

TALKING WITH YOUR PATIENT ABOUT CLONOSEQ MRD RESULTS

Many clonoSEQ® patients find it informative to review and discuss their clonoSEQ MRD results with their clinician. Below are some common questions that patients may ask about their clonoSEQ results. As with any test, clonoSEQ MRD results should always be interpreted by a medical professional.

My clonoSEQ result says “[n] residual clonal cells per million nucleated cells”. What does that mean?

All clonoSEQ MRD results are expressed as a number out of 1 million. You can think of it as the number of cancer cells present out of 1 million total cells from the sample that was analyzed.

Because clonoSEQ reports MRD results this same way every time, the numerical MRD values can be compared from one testing time point to another. This allows you to directly observe changes and trends in your disease level over time.

The actual number of cells analyzed in your sample may be higher or lower than 1 million. You can tell how many cells were actually analyzed from this particular sample by looking in the Results Summary on page 1 of the clonoSEQ report.

If my clonoSEQ MRD result is zero, does that mean my cancer is gone?

A clonoSEQ MRD result of zero means that within the sample that was tested, there was no evidence of disease. clonoSEQ is a very sensitive test so, in general, this result is a good sign that any remaining disease is likely to be limited.^{1,2} However, it does not necessarily mean that your cancer is completely gone.

While testing a bone marrow (or blood) sample is a very useful way to get an understanding of how much cancer remains in your body, the sample tested may not always represent the complete picture of your disease. This is one reason why continuing to monitor your MRD over time can be useful.

My MRD went up [or down] vs. the last time I was tested. How confident can I be that this is a real increase [decrease]? What does it mean?

clonoSEQ results have been demonstrated to be highly accurate, but all tests have some variation associated when reporting quantitative values.^{1,2}

One way that we can know if a change in MRD level is “real” is by looking at the range (also called a confidence interval) provided in the clonoSEQ report for each of the two results that are being compared. For example, if your current MRD value is higher than your previous MRD value and the ranges (confidence intervals) do not overlap, then we can assume that the current result represents a true increase in your tumor level.

When comparing two MRD results, it is important to confirm that the results are generated from the same type of sample (e.g., two bone marrow samples or two blood samples).

More generally, the clinical significance of any change in MRD may depend on many factors, including how much the MRD level changed and how fast that change happened. It’s important that you consider any change in your MRD level along with other signs and symptoms we are following and also put the result in the context of your specific treatment plans and goals.

My MRD went down vs. the last time I was tested, but it was still detectable. What does this tell me about my prognosis?

In general, studies have shown that patient outcomes are better when the trend in tumor burden is decreasing rather than increasing.^{3,4}

Assuming that we are comparing two MRD results generated using the same sample type (e.g., two bone marrow samples or two blood samples), if your current MRD value is lower than your previous MRD value and the ranges (confidence intervals) do not overlap, then we can assume that the current result represents a true decrease in your disease level.

A decrease in MRD may be an indication that your treatment plan has been working. How we interpret your specific level of remaining disease depends on when the test was done, what treatment(s) you have received and where you are in your treatment course. It also depends on the number of cells that were tested as well as the type of sample. We (your doctor and care team) will determine what is the right path forward for you based on consideration of your MRD trend as well as other signs and symptoms we are following, with your specific treatment goals and plans in mind.

My clonoSEQ result says “[n] per million” but then it says that <1M cells were assessed...what does that mean for my result?

The actual number of cells analyzed in your sample may be higher or lower than 1 million; we can tell how many cells were analyzed from this particular sample by looking in the Results Summary on page 1 of the clonoSEQ report.

If <1 million cells were analyzed, we can look at the range (also known as a confidence interval) that is provided in the report to understand how much possible variability there was in the result. In general, the more cells that are analyzed by the clonoSEQ test, the smaller the possible range around your test result will be.

How do I know when my MRD should be tested again?

Knowing your current MRD status can be useful as a way to get an up-to-date assessment of your level of disease and to help you plan for what may be ahead. To see how MRD is changing over the course of treatment or during remission, you can be periodically re-tested.

There are some guidelines that doctors can reference which have been developed by national or international medical organizations which suggest time points when MRD assessment may be useful.⁵⁻⁹

In general, how often to test MRD is a decision that is customized for each patient. Insurance companies that cover clonoSEQ usually leave it up to clinicians to decide what is the right frequency to test. We (your doctor and care team) will determine the right frequency for testing your MRD based on your past MRD results as well as other signs and symptoms we are following, and with your specific treatment goals and plans in mind.

1. clonoSEQ®. [technical summary]. Seattle, WA: Adaptive Biotechnologies Corporation; 2020.
2. Ching T, et al. *BMC Cancer*. 2020;20:612.
3. Martinez-Lopez J, et al. *Blood Advances*. 2020;4:14.
4. Wood B, et al. *Blood*. 2018;131(12):1350-1359.
5. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Multiple Myeloma V.1.2021.
6. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Acute Lymphoblastic Leukemia V.1.2020.
7. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Chronic Lymphocytic Leukemia V.4.2020.
8. Kumar S, et al. *Lancet Oncol*. 2016;17(8):e328-46.
9. Hallek M, et al. *Blood*. 2018;131(25):2745-2760.

clonoSEQ is available as an FDA-cleared *in vitro* diagnostic (IVD) test service provided by Adaptive Biotechnologies to detect measurable residual disease (MRD) in bone marrow from patients with multiple myeloma or B-cell acute lymphoblastic leukemia (B-ALL) and blood or bone marrow from patients with chronic lymphocytic leukemia (CLL). clonoSEQ is also available for use in other lymphoid cancers as a CLIA-validated laboratory developed test (LDT) service. For important information about the FDA-cleared uses of clonoSEQ including test limitations, please visit clonoSEQ.com/technical-summary.