

Cellular therapies are being increasingly explored both for regenerative (stem cells) and for immunotherapy (T and NK cells) purposes. In fact, cells from normal familial or unrelated donors are used as part of established curative strategies for genetic diseases (e.g. severe blood and metabolic disorders) and for malignancies (e.g. high-risk leukemias). This group of diseases are responsible for most morbidity and mortality in the pediatric age group after accidents.

The RITA program (Reparto Inderdisciplinare Terapia Avanzata) was specifically developed to provide access to cellular therapies for the tertiary care pediatric referral center in Tuscany. This program was designed to comply with international regulations of good laboratory and clinical practices summarized by the Joint Accreditation Commission of ISCT and EBMT (i.e. the International Society for Cellular Therapies and the European group for Blood and Marrow Transplantation) (www.jacie.org).

Clinical research activity is currently focusing on the use of partially matched family donors for the cure of β -thalassemia major and neuroblastoma. Thalassemia major is the most frequent genetic disorder and results in a severe blood disease that can be cured by HLA-compatible stem cell transplantation. Most patients however, lack a compatible donor but have a partially matched (haploidentical) family donor. The use of purified stem cells from haploidentical family donors in an initial series of 13 patients (4 of which done at our institution) performed according to a defined clinical protocol developed by the group of professor Guido Lucarelli, the leading world authority in transplant for thalassemia, was associated with a 61% cure rate and no transplant-related mortality (5 of 12 patients rejected and returned thalassemic).

High-risk neuroblastoma is responsible for most deaths due to malignancy in the pediatric age group as a single pathological entity. Its curability at diagnosis is around 20-30% and no established treatment option is available for relapsed patients. This disease is a well known target for immune effector cells, particularly T and NK cells. In partially matched allogeneic transplantation both these immune effector cells may come into play with a synergistic activity in which HLA mismatches may activate both NK and T cells with different mechanisms. In fact, neuroblastoma cells that try to escape T cell killing by down-modulating class I expression may become unable to inhibit NK lysis and viceversa. In an initial series of 4 patients in 2nd or subsequent remissions (all done at our institution) performed according to a defined clinical protocol developed in collaboration with the Istituto Gaslini, the Italian referral center for neuroblastoma, there was one death possibly due to chronic lung GVHD and 3 patients with stable disease at a median follow up of 7 months.