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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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a. REPORT	b. ABSTRACT	c. THIS PAGE		19	Jeffery Auletta, M.D. - Sr Vice President and Chief Scientific Director
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Grant Award N00014-24-1-2057

DEVELOPMENT OF MEDICAL TECHNOLOGY
FOR CONTINGENCY RESPONSE TO MARROW TOXIC AGENTS
QUARTERLY RESEARCH PERFORMANCE REPORT
SUBMITTED January 12, 2024

Office of Naval Research

And

The National Marrow Donor Program® d/b/a NMDP

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 World Headquarters and NMDP contracted 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 immunobiology 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. 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. Specific Aim 1: Develop and Maintain the Radiation Injury Treatment Network (RITN) to prepare for the care of patients resulting from a hematopoietic toxic event

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. Specific Aim 2: 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. Specific Aim 3: Perform Immunogenetic and Genomic Studies in Transplantation and Cellular Therapy

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. Specific Aim 4: Conduct Observational and Prospective Clinical Trials in Transplantation and Cellular Therapy

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

Specific Aim 1: Develop and Maintain the Radiation Injury Treatment Network (RITN) to prepare for the care of patients resulting from a hematopoietic toxic event

Activity 1-1: 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.
    - Three RITN hospitals have been chosen to host two sessions.
        - Avera McKennan (Sioux Falls, SD)
        - Banner-University Medical Center (Tucson, AZ)
        - Mount Sinai (New York, NY)
    - Dates yet to be determined.
- Radiation Emergency Assistance Center/Training Site (REAC/TS) Management of Radiation Illnesses and Injuries 2-day course is being piloted this fiscal year. This course was developed to integrate physicians, practitioners, nurses, and other healthcare providers, as well as other

disciplines in the healthcare field to the practical aspects of initial hospital management of irradiated and/or contaminated patients through lectures and hands-on practical exercises.

The course will focus on the fundamentals of radiobiology along with the medical care and management of patients involved with radiological and/or nuclear incidents. Topics include radiation physics; radiation detection/measurement/ identification; early evaluation and treatment of the acute radiation syndrome (ARS), and cutaneous injuries, contamination control; and mitigating risks to patients, providers, and facilities.

  - Orlando Health has been chosen to host.
  - Dates yet to be determined.

- FY2024 RITN Biennial Workshop
  - Planning Committee
    - Named in November 2023 and continues to plan for the July 9-10, 2024 Workshop.
    - Members representing RITN hospitals: Children's Mercy Hospital, Dana Farber Cancer Institute, Duke University, Emory University, Massachusetts General, Mayo Clinic Rochester, MD Anderson, Roswell Park Comprehensive Cancer Center, Rush University Medical Center, Stanford-Pleasanton, University Hospitals Seidman Cancer Center, University of Utah, University of Virginia, and West Virginia University Hospitals.
    - Members representing federal partners: the Administration for Strategic Preparedness and Response (ASPR), Armed Forces Radiobiology Research Institute (AFRRI), Association of State and Territorial Health Officials (ASTHO), Biomedical Advanced Research and Development Authority (BARDA), National Association of County and City Health Officials (NACCHO), and the National Institute of Allergy and Infectious Diseases (NIAID)/National Institutes of Health (NIH).
  - The call for abstracts tentatively set for late January with registration beginning in the spring of 2024.

Hospital radiation disaster preparedness

- Annual disaster readiness tabletop exercises (drills) will be scheduled for current RITN hospitals to participate for their annual task completion. Six sessions will be offered between June and August 2024.
- Additional disaster readiness exercises (drills) have yet to be scheduled: Saipan exercise and training, two Functional exercises, two Regional Tabletop exercises, one hospital coalition Tabletop exercise, and one exercise to be determined.

Hospital network growth

- Appropriate growth helps ensure support of 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:
    - Nashville, TN
    - Los Angeles, CA

        - San Antonio, TX
        - Memphis, TN
        - Phoenix, AZ
        - New Orleans, LA
        - Albuquerque, NM
    - Specific hospitals
        - Children's Hospital Los Angles (CHLA)
        - Corewell East Beaumont Children's Hospital (Royal Oak, MI)
        - University of Tennessee (Nashville, TN)

Federal partnership development

- Association of Healthcare Preparedness Professionals (AHEPP)
    - AHEPP's mission is to provide healthcare and other preparedness professionals with opportunities for networking, resource sharing, continuing education, and scholarly exchange (ahepp.org).
    - RITN will be in attendance to network and further relationships with current hospital emergency managers as well as use the opportunity to recruit new hospitals for growth.
- National Association of County and City Health Officials (NACCHO) Preparedness Summit
    - The NACCHO Preparedness Summit's theme is "Public Health, Healthcare, and Emergency Management: Aligning to Address Cascading Challenges," and will provide an opportunity for sectors to come together, align missions, and discover better ways to work as true partners to meet the challenges of today and tomorrow.
    - RITN is a member of the Radiation Workshop Planning Committee which will conduct a 1-day radiation-specific planning workshop Sunday, March 24, 2024, and is expected to have over 100 people attend.

Specific Aim 2: Development of Science and Technology for Rapid Identification of Matched Donors

Activity 2-1: 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.

Activity 2-2: Modeling and analysis of registry coverage for the Warfighter

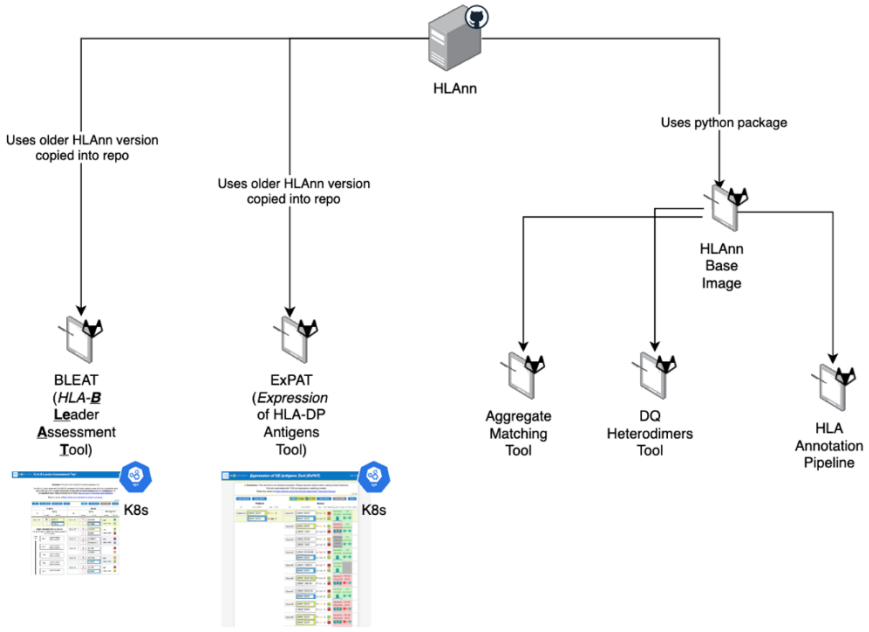
This quarter, proposed improvements to population genetic mappings based on self-identified race and ethnicity were evaluated. These mappings demonstrated improved matching performance through HapLogic and also increased the sample size for some populations that in turn improves the produced haplotype frequencies. A manuscript entitled "Combined imputation of HLA genotype and self-identified

race leads to better donor-recipient matching" was published in *Human Immunology* (Oct 2023) (https://pubmed.ncbi.nlm.nih.gov/37867095/).

In addition, efforts to increase the flexibility of the registry modeling codebase to handle more scenarios (number of matches or mismatches out of total HLA allele number) continued. Validation on the revamped code base was completed, and end-to-end processing time for registry modeling runs was reduced. Finally, new statistics for donor availability from the last two years were refreshed in preparation for future modeling scenarios.

Activity 2-3: Development of science and technology for rapid communication of HLA data

New functionality was added to the HLA Annotation pipeline to prepare for automation of typing coverage evaluations. Feedback was collected from users in November, and improvements for usability are in progress. Meanwhile, the gene feature service database was replatformed and the data repopulated for use. The service is now deployed on a platform with backup and support, and GFE service was updated to properly handle exceptions. The infrastructure build is in progress for handling HLA data across different use cases combining various previously developed services is shown below.



Activity 2-4: Use of population genetics and machine learning to automate the donor selection process

During the last quarter, two presentations on machine learning and statistical models applied to patient transplant outcomes were shown at the annual ASHI (American Society for Histocompatibility and Immunogenetics) meeting in October, 2023. One presentation explored the potential for machine learning to assist in balancing trade-offs in HCT outcomes including proposing a machine learning framework to

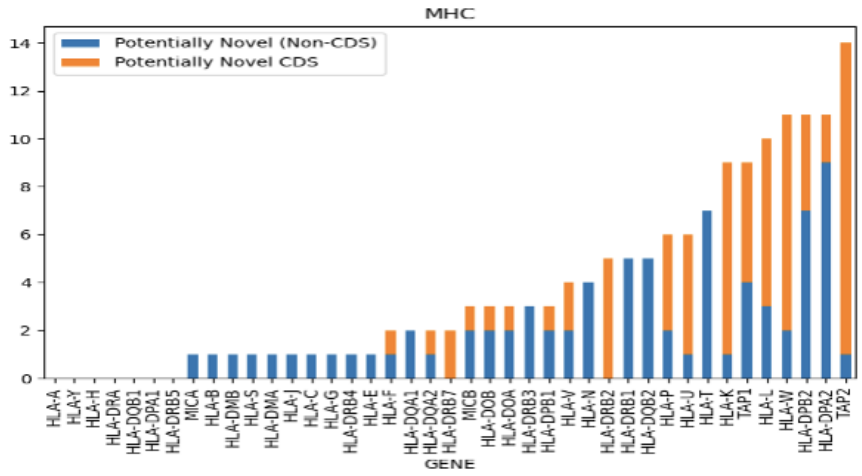
balance competing HSCT, leveraging multi-objective optimization on CIBMTR data, using self-organizing maps to analyze high-dimensional data, in order to inform personalized HCT decision making. Additional work explores classical statistics and machine learning, models overall and event-free survival probabilities, applies explainable artificial intelligence methods to interpret predictions, and calculates substitution ratios for donor traits to decode the influence of donor age, HLA matching, and relatedness on HCT success for patients with leukemia.
Another abstract was presented at the American Society of Hematology (ASH) annual meeting in December 2023 entitled, "Is the Youngest Donor Always the Best Choice to Optimize Outcomes for Matched Unrelated Allogeneic Transplant? Improving Precision Using Novel Statistical Methodology". Our recently published research has shown that use of younger donors is associated with superior survival for recipients of allogeneic hematopoietic stem cell transplant (HSCT). But we had not explored the donor age impact on other outcomes, or the impact of smaller age differences (<4 years) when balanced against other factors. We reported results using our recently developed machine learning survival methodology, Nonparametric Failure Time Bayesian Additive Regression Trees (NFT BART). Here we study patient-specific optimization of donor selection for overall survival (OS) and event-free survival (EFS including events of death, relapse, graft failure/rejection, or moderate/severe chronic graft vs. host disease, GVHD).

Using our novel NFT BART methodology, we showed that donor selection to optimize HSCT outcomes can be improved by considering both OS and EFS. This weighted optimization strategy balances outcomes, prioritizing OS while also allowing for consideration of EFS when OS is likely similar between donors. Additionally, this supports previous research showing that choosing among donors from 18 to 30 with resultant minimal differences in outcomes that are negligible allowing for more flexibility in donor selection. A manuscript is under development for submission later this year.

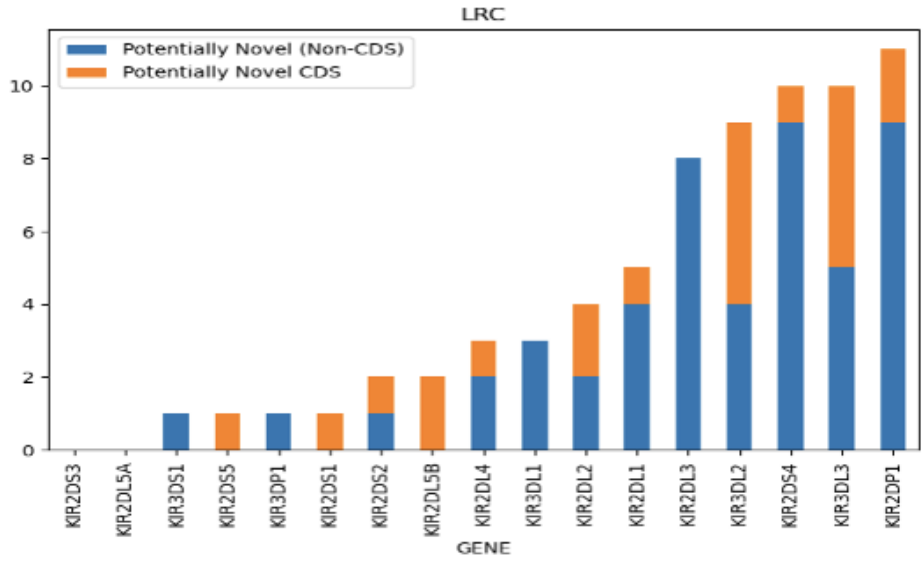
Specific Aim 3: Perform Immunogenetic and Genomic Studies in Transplantation and Cellular Therapy

Activity 3-1: 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

During the last quarter, a small pilot was conducted to evaluate the ability to generate and evaluate novel immunogenetic data on transplant donor and recipient pair samples. Eight samples were selected for full genomic sequence typing of the Major Histocompatibility Complex, Leukocyte Receptor Complex, and Killer Cell Immunoglobulin-like Receptors. Exploration of this data identifies potential novel alleles and areas of currently unknown impact on HCT. The number of potential novel alleles identified with this sequencing is shown in the two figures below.



Number of potentially novel alleles per gene



Number of potentially novel alleles per gene

Activity 3-2: 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: Molecular Evaluation of AML patients after Stem cell transplant to Understand Relapse Events". To date, 18 centers have committed to participate in the study and combined plan to enroll >250 patients per year. Seventeen of 18 sites have received local IRB approval for the protocol. Sixteen sites have fully opened the study and have enrolled a total of 103 patients through September December 2023.

Activity 3-3: 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.

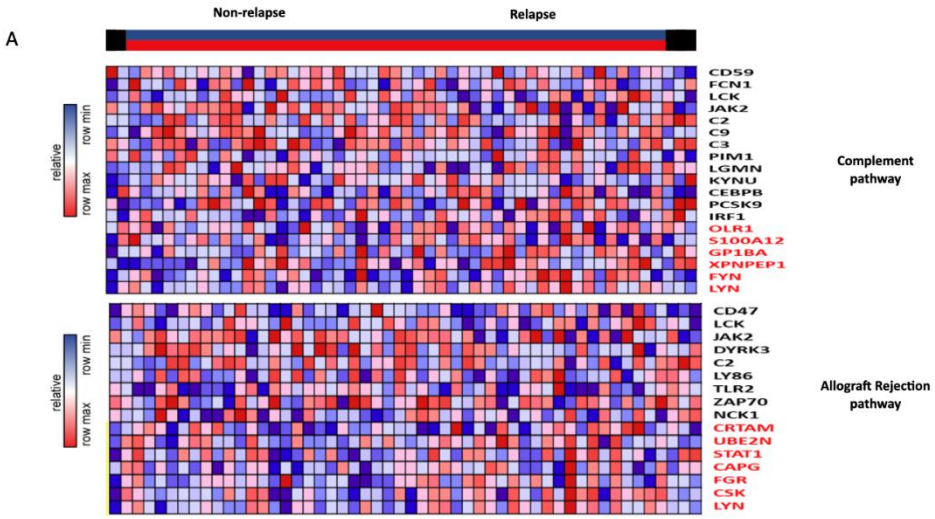
The primary aim of this study is to evaluate PBSC graft stem cell and associated immune cell composition and to determine at 12-months of follow-up how either the comprehensive graft cellular composition profile or specific graft composition elements influences the primary outcomes of time to neutrophil 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 568 product samples were received and tested through December 31, 2023, with 65 tested in the last quarter. Preliminary analyses focused on graft composition correlation with donor characteristics and the impact of cryopreservation are underway. Initial results were presented as oral abstracts at the 2023 ASH annual meeting and abstracts submitted to the 2024 EBMT annual meeting:

- MAIT Cell Frequencies within PBSC Grafts Are Associated with Donor CMV Serostatus and Age: An Initial Analysis from the DKMS and NMDP Graft Composition Study
- Cryopreservation Changes the Immune Effector Cell Composition of Peripheral Blood Stem Cell Grafts: An Analysis from the DKMS and NMDP Graft Composition Study

Activity 3-4: Determine the impact of non-HLA genes and gene expression on allogeneic cell transplantation

During the past quarter, a manuscript entitled, "Proteomics to predict relapse in patients with myelodysplastic neoplasms undergoing allogeneic hematopoietic cell transplantation", was accepted for publication in December 2023 in *Biomarkers Research.* As part of the results reported in this manuscript, proteins involved in the complement or allograft rejection pathway were found to have differing patterns of expression in samples from patients that experience relapse or non-relapse after transplant, as seen in the figure below.



A manuscript entitled "CYTO-SV-ML: a machine learning framework for discovery and classification of cytogenetic structural variants using whole genome sequencing data" was also submitted to B*MC Medical Genomics* in November, 2023.

Specific Aim 4: Conduct Observational and Prospective Clinical Trials in Transplantation and Cellular Therapy

Activity 4-1: Conduct clinical outcomes research using the CIBMTR research database and repository.

Observational Research

- Published 13 manuscripts in peer-reviewed journals during the last quarter (see publications below).

- A total of 38 abstracts were submitted presented to at the 2023 American Society of Hematology (ASH) annual meeting to be held in San Diego, CA, December 9-12, 2023. Presentation title and type [oral (N=28) or poster (N=11) abstract] are listed in the table below. Abstracts were published in a supplement to the journal Blood in November 2023.

Table. Presentations at the 2023 ASH Annual Meeting

Title	Presentation type
Real-World Evidence in the United States (US) of the Impact of Bridging Therapy Prior to Axicabtagene Ciloleucel (Axi-Cel) for the Treatment of Relapsed or Refractory Large B-Cell Lymphoma (R/R LBCL)	**Oral**
The Composite Health Risk Assessment Model (CHARM) to Predict 1-Year Non-Relapse Mortality (NRM) Among Older Recipients of Allogeneic Transplantation: A Prospective BMT-CTN Study 1704	**Oral**
Multicenter, Real-World Study in Patients with R/R Large B-Cell Lymphoma (LBCL) Who Received Lisocabtagene Maraleucel (liso-cel) in the United States (US)	**Oral**
Rabbit Antithymocyte (rATG) Exposure and Outcomes after Hematopoietic Cell Transplantation: A Real World Experience from BMT CTN 1202	**Oral**
Real-World Outcomes of Brexucabtagene Autoleucel (Brexu-cel) for Relapsed or Refractory (R/R) Mantle Cell Lymphoma (MCL): A CIBMTR Subgroup Analysis of High-Risk Characteristics	**Oral**
Long-Term Outcomes after Unrelated Marrow Transplantation for Aplastic Anemia with Optimized Cyclophosphamide Dose (BMT CTN 0301)	**Oral**
Age-Related Differences in Utilization of Allogeneic HCT for Acute Myeloid Leukemia in California: Results of a Population-Based, Novel Linked Dataset	**Oral**
Out-of-Pocket Costs and Financial Hardship Among Participants of the BMT CTN 1102 Study	**Oral**
Predictors of Cytokine Release Syndrome and Neurotoxicity in Patients with Large B-Cell Lymphoma and Their Impact on Survival	**Oral**
Impact of Publicly Reported Center Specific Analysis on Patient Selection Practices for Hematopoietic Stem Cell Transplantation	**Oral**
Factors Associated with Treatment Receipt in Medicare Beneficiaries Diagnosed with Acute Myeloid Leukemia	**Oral**

Donor Hematopoietic Cell Telomere Length and Magnitude of Post-HCT Shortening Predict Survival in Early Stage Leukemia and Myelodysplastic Syndrome	**Oral**
Large-Scale Post-Transplant TCR Deep Sequencing Reveals a Major T Cell Diversity Bottleneck with Post-Transplant Cyclophosphamide with Implications for Both Efficacy and Toxicity: Results of the BMT CTN 1801 Study	**Oral**
Measurable Residual IDH2 before Allogeneic Transplant for Acute Myeloid Leukemia	**Oral**
Ibrutinib Added to Standard Conditioning and As Consolidation Therapy Following Autologous Hematopoietic Stem Cell Transplantation (AutoHCT) for Relapsed/Refractory Activated-B-Cell Subtype Diffuse Large B-Cell Lymphoma (ABC-DLBCL): Primary Analysis of the US Intergroup Double-Blind Randomized Phase III Study Alliance A051301/BMT-CTN 1201	**Oral**
Machine Learning Validates Risk Biomarkers of Chronic Graft-Versus-Host Disease in 936 Patients from BMT CTN 0201 & 1202 Cohorts	**Oral**
Chimeric Antigen Receptor (CAR) T Cell Infusion for Large B Cell Lymphoma in Complete Remission: A Center for Internation Blood & Marrow Transplant Research (CIBMTR) Analysis	**Oral**
Autologous Transplant (auto-HCT) Is Associated with Improved Clinical Outcomes Compared to CAR-T Therapy in Patients (pts) with Large B-Cell Lymphoma (LBCL) Achieving a Complete Remission	**Oral**
CD33 CAR T-Cells (CD33CART) for Children and Young Adults with Relapsed/Refractory AML: Dose-Escalation Results from a Phase I/II Multicenter Trial	**Oral**
Post-Transplant Cyclophosphamide Eliminates Disparity in GvHD-Free, Relapse-Free Survival and Overall Survival between 8/8 Matched and 7/8 Mismatched Unrelated Donor Hematopoietic Cell Transplantation in Adults with Hematologic Malignancies	**Oral**
Patient-Reported Outcomes of BMT CTN 1703: A Randomized Phase III Study for GVHD Prophylaxis - A Quality of Life Evaluation	**Oral**
Post-Hoc Analysis of Measurable Residual Disease from BMT-CTN 1506/Morpho: FLT3-ITD Variant Allele Frequency and Survival Are Highly Correlated	**Oral**

Real World Outcomes with Idecabtagene Vicleucel (Ide-Cel) CAR-T Cell Therapy for Relapsed/Refractory Multiple Myeloma	**Oral**
MAIT Cell Frequencies within PBSC Grafts AreAssociated with Donor CMV Serostatus andAge: An Initial Analysis from the Dkms andNMDP Graft Composition Study	**Oral**
Real-World Outcomes of Brexucabtagene Autoleucel (brexu-cel) for Relapsed or Refractory (R/R) Adult B-Cell Acute Lymphoblastic Leukemia (B-cell ALL): Evidence from the CIBMTR Registry	**Oral**
Cryopreservation Changes the Immune Effector Cell Composition of Peripheral Blood Stem Cell Grafts: An Analysis from the DKMS and NMDP Graft Composition Study	**Oral**
Hematopoietic Stem Cell Transplantation for Fanconi Anemia: Outcome and Prognostic Factors for Survival and Subsequent Neoplasms	**Oral**
Reduced Intensity Haploidentical Bone Marrow Transplantation in Adults with Severe Sickle Cell Disease: BMT CTN 1507	**Oral**
Comparative Effectiveness of Axicabtagene Ciloleucel Vs Historical Standard-of-Care in Patients with Relapsed or Refractory Follicular Lymphoma: An Analysis of CIBMTR and SCHOLAR-5 Data	**Poster**
HLA-DRB1 Hed Is Associated with Improved Survival and Decreased Relapse in Patients with Hematologic Malignancies Following Allogeneic Hematopoietic Stem Cell Transplant	**Poster**
Monoallelic Pathogenic Variants in Hemophagocytic Lymphohistiocytosis Genes Are Uncommon and Not Associated with Hematopoietic Cell Transplantation Outcomes in Severe Aplastic Anemia	**Poster**
Caregiver Perspectives on Housing, Finances and Employment Post-Allogeneic Hematopoietic Cell Transplant	**Poster**
Persistence of FLT3-TKD in Blood Prior to Allogeneic Transplant Is Associated with Increased Relapse and Death in Adults with AML in First Remission	**Poster**
Durable Efficacy and Manageable Safety in Patients Age ≥ 75 Years with Relapsed/Refractory Large B-Cell Lymphoma Treated with Tisagenlecleucel in the Real-World Setting	**Poster**

Real-World Tisagenlecleucel Outcomes in Richter-Transformed Chronic Lymphocytic Leukemia: A Center for International Blood & Marrow Transplant Research (CIBMTR) Analysis	**Poster**
Is the Youngest Donor Always the Best Choice to Optimize Outcomes for Matched Unrelated Allogeneic Transplant? Improving Precision Using Novel Statistical Methodology	**Poster**
Measurable Residual IDH1 before Allogeneic Transplant for Acute Myeloid Leukemia	**Poster**
Measurable Residual FLT3-ITD before Allogeneic Transplant for Acute Myeloid Leukemia	**Poster**
Prediction of Graft-Versus-Host Disease (GVHD) in Recipients of Hematopoietic Cell Transplant(alloHCT) from a Single Mismatched Unrelated Donor Using a Highly Multiplexed Proteomics Assay: MHC-Pepseq	**Poster**

Research data collection and systems enhancements
During the past quarter, CIBMTR continued support for electronic data submission initiatives, production FormsNet[SM] Recipient, FormsNet[SM] 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.

FormsNet3[SM] (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:

- Technology upgrade for the latest functionality that is used in all grids within FN3
- Refactoring of form reprocessing tool (allows CIBMTR staff to reprocess en masse) to improve performance
- Existing functionality utilizing clinicaltrials.gov was updated to support new APIs released by Clinicaltrials.gov
- Improvement to functionality for Check All that Apply fields-ensuring smart navigation and error messages are accurate for end-users
- Enhancement to audit functionality to remove redundant manual entry for CIBMTR auditors
- Donor Center Forms Due performance improvements
    - IDM test result automation
- Developed and tested the following forms that were released in October 2023:

Form	Form Name	Category

2100R9	Post-Infusion Follow-up	Revised Recipient Form
3004R2	Genetic Mutation Report Form	Revised Recipient 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:
  - Support of updates to the FN3 Consent Tool with updates to the AGNIS 2815 form
- 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.
  - One AGNIS form was released to production:
    - 2815 Consent Tool
  - Eight AGNIS forms were released to external test and are awaiting external partner testing before they will move to production:
    - 2815 Consent Tool
    - 2400 Pre-Transplant Essential Data
    - 2402 Pre-TED Disease Classification
    - 2006 Hematopoietic Stem Cell Transplant Infusion
    - 4006 Cellular Therapy Infusion
    - 4000 Pre-Cellular Therapy Essential Data
    - 4100 Post-Cellular Therapy Essential Data
    - 4101 Post-Cellular Therapy Follow-Up

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 29 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.
- Completed the annual Center Volumes Data Reporting project for 2023
- Continued enhancing study information and visualizations to support our Clinical Research Outcomes team.

- Enhanced Sample Inventory data reporting dashboards with data from other CIBMTR systems
- Provided Cord Blood Banks a new patient level supplemental report in the Quarterly Cord Blood Quality Report
- Extended Survivorship Plan project to additional external centers
- Began planning to integrate the Veeva clinical data management system into NMDP systems.
- Completed development of additional Quality Control reports for internal partners.
- 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 regular delivery of monthly data extracts directly from UDM comprised of thousands of patient outcome variables for statistical analysis.
- Continued development of discrete data domains focused on relapse, GVHD, infection, engraftment, lines of therapy, and numerous disease-specific data sets.
- Continued delivery of monthly and quarterly CAR T-cell data sets to our Japanese (JDCHCT) and pharmaceutical partners.
- 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.

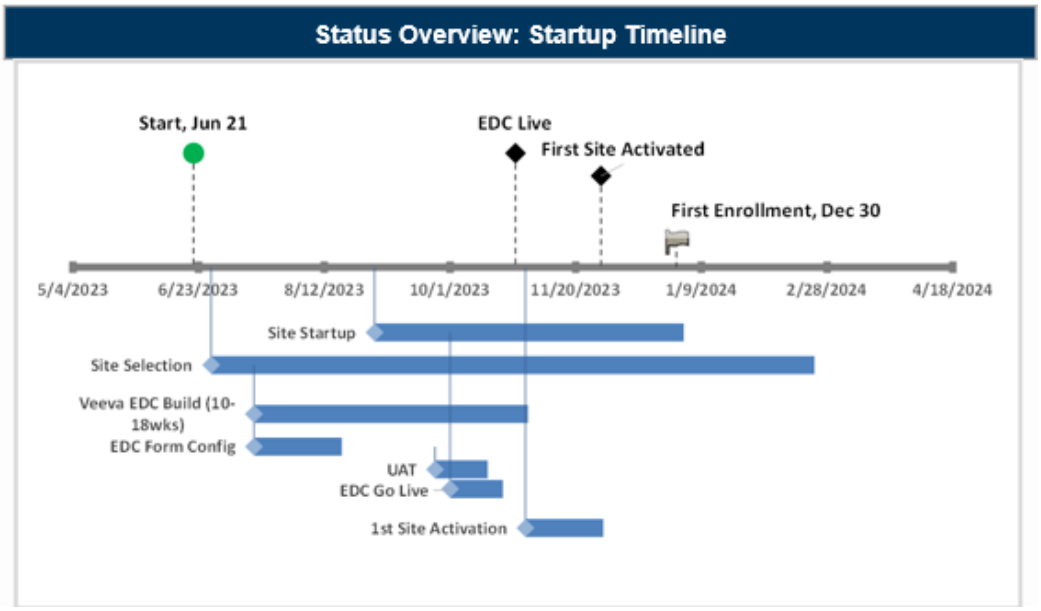
Enhance Data Sharing and Visualization
Deliver data visualization and analytic tools that will enable stakeholders to more efficiently interact with data to identify relevant trends and patterns.

- A new application (PartnerShare–StudyLink BMTCTN) has been released to production for external users. This application is designed for users at the Registry-Level who specifically have research needs in the Clinical Trials Network which span multiple centers' data. Data is anonymized and presented to the users based on the rules set by their study parameters.
- Virtual Survivorship, an application which presents pre-formatted reports designed for patient consumption, has been released to production for use by the centers.
- Continued enhancement of the PartnerShare product is now focusing on incorporating Gene Therapy in the deliverable.
- The public web portal now displays more data related to the studies related to the Public Datasets.

Activity 4-2: 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 activation of a new prospective clinical trial protocol designed to build upon the successful MMUD post-transplant cyclophosphamide platform (timeline below). The study protocol entitled, "OPTIMIZE: A Phase II Study of Reduced Dose Post Transplantation Cyclophosphamide as GvHD Prophylaxis in Adult Patients with Hematologic Malignancies Receiving HLA-Mismatched Unrelated Donor Peripheral Blood Stem Cell Transplantation" was approved by the NMDP IRB in September 2023. The study will enroll up to 170 subjects at up to 50 participating sites with

a goal of activating 20 sites by the end of September 2024. Three sites were activated and 2 subjects consented through the end of December 2023. Funds from this grant will support protocol defined correlative studies to evaluate immune reconstitution and explore mechanisms of relapse post-transplant.



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