Clinical Value of Flow Cytometry MRD Testing

The objectives of treating cancer patients are to reduce/minimize the tumor burden and then hopefully go further and obtain a remission of the disease. For hematologic malignancies, post-treatment, if there is any remaining (residual) cancer cells in the body, they can become active, proliferate, and relapse the disease in patients. MRD detection is an indicator that the treating treatment was not completely effective or that the treatment was inadequate and needs to continue longer. MRD may also be an indication that all cancer cells did not respond to the given therapy or that malignant cells have become resistant to the anti-cancer therapies used. When a treated patient tests MRD negative (absence of residual cancer cells), this outcome is predictive of long remission periods and prolonged survival rates. MRD testing provides great clinical value by acting as a gauge to direct cancer treatments and to provide better patient care.

Unlike solid tumors, blood cancers such as multiple myeloma (MM), chronic lymphocytic leukemia (CLL), acute lymphoblastic leukemia (ALL) and acute myeloid leukemia (AML) can be monitored by measuring the presence and frequency of cancerous cells in the peripheral blood or bone marrow. Well-established MRD flow cytometry panels have been used universally and extensively to allows for statistically relevant, confident identification of clusters of at least fifty events at the lowest sensitivity threshold. It should be noted that a cluster containing as few as ten events with a clearly aberrant immunophenotype may be sufficient for confident MRD assessment for Multiple Myeloma at multiple time points following treatment.

MRD-based risk groups. There are several well-established MRD flow panels that have been used extensively by NeoGenomics to detect and measure the presence of malignant cells at low frequency. The expression of several cell surface markers can easily be monitored by flow cytometry in CLL, MM, and B-cell Precursor ALL patients. In addition to its prognostic/diagnostic relevance, recent guidelines of the FDA is starting to pay attention the use of MRD testing as a predictive biomarker/endpoint for novel cancer drug development. NeoGenomics’ flow cytometry MRD results have provided great clinical value to the pharmaceutical industry in the development of new and improved cancer therapies.

Flow Cytometry MRD Panels

Multiple myeloma (IMM) MRD Panel

CD45, C100, C20D, C27D, C38D, CD45, C56D, CD81, CD117, CD138, Ckappa, and Lamba

This IMM MRD panel has been shown to detect MRD in patients with previously diagnosed and treated multiple myeloma. The limit of detection is 0.001%.

Chronic lymphocytic leukemia (CLL) MRD Panel

CD45, CD3, CD5, CD19, CD202, (or RORC), CD43, CD79b, CD10

This CLL MRD panel follows the strategy developed by the European Research initiative in CLL (ERIC) and can detect MRD at the 0.01% level. This examination has become increasingly important as specific CLL treatments improve. Detecting MRD above 0.01% is reported to be an independent predictor of progression-free survival and overall survival in CLL patients treated with chemoimmunotherapy. The prognostic value of achieving MRD-negative status with other CLL therapies is under investigation in clinical trials.

B-Cell/B-precursor Acute Lymphoblastic Leukemia (B-ALL) MRD Panel

CD45, CD3, CD9, CD10, CD19, CD20, CD34, CD38, CD56, CD103/CD33, CD71, Sylven

This B-ALL MRD panel follows the strategy developed by the Children’s Oncology Group (COG) and can detect MRD at the 0.01% level. The B-ALL MRD is highly predictive of relapse in patients treated for acute lymphoblastic leukemia.

Conclusion

The evolution of regulatory science to allow innovative approaches, such as MRD, to the development of new therapeutic treatments for hematologic malignancies could expedite approval of drugs that could potentially improve patient outcomes. Incorporation of MRD into clinical trial evaluation protocols in which sequential analysis can be performed may determine the efficacy of novel investigational drugs earlier by acting as a surrogates biomarker of patient outcome and endpoint in clinical trials and have substantial clinical and regulatory advantages. Since MRD measures tumor burden at levels that are undetectable through conventional lab techniques, it can also potentially act as a clinical and regulatory endpoint, which supports use in future clinical trials as well as for clinical decision making. NeoGenomics’ flow cytometry MRD data provides unparalleled level of expertise, service, flexibility, and scalability. The data shown and generated by NeoGenomics displays the quality and utility of MRD analysis in the context of patient monitoring.

Ongoing and future clinical trials will continue to evaluate the definition and the role of MRD in treatment decision-making. On the one hand, the achievement of an MRD-negative status does not necessarily mean that treatment should be stopped, questioning whether it is necessary to change treatment or dosage, improving the depth of response. However, before developing new and or escalating of current strategies based on MRD status, other information such as on positive patients or de-escalating treatment for MRD-negative patients, we need to determine if sustained MRD negativity should be viewed as the goal of any treatment. Continued use of MRD as a biomarker in clinical trials will provide information that will help define the most appropriate time point for its evaluation as a clinical endpoint.

References