NORTHWEST
MULTIPLE MYELOMA FIGHTERS

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The Role of MRD in Treatment Decisions

Edited transcript of audience questions and answers

Q. I have been MRD negative for about a year, and my physician is suggesting I could stop treatment. I had previously been told to wait two years. What is the current thinking on how long to maintain MRD negativity before stopping?

A. There is no definitive answer yet. The scenario varies depending on treatment history and trial context. In practice, one common approach is testing at 12 months post-transplant, then again 12 months later — putting patients roughly three years from diagnosis before a discontinuation decision. That aligns with MRC11 data showing that MRD negativity at three years post-transplant correlates with significantly lower progression risk. Whether 12 months of MRD negativity is equivalent to 24 or 36 months is not established. This remains a gray area, and there are likely several reasonable approaches. The conversation with your physician matters more than a fixed rule.

Q. My husband has been on daratumumab for 70 rounds and his M-spike has stayed stable at 0.1–0.2. He has not had MRD testing. Should we request it, and could it support a decision to stop daratumumab?

A. MRD testing is most meaningful when conventional markers — M-spike, urine protein, free light chains — are negative. If an M-spike is still detectable, that measurable disease is the more relevant indicator. Daratumumab can artificially elevate the M-spike reading by about 0.1, and there is a test that corrects for that interference. If the corrected result still shows an M-spike, then the disease remains measurable by standard methods, and MRD testing would not add much. The data supporting treatment discontinuation applies to patients with no detectable disease by blood or urine markers. In this situation, MRD testing is unlikely to change management.

Q. What does a "log increase" mean in the context of MRD results?

A. A log increase means the MRD level rose by a factor of ten. For example, moving from 10^{-4} to 10^{-3} is one log. This is visible on the clonoseq report as a plot showing the clone count over time. It is not a calculation patients typically need to do themselves — the report makes it fairly clear. Reviewing the result with your physician is the right approach.

Q. I have never achieved MRD negativity on next-generation sequencing, though I have had negative results by flow cytometry. Which test should guide treatment decisions, including whether to continue maintenance?

A. Next-generation sequencing — genetic testing such as clonoseq — is the standard for treatment decisions in the U.S. The highly sensitive flow cytometry method referenced in research, called EuroFlow, is used at very few centers, possibly only Mayo Clinic in the U.S. For most patients, flow cytometry results are not the basis for discontinuation decisions. If you have not achieved negativity by NGS, continuing treatment based on that result is consistent with current evidence.

Q. What is the difference between clinical progression and MRD progression?

A. Clinical progression means new or worsening CRAB criteria: bone lesions, anemia, elevated calcium, or renal failure. Biochemical progression — a rising M-spike or free light chains — can also prompt treatment before overt clinical symptoms appear, though physicians do not always treat biochemical progression immediately. MRD progression is different: it means the MRD level has increased by one log on testing, even if no changes are visible in standard blood or urine markers. MRD progression predicts a higher likelihood of clinical progression within two to three years. Whether MRD progression should automatically trigger treatment changes the same way clinical progression does is still an open question — the data suggests it should, but how these categories were defined across studies is not always consistent.

Q. I have light-chain myeloma and my oncologist monitors my kappa free light chains rather than an M-spike. How does this affect MRD testing and when it becomes relevant?

A. Light chains serve the same role as the M-spike: a measurable indicator of disease. MRD testing becomes relevant only when conventional markers — free light chains, serum protein electrophoresis, urine protein, bone marrow flow cytometry — are all negative. If your free light chains are still elevated, that is your primary marker to track. The goal at that stage is normalizing the free light chain ratio, not pursuing MRD testing. Once all standard markers are negative, that is when MRD adds diagnostic value.

Q. For a patient in complete response after relapse on a pomalidomide/daratumumab regimen, who has never had MRD testing during this treatment line, how often should MRD be tested?

A. There is no established frequency for this situation. The data supporting MRD-guided treatment discontinuation comes primarily from newly diagnosed patients in trials like Perseus and MIDAS. That evidence does not extend cleanly to patients in the relapsed setting on regimens like pomalidomide/daratumumab. In this case, MRD testing would be more for personal knowledge than for driving a treatment decision. If your physician has indicated that the current regimen will not change regardless of MRD results, testing remains optional. It is reasonable to ask about it; it is also reasonable to skip it.

Q. If a patient never achieves MRD negativity, does treatment need to continue indefinitely?

A. In general, yes — persistent MRD positivity is a reason to continue treatment. There are cases where patients have stopped due to intolerance and done well even while MRD positive, but those are not planned discontinuations. They happen when side effects make continuation impossible. The weight of evidence does not support elective stopping in patients who remain MRD positive. That said, this is always an individualized conversation. There is nuance depending on stability, duration of positivity, and overall clinical picture. The general principle is to continue if MRD positivity persists.