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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			Jeffery Auletta, M.D. - Sr Vice President and Chief Scientific Director
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Grant Award N00014-21-1-2954

DEVELOPMENT OF MEDICAL TECHNOLOGY

FOR CONTINGENCY RESPONSE TO MARROW TOXIC AGENTS

QUARTERLY RESEARCH PERFORMANCE REPORT

SUBMITTED January 14, 2022

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

N00014-21-1-2954

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 to improve outcome 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 of marrow toxic injuries. The NMDP manages a network of centers that work in concert to facilitate unrelated HCT. The Radiation Injury Treatment Network (RITN), comprised of a subset of NMDP's network centers, is dedicated to radiological disaster preparedness activities and develops procedures for response to marrow toxic mass casualty incidents.

B. Development of Science and Technology for Rapid Identification of Matched Donors
Disease stage at the time of transplantation is a significant predictor of survival, decreasing the time to identify the best matched donor is critical. Methods are under development to rapidly provide the best matched 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 are focused on strategies to maximize disease control while minimizing the toxicity related to alloreactivity in HCT.

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:**
    - RITN Biennial (FY2022) Workshop "Past Informing the Present, Past Improving the Plan for a Rad/Nuc Incident" is (1) Targeted towards physicians and other healthcare providers, support staff, hospital and hospital system administrators, emergency managers, research scientists, and appropriate federal agency staff that would be involved in radiation response and treatment of patients with radiation-induced bone marrow injury; and (2) Will (a) highlight recent developments in Covid pandemic response and applicable lessons we have learned, (b) review and disseminate novel radiation countermeasures and dosimetry, (c) discuss optimizing triage and on the ground federal resources, (d) present strategies to ensure the availability and appropriate use of medical and psycho-social supportive care and resilience, and (e) explore applying telemedicine as a force multiplier for care and education.
        - Planning Committee continues to meet monthly to plan for August 2022.
        - The call for abstracts was sent in late December and general participant registration will begin in early 2022.

        - Committee members represent RITN hospitals: Dana Farber Cancer Institute, Duke University, Mayo Clinic Rochester, North Shore University Hospital, and the University of Iowa; as well as federal partners: The Assistant Secretary for Preparedness and Response (ASPR) and the Biomedical Advanced Research and Development Authority (BARDA).

    - Emergency Management of Radiation Victims 1-day course (1) Has an intended 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 discuss the fundamentals of radiation physics, radiation detection/measurement/identification, prevention of the spread of contamination, how to minimize radiation dose to victims and providers, and the role of medical/health physicists in caring for contaminated victims with instruction provided by the Radiation Emergency Assistance Center/Training Site (REAC/TS).
        - One course tentatively scheduled for FY2022.
        - Dates and location have yet to be determined.

    - 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.
        - One, half-day course tentatively scheduled for the afternoon of Wednesday, August 3 (day before biennial RITN Workshop) at the Westin Alexandria Old Town.
        - Two, half-day courses with yet-to-be-determined dates and locations tentatively planned.

- **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 dates will be offered to ensure as much participation as possible from centers.
    - Additional disaster readiness exercises (drills) will resume pre-COVID scheduling. To be scheduled: one Full-scale exercise, two Functional exercises, and three Regional Tabletop exercises.
    - Assist Nebraska Medicine in streamlining the interactions they have with national specialty organizations such as RITN as well as potentially supporting them in their regional exercise (drill).

- **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 Assistant Secretary for Preparedness and Response plans for response to a radiological/nuclear disaster with-in the continental U.S.
    - Planning the addition of three new hospitals to the RITN.

- **Federal partnership development:**
    - Support the Gryphon Scientific's Center for Disease Control (CDC) funded project as a subcontractor to assess United States laboratory capabilities for ionizing radiation related testing.
        - Analysis has begun and the preliminary data is available for workgroup members. November and December meetings were canceled due to holidays and analysis is in progress.

- **Other projects:**
    - RITN Automated Tracking System project seeks to develop an integrated means to collect, review, report and store data related to the activity and annual task deliverables of the hospitals that are part of its' network. This system should automate where feasible all steps that are currently manually accomplished. Users of this system range from staff at RITN headquarters to staff at each individual RITN center across the United States.
        - RFP created, distributed, reviewed and is in the process of completion.

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

In the last quarter, registry modeling software was updated for more efficient utilization and preliminary validation for mismatch levels was performed. HLA frequencies were updated to use the latest curated reference for 2020, an upgrade from the 2017 HLA frequencies used in previous modeling. In addition, a preliminary analysis to better understand the contribution of racially and ethnically diverse donors for matching in diverse groups was performed. In addition, preliminary code was developed for validation of registry modeling through simulations of donor registry searches with patient matching criteria. In the next quarter, the updated software will be applied to the latest representative statistics on warfighter race and ethnic composition. These results will aid in preparation for coverage of warfighters of diverse race and ethnic backgrounds in case of radiation emergencies.

Development of science and technology for rapid communication of HLA data

The previously developed gene feature enumeration (GFE) software was updated to handle versioned references for key immunogenetic genes of interest, e.g. HLA, and allow for unique identification of gene sequences in the database. Additional development was performed for gene sequence alignment and nucleotide polymorphism scoring to identify and track the frequency of new and predetermined variants of interest in HLA genes from histocompatibility markup language input files from large populations. Further development to allow for community collaboration and identification and tracking of submitters and submissions will be pursued in the next quarter during a hackathon in preparation for the next International Histocompatibility Working Group meeting. These tools allow for rapid communication of HLA data to promote both research studies that rely on HLA data and the operational matching of patients and donors.

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

In this quarter, we explored preliminary time-to-event and multiple competing risk statistical and machine learning models to predict overall and event-free survival after allogeneic stem cell transplant. Event-free survival is defined as survival where the patient does not experience any significant adverse events including graft rejection, moderate or severe chronic graft versus host disease, or relapse. The analysis utilized a dataset consisting of ~5,000 patients with leukemia who underwent a first allogeneic hematopoietic stem cell transplant between 2016 and 2018 in the United States. Records with more than 20% missing data were not retained and a subset of variables was selected such that the dataset for analysis included 8 survival/competing risk outcome variables and 76 explanatory variables. We seek to evaluate predictions and model performance for overall survival, event-free survival, and competing risk outcomes based on the explanatory variables, and to rank the relative importance of covariates and the effects of the most important variables. The dataset was divided into training and validation subsets consisting of 80% and 20% of the population, respectively. Cox proportional hazards model, Ridge – Elastic Net – Lasso, Extreme Gradient Boosting – tree based, Random survival forests, Neural networks, and Generalized additive models were applied. Model building, evaluation, and deployment are a continuous process. Utilizing an iterative approach, we seek to improve upon previous results each time and anticipate availability of preliminary results next quarter.

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 NMDP/CIBMTR maintains a research repository of peripheral blood samples from transplant donors (pre-donation) and recipients (pre-transplant). These samples are routinely genotyped through the ongoing Donor/Recipient Pair project to ensure sample identity and enhance the immunogenetic data available for histocompatibility research. This sample inventory and upgraded data are critical for expanding and optimizing research scenarios for evaluation of the role of HLA and other immunogenetic factors in HCT. Last year, additional Donor/Recipient transplant pair samples were selected to enhance study cohorts evaluating the contemporary treatment strategies for performing matched and mismatched transplants utilizing related and unrelated donors. In addition, the range of possible cases for inclusion was examined and selected to maximize representation of racial and ethnic diversity. The HLA typing from more than 2,600 related and 5,500 unrelated HCT donor (or cord) and recipient pairs was ordered in preparation for high resolution sequence analysis. In the last quarter, the typings were received and potential discrepancies resolved. Collated documentation and a complete dictionary and requirements for linkage to other systems for future query was compiled. Requirements for migration of historical data to new database systems were also delivered. The data from this project will impact crucial research studies that will provide guidelines into the selection of best donors and cord blood units for the most favorable patient outcomes after transplant.

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.

Planning continued on a project designed 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 unrelated donor 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 finalize the study protocol that is titled, "MEASURE: Molecular Evaluation of AML patients after Stem cell transplant to Understand Relapse Events". the protocol was submitted to and approved by the NMDP IRB in late December. A site selection questionnaire was developed and distributed to 15 candidate centers to solicit interest in participating in the study. To date, 9 centers have responded with an intent to participate in the study and have committed to enroll >250 patients per year. The protocol team planned an investigator meeting with the site principal investigators that will be held at the annual Tandem meeting scheduled for February 4, 2022 in Salt Lake City, but recently postponed to April 2022.

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.

Analyses include:

- Stem cell subset composition (not just number) influences time to engraftment and immune reconstitution
- Both conventional and novel unconventional T cell subsets within the graft influence GVHD, relapse, infection and immune reconstitution after transplant
- Natural killer cells have a role in transplant biology and number and phenotype in the donor graft influence GVHD, relapse, infection and immune reconstitution after transplant.
- The myeloid/antigen presenting cell compartment of the graft influences infection risk and immune reconstitution, thus play a role in long term patient outcome

The secondary aims of this study are:

- Explore potential associations of favorable PBSC graft composition features that may be predicted by analysis of peripheral blood samples at time of unrelated donor work-up such that these biomarkers could be incorporated into donor selection algorithms.
- Evaluate graft composition association with >12-month outcomes for overall survival, primary disease relapse, DFS and the incidence of late transplant effects including, but not limited to, chronic GVHD, diseases of the cardiovascular, pulmonary, and endocrine systems, dysfunction of the thyroid gland, bone diseases and the development of secondary primary malignancies.

- Establish a cohort of pre-transplant recipient and pre-donation adult unrelated donor biologic samples (whole blood, plasma, viable PBMC and viable donor PBSC graft mononuclear cells) collected prospectively from donors and patients enrolled on this study. This important biospecimen resource will be critical for the support of additional protocol team defined allogeneic HCT related correlative studies that will extend the knowledge gained from the primary study.

During the past quarter the immunophenotyping panel was finalized and accrual was initiated for U.S. based donors. A total of 11 product samples were received and tested through December 31, 2021. Testing costs are covered under a previous year grant while staff support is funded under this grant.

Even when patient and donor are HLA matched, post-transplant complications occur, therefore, other loci may play a role

With pre-transplant whole genome sequencing results from a cohort of 494 patients with MDS and their respective donors, we sought to identify the contribution of genomic factors to the prediction of overall survival outcomes following allogeneic HCT. Previously we identified a number of genomic factors that correlated well with transplant overall survival outcomes in this cohort. Using the random survival forests, we built prediction models first with the foundation of the known revised international prognostic scoring system data (base model) on these patients. Then we added other known clinical patient data (clinical model = base model + MDS type, hypomethylating agent treatment, chemo data) and lastly added the previously selected genomic candidates (full model). In the below figure, we show the preliminary results for this analysis. The concordance index of the model for prediction of overall survival for the full model over the base model is a striking increase of almost 0.2. These preliminary results show promise for the contribution of genomic features to the evaluation of transplant outcomes for patients with MDS.

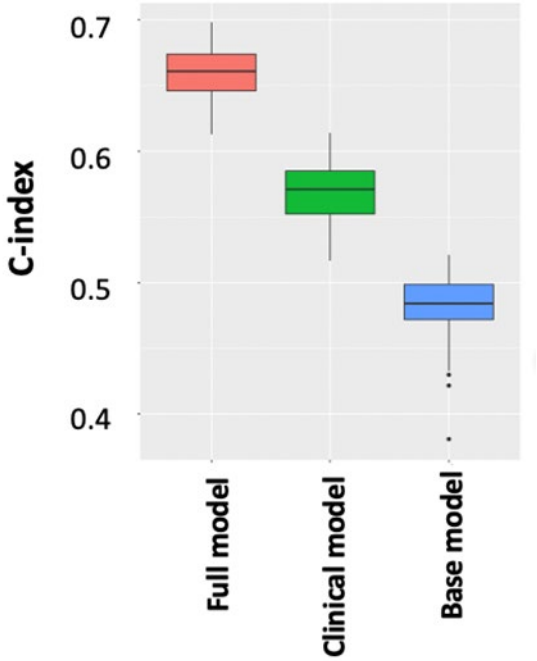

Figure: Transplant overall survival prediction model results showing the concordance index from random survival forest application using a Base model (IPSS-R score), Clinical model (base model + additional clinical data), and Full model (Clinical model + Genomic data).

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 32 abstracts were presented at the 2021 American Society of Hematology Annual Meeting held in December in Atlanta, GA. Presentation titles and type are detailed in the table below and abstracts published in Blood (https://ashpublications.org/blood.issue/138/Supplement%201).
- A total of 23 abstracts were accepted for presentation at the 2022 BMT Tandem Annual Meeting originally scheduled to be held Feb. 2-6 in Salt Lake City, UT. The meeting was recently postponed and rescheduled for April 23-26 due to current pandemic surge. Presentation titles and type are detailed in the table below. Abstracts will be published in an upcoming issue of Transplantation and Cellular Therapy Journal.
- A total of 384 proposals were received for consideration within the 15 CIBMTR Working Committee meetings to be held at the 2022 annual Tandem BMT Meeting. A total of 88 were accepted for presentation in the various working committee meetings. Final selection of proposals for activation in the 2022-2023 academic year (July 1, 2022-June 30, 2023) will occur following the Tandem BMT meeting.

Table: CIBMTR presentations at 2021 American Society of Hematology Annual Meeting

Title	Status
Saturday, December 11, 2021	
Single HLA Class I Mismatches with High Peptide Divergence in the Graft-Versus-Host Direction Are Associated with Inferior Survival after 9/10 HLA-Matched UD-HCT: A Retrospective Study from the CIBMTR	Oral
Efficacy and Long-Term Outcomes of Autologous Stem Cell Transplant (ASCT) for Patients with POEMS Syndrome (Polyneuropathy, Organomegaly, Endocrinopathy, Monoclonal Protein, Skin Changes): A CIBMTR Analysis	Oral
Haploidentical Vs. Matched Unrelated Donor Transplants Using Post-Transplant Cyclophosphamide for Lymphoma: A Joint CIBMTR/EBMT Study	Oral

Title	Status
Deleterious Germline Variants Are Present in Patients with Myelodysplastic Syndrome of All Ages Treated with Related Allogeneic Stem Cell	Oral
The Impact of Pre-Apheresis Health Related Quality of Life on Peripheral Blood Progenitor Cell Yield and Donor's Health and Outcome: Secondary Analysis of Rdsafe and BMT CTN 0201	Poster
The Impact of Pre-Apheresis Health Related Quality of Life on Peripheral Blood Progenitor Cell Yield and Donor's Health and Outcome: Secondary Analysis of Rdsafe and BMT CTN 0201	Poster
Sunday, December 12, 2021	
Health-Related Quality of Life in a Biologic Assignment Trial of Reduced Intensity Hematopoietic Cell Transplantation Based on Donor Availability in Patients Aged 50-75 with Advanced Myelodysplastic Syndrome	Oral
Real-World Efficacy and Safety Outcomes for Patients with Relapsed or Refractory (R/R) Aggressive B-Cell Non-Hodgkin's Lymphoma (aBNHL) Treated with Commercial Tisagenlecleucel: Update from the Center for International Blood and Marrow Transplant Research (CIBMTR) Registry	Oral
The Impact of Somatic Mutations on Allogeneic Hematopoietic Cell Transplantation in Chronic Myelomonocytic Leukemia: A Center for International Blood and Marrow Transplant Research (CIBMTR) Analysis	Oral
Late Effects after Allogeneic Hematopoietic Cell Transplantation Among Children and Adolescents with Non-Malignant Disorders: A Report from the Center for International Blood and Marrow Transplant Research (CIBMTR)	Oral
Prompt CR Plus Consolidation Therapy Yields Improve Survival after Allogeneic Transplantation for AML Patients Receiving Myeloablative, but Not Reduced-Intensity Conditioning: A CIBMTR Analysis	Oral
Real-World Outcomes of Axicabtagene Ciloleucel (Axi-cel) for the Treatment of Large B-Cell Lymphoma (LBCL): Impact of Age and Specific Organ Dysfunction	Oral
Lessons from an Ongoing, Multi-Center Trial Involving Biospecimen Collection for Prospective Microbiome and Immune Profiling in Patients Undergoing Reduced Intensity Conditioning Allogeneic HCT	Poster
The Incidence and Impact of Clostridioides Difficile Infection (CDI) on Outcomes after Allogeneic Hematopoietic Cell Transplant (alloHCT) – a CIBMTR Study	Poster

Title	Status
COVID-19 in Pediatric Hematopoietic Cell Transplant Recipients: A CIBMTR Study	Poster
Cryopreservation of Allogeneic Hematopoietic Cell Grafts Did Not Adversely Affect Early Post-Transplant Survival during the First Six Months of the COVID-19 Pandemic	Poster
A Refined Model of HLA-DP Permissiveness Improves Stratification of Acute Graft-Versus-Host Disease Risks after Unrelated Hematopoietic Cell Transplantation: A Retrospective Study from the CIBMTR	Poster
Bacterial Prophylaxis in Patients with Acute Gvhd; Who Is at Risk for Bloodstream Infections?	Poster
Monday, December 13, 2021	
Peri-Transplant Alemtuzumab Levels Predict Risk of Secondary Graft Failure and Inversely Impact CXCL9 Levels after RIC HCT (A Correlative Biology Study to BMT-CTN 1204 RICHI)	Oral
Donor Socioeconomic Status As a Predictor of Altered Immune Function and Treatment Response Following Hematopoietic Cell Transplantation for Hematologic Malignancy	Oral
Trends in Use and Outcomes of Autologous and Allogeneic Hematopoietic Cell Transplantation in Racial/Ethnic Minorities	Oral
Racial and Socioeconomic Disparities in Long-Term Outcomes in ≥ 1 Year Allogeneic Hematopoietic Cell Transplantation Survivors: A CIBMTR Analysis	Poster
Impact of Allogeneic Hematopoietic Cell Transplantation (HCT) As Consolidation Following CD19 Chimeric Antigen Receptor (CAR) T Cell Therapy for Treatment of Relapsed Acute Lymphoblastic Leukemia (ALL)	Poster
Identification of Novel Prognostic Biomarkers DDX11 and CHD1 of Allogeneic Hematopoietic Cell Transplantation Outcomes for Patients with MDS: A CIBMTR Comprehensive Genomic Screening	Poster
Genomic Subgroups Impact Post-Transplant Survival in Patients with Myelodysplastic Syndrome: A CIBMTR Analysis	Poster
Impact of Center Experience with Donor Type and Treatment Platform on Outcomes: A Secondary Analysis BMT CTN 1101	Poster

Title	Status
Impact of HLA Molecular Mismatch on Haploidentical Hematopoietic Stem Cell Transplantation: A Center for International Blood and Marrow Transplant Research Study	Poster
Trends in Allogeneic Hematopoietic Cell Transplantation Utilization and Estimated Unmet Need Among Medicare Beneficiaries with Acute Myeloid Leukemia	Poster
Improved Overall Survival of Patients Treated with Abatacept in Combination with a Calcineurin Inhibitor and Methotrexate Following 7/8 HLA-Matched Unrelated Allogeneic Hematopoietic Stem Cell Transplantation: Analysis of the Center for International Blood and Marrow Transplant Research Database	Poster
Major ABO Incompatibility Significantly Influences the Survival and Outcomes after Allogeneic Hematopoietic Cell Transplantation in Leukemia – CIBMTR Analysis	Oral
Impact of Autologous Hematopoietic Cell Transplant (HCT) Followed By Dendritic Cell/Myeloma Fusion Vaccine with Lenalidomide Maintenance in Increasing Multiple Myeloma (MM) Immunity (BMT CTN 1401)	Oral
Superior Outcomes with Fludarabine-Busulfan (Flu/Bu) Based Conditioning for Allogeneic Hematopoietic Cell Transplantation in Myelofibrosis - a Comparative Analysis By CIBMTR	Oral

Table: CIBMTR presentations at 2022 BMT Tandem Annual Meeting – presentation dates/times pending revised schedule for postponed meeting.

Title	Status
Outcomes of Allogeneic Hematopoietic Cell Transplantation in Blastic Plasmacytoid Dendritic Cell Neoplasm: A CIBMTR Analysis	Poster
A Pilot Study Exploring the Link between Donor-Engrafted Clonal Hematopoiesis and Outcomes of Allogeneic Hematopoietic Cell Transplantation from Older Matched Sibling Donors	Poster
Improved Overall Survival of Patients Treated with Abatacept in Combination with a Calcineurin Inhibitor and Methotrexate Following Allogeneic Hematopoietic Stem Cell Transplantation: Analysis of the Center for International Blood and Marrow Transplant Research Database	Poster

Title	Status
Effect of Autograft CD34 + Dose on Outcome in Pediatric Patients Undergoing Autologous Hematopoietic Stem Cell Transplant for Central Nervous System Tumors.	Poster
Impact of CD34+ Cell Dose on Outcome Among Children Undergoing Autologous Hematopoietic Stem Cell Transplant for High-Risk Neuroblastomas.	Poster
Single HLA Class I Mismatches with High Peptide Divergence in the Graft-Versus-Host Direction Are Associated with Inferior Survival after 9/10 HLA-Matched UD-HCT: A Retrospective Study from the CIBMTR	Poster
Return to School Practices after Hematopoietic Cell Transplantation: A Survey of Transplant Centers in the United States	Poster
What Do Patients Think about Palliative Care? A National Survey of Hematopoietic Stem Cell Transplant Recipients	Poster
Enhancing Administrative Claims Data to Identify and Address Barriers to Treatment: NMDP Search and CMS Medicare Claims Merged Dataset	Poster
Humoral Immunogenicity of Sars-Cov-2 Vaccination in the First Year after Hematopoietic Cell Transplant or Chimeric Antigen Receptor T Cell Therapy: A CIBMTR and BMT CTN Study	Poster
The Use of Search Summary Score Tool for Rapid Unrelated Bone Marrow Search Assessment	Poster
A Tool to Assess Functional HLA-DPB1 Variation in Transplantation	Poster
Unrelated Donor Registry HLA Match Likelihoods in the Mismatched Setting	Poster
A report from the National Marrow Donor Program: Neither COVID-19, nor cryopreservation, prevented allogeneic product infusion.	Poster
Impact of Bortezomib-Based Vs. Lenalidomide Maintenance Therapy on Outcomes of Patients with High-Risk Multiple Myeloma	Oral
A refined model of HLA-DP permissiveness improves stratification of acute graft-versus-host disease risks after unrelated hematopoietic cell transplantation: a retrospective study from the CIBMTR	Oral

Title	Status
Mutation Analysis in Patients with High-Risk Myelodysplastic Syndrome Receiving Allogeneic Hematopoietic Cell Transplantation Based on Biological Donor Availability: Blood and Marrow Transplant Clinical Trials Network (BMT CTN) Study 1102.	Oral
Trends in Late Mortality Amongst Two-Year Survivors of Pediatric and Young Adult Allogeneic Hematopoietic Cell Transplantation for Acute Leukemias: On Behalf of the CIBMTR Late Effects Working Committee	Oral
Chimeric Antigen Receptor t-Cell (CAR-T) Therapy Recipients and Worsening Financial Impact over Time: A Mixed Methods Longitudinal Study	Oral
Impact of Donor Socioeconomic Status on Recipient Outcomes Following Hematopoietic Cell Transplantation	Oral
Racial and Ethnic Diversity on Blood and Marrow Transplant Clinical Trials Network (BMT CTN) Trials – We Can Do Better.	Oral
Haploidentical Versus Matched Unrelated Donor Transplants for Lymphomas Using Post-Transplant Cyclophosphamide: A Joint CIBMTR/EBMT Study	Oral
Cryopreservation of Allogeneic Hematopoietic Cell Grafts Did Not Adversely Impact Early Post-Transplant Survival during the First Six Months of the COVID-19 Pandemic	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
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:

- The Japanese multi-language support, allowing FormsNet system and forms to display in a language other than English, was updated in October 2021 to reflect two Cellular Therapy form revisions.
- New capability for users to view and respond to queries in the CRID assignment tool.
- Continued monthly security monitoring and incorporating fixes to security vulnerabilities within the month.
- System maintenance to upgrade FN3 technologies to the latest revisions.

- Two, new internal tools: 1) to support and maintain studies in FN3 2) to support translations with the multi-language capabilities in FN3 were created, with a planned January release.

- Infectious Disease Marker (IDM) Tool:
    - New IDM PDF Report Permanent Solution is complete and obviated the need for any licensing.
    - Ensures future PDF software upgrades do not interfere with center submission.
- FDM: Completed several proactive security vulnerability fixes revealed by new scans

- AGNIS Mapping Tool (FDM): Create new tables & change translator table into flat view. Added grids for CRF reports with export enabled, which speeds up and improves AGNIS form metadata mapping.

- Phase 1 of 2 for the Upstream CRID Assignment Project is Complete
    - Create New Patient, Update Patient, and Infusion Trigger work are fully tested in lower environments across NMDP enterprise (MatchSource to Formsnet).

- Developed and released the following data collection forms in October 2021.

Form	Form Name	Category
2003R1	Gene Therapy Product	New recipient form
2037R3	Leukodystrophies Pre-Infusion	Revised recipient form
2137R3	Leukodystrophies Post-Infusion	Revised recipient form
2400R9	Pre-Transplant Essential Data	Revised recipient form
2450R6	Post-Transplant Essential Data	Revised recipient form
2814R4	Indication for CRID Assignment	Revised recipient form
2900R5	Recipient Death Data	Revised recipient form

Electronic data submission/AGNIS

CIBMTR continued support for electronic data submission initiatives and production AGNIS customers. Effort focused on development of new AGNIS instances of CIBMTR disease specific forms, and support for CIBMTR form revision updates to existing forms. The team is in process of completing communication, educational and technical project implementations to lower AGNIS submission burden and increase the client-base including but not limited to:

- Increasing the reuse of existing AGNIS modules when supporting form revisions and other Forms Builder reports enhancements
- Additional AGNIS reports and enhancements to the AGNIS test environments to help support external users when they are testing new AGNIS 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.
- Four AGNIS forms were released to production:
    - 2000r6 – Recipient Baseline Data
    - 2100r6 – Post-HCT Follow-up Data
    - 2018r6 – Lymphoma Pre-Infusion
    - 4000r7 – Pre-Cellular Therapy Essential Data Form
- One was released for External Test environment for center/vendor testing:
    - 4006r5 – Cellular Therapy Infusion

- Exciting updates to Enhanced Change Notes were introduced and communicated to stakeholders:
    - Substantially new automated process saves time and manual effort.
    - The automation detects changes either missed by or changed after the previous notes which reduces errors, improves center/vendor satisfaction, and reduces emails.
    - Minor updates were made to the new AGNIS User Site which was introduced in September 2021. The new site can be found here: https://sites.google.com/view/agniscibmtr/about-agnis?authuser=0

Automated data exchange using electronic data collection systems that interface directly with source health and laboratory records:
Using data extracted directly from data collection systems at partner centers, CIBMTR successfully populated laboratory data points on 26 forms at both pre-infusion and post-infusion time points. As CIBMTR continues to add form fields through periodic updates, partner transplant centers will continue to see increased benefits, including time savings.

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 Operational Data Warehouse utilized for delivery of key data to stakeholders. Accomplishments include:

- Incorporated ongoing forms revisions into the warehouse.
- Enhanced processes to support CIBMTR's Domestic and International CPI Processes.
- Completed Cord Blood Bank requests to the Cord Blood Data Quality Report.

Unified Domain Model
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 delivery of monthly and quarterly CAR T-cell data sets to our Japan and pharmaceutical partners
- Delivered 4 Periodic Safety Update Reports (PSUR) for two CAR T-cell therapies. Continued transitioning HCT data from the Research Database to the Unified Domain Model and delivered the first set of Stem Cell Therapeutic Outcomes Data required for the HRSA SCTOD quarterly report.
- Delivered 2 new data extracts combining data from the new Unified Domain Model database with older data from the Research Database, as we work toward sunsetting the Research Database.

- Continued work on adding human leukocyte antigen data (HLA) data to the Unified Domain Model

Enhance Data Sharing and Visualization
Deliver data visualization and analytic tools that will harness the power of big data.

- Created reports in new Business Intelligence tool, Looker, to support CIBMTR Prospective Research team needs.
- Created new Business Intelligence reports to support ePRO Data Quality efforts.
- 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.

Data Operations Dashboard
Published the annual TCSA reports: Annual Specific Survival Report and the Center Specific Univariant reports.

Center Performance Analytics
Annual update of the Center Performance Analytics (CPA) application with a refresh of new/current data.

Publications

1. Pasvolsky O, Yeshurun M, Fraser R, et al. Maintenance therapy after second autologous hematopoietic cell transplantation for multiple myeloma. A CIBMTR analysis. Bone Marrow Transplantation. doi:10.1038/s41409-021-01455-y. Epub 2021 Oct 4. Impact Factor: 5.48

2. Bhatt VR, Wang T, Chen K, et al. Chronic Graft-Versus-Host Disease, Non-Relapse Mortality and Disease Relapse in Older versus Younger Adults Undergoing Matched Allogeneic Peripheral Blood Hematopoietic Cell Transplantation: A CIBMTR Analysis. Transplantation and Cellular Therapy. doi:10.1016/j.jtct.2021.10.002. Epub 2021 Oct 9. Impact Factor: *See Below

3. Cancio M, Hebert K, Kim S, et al. Outcomes in hematopoietic stem cell transplantation for congenital amegakaryocytic thrombocytopenia. Transplantation and Cellular Therapy. doi:10.1016/j.jtct.2021.10.009. Epub 2021 Oct 17. Impact Factor: *See Below

4. Hamadani M, Gopal AK, Pasquini MC, et al. Allogeneic Transplant and CAR-T Therapy After Autologous Transplant Failure in DLBCL: A Noncomparative Cohort Analysis. Blood Advances. doi:10.1182/bloodadvances.2021005788. Epub 2021 Oct 21. Impact Factor: 6.79

5. Phelan R, Im A, Hunter RL, Inamoto Y, et al. Male-specific late effects in adult hematopoietic cell transplantation recipients: a systematic review from the Late Effects and Quality of Life Working Committee of the Center for International Blood and Marrow Transplant Research and Transplant Complications Working Party of the European Society of Blood and Marrow Transplantation. Transplantation and Cellular Therapy. doi:10.1016/j.jtct.2021.10.013. Epub 2021 Oct 29. Impact Factor: *See Below

6. Fuchs EJ, McCurdy SR, Solomon SR, et al. HLA informs risk predictions after haploidentical stem cell transplantation with post-transplantation cyclophosphamide. Blood. doi:10.1182/blood.2021013443. Epub 2021 Nov 1. Impact Factor: 22.11

7. Zou J, Wang T, He M, Bolon YT, et al. Number of HLA mismatched eplets is not associated with major outcomes in haploidentical transplantation with post-transplantation cyclophosphamide: A Center for International Blood and Marrow Transplant Research Study. Transplantation and Cellular Therapy. doi:10.1016/j.jtct.2021.11.001. Epub 2021 Nov 11. Impact Factor: *See Below

8. O' Donnell PV, Brunstein CG, Fuchs EJ, et al. Umbilical cord blood or HLA-haploidentical transplantation: Real world outcomes vs randomized trial outcomes. Transplantation and Cellular Therapy. doi:10.1016/j.jtct.2021.11.002. Epub 2021 Nov 11. Impact Factor: *See Below

9. Sidana S, Kumar S, Fraser R, et al. Impact of induction therapy with VRD vs. VCD on outcomes in patients with multiple myeloma in partial response or better undergoing upfront autologous stem cell transplantation. Transplantation and Cellular Therapy. doi:DOI: 10.1016/j.jtct.2021.10.022. Epub 2021 Nov 12. Impact Factor: *See Below

10. Tan CR, Estrada-Merly N, Landau H, et al. A second autologous hematopoietic cell transplantation is a safe and effective salvage therapy in select relapsed or refractory AL amyloidosis patients. Bone Marrow Transplantation. doi:10.1038/s41409-021-01527-z. Epub 2021 Nov 20. Impact Factor: 5.48

11. Meyers G, Hamadani M, Martens MJ, et al. Lessons learned from early closure of a clinical trial for steroid-refractory acute GVHD Bone Marrow Transplantation. doi:10.1038/s41409-021-01529-x. Epub 2021 Nov 23. Impact Factor: 5.48

12. Luznik L, Pasquini M, Logan B, et al. Randomized Phase III BMT CTN Trial of Calcineurin Inhibitor-Free Chronic Graft-Versus-Host Disease Interventions in Myeloablative Hematopoietic Cell Transplantation for Hematologic Malignancies. Journal of Clinical Oncology. doi:10.1200/JCO.21.02293. Epub 2021 Dec 2. Impact Factor: 44.54

13. Hamadani M, Ngoya M, Sureda A, et al. Outcome of allogeneic transplantation for mature t-cell lymphomas: impact of donor source and disease characteristics. Blood Advances. doi:10.1182/bloodadvances.2021005899. Epub 2021 Dec 3. Impact Factor: 6.79

14. Epperla N, Hamadani M. Double-refractory Hodgkin lymphoma: tackling relapse after brentuximab vedotin and checkpoint inhibitors. Hematology / the Education Program of the American Society of Hematology. 2021 Dec 10; 2021(1):247-253. doi:10.1182/hematology.2021000256. Epub 2021 Dec 10. Impact Factor: 3.06

* The American Society of Blood and Marrow Transplant was renamed as The American Society of Transplant and Cellular Therapy in 2020. The change led to an update to the name of the society journal from Biology of Blood and Marrow Transplant (Impact Factor: 3.9) to the Journal of Transplant and Cellular Therapy resulting in a reset of the impact factor.