Abstract

Purpose: The detection of minimal residual disease (MRD) in patients with acute myeloid leukemia (AML) may improve future risk-adapted treatment strategies. We assessed whether MRD-positive and MRD-negative patients with AML benefit differently from the graft-versus-leukemia effect of allogeneic hematopoietic stem-cell transplantation (alloHSCT).

Methods: A total of 1,511 patients were treated in subsequent Dutch-Belgian Hemato-Oncology Cooperative Group and the Swiss Group for Clinical Cancer Research AML trials, of whom 547 obtained a first complete remission, received postremission treatment (PRT), and had available flow cytometric MRD before PRT. MRD positivity was defined as more than 0.1% cells with a leukemia-associated immunophenotype within the WBC compartment. PRT consisted of alloHSCT (n = 282), conventional PRT by a third cycle of chemotherapy (n = 160), or autologous hematopoietic stem-cell transplantation (n = 105).

Results: MRD was positive in 129 patients (24%) after induction chemotherapy before proceeding to PRT. Overall survival and relapse-free survival were significantly better in patients without MRD before PRT compared with MRD-positive patients (65% ± 2% *v* 50% ± 5% at 4 years; $P = .002$; and 58% ± 3% *v* 38% ± 4%; $P < .001$, respectively), which was mainly because of a lower cumulative incidence of relapse (32% ± 2% compared with 54% ± 4%; $P < .001$, respectively). Multivariable analysis with adjustment for covariables showed that the incidence of relapse was significantly reduced after alloHSCT compared with chemotherapy or autologous hematopoietic stem cell transplantation (hazard ratio [HR], 0.36; $P < .001$), which was similarly exerted in both MRD-negative and MRD-positive patients (HR, 0.38; $P < .001$; and HR, 0.35; $P < .001$, respectively).

Conclusion: The graft-versus-leukemia effect of alloHSCT is equally present in MRD-positive and MRD-negative patients, which advocates a personalized application of alloHSCT, taking into account the risk of relapse determined by AML risk group and MRD status, as well as the counterbalancing risk of nonrelapse mortality.