

The Role of Allogeneic Stem Cell Transplantation in MDS

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Allogeneic SCT (alloSCT) is the treatment of choice for patients with MDS who have a histocompatible donor, but the question is up to which age? Patients with early stages of MDS may profit optimally from alloSCT, with long-term DFS in more than 50% of patients. Longer disease duration before transplantation is associated with an increased TRM after transplantation. A recent analysis confirmed that delayed transplantation may result in maximized overall survival for low risk MDS1. They hypothesized that the optimal timing of transplantation for this cohort is at the time of development of a new cytogenetic abnormality, the appearance of a clinically important cytopenia or an increase in the percentage of marrow blasts. Whether patients with advanced stages of MDS should receive remission-induction chemotherapy prior to the transplant conditioning remains a point for discussion. Retrospective analyses showed conflicting data. Interpretation of the data is hampered by selection biases in the two treatment approaches. Therefore, the EBMT has launched a prospective study for this question (www.ebmt.org: Chronic leukemia; protocol: Allo-MDS 2x2). The results of allSCT with unrelated donors have improved markedly in recent years.² The American National Marrow Donor Program (NMDP) reported an improved DFS in more recently performed transplantations in a cohort of 510 patients with MDS transplanted with unrelated donors. The relative risk for DFS was 1.43 (95% confidence interval: 1.01–2.01) for transplantations performed between 1988 and 1993 versus more recent transplantations³.

The idea to reduce the intensity of the conditioning regimen has been developed in view of the high TRM of conventional marrow ablative conditioning regimens. The principle of RIC regimens is based on intensive immune suppression during conditioning and/or after stem cell infusion to facilitate donor engraftment and to establish complete donor chimerism. It is difficult to reconcile the contribution of RIC regimens to the improved outcome of alloSCT in view of the recently improved outcome of transplantation with marrow ablative regimens and the heterogeneity of the patient populations (age, co-morbidity, stage of disease).⁴ For this reason, the EBMT has launched a prospective randomized study comparing RIC regimens with standard conditioning regimens in patients with MDS older than 50 years.

The question remains whether autoSCT is a good alternative for alloSCT? In a recent study the 4-year DFS of the patients with a donor was 46%, higher than the DFS of 26% in patients without a donor. Subgroup analysis showed that the advantage of the presence of an HLA-identical sibling donor was only apparent in the patient group with intermediate and high risk cytogenetics.

General conclusion: allogeneic SCT may be considered the curative treatment option of choice. The upper age limit for alloSCT is mainly mandated by co-morbidity and general condition of the patient (frailty index) rather age of 60 or 70 years. For patients lacking an suitable donor, treatment with autoSCT or chemotherapy may be a good alternative for MDS patients with good-risk cytogenetic characteristics.

References

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