ACUTE LYMPHOBLASTIC LEUKEMIA

PEDIATRIC PATIENT

Highlights

- clonoSEQ Tracking (MRD) testing revealed early signs of relapse post-transplant.
- Physician had opportunity to prepare options for follow-up treatment, allowing him to act quickly once relapse was confirmed.

Actual results may vary. Limited to one patient case.

clonoSEQ®

Physician's Perspective*

"When a patient has morphologic relapse, you feel anxious and need to act. Knowing that a patient is relapsing by detecting disease at a much lower level gives us a window of time to prepare instead of having to act immediately when a kid comes in with packed marrow and a fever.

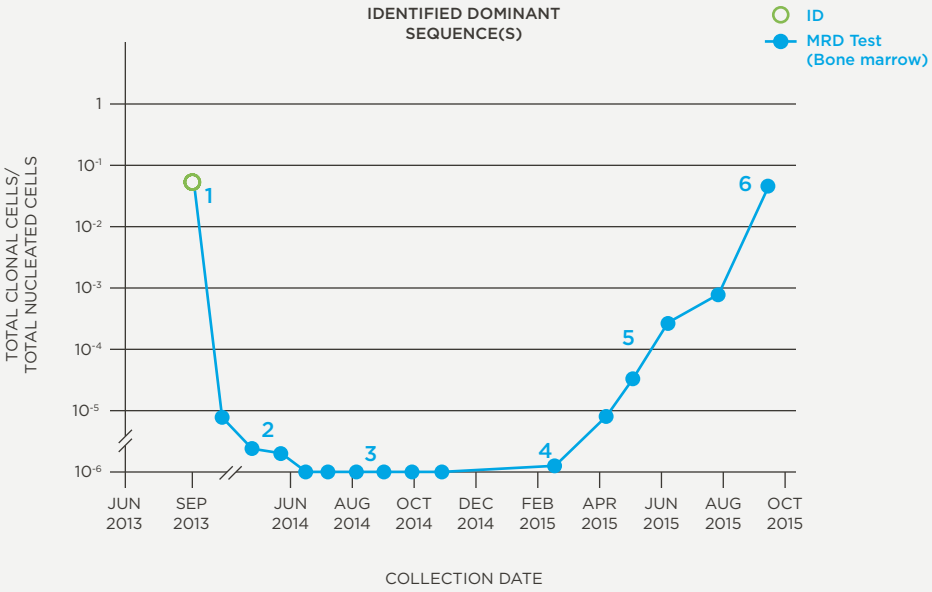
Once a positive MRD test comes back, I increase the frequency of testing in order to stay on top of disease. In the case of this patient, upon the first positive MRD test, we banked T cells in case the patient was eligible for an immunotherapy trial. Once he relapsed, I enrolled him immediately in a CAR-T trial, and since that treatment two years ago he has been in remission.

People say that there is no advantage to detecting disease earlier, but that's changing. We have new transplant modalities, immunotherapies like blinatumumab, and many CAR trials available, so detecting disease early may be advantageous to the patient."

Patient History

- Pre-adolescent male diagnosed with B-acute lymphoblastic leukemia
- Decision to proceed to allotransplant was made after low-level MRD remained following several rounds of chemotherapy
- Patient received unrelated donor transplant in early 2014. Patient's chimerism was dropping post-transplant but patient remained MRD-negative by flow. NGS detected MRD+ in April 2015. Five months later, MRD+ detected was by flow
- Patient recurred in September 2015 and was enrolled in CAR-T therapy trial in November 2015

***Clinician has received compensation to participate in advisory meetings sponsored by Adaptive. Clinician's research has also been supported, in part, via product grants.**



Use of the clonoSEQ Assay

1. Physician ordered Clonality (ID) test so that he would have freedom to use clonoSEQ MRD testing in the future if desired.
2. MRD was detectable at 30, 60 and 90 days post-transplant.
3. The patient was clonoSEQ MRD-negative in the bone marrow at 4, 5, 6, 7, 8, and 9 months post-transplant.
4. One year post-transplant, MRD was detected by clonoSEQ (1 leukemic molecule / million cells). The patient remained MRD-negative by flow. Assessment of chimerism revealed that patient had lost his graft.
5. Physician made decision to conduct monthly clonoSEQ MRD evaluation. The patient's MRD continued to rise month-over-month. Options for further treatment discussed; decision made to bank T cells for potential CAR-T treatment.
6. MRD continued to increase, and morphologic relapse was observed (7 months after initial positive MRD test). Patient received CAR-T therapy in November 2015 as part of a trial and has been in remission for 2 years.

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 or multiple myeloma.

clonoSEQ 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.

clonoSEQ is a single-site assay performed at Adaptive Biotechnologies.

Special Conditions for Use:
- For *in vitro* diagnostic use.
- For prescription use only (Rx only).

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

For important information about the FDA-cleared uses of clonoSEQ, including test limitations, visit clonoSEQ.com/technical-summary.

Contact Adaptive Clinical Services
(888) 552 8988
clinicalservices@adaptivebiotech.com