



**REVEAL
PREVIOUSLY
UNSEEN
DISEASE
WITH
CLONOSEQ**

clonoSEQ®
amplify answers™

What gets measured gets managed™

clonoSEQ®

DISEASE BURDEN

JAN

APR

JUL

OCT

DEC

SENSITIVITY

clonoSEQ detects measurable residual disease (MRD) at the level of a single cancer cell among a million cells.⁴ The assay provides a continuous measure of MRD, with its sensitivity limited only by the amount of DNA analyzed.¹ Measuring MRD at such low levels offers prognostic value to clinicians as they assess how patients respond to treatment.¹

SPECIFICITY

clonoSEQ enables identification and tracking of individual cancer cells. Once the DNA sequences associated with these cancer cells are identified, the presence of each specific sequence can be assessed in subsequent MRD samples, enabling clinicians to gain a more precise understanding of disease burden over time.^{1,4}

STANDARDIZATION

clonoSEQ has undergone extensive analytical and clinical validation, fulfilling the defined requirements for regulatory review.¹ The consistency demonstrated in these validation studies meets the high bar for standardization required by cooperative groups and drug developers, while also enhancing patient management in the clinic.

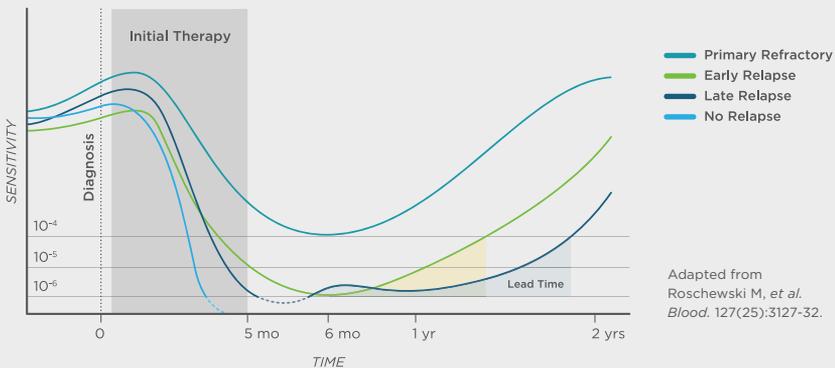
THE POWER OF MRD TESTING

Measurable (or minimal) residual disease (MRD) refers to the small number of cancer cells that can remain in a patient's body after treatment and may be early indicators of disease recurrence. These residual cells are present at such low levels that they typically cause no signs and symptoms, and more refined and sensitive techniques are required to identify them.⁴

In cancer treatment, MRD testing using next-generation DNA sequencing (NGS) is an effective way to determine how treatment has impacted disease burden.⁴ MRD can help clinicians assess response to therapy, monitor the durability of response,⁵ and it may be an early indicator of recurring disease.⁶ MRD assessment is also being used to inform drug development and as an endpoint in multiple clinical trials.

KEY ADVANTAGES OF NGS MRD ASSESSMENT

- Adds unprecedented insight for understanding response to therapy
- Goes beyond a simple “Yes/No” MRD result by quantifying residual disease levels
- Assesses the presence of malignant cells at levels below the detection limit of conventional cytomorphological methods, enabling more timely decisions about how and when to intervene⁴



The clonoSEQ Assay

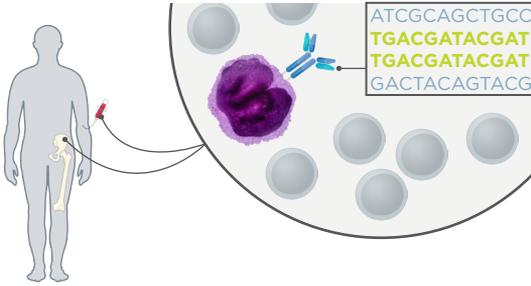
- **Deep sensitivity enabling MRD assessment in blood or marrow**
- **Enhanced clinical insight with limited input material**
- **Precision and reproducibility clinicians can trust**
- **Clinically validated in multiple myeloma and acute lymphoblastic leukemia (ALL)**

The clonoSEQ Assay is a highly accurate and sensitive method of assessing MRD in lymphoid malignancies. The assay was specifically designed to identify the unique molecular signature of malignant lymphoid cells which can be quantified and tracked throughout the course of treatment. clonoSEQ leverages NGS and groundbreaking advances in chemistry and bioinformatics to identify and track individual cancer cells with a sensitivity limited only by the amount of DNA analyzed.¹

Clinical Practice Guidelines recommend assessing MRD after each stage of treatment for multiple myeloma (MM)—following induction, prior to high-dose therapy or autologous stem cell transplant, following consolidation, and during maintenance (at times of suspected complete response).^{2,3} In a growing number of lymphoid malignancies, MRD is becoming an essential metric to inform and enhance treatment decisions at multiple points throughout treatment. Clinicians and drug developers alike look to the clonoSEQ Assay as a new accepted standard to assess MRD status.

[Learn more at clonoSEQ.com/doctors](https://clonoSEQ.com/doctors)

How the clonoSEQ Assay works*



Step 1: Clonality (ID) Test

Identify the patient's unique cancer

DNA sequence(s)

The clinician provides a high disease load sample (blood or bone marrow) from the patient's initial diagnostic work-up. The clonoSEQ Assay identifies the dominant DNA sequence(s) that are typically associated with malignancy.¹

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

```
ATCGCAGCTGCCATCGCAGCTGCCTCGCAGCTGCATCGCAA
TGACGATACGATTGACGATACGATTGACGATACGATTGACG
TGACGATACGATTGACGATACGATTGACGATACGATTGACG
TGACGATACGATTGACGATACGATTGACGATACGATTGACG
GACTACAGTACGGACTACAGTACGGACTACAGTACGGACTA
GCATCGCAAACGCATCAGCATCGAGGCATAGCCATCAGCAT
CGCTACGTCAGCAGCATCGACGATGCAGCATCAGGCATCAG
GCATCGCAAACGCATCAGCATCGAGGCATAGCCATCAGCAT
AAATCGCATCGTACGATCGACTACGATCGAGACTCAGCAG
```

Step 2: Tracking (MRD) Test

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

The clonoSEQ Assay tracks the patient's identified dominant DNA sequence(s) in blood or bone marrow samples—taken during or after treatment—to assess how disease burden has changed. The assay also identifies any newly emerging sequences of interest.¹

- Tracks changes in disease burden over time
- Enables monitoring in blood, potentially reducing the need for invasive bone marrow biopsies or radiation exposure from CT scans

*The clonoSEQ Assay is regulated under CLIA and has not been cleared or approved by the FDA. The assay should only be used taking into account all available information and should not be used as the sole determinant to guide patient care.

Enhancing treatment decisions**

clonoSEQ reports are provided in a simple and clear format allowing clinicians to identify and track throughout treatment specific DNA sequences associated with malignancy.

CLONALITY (ID) REPORT

CLONALITY RESULT

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

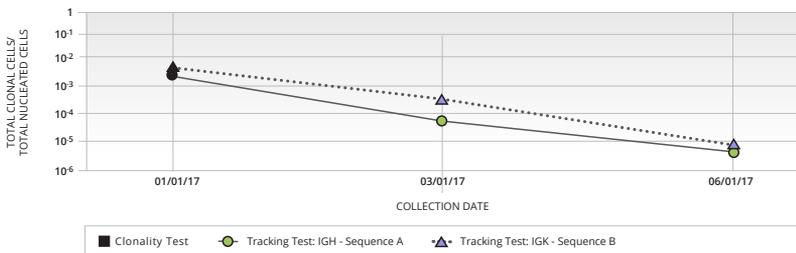
RESULTS SUMMARY

- Genomic DNA was extracted from a bone marrow sample.
- There were two sequences identified that met the criteria for a "dominant" sequence.
- These sequences have been tagged for tracking in other samples from this patient.
- This is consistent with a lymphoid selection, expansion, or hyperproliferation.
- ▶ **The test result should only be used taking into account all available clinical information and should not be used as the sole determinant to guide patient care and management.**

The Clonality (ID) Report provides an overview of the dominant lymphocyte sequences (associated with malignancy) that were identified in a patient's immune repertoire.¹

TRACKING (MRD) REPORT

IDENTIFIED DOMINANT SEQUENCE(S)



The number of clonal cells may vary by sample type. As such, changes in clonal cell values over time are best compared using the same sample type.

Subsequent Tracking (MRD) Reports measure the presence of each tracked clone and identify newly emerging clones of interest. Each report includes previously identified and tracked clones, resulting in a visual representation of disease burden over time that can be easily communicated to patients and clinical staff.¹

**Assay limitations include false positive or false negative results that may occur for reasons including, but not limited to: sample mix up; misidentification; technical and/or biological factors.



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 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

Actionable results—delivered within 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 the secure clonoSEQ Portal, or receive secure fax reports

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

1. Data on file.
2. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology [NCCN Guidelines®] for Multiple Myeloma V.3.2017. Accessed November 1, 2017.*
3. Kumar S, et al. *Lancet Oncol.* 2016; 17(8):e328-46.
4. Sherrod AM, et al. *Bone Marrow Transplantation.* 2015; 51:2-12.
5. Martinez-Lopez J, et al. *Blood.* 2014; 123(20):3073-3079.
6. Takamatsu H, et al. *Ann of Oncol.* 2017; 28(10):250-2510.

*NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way.