IBMTR/ABMTR Mortimer M. Bortin Awards for Best Clinical Abstracts

Mortimer M. Bortin, M.D., was one of the founding members of the International Bone Marrow Transplant Registry and served as its Scientific Director for 20 years. The Mortimer M. Bortin Award, established to commemorate Dr. Bortin's contributions to the field of transplantation, is presented each year to investigators submitting abstracts to the Tandem BMT Meetings. The abstracts must address important issues in clinical blood and marrow transplantation and be of outstanding scientific merit. This year three $1,000 awards will be presented on behalf of the Mortimer B. Bortin Fund Awards Committee. The awards are supported by an unrestricted educational grant from ILEX Oncology, Inc.

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A SUCCESSFUL APPROACH OF G-CSF PRIMED HAPLOIDENTICAL BONE MARROW TRANSPLANTATION WITHOUT EX-VIVO T CELL DEPLETION FOR HIGH-RISK LEUKEMIA

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HLA-haploidentical hematopoietic stem cell transplants (HSCT) have been associated with high incidences of lethal graft versus host disease (GVHD), host versus graft rejection (HVGR), delayed immune reconstitution and infection. We designed a haploidentical HSCT protocol which focuses on engraftment and sequential immunosuppression to prevent both HVGR and GVHD, eventually to achieve a stable engraftment without clinical GVHD. Twenty-eight high-risk leukemia patients underwent haploidentical G-CSF-primed bone marrow transplants without ex-vivo T cell depletion. All patients received the same chemoradiation conditioning regimens. GVHD prophylaxis consisted of anti-thymocyte globulin, cyclosporin A, methotrexate and mycofenolate mofitel. Thirteen patients received additional Basiliximab anti-CD25 mAb. All patients achieved trilineage engraftment, a median of 19 and 21 days for neutrophil and platelet. G-CSF donor priming significantly increased CD34+ and CFU-GM cells. More importantly, it significantly reduced lymphocytes and reversed CD4+/CD8+ ratio in the donor marrow grafts. The incidence of grade II-IV acute GVHD was 0% and 33% with and without the anti-CD25 mAb ($p<0.05$). The CD3+/CD8+ T cells, CD19+ B cells and CD16+/CD56+ NK cells recovered within 6-12 months. Of 28 patients, 21 are alive with minimal chronic GVHD and Karnofsky performances of 100% during a median follow-up of 19 months. Disease free survivals were 92% and 60% with and without anti-CD25 mAb ($p<0.04$). The probability of over all disease free survival at 2 years is 72%. In summary, G-CSF primed marrow grafts along with sequential immunosuppressants, especially the anti-CD25 mAb, could achieve excellent engraftment, proper immune reconstitution, and virtual control of grade II-IV acute GVHD.

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UNRELATED UMBILICAL CORD BLOOD TRANSPLANTATION FOR HURLER SYNDROME

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Background: Hurler syndrome (HS, MPS-I) causes progressive central nervous system deterioration, cardiovascular disease and death in childhood. Allogeneic bone marrow transplantation (BMT) before two years of age halts disease progression and prolongs life, however many children lack an appropriate donor. We investigated the feasibility of unrelated umbilical cord blood (UCB) with a myeloablative, non-TBI containing preparative regimen as an alternative source of hematopoietic stem cells for transplantation in children with HS. **Methods:** Nineteen consecutive children with HS received busulfan, cyclophosphamide and ATG followed by unrelated UCB transplants at Duke University Medical Center between 12/95 and 7/02, and were evaluated for engraftment, toxicity and effects of this therapy on the natural history of the disease. **Results:** UCB donors with normal α-L-iduronidase levels delivering a median cell dose of 8.55×10^7 cells/kg and discordant for 0-3 HLA markers were identified. Seventeen of the 18 evaluable patients engrafted after their initial UCB transplant, and the remaining child engrafted after a second UCB transplant. The median time to engraftment (ANC >500/μL) was 24 days. Five patients experienced grade 2 or 3 acute GVHD, and no children developed extensive chronic GVHD. Seventeen of the 19 children (89%) are surviving with complete donor chimerism and normal leukocyte α-L-iduronidase levels for a minimum of 100 days and a median of 748 days post transplant. Significant improvement was seen in many disease manifestations including orthopedic disease, skeletal growth, and neurodevelopment, with children achieving and maintaining a normal velocity of neurocognitive development within one year post transplant. **Conclusions:** UCB is a readily available stem cell source for allogeneic transplantation in patients with HS. Durable engraftment can be achieved without the use of TBI. UCB transplantation favorably alters the natural history of HS and should be strongly considered for all children with HS eligible for transplantation therapy.

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MYOCARDIAL ANGIOGENESIS AND MYOGENESIS BY DIRECT INJECTION OF AUTOLOGOUS MARROW STEM CELLS IN HUMANS

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Following methodology we and others developed in porcine models of acute and chronic myocardial ischaemia, we are attempting to produce angiogenesis and myogenesis in humans by direct intramyocardial injection of cells derived from patient's own bone marrow. A randomized placebo controlled trial is currently underway but interim data of the the first three "roll out" patients, who all recieved cell injections, is presented here. All patients were male with severe coronary artery disease and had undergone coronary artery grafting on more than one occasion. None of the patients were candidates for further revascularisation surgery or percutaneous angioplasty and stenting. All patients had regions of myocardium that were demonstrated viable but became ischaemic creating pain and loss of function on exertion. On the day of the procedure, patients had 40 mls bone marrow extracted which then underwent Ficoll gradient centrifugation to obtain the mononuclear layer. The cells were resuspended to obtain a cell concentration of 10, 000, 000 per ml. Simultaneously patients underwent intraventricular NOGA mapping to determine regions of ischaemic but viable myocardium. Between 10-13 carefully targetted sites were then directly injected with 0.1 mls of the autologous marrow cell suspension. All patients tolerated the procedure

without incident. The table shows baseline and three month assessments. The current study is designed for final follow up assessment at 6 months. These data show that reinjection of fractionated autologous bone marrow using the NOGA catheter system is feasable and safe. The data though limited are encouraging and the randomized trial is ongoing.

INTERIM RESULTS AT 3 MONTHS, INITIAL "ROLL OUT" PATIENTS						
	EXERCISE TIME-MINS		ANGINA EVENTS/WEEK		NITRATE USE/WEEK	
	BASELINE	3 MONTHS	BASELINE	3 MONTHS	BASELINE	3 MONTHS
Patient 1	3.1	3.8	9	1	11	2
Patient 2	3.9	4.3	21	1	20	1
Patient 3	4.6	5.9	64	56	64	28