MULTIPLE MYELOMA

ADULT PATIENT

Highlights

- Standard-risk myeloma patient in sCR following autologous stem cell transplant
- Patient entered maintenance protocol but discontinued maintenance due to toxicity
- clonoSEQ Tracking (MRD) Test revealed early signs of relapse 3 years post-transplant
- Clinical relapse observed 6 months after initial MRD-positive clonoSEQ test result

Actual results may vary. Limited to one patient case.

clonoSEQ®

Physician's Perspective*

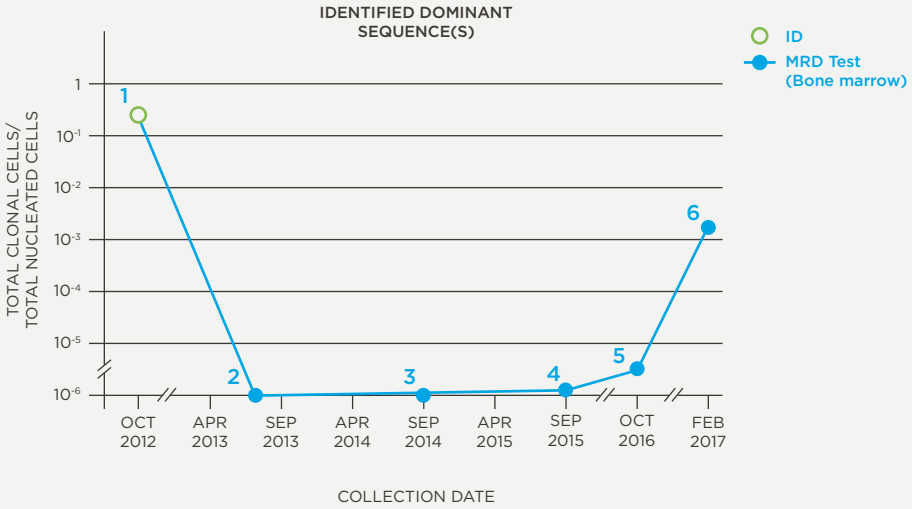
"It's clear you can say that an MRD-negative result in a low-risk patient bodes well. What you don't know is if continuing maintenance will change anything. In this case, the patient was standard-risk and wasn't tolerating maintenance well, I used the MRD-negative clonoSEQ result to justify stopping therapy. I then continued to follow MRD, hoping to use it as an early indicator of relapse. When I saw that first low-level MRD+ result, I wasn't ready to treat, but I did decide to see him more frequently and the relapse occurred very quickly thereafter.

You never know how fast people are going to progress. The problem is that if someone has a very low MRD level, the disease could progress quickly or it could take a year before it becomes anything. The same is true with a small rise in an M-spike, though. In that case, we might see the patient sooner, get a PET scan sooner, and generally be more vigilant about monitoring to see if the disease is coming back. I use an MRD-positive clonoSEQ result in the same way."

Patient History

- Late 50s male diagnosed with multiple myeloma with standard-risk features
- Achieved stringent CR following hyper-CVAD and RVD induction regimen and proceeded to autologous stem cell transplant
- Post-transplant, received 4 cycles of RVD consolidation therapy and began monitoring residual disease via clonoSEQ
- Initiated on lenalidomide maintenance protocol, but developed pancytopenia after one year and discontinued maintenance
- Patient eventually progressed to clinical relapse 2.5 years after maintenance was discontinued

***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. clonoSEQ Clonality (ID) test performed on high-disease load bone marrow sample (collected at diagnosis in October 2012) to identify sequences for subsequent measurable residual disease (MRD) testing.
2. clonoSEQ Tracking (MRD) Test results from a sample collected in July 2013 during post-transplant consolidation therapy found no evidence of residual disease in the bone marrow.
3. clonoSEQ Tracking (MRD) test in September 2014 showed continued MRD negativity, so maintenance was discontinued and patient's MRD was tracked using clonoSEQ on an ongoing basis.
4. During routine clonoSEQ testing two years later in August 2016, a low level of residual disease (9 residual cells per million) was detected. Patient was otherwise in sCR.
5. MRD levels continued to rise; the frequency of testing was increased from one year to every six months.
6. Clinical relapse was observed six months after initial MRD-positive clonoSEQ result.

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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