nmdp BioTherapies℠

FIND CURES. SAVE LIVES.

PAVING THE WAY TO SUCCESSFUL CELL THERAPY CLINICAL TRIALS WITH A COMPREHENSIVE APPROACH AND PATIENT SUPPORT

The cellular therapy field, which includes hematopoietic cell transplantation (HCT), is evolving rapidly and clinical trials are key to that advancement. However, cell therapy clinical trials come with unique challenges and complexity—from trial design to patient or donor selection to long-term follow up—that impact the clinical trial sponsor, investigators, clinical trial sites, physicians, and patients and their caregivers.

NMDP℠ has more than 35 years of experience in the cell therapy space. In that time, we have developed capabilities to overcome these challenges and successfully lead academic and industry clinical trials as well as expand patient access to trials.

Our support spans the clinical trials continuum that starts with our CIBMTR® (Center for International Blood and Marrow Transplant Research®) CRO Services for clinical trial design and management and ends with outcomes collection, research and long-term follow up. It also includes the NMDP Jason Carter Clinical Trials Search and Support Program, which helps patients understand, find and enroll in clinical trials. Our mission is to save lives through cellular therapy, and saving lives is rooted in research and clinical trials that advance therapy options so more patients can get the treatment they need.

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Effectively leading cell therapy clinical trial execution requires experience

CIBMTR® is a research collaboration between NMDP℠ and the Medical College of Wisconsin®. That means those conducting academic or industry clinical trials can leverage a powerhouse of support and the established infrastructure and stability that goes along with it.

CIBMTR facilitates critical observational and interventional research through scientific and statistical expertise, a large network of centers, and a unique database of long-term clinical data for more than 630,000 people who have received HCT and other cellular therapies.

We are both a sponsor running our own clinical trials and a CRO running trials for other organizations. Our 70+ person CIBMTR CRO Services team focuses only on cell therapy and HCT clinical trial design and oversight, with a focus on partnership with organizations for the highest-impact clinical trials.

Our collaborative nature has ensured the successful execution of industry and academic studies and given many patients access to life-saving treatments.

Our CIBMTR CRO Services supports industry trials through NMDP BioTherapies℠. Since 2016, NMDP BioTherapies has formed partnerships with more than 50 biopharmaceutical companies to advance the development of cell and gene therapies through industry-leading solutions.

Our partnerships have evolved over time. They typically began in early clinical and pre-clinical trial development when NMDP BioTherapies first launched and now include later-stage clinical development and commercial launch as the industry advances.

Cell therapy and HCT clinical trials and correlative study management expertise

20+ years of clinical trials experience	**45,600+** patients and donors enrolled in clinical trials since 2001
9 active studies under IND/IDE authorization from the U.S. FDA	**26** active clinical studies in design, enrollment and follow up

Academic center and industry investigators benefit from our in-house cell therapy and HCT experts and infrastructure. Our HCT and cell therapy physicians offer clinical insights to help sponsors and investigators optimize protocol design and lay the groundwork for a successful clinical trial.

Established relationships and contracts with investigational sites, donor centers and research lab partners throughout the United States allow us to:

- Successfully recruit sites to participate on trials
- Complete site start up faster
- Expedite processes throughout the duration of the study

Active investigational transplant center sites in our CIBMTR CRO clinical trials network

*The blue pins represent the nearly 250 investigational transplant center sites in our U.S. clinical trials network.

CIBMTR CRO Services Capabilities

Our CIBMTR CRO Services offers full CRO capabilities to support clinical trials in all phases, with specific expertise in Phase I and Phase II trials. Our capabilities can be used as full CRO services or based on specific needs.

PROTOCOL DEVELOPMENT AND APPROVALS

Oversee protocol design with physician oversight and consultation including population analysis, statistical support, and patient and caregiver consultation

PROJECT MANAGEMENT

Consent Form creation, stakeholder coordination, investigator meetings and trainings, and study milestone tracking

SITE SELECTION, START UP AND MANAGEMENT

Select and train sites and oversee site start up, enrollment and protocol compliance

DATABASE BUILD AND DATA MANAGEMENT

Manage electronic data capture, including database programming and testing; data aggregation, cleaning and real-time analytics; query and site data qualifying; and data transfer

STUDY MONITORING

Oversee on-site and remote monitoring to ensure data accuracy and mitigate risks

LAB AND RESEARCH S AMPLE OVERSIGHT

Manage central pharmacies and collect and track research samples

STATISTICS AND DATA ANALYSIS

Provide feasibility assessments, trial design and sample size estimation; develop statistical analysis plan; and provide statistical support for regulatory reporting, Data Safety Monitoring Board (DSMB), and interim and final analyses

PATIENT-REPORTED OUTCOMES COLLECTION

Centrally administer patient-reported outcomes and other surveys

MEDICAL AND SAFETY MONITORING

Provide Medical Monitor and DSMB services, including system notifications for real-time reporting and regulatory body triage

CONTRACTS AND FINANCIAL ADMINISTRATION

Facilitate expedited site contracting under umbrella of existing Master Study Agreements, budget creation and tracking, and site and subject payments

CIBMTR CRO Services support for abatacept clinical trials

In December 2021, the FDA approved abatacept for the prevention of acute graft-versus-host disease (aGVHD) for patients aged 2 and older who received a matched or mismatched unrelated donor (MMUD) transplant. It is the first FDA-approved drug for the prevention of aGVHD and will increase access to HCT for more patients with hematologic malignancies and disorders.

The FDA based its approval on the safety and efficacy data from two separate studies: the Phase II clinical trial GVHD-1 (also known as ABA2) and a confirmatory observational study, GVHD-2. Our CIBMTR CRO Services prospectively supported the multi-center, ABA2 study that included a double-blind, placebo-controlled cohort and open-label, single-arm cohort.

The GVHD-2 study used real-world data provided by CIBMTR to further evaluate the impact of abatacept on the survival of HCT recipients with a 7/8 MMUD.

Researchers used an Inverse Probability Treatment Weighting (IPTW) regression analysis with propensity score weighting to minimize any potential treatment selection bias caused by using real-world control data from CIBMTR. This data was one component of determining the clinical effectiveness of abatacept and emphasizes the impact our CIBMTR Research Database has on improving outcomes for patients.

Our CIBMTR CRO Services is supporting the currently enrolling ABA-3 (NCT04380740). The multicenter randomized, double-blind, Phase II trial is investigating extended dosing of abatacept in MMUD recipients with a goal to reduce the risk of chronic GVHD.

Allogeneic Cell Therapy Clinical Trial Support Beyond Traditional Services

NMDP offers academic and industry clinical trial support for allogeneic cell therapies beyond the support provided by a traditional CRO. We have managed the NMDP Registry℠—the most diverse registry of potential unrelated donors and cord blood units in the world—for more than 35 years.

In that time, we have facilitated more than 120,000 cell therapies, the vast majority of which were time-sensitive allogeneic transplants.

That allowed us to develop sophisticated search and match and logistics capabilities to identify donors that match the characteristics an investigator needs and deliver the cells where they are needed.

In partnership with NMDP BioTherapies, our CIBMTR Bioinformatics Consulting Service provides models, analyses and interpretations to help sponsors define their targets and build their off-the-shelf cell banks.

We also offer Adult Allogeneic Cell Sourcing and Cord Blood Unit Sourcing services through NMDP BioTherapies for cell therapies in clinical trials or commercially available. This allows sponsors to access high-quality starting material for their therapy.

A supported patient is an empowered patient

When patients understand all their treatment options—including clinical trials—they can make informed decisions. However, it can be difficult for patients to find and join clinical trials. That is why we launched the **NMDP Jason Carter Clinical Trials Search and Support Program** in 2017.

The Clinical Trials Search & Support Program simplifies clinical trials access for patients, their families and their care teams through navigational and financial support.

Clinical Trials Search and Support Program by the numbers

1,700+ patients connected to clinical trials since 2017	**97%** of connected patients received clinical trial travel financial assistance	**$972,000+** in clinical trial travel financial assistance provided

Clinical Trial Navigational Support

Our **clinical trials navigators** provide high-touch support for patients and create efficiencies for care teams.

Clinical trials navigators:

- Conduct a national clinical trials search on behalf of patients with any benign or malignant hematology diagnoses—not limited to HCT and cell therapy trials
- Identify potential clinical trial options for uninsured or undocumented patients
- Provide general education on clinical trials in English or Spanish to help patients prepare for a clinical trial visit
- Navigate patients through the health care system so they can gather medical records for a clinical trial visit
- Apply for grants to help patients with travel costs to participate in clinical trials

A navigator is available at every point as the patient explores and enrolls in a clinical trial.

The **Clinical Trials Search & Support website** (CTSearchSupport.org) is an easy-to-use, intuitive platform patients and their care teams can use to identify open clinical trials for all benign and malignant hematology diagnoses.

The search tool is not limited to HCT and cell therapy, and it includes clinical trials beyond those sponsored by NMDP. Users can filter results based on patient need, diagnosis, phase of treatment, age and location.

The website also includes **educational resources and videos** to help patients learn about the clinical trials process, treatment options available through a clinical trial and clinical trial results.

We formatted and wrote the website for patients to understand. This promotes patient empowerment over their treatment and stronger communication between patients, families and care teams.

Clinical Trials Financial Support

Patients and their family members usually have out-of-pocket expenses when they participate in a clinical trial, including travel costs such as:

- Air travel
- Ground transportation (e.g., gas, parking and public transit)
- Accommodations (e.g., hotel, temporary housing and incidentals)

The NMDP offers financial assistance for travel expenses to help patients overcome financial barriers to clinical trial access.

Financial assistance is available for patients enrolled or in the process of enrolling in a clinical trial for a benign or malignant hematologic disorder.

Bringing optimal visibility to clinical trials can be a challenge for sponsors

Researchers, physicians and other health professionals can apply to have their clinical trials highlighted in the "Featured Trials" section on the Clinical Trials Search & Support website.

Featured Trials do more for patients in one or more of the following categories:

- **High Impact:** addresses a known issue or gap in care, impacts clinical practice, etc.
- **Patient-Centered:** travel costs covered, informed consent written in plain language, etc.
- **Focused on Diversity, Equity and Inclusion:** staff trained on cultural and anti-bias practices, trial locations in rural and urban areas, etc.
- **Accessible:** broad eligibility requirements, number of trial locations, etc.

These trials are listed on the user-friendly website for easy navigation for patients and clinicians.

CIBMTR CRO Services Patient-centric Approach

Our CIBMTR CRO Services team prioritizes patient-centric components in clinical trial design and oversight. We aim to ensure clinical trials are accessible for all patients. In doing so, clinical trial results will more accurately represent the full population of patients who may need cell therapy.

For example, to support trials that target recruitment of patients who are ethnically diverse, the team may select hospitals with high populations of ethnically diverse patients to participate. To ensure informed consent forms are written in plain language for patients, the team solicits feedback from recipients and caregivers.

In addition, our CIBMTR CRO Services team strives to incorporate **patient-reported outcomes (PROs)** into academic and industry clinical trials to understand the treatment impact from the patient's perspective.

The team collects PRO data at time points that parallel those at which treatment centers submit their clinical outcomes data from health care records, including:

- Pre-infusion
- Day 30 (non-HCT cell therapy only)
- Day 100
- Day 180
- Year 1
- Annually

In 2022, CIMBTR CRO Services collected 1,065 PRO surveys from 390 patients at 19 treatment centers

PROs are the most accurate measurement of the patient's experience with disease and treatment because they are collection directly from the patient.

Outcomes data supports observational studies and informs prospective studies and clinical trials

Working with our CIBMTR CRO Services gives investigators a direct link to the **CIBMTR Research Database** for historical control analysis and real-time comparison of patient populations by center.

The database contains cellular therapy information for recipients and, in the case of allogeneic HCT, their donors.

CIBMTR Research Database
350+ centers in international network
30+ countries represented
630,000+ patients in the database

CIBMTR collaborates with centers from around the world to collect clinical outcomes information for therapies performed worldwide including:

- Allogeneic transplants
- Autologous transplants
- Other cellular therapies

This includes outcomes data for nearly all allogeneic transplants and approximately 80% of the autologous transplants performed in the U.S.

We offer access to descriptive statistics for populations of interest and/or a univariate analysis of overall survival to aid in clinical decision-making, protocol development or other information-specific needs.

Conducting clinical outcomes research using the CIBMTR Research Database is a core activity of CIBMTR.

These studies address a wide range of issues and focus on questions that are difficult or impossible to address in single-center studies or randomized trials because:

- The diseases studied are uncommon
- Single centers treat few patients with a given disorder
- Not all important questions are amendable to a randomized research design

CIBMTR also supports investigators in conducting cellular therapy observational studies.

Medicare Coverage with Evidence Development (CED) studies

Many patients with specific diseases and/or at certain ages cannot access cell therapy in the U.S. because it is not covered by the Centers for Medicare and Medicaid Services.

However, CED studies allow Medicare to provide coverage to patients enrolled in clinical studies that inform policy decisions.

CIBMTR is facilitating five Medicare CED studies focused on:

- Myelodysplastic syndrome (MDS
- Myelofibrosis
- Multiple myeloma for elderly patients
- Sickle cell disease for adolescents and adults

These national clinical studies have allowed nearly 8,000 patient to receive HCT with Medicare reimbursement.

Cell and Gene Therapy Clinical Outcomes Initiatives

In addition to receiving data on HCT recipients, CIBMTR collects data for patients who receive other cell therapies.

Currently, most data are for chimeric antigen receptor T-cell (CAR-T) therapies for hematologic cancers.

In 2020, CIBMTR also began developing capabilities to support long-term follow up for emerging gene therapies for multiple diseases. CIBMTR received infusion data for 14 gene therapy products in 2022.

CIBMTR Non-HCT Cell Therapy Outcomes Data Collection in 2022

214 centers submitted data for **10,976** patients.
6,646 patients treated for lymphoma and **1,401** patients treated for ALL.

Long-term follow-up studies

CIBMTR partners with pharmaceutical companies to collect long-term follow-up data for post-approval studies required by the Food and Drug Administration (FDA) for cell and gene therapies.

The FDA requires pharmaceutical companies that commercialize genetically engineered cell therapies to follow therapy recipients for up to 15 years to evaluate safety and efficacy.

Cellular Immunotherapy Data Resource (CIDR)

The CIDR collects outcomes data about the long-term safety and efficacy of non-transplant cell therapies for all cancers, including solid tumors. These data support observational studies and inform prospective studies and clinical trials.

CIBMTR receives funding from the National Institutes of Health to serve as the CIDR as part of the Cancer MoonshotSM to accelerate cancer research, under the Immuno-Oncology Translational Network (IOTN). The Cancer Moonshot helps scientists in different organizations nationwide to join and quickly develop new immune therapies to prevent or cure cancer.

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Clinical trials are critical to improve outcomes for patients and advance the science of life-saving cell therapies. With the unique challenges and complexities of these innovative treatments, academic and industry sponsors can benefit from the synergies NMDP and NMDP BioTherapies offer through CIBMTR including:

- End-to-end clinical trial design, operations and logistics support
- Built-out clinical infrastructure with single Institutional Review Board (sIRB), dedicated DSMB, master contracts and 21 CFR part 11 compliant technology
- Access to patients and allogeneic donors for research
- Models, analyses and interpretations to help sponsors define their targets
- Direct link to the CIBMTR Research Database with information on more than 630,000 patients
- Industry-leading infrastructure to collect and analyze patient outcomes data

With careful planning, execution and patient support, cell therapy clinical trials will pave the way for new treatments for patients.

Contact us to learn how our CRO Services professionals can support your transplant and cell and gene therapy trials:

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