

## INTRODUCTION

$\beta$ -Thalassemia major is a genetic defect that causes reduced or absent  $\beta$ -globin synthesis, results in an imbalanced accumulation of  $\alpha$ -globin chains and ineffective erythropoiesis with hemolysis.<sup>(1)</sup> The hallmarks of treatment include regular red blood cell (RBC) transfusions with iron chelation therapy for transfusion-related iron overload and supportive care to treat the complications of iron overload.<sup>(2,3)</sup> However, the only curative therapy is replacement of the defective gene by hematopoietic cell transplantation.<sup>(4-6)</sup>

Over the past 2 decades, bone marrow transplantation as a therapeutic option for thalassemia has undergone considerable investigation and refinement. Analysis of the first large series of patients undergoing hematopoietic stem cells transplantation (HSCT) for thalassaemia identified 3 independent prognostic factors for outcome in children: hepatomegaly, liver biopsy with evidence of portal fibrosis and irregular compliance with chelation therapy. These factors form the basis of the Pesaro classification into good, intermediate and poor risk (Class 1, 2 and 3 respectively).<sup>(4-6)</sup> In the initial reports, outcomes after transplantation were affected significantly by the pre-transplantation risk status.

Modifications to the conditioning regimen have been used to reduce the risk of transplantation-related complications in high-risk recipients. However, outcomes after transplantation have become more similar.<sup>(7-10)</sup> The most recent results after human leukocyte antigen (HLA)-matched sibling bone marrow transplantation (BMT) for Pesaro class I or II and class III recipients show thalassemia-free survival probabilities of 87%, 85%, and 80%, respectively. Despite these improvements, pre-transplantation transfusion exposures and organ damage from iron overload still appear to impact transplantation outcomes negatively. In the most recent update, the transplantation-related mortality in class I or II and class III patients was 3% and 10%, respectively, and 8% to 12% of pediatric recipients experienced graft rejection after BMT.<sup>(6)</sup>

One of the main features of thalassemia is the variable degree of raised ferritin level that has been used also as a marker for iron overload pre-hematopoietic stem cells transplantation.<sup>(7,8)</sup> Also due to frequent blood transfusions there is an increased incidence of HCV infection which is a small (55–65 nm in size), enveloped, positive-sense single-stranded RNA virus of the family Flaviviridae which is the cause of hepatitis C in humans.<sup>(9)</sup> HCV infection and liver disease is an important cause of morbidity and mortality among recipients of bone-marrow transplantation (BMT). Hepatic GVHD is a common complication following BMT and an important cause of liver-related mortality. The high prevalence of HCV may have contributed to the outcome of hepatic GVHD and VOD.<sup>(10)</sup>