CLONOSEQ MRD TESTING IN MULTIPLE MYELOMA: A POTENTIAL CLINICAL PATHWAY

Based on available evidence, the following clinical strategy reflects a potential approach for integrating clonoSEQ® MRD testing into the management of multiple myeloma patients:

Key Takeaways

- Perform Clonality (ID) assessment at time of diagnosis to establish tumor-specific DNA sequences to track; use a fresh or archived marrow sample collected prior to initiation of treatment to enable future MRD assessment.
- Assess MRD in the bone marrow after each treatment stage:[1]
  - Post-induction
  - Post high-dose therapy/ASCT
  - Post-consolidation
  - Post-maintenance
- During maintenance, monitor MRD in the bone marrow at least every 12 months.[1]
- In patients achieving sustained MRD negativity (defined as MRD negativity in the bone marrow at 2 consecutive time points a minimum of 1 year apart), consider whether to discontinue maintenance.[2,3]
- In patients who have discontinued therapy, consider monitoring MRD in the bone marrow at least every 12 months.[1,2]
- Interim peripheral blood MRD assessments* may be useful in certain circumstances.[4]

Other testing approaches may be medically appropriate and final testing decisions should be made by the patient's healthcare provider. The results obtained from the clonoSEQ Assay should always be used in combination with the clinical examination, patient medical history, and other findings.

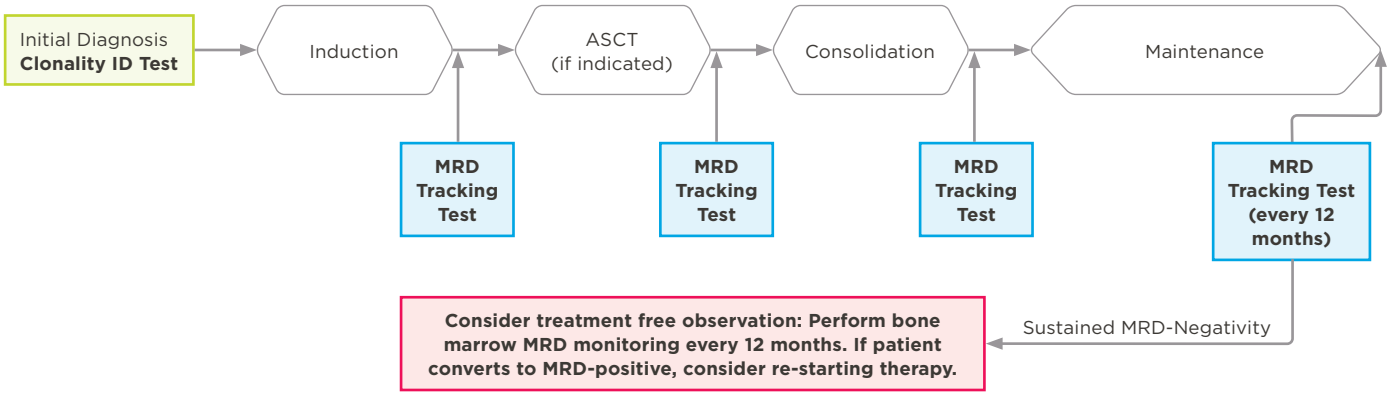
Supporting Data, Guidelines and References

The data generated from the DFCI 10-106 study (NCT01208662) support the importance of serial MRD monitoring in myeloma.[5] See study design below:

MRD assessment time points:

- clonoSEQ MRD monitoring in bone marrow should be performed at baseline, post-induction, 30 days post-transplant (if applicable), post-consolidation, and post-maintenance.[1]
- Subsequent clonoSEQ MRD monitoring should be performed at least every 12 months in the bone marrow.[1] Interim peripheral blood MRD assessments may be useful in certain circumstances.[4]

Multiple Myeloma Patient Pathways (based on DFCI 10-106)[5]



Summary of supporting data:

- MRD is shown to be highly prognostic of patient outcomes (MAIA, CASTOR, POLLUX, IFM2009, Munshi meta-analysis, etc.)[6-10] and has been shown to be more prognostic than standard response measures such as CR and sCR.[11-13]
- Data from the IFM2009 study showed that patients who achieved MRD-negativity had the best outcomes, regardless of whether they received transplant or not.[9]
- Ongoing clinical studies are assessing the feasibility of discontinuing therapy based on MRD status.[2,3] Preliminary data from the MASTER trial (NCT03224507) shows that none of the 40 patients who have discontinued therapy based on MRD negativity have relapsed (follow-up: 0.7 – 15.3 months).[2]
- Serial clonoSEQ MRD monitoring should be performed at least every 12 months in the bone marrow.[1,2] Interim peripheral blood MRD assessments may be useful in certain circumstances.[4]

Summary of guidelines:

- NCCN clinical practice guidelines recommend assessing MRD after each treatment stage: post-induction, post high-dose therapy/ASCT, post-consolidation, post-maintenance.[1]

1. NCCN Clinical Practice Guidelines in Oncology: Multiple Myeloma. Version 4.2021.
2. Costa L et al. EHA 2020. EP928.
3. ClinicalTrials.gov. NCT04071457. Accessed June 2, 2021.
4. Vij R, et al. *Clin Lymphoma Myeloma Leuk*. 2014;14(2):131-139.
5. ClinicalTrials.gov. NCT01208662. Accessed June 2, 2021.
6. Facon T, et al. *N Engl J Med*. 2019;380(22):2104-2115.
7. Mateos M, et al. *Clin Lymphoma Myeloma Leuk*. 2020;20(8):509-518
8. Avet-Loiseau H, et al. *J Clin Oncol*. 2021;39(10):1139-1149.
9. Perrot A, et al. *Blood*. 2018;132(23):2456-2464
10. Munshi N, et al. *Blood* Adv. 2020;4(23):5988-5999.
11. Lahuerta JJ, et al. *Journal of Clinical Oncology*. 2017:JCO2016692517.
12. Cedena MT et al. *PLoS One*. 2020;15(8):e0237155.
13. Avet-Loiseau H et al. ASH 2015. Abstract 191.

clonoSEQ is available as an FDA-cleared *in vitro* diagnostic (IVD) test service provided by Adaptive Biotechnologies to detect minimal residual disease (MRD) in bone marrow from patients with multiple myeloma or B-cell acute lymphoblastic leukemia (B-ALL) and blood or bone marrow from patients with chronic lymphocytic leukemia (CLL). clonoSEQ is also available for use in other lymphoid cancers and specimen types as a CLIA-validated laboratory developed test (LDT). For important information about the FDA-cleared uses of clonoSEQ including test limitations, please visit clonoSEQ.com/technical-summary.

*Blood-based clonoSEQ testing in myeloma is available as a CLIA-validated LDT and has not been cleared or approved by the FDA.

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