EDITORIAL

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# Finding the perfect recipe for success

Familial hemophagocytic lymphohistiocytosis (FHLH) is a rare genetic disease for which optimal therapy includes consolidation with a hematopoietic stem cell transplant (HSCT). The HLH-1994 study demonstrated a 3-year survival of 62% in patients who received HSCT.[1] The conditioning regimen was myeloablative carrying with it significant morbidity and mortality from the resulting organ toxicity. As several studies have shown that 20%–30% donor chimerism is sufficient in most cases to eliminate the clinical manifestations of FHLH, an attempt was made to reduce the toxicity of the conditioning regimen by reducing the myeloablative aspects and replacing them with more immunoablative components. Several single institution reports demonstrated the effectiveness of this approach[2,3] achieving overall survival rates of 80%–100%, although this was accompanied by significant issues with mixed chimerism and nonengraftment. In the Bone Marrow Transplant Clinical Trials Network (BMT-CTN) protocol 1204 multi-institutional trial similar results were obtained with only a third of patients achieving sustained donor engraftment with the initial transplant, and the remainder requiring subsequent transplants to achieve this.[4] Although the 1-year survival achieved 80%, this dropped to 67% by 18 months. Although significant progress was made in reducing transplant related mortality, clearly additional changes to the conditioning regimen are needed to achieve improved engraftment.

As HSCT is optimized to reduce morbidity and mortality, there is an increasing need to make transplant available to all patients diagnosed with FHLH by the use of alternative donor sources. In this article, Jia et al[5] demonstrated the feasibility of using haploidentical donors as a stem cell source for the treatment of FHLH using a reduced-intensity conditioning regimen. Their observation of mixed donor chimerism is quite consistent with the results seen in the reduced-intensity regimen studies above. Although the number of patients is small, they were able to achieve 80% survival using this alternative donor source. The successful use of haploidentical donors using a reduced intensity conditioning regimen opens the door for practically all patients with FHLH to have a donor and thus proceed with HSCT. This provides us with the platform to further optimize the portion of the conditioning regimen to reduce the number of patients needing additional transplants or stem cell boosts.

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## CONFLICT OF INTEREST

I have no competing interests.

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