IMPROVING OUTCOMES AFTER HEMATOPOIETIC CELL TRANSPLANTATION IN FA IN LOW-RESOURCES COUNTRIES: THE EXPERIENCE FROM CURITIBA

C Bonfim [a,b,c], ra Mutori [a], ACM Lima [a], S Nichele [a,c], D Pilonetto [a], G Loth [a,b], J Trennepohl [a], AM Rodrigues [a,b], P Pelegrina [b], R Pasquini [a]

[a] *Hospital de Clínicas da Universidade Federal do Paraná (UFPR), Curitiba, PR, Brazil*
[b] *Hospital Pequeno Príncipe/Instituto de Pesquisa Pelé Pequeno Príncipe, Curitiba, PR, Brazil*
[c] *Hospital Nossa Senhora das Graças, Curitiba, PR, Brazil*

Introduction: Fanconi Anemia (FA) is a rare and challenging disease to manage, and there is a substantial gap between treatments available in high- versus low- and middle-income countries. Although hematopoietic cell transplantation (HCT) is the only curative treatment for the hematological complications related to this disease, this procedure is highly complex, requiring sophisticated infrastructures and trained personnel. **Objective:** Describe the outcomes after matched related, unrelated and haploidentical HCT for 216 FA patients in aplastic phase in Curitiba, Brazil. **Results:** The median age was 9-years (range: 3-32); all patients were in aplastic phase and received bone marrow as the stem cell source. 1st group: Matched Related Donors (MRD): 101 pts were transplanted between 1999-2021. Median follow-up: 9.6 years; 83 received HCT from matched siblings while 18 had other MRD. All patients received a simple preparatory regimen with Cyclophophamide (CY) 60 mg/kg with (n = 12) or without rabbit-ATG (n = 89) and GVHD-prophylaxis with cyclosporine and methotrexate (csa + MTX;96%) or mycophenolate (csa +MMF;4%). Six patients had primary or secondary graft failure (GF), all received a 2nd transplant, and 5 are alive and engrafted. Eight patients died at a median of 545 days after transplant (range: 3- 6271). Two-year transplant-related-mortality (TRM):4%. 10-year overall survival (OS) was 94%, and all patients transplanted in the past ten years are alive (n = 42). This regimen was well tolerated with a low TRM and acute and chronic GVHD incidence. 2nd group: Unrelated donors:75pts were transplanted between 2003-2021; median follow-up:6-years. HLA-compatibility: 10/10 (n = 68) and 9/10 (n = 7). 73% of donors were found in the Brazilian donor registry. All patients received a non-irradiation regimen including CY 60 mg/kg + Fludarabine + ATG, and the majority received csa + MTX as GVHD prophylaxis. GF was observed in two patients, and one is alive and well after a 2nd transplant.15pts died at a median of 117 days post-HCT (range: 3-4379), and infections were the major cause of death in 60% of patients. The day-100 CI of acute GVHD and 2-year CI of chronic GVHD was 17% and 25%, respectively. 5-year OS was 79%. 3rd group: Haploidentical donors:40pts were transplanted between 07/2013 to 01/2022, 31 patients received a preparatory regimen with Fludarabine + TBI (200) + rabbit-ATG, and 9 received Fludarabine + TBI(200) + Campath. GVHD prophylaxis with post-transplantation cyclophosphamide (PTCy) 50-60 mg/kg (total dose) + csa + MMF. Three patients in the ATG group had primary or secondary GF, received a 2nd haplo-PTCy transplant, and died. The CI of day-100 acute GVHD was 27%. The 2-year CI of chronic GVHD was 51% for the ATG group and 25% for the Campath group (p = 0.15). Six patients died at a median of 209 days due to rejection (n = 3) or GVHD (n = 3). 3-year OS was 85%. All patients in the Campath group are alive. **Conclusions:** These results show the feasibility of performing HCT for patients with FA in aplastic phase in Brazil. This experience also reflects more than 40 years of dedication to the treatment of FA and is based on strong national and international collaborations. These simple but effective preparatory regimens can lead to excellent outcomes, serve as a guideline, and be reproducible in other countries with similar resources.

https://doi.org/10.1016/j.htct.2022.09.538

EFEITO INSTRUCIONAL DE TOPOGRAFIAS MICROMOLDADAS PARA EXPANSÃO IN VITRO DE CÉLULAS TRONCO ESQUELÉTICAS E PROGENITORES DA MEDULA ÓSSEA HUMANA

TPEG Lopes [a,b,c,d], RB Dias [a,b,c], S Pernini [a,b], C Fontenelle [e], P Mannarino [e], A Maiolino [b,c], ASCP Campos [d,e], TL Pereira [d,e], M Farina [d,e], DC Bonfim [a,b,c]

[a] *Programa de Pós-graduação em Ciências Morfológicas, Instituto de Ciências Biomédicas, Universidade Federal do Rio de Janeiro (UFRJ), Rio de Janeiro, RJ, Brasil*
[b] *Laboratório de Biomineralização, Instituto de Ciências Biomédicas, Universidade Federal do Rio de Janeiro (UFRJ), Rio de Janeiro, RJ, Brasil*
[c] *Laboratório de Biologia Celular Aplicada a Medicina, Instituto de Ciências Biomédicas, Universidade Federal do Rio de Janeiro (UFRJ), Rio de Janeiro, RJ, Brasil*
[d] *Laboratório de Cultura e Criopreservação de Medula Óssea (LCCMO), Universidade Federal do Rio de Janeiro (UFRJ), Rio de Janeiro, RJ, Brasil*
[e] *Hospital Universitário Clementino Fraga Filho (HUCFF), Universidade Federal do Rio de Janeiro (UFRJ), Rio de Janeiro, RJ, Brasil*

Objetivo: Em face a descoberta de marcadores para a identificação das Células tronco esquelética (SSC) e de seus progenitores da medula óssea humana, iniciamos um estudo para avaliar se o uso dessas populações possui algum benefício em termos de potencial regenerativo (osteocondrogênico). Inicialmente, separamos e cultivamos duas frações de células da medula óssea: PDPN- CD146+ (osteoprogenitores) e as células PDPN+ CD146-, que incluem as SSCs e os condroprogenitores. No entanto, observamos uma mudança no fenótipo dessas células após seu cultivo em um sistema *in vitro* tradicional (2D). No que tange ao sistema de cultivo, estudos demonstram que o cultivo de células-tronco/progenitoras sobre topografias específicas, moldadas para mimetizar o ambiente *in vivo*, podem regular seu fenótipo e potencial biológico. Dessa forma, o presente estudo visa avaliar a manutenção das