Detection of micrometastatic disease in bone marrow: is it ready for prime time?

Minimal residual disease (MRD), or isolated tumor cells (ITCs) in bone marrow, may be the source of potentially fatal overt distant metastases in solid tumors even years after primary treatment. MRD can be detected by immunohistochemical methods using antibodies directed against cytokeratins or cell-surface markers or molecular, polymerase chain reaction-based techniques. Among solid tumors, the clinical relevance of MRD has been most extensively studied in breast cancer patients. Recently, the highest level of evidence for the prognostic impact of MRD in primary breast cancer was reached by a pooled analysis comprising more than 4,000 patients, showing poor outcome in patients with MRD at primary therapy. Yet the clinical application of MRD detection is hampered by the lack of a standardized detection assay. Moreover, clinical trial results demonstrating the benefit of a therapeutic intervention determined by bone marrow status are still absent. Recent results suggest that, in addition to its prognostic impact, MRD can be used for therapy monitoring or as a potential therapeutic target after phenotyping of the tumor cells. Persistent MRD after primary treatment may lead to an indication for extended adjuvant therapy. However, until clinically relevant data regarding successful therapy of MRD are available, treatment interventions on the basis of MRD should only be performed within clinical trials.