Immunophenotyping in multiple myeloma: Patients without minimal residual disease live longer

The diagnostic significance of minimal residual disease (MRD) in patients with multiple myeloma has been examined in numerous studies and is the subject of much controversial discussion. Existing data has to date been extremely heterogeneous with regard to patient collectives, therapies, number of cases, and the methodology via which MRD was detected. However, since the presentation of the meta-analysis by Munshi et al. (JAMA Oncol 2017), it can be considered as proven that MRD negativity after first-line therapy is one of the strongest surrogate markers for prolonged overall survival. MLL offers MRD testing for myeloma patients using both blood and bone marrow, allowing sensitivity of 10-5 to be achieved, which was set as the standard by the International Myeloma Working Group (IMWG).

In the meta-analysis by Munshi et al., 21 studies were included in which patients with newly diagnosed multiple myeloma were treated and the MRD status was examined. The effect of the MRD status on progression-free (PFS) and overall survival (OS) was analyzed. 14 studies with 1,278 patients contained data on PFS and 12 studies with 1,100 patients on OS. MRD-negative patients had a significantly better PFS (Hazard Ratio [HR]: 0.41; p < 0.001) and OS (HR: 0.57; p < 0.001) than patients with MRD. The median MRD-negative patient lived for 54 months without progression, while the figure for MRD-positive patients was just 26 months. The median OS was 98 months without and 82 months with MRD.

Even in patients who achieve a complete response (CR), the MRD status is still a clearly discriminating parameter: In these patients, a positive MRD status also equates to a shorter PFS (HR: 0.44; p < 0.001) and a shorter OS (HR: 0.47; p < 0.001) than in those with a negative MRD status. The median MRD-negative patient with a complete response lived for 56 months without renewed progression, while this value was 34 months for MRD-positive patients. The median OS was 112 months without and 82 months with MRD.

Correspondingly, in numerous recent clinical (avada) studies the MRD status was implemented as a secondary end point which is inherently available significantly more rapidly than PFS and OS data. Even the detection of a CR according to the criteria of the IMWG is often only possible significantly after achieving MRD-negativity due to the long half-life period of the clonal immunoglobulins in the serum.

The detection of circulating plasma cells in peripheral blood before therapy or after performing an autologous stem cell transplant is also significantly associated with the prognosis of multiple myeloma. For example, Chakrabartty et al. (Haematologica 2017) showed that the PFS and OS for patients in which circulating plasma cells were detected neither before nor after therapy was significantly longer (5-year OS 83% vs. 43%, p < 0.001). Furthermore, this also has the advantage that the testing can be performed independently of the quality and quantity of a bone marrow aspirate.

MLL offers immunophenotyping tests utilizing both peripheral blood as well as bone marrow for patients with multiple myeloma, whereby a sensitivity of 10-5 (one myeloma cell among 10,000 cells) can be guaranteed. These tests therefore fulfill the strict criteria prescribed by the IMWG.

Literatur