



EBMT Paediatric Diseases Working Party
**Combined Organ and Stem Cell
Transplantation in Children
(COST4KIDS) Subcommittee**
Goals and action plan 2018 - 2022

Goals

In keeping with the mission and aims of the Paediatric Diseases Working Party (PDWP) of the European Group for Blood and Marrow Transplantation (EBMT) the Combined Organ and Stem Cell Transplantation in Children Subcommittee (PDWP-COST4KIDS) activities are aiming at exploring the role of haematopoietic stem cell transplantation (HSCT) and cellular therapies as a strategy to induce functional tolerance after paediatric solid organ transplantation (SOT). The motivation to this subcommittee is mediated by the need to find alternatives to the life-long use of immunosuppressive agents needed for successful SOT. The inevitable toxicity of conventional immunosuppression treatment (IS) significantly increases the risk of infection and cancer together with a risk of chronic organ rejection, compromising the quality of life of these children. Long-term IS does not prevent chronic rejection with estimated long-term graft survival between 5 and 20 years, depending on the transplanted organ. Moreover, the costs of IS over a life time with all the expenses related to increased post-transplant morbidity exceed the costs of a combined transplant and have substantial financial impact on the European healthcare system. Taken all this together along with the continuous increase of organ shortage and the knowledge that most of HSCT patients are free of IS one year after HSCT, justify the need for more effective and safer approaches. Although preclinical models and isolate successful series of pilot trials have been reported, the establishment of durable tolerance through HSCT, the application of HSCT in SOT is now limited by the potential toxicity of conditioning regimens, the risk of graft versus host disease (GVHD) and the challenge of HLA mismatch.

In the last decade a great experience with haploidentical HSCT has been acquired allowing wider indications as well as more effective measures to induce sustained tolerance. Nowadays, cell-based therapies are being used with increasing frequency to induce tolerance and immunomodulation but still some challenges have to be overcome in order to implement these practices routinely in paediatric transplant care

We consider that by sharing knowledge and expertise with the support of the EBMT we may help to establish safe and feasible combined transplant programs. We do hope that COST4KIDS will permit implementation of this approach progressively in selected cases.

Our goals are:

1. Creation of a self-sustaining network of physicians and researchers involved in HSCT and cell therapies for inducing tolerance after paediatric SOT.
2. Promote and implement the haematopoietic mixed chimerism concept as strategy to achieve functional immune tolerance in paediatric SOT in order to foster the translation of research into clinical practice in Europe.
3. Generate a debate of a new state of the art of paediatric solid transplantation free of IS and based on haematopoietic mixed chimerism induced by HSCT.
4. Promote education and training activities to overcome gaps in translation of scientific findings for EBMT members, as well as other audiences, including non-EBMT member transplant professionals, patients and their families.

5. Propose international prospective trials considering experts in SOT and HSCT combining transplantation (SOT and HSCT) emphasising risk-adjusted approach as well as evaluation of QoL.
6. Promote active participation in international registries for data collection and integration where data will be exploited for scientific purposes and improving patient care.
7. Integrate patient and family in this development to harmonise clinical care.
8. Interact with other PDWP subcommittees and WPs of the EBMT as appropriate

Main Projects

1. Education and training activities for SOT and HSCT combined transplant for physicians and nurses and other healthcare professionals and patient associations.
2. Collaboration with European SOT programs interested in tolerance induction. These will be achieved by invitation to scientific meetings
3. EBMT PDWP-COST4KIDS fellowship program for HSCT and SOT researchers focused on young investigators
4. Others as proposed by other members and subcommittees.

Action plan

1. Workshops, webinars and meetings discussing current studies and challenges and identify new opportunities. We will consider invite relevant external experts in the field.
2. Organisation of Training Schools targeting young investigators to gain technical expertise and exchange of best practices.
3. Collection of information through registries for evaluation, study and exploitation of post-transplant results
4. Promote the interchange of researchers, clinicians through secondments
5. Dissemination of knowledge and findings through conference communications and scientific publications in specialised and peer-reviewed journals either in the form of original, review, or technical articles reporting protocols or methodology.
6. Prospective studies and clinical trials proposal