CLONOSEQ MRD TESTING AND FIXED-DURATION THERAPY IN CLL: A POTENTIAL CLINICAL PATHWAY

Based on available evidence, the following clinical strategy reflects a potential approach for integrating blood-based clonoSEQ MRD testing into the management of patients with CLL on fixed duration venetoclax-containing* regimens:

Key Takeaways

- Perform clonality (ID) assessment at time of diagnosis to establish patient-specific sequences to track; use a fresh blood or marrow sample collected prior to initiation of treatment.
- Assess MRD at 6 months and 3 months prior to completion of a fixed duration regimen (i.e., at months 6 and 9 of a 12-month regimen).[1]
- Assess MRD at end of therapy (EOT).[1, 2]
- Assess MRD at least once 3 months post-treatment to determine disease kinetics.[1]
- Implement MRD surveillance every 3-6 months thereafter.[1,3,4,5]

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.

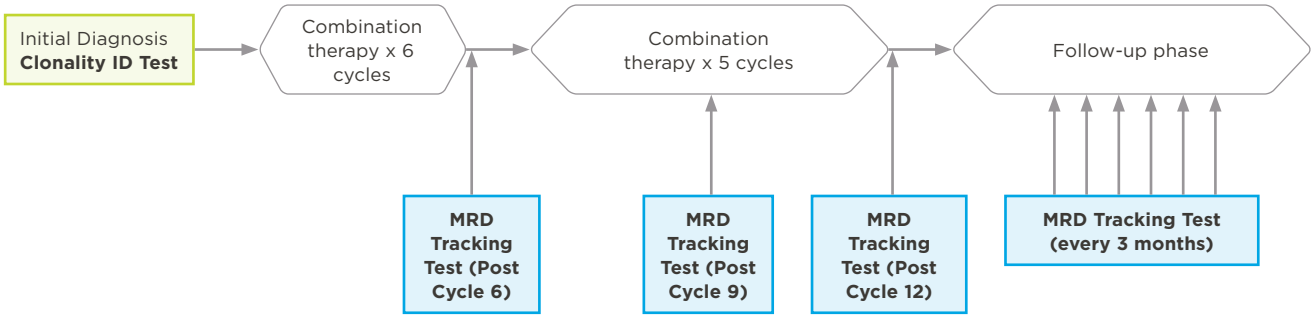
Supporting Data, Guidelines and References

The data generated in CLL14 support the importance of understanding kinetics of response and growth rate at the end of fixed duration therapy.[1] See study design below:

CLL14 assessment timepoints:

- MRD monitoring in peripheral blood was performed at baseline and post-cycles 6, 9, and 12 (end of treatment), and then serially every 3 months.[1,3,4]

CLL MRD Patient Pathways (based on CLL14)



*Adaptive Biotechnologies does not recommend or endorse any particular course of treatment

Summary of supporting data:

- For patients MRD-positive at 10^{-4} at end of therapy (EOT), some have decreasing levels of disease (or evidence of continued response), while others have evidence of increasing tumor growth despite therapy.[3]
- Additionally, understanding growth rate post-therapy was prognostic of relapse.[3]
- For fixed-duration therapies, these data support MRD testing at an interval prior to EOT and at EOT to define response over time, kinetics, and the potential need to modify treatment course.[1,3,4]
- Serial monitoring post-therapy discontinuation can be used to assess for potential molecular relapse.[1,3,4]

Summary of guidelines:

- NCCN Clinical Practice Guidelines state that evidence from clinical trials suggests that undetectable MRD in the peripheral blood after the end of treatment is an important predictor of treatment efficacy.[2]
- In guidelines, response assessment is suggested at least 2 months after completing fixed duration therapy.[6]

1. Al-Sawaf O et al. *Lancet Oncol*. 2020;21(9):1188-1200.
2. NCCN Clinical Practice Guidelines in Oncology: Chronic Lymphocytic Leukemia. Version 4.2021.
3. Al-Sawaf O et al. ASH 2020. Abstract 127. https://ash.confex.com/ash/2020/webprogram/Paper136977.html
4. Al-Sawaf O et al. ASH 2020. Abstract 1310.https://ash.confex.com/ash/2020/webprogram/Paper134865.html
5. ClinicalTrials.gov. NCT04560322. Accessed June 4, 2021.
6. Hallek M, et al. *Blood*. 2018;131(25):2745-2760.

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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