**Eytan M. Stein, MD**
Assistant Attending Physician
Director, Program for Drug Development in Leukemia
Leukemia Service, Department of Medicine
Memorial Sloan Kettering Cancer Center
New York, New York

**How does the concept of measurable residual disease (MRD) apply to therapy today and moving forward?**

Measurable residual disease (MRD) is defined as the presence of leukemic blasts at a threshold less than 5% of marrow cellularity. The presence of MRD following intensive induction chemotherapy typically translates to poorer outcomes in the post-transplant setting. Therefore, MRD negativity is often a goal of therapy. The concept of MRD is perplexing in practice because 1) we have yet to determine the optimal way to achieve MRD negativity, and 2) some patients who are MRD positive will become MRD negative without further therapy. The randomized QUAZAR AML-001 study provided some insight.[1] In this study, patients received either oral azacitidine or placebo. What is interesting in the trial is that nearly 20% of patients in the placebo arm converted from MRD positivity to MRD negativity without any further therapy. This is likely the result of the timing of MRD measurement, wherein patients progressing towards MRD negativity were simply measured too early.

A third conundrum is that about 30% of patients who are MRD negative prior to transplant will relapse in the post-transplant setting and, likewise, about 30% of patients who are positive prior to transplant will not relapse after transplant. This demonstrates that the positive predictive value of our current approach to MRD testing is lacking. Clearly, we are in need of improved MRD testing to more accurately identify residual leukemic cells. We also need improved understanding of the kinetics of MRD and how MRD status changes in patients, as well as well-designed trials to determine if elimination of MRD actually translates into a survival benefit.

***For more information on the treatment landscape in AML, please view the full newsletter by clicking here.*** (https://managingaml.com/ce-education/46-surveying-the-treatment-landscape-therapeutic-advancements-affecting-treatment-decisions-in-aml)

**Reference:**

1. Wei AH, Döhner H, Pocock C, et al. Oral azacitidine maintenance therapy for acute myeloid leukemia in first remission. *N Engl J Med.* 2020;383(26):2526-2573.