clonoSEQ®
By Adaptive

Blood cancer care is always advancing. Aim higher with clonoSEQ.

All 31 NCCN® Member Institutions use clonoSEQ to track minimal residual disease (MRD) at a sensitivity of 1 cancer cell in 1 million healthy cells.[1,2*] Use clonoSEQ in routine clinical practice to help predict patient outcomes and support treatment decisions in lymphoid malignancies.[3-9]

JOIN THE MOVEMENT AND DETECT DEEPER

*Given adequate sample material.

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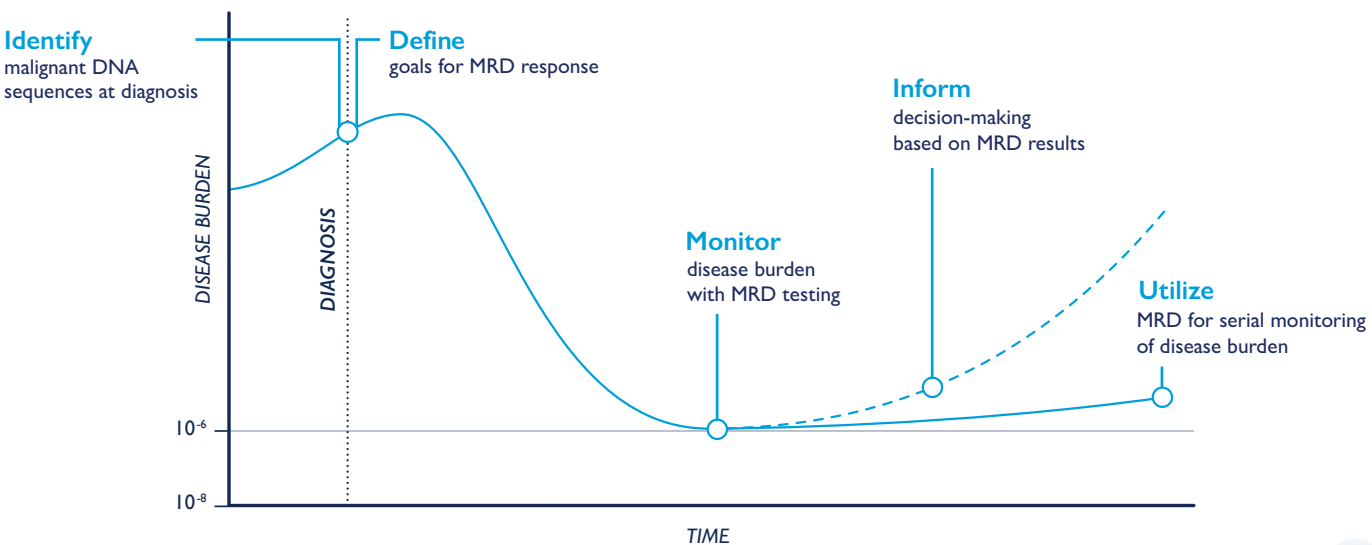
Aim higher in lymphoid cancer management

Why use MRD to assess disease burden?[1,7-10]

- MRD is the number of cancer cells that can remain in the body during and after treatment
- These very low levels of cancer cells do not cause symptoms
- MRD is shown to be highly prognostic of outcomes in multiple myeloma, CLL, and B-ALL

How leading cancer centers use MRD



Aim higher than complete response

Why MRD matters

Treatments are constantly advancing

Today's treatment regimens are driving deeper responses than ever in lymphoid malignancies[8,11,12]

Complete response may not be all that complete

Newer therapies are helping more patients achieve a complete response (CR), but most of these patients will eventually relapse[5,13-15]

MRD can help standardize assessment

The difference between complete response and outcomes illuminates the need to enhance traditional assessment techniques with sensitive tools like clonoSEQ MRD testing[15-17]

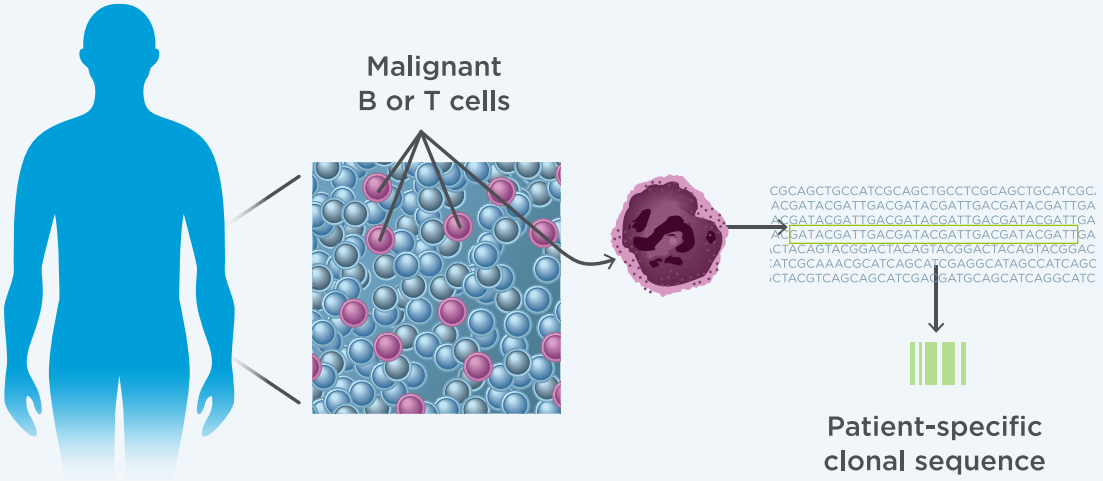
Physician's Perspective

"The disconnection between CR and long-term efficacy suggests that persistent disease remains undetected, and measuring deeper responses is necessary to predict and improve long-term outcomes."[12]

Dr. Avet-Loiseau

Aim higher with state-of-the-art technology

How clonoSEQ works



clonoSEQ identifies the dominant DNA sequence(s) associated with malignancy in a high disease burden sample from the patient's diagnosis or relapse, generating MRD results that are a direct measure of the tumor, not a surrogate of disease.[1,10]

clonoSEQ technology allows you to detect MRD at a sensitivity of 10^{-6}, **identifying 1 cancer cell in a million healthy cells.**[1*]

*Given adequate sample material.
BCR, B-cell receptor; TCR, T-cell receptor.

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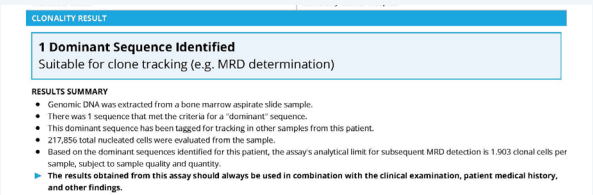
Aim higher throughout treatment and beyond

The clonoSEQ report

Clonality (ID) Report


CLONALITY RESULT

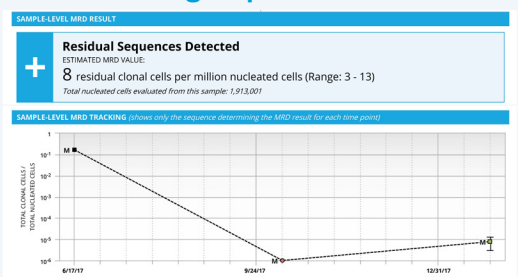
1 Dominant Sequence Identified
Suitable for clone tracking (e.g. MRD determination)

RESULTS SUMMARY

- Genomic DNA was extracted from a bone marrow aspirate slide sample.
- There was 1 sequence that met the criteria for a "dominant" sequence.
- This dominant sequence has been tagged for tracking in other samples from this patient.
- 217,856 total nucleated cells were evaluated from the sample.
- Based on the dominant sequences identified for this patient, the assay's analytical limit for subsequent MRD detection is 1.903 clonal cells per sample, subject to sample quality and quantity.
- **The results obtained from this assay should always be used in combination with the clinical examination, patient medical history, and other findings.**

- Identifies dominant sequences related to the patient's cancer and is required for subsequent MRD tracking[1]
- Uses a high disease burden bone marrow/blood sample from a specimen obtained at diagnosis or relapse[1]
- For CLL patients, IGHV mutation status is included in the Clonality (ID) report (not pictured)*

MRD Tracking Report



- Visually tracks patient-specific dominant DNA sequences identified by the Clonality (ID) test and detects any newly emerging sequences[1]
- Detects changes in disease burden over time[1]
- Supports routine MRD monitoring throughout treatment and into remission

*IGHV testing is available as a CLIA-validated LDT and has not been cleared or approved by the FDA.
IGHV, immunoglobulin heavy chain variable region.

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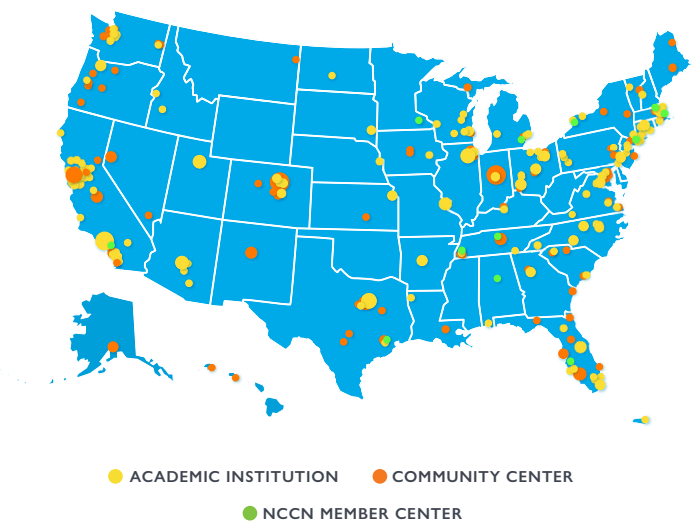
Aim higher and join other leading cancer centers

The clonoSEQ community



Hundreds of centers routinely use clonoSEQ to measure MRD in lymphoid malignancies[2]:

- >20,000 unique patients tested
- All 31 NCCN® Member Institutions currently testing in clinical practice
- >90 peer-reviewed publications
- Test of choice for >40 biopharma companies in >190 clinical trials

Scan to view case studies and insights on how top clinicians use clonoSEQ to elevate patient care

Aim higher with sensitive MRD detection

Why choose clonoSEQ?

Sensitivity

Detect MRD at low levels that correlate with patient outcomes, helping to avoid false positives[1,10*]

Specificity

Precisely identify and quantify tracked malignant cells, helping to remove subjectivity from your assessment of disease burden[1]

Standardization

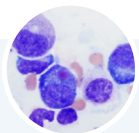
Ensure consistency and reproducibility of results across patients and over time[10]

clonoSEQ is the first and only FDA-cleared assay to detect MRD in multiple myeloma, CLL, and B-ALL

*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.

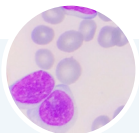
Aim higher in routine multiple myeloma and CLL care

Why so many clinicians use clonoSEQ



Multiple myeloma

- Clinical studies indicate that MRD negativity with clonoSEQ was the **strongest predictor** of progression-free survival (PFS) (vs traditional risk factors like cytogenetics and staging at diagnosis)[18]
- Patients who **intensified or changed therapy** based on MRD-positive results experienced significantly better PFS than those who did not[7]
- MRD testing is **recommended by clinical practice guidelines** at multiple times during and after treatment[19]

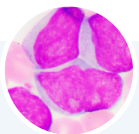


Chronic lymphocytic leukemia (CLL)

- clonoSEQ can identify IGHV mutation status, an **important prognostic indicator** in CLL[20,21]
- clonoSEQ MRD has been shown to sensitively measure the deep responses achievable with many current therapies and was **highly predictive of outcomes** regardless of sample type (blood or bone marrow)[1,11,22]
- Studies have shown that serial MRD testing during and after treatment can identify **MRD relapse kinetics**[9,23]

Aim higher in routine ALL care

Why so many clinicians use clonoSEQ



Pediatric acute lymphoblastic leukemia (ALL)

- MRD assessment is **recommended by clinical practice guidelines**, making it an essential component of patient evaluation over the course of sequential therapy[24]
- clonoSEQ provided **greater prognostic and predictive value** vs multiparameter flow cytometry (MFC)[25]
- MRD detection with clonoSEQ was shown to be predictive of outcomes in both **pre- and post-transplant patients**[25]

Adult acute lymphoblastic leukemia (ALL)

- clonoSEQ provided **greater prognostic value** than flow; 17 out of 25 patients who were MRD negative by MFC had residual disease by clonoSEQ and experienced poorer survival[26]
- clonoSEQ MRD status based on bone marrow and peripheral blood samples was **highly concordant**[27*]
- Supporting clinical practice guidelines, studies have demonstrated the **prognostic significance of MRD** measurements during and after induction therapy[28]

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

We aim higher for patients

Adaptive Assist Patient Support Program

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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 (eg, 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.

IGHV

- CLL Clonality (ID) Tests will also produce an IGHV status result, which is provided as a CLIA-validated laboratory developed test (LDT) but which has not been cleared or approved by the FDA.

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Aim higher in everyday lymphoid cancer care

The value of MRD: Today's treatment regimens are driving deeper responses than ever in lymphoid malignancies, reinforcing the need for sensitive assessment with tools like clonoSEQ® MRD testing.[5,8,11-17]

The power of clonoSEQ: With a sensitivity of 10^{-6}, clonoSEQ can precisely detect remaining cancer cells to help inform clinical decision-making.[1]*

The application in care: clonoSEQ is the first and only FDA-cleared assay to detect MRD in multiple myeloma, CLL, and B-ALL, and is included in clinical practice guidelines.[18,21,23,27]

The support for practices: Adaptive offers streamlined ordering, Adaptive Assist™, clinical consultations, pathways, and case studies.

LEARN MORE ABOUT ELEVATING MRD ASSESSMENT IN YOUR PRACTICE AT clonoSEQ.com/AimHigher

*Given adequate sample material.

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