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14. ABSTRACT

1. Contingency Preparedness: Collect information from transplant centers, build awareness of the Transplant Center Contingency Planning Committee and educate the transplant community about the critical importance of establishing a nationwide contingency response plan.

2. Rapid Identification of Matched Donors: Increase operational efficiencies that accelerate the search process and increase patient access are key to preparedness in a contingency event.

3. Immunogenic Studies: Increase understanding of the immunologic factors important in HSC transplantation.

4. Clinical Research in Transplantation**:** Create a platform that facilitates multicenter collaboration and data management.

15. SUBJECT TERMS
Research in HLA Typing, Hematopoietic Stem Cell Transplantation and Clinical Studies to Improve Outcomes

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Grant Award N00014-23-1-2057

DEVELOPMENT OF MEDICAL TECHNOLOGY

FOR CONTINGENCY RESPONSE TO MARROW TOXIC AGENTS

QUARTERLY RESEARCH PERFORMANCE REPORT

SUBMITTED January 13, 2023

Office of Naval Research

And

The National Marrow Donor Program®

500 5th St N

Minneapolis, MN 55401

I. Heading

PI: Jeffrey Auletta, M.D.
National Marrow Donor Program
N00014-23-1-2057
Development of Medical Technology for Contingency Response to Marrow Toxic Agents

II. Scientific and Technical Objectives

The main goal of all activities funded through this grant is to develop, test and mature the ability of the NMDP Coordinating Center and NMDP contracted network sites network sites to address contingency events wherein civilian or military personnel are exposed to marrow toxic agents, primarily ionizing radiation or chemical weapons containing nitrogen mustard. As a result of prior efforts in this regard a solid foundation has been established. The proposed new activities will continue to enhance and expand our capabilities in each of the four focus areas. Contingency preparedness activities will continue to integrate NMDP's role with federal, state and local agencies.

An accident, a military incident, or a terrorist act in which a number of individuals are exposed to marrow toxic agents will result in injuries from mild to lethal. But the extent of individual injuries and the likelihood of recovery in many cases will not be apparent until days or weeks after the event. Casualties will be triaged by first responders, and those with major marrow injuries who will need aggressive medical support and may be ultimately candidates for hematopoietic cell transplantation (HCT) will need to be identified. While these patients are being supported, HCT donor identification activities will be initiated because it will not be initially clear which ones may ultimately require HCT. NMDP-approved transplant centers will provide a uniform and consistent clinical foundation for receiving, evaluating and caring for casualties. NMDP Coordinating Center will orchestrate the selection and testing necessary to rapidly identify the best available donor or cord blood unit for each patient utilizing its state-of-the-art communication infrastructure, sample repository, laboratory network, and human leukocyte antigen (HLA) expertise. NMDP's on-going immunobiologic, bioinformatics and clinical research activities promote studies to advance the science and technology of HCT transplantation and directly translate research results to improve outcomes and quality of life for the patients.

Importantly, most individuals with near-lethal marrow toxic injuries will recover their own marrow function provided they receive intensive supportive care from the medical professionals that are part of the contingency response community.1 These professionals can save the lives of persons with severe marrow suppression using the knowledge and skills practiced every day to treat patients undergoing HCT coordinated through the NMDP.

III. Approach

A. Contingency Preparedness

HCT teams are uniquely positioned to care for the casualties with marrow toxic injuries, such as Acute Radiation Syndrome (ARS), from exposure to ionizing radiation or chemicals. The NMDP manages a network of hospitals that work in concert to facilitate unrelated HCT. The Radiation Injury Treatment Network (RITN), comprised of a subset of NMDP's network centers as well as non-NMDP network centers, is a national network of medical centers with expertise in the management of bone marrow failure and works with partners from other medical specialties to assist with managing ARS and its health-related consequences in response to marrow toxic mass casualty incidents.

B. Development of Science and Technology for Rapid Identification of Matched Donors
Rapid progression to successful transplantation following a marrow toxic exposure or disease diagnosis affects survival. Decreasing the time to identify the optimal donor is critical. Methods are under development to rapidly identify and provide the optimal donor for HCT.

C. Immunogenetic Studies in Transplantation
Improving strategies to avoid and manage complications due to graft alloreactivity is essential to improve the outcomes of HCT. Research efforts focus on strategies to maximize success of HCT while minimizing the toxicity related to alloreactivity between the donor graft and the recipient.

D. Clinical Research in Transplantation
Clinical research creates a platform that facilitates multi-center collaboration and data management to address issues important for managing radiation exposure casualties. Advancing the already robust research capabilities of the NMDP network will facilitate a coordinated and effective contingency response.

IV. Updates

A. Contingency Preparedness

Maintain the Radiation Injury Treatment Network (RITN) to prepare for the care of patients resulting from a hematopoietic toxic event

Radiation disaster and countermeasure research education

- Advanced HAZMAT Life Support (AHLS) for Radiological Incidents & Terrorism 4-hour course (1) Has a target audience of physicians, physician multipliers, nursing staff, administrators and coordinators from departments such as bone marrow transplant, hematology, oncology, radiation safety, nuclear medicine, and the emergency department, as well as emergency management, and first responders; and (2) Will include interactive lectures and tabletop exercises that trains healthcare professionals to evaluate and care for irradiated and radiologically contaminated patients.
- TBD – Two, half-day courses hosted by a TBD RITN hospital

Radiation disaster preparedness training
No updates at this time.

Hospital radiation disaster preparedness

- Annual disaster readiness tabletop exercises (drills) will be scheduled for current RITN centers to participate for their annual task completion. Six sessions will be offered between June and August 2023.
- Additional disaster readiness exercises (drills) have yet to be scheduled: one Full-scale exercise, five Functional exercises, and three Regional Tabletop exercises.

Hospital network growth

To ensure the appropriate growth in a direction that supports the vision and needs of the Department of Defense-Office of Naval Research as well as the Department of Health and Human Services Administration for Strategic Preparedness and Response plans for response to a radiological/nuclear disaster with-in the continental U.S.

- Targeted hospitals in the following cities:
    - Atlanta, GA
    - Nashville, TN
    - Los Angeles, CA
    - San Antonio, TX
    - Dublin, CA
    - Memphis, TN
    - Phoenix, AZ
    - New Orleans, LA
    - Albuquerque, NM
- Specific hospitals:
    - Children's Healthcare of Atlanta (CHOA)
    - Skyline Medical
    - Children's Hospital Los Angles (CHLA)
    - Stanford (Dublin, CA)
    - Corewell East Beaumont Children's Hospital (Royal Oak, MI)

Federal partnership development

- National Association of County and City Health Officials (NACCHO) Preparedness Summit
    - Recovering from a long pandemic response, there is a need to redefine not only the endemic phase of COVID-19, but reassess responses to natural disasters, emerging infectious diseases, terrorist threats, climate issues, and maintenance of all-hazards plans. "Recover. Renew: Reprioritizing All-Hazards Preparedness" is the theme and will give attendees the opportunity to reevaluate issues (old and new) in preparedness, share resources, build skills, and to network with others in the industry.
- RITN is a member of the Radiation Workshop Planning Committee which is planning a 1-day radiation-specific planning workshop prior to the Preparedness Summit.

B. Development of Science and Technology for Rapid Identification of Matched Donors

Expand the genetic diversity of the registry through continued addition of adult donors and cord blood units, utilizing high volume HLA typing methodologies

No activity to report this quarter.

Modeling and analysis of registry coverage for the Warfighter

Population genetics-based registry models projected donor coverage for warfighters as potential patients approaches but does not reach 100% when considering HLA match levels down to 5 of 8 matching alleles. Over the last quarter, additional methods and data sources for validation of registry models was investigated. Our models seek to better understand the contribution of racially and ethnically diverse donors for matching in diverse groups. Current resources for validation of these results through simulations of donor registry searches with patient-donor HLA match criteria require more frequent and comprehensive data updates and greater flexibility in matching rules along with the ability to consider outcome probabilities in the presence of missing data. Previously, registry models were restricted in the number of mismatched HLA alleles that could be calculated. New code explores allowing another level of mismatch. Registry searches were conducted for the purposes of validating modeled results and continue to be evaluated for quality testing and assessment of model result accuracies. This modeling aids in preparation for coverage of potential donor sources to Warfighters of diverse race and ethnic backgrounds in case of radiation emergencies.

Development of science and technology for rapid communication of HLA data

During the past quarter, a manuscript, titled "Assessment of HLA-DPB1 Genetic Variation with an HLA-DP Tool and Implications in Clinical Transplantation", was submitted for publication. Genetic variation in HLA-DPB1 exon 2 defines permissive and non-permissive TCE groups, and exons 2 and 3 (in linkage with rs9277534) inform low- and high-expression allotypes with varying implications for transplant outcomes identified in previous studies (Figure 1). In this study, 356,272 exon 2 –exon 3 phased sequences from individuals were analyzed across five self-identified race and ethnicity categories: White, Hispanic, Asian or Pacific Islander, Black or African American, and American Indian or Alaskan Native. The complex relationship between TCE and expression models was explored, and the importance of exon 3 sequence data was uncovered through this analysis. Archived donor search lists for 2,545 patients who underwent transplantation from an HLA-11/12 unrelated donor mismatched for a single HLA-DPB1 allele were analyzed. Depending on the order in which TCE and expression criteria are considered, some patients have different TCE- and expression-favorable donors in terms of transplant outcome risk. In addition, many expression-favorable alternatives exist in the search lists were uncovered. A novel tool called ExPAT (Expression of HLA-DP Assessment Tool), consisting of a public web application, Python

code package, and analysis pipeline was developed and launched to facilitate exploration of HLA-DP genetics and impact on expression and improved matching of transplant donors and patients.

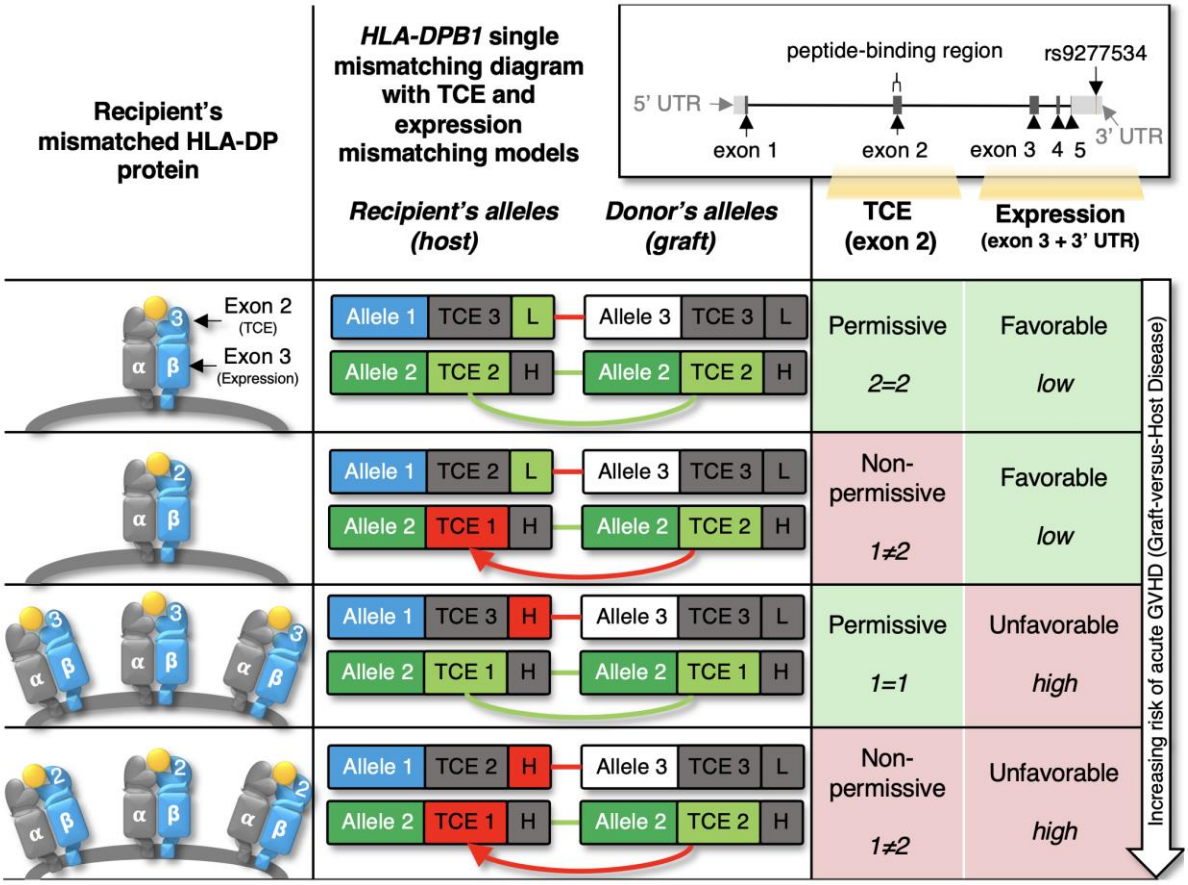

Figure 1: The relationship between HLA-DPB1 genetics and protein expression in transplant donors and patients (recipients) is shown in order of increasing risk of acute Graft versus Host disease for the patient. The ExPat tool facilitates categorization of patient and donor genotypes and combinations to aid in selection of the best donor match for the patient.

Use of population genetics and machine learning to automate the donor selection process

Apply BART NFT method to prediction of transplant outcomes

A new model has been developed based on the BART NFT methodology to assist with donor selection in situations where there is a tradeoff between the factors that affect overall survival (OS) and event free survival (EFS) in an 8/8 matched unrelated donor setting. A machine learning based model was developed that provides estimates of both OS and EFS and this was applied to a historical dataset to evaluate the alternative matched donors not selected compared the donor that was selected. This new method demonstrates that historically donors were not selected optimally (according to the model) with regard to sex and age of the donor impacting OS and EFS. A model for generating a weighted blend of OS/EFS outcome has been proposed. This approach is being developed into a pilot web application for interactive prospective use to validate the approach.

Expand previous work on optimizing donor selection in the HLA matched (8 of 8 alleles) setting to focus on mismatched transplants, specifically those performed under new clinical protocols for multiple mismatched and haploidentical donor transplants

During the past quarter a dataset has been prepared covering the period 2016-2019 across all available categories of matching and mismatching to inform the development of machine learning models that can inform the decision of which cell source to use (not just selecting among options within a category).

Donor Cell Source	Number
Unrelated	16424
Matched sibling	8399
Matched relative	456
One antigen mismatched relative	258
>one antigen mismatched relative	5978
URD single cord	901
URD multiple cords	916

Preliminary results have shown that this data driven approach can provide recommendations in certain contexts that are not in agreement with the standard consensus for selecting donors. For example, in the standard consensus donor selection approach, an 8/8 donor is always preferable to a 7/8 donor regardless of the ages of the donors. A model that can identify specific situations where deviation from this central dogma has the potential to change practice and improve outcomes.

In addition, a manuscript entitled "Machine Learning Approach to Predicting Overall Survival After Allogeneic Hematopoietic Cell Transplantation" was drafted. Several prognostic scores and models for predicting the outcomes of allogeneic hematopoietic cell transplantation (allo-HCT) have demonstrated utility in stratifying patients into risk classes but struggle to make accurate individualized predictions. A machine-learning pipeline for predicting one-year overall survival after hematopoietic cell transplantation (HCT) was developed using a set of readily available clinical variables. Transplant records from the Center for International Blood and Marrow Transplant Research (CIBMTR) database restricted to the years 2014 - 2018 in the United States (N=36,538) were utilized. The dataset was split into training (85%) and test (15%) sets. Several machine learning models were built using the selected features, and their predictive performances were evaluated. XGB was identified as the best model and also performed better than standard logistic regression, C-index 0.76 vs. 0.63. The top-ranked predictors (features) identified by the XGB model include patient-related factors (recipient age and Karnofsky performance status), disease-related factors (disease type and status at time of HCT), and transplant-related factors (donor/recipient sex and CMV serostatus match, conditioning regimen, donor type, donor age group). Potential uses of this clinically based machine learning pipeline include (1) providing a personalized prognostic assessment, (2) informing clinical decisions regarding donor selection and conditioning regimen choices, (3) generation of testable hypotheses that could potentially guide future trials, and (4) establishing a baseline, upon which the added value of integrating more costly high dimensional data, such as omics data, can be evaluated.

Expand the genetic diversity of the registry through continued addition of adult donors and cord blood units, utilizing high volume HLA typing methodologies

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Apply and validate HLA imputation and annotation methods for flexible and batch application toward improved matching

During the past quarter we released a new open-source imputation algorithm for HLA https://github.com/nmdp-bioinformatics/py-graph-imputation/. This new method builds on previous methods with extensions for addressing individuals with mixed, missing or misassigned race/ethnicity and addresses the problem sampling error in population frequency data. The new method was validated on simulated and clinical data and has been shown to perform consistently better than the imputation method used in routine clinical practice for determining match probabilities in routine donor registry search (Figure 2).

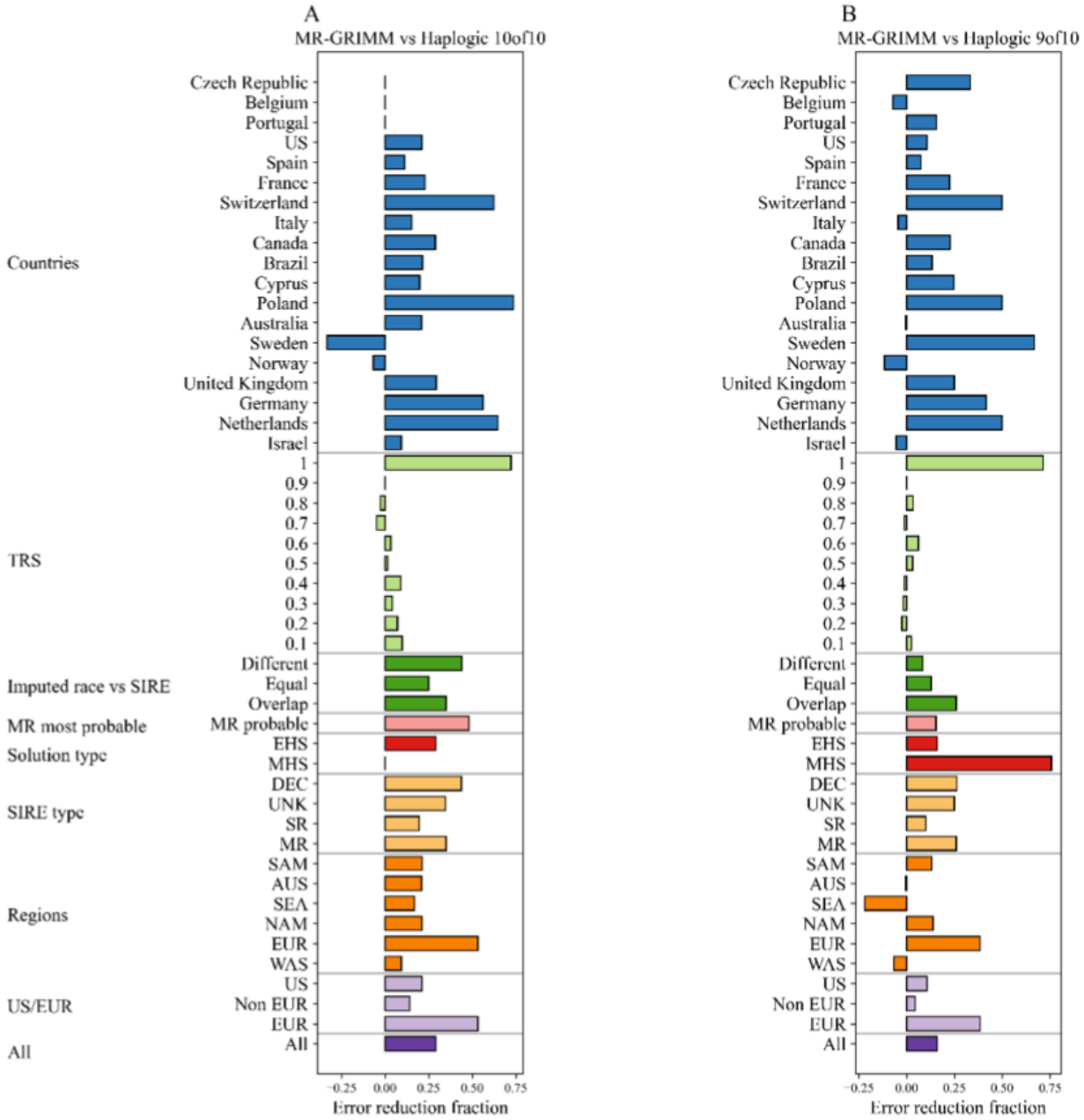


Figure 2. Reduction in error (difference between AUC and 1) of new graph-based imputation method (MR-GRIMM) compared to the imputation method used in operations (HapLogic). The AUC the area under the receiver-operator characteristic curve measured for full match-10 of 10 (A) and single mismatch -9 of 10 (B), for all patient-donor pairs from the real-life dataset stratified in 8 different dimensions. Bars to the right indicate improvement with the new method.

C. Immunogenetic Studies in Transplantation

Evaluate HLA disparity and impact on HCT by adding selected pairs to the Donor/Recipient Pair project utilizing sample selection criteria that optimize the new data generated by the typing project

The Donor/Recipient Pair project continues to enroll the most recent related and unrelated transplant pairs to ensure that changes in practice can be evaluated using quality-controlled high resolution HLA data. Strategic selection of pairs for testing and optimization of practices associated with data storage and management ensure that investigators have timely access to robust, high-quality data to analyze the impact of matching as either the focus of or as a variable in CIBMTR-approved research studies. This period, migration of DRPP unrelated transplant pair inventory to a new database was completed to allow for continued access and platform support. Additionally, user acceptance testing was completed on the migrated data and tools. Finally, the audit of four additional sample groups was completed. In collaboration with stakeholders from various business units, an improved process has been established to optimize the efficiency with which pairs are submitted for typing moving forward.

Development of a national framework to standardize measurable residual disease evaluation in the clinical care of patients receiving allogeneic transplant for acute myeloid leukemia

While allogeneic HCT is a curative therapy for many patients with acute myeloid leukemia (AML), the risk of relapse even after achieving a cytomorphological complete remission (CR) is the most common form of treatment failure and death. Transplant-related morbidity and mortality is a major obstacle for the effective use of alloHCT, resulting in the potential under- or over-utilization of conditioning regimen intensity to prevent AML relapse. The presence of residual leukemic burden, known as measurable residual disease (MRD), prior to transplant is associated with worse outcomes after transplantation. AML MRD testing is not standardized, and no clear path to translate findings from research laboratories to clinical transplant settings currently exists.

A multicenter prospective observational study was launched in 2022 to address this issue by developing a coordinated national framework to 1) allow collection of leftover initial AML diagnosis material from patients who have received alloHCT in US centers, 2) prospectively collect samples from AML patients after alloHCT to determine optimal timing and method for post-alloHCT MRD monitoring and 3) implement findings from phases 1 and 2, together with a central reference laboratory, to allow local centers to perform standardized MRD testing pre or post alloHCT. This would allow both selection of conditioning intensity, but also inform post-transplant maintenance and allow patient selection for novel clinical trials.

During the past quarter the protocol team continued to meet regularly to manage the IRB approved and ClinicalTrials.gov registered study protocol entitled, "MEASURE: **M**olecular **E**valuation of **A**ML patients after **S**tem cell transplant to **U**nderstand **R**elapse **E**vents". To date, 17 centers have committed to participate in the study and combined plan to enroll >250 patients per year. Ten of 17 sites have received local IRB approval for the protocol. All sites have initiated submission of regulatory documents required for

participation. Site initiation visits were completed for 7 sites with 1 more scheduled for early next quarter. Two sites have fully opened the study and has enrolled 8 patients.

Determine the impact of peripheral blood stem cell graft composition on the outcome of hematopoietic cell transplantation

While allogeneic HCT offers potentially curative therapy to patients with a variety of benign and malignant diseases, both acute and chronic GVHD continue to plague the field and often limit the longevity and quality of life for patients. The composition of PBSC grafts has been evaluated in multiple studies to attempt to discern associations between various cellular subsets and outcomes. The BMT CTN 0201 randomized trial of bone marrow versus PBSC found that PBSC grafts were associated with a higher risk of cGVHD and worse quality of life following unrelated donor HCT compared to BM. A correlative study of graft immunophenotype failed to identify any associations between PBSC graft composition and outcomes. However, the PBSC cohort included only 147 evaluable products limiting the power to evaluate various cellular subsets. The association between PBSC graft immunophenotype and outcomes remains unclear.

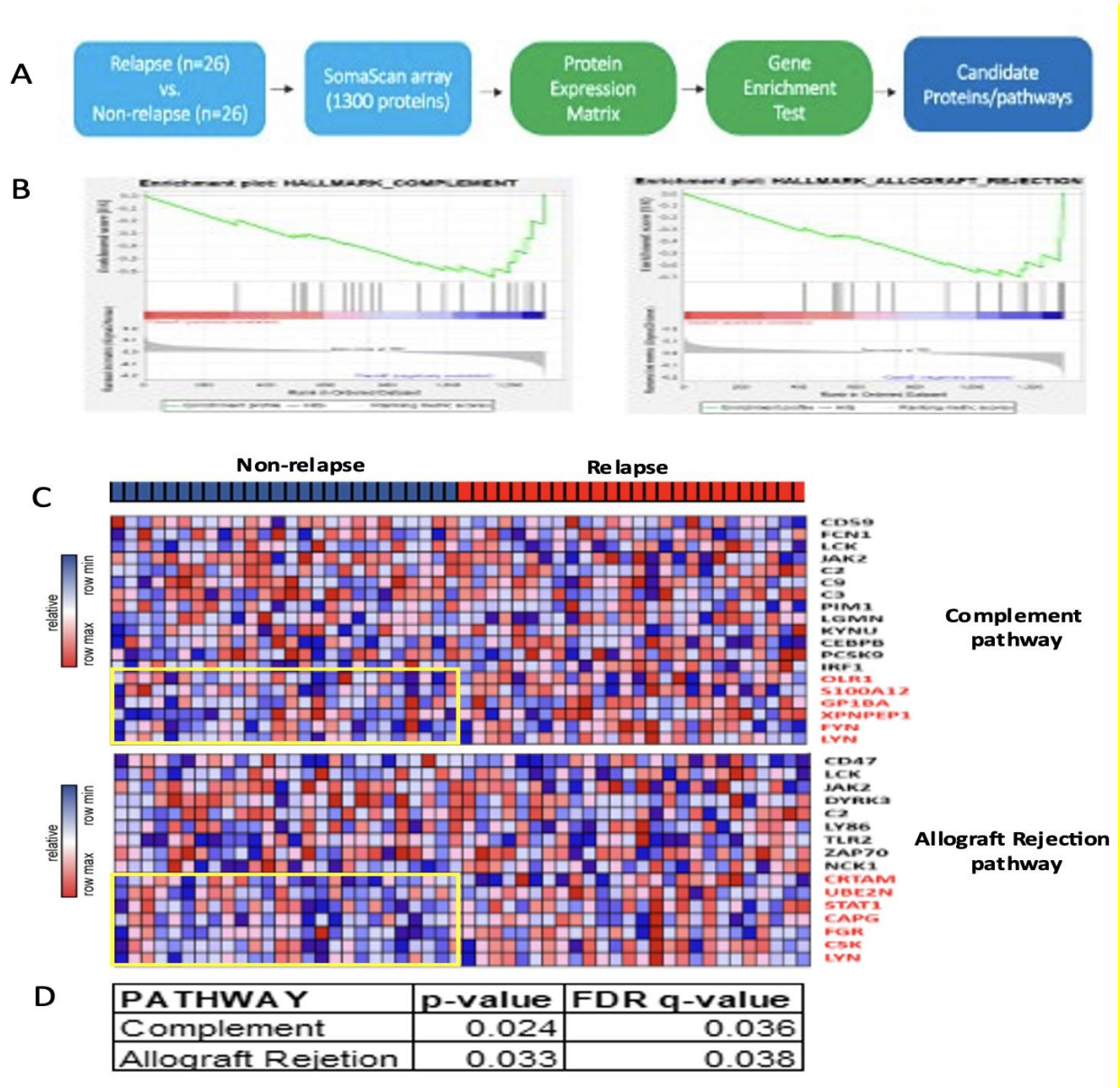
The primary aim of this study is to evaluate PBSC graft stem cell and associated immune cell composition and to determine at 12-months of follow-up how either the comprehensive graft cellular composition profile or specific graft composition elements influences the primary outcomes of time to neutrophil engraftment and overall survival. Secondary outcomes of interest include, but not limited to, incidence of acute and chronic GVHD, primary disease relapse, TRM, and DFS. The study will evaluate approximately 2,100 PBSC products over a 3-year accrual period with 1,100 collected in the U.S. through the NMDP and an additional 1,000 collected in Germany for U.S. based patients through the DKMS. The U.S. testing will be supported through the ONR (prior grant years and the current) and DKMS will support testing of German collected products. Data will be merged with CIBMTR collected clinical outcomes for analysis and correlation with clinical outcomes.

During the past quarter accrual continued for U.S. based donors. A total of 294 product samples were received and tested through December 31, 2022 with 69 tested in the last quarter. Testing costs are covered under this grant while staff support is funded under a subsequent grant. The DKMS laboratory continued efforts to establish the standardized immunophenotyping panel for testing of Germany based donors. The study team met several times to finalize plans for concordance testing between the U.S. and DKMS laboratories. Concordance testing using known controls supplied by the NMDP testing laboratory will be performed in the next quarter. Accrual of German donors has begun on a limited basis and will be expanded following successful completion of the concordance evaluation to ensure that data is being consistency captured in both the U.S. and German laboratories. Testing of German donors will be fully funded by DKMS.

Determine the impact of non-HLA genes and gene expression on allogeneic cell transplantation

This quarter, a manuscript entitled “Proteomics to predict relapse in patients with myelodysplastic syndromes undergoing allogeneic hematopoietic cell transplantation” was drafted. Disease relapse remains a major barrier to success for allogeneic hematopoietic cell transplantation (allo-HCT) in myelodysplastic syndromes (MDS). While certain high risk genomic alterations have been found to associate with increased risk of relapse, additional predictors of relapse remain to be identified. The hypothesis is that unique proteomic signatures in MDS patients prior to allo-HCT could serve as biomarkers for relapse risk. Using

CIBMTR outcomes data, 52 MDS patients with or without relapse after allo-HCT were identified and their proteomic profile analyzed from pretransplant blood samples in a matched case-control design where 26 patients who did not have disease relapse after allo-HCT (controls) were matched with 26 patients who experienced relapse. Proteomic assessment was conducted using the Slow Off-rate Modified Aptamers (SOMAmer) based assay. In a gene set enrichment analysis (GSEA) of relapse associations, the hallmark complement and hallmark allograft rejection pathways were noted to be statistically enriched (p value<0.05, FDR<0.05) (see Figure 1). In addition, epigenetic signatures in these immune pathway genes were found to be modulated on their *cis*- and transcription regulatory elements, which differentially sensitize the immune response in MDS patients. These findings indicate that proteomics may provide novel biomarkers of MDS relapse.



PATHWAY	p-value	FDR q-value
Complement	0.024	0.036
Allograft Rejetion	0.033	0.038

Figure 3. Allograft rejection and complement pathways were enriched in MDS relapse group by proteomics gene set enrichment analysis. A. Describes the workflow used for proteomic analysis. B. The profile of the ES score and positions of DE gene candidates in the rank list from GSEA leading edge

analysis. C. Protein expression heatmap for tow representative pathways: complement pathway and allograft rejection pathway. Differentially expressed proteins between non-relapse and relapse groups are highlighted in red. D. The normal p value and FDR q-value for the complement and allograft rejections pathways.

D. Clinical Research in Transplantation

Conduct clinical outcomes research using the CIBMTR research database and repository.

Observational Research

- Published 14 manuscripts in peer-reviewed journals during the last quarter (see publications below).
- A total of 31 abstracts were presented at the 2022 American Society of Hematology (ASH) Annual Meeting held Dec. 10-13 in New Orleans, LA. Presentation titles and type are detailed in table 1 below. Abstracts are posted on the ASH annual meeting website and published in Blood.
- A total of 21 abstracts were submitted and accepted for presentation at the 2023 BMT Tandem Meetings of the CIBMTR and American Society for Transplant and Cellular Therapy to be held February 15-19 in Orlando, FL. Presentation titles and type are detailed in table 2 below. Abstracts will be published in a supplemental to the Journal of Transplant and Cellular Therapy next quarter.

Table 1: CIBMTR presentations at 2022 ASH Annual Meeting

Title	Status
Does Race/Ethnicity Impact Umbilical Cord Blood Transplant Outcomes in a Contemporary Era?	Oral
Association between patient-reported outcomes and the social transcriptome profile as a predictor of clinical outcomes following hematopoietic stem cell transplant	Oral
Graft Failure in MDS and Acute Leukemia Patients After Allogeneic Stem Cell Transplantation Receiving Post Transplant Cyclophosphamide	Oral
Younger Matched Unrelated Donors Confer a Decreased Relapse Risk As Compared to Older Sibling Donors for Adult B-Cell ALL Patients Undergoing Allogeneic Hematopoietic Cell Transplantation	Oral
Comparison of Allogeneic Hematopoietic Cell Transplantation Outcomes from Younger Matched Unrelated Donor Versus Older Sibling Donor for Acute Myeloid Leukemia	Oral
Germline-somatic interactions drive JAK2-mediated clonal expansion in myelofibrosis.	Oral
A Real-World Evidence Comparison of One-Year Overall Survival and Relapse-Free Survival Between Patients Treated with Abatacept in Combination with a Calcineurin Inhibitor and Methotrexate versus Antithymocyte Globulin or Post-Transplant Cyclophosphamide Following Allogeneic Hematopoietic Cell Transplantation	Oral
Real-World Outcomes for Patients with Relapsed or Refractory (R/R)Aggressive B-Cell Non-Hodgkin's Lymphoma (aBNHL) Treated withCommercial Tisagenlecleucel: Subgroup Analyses from the Center for International Blood and Marrow Transplant Research (CIBMTR) Registry	Oral
Clinical outcomes following allogenic transplant with omidubicel or other donor sources in patients with hematologic malignancies: comparison of clinical trial results to external controls drawn from the CIBMTR database	Oral
Development of A risk score to predict the incidence of acute graft versus host disease after allogeneic hematopoietic cell transplantation (HCT)	Oral
Observational cohort study of people living with HIV treated with CD19-directed CAR T cell therapy for B-cell lymphoid malignancies	Oral
Improved Outcomes of UM171-Expanded Cord Blood Transplantation Compared with Other Graft Sources: A Real-World Database Study	Oral
Ongoing Risk of Unrelated Donors Testing Positive for COVID-19 Following Medical Clearance and Impact on Operations: A Report from the National Marrow Donor Program	Oral
Associations of Minor Histocompatibility Antigens with Clinical Outcomes Following Allogeneic Hematopoietic Cell Transplantation	Oral
Post-Transplant Cyclophosphamide, Tacrolimus, and Mycophenolate Mofetil As the New Standard for Graft-Versus-Host Disease (GVHD) Prophylaxis in Reduced Intensity Conditioning: Results from Phase III BMT CTN 1703	Oral
International Collaborative Study to Compare the Prognosis for Acute Leukemia Patients Transplanted with Intensified Myeloablative Regimens	Poster
Impact of center specific analysis on hematopoietic cell transplant center volumes	Poster
Comorbidities, Toxicities and Efficacy Outcomes after Chimeric Antigen Receptor T-cell Therapy in B cell Lymphoma	Poster

Title	Status
Impact of Age on Outcomes after CD19 Directed CAR T Cell Therapy for Large B Cell Lymphomas: Real World Experience from the Center for International Blood & Marrow Transplant Research (CIBMTR)	Poster
Racial, ethnicity and socioeconomic disparity in outcome of patients with chronic graft-versus-host disease	Poster
Utilization of Autologous HCT in Multiple Myeloma: A novel linkage of CIBMTR, cancer registry and hospitalization data in California	Poster
Subsequent Solid Neoplasms Following Hematopoietic Cell Transplantation (HCT) for Hematologic Malignancies: Comparing Center For International Blood And Marrow Transplant Research (CIBMTR) and California Cancer Registry (CCR) Data	Poster
Comparison of vital status and cause-specific mortality after Hematopoietic Cell Transplantation between the Center for International Blood and Marrow Transplant Research and the California Cancer Registry: a record-linkage analysis from 1991 to 2018	Poster
Access: A Multi-Center, Phase II Trial of HLA-Mismatched Unrelated Donor Hematopoietic Cell Transplantation with Post-Transplantation Cyclophosphamide for Patients with Hematologic Malignancies	Poster
Quality of Life in Patients Undergoing Double Umbilical Cord Blood vs. Haploidentical Marrow Transplantation: a QOL Analysis Report of BMT CTN 1101	Poster
Comparable Incidence Rates of Hematologic and Non-Hematologic Malignancies, Thrombotic Events, and Autoimmune Disorders in Unrelated Adult Donors Undergoing Bone Marrow Collection Versus Peripheral Blood Stem Cell Mobilization with Recombinant Human Granulocyte Colony-Stimulating Factor (rHuG-CSF): Results of the Donor Long-Term Follow-up Study By the National Marrow Donor Program (NMDP)	Poster
An Exploration of Unrelated Donor Existence for Patients Who Received Haploidentical Hematopoietic Cell Transplants	Poster
Analysis of US Registry Data on Patient Characteristics, Treatment Patterns and Outcomes of Patients Receiving Extracorporeal Photopheresis with or without Ruxolitinib	Poster
Veno-Occlusive Disease Risk and Other Outcomes in Patients with B-Cell Precursor Acute Lymphoblastic Leukemia Who Received Inotuzumab Ozogamicin and Proceeded to Hematopoietic Stem Cell Transplantation: A Registry-Based, Observational Study	Poster
Shared Graft Versus Leukemia Minor Histocompatibility Antigens in DISCOVeRY-BMT	Poster
Genome-Wide Non-HLA Mismatches Improve Risk Stratification for Overall Survival and Cause Specific Mortality after Unrelated Donor Allogeneic HCT	Poster

Table 2. CIBMTR presentations at 2023 BMT Tandem Meetings

Title	Status
Posttransplant Cyclophosphamide-Based Transplantation from Haploidentical Donors Has Similar Outcomes As Unrelated Donor Transplantation in Myelofibrosis: A Center for International BMT Research (CIBMTR) Study	Oral
Comparison of Allogeneic Hematopoietic Cell Transplantation Outcomes from Younger Matched Unrelated Donor Versus Older Sibling Donor for Acute Myeloid Leukemia	Oral
Younger Matched Unrelated Donors Confer a Decreased Relapse Risk As Compared to Older Sibling Donors for Adult B-Cell ALL Patients Undergoing Allogeneic Hematopoietic Cell Transplantation	Oral
Associations of Minor Histocompatibility Antigens with Clinical Outcomes Following Allogeneic Hematopoietic Cell Transplantation	Oral
Improved Relapse-Free Survival (RFS) for Pediatric and Young Adult Patients with Relapsed or Refractory (R/R) B-Cell Acute Lymphoblastic Leukemia (B-ALL) and Low or Intermediate Preinfusion Disease Burden Treated with Tisagenlecleucel: Results from the CIBMTR Registry	Oral
Shared Graft Versus Leukemia Minor Histocompatibility Antigens in Discovery-BMT	Oral
HLA Evolutionary Divergence Does Not Predict Relapse and Survival Following Allogeneic Hematopoietic Stem Cell Transplant for Myeloid and Lymphoid Malignancies	Poster
Access: A Multi-Center, Phase II Trial of HLA-Mismatched Unrelated Donor Hematopoietic Cell Transplantation with Post-Transplantation Cyclophosphamide for Patients with Hematologic Malignancies	Poster
Impact of Public Reporting of Center-Specific Analysis Scores on Hematopoietic Cell Transplant Center Volumes	Poster
An Exploration of Unrelated Donor Existence for Patients Who Received Haploidentical Hematopoietic Cell Transplants	Poster
Association between Patient-Reported Social Determinant of Health Outcomes and a Social Genomics Profile in Allogeneic Hematopoietic Cell Transplantation: A Center for International Blood and Marrow Transplant Research (CIBMTR) Analysis	Poster
Can You Spare 100 Days? The Allogeneic Hematopoietic Cell Transplant Caregiver Requirement	Poster
Can You Spare 100 Days? Allogeneic Hematopoietic Cell Transplant Caregiver Requirements from the Perspective of Recipients and Caregivers	Poster
Does Race/Ethnicity Impact Umbilical Cord Blood Transplant in a Contemporary Era?	Poster
Delayed CD4+ T Cell Recovery after Allogeneic Hematopoietic Cell Transplantation Is Associated with Decreased Overall Survival in Adult but Not Pediatric Recipients	Poster
Patient-Reported Outcomes in Long-Term Survivors of Autologous Hematopoietic Cell Transplantation (AHCT) for Hodgkin (HL) and Non-Hodgkin Lymphoma (NHL): Secondary Analysis from Two Multicenter Randomized Controlled Trials (RCT) of Hematopoietic Cell Transplant Survivorship Interventions	Poster

Title	Status
Ph-Positive ALL Patients Who Are Treated with Tyrosine Kinase Inhibitors Have Similar Post-Transplant Survival As Ph-Negative Patients	Poster
Ongoing Risk of Unrelated Donors Testing Positive for COVID-19 Following Medical Clearance and Impact on Operations: A Report from the National Marrow Donor Program	Poster
Trends in Utilization of Autologous and Allogeneic Hematopoietic Cell Transplantation in Racial/Ethnic Minorities	Poster
Disease-Specific Overall Survival Prediction after Allogeneic Hematopoietic Cell Transplantation	Poster
A Retrospective Analysis of Genotype Copy Number (GCN) in Unrelated Donor Transplants and Future Implications for Mismatched Transplants	Poster

Research data collection and systems enhancements
During the past quarter, CIBMTR has continued support for electronic data submission initiatives, production FormsNet Recipient, FormsNet Donor, and AGNIS customers, as well as Data Warehouse users. Progress has been made on the following critical projects to upgrade our technology supporting the program:

Simplify Data Acquisition
To acquire timely, high quality, data with less administrative burden to current and new partners/patients.

FormsNet (FN3)
Continued the quarterly releases of recipient form revisions to be current with existing treatment practices, as well as implemented revisions of forms to support the cellular therapies registry. Completed and in-process enhancements within Data Capture applications include:

- Added collection fields within FN3 and updated tools for supporting the Data Transformation Initiative, with a planned January release
- New development and testing was completed for the Upstream CRID Assignment Project for a January 27th release to production:
    - Formsnet3 was configured to capture patient demographic and infusion data already captured by the NMDP MatchSource application to assign a CRID at the time of infusion and to autocomplete and make applicable forms due
    - This project will reduce center data entry, improve CIBMTR reporting capabilities, improve data quality, and reduce the troubleshooting between CIBMTR and transplant centers to reconcile discrepancies.
- Enhancements to internal tool User Interface (UI) features to support reprocessing multiple forms at a single time, with a planned January release
- FormsNet3 Forms Definition Manager (FDM): Completed several proactive security vulnerability updates revealed by new scans
- FDM/AGNIS Mapping Tool:
    - Further configuration of tool to connect to new Cancer Data Standards Registry and Repository (caDSR) API
- Study updates were made to the FN3 Donor Form 3000
  Audit Migration to FN3:

- Completed major pieces of functionality for Audit Patient and Event Randomization (released month by month) that reduce manual work, increase data quality, reporting capabilities, and configurability for the future

- Developed and tested the following for release in January 2023:

Form	Form Name	Category
3000r7	Protocol Deviation Form	Revised Donor Form

Electronic data submission/AGNIS
CIBMTR continued support for electronic data submission initiatives and production AGNIS customers. Effort focused on support for CIBMTR form revision updates to existing forms.

- Recent AGNIS and other electronic data submission accomplishments:
- The AGNIS team continues to release forms for centers to use in data submission to the CIBMTR as well as address questions or issues raised by centers and their vendors.
- Three AGNIS forms were released to production:
  - 2900r5 Patient Death Data
  - 2450r6 Post-Transplant Essential Data
  - 2400r9 Pre-Transplant Essential Data
- One AGNIS form was released to external test and is awaiting external partner testing before it can move to production:
  - 2814r4 Indication for CRID Assignment
- Formsnet3 (FN3) Methicillin spelling error was also corrected in AGNIS mappings and documentation
- FN3 Number of Repetitions Update to the 2400r9 was updated in AGNIS mappings and documentation
- FN3 Update to allowable decimals places on Question 80 of Forms 2006r6 were updated in AGNIS mappings and documentation

Automated data exchange using electronic data collection systems that interface directly with source health and laboratory records
CIBMTR has continued to update its reporting application to exchange additional discrete electronic data records. Using the data extracted directly from data collection systems at partner centers, CIBMTR further expanded capabilities to populate additional laboratory data points on 26 forms at both pre-infusion and post-infusion time points. These expanded capabilities provide partner transplant centers with improved time savings and eliminate the potential of manual data entry errors. The underlying structures for data exchange and storage were updated based on current standards – these updates are the foundation upon which we will be able to expand the types of data that can be exchanged electronically.

Simplify Data Analysis
Collect & analyze more data more frequently without increasing the burden on centers.

Integrated Data Warehouse (IDW)
CIBMTR continued to increase the capabilities of the IDW, which is the Operational Data Warehouse utilized for delivery of key data to stakeholders. Accomplishments include:

- Incorporated ongoing forms revisions into the warehouse
- Continued enhancing processes to support CIBMTR's Domestic and International CPI Processes.

- Continued enhancing study information and visualizations to support our Prospective Research team.
- Began development to enhance our Sample Inventory data processes with Labvantage
- Began planning to produce dashboards pairing Sample Inventory data with data from other CIBMTR systems
- Completed 2022 Center Volumes Data Reporting project.
- Provided ePRO data for use in Data Back to Centers (DBtC) dashboard.
- Provided Survivorship Plans for external partners use through the DBtC portal.
- Provided variable-specific audit instructions for Japanese Data Center Hematopoietic Cell Transplantation.

Unified Domain Model (UDM)
Continuing the process of building this single source of truth of data that will contain high quality, validated data readily available to researchers for immunobiology, outcomes, and other types of analyses.

- Continued transitioning HCT data from the Research Database to the Unified Domain Model (UDM) including delivery of 15 data extracts directly from UDM and continued development of a relapse-specific data domain.
- Continued delivery of monthly and quarterly CAR T-cell data sets to our Japan (JDCHCT) and pharmaceutical partners.
- Completed data design review for upcoming Gene Therapy data extracts
- Continued refinement and delivery of Periodic Safety Update Reports (PSUR) for CAR T-cell therapies.
- Provided quarterly Stem Cell Therapeutic Outcomes Data required for the HRSA SCTOD quarterly report.

Enhance Data Sharing and Visualization
Deliver data visualization and analytic tools that will enable stakeholders to more efficiently interact with data to identify relevant trends and patterns.

- Enhanced the Data Back to Centers (DBtC) dashboard and Data Back to Centers Download (DBtC-Download) to leverage the extracts produced from UDM and the HCT Centralization project. We continue to grow and enhance this application each month with new data and charts.
- The Center Performance Application (CPA) received its annual data update; introducing several new variables and associated charts
- Transplant Center Specific Analysis (TCSA) annual survival report was generated and published for the participating centers. Additionally, the related Center Specific Univariant reports were also generated and made available to each center.
- The One-Year Survival Outcomes calculator was rebuilt using QlikView to alleviate the dependency on aging technology.
- The One-Year Survival Outcomes calculator received its annual update and refined its calculations by adding additional variable option values.
- Business Intelligence Data Sharing- Continued expansion of business intelligence tool capabilities. Adding to the existing suite of external Business Intelligence data sharing applications including the introduction of more data, dimensions and measures, stakeholder groups, and continuing data quality initiatives.

Conduct clinical trials on the use of HLA mismatched graft sources to expand access to all patients in need of allogeneic cell transplantation

During the last quarter, work continued on the development of a new prospective clinical trial protocol designed to build upon the successful MMUD post-transplant cyclophosphamide platform. The team incorporated feedback received through several scientific advisory meetings with leading transplant and clinical research professionals to seek input on study design and approach. Funds from this grant will support protocol defined correlative studies to evaluate immune reconstitution and explore mechanisms of relapse post-transplant.

Publications

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