ACUTE LYMPHOBLASTIC LEUKEMIA

YOUNG ADULT PATIENT

Highlights

- clonoSEQ Tracking (MRD) Testing in the peripheral blood revealed early signs of relapse post-transplant
- Patient achieved remission after CAR-T trial
- Patient continues to be monitored for MRD with peripheral blood samples

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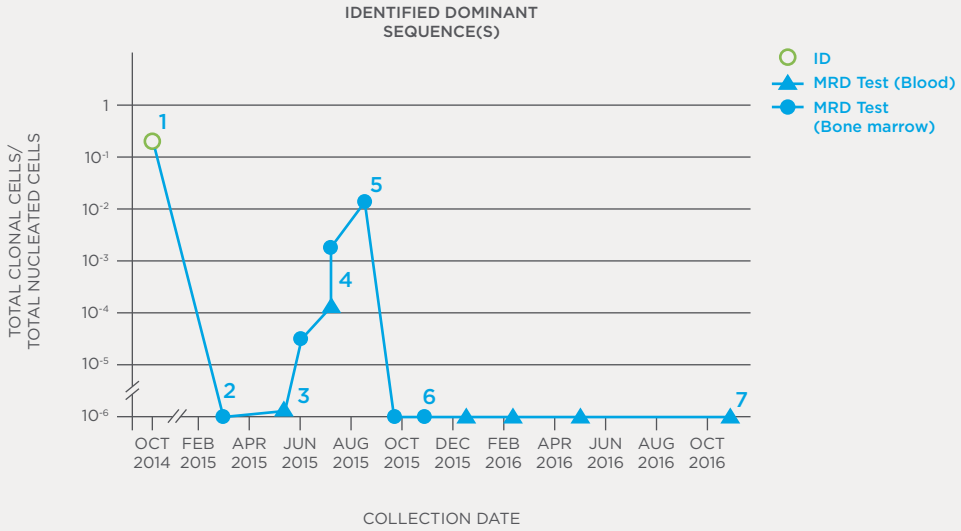
Physician's Perspective*

"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, so post-transplant, it is my standard of care to assess the patient's MRD by clonoSEQ. This patient was MRD-positive in the peripheral blood 6 months post-transplant. MRD continued to rise in additional follow-up assessments in the peripheral blood and bone marrow. It is important to note that during this 3-month period of positive clonoSEQ (MRD) Tracking Test results, the patient was flow cytometry MRD-negative. As we could identify the impending relapse early based on the rising trend in MRD, I decided to refer the patient for the trial. I continue to monitor the patient's MRD in the peripheral blood about every 2-3 months."



Patient History

- Late-30s female with ALL diagnosed 9 months post-partum
- Refractory to Hyper-CVAD + Linker regimen
- Received allogenic transplant in late 2014
- Post-transplant flow cytometry results were MRD-negative for an additional three months while clonoSEQ peripheral blood and bone marrow results were MRD-positive
- Patient could enroll in CAR-T trial as the relapse was detected early and the patient still met the study eligibility criteria

Use of the clonoSEQ Assay**

1. Transplant physician sent bone marrow sample for clonoSEQ (ID) Test so that clonoSEQ (MRD) Tracking could be carried out post-transplant.
2. Day 90 post-transplant, the patient was MRD-negative by clonoSEQ.
3. 3 months later, the clonoSEQ (MRD) Tracking Test revealed the presence of measurable residual disease (MRD).
4. Repeat peripheral blood and bone marrow clonoSEQ results were MRD-positive. During this time, the patient was MRD-negative by flow cytometry.
5. Patient enrolled in CAR-T study.
6. Post-CART therapy, the patient was MRD-negative in the bone marrow.
7. The patient continues to be monitored by clonoSEQ Tracking (MRD) Test in the peripheral blood every 2-3 months, and is MRD-negative as of the latest assessment.

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

**Results may vary. clonoSEQ results 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.

ACUTE LYMPHOBLASTIC LEUKEMIA

YOUNG ADULT PATIENT

Highlights

- Post-transplant clonoSEQ Tracking (MRD) Testing revealed measurable residual disease (MRD); flow cytometry results did not detect measurable residual disease
- MRD continued to decline until patient became MRD-negative
- Patient continues to be monitored for MRD with peripheral blood samples

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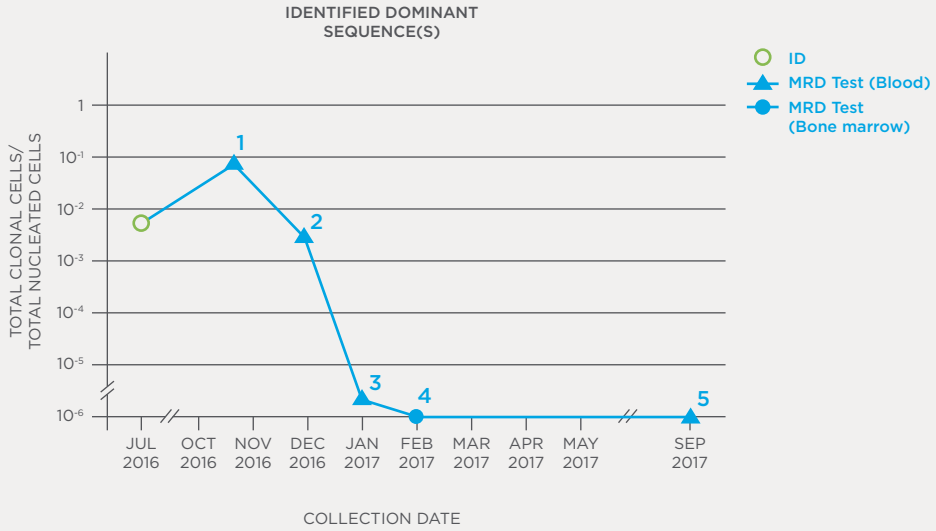
Physician's Perspective*

"This patient was told that he was MRD-negative in the bone marrow by flow cytometry when he was referred to me for transplant. My standard of care is to take a peripheral blood clonoSEQ Tracking (MRD) test prior to transplant. This test showed that the patient was MRD-positive. My experience is that patients who are MRD-negative prior to transplant have better outcomes post-transplant."



Patient History

- Mid-30s male with ALL
- Patient received pediatric induction regimen followed by consolidation therapy
- Pre-transplant flow cytometry MRD was negative and clonoSEQ Tracking (MRD) Test was MRD-positive. Patient received allogenic stem cell transplant
- Immunosuppression therapy was discontinued post-transplant
- Patient continues to be monitored by clonoSEQ Tracking (MRD) Tests with peripheral blood samples

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Use of the clonoSEQ Assay**

1. Prior to transplant, the patient was MRD-negative in the bone marrow by flow cytometry. The patient was MRD-positive in the peripheral blood by clonoSEQ. The patient then received an ASCT in November 2016.
2. Day 28 post-transplant, the patient continued to have a high level of MRD present in the peripheral blood. Due to this, immunosuppression was discontinued.
3. Day 60 post-transplant, the clonoSEQ (MRD) Tracking Test detected only 1 malignant cell in 1,000,000 total nucleated cells.
4. To confirm response in the bone marrow, MRD was assessed by clonoSEQ Day 90 post-transplant. The result was MRD-negative.
5. MRD will continued to be monitored by the clonoSEQ Tracking (MRD) Test in the peripheral blood. About 11 months post-transplant, the patient continues to be MRD-negative in the peripheral blood.

ACUTE LYMPHOBLASTIC LEUKEMIA

ADULT PATIENT

Highlights

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

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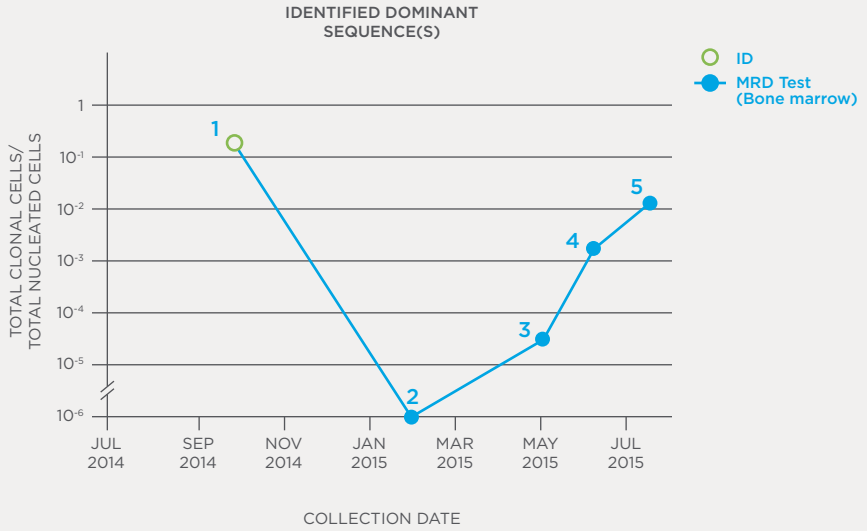
Physician's Perspective*

"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 Test 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

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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 showed no evidence of disease by morphology or flow cytometry. Blood counts were normal and MRD was undetectable by clonoSEQ.
3. 170 days post-transplant, patient's bone marrow 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 showed no evidence of disease by morphology or standard flow cytometry, but MRD 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.

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.

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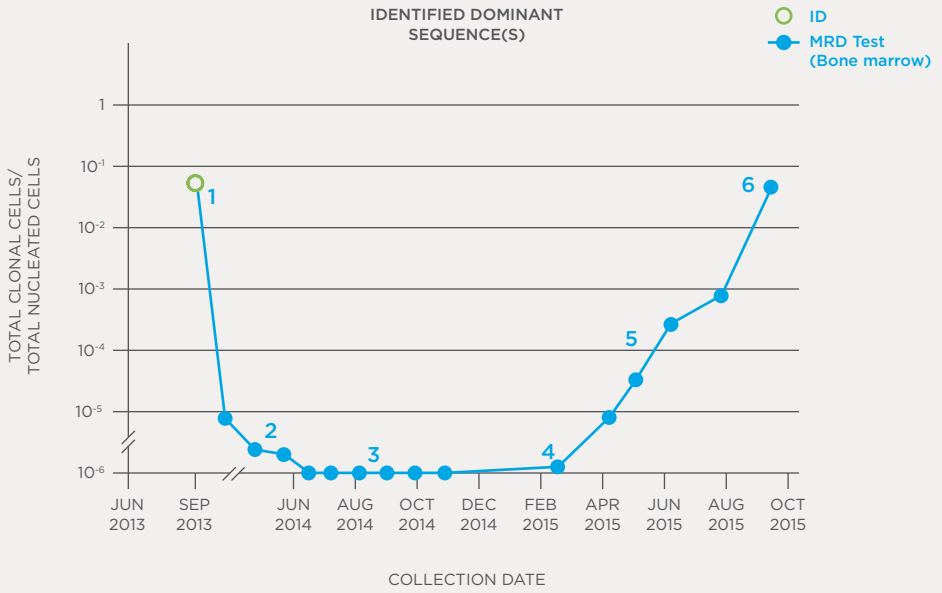
Physician's Perspective*

"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 by flow
- Patient recurred in September 2015 and was enrolled in CAR-T therapy trial in November 2015

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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.

Learn more at clonoSEQ.com

Contact Adaptive Clinical Services
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The clonoSEQ Assay is regulated under CLIA and has not been cleared or approved by the FDA. clonoSEQ should only be used taking into account all available clinical information.

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