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Haploidentical hematopoietic cell transplantation: Current status and future prospects

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Abstract

HLA-Haploidentical HCT has emerged as a front-runner for alternate donor transplantation for hematological malignancies over the past decade. The primary reason has been the employment of post-transplantation cyclophosphamide (PTCy) as GVHD prophylaxis, which by dint of both its ease of application and impressive outcomes, has made haploidentical HCT feasible across the globe. Large registry-based studies have confirmed the equivalence of this approach as compared to matched related and unrelated donor sources in acute leukemia as well lymphomas, with low incidences of both acute and chronic GVHD. However, the risk of relapse has remained unchanged across the donor sources depending on the nature of the underlying malignancy. Moreover, the suitability of this approach remains questionable in younger children and those with non-malignant disorders. Adoptive immunotherapy following haploidentical HCT has barely been used due to concerns related to GVHD. However, several recent studies have shown that early G-CSF mobilized donor lymphocyte infusions (DLI) can reduce the relapse risk in relapsed/refractory leukemia. The use of T cell costimulation blockade with CTLA4Ig in conjunction with PTCy has shown to improve reconstitution of Tregs early after haploidentical HCT in children with aplastic anemia. The same approach when used in children with leukemia was not associated with increased relapse. Interestingly, CTLA4Ig does not block natural killer (NK) cell activation and might even potentiate its cytotoxicity. Based on this principle, employment of CTLA4Ig-primed DLI in patients with advanced leukemia showed marked proliferation of mature NK cells which correlated with disease-free survival with low incidences of GVHD and non-relapse mortality. This approach has been shown to be effective in both lymphoma as well as myeloma in pilot studies. However, the success of any such approach rests on the appropriate selection of the donor vis-à-vis graft composition. It remains to be seen whether haploidentical HCT with unique approaches to NK cell mediated immunotherapy post-HCT might re-position this as a preferred option for advanced malignancies. This approach with universal donor availability might pave the way for innovative immunotherapies for solid tumors as well.

Biography

Suparno Chakrabarti is the Head of the Department for Blood and Marrow Transplantation and Hematology at Dharamshila Narayana Hospital and Research Centre, and Cellular Therapy & Immunology at Manashi Chakrabarti Foundation, India. He initiated the first Haploidentical BMT program in India and along with Dr Sarita Jaiswal and has developed this as a sustained alternate donor program with over 125 Haploidentical transplants in the past eight years. They have innovated newer methods of carrying out haploidentical BMT in patients with advanced leukemia as well as aplastic anemia with excellent results. His key area of research is Transplant immunology in relation to Haploidentical BMT. He trained in Internal Medicine at PGIMER, Chandigarh in India. Subsequently, he spent 13 years in the UK, initially as a research fellow and subsequently as a consultant in the field of BMT. During this period, he played a substantial role in developing Campath-1H based T cell depletion and reduced intensity conditioning. The bulk of his research also focused on post-transplant virus infections and immune reconstitution. He received FRCPATH based on his published work. He has over 100 publications to his credit. He also runs a charitable organization for children with blood diseases.

Publications

1. EBV-related disease following haematopoietic stem cell transplantation with reduced intensity conditioning, Sarita Rani Jaiswal; Shamsuz Zaman; Suparno Chakrabarti; ... Paul V. O'Donnell, 2016 in Biology of Blood and Marrow Transplantation, DOI: 10.1016/J.BBMT.2015.11.010
2. CD56-enriched donor cell infusion after post-transplantation cyclophosphamide for haploidentical transplantation of advanced myeloid malignancies is associated with prompt reconstitution of mature natural killer cells and regulatory T cells with reduced incidence of acute graft versus host disease: A pilot study, Sarita Rani Jaiswal; Shamsur Zaman; Murugaiyan Nedunchezhian; ... Paul O'donnell, Published: 2017 in Cytotherapy, DOI: 10.1016/J.BBMT.2015.11.010
3. Improved Outcome of Refractory/Relapsed Acute Myeloid Leukemia after Post-Transplantation Cyclophosphamide-Based Haploidentical Transplantation with Myeloablative Conditioning and Early Prophylactic Granulocyte Colony-Stimulating Factor-Mobilized Donor Lymphocyte Infusions, Sarita Rani Jaiswal; Shamsuz Zaman; Suparno Chakrabarti; ... Paul V. O'Donnell;Published: 2016 in Biology of Blood and Marrow Transplantation, DOI: 10.1016/J.BBMT.2016.07.016
4. CTLA4Ig-based T-cell costimulation blockade is associated with reduction of adenovirus viremia following post-transplantation cyclophosphamide-based haploidentical transplantation; Bone Marrow Transplantation 2020-03-14 | journal-article, DOI: 10.1038/s41409-019-0549-6
5. Natural killer cell-based immunotherapy with CTLA4Ig-primed donor lymphocytes following haploidentical transplantation; Immunotherapy, 2019-10-03 | journal-article; DOI: 10.2217/imt-2019-0037

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