Managing Myeloma

How do we define minimal residual disease and what is its significance in clinical practice?

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Welcome to *Managing Myeloma*. I am Dr. Faith Davies and today I would like to discuss how we define minimal residual disease and its significance in clinical practice. With many of the new treatment approaches, we are able to achieve complete response in a high percentage of patients. That would mean no evidence of an M-component, normalization of serum-free light chains, and no evidence of malignant plasma cells on morphology in the bone marrow. That has really meant that we have been able to develop more sensitive techniques to detect low levels of disease. These techniques include things like flow cytometry as well as next-generation sequencing techniques to detect MRD on the molecular level. Both of these technologies have some positive points as well as some drawbacks. The important thing for a practicing physician is to know the sensitivity of the test; not just to be able to say whether the patient is MRD negative or positive, but to say what level the patient has their MRD at, be that one tumor cell in 10^4 normal cells or one tumor cell in 10^6 normal cells.

As far as the practicalities of these technologies, we know that patients who are MRD negative have a prolonged progression-free and overall survival. Certainly it should be something that we are trying to aim for when we are treating our patients. There is now plenty of data to suggest that this prognostic evidence is not only present in newly diagnosed patients but also relapsed patients and patients treated with some of the more novel therapies such as antibodies. It is also important for patients with high risk cytogenetics; in that group of patients, if a patient is MRD positive and has high risk cytogenetics, those patients have a particularly poor outcome.

Some of the outstanding questions, though, are from a very practical basis. If a patient remains MRD positive, should we be thinking about intensifying treatment? If a patient is MRD negative, should we think about stopping treatment? Then there are simple things like when is the best time to test for MRD; and is one MRD test enough or do we need to do a number of tests to confirm that the patient is in sustained MRD? At the moment, there is a lot of research going on in this area, and there are a lot of groups coming together involving both industry, academia, as well as some of the regulatory groups and patient groups trying to get some consensus on how we should think about this moving forward.

Thank you for spending some time with me today and I hope you enjoyed viewing this activity.