

Umbilical Cord Blood (UCB) Transplantation for Patients with Hematologic Malignancies

Researchers with the Bone Marrow and Stem Cell Transplant program at the Abramson Cancer Center of the University of Pennsylvania are seeking to hasten immune system reconstitution and hematopoietic recovery in patients with hematologic malignancies receiving umbilical cord blood (UCB) transplantation.

UCB represents a promising source of stem cells for patients with advanced hematologic diseases for whom hematopoietic stem cell transplantation (HSCT) may be life saving. The benefits of UCB transplantation after HSCT are well established. Cryopreserved UCB grafts offer a rich source of hematopoietic stem cells (HSCs) and naïve donor T cells. The grafts are immediately available from a rapidly growing list of national and international cord blood banks. Since there is a lower incidence of graft versus host disease than that seen after transplantation of unrelated blood or bone marrow stem cells, the requirement for HLA matching is less stringent. The major limitation of UCB HSCT is delayed hematopoietic and immune reconstitution.

Researchers with the Bone Marrow and Stem Cell Transplant program at Penn are performing a Phase I clinical trial that seeks to address these limitations of UCB transplantation. Building upon an earlier trial at Penn that established the safety of delayed infusion of costimulated allogeneic T cells in patients with advanced hematologic malignancies, this trial will assess the safety (in terms of graft versus host disease) of UCB-derived T cells expanded *ex vivo* via CD3/CD28 costimulation and reinfused at the time of UCB HSCT. A secondary endpoint of the trial will be to study time to engraftment and immune reconstitution in recipients of this therapy. Patients with hematological malignancies who are eligible and appropriate for UCB transplantation can be enrolled if they do not have a suitable related or unrelated donor available, and have a suitable umbilical cord blood graft identified.

Cord blood units are selected if they are frozen in two aliquots with sufficient cell numbers to support a transplant. This protocol adds another option for patients who require allogeneic SCT but who do not have a suitable matched sibling or unrelated donor. Patients with hematologic malignancies may be referred to any member of our transplant group and will be considered for umbilical cord blood transplant if a suitable family member or well matched unrelated donor cannot be identified in a timely manner. For specific questions regarding this trial, please contact Dr. Elizabeth Hexner or Dr. David Porter.



Figure 1. Gathered from placental tissue, umbilical cord blood offers a rich source of hematopoietic stem cells.

CASE STUDY

Ms. B, a 42 year old woman with high risk acute myelogenous leukemia in first remission, first presented at Penn in December 2008 with a white blood count of 60,000 composed primarily of myeloblasts. Cytogenetic studies showed deletion of chromosome 7 and multiple other abnormal clonal rearrangements. Her cells also expressed an internal tandem duplication of FLT3. She received standard induction chemotherapy with idarubicin and cytarabine. A biopsy on day 14 showed residual disease and she received retreatment. At 28 days after her second course of induction chemotherapy, her white blood count was 2000/ μ L with a normal differential, her hemoglobin was 10 g/dL and her platelet count 70,000/ μ L. A bone marrow biopsy showed less than five percent blasts and one of 20 cells still had deletion of chromosome 7 and multiple cytogenetic abnormalities. She was in a minimal disease state but considered incurable with standard chemotherapy. For Ms. B, allogeneic stem cell transplantation offered the only chance of long-term cure. However, HLA typing of two siblings did not identify a match, nor were any well matched donors identified through a preliminary search of the National Marrow Donor Program registry. A subsequent search for potential cord blood units identified a unit comprised of a 5×10^7 total nucleated cells/kg, matched at 5 of 6 HLA antigens tested and frozen in two aliquots. The cord blood was requested and delivered within one week of the search.

The identification and rapid delivery of a well matched cord blood unit allowed Ms. B, a patient with very high-risk disease, to proceed from search to transplant within one month. She is currently undergoing cord blood transplantation. The addition of activated T cells to the traditional cord blood graft may speed graft recovery and immune reconstitution; this hypothesis will continue to be tested during this and subsequent clinical trials.

Our Team of Faculty

The Bone Marrow and Stem Cell Transplant program at the University of Pennsylvania and Abramson Cancer Center is the largest transplant center in the region. Our vibrant research mission is supported by many clinical trials for both autologous and allogeneic SCT. Transplant options are available for most patients and are performed with autologous stem cells, matched sibling and unrelated donors, and umbilical cord blood. We have active programs using both conventional allogeneic SCT and for non-myeloablative allogeneic (“mini”) transplantation. We are committed to premier clinical care and strive to work collaboratively with patients’ referring physicians.

Hematologic Malignancy Physicians

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Location

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To refer a patient and/or consult with a doctor:

Patients with hematologic malignancies may be referred to any member of our transplant group and will be considered for umbilical cord blood transplant if a suitable family member or well matched unrelated donor cannot be identified in a timely manner.

For specific questions regarding the UCB trial, please contact:

Dr. Elizabeth Hexner at 215.614.1847 or Dr. David Porter at 215.662.2862

