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TARGETED THERAPIES

Imatinib prior to allogeneic HSCT therapy improves both relapse and nonrelapse survival in patients with Ph$^+$ALL

A retrospective analysis of Japanese transplant registry data has demonstrated that imatinib therapy before allogeneic haematopoietic-stem-cell transplantation (allo-HSCT) improves both relapse and nonrelapse survival in patients with Philadelphia-chromosome-positive acute lymphoblastic leukaemia (Ph$^+$ALL).

> “...the risk of nonrelapse-related mortality was also reduced in the imatinib cohort...”

“Ph$^+$ALL (*BCR–ABL*-positive ALL) is one of the most-prevalent genetically defined subtypes of adult ALL, and was the subtype with the poorest prognosis until recently,” says Shuichi Mizuta, lead investigator of this study. “The introduction of a combination chemotherapy regimen incorporating imatinib has markedly improved outcomes in Ph$^+$ALL, but uncertainty remains regarding the extent of this benefit that is attributable to imatinib,” continues Mizuta.

To address this uncertainty, Mizuta and coauthors analysed Japan Society of Hematopoietic Cell Transplantation Transplant Registry Unified Management Program (TRUMP) data on disease outcomes in 738 patients, 542 of whom received imatinib prior to allo-HSCT for Ph$^+$ALL and 196 of whom did not receive imatinib. The 5-year overall survival was 59% in the imatinib cohort and 38% in the non-imatinib cohort; 3-year cumulative incidence of relapse was 23% versus 39%, and relapse was the cause of 40% and 47% of all deaths in these cohorts, respectively.

Interestingly, the risk of nonrelapse-related mortality was also reduced in the imatinib cohort compared with the non-imatinib group in both univariate (HR 0.65; $P<0.001$) and multivariate analyses (HR 0.55; $P=0.005$), despite the former cohort comprising larger proportions of older individuals and recipients of unrelated and/or HLA-mismatched transplantations. The authors suggest that this finding might reflect increased sustained remission that provides additional time to identify suitable donors; treatment with imatinib resulted in a higher rate of pre-transplant *BCR–ABL* negativity than observed with other regimens (64% versus 34%).

These findings suggest a therapeutic benefit of imatinib in Ph$^+$ALL that is related to an increased disease response prior to allo-HSCT. Indeed, “the clinical relevance of HSCT for Ph$^+$ALL in the current era of tyrosine kinase inhibitors is still an open question,” Mizuta concludes.

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Original article Mitzuta, S. *et al*. Pre-transplant administration of imatinib for allogeneic hematopoietic stem cell transplantation in patients with *BCR–ABL*-positive acute lymphoblastic leukemia. *Blood* doi:10.1182/blood-2013-11-538728