

clonoSEQ®

**ARE YOU
SEEING THE
FULL PICTURE?**



**The 1st and only FDA-cleared assay to
detect and monitor MRD in patients with
CLL, multiple myeloma, and B-ALL**

MEASURABLE RESIDUAL DISEASE

Complete your patient's clinical picture by tracking measurable residual disease (MRD) at regular timepoints



SENSITIVITY

clonoSEQ can detect a single cancer cell among 1 million cells (given sufficient sample input). Measuring MRD at such deep sensitivity offers prognostic value to clinicians as they assess how patients respond to treatment.^{1,6}

SPECIFICITY

clonoSEQ identifies and tracks individual cancer cells, thus enabling clinicians to gain a more precise understanding of disease burden over time.^{1,6}

STANDARDIZATION

clonoSEQ has undergone extensive analytical and clinical validation, fulfilling the requirements for FDA clearance for in vitro diagnostic use.^{1,6} clonoSEQ meets the high bar for standardization required by cooperative research groups and drug developers, while also enhancing clinical patient management.

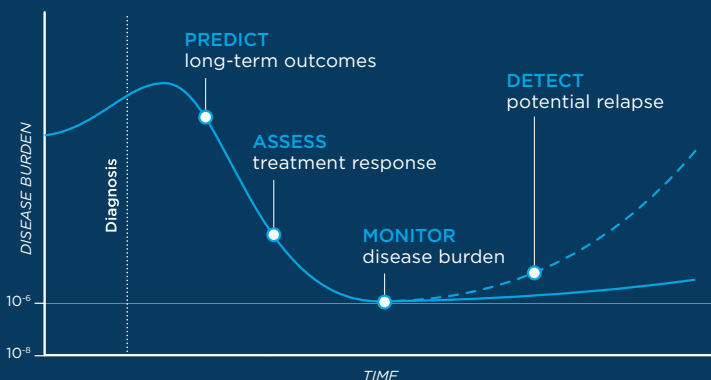
THE POWER OF MRD TESTING

Measurable (or minimal) residual disease (MRD) refers to the small number of cancer cells that can remain in a patient's body during and after treatment and may eventually cause disease recurrence. These residual cells typically cause no physical signs or symptoms and are present at such low levels that more sensitive techniques are required to identify them.

Studies have demonstrated the strong correlation between MRD and risk of recurrence, as well as the prognostic significance of MRD measurements during and after therapy.¹ Monitoring MRD at various points throughout the course of treatment and remission provides important insight into the status of a patient's disease and can help guide clinicians in developing personalized treatment approaches. Serial MRD assessment can help clinicians predict patient outcomes, assess response to therapy, monitor disease burden, and detect potential relapse.¹

BENEFITS OF NGS MRD TESTING WITH CLONOSEQ

- MRD results help predict long-term patient outcomes¹
- Precise quantification of MRD enables accurate assessment of response to therapy¹
- Deep sensitivity enables timely patient management decisions





The 1st and only FDA-cleared assay to detect and monitor MRD in patients with CLL, multiple myeloma, and B-ALL

- MRD detection at a level of one cell in 1 million*
- Enhanced clinical insight with limited sample input material
- Accuracy and reproducibility to inform patient care
- Currently utilized for MRD testing by 30 out of 30 of National Comprehensive Cancer Network® (NCCN®) Member Institutions

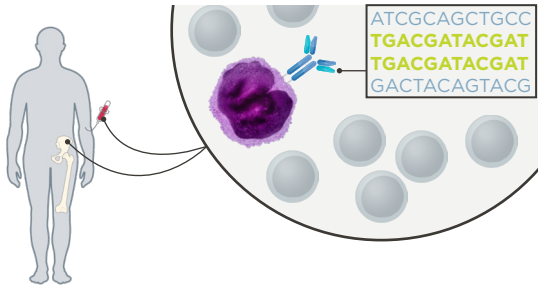
The clonoSEQ® Assay is an accurate, sensitive, and standardized method of assessing MRD in bone marrow samples from patients with B-cell acute lymphoblastic leukemia (ALL) or multiple myeloma, and blood or bone marrow from patients with chronic lymphocytic leukemia (CLL). The assay identifies the unique molecular signature of malignant lymphoid cells, which can be quantified and tracked over time. clonoSEQ leverages the power of next-generation sequencing (NGS) to accurately and reliably assess how disease burden changes over time in response to treatment or during remission.¹

Clinical practice guidelines in hematological malignancies recognize that MRD status is a reliable indicator of clinical outcome and response to therapy. In **acute lymphoblastic leukemia** (ALL), MRD assessment has been established as an essential component in clinical management. Guidelines recommend MRD assessment, by methods including NGS, to occur upon completion of initial induction and at additional time points based on the regimen used.²

In **multiple myeloma**, MRD assessment by methods including NGS is recommended in guidelines after each treatment stage (e.g., after induction, high-dose therapy/ASCT, consolidation, maintenance). MRD tests can also be initiated at the time of suspected complete response.³

In **chronic lymphocytic leukemia**, clinical practice guidelines recommend the complete eradication of disease as a treatment goal and include MRD assessment in blood or bone marrow using a technology with high sensitivity.^{4,5}

How the clonoSEQ Assay works



Clonality (ID) Test

Identifies the patient's unique cancer DNA sequence(s)

clonoSEQ identifies the dominant DNA sequence(s) associated with malignancy in a high disease load bone marrow or blood sample from the patient's initial diagnostic work-up.¹

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ATCGCAGCTGCCATCGCAGCTGCCTCGCAGCTGCATCGCAA
TGACGATACGATTGACGATACGATTGACGATACGATTGACG
TGACGATACGATTGACGATACGATTGACGATACGATTGACG
TGACGATACGATTGACGATACGATTGACGATACGATTGACG
GACTACAGTACGGACTACAGTACGGACTACAGTACGGACTA
GCATCGCAAACGCATCAGCATCGAGGCATAGCCATCAGCAT
CGCTACGTCAGCAGCATCGACGATGCAGCATCAGGCATCAG
```

- Required once for new patients to enable disease tracking
- Identifies trackable dominant sequences in most patients
- Does not require patient-specific customization

Tracking (MRD) Test

Use the sequence(s) identified by the Clonality (ID) Test to measure and track MRD

clonoSEQ tracks the patient-specific dominant DNA sequence(s) in follow-up samples to assess how disease burden has changed. The assay also identifies and reports any newly emerging sequences of interest.¹

- Tracks changes in disease burden over time
- Can be performed at any point during or after treatment or while a patient is in remission

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.

Subsequent Tracking (MRD) Reports measure the presence of each tracked sequence and identify newly emerging sequences of interest. Each report includes previously identified and tracked sequences, resulting in a visual representation of disease burden over time that can be easily shared with patients and clinical staff.



Ordering the clonoSEQ Assay

Online order completion

Enables patient data to be stored securely and accessed for future orders, eliminating the need for repetitive data entry.

Automated order verification

Ensures your order includes all the required information, reducing the likelihood of follow-up calls or processing delays.

Shipping materials provided

Upon request, we can provide kits to help you collect and ship fresh and frozen specimens.

Rapid, actionable results

Delivered in approximately 7 days (fresh specimens) or 14 days (archived specimens) from the date of sample receipt and reconciliation.

Secure report access

View and search results for all of your patients through our secure online Diagnostics Portal, or choose to receive secure fax reports.

Adaptive's Clinical Services team is ready to assist you with ordering clonoSEQ at (888) 552-8988.

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.

1. clonoSEQ®. [technical summary]. Seattle, WA: Adaptive Biotechnologies Corporation; 2020.;
2. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Acute Lymphoblastic Leukemia V.1.2020. © National Comprehensive Cancer Network, Inc. 2020. All rights reserved. Accessed [February 19, 2020]. To view the most recent and complete version of the guideline, go online to NCCN.org.; 3. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Multiple Myeloma V.2.2020. © National Comprehensive Cancer Network, Inc. 2020. All rights reserved. Accessed [February 19, 2020]. To view the most recent and complete version of the guideline, go online to NCCN.org.; 4. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Chronic Lymphocytic Leukemia/Small Lymphocytic Leukemia V.4.2020. © National Comprehensive Cancer Network, Inc. 2020. All rights reserved. Accessed [February 19, 2020]. To view the most recent and complete version of the guideline, go online to NCCN.org.; 5. Hallek, M., et al. *Blood*. 2018, 131(25):2745-2760.; 6. Ching T, et al. *BMC Cancer*. 2020;20:612.

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