

CHRONIC LYMPHOCYTIC LEUKEMIA

ADULT PATIENT

Highlights

- Post-transplant CLL patient monitored with clonoSEQ Tracking (MRD) Test using peripheral blood samples
- Detectable MRD post-transplant guided use of additional therapy
- Regular MRD testing being used to monitor continued success of treatment

Physician's Perspective*

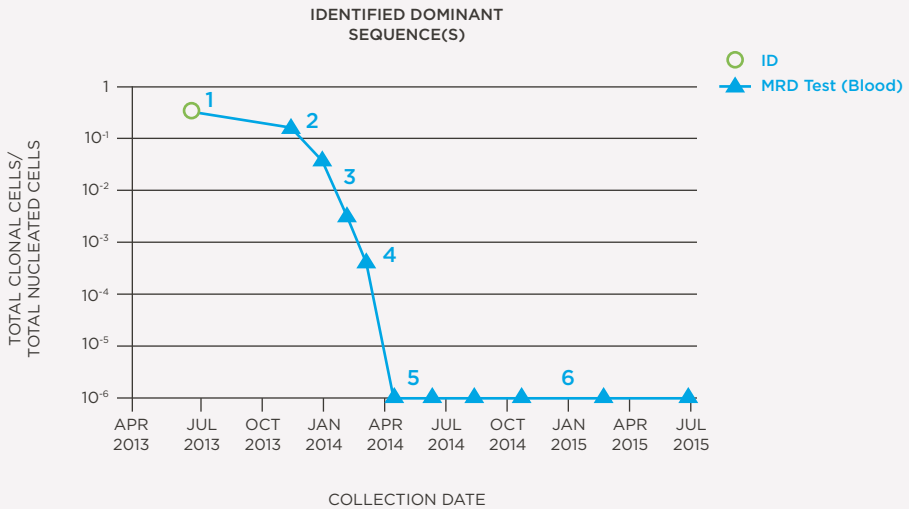
“My general practice is to give a post-transplant patient a year to become U-MRD6. In the case of this patient, however, the disease really didn't seem to be responding to transplant so I decided to act early.¹ Drug treatment with rituximab followed by immunosuppression taper allowed for the graft-versus-leukemia effect to take hold and the patient was able to achieve stable molecular remission.² If the patient's disease should start to go up in the future, I will monitor it closely and consider intervening when it reaches a level of about 10,000 leukemic molecules/million cells.”

Patient History

- Late 60s male with relapsed chronic lymphocytic leukemia (CLL)
- Patient had been under treatment and observation for several years prior to transplant. Based on a variety of factors, the decision to proceed with allogeneic transplant was made.

*Clinician has received equity compensation as a member of Adaptive's Scientific Advisory Board. Clinician's research has also been supported, in part, via product grants.

clonoSEQ is available as an FDA-cleared *in vitro* diagnostic (IVD) test service provided by Adaptive Biotechnologies to detect measurable 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 as a CLIA-validated laboratory developed test (LDT) service. For important information about the FDA-cleared uses of clonoSEQ including test limitations, please visit clonoSEQ.com/technical-summary.



Use of the clonoSEQ Assay

- 1 Physician sent a blood sample for clonoSEQ Clonality (ID) Test in preparation for subsequent peripheral blood MRD monitoring post-transplant.
- 2 Eight-weeks post transplant, the level of disease detectable in the patient's blood remained high. Anti-CD20 therapy with rituximab was initiated.¹
- 3 At six and ten weeks after therapy, a clonoSEQ Tracking (MRD) Test showed a trend in reduction of MRD.
- 4 To further reduce disease levels, immune suppression was tapered to induce graft-versus-leukemia effect.
- 5 clonoSEQ Tracking (MRD) Test did not detect measurable residual disease (MRD) beginning four months after immunosuppression tapering was initiated.
- 6 Subsequent MRD monitoring with the clonoSEQ Tracking (MRD) Test has continued, with samples taken every 2 months for the first six months, and then every four months thereafter. The patient continued to have undetectable MRD (U-MRD6).

Intended Use:

The clonoSEQ Assay is an *in vitro* diagnostic that uses multiplex polymerase chain reaction (PCR) and next-generation sequencing (NGS) to identify and quantify rearranged IgH (VDJ), IgH (DJ), IgK and IgL receptor gene sequences, as well as translocated BCL1/IgH (J) and BCL2/IgH (J) sequences in DNA extracted from bone marrow from patients with B-cell acute lymphoblastic leukemia (ALL) or multiple myeloma (MM), and blood or bone marrow from patients with chronic lymphocytic leukemia (CLL).

The clonoSEQ Assay measures minimal residual disease (MRD) to monitor changes in burden of disease during and after treatment. The test is indicated for use by qualified healthcare professionals in accordance with professional guidelines for clinical decision-making and in conjunction with other clinicopathological features.

The clonoSEQ Assay is a single-site assay performed at Adaptive Biotechnologies Corporation in Seattle, Washington.

Special Conditions for Use:

- For *in vitro* diagnostic use.
- For prescription use only (Rx only).

Limitations:

ALL, MM, and CLL

- MRD values obtained with different assay methods may not be interchangeable due to differences in assay methods and reagent specificity.
- The results obtained from this assay should always be used in combination with the clinical examination, patient medical history, and other findings.
- The clonoSEQ Assay is for use with specimens collected in EDTA tubes.
- Results may vary according to sample time within the course of disease or by sampling site location.
- The assay may overestimate MRD frequencies near the limit of detection (LoD).
- The MRD frequency LoD varies based on the amount of gDNA that is tested and using lower gDNA input may prevent MRD detection at low frequencies.
- Sample processing and cell enrichment strategies may affect the measured MRD frequency.
- The volume and cellularity of sampled input material may affect the ability to detect low levels of disease.
- False positive or false negative results may occur for reasons including, but not limited to: contamination; technical and/or biological factors such as the type of rearrangement or the size of the junction region.
- The assay has been validated with the Illumina NextSeq500 and 550.

For CLL

- MRD is based on measurements of tumor cells detected in peripheral blood and/or bone marrow. However, patients may have significant residual disease in unassessed compartments and U-MRD in one compartment cannot fully rule out the presence of disease in the other compartment, for example, U-MRD in blood may not be the same in bone marrow. Therefore assessment of MRD in CLL should employ a multimodal approach including clinical examination, patient medical history, and other findings.
- Outcome for patients with MRD detectable in bone marrow but not in peripheral blood (PB-/BM+) may differ according to type of therapy.
- This assay is capable of monitoring specific tumor clonotypes. The association between MRD assessments and patient clinical status for the purpose of monitoring changes in disease (e.g., relapse, remission, stable disease) has not been demonstrated.
- The value of MRD in CLL for previously untreated or “watch and wait” patients is not established.
- CLL is a heterogeneous disease. MRD values and expectations for outcome may not be generalizable across treatments. Changes in MRD should be interpreted with caution when used to evaluate disease burden in therapies that have not been validated.
- Regardless of MRD status, cytogenetics play an independent role in patient risk status and its impact on PFS/OS.

Contact Adaptive Clinical Services

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1. Logan AC, et al. *Leukemia*. 2013;27(8):1659-65.
2. Arai S, et al. *Blood*. 2012;119(25):6145-54

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