ACUTE LYMPHOBLASTIC LEUKEMIA

ADULT PATIENT

Highlights

- Sensitivity of clonoSEQ MRD Assay allowed for early detection of relapse in post-transplant adult ALL patient
- Physician began preparations for patient enrollment in CAR-T clinical trial

Actual results may vary. Limited to one patient case.

clonoSEQ®

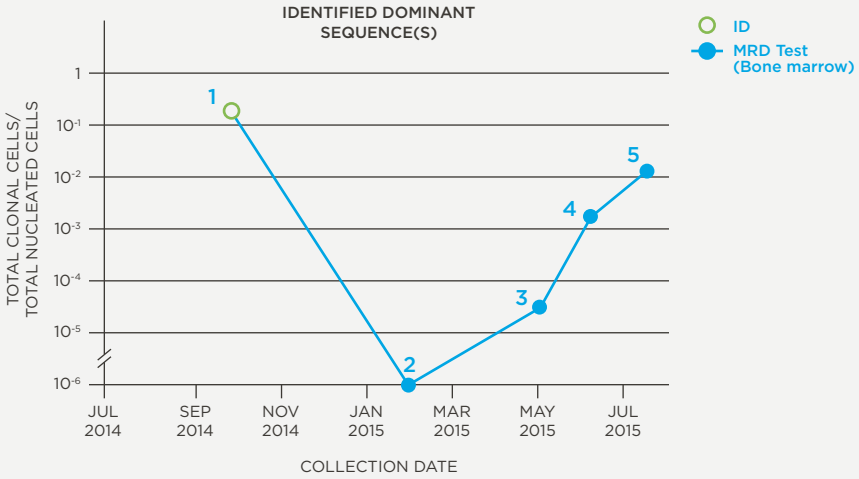
Physician's Perspective*

"When we rely on morphology alone, we are often surprised when a patient's bone marrow looks beautiful at day 180 post-transplant and then six months later they show up with circulating blasts. For this patient, the sensitivity of the clonoSEQ MRD Assay allowed for early disease detection, providing me with time to prepare my patient and his other doctors for what would come next, which in this case was enrollment in a CAR-T cell clinical trial. When the follow-up MRD test came back positive and at a higher level (time-point 4), everything was already in place. My patient was able to move on to his next treatment while still relatively healthy and he was pleased that the latest technologies were guiding his treatment."

Patient History

- Late 30s male with no medical history diagnosed with precursor B-ALL (normal cytogenetics) in June 2014
- No significant bone marrow response seen after initial induction (on day 14) or extended induction (day 28)
- Refractory to salvage therapy with morphologic disease persisting in bone marrow, so referred for allo-transplant
- Disease burden too high for immediate transplant, so patient was enrolled in a clinical trial of a CD22-targeted antibody drug conjugate
- After one cycle of trial therapy patient was in morphological remission but with MRD detected by flow cytometry at 10^{-3}, so decision was made to proceed to transplant
- Unrelated donor, ablative transplant carried out November 2014

***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. Transplant physician sent bone marrow sample for clonoSEQ Clonality (ID) Test before patient was enrolled in clinical trial so that clonoSEQ MRD tracking could be carried out post-transplant.
2. 80 days post-transplant, patient's bone marrow sample showed no evidence of disease by morphology or standard flow cytometry. Blood counts were normal and MRD was undetectable by clonoSEQ.
3. 170 days post-transplant, patient's bone marrow sample showed no evidence of disease by morphology or standard flow cytometry, but MRD was detected by clonoSEQ. Based on this result, immunosuppression was tapered off.
4. 210 days post-transplant, patient's bone marrow sample showed no evidence of disease by morphology or standard flow cytometry, but MRD was again detected by clonoSEQ, this time at a higher level.
5. The patient's MRD level continued to rise, confirming that the patient was proceeding to clinical relapse and supporting decision to enroll in a CAR-T clinical trial. At 250 days post-transplant, increased disease burden as assessed by clonoSEQ was also detected for the first time by flow cytometry.

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.

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