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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.

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Research in HLA Typing, Hematopoietic Stem Cell Transplantation and Clinical Studies to Improve Outcomes

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DEVELOPMENT OF MEDICAL TECHNOLOGY
FOR CONTINGENCY RESPONSE TO MARROW TOXIC AGENTS
QUARTERLY RESEARCH PERFORMANCE REPORT
SUBMITTED July 13, 2023

Office of Naval Research

And

The National Marrow Donor Program®

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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 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.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.
    - Due to cancelation of REAC/TS sponsorships, four additional RITN hospitals will host two 4-hour sessions on radiological incidents and terrorism. This is in addition to the one RITN hospital in the FY2023 budget (West Virginia University Hospital, Morgantown, WV) which was hosted and completed April 11, 2023.
        - Additional hospitals:
            - Corewell Health (Grand Rapids, MI) - hosted and completed June 4 and June 5, 2023
            - University of Wisconsin (Madison, WI) - will be hosted and completed July 26, 2023
            - Orlando Health, (Orlando, FL) - will be hosted and completed August 7, 2023
            - Temple University (Philadelphia, PA) - will be hosted and completed September 7, 2023

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 hospitals to participate for their annual task completion. Seven sessions are being offered between June and August 2023: June 23 (conducted and completed), July 18, July 27, August 8, two on August 9, and August 16, 2023.
- Two additional disaster readiness exercises (drills) were scheduled, conducted, and completed: Maryland Healthcare Coalitions (April 20, 2023) and Guam (February 28, 2023).

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 approached:
    - Children's Healthcare of Atlanta (CHOA) (Atlanta, GA) - in process of signing agreement
    - Skyline Medical (Nashville, TN)
    - Children's Hospital Los Angeles (CHLA) (Los Angeles, CA)
    - Stanford-Pleasanton (Pleasanton, CA) - in process of signing agreement
    - Corewell East Beaumont Children's Hospital (Royal Oak, MI)
    - Cooper Health (Camden, NJ)
    - LCMC (New Orleans, LA)

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).
    - Activities under this section are complete.
- National Association of County and City Health Officials (NACCHO) Preparedness Summit
    - In 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 for the summit 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 conducted a 1-day radiation-specific planning workshop Sunday, April 23, 2023 with over 100 attendees.

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

During the past quarter, a total of 71,856 newly registered volunteer donors were HLA typed and added to the Be The Match Registry.

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. 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.

Over the last quarter, we produced registry modeling results using new validated code engineered to improve the capabilities and efficiency of registry analysis, including the ability to calculate a wider range of HLA matches and mismatches. This modeling aids in preparation for coverage of potential donor sources to Warfighters of diverse race and ethnic backgrounds in case of radiation emergencies. We also initiated design for a tool to provide summary projections of donor existence in populations with a variety of diversity ratios. In addition, an abstract summarizing the Warfighter modeling was submitted for presentation at the 2023 Military Health System Research Symposium and accepted for poster presentation.

Development of science and technology for rapid communication of HLA data

During the last quarter, two manuscripts were accepted for publication. The first was a manuscript titled "Genotype List String 1.1: Extending the Genotype List String grammar for describing HLA and Killer-cell Immunoglobulin-like Receptor genotypes" was published in the journal *HLA: Immune Response Genes*. This paper is an update to a data standard developed under this grant for the rapid and accurate communication of HLA data. This new version includes an extension to support ambiguity in terms of the gene content which results from large-scale genotype of systems like KIR, the NK receptors that bind HLA. The second was a manuscript, titled "Assessment of HLA-DPB1 Genetic Variation with an HLA-DP Tool and Implications in Clinical Transplantation", was accepted for publication by the journal *Blood Advances*. This manuscript describes genetic variation in HLA-DPB1 exon 2 that 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. 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.

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

A new methodology using machine learning was developed in last quarter entitled "Navigating the Trade-offs of HCT and the use of machine learning-driven decision support tools." Here, time-to-event modeling was used along with multi objective optimization to compare the tradeoffs for impact to patient survival in selection of specific donor characteristics against others. A manuscript demonstrating applications of these methods in selection of donors is planned to be drafted next.

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 for high resolution HLA typing to ensure that changes in practice can be evaluated using quality-controlled 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, new sample groups were selected for typing upgrades, including 823 related donor-recipient transplant pairs and 1177 unrelated donor-recipient transplant pairs. Through collaboration across the immunobiology and bioinformatics research team, analysis of validation processes will lead to increased assessment and automation to evaluate typing results through the next year. A small pilot for greater coverage and study of immunogenetic regions is also being planned.

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, 18 centers have committed to participate in the study and combined plan to enroll >250 patients per year. Fourteen of 18 sites have received local IRB approval for the protocol. All sites have initiated submission of regulatory documents required for participation. Twelve sites have fully opened the study and have enrolled a total of 30 patients through June 2023.

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 446 product samples were received and tested through March 31, 2023, with 81 tested in the last quarter. Preliminary analyses focused on graft composition correlation with donor characteristics and the impact of cryopreservation are

underway. Testing costs are covered under a subsequent grant while staff support is funded under this grant. 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 new manuscript entitled "Donor germ-line variants associate with outcomes of allogeneic hematopoietic stem cell transplantation in patients with MDS" was prepared from analysis of data funded under his grant and submitted for publication consideration. In this manuscript, genome-wide association analysis was conducted to determine whether germ-line genetic variants in transplant donors impact overall survival in patients with MDS after allo-HCT. Here, we identified three genetic loci (Table XXX) associated with overall survival, and the identification of these loci may lead to improvement of predictive algorithms and optimization of donor selection for future allo-HCT.

Table 1: Summary statistics for the top associations in both the full donor cohort as well as the set of unrelated donors.

Cohort	SNP	rsID	HR	P	MAF	HR-REL	P-REL	HR-TRM	P-TRM	Annotation
All donors	chr7:142509064:C:T	rs111224634	5.96	$2.39x10^{-8}$	0.012	5.04	$1.89x10^{-5}$	4.81	$8.78x10^{-4}$	Upstream TRBV6
Unrelated donors	chr1:161408186:C:A	None	15.03	$4.77x10^{-10}$	0.010	4.73	0.149	14.08	$1.59x10^{-7}$	intergenic
Unrelated donors	chr7:142509064:C:T	rs111224634	6.67	$4.96x10^{-9}$	0.015	5.47	$1.10x10^{-5}$	5.41	$4.10x10^{-4}$	Upstream *TRBV6*
Unrelated donors	chr3:35469184:C:T	None	7.88	$1.26x10^{-8}$	0.123	2.48	0.22	9.63	$8.96x10^{-8}$	intergenic

SNP=Single Nucleotide Polymorphism represented in GrCH38; HR=Hazard Ratio; P=P-value; MAF=Minor Allele Frequency; HR-REL=Hazard Ratio with relapse; P-REL=P-value with relapse; HR-TRM=Hazard Ratio with Treatment Related Mortality; P-TRM=P-value with Treatment Related Mortality

D. Clinical Research in Transplantation

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

Observational Research

- Published 23 manuscripts in peer-reviewed journals during the last quarter (see publications below).
- A total of 6 abstracts were presented at the 2023 European Society for Blood and Marrow Transplant (EBMT) annual meeting held in Paris, France, April 23-26, 2023. Presentation titles and type are detailed in table 2 below. Abstracts will be published in a supplement to the journal Bone Marrow Transplantation later this year.
- A total of 4 abstracts were presented at the 2023 American Society of Clinical Oncology annual meeting held in Chicago, IL, June 2-6, 2023. Presentation titles and type are detailed in table 3 below. Abstracts are available online.

Table 2. CIBMTR presentations at 2023 EBMT Meeting

Title	Status
Global trends in demand for mismatched unrelated donor transplants have positively impacted racially and ethnically diverse candidates for hematopoietic cell transplantation posttransplant.	Poster
Social functioning after transplantation and cellular therapy: Initial patient-reported outcomes results from the CIBMTR.	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
Machine learning for risk biomarkers of chronic graft-versus-host disease in 936 patients from BMTCTN 0201 & 1202 cohorts.	Poster
Survival outcomes at 1-year post-allogeneic HCT between patients treated with abatacept in combination with CNI+MTX versus ATG or PT-CY: A real-world evidence comparison.	Oral
Optimizing haploidentical donor selection for pediatric hematopoietic cell transplant.	Oral

Table 3. CIBMTR presentations at 2023 ASCO Meeting

Title	Status
Real-world early outcomes of axicabtagene ciloleucel for relapsed or refractory (R/R) follicular lymphoma (FL)	Poster
Rates of cytokine release syndrome (CRS) and immune effector cell–associated neurotoxicity syndrome (ICANS) from Center for International Blood and Marrow Transplant Research (CIBMTR) data on US subjects (SUBJ) with lymphoma following chimeric antigen receptor T cell therapy (CAR-T)	Poster
Biologic indicators of donor socioeconomic disadvantage and recipient mortality following allogeneic hematopoietic cell transplantation	Oral
Real-world outcomes of brexucabtagene autoleucel (brexu-cel) for relapsed or refractory (R/R) mantle cell lymphoma (MCL): A CIBMTR subgroup analysis by prior treatment	Oral

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 functionality for supporting the Data Transformation Initiative
- Upstream CRID Assignment was introduced to transplant centers on January 27, 2023 A total of 19 centers are now using this functionality in production.
  - Additional enhancements will be added in July 2023
- Enhancements to FN3 Transfer Tool to provide email notifications to affected transplant center when a transfer has been declined.
- Development completed for FN3 to call a web service to validate cytogenetic karyotype data entered as an ISCN compatible string, with a planned July 2023 release
- Introducing TED and CRF reporting levels for cellular therapy, with a planned July 2023 release
- Introducing new consent status, Reconsent Pending, to allow CIBMTR to proactively identify when a recipient may need to be reconsented, with a planned July 2023 release
- FormsNet3 Forms Definition Manager (FDM): Completed several proactive security vulnerability updates revealed by new scans
- Enhanced internal FDM editors for validation and events & actions rules
- Study updates were made to the FN3 Donor Form 3000
  - Audit Migration to FN3:
  - Testing in progress 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 forms that were released in April 2023:

Form	Form Name	Category
3000r7	Protocol Deviation Form	Revised Donor Form
2103r1	Gene Therapy Persistence Form	New 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:
- 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:
    - 2450r7 Post-Transplant Essential Data
  - Four Three forms were released to external test and are awaiting external partner testing before they will move to production:
    - 2199 Donor Lymphocyte Infusion
    - 4003 Cellular Therapy Product
    - 2006 Hematopoietic Stem Cell Transplant Infusion
    - 4006 Cellular Therapy Infusion

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 29forms 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.

- Recent electronic data collection accomplishments
  - Ability to populate ANC on:
    - 2450r7 Post-Transplant Essential Data
    - 2100r8 Post-Infusion Follow-up
  - Ability to populate Labs at Diagnosis on:
    - 2402r7 Disease Classification

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 Clinical Research Outcomes team.
- Enhanced Sample Inventory data repotting dashboards with data from other CIBMTR systems
- Provided Cord Blood Banks additional reporting data in the Quarterly Cord Blood Quality Report
- Provided additional ePRO data for use in Data Back to Centers (DBtC) dashboard.
- Updated Survivorship Plans for external partners use through the DBtC portal based on data consumer feedback
- 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.
- 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.

- 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.
- Portal upgrade complete. Enterprise solution now has new hardware and has been upgraded to the latest version of SharePoint
- Kicked off a project supporting data sharing for partners with data specific to BMTCTN initiatives
- Kicked off a project supporting registry-to-registry data sharing which will give our partner organizations the ability to collaborate with each other.
- Kicked off the annual update of the Center Volumes (CVDR) application

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 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 submitted to and approved with stipulations by the NMDP IRB in June 2023. Enrollment on the trial is anticipated to start in the next two quarters. Funds from this grant will support protocol defined correlative studies to evaluate immune reconstitution and explore mechanisms of relapse post-transplant.

Publications

1. Cusatis R, Balza J, Uttke Z, et al. Patient-reported cognitive function among hematopoietic stem cell transplant and cellular therapy patients: A scoping review. Quality of Life Research. doi:10.1007/s11136-022-03258-0. Epub 2022 Oct 6. Impact Factor: 4.14

2. Olson TS, Frost BF, Duke JL, et al. Pathogenicity and impact of HLA class I alleles in aplastic anemia patients of different ethnicities. Journal of Clinical Investigation Insight. 2022 Nov 22; 7(22):e163040. doi:10.1172/jci.insight.163040. Epub 2022 Oct 11. PMC9746824. Impact Factor: 9.48

3. Boyiadzis M, Zhang MJ, Chen K, et al. Impact of pre-transplant induction and consolidation cycles on AML allogeneic transplant outcomes: A CIBMTR analysis in 3113 AML patients. Leukemia. doi:10.1038/s41375-022-01738-3. Epub 2022 Oct 12. Impact Factor: 12.88

4. Pagliuca S, Gurnari C, Hercus C, et al. Molecular landscape of immune pressure and escape in aplastic anemia. Leukemia. doi:10.1038/s41375-022-01723-w. Epub 2022 Oct 17. Impact Factor: 12.88

5. Cusatis R, Martens MJ, Nakamura R, et al. Health-related quality of life in reduced intensity hematopoietic cell transplantation based on donor availability in patients aged 50-75 with advanced myelodysplastic syndrome: BMT CTN 1102 American Journal of Hematology. doi:10.1002/ajh.26768. Epub 2022 Oct 17. Impact Factor: 10.05

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