Introduction to the Series on Measurable Residual Disease

Jerry Radich

Fred Hutchinson Cancer Center, Seattle, WA, USA

Correspondence: J. Radich
jradich@fredhutch.org

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Measurable residual disease (MRD) is playing an increasingly important role in the management of patients with hematologic malignancies. The detection of MRD, be it by flow cytometry or genetic assays, is associated with an increased risk of relapse in myeloid and lymphoid malignancies, and MRD is now being used to determine treatment strategies during therapy and is being explored as an endpoint in phase II clinical trials.

Across many diseases and studies, the association of MRD with outcomes (relapse and survival) is remarkably consistent, despite differences of therapy, time-points at which it is measured, populations (pediatric *vs*. adults) or methods being used to measure MRD. However, there are many other features of MRD that need to be explored.

First, there are several methodological questions. Do some of the newer genetic approaches (next-generation sequencing, droplet digital polymerase chain reaction) predict outcome better than other standard approaches (flow cytometry)? Does increased sensitivity necessarily make for a better MRD assay (as with increasing sensitivity, most patients may have residual disease, yet not relapse). With better assays, can we move from the painful and costly bone marrow biopsy to peripheral blood testing (*à la* chronic myeloid leukemia)?

Second there are biological questions, as MRD is not just a measure of disease burden, it is also a measure of disease biology. Why do some patients easily achieve an MRD-negative state, while others do not? Why do some patients with residual disease not relapse, while some without MRD, do relapse? With the advent of single-cell genotyping, can we determine now which gene mutation(s) in which cell subtype influence MRD and relapse?

Lastly, there are clinical questions. How do we best use MRD to guide therapy? Does changing therapy based on MRD really affect the outcome? Can we eventually use MRD as an early endpoint for clinical trials? And, if so, will it be better to use MRD as a smart, quantitative variable rather than a dumb, categorical variable?

Given its increasing importance in clinical and research applications, we have decided to give MRD our full attention with reviews of MRD in acute lymphoblastic leukemia, acute myeloid leukemia, chronic myeloid leukemia, chronic lymphocytic leukemia, and myeloma. In this issue we start with acute lymphoblastic leukemia, acute myeloid leukemia, and chronic myeloid leukemia;[1-3] chronic lymphocytic leukemia and myeloma will soon follow. We have asked experts in the field to create succinct, interesting, informative and entertaining reviews, guided by the principle of producing a work that they themselves would want to read. Once the series has been completed, I will end with a summary and a look forward.

We at *Haematologica* hope that you enjoy the series and, as always, we welcome your comments and suggestions.

Disclosures

No conflicts of interest to disclose.

References

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