# Defining Who Benefits from HSCT in CML

BY SARAH DIGIULIO

In the era of tyrosine kinase inhibitors (TKIs), allogeneic (allo) hematopoietic stem cell transplantation (HSCT) may still be considered a potentially curative option for patients with chronic myelogenous leukemia (CML), especially for patients with advanced disease. That was the conclusion of a recent study that compared outcomes for CML patients treated in the pre- and post-TKI era (***Clinical Lymphoma, Myeloma & Leukemia 2015:15;S129-S140***)—confirming similar conclusions found in previous work and also highlighting the importance of pre-transplant minimal residual disease status.

"Our data confirm what other retrospective studies already have shown, that the results of allotransplantation for CML patients improved in recent years, with more than half of patients being alive and leukemia-free at three years, despite the use of pre-transplant TKI," Ali N. Chamseddine, MD, of Gustave Roussy Cancer Campus in Villejuif, France, explained in an email.

A second main finding was that there were favorable outcomes at three years in patients who were minimal residual disease-negative before transplant, Chamseddine said—with leukemia-free survival and overall survival being significantly higher for those patients than in patients who were minimal residual disease-positive before transplant.

"This suggests that achieving a pre-tansplantation minimal residual disease-negative status is vitally important. It also highlights the need for effective TKIs in minimal residual disease-positive patients in whom non-myeloablative conditioning regimens is planned," he explained.

The emergence of tyrosine kinase inhibitors (TKIs) has changed the treatment landscape of CML, causing a dramatic decline of the HSCT in front-line-eligible transplant recipients, Chamseddine said. But because transplant is still the reference-standard therapy for patients with CML who do not respond to TKI treatment or those who have advanced disease, it is critical to know who can benefit when from transplant, as well as the role of TKIs for patients who undergo transplant.

## Study Details

The researchers analyzed data for 69 patients with Philadelphia chromosome-positive CML—39 patients were treated in the pre-TKI era (1989-2001) and 30 patients were treated in the TKI era (2002-2013)—all of whom underwent allo-HSCT at the Gustave Roussy Cancer Campus. Additional analyses were done for the patients treated in the latter group, for whom detailed data about TKI treatment and minimal residual disease status were available.

The data showed:

- At three years, the leukemia-free survival and overall survival were higher in the patients treated in the TKI era (66% and 71% respectively) compared with patients treated in the pre-TKI era (63% and 57%); and
- Leukemia-free survival and overall survival at three years for the pretransplantation minimal residual disease-negative patients were significantly higher (83% and 94% respectively) compared with the minimal residual disease-positive patients (43% and 46%).

## Confirmatory Findings

The findings from this study are concordant with other retrospective studies, Chamseddine said—showing that even though TKIs have significantly delayed transplantation for most patients who eventually undergo it, outcomes are not significantly affected by the delay. Overall survival at three years was 63 percent for patients transplanted in the pre-TKI era compared with 57 percent for those transplanted in the TKI era, according to these data, he said. And the findings highlight that pre-transplant TKI use was valuable in terms of achieving a more prolonged and profound negative minimal residual disease rate, which led to better post-transplant outcomes, he added.

What practicing clinicians should know about these findings, Chamseddine explained, is that "allo-HSCT no longer has a role in first-line treatment in chronic phase-CML, but two groups of patients—those with advanced disease and those who are intolerant to TKI therapy—do benefit from allo-HSCT. And pre-transplant negative minimal residual disease is significantly associated with better outcomes."