developed and sponsored by AbbVie. This activity is intended for United States and Puerto Rico health care professionals only.

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Dr. Davids:

I’m Dr. Matthew Davids, associate professor of medicine at Harvard Medical School and the director of clinical research for the division of lymphoma at Dana-Farber Cancer Institute in Boston, Massachusetts.

Thank you for joining me as I discuss depth of remission in CLL. The traditional measure of depth of response has been complete response, or CR, defined as the absence of morphologic evidence of CLL in the marrow, no cytopenias, all lymph nodes less than 1.5 cm, no splenomegaly or hepatomegaly, and an absolute lymphocyte count less than 4000 per microliter. More recently, some clinical trials are also measuring minimal residual disease, or MRD.

In CLL, MRD negativity is most commonly defined as less than 1 CLL cell per 10,000 leukocytes (10^{-4}). It is important to understand that MRD negativity is not a yes or no determination, but rather that a sample is negative at a certain threshold. Many clinicians are now using the term undetectable MRD. This is because MRD negative implies the complete absence of CLL cells, whereas undetectable implies that, based on the power of the test, we do not detect any CLL cells, but they could still be present at a very low level.

MRD can be evaluated in the bone marrow or in peripheral blood. Recent trials have demonstrated fairly good concordance of results from the blood and bone marrow, which may lead to increased use of blood-based MRD assays in the clinic in the future. Flow cytometry is the most common method used to assess MRD. Other more sensitive methods for measuring MRD include PCR and next-generation sequencing via the clonoSEQ platform, which has recently been FDA cleared and approved for Medicare reimbursement.

With fixed-duration chemotherapy, achievement of undetectable MRD has been associated with improved clinical outcomes, including progression-free survival and overall survival. Emerging data suggest that undetectable MRD may also correlate with improved clinical outcomes for time-limited novel agent-based therapies. It is important to note that some novel agents contribute to progression-free survival without typically achieving undetectable MRD. MRD is currently being evaluated in clinical trials for its value in treatment decision making, particularly with regard to defining the optimal duration of novel agent-based combination therapies.

In patients with a long life expectancy and good functional status, undetectable MRD remains an appropriate goal regardless of age. For those with short life expectancy due to other health conditions, palliation is appropriate. Most older patients with CLL fall somewhere in between, requiring that clinicians balance a variety of considerations when recommending therapy. As novel therapies and combination strategies emerge and tolerability and toxicity improve, the number of patients who will be candidates for time-limited treatment strategies that can achieve a good depth of remission will likely expand.

ReachMD Announcer:

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