CLONOSEQ MRD TESTING IN TRANSPLANT-INELIGIBLE 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 (MM) patients not eligible for hematopoietic cell transplant (HCT):

Key Takeaways

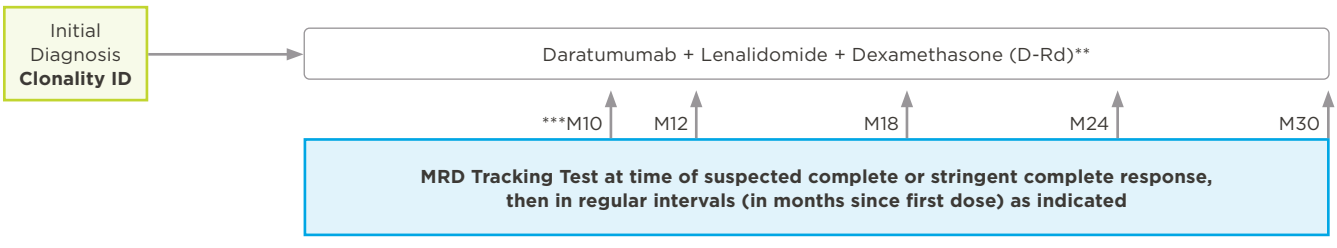
- Perform Clonality (ID) assessment at time of diagnosis to establish tumor-specific DNA sequences to track; use a fresh or archived marrow sample collected prior to initiation of treatment to enable future MRD assessment.[1]
- According to NCCN guidelines, MRD assessment is indicated post-induction and during therapy as needed for prognostication.[1]
- Consider evaluation of minimal residual disease (MRD) via bone marrow aspirate obtained at the time of suspected complete or stringent complete response and at 12, 18, 24, and 30 months after the first dose in patients who had a complete response or better.[2,3]
- 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 MAIA study (NCT02252172) support the important prognostic value of MRD negativity for transplant-ineligible MM.[2] See study design below:

Transplant-Ineligible Multiple Myeloma MRD Patient Pathway (based on the MAIA study)



*Blood-based clonoSEQ testing in myeloma is available as a CLIA-validated LDT and has not been cleared or approved by the FDA.
**Adaptive Biotechnologies does not endorse any particular course of treatment.
***Median time to a CR or better was 10.4 months.

MRD assessment time points:

- In the MAIA study, a large recent trial involving transplant ineligible patients randomized to Rd versus D+Rd, clonoSEQ MRD monitoring in bone marrow was performed at baseline, at time of suspected CR/sCR and at 12, 18, 24 and 30 months post cycle 1 day 1 (+/-1 month) in patients who have a complete response or better.[2,3]
- The median time to a complete response or better In the MAIA study (i.e. time to first MRD assessment) was 10.4 months in the group of patients receiving daratumumab.[2]

Summary of supporting data:

- In patients deemed not suitable for high-dose chemotherapy and ASCT, treatment with multi-agent combinations including bortezomib/ lenalidomide/ dexamethasone (RVd), daratumumab/lenalidomide/dexamethasone (D+Rd), and lenalidomide/low-dose dexamethasone (Rd) are listed as preferred options according to NCCN guidelines.[1]
- In the MAIA study, MRD negativity by NGS ($<10^{-5}$) was associated with significantly longer progression-free survival, irrespective of treatment arm.[2,3]
- In a recent meta-analysis comprised of patients treated with a diverse array of therapeutic regimens, MRD negativity was associated with significantly improved PFS and OS in the transplant-ineligible NDMM subgroup.[5]
- Data from the IFM2009 study showed that patients who achieved MRD-negativity had the best outcomes, regardless of whether they received transplant or not.[6]
- MRD negativity at 10^{-5} sensitivity threshold by NGS is the primary endpoint of the forthcoming CEPHEUS Trial evaluating the efficacy and safety of D-VRd vs VRd alone.[7]

Summary of guidelines:

- NCCN clinical practice guidelines recommend assessing MRD (with a sensitivity of at least 10^{-5}) after each treatment stage: post-induction, post-consolidation, and post-maintenance.[1]
- MRD tests should be initiated only at the time of suspected complete response.[1]
- DNA sequencing assay on bone marrow aspirate should use a validated assay.[1]
- ASCO and CCO Joint Guidelines recommend the goal of initial therapy for transplant-ineligible patients as the achievement of the best quality and depth of remission.[8]

1. NCCN Clinical Practice Guidelines in Oncology: Multiple Myeloma. Version 4.2021.
2. Facon T, et al. *N Engl J Med*. 2019;380(22):2104-2115.
3. Kumar et al. *Blood*. 2020. 136 (Supplement 1): 24–26.
4. Vij R, et al. *Clin Lymphoma Myeloma Leuk*. 2014;14(2):131-139.
5. Munshi NC, et al. *Blood Adv*. 2020;4(23):5988-5999.
6. Perrot A, et al. *Blood*. 2018;132(23):2456-2464.
7. Zweegman S, et al. J Clin Oncol. 2019;37(15_suppl):TPS8056–TPS.
8. Mikhael J, et al. J Clin Oncol. 2019;37(14):1228-1263.

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.

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