



Voices of MRD: Where We've Been, Where We Are Now and Where We're Going

AUDIENCE QUESTIONS ANSWERED

Lymphoma

1. Is there an indication for MRD for Follicular Lymphoma?

For follicular lymphoma, MRD is now in clinical trials and hopefully in the future it will help in making treatment decisions about consolidation and maintenance. It has prognostic value in follicular lymphoma.

2. Regarding lymphoma, does MRD have any prognostic value in primary lymphoma of the bone/diffuse large B cell lymphoma (DLBCL)?

MRD in peripheral blood has a prognostic value in DLBCL.

3. How is MRD used for patients with high grade lymphoma?

MRD is currently not part of the standard follow up or surveillance testing done in diffuse large B cell lymphoma or Burkitt's lymphoma, but there are studies that showed prognostic value of MRD when done after completion of chemotherapy.

4. Are there any MRD tests available for pre-B-cell lymphoblastic lymphoma with Philadelphia-like genomic mutation?

Yes. MRD could be done by next generation sequencing on peripheral blood (clonoSEQ® testing/Adaptive).

5. Are there MRD tests for lymphoma? If so, what kind of samples are needed? How is it done?

MRD can be done on peripheral blood in diffuse large B cell lymphoma, follicular lymphoma and mantle cell lymphoma by next generation sequencing (clonoSEQ® testing/Adaptive).

6. How do you interpret a positive MRD test result for an aggressive lymphoma patient? When should you go to treatment based on MRD testing results?

If a patient has a positive MRD test, I recommend obtaining imaging to check for relapse. There are no studies to show that treatment based on positive MRD results without clinical or radiographic relapse improves survival in patients with lymphoma.

7. How is MRD testing used differently with high grade lymphomas vs. indolent ones?

Currently, MRD testing is considered prognostic in both high grade and indolent lymphoma but there is no data to guide modification of treatment based on MRD testing except in patients with B lymphoblastic lymphoma.

8. At what point in follicular lymphoma would MRD testing be indicated? After treatment and maintenance, as an alternative to imaging?

MRD testing for surveillance in follicular lymphoma may be used by some oncologists as an alternative to imaging, but it is not currently the standard of care.

Acute Myeloid Lymphoma (AML)

9. Is there any value to testing MRD in AML if in remission for over four years?

I do not believe so.

10. Is there value to MRD testing in AML if in remission after standard Induction and Consolidation chemo?

Yes. MRD could be done on bone marrow biopsy by multicolor flow cytometry or next generation sequencing or by polymerase chain reaction (PCR) for specific genetic alterations if found initially. The positive MRD precedes clinical relapse and if found, the patient needs to be started on salvage treatment and considered for allogeneic stem cell transplant.

11. Why is MRD not considered standard of care for AML?

Because more studies are needed to validate that early treatment based on MRD improves outcome.



Chronic Lymphocytic Leukemia (CLL)

12. In what circumstances might MRD be valuable to a CLL patient undergoing a specific treatment?

Today MRD is mostly a research tool, but it can be very helpful in predicting the duration of response to some, but not all, therapies.

13. How do you anticipate the role of MRD to evolve as it relates to treatment decisions in CLL?

Based on trends in research, it is reasonable to anticipate that MRD may be used to determine when to stop some therapy and when to intensify therapy in the future.

14. Under what circumstances would MRD be appropriate for CLL?

MRD is appropriate to further monitor depth of response once a low or normal absolute lymphocyte count has been reached with some chemo-immunotherapy and novel therapy treatments, but not with all.

15. In what circumstances will Medicare currently cover MRD testing in connection with one's CLL therapy? And for which therapies? And what is the trend?

MRD is usually done by flow cytometry and Medicare pays for the test if ordered for the proper indications. Next generation sequencing (clonoSEQ®) is increasingly being used in clinical settings as it can look deeper for residual disease, and it too will be covered by Medicare in the proper circumstances. It is always best to check with your healthcare team and insurance to see what is and isn't covered. Insurance is trending toward increased coverage.

MRD Testing and Transplant

16. Is MRD testing used post auto transplant? If not, why?

It depends on the disease. However, in general, many doctors send for MRD testing whenever a bone marrow is performed after transplant.

17. Would it be beneficial for a patient who had negative MRD before transplant to have it done again after transplant, or after maintenance treatment?

It depends on the disease. MRD is often checked in the post-transplant setting (usually at least once in the first months after transplant). There is not a clear role for repeat MRD testing after maintenance treatment. This should be discussed with your doctor.

18. Should MRD testing be used to make a decision to go for autologous stem cell transplantation (ASCT) and eventually post-transplant to measure results and decide about maintenance?

It depends on the disease. Usually, MRD status does directly impact the decision for autologous transplant. However, it is commonly checked after transplant to assess disease status. There is not a clear answer as to how MRD status after transplant should impact the decision for maintenance. This should be discussed with your doctor.

MRD Testing (frequency, results, frequently asked questions)

19. How often should MRD testing be done after MRD negativity is achieved? When is the best time to do the MRD test? Right after treatment or waiting a few months?

MRD testing is highly dependent on the type of cancer and a patient's individual treatment plan. Patients may be tested after the final cycle of combination therapy, after bone marrow transplantation, during treatment to confirm the depth of remission, after one year on maintenance therapy, at regular intervals after treatment is completed, or at other specific times as recommended by the doctor.

20. How should low numbers be interpreted and what does "0" really mean in flow cytometry tests?

A low number of MRD means that there is still some detectable disease present. Depending on the specific disease, this may or may not influence therapy decisions. Having zero MRD means that no residual disease can be detected with the flow cytometry test.



Defining MRD Testing

21. What is the difference between the term “MRD” and “no detectable disease”?

“MRD” refers to measurable/minimal residual disease. A test showing no evidence of MRD is equivalent to saying that there is no detectable disease.

22. What efforts are being done to reduce the LOD on quantitative detection tests (example, qPCR tests for CML patients) and therefore “shift the goal posts” on the definition of MRD?

Some researchers are looking into more sensitive tests for MRD across a variety of cancers, and the definition of MRD positivity is dependent on the specific test. For example, if one MRD test is only capable of detecting 1 abnormal cell out of 10,000 cells, then it is possible to be “MRD negative” by this test but “MRD positive” by a test that is capable of detecting 1 abnormal cell out of 1,000,000 cells. Therefore, the prognostic impact of MRD should always be considered in the context of the sensitivity of the specific test used.

General MRD Questions

23. If you are a patient and you have an MRD test coming up, what are 3 questions to ask your doctor about MRD testing?

The MRD Testing Collaborative has developed a list of questions about MRD testing that can be helpful as you prepare to meet your doctor and find more about MRD testing.

- [Questions to Ask Your Doctor Worksheet](#)
- [Questions to Ask Your Doctor Reminder Card](#)

24. What is the name of the Next Gen MRD test now approved by the FDA?

clonoSEQ®

25. Please explain clonoSEQ, and who should have it?

clonoSEQ® is the first and only FDA-cleared test that detects, counts, and tracks minimal residual disease (MRD) in blood or bone marrow samples from patients with chronic lymphocytic leukemia (CLL) and bone marrow samples from patients with multiple myeloma or B-cell acute lymphoblastic leukemia (B-ALL). clonoSEQ identifies the specific DNA sequence(s) associated with a patient’s cancer and can detect one single cancer cell among a million healthy cells (provided sufficient sample material). clonoSEQ helps patients and their doctors monitor blood cancer, manage ongoing decisions, and move forward with confidence. For more information please talk with your doctor or visit clonoSEQ.com.

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