Thrombopoietic agents hold promise for patients with severe or refractory ITP, and for patients prior to planned procedures. As experience accumulates, and assuming long-term safety is documented, extension to other settings can be considered, including the use of these agents in maintenance treatment to avert the side effects of existing treatments. However, not all ITP patients respond to TPO receptor agonists, and predictors of response would be helpful. Furthermore, usage will need to be considered in the context of recent studies suggesting that high doses of dexamethasone on presentation may favorably alter the natural history of the disease and the fact that some patients achieve a “cure” after splenectomy or a single course of rituximab.

The potential use of TPO receptor agonists is also evident in patients suffering from thrombocytopenia caused by conditions with fewer treatment options, including myelodysplasia, viral hepatitis (to permit use of antiviral therapies), and chemotherapy-induced thrombocytopenia (where it can be shown that thrombocytopenia requires transfusion or limits otherwise life-prolonging treatment), among others. The studies by Jenkens et al with eltrombopag in this issue and related studies with this and other TPO receptor agonists portend a potentially exciting new approach to the treatment of patients with ITP and other causes of severe thrombocytopenia.

The author has served as a consultant for Amgen and Glaxo-Smith-Kline.

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No more transplantation in CML?

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Allogeneic stem cell transplantation has been considered the only curative therapy for chronic myeloid leukemia (CML). However, since 1999 the number of transplantations reported to scientific groups has substantially dropped.

In this issue, Hehlmann and colleagues report the results of a large randomized study comparing allogeneic stem cell transplantation versus the best available drug treatment. Of 621 patients included in the study, 354 were eligible for stem cell transplantation and 135 patients actually received a matched transplant. The patients included in the group that did not undergo transplantation were treated with interferon and hydroxyurea, or low-dose AraC and then with imatinib at the time the drug was available. The results of this important study demonstrate the superiority of the drug treatment group with a significantly better outcome. The difference is marked at 3 years after diagnosis, the 2 curves being indistinguishable at 8 years.

There has been substantial progress in recent years in the management of CML with the remarkable efficacy of imatinib. Before the imatinib era, the treatment of CML patients was restricted to allogeneic stem cell transplantation or interferon-based regimens. These therapies were indicated in the majority of patients younger than 70 years. Allogeneic transplantation was considered for patients younger than 40 years for those with a matched related donor. Although the optimal timing of transplantation was frequently discussed, a number of papers have shown little difference in long-term outcome among patients who underwent transplantation in the first 12 months after diagnosis compared with those who underwent transplantation after 1 year. Although the procedure carries a risk of death, it is obvious that transplantation is still considered as the only curative therapy with patients in complete response without any maintenance therapy. Interferon (IFN)–based regimens are no longer used as front-line therapy. However, the combination of IFN and AraC has been considered the gold standard until imatinib demonstrated its superiority.

Despite the toxicity of this combination, the treatment induced complete cytogenetic responses in patients who could tolerate 2 or 3 years of the treatment. Of interest, patients who achieved sustained cytogenetic responses had significant survival improvement. A similar observation has been published with imatinib. Given the recent update of the International Randomized Study of Interferon and STI 571 (IRIS) trial, it is obvious that any comparison between transplantation and imatinib would conclude in imatinib’s favor. Allogeneic stem cell transplantation could again play a role in case of imatinib resistance. But the recent impressive results of the second generation of tyrosine kinase inhibitors will probably delay the time of transplantation in the course of the disease. However, these new inhibitors could also be used for reducing the tumor burden before performing stem cell transplantation. Nevertheless, the study of Hehlmann et al clearly reinforces the message previously published that allogeneic stem cell transplantation cannot be recommended for front-line therapy.

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