HEMATOLOGY

Allo SCT offers hope as second-line therapy for CML

Imatinib is now established as the first-line therapy for patients with chronic myeloid leukemia (CML), resulting in a decreased need for allogeneic hematopoietic stem cell transplantation (allo SCT). Nonetheless, allo SCT remains an important treatment option, especially for patients who fail to respond to imatinib or develop disease progression. The optimal second-line treatments for these patients have not been established, and randomized trials assessing allo SCT in the imatinib era are scarce. Saussele and coauthors used interim safety data from the randomized German CML Study IV trial to determine the role of allo SCT. "One of the goals of the randomized CML Study IV was to determine the role of allo SCT in the imatinib era. We conclude that allo SCT could become the preferred second-line option after imatinib failure for suitable patients with a donor" reports Susanne Saussele, lead investigator of the study.

This 5-arm study randomized 1,241 patients to receive either 400 mg imatinib, 800 mg imatinib, 400 mg imatinib and interferon, 400 mg imatinib and cytarabine, or 400 mg imatinib after failure with interferon. In total, 84 patients received a transplant, with 64% of donors being unrelated and 36% related to the transplant recipient. To define the tumor load, the cytogenetic status was analyzed before transplantation. Almost 70% of patients in chronic phase achieved a cytogenetic response, and 10% achieved major molecular remission. In patients with advanced phase disease, 42% achieved a cytogenetic response and 10% achieved major molecular remission.

The outcomes of 53 chronic phase patients who received a transplant were compared with 106 matched patients who did not have a transplant. At 3 years, the survival after diagnosis for the 53 patients who received allo SCT (91.9%, 95% CI 82.9–97.8%) was not different from the 106 matched patients who did not receive a transplant (95.9%, 95% CI 91.1–98.9%). Of the 106 patients who had a transplant, four received a second-line tyrosine kinase inhibitor before transplant, four progressed and were treated with chemotherapy, two died while on imatinib treatment and 96 are still in continued chronic phase while on imatinib. Importantly, a low transplant mortality rate and good long-term survival for patients undergoing transplant was observed. Saussele comments "The outcome after allo SCT in the imatinib era appears to be superior to that in the pre-imatinib era. The transplantation-related mortality is only 8% compared with more than 20% previously."

"We conclude that reduction of tumor load by initial imatinib therapy and improvement in transplantation procedures translate into improved outcome of patients after hematopoietic stem cell transplantation" explains Saussele's team. "In view of the curative potential of transplantation and survival results that were equally good as with imatinib treatment, allo SCT could become the preferred second-line option after failure of first-line tyrosine kinase inhibitor therapy". The investigators plan to assess treatment outcomes after first-line tyrosine kinase inhibitor therapy and will recommend allo SCT if there are indications of a lack of response to interferon treatment and will consider this approach when treatment outcome is suboptimal.

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