CHEMOSENSITIVE RELAPSES AFTER CHEMOTHERAPY AND AUTOLGOUH HSCT: SOURCES OF HSCT INCLUCED HLA-MATCHED SIBLINGS (n = 41), MATCHED UNRELATED DONORS (n = 6) AND PARENTS (n = 1). FORTY-FIVE PATIENTS RECEIVED MYELOBLASTIC AND 3 RECEIVED REDUCED DENSITY CONDITIONING. THE MEDIAN EFS AND OS WERE 38 AND 40 MONTHS AND AT 160 MONTHS, THE EFS AND OS WERE 47% AND 50%. WHEN PATIENTS WITH DIFFUSE LARGE B-CELL LIPOMATOSIS WERE SEPARATELY ANALYZED, THE EFS AND OS AT 40 MONTHS WERE ABOUT 52% AND NONE OF THE PATIENTS HAD DISEASE RELAPSE OR MORTALITY THEREAFTER.

CONCLUSION: WE DEMONSTRATED THAT ALLOGENEIC HSCT MAY OFFER A CURE FOR HIGH RISK NHL PATIENTS. OUR RESULTS COMPARED FAVORABLY WITH THOSE REPORTED IN THE LITERATURE.

19 RECIPIENT OUTCOMES DATA COLLECTION AND REPORTING FOR CORD BLOOD BANK FOLLOW-UP AND QUALITY ASSURANCE PURPOSES: THE NATIONAL MARROW DONOR PROGRAM® EXPERIENCE

HAILE, M.1, CONFER, D.1, WELTE, K.1, MATLACK, M.1, KING, R.1, BOO, M.1, KURTZBERG, J.1. 1. NATIONAL MARROW DONOR PROGRAM, MINNEAPOLIS, MN; 2. DUKE UNIVERSITY MEDICAL CENTER, DURHAM, NC.

Cord blood banks (CBB) are required to monitor clinical outcomes of cord blood unit (CBU) transplants performed by transplant centers (TC). Obtaining accurate and timely follow-up data on clinical outcomes from the TC can be very difficult. The National Marrow Donor Program (NMDP), by virtue of their comprehensive activities with member network centers, collects outcomes data on recipients transplanted with either cord blood or adult donor cells. NMDP member transplant centers are required to submit data at defined intervals as part of their participation agreement. A system is in place to monitor compliance that includes a due process procedure for non-compliant centers. Recipients sign an IRB-approved consent form for data submission to the NMDP. All submitted data are verified through system checks at time of data entry. Identified errors are subject to a formal error correction process. Transplant centers are audited on a four year cycle to assure the accuracy and integrity of the data provided. At any given time, >90% of NMDP centers are compliant with forms submission requirements. The data elements include information on the results of the thaw, infusion related reactions, preparative regimens, neutrophil and platelet engraftment, GVHD, relapse, survival, and death. Member cord blood banks receive a quarterly report from the NMDP which includes comprehensive data on the individual recipients for which their CBUs were used. The data include recipient demographics, infused cell dose, degree of HLA match, engraftment, GVHD, relapse, survival, and cause of death. While outcomes data are reported quarterly to member banks, thaw data are reported and reviewed on a continuous basis. TNC recoveries that are low (<60%) or high (>100%) are reviewed by NMDP staff to detect problems with CBU potency that might be linked to a certain bank, shipping procedure or thawing protocol at a TC. Future directions include trend analysis reports and reviews with the NMDP Quality Standards subcommittee. The NMDP’s process for reporting quality assurance data to member banks is a valuable service that is unlikely to be feasible in a single bank.

ISOPHOSPHORAMIDE MUSTARD-LYSINE (IPM-L; ZIO-201): A NEW ALKYLATOR FOR BONE MARROW TRANSPLANTS

MORGAN, L.1, STRICK, K.1, RODGER, A.1, YARRIS, B.1, WAND, W.1, PAPAGIANNIS, C.1, GALE, R.P.1, DEKK-TEK, INC, NEW ORLEANS, LA; 2. CANCER MEDICA, LLC, BIRMINGHAM, AL; 3. SOUTHERN RESEARCH INSTITUTE, BIRMINGHAM, AL; 4. CHEMISTRY DEPARTMENT, UNIVERSITY OF NEW ORLEANS, LA; 5. MPI RESEARCH, MATTAWAN, MI; 6. ZIOPHARM ONCOLOGY, CHARLESTON, MA.

Alkylators are widely used in conditioning regimens for bone marrow transplants. IPM is a bi-functional alkylator with cross-linking through C-C base sequences resulting in irreparable interstrand DNA cross-linking producing cell death. IPM alkylates DNA as a phosphorodiamidate and may cross-link DNA differently from phosphoramidate mustard (PM) the major DNA-crosslinking moiety of cyclophosphamide (CPA). IPM is active in diverse cancer models but its chemical instability has hampered pharmaceutical development; CPA and ifosfamide (IFOS) were developed as alternatives. We stabilized IPM with lysine (IPM-L; ZIO-201) and tested it in preclinical sub-acute pharmacology and toxicology models and in mice with human cancer xenografts. ZIO-201 and IPM were given IV daily × 3 d. ZIO-201 sub-acute LD50/10 in adult mice was 133 and 220 mg/kg (combined sexes) compared to 119 and 149 mg/kg for IPM. Bone marrow failure was the dose-limiting toxicity (DLT) of both drugs. In the MX-1 human breast cancer model, ZIO-201 was better than IPM. MTD: 93 vs. 40 mg/kg/dose and tumor versus control life extension (T-C): 10.2 versus 2.1 d. Because ZIO-201 (unlike cyclophosphamide [CPA] and ifosfamide [IFOS]) is not metabolized to acrolein or acetaldehydes, there was no kidney, bladder or CNS toxicity. ZIO-201 is in phase-1 trials in humans: data will be presented. Using ZIO-201 may increase the safety and efficacy of this class of alkylators in clinical settings where high-dose CPA and IFOS are used, like bone marrow transplants. Possible dose increases and activity in CPA- and IFOS-resistant cancers may broaden the target range. Supported by grant R44 CA83552 from the NCI/ SBIR program.

ADOPTIVE IMMUNOTHERAPY WITH TUMOR-DERIVED DONOR LYMPHOCYTES AFTER ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION

HARDY, N.M.1, FELIXES, V.1, MARRIOTT, J.1, CARTER, C.1, JUNE, C.1, LECINE, B.1, HAKEM, F.1, VONDERBECKE, K.1, GRESS, R.1, READ, E.1, FOJAIL, D.1, BISHOP, M.R.1, NATIONAL CANCER INSTITUTE, NATIONAL INSTITUTES OF HEALTH (NIH), BETHESDA, MD; 2. CLINICAL CENTER, NIH, BETHESDA, MD; 3. UNIVERSITY OF PENNSYLVANIA, PHILADELPHIA, PA.

Treatment of refractory or recurrent malignancy with donor lymphocyte infusion (DLI) after allogeneic hematopoietic stem cell transplantation (allo-HSCT) is limited in efficacy, and graft-versus-tumor (GVT) is often accompanied by graft-versus-host disease (GVHD). After allo-HSCT, lymphocytes infiltrating residual tumor are likely of donor origin. Compared with DLI, they may provide enhanced antigen specificity and maintain tumor-specific homing, thus generate better GVT with less GVHD. We are testing this hypothesis through administration of ex-activated tumor-derived lymphocytes (TDL) after allo-HSCT. Clinical evaluation of TDL therapy was initiated with a 51-year-old woman for metastatic breast cancer whose disease progressed after matched-sibling allogeneic HSCT and subsequent conventional therapy plus DLI. Metastases were surgically removed two weeks after administration of unmanipulated DLI. Lymphocytes were isolated from 9.4 cm of tumor and expanded for 14 days with anti-CD3/CD28-coated magnetic beads (3:1 bead-to-total nucleated cell ratio) and media containing IL-2 (100 or 1000 IU/mL). The cell products from the two culture conditions were similar. The process yielded 42.5 × 10^10 cells, 33% expressing CD3, and generated 14.7 × 10^9 TDL, 85% expressing CD3 (a 3.1-log T cell expansion). There was no tumor contamination of the T cell product by immunohistochemistry. Chimerism analysis revealed the TDL to be of donor origin. Flow cytometry showed an increase in the CD4/CD8 ratio from 1.3 to 1.9 after expansion. 76% of CD8 and 31% of CD4 cells secreted IFN-γ, and none secreted IL-2. IL-4 or IL-10, 76% of CD8 and 57% of CD4 cells expressed CXCR3. Three infusions of TDL were given in a dose-escalating manner (S, 25 and 100 × 10^8 CD3 Cells/kg). Two additional infusions were given in conjunction with low-dose IL-2, the second of which was preceded by one cycle of paclitaxel and trastuzumab cytoreductive therapy. No infusion-related or delayed toxicities were observed. The patient had no evidence of GVHD, even after the highest dose of 10^8 allogeneic T cells. Evaluation of the remaining thoracic lesion demonstrated progressive disease after the first two TDL infusions, transient disease stability after the third and fourth infusions, and at present, the patient has stable disease one month after the fifth infusion. This is the first clinical report of the application of TDL and represents a novel approach for adoptive immunotherapy in the setting of allo-HSCT.