RESEARCH Matters

Winter 2023

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Association for the Accreditation of Human Research Protection Programs, Inc. — *Full* Accreditation

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RESEARCH AROUND McLAREN

McLAREN CENTER FOR RESEARCH AND INNOVATION CONTRIBUTES TO NEW COVID-19 STANDARD OF CARE

The McLaren Center for Research and Innovation organized the participation of three Michigan-based McLaren Health Care hospitals in a nationwide clinical trial that resulted in a new standard of care for patients with severe COVID-19 to avoid dangerous blood clots. A comprehensive program facilitating McLaren Health Care's participation in clinical trials, the McLaren Center for Research and Innovation began its participation in the COVID-PACT study in November 2020, resulting in its outcomes being published in September.

Mark Zainea, MD

Published in *Circulation*, the medical journal of the American Heart Association, results from COVID-PACT will guide the future of care for critically ill ICU patients with severe COVID-19, setting a new standard of care for other physicians to follow when treating this patient population.

A nationwide study comprising 34 sites and 390 patients, cardiologist Dr. Mark Zainea, at McLaren Macomb in Mount Clemens, led McLaren's participation in COVID-PACT and was listed among the published study's authors. Also included were internist Dr. Elizabeth Pionk and vascular surgeon Dr. Nicolas Mouawad at McLaren Bay Region in Bay City, and pulmonologist Dr. Chintalapudi Kumar at McLaren Greater Lansing.

The published study demonstrated a 44 to 45 percent reduction in the development of potentially dangerous blood clots.

"Blood clots have been some of the most harmful and impactful side effects of a COVID-19 diagnosis, causing endless damage to the patient even after they've initially recovered from the virus," Dr. Zainea said. "As we started to learn more about how to treat this virus, addressing the risk for developing blood clots was an initial concern. To be part of the nationwide effort to develop a treatment has been an incredibly rewarding process for all of us."

The critically ill patients who qualified for the trial were those who were hospitalized in an intensive care unit with severe COVID-19. Patients were treated with high-flow supplemental oxygen to address their low blood-oxygen levels, though they were still at risk for the development of potentially life-threatening blood clots, further lowering their blood oxygen levels and increasing the risk for additional health complications.

The aim of the study was to determine the benefit and impact of anticoagulant medications on the ultimate recovery of these patients. Those enrolled in the trial were given either a standard dose of the anticoagulant medication heparin with or without the addition of the anticoagulant and antiplatelet medication clopidogrel. Others were given a full dose of heparin, also with or without the addition of clopidogrel. All enrolled patients

were provided with one of these forms of therapy. Of those 390 patients, 16 were enrolled from McLaren facilities around the state.

The peer-reviewed results of this randomized-controlled study demonstrated a significant benefit of a therapy with a full dose of heparin without the addition of clopidogrel in the recovery of patients previously experiencing severe COVID-19.

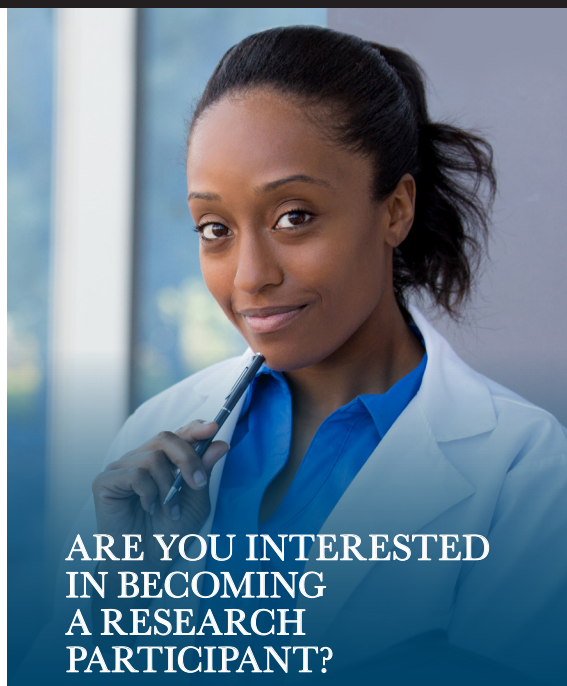
COVID-PACT RESEARCH COORDINATOR

MCRI would like to acknowledge the hard work of Emily Paschall on the COVID-PACT clinical trial. She is a full time Clinical Research Coordinator at our McLaren Macomb location. Emily worked diligently with the investigators involved to enroll patients in this ground-breaking study. Her hard work and dedication to this, as well as many other clinical trials is consistently acknowledged by industry sponsors, investigators, and her team members. We are lucky to have her as a member of the department. Thank you, Emily!

Emily Paschall

DO YOU HAVE A RESEARCH PROJECT THAT NEEDS FUNDING?

McLaren Health Care has formed a corporate level Research Funding Committee. This committee has been created to establish a system-wide strategic plan and process for awarding research funding to investigators. One goal of this committee is to support and strengthen investigator-initiated research within the corporation. Awards of up to $5,000 will be awarded to individuals involved in Graduate Medical Education Research (Residents and Fellows). Awards of up to $20,000 will be awarded to non-GME individuals interested in pursuing Investigator-Initiated research. Non-GME awards are open to all McLaren employees or affiliated providers. These funds are to be used for the conduct of the observational or interventional research study and will be awarded on a quarterly basis. Due dates for application submissions are January 1st, April 1st, July 1st, and October 1st of each year. The application process can be accessed at: www.McLaren.org/FundingApplication. Required information for the application includes a detailed description of the research project, as well as a proposed budget.



ARE YOU INTERESTED IN BECOMING A RESEARCH PARTICIPANT?

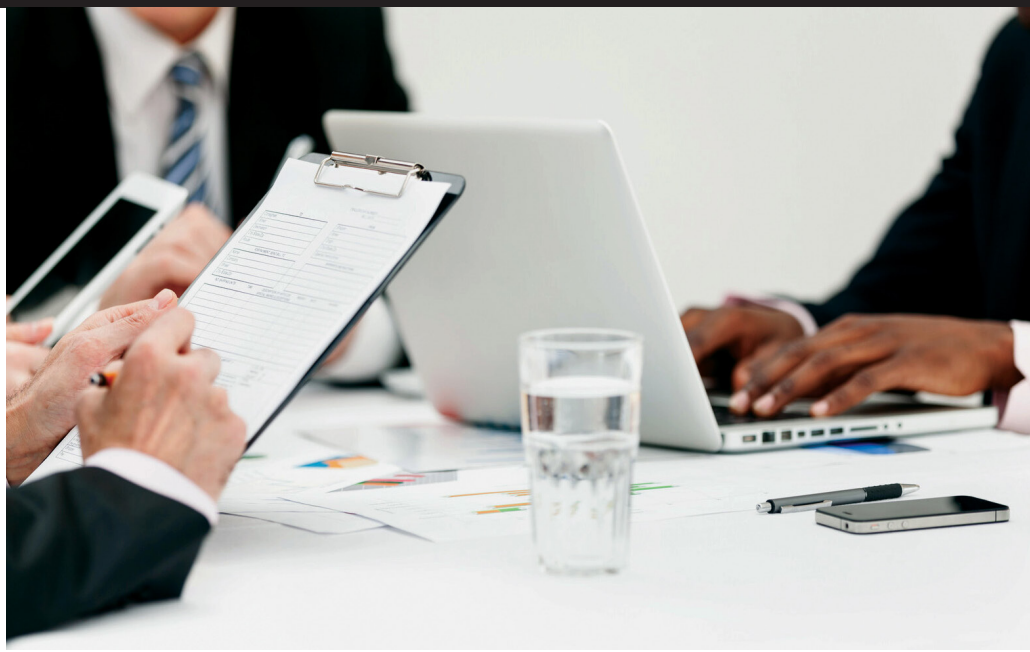
For information on enrolling in a clinical trial please visit our website at www.mclaren.org/main/clinical-research-trials. Here you will find a list of open enrolling studies at McLaren, including which hospital the research is being done at and contact information for each study.

We have enrolling studies for the following conditions (not a complete list):

- **Diabetes**
- **Orthopedic Surgery**
- **COVID-19**
- **High Blood Pressure (Hypertension)**
- **Stroke**
- **Heart Attacks / Heart Failure / Heart Disease**
- **Kidney Diseases**
- **Lung Diseases**
- **Peripheral Artery Disease**
- **Carotid Artery Disease**
- **Mastectomy**
- **Various Cancers**
  - **Breast**
  - **Lung**
  - **Prostate**
  - **Multiple Myeloma**
- **Patients who underwent intracranial aneurysm coiling**
- **Drug study for patients with recent acute coronary syndrome**

For a complete list of conditions, please visit our website listed above.

RESEARCH AROUND McLAREN



CLINICAL TRIAL ACUITY SCORING

The ability to quantify protocol specific workloads can have a significant impact on the efficiency and success of a research institution. Unfortunately, a standardized method of estimating required resources to carry out a clinical trial does not yet exist. Assessing the acuity of a clinical trial before agreeing to participate is intended to prevent the problem of taking on protocols that cannot adequately enroll subjects. Scoring clinical trial protocols with an acuity tool allows research administration to better understand the site resources needed to successfully enroll and conduct study activities. This assessment provides the institution with data to support funding requests, staffing needs, physical space, and equipment requests. A clinical trial acuity scoring tool also prevents bias when making decisions about which study opportunities to add to a portfolio, and which are best to decline.

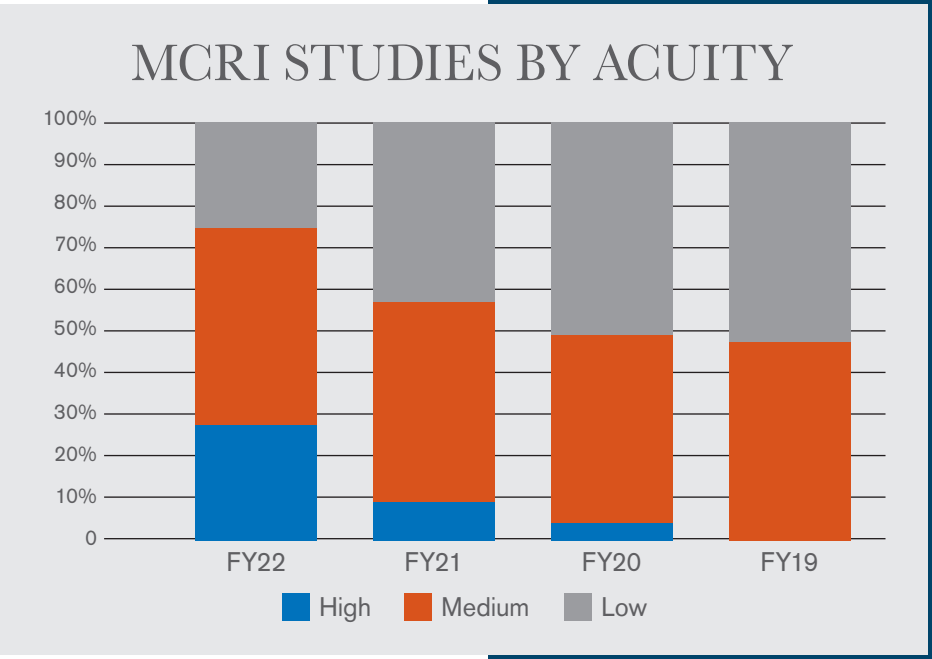
Predicting the resources needed to operationalize a clinical trial is also essential to the process of negotiating the clinical trial contract and budget. Without using cumbersome and detailed effort tracking software, it can be very challenging to understand the amount of time and effort that is spent on each procedure and assessment in any given protocol. Due to increasing complexity of protocols and research institutions with finite resources, it is critical to have a method to evaluate, quantify and document the amount of time and effort that will be required to operationalize the protocol. This data provides justification for the contract and budget specialists to communicate with the sponsor to ensure the research institution has the proper financial support for their portfolio.

Some research institutions have created their own methods of assessing clinical trial acuity and McLaren Center for Research and Innovation is actively testing our own acuity scale, as well. The primary data points being evaluated include phase and type of study, participant setting, data reporting requirements, monitoring oversight, complexity and frequency of patient procedures, visit frequency, anticipated study duration and rate of enrollment. The most difficult data point to estimate is patient enrollment. How many patients anticipated to enroll and at what rate is very challenging for even the most seasoned investigator to estimate. Factoring in the wrong enrollment rate

can significantly affect the amount of time and effort output thereby affecting the protocol's overall acuity score. This may result in over or under estimation of resources required. Getting this estimate right can mean the difference between success and failure of any given trial.

Low acuity studies are typically registries, data collections, or studies that have limited follow up or sponsor assisted follow up. These studies typically do not require a significant amount of time from the coordinators, they do not require specialized staffing or large amounts of money in the sponsor budget to cover costs. They typically do not have tests or procedures that are being done for research purposes and nearly all activity is considered standard of care. Studies like this can possibly move into the medium category if enrollment is extremely high and will be taking up a significant portion of the coordinator's time.

Medium acuity studies make up the bulk of our current portfolio. They are typically Phase 3 out-patient drug or device trials, that involve a moderate follow up schedule, some non-standard tests or procedures, and have a steady rate of enrollment. Excessive enrollment, frequent protocol deviations, violations, or serious adverse events can increase time and effort significantly and the study could fall into a high acuity category should any of these estimates be off.



High acuity trials typically involve multiple ancillary departments within the hospital, often involve inpatients, pharmacy, frequent or timed tests for research purposes, long hours or even night and weekend hours for coordinators, and involve a large volume of data collection, with anticipated frequent AE/SAE reporting. These trials require significant amounts of budgeted funds to cover these extra costs, so knowing up front is vital to the success of the budget negotiation process.

In evaluating our portfolio over the past several years, we have seen a dramatic increase in the acuity of our clinical trials. In 2022 we had 28% of our trials falling into the high acuity category, as opposed to 0% in 2019.

It is extremely difficult for any single tool to effectively evaluate everything required to conduct a clinical trial. However, even an imperfect acuity scoring tool puts a research institution at an advantage over those that do not utilize any such tools. Having data to determine which protocols belong in our portfolio and justification for staffing needs and increased budgets can poise MCRI for greater success in the long term. Enrolling what we agree to in the studies that we take on, creates strong relationships with sponsors who will return time and time again to sites that reliably deliver what is promised.

RESEARCH AROUND McLAREN

Asfar Azmi, PhD

CANCER METABOLISM DRUG STUDIED AT KARMANOS MOVES INTO THE PHASE 1 CLINICAL TRIAL STAGE, TARGETS LATE-STAGE PANCREATIC CANCER

Researchers at the Barbara Ann Karmanos Cancer Institute have seen pre-clinical activity of a cancer metabolism drug that has now entered Phase 1 clinical trials. This clinical trial will study the combination of chemoradiation to treat locally advanced and surgically inoperable pancreatic cancer.

The drug is called CPI-613® (devimistat), developed by Cornerstone Pharmaceuticals (Cranbury, New Jersey). Devimistat is a particular class of anti-mitochondrial drug that inhibits the tri-carboxylic acid cycle by working on enzymes involved with cancer cell energy metabolism. Devimistat can be given at lower doses and presents fewer side effects. In combination with gemcitabine and intensity-modulated radiation (Gem-RT) therapy, the ongoing Phase 1 will investigate the maximum dose of devimistat that can be safely given to pancreatic cancer patients. Currently, two patients are enrolled in this trial.

This open-label, dose-escalation study will be conducted at the Medical College of Wisconsin (MCW) in Milwaukee. The translation study done by researchers at Karmanos was in partnership with former Karmanos and Wayne State University (WSU) fellow Mandana Kamgar, MD, principal investigator of the devimistat Phase 1 clinical trial.

“Pancreatic cancer is a deadly disease without effective drugs. Chemo and radioresistance continue to be an overwhelming obstacle to effective pancreatic cancer treatment,” explained Asfar Azmi, PhD, leader of the Molecular Therapeutics Research Program (MT), director of the Pancreas Cancer Research Initiative at Karmanos and associate professor at WSU School of Medicine.

"Emerging evidence supports the model that metabolic reprogramming and mitochondrial metabolism allow malignant cells to adapt to conventional therapies. Carbohydrates are a preferred energy source in tumor cells, and the tumor microenvironment generally favors glycolysis and oxidative phosphorylation (OXPHOS). A shift in mitochondrial energetics towards high OXPHOS has recently been shown to confer pancreatic cancer resistance to gemcitabine, a commonly used chemotherapy. Enhanced mitochondrial respiration modulates known radioresistance pathways, including cell-cycle checkpoint mechanisms, DNA repair processes and redox balance. These observations strongly suggest that selective inhibition of hyperactive mitochondrial metabolism can be used to potentiate current chemo and radio-based treatments against pancreatic cancer."

"Our pre-clinical studies in cellular and 3D models demonstrate that devimistat can favorably re-wire the altered tumor metabolism to make pancreatic tumors sensitive to chemoradiation therapy. This combination is anticipated to enhance the efficacy of chemoradiation and improve survival outcomes of patients with deadly and by-far incurable pancreatic cancer," concluded Dr. Azmi.

Team members at Karmanos who continue to work on this study are Dr. Husain Yar Khan, research scientist in the Department of Oncology at WSU School of Medicine, and Dr. Jessica Back, member of the Tumor Biology and Microenvironment Research Program at Karmanos, associate director of Molecular Imaging and Cytometry Core (MICR) and assistant professor of oncology, WSU School of Medicine. Pre-clinical metabolomic studies were supported by a collaboration with Dr. Jing Li, member of the MT Research Program, director of Pharmacology and Core at Karmanos Cancer Institute and professor of oncology at WSU School of Medicine.

Dr. Azmi's team is leading the correlatives research on biopsies from the trials and hopes to obtain a federal grant to investigate further the future clinical use of devimistat and chemoradiation in pancreatic cancer.

RESEARCH AROUND McLAREN

Craig Cole, MD

PROVIDING INSIGHT ON CARE AND CLINICAL TRIAL PARTICIPATION OF AFRICAN AMERICAN MULTIPLE MYELOMA PATIENTS

Craig Cole, MD, hematologist and oncologist at the Karmanos Cancer Institute at McLaren Greater Lansing, and member of the Hematology Oncology and the Multiple Myeloma and Amyloidosis Multidisciplinary Teams (MDTs), joined both OncLive and WebMD to discuss multiple myeloma (MM) care for minority patients. Each podcast touches on the roots of health disparities in MM, barriers in diagnosis, awareness of MM in the local community, screening for monoclonal gammopathy of undetermined significance and clinical trial enrollment among African American MM patients.

OncLive

Joseph Mikhael, MD, the chief medical officer of the International Myeloma Foundation, interviews Dr. Cole for OncLive Insights. The discussion focuses on the disparities in survival and incidence rates between patient populations, especially between Black Americans and White Americans diagnosed with MM.

To watch all four episodes of this series, look for *"Dr. Craig Cole joins discussion on disparities and multicultural care for multiple myeloma patients"* in the news section at **karmanos.org/healthcareprofessionals**.

WebMD

John Whyte, MD, MPH, host of WebMD's Health Discovered podcast, welcomes Dr. Cole to talk about the fight for equity in multiple myeloma care. Robert Brooks was also interviewed on the podcast. Brooks is a Karmanos MM survivor who participated in a clinical trial under the care of Jeffrey Zonder, M.D., hematologist and oncologist, leader of the Multiple Myeloma and Amyloidosis MDT, and member of the Hematology Oncology MDT.

To listen to the WebMD podcast, look for "IN THE NEWS: The Fight for Equity in Multiple Myeloma Care" in the news section at **karmanos.org/healthcareprofessionals**.

GRADUATING FELLOW AND KARMANOS BREAST CANCER SPECIALIST

CO-AUTHOR MANUSCRIPT ON TRIPLE NEGATIVE BREAST CANCER WITH BMT FACULTY

Hadeel Assad, MD, medical oncologist, member of the Breast Cancer Multidisciplinary Team (MDT) and Phase 1 Clinical Trials Program at Karmanos, along with hematology and medical oncology graduating fellow at Karmanos and Wayne State University (WSU) School of Medicine, Bayan Al-Share, MD, co-authored "Role of High-Dose Adjuvant Chemotherapy (HDC) Followed by Autologous Stem Cell Transplantation (ASCT) in Locally Advanced Triple-Negative Breast Cancer (TNBC): A Retrospective Chart Review," published in Hindawi Journal of Oncology. Co-leaders of Karmanos' Bone Marrow & Stem Cell Transplant (BMT) MDT, Voravit Ratanatharathorn, MD, and Joseph Uberti, MD, PhD, along with BMT members Abhinav Deol, MD, Asif Alavi, MD, Dipenkumar Modi, MD, Andrew Kin, MD, and Lois Ayash, MD, contributed to the research. Judith Abrams, PhD, member of the Tumor Biology and Microenvironment Research Program at Karmanos, also collaborated in the study.

"Due to the robustness of the BMT database at Karmanos, we are able to evaluate many scientific questions related to transplant patients and encourage our HemOnc fellows to take advantage of this unique opportunity," explained Dr. Assad. "This is the first study in many years that involved collaboration between both breast and transplant oncologists. We reviewed 29 women with confirmed TNBC treated with HDC and ASCT between 1995 and 2001. We excluded patients with unknown HER2/neu status and selected for high-risk features such as T4 disease or >4 regional node involvement. Our study revealed prolonged DFS and OS with acceptable side effect profile. We concluded that re-evaluation of this approach in this subset of high-risk breast cancer in prospective randomized studies may be worthwhile, realizing the recent approval of immunotherapy and adjuvant Olaparib, a subset of patients will also have to be taken into account."

Hadeel Assad, MD

Bayan Al-Share, MD

To read this study, look for this article in the news section at karmanos.org/healthcareprofessionals.

RESEARCH AROUND McLAREN

Jennifer Beebe-Dimmer, PhD, MPH

COLLABORATIVE KARMANOS, WAYNE STATE AND DUKE UNIVERSITY RESEARCH TEAMS

IDENTIFYING GENE MUTATION IN BLACK MEN THAT CAUSES EARLY PROSTATE CANCER

Researchers at Barbara Ann Karmanos Cancer Institute and Wayne State University have recently found inherited genetic variants mostly involved in the body's response to acquired DNA damage that may be responsible for early-onset prostate cancer among some Black men.

Jennifer Beebe-Dimmer, PhD, MPH, leader of the Population Studies and Disparities Research (PSDR) Program, scientific director of the Epidemiology Research Core (ERC) at Karmanos, and professor of Oncology at Wayne State University (WSU) School of Medicine, led the Karmanos and WSU team for the study titled, "Germline Variants in DNA Damage Repair Genes and HOXB13 among Black Patients with Early-Onset Prostate Cancer," recently published in the American Society of Clinical Oncology's JCO Precision Oncology. Researchers were interested in identifying genetic variants in Black men diagnosed with early-onset prostate cancer.

"The objective of this study was to examine the prevalence and spectrum of known mutations in cancer susceptibility genes in primarily DNA damage response pathways in African American men diagnosed with early onset prostate cancer," explained Dr. Beebe-Dimmer. "Our knowledge about the importance of these genes in black men with prostate cancer lags far behind our knowledge in men of European descent."

One of the risk factors for prostate cancer is a family history of the disease, particularly when there is a father, brother or son who is diagnosed before age 65. These men are usually encouraged to speak with their doctor before the age of 50 to talk about their risk. However, if they are Black, they should speak with their doctor at age 45. Black men are more likely to be diagnosed with prostate cancer and die from the disease than their non-Hispanic White male counterparts, who are usually the subjects of most prostate cancer research.

"In the absence of genetic information, a family history of prostate cancer, particularly among close relatives - fathers, brothers and sons - is often used as a proxy measure of inherited genetic predisposition. There is a similar logic in looking at men with earlier onset disease. The thought is that these men have an inherited predisposition to disease, which is why it manifests at an earlier age," said Dr. Beebe-Dimmer.

The team examined the DNA of over 700 Black men, 62 years old and younger, who had been diagnosed with early-onset prostate cancer. From the gene sequence, they found about 4 percent of the men had HOXB13 (a gene first discovered in White men with hereditary prostate cancer) and decided to take a closer look.

The team hopes their findings on the genetic variants among Black men will help reduce the number of early-onset prostate cancer diagnoses and deaths from the disease. With this, they hope men who know they have a family history of prostate cancer will also consider genetic testing and talk to their doctors about prostate cancer screening.

"Mutations in the genes identified in this study not only help us to understand the underlying biology of prostate cancer in African American men, but our new knowledge of these mutations may also be used in the development and use of targeted treatments, as well as screening for earlier detection of disease in unaffected family members," concluded Dr. Beebe-Dimmer.

For four years, Dr. Beebe-Dimmer has been working on this research with a group of Karmanos and WSU School of Medicine researchers, including Matthew Trendowski, PhD, WSU medical student; Tara Baird, manager of the ERC, Karmanos and WSU; and Julie Ruterbusch, MPH, co-director of the ERC, member of the PSDR Program at Karmanos and WSU research assistant. This research was also in collaboration with Duke University – that team led by the senior author, Kathleen Cooney, MD. The Department of Defense and the National Institutes of Health funded the study.

Tara Baird

Julie Ruterbusch, MPH

Matthew Trendowski, PhD

RESEARCH AROUND McLAREN

OCHECE RECEIVES SUPPLEMENTAL AWARD FOR SEXUAL ORIENTATION AND GENDER IDENTITY COMMUNITY RESEARCH

The National Cancer Institute (NCI) has awarded the Barbara Ann Karmanos Cancer Institute's Office of Cancer Health Equity & Community Engagement (OCHECE) supplemental funding to the P30 Cancer Center Support Grant (CCSG), also known as the Core Grant*. The $150,000 award will support the "Enhancing Sexual Orientation and Gender Identity (SOGI) Data Collection" project led by OCHECE.

"SOGI stands for sexual orientation and gender identity. It is important to have a systematic and accurate collection of SOGI data because it gives healthcare systems the enhanced ability to monitor and identify disparities in cancer incidence and mortality for LGBTQIA patients, as well as the quality of care provided for this group of patients," said Brittany Dowe, MPH, director of OCHECE. "This additional funding is important to help strengthen the standardization across Karmanos Cancer Institute's 16 locations for collection of SOGI data."

OCHECE leads Karmanos' community outreach and engagement efforts across the 46 Michigan counties the network serves. The organization creates opportunities for diverse community members and organizations to engage in discussion, research and strategy with Karmanos and Wayne State University researchers, scientists and physicians. The goal is to reduce the cancer burden and improve cancer outcomes across all populations.

Learn more about OCHECE, visit: **karmanos.org/ochece**.

OCHECE has partnered with LGBT Detroit, Corktown Health and the National LGBT Cancer Network for the SOGI project. The project has four goals:

1. Identify oncology provider-level and patient-level barriers to the collection of SOGI data
2. Develop and conduct training for oncology providers and staff on rationale and strategies for collecting the data
3. Develop and implement a campaign to increase patient awareness and knowledge of SOGI data collection
4. Implement and evaluate the data through both paper-based forms and electronic medical records throughout the Karmanos Cancer Network sites within McLaren Health Care.

**The P30 grant, awarded by the NCI, supports enhancing multidisciplinary approaches and collaborative research efforts in treating cancer.*

KARMANOS RECEIVES RENEWAL OF MEMBERSHIP IN PRESTIGIOUS PROSTATE CANCER CLINICAL TRIALS CONSORTIUM

Elisabeth Heath, MD, FACP, leader of the Genitourinary Oncology Multidisciplinary Team (MDT) and member of the Phase 1 Clinical Trials MDT at the Barbara Ann Karmanos Cancer Institute, has received grant renewal from the U.S. Department of Defense to continue membership in the prestigious Prostate Cancer Clinical Trials Consortium (PCCTC) program.

The Prostate Cancer Clinical Consortium Award is a peer-reviewed, competitive grant. Peers include scientific researchers at universities and cancer centers across the nation. Karmanos has been part of the consortium since 2008. The award allows our physicians and researchers the opportunity to participate in numerous clinical trials, translate laboratory findings to the clinic and offer cutting-edge clinical trials to prostate cancer patients in Metro Detroit. The budget amount for the new four-year grant renewal is $1,847,997.

Dr. Heath will continue to direct Karmanos' involvement in the consortium. Dr. Heath is the associate center director of Translational Sciences, professor of Oncology at Wayne State University (WSU) School of Medicine and the Patricia C. and E. Jan Hartmann Endowed Chair for Prostate Cancer Research at Karmanos and WSU.

"This grant has provided us with the opportunity to offer cutting edge clinical trials in prostate cancer," said Dr. Heath. "We appreciate the collaboration and partnership with other PCCTC member sites and colleagues to advance science in prostate cancer."

Dr. Heath's co-principal investigator is Frank Cackowski, MD, PhD, medical oncologist, member of the Genitourinary Oncology MDT and assistant professor of Oncology at WSU.

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Elisabeth Heath, MD, FACP

Frank Cackowski, MP, PhD

RESEARCH AROUND McLAREN

LIFE-SAVING STUDY: CLINICAL TRIAL GIVES PANCREATIC CANCER PATIENT RENEWED HOPE

Her quest for clinical trial options led her to Karmanos

In the fall of 2020, when Cathleen Janosko noticed she had an upset stomach and felt more tired than usual, she did not think much of it. After all, many people experience those symptoms from time to time.

But a few months later, when those vague symptoms turned into a deep-seated pain in her upper right abdomen, she knew something was not right.

Janosko, who lives in rural southeast Ohio, went to a local hospital for an ultrasound. Then her doctor called with the news: the scan showed a mass in her liver. Subsequent computed tomography (CT) revealed more masses in her pancreas and lower abdomen. The diagnosis was Stage 4 pancreatic cancer.

“I was devastated and very scared,” said 63-year-old Janosko. “I knew my cancer was life-threatening. I also thought of my parents. I had lost my father to lung cancer and my mother to uterine cancer.”

That was the beginning of Janosko’s cancer journey. Thankfully, subsequent testing and loads of late-night research on the specifics of her disease led her to the Clinical Trials Program at the Karmanos Cancer Center.

Today, nearly a year after enrolling in a clinical trial that targets the specific genetic driver of her cancer, Janosko has no visible sign of the disease. Her extraordinary outcome offers hope to future cancer patients–including those with late-stage pancreatic cancer.

A particularly deadly disease

Due partly to the pancreas’ location in the upper area of the abdomen, it can be challenging to diagnose the disease at an early stage. By diagnosis, for most patients, the disease has often metastasized and spread to other organs, thus eliminating surgical treatment options. This was the case for Janosko.

According to the American Society of Clinical Oncology, the five-year survival rate for pancreatic cancer is just 11 percent. The survival rate for patients

with Stage 4 disease is around 2 to 3 percent.

For these reasons, Janosko's local hospital doctors did not offer her much hope.

"They said there was nothing more they could offer besides chemotherapy, with no subsequent testing," she explained. "They gave me just two to six months to live. That's when I began doing my research."

Janosko transferred to a larger area hospital where she began receiving chemotherapy. Doctors there also performed a genetic test on the tumor. The results exposed a targetable gene fusion called NRG1, which is rare in cancers.

"I had been researching all I could about the disease on various pancreatic cancer support group websites," Janosko said. "I noticed many survivor stories had involved clinical trials. I also learned there are trials targeting NRG1 fusion in many cancers, including pancreatic cancer. The sites also noted the importance of getting into a clinical trial early to achieve the best results."

Ten-and-a-half months of chemotherapy had reduced Janosko's tumors slightly, but there was not much progress.

"I uploaded my medical information to an independent virtual tumor board that gives unbiased reviews of treatment options to patients with advanced-stage disease," outlined Janosko. "They said a clinical trial targeting the NRG1 fusion would be my best option. After further online research, I learned the Karmanos Cancer Center in Detroit was the closest hospital offering this specific clinical trial."

Targeted treatment

Large academic centers and research institutes like the Barbara Ann Karmanos Cancer Institute offer the broadest portfolio of clinical trials. At any one time, Karmanos offers approximately 250 active trials.

This broad portfolio is what led Janosko to Karmanos.

Najeeb Al-Hallak, MD, MS

In December 2021, she and her husband, John, drove nearly 300 miles to Detroit to meet with Najeeb Al-Hallak, MD, MS, medical oncologist at Karmanos. After reviewing her case. Dr. Al-Hallak said Janosko was a good candidate for the clinical trial she had identified.

"Cathleen's lab results indicated a rare NRG1 fusion, which we think is a driver for cancer growth," explained Dr. Al-Hallak, a member of the Gastrointestinal and Neuroendocrine Oncology and the Phase 1 Clinical Trials Multidisciplinary Teams at Karmanos. "Our particular clinical trial is very much targeted to that mutation.

"She was concerned about enrolling in the trial but realized it was her best option. She followed the science and made a courageous decision to enroll."

"Enrolling in the trial was exciting but also scary," Janosko admitted. "Dr. Al-Hallak said that although he hadn't previously had a pancreatic cancer patient

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RESEARCH AROUND McLAREN

LIFE-SAVING STUDY: CLINICAL TRIAL GIVES PANCREATIC CANCER PATIENT RENEWED HOPE

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take this drug, he felt I was a great candidate for the trial."

Cathleen and John make the four-and-a-half-hour trip every two weeks to Karmanos' Detroit location, where she receives the experimental drug intravenously. She will finish the treatment in late 2023.

Janosko's decision paid off tremendously. In February 2022, a positron emission tomography (PET) scan showed no visible tumors. The latest updated CT scan from October 2022 confirmed that her cancer is still in remission with no measurable tumors or metastatic disease. Janosko said she had not experienced side effects from the treatment.

"Her case is nothing short of amazing," Dr. Al-Hallak said. "Scans show no visible cancer and Cathleen is in remission. She'll continue receiving the drug through the two-year clinical trial period. I truly believe her case will have a very positive outcome."

Dr. Al-Hallak added that the tumor genetic data opened further treatment possibilities for Janosko when none seemed readily available.

Janosko also encourages other cancer patients to consider enrolling in a clinical trial.

"My results are nothing less than a miracle," she said. "Dr. Al-Hallak and his team at Karmanos have always treated us with the best care.

"The ongoing cancer research gives me hope that doctors will be able to find more drugs that work for different cancers. Clinical trials are important because they help determine what works. Look for a medical team that addresses your specific cancer and doesn't treat you like every other patient. My treatment was tailored to me, which has made all the difference."

KARMANOS RECEIVES RENEWAL OF MEMBERSHIP IN PRESTIGIOUS PROSTATE CANCER CLINICAL TRIALS CONSORTIUM

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The Prostate Cancer Clinical Consortium Award was established in 2005 to support the collaborations and resources necessary to rapidly execute Phase II or Phase I/II clinical trials of therapeutic agents or approaches for the management or treatment of prostate cancer. The overarching goal of the award is to combine the efforts of leading investigators to bring to market novel therapeutic interventions that will ultimately decrease the overall impact of prostate cancer.

EQUIP CORNER

Susmita Jain

BEST PRACTICE IN RESEARCH DATA MANAGEMENT AND PROTECTION

By Susmita Jain, Research QI and Education Specialist, McLaren Health Care

Why Data Management is Important?

With the evolution of the digital age, technology continues to play a very important role in clinical research. Keeping the dynamic nature of the technology in mind, and its challenges, the regulatory bodies are putting intense scrutiny on data protection and data privacy in clinical trial procedures and policies. We are aware that all research involves some risk. Research participants are more vulnerable than ever as researchers use third party applications for data storing and sharing online. This research data must be protected from loss, theft, cyber-attack, hardware failure, natural disaster etc. The more sensitive the data, the more significant these threats become. In 2021, according to Politico, approximately 50 million people in the U.S. faced a health-data breach. Data breaches pose huge privacy and security concerns for researchers and can cost the health-care industry billions of dollars. To avoid such crisis, we need to develop privacy and security practices in research data management that also fit with the regulatory requirements.

The Principal Investigator (PI) is responsible for all aspects of the research, including the collection, transmission, storage, backup, and security of data. This is both while the research is being conducted and once it has been completed. It is the responsibility of the PI to ensure those listed as key personnel are informed and trained on the procedures related to data management. The PI must report any breaches in confidentiality to the MHC Institutional Review Board (IRB) within seven days of becoming aware of the event.

What is Data management plan?

A data management plan (DMP) details how you will treat your data during a research study and what happens with the research data once the research

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is completed – all in keeping compliance with the applicable regulatory requirements. It covers all the research stages from data collection, and organization, through quality assurance/quality Improvement (QA/QI). This includes documentation and use of the data, data storage and sharing with others. It will include:

- How will the data be created?
- How will the data be captured and in what format?
- How much data will be collected? And how often should it be collected?
- How will you organize your data?
- What tools or software will be required to read or view the data?
- What will be the quality assurance and quality control mechanisms at each stage?
- How long will the data be accessible?
- How will data be stored and protected over the duration of the project?
- How will data be preserved, shared and made available for future use?
- How will the data be destroyed once the project terms are over?

Understand the Regulatory Requirements:

Before creating your plan, it is very important to familiarize yourself with the applicable laws and regulations that require data to be safe and confidential.

Although the term "data management plan" is not included in the FDA regulations, Federal regulations for human subjects research require an IRB to determine that adequate provisions to protect the privacy of subjects and the confidentiality of data are in place and that researchers include adequate data management and protection plan for minimizing these risks.

As applicable to research, the following are certain regulatory guidelines related to data privacy and data sharing:

- FDA Privacy Act Regulations (21 CFR part 21)
- FDA Technology Modernization Action Plan (TMAP)
- FDA Office of Digital Transformation
- HHS Privacy Act regulations (45 CFR Part 5b)
- NIH's 2003 Data Sharing Policy
- NIH Data Management & Sharing (DMS) Policy, will be effective January 25, 2023
- The Health Insurance Portability and Accountability Act of 1996 (HIPAA)

Here are some reminders and tips for the research members while creating your data management plan:

Prior to submitting your application to MHC's IRB, create guidelines related to your research outlining how data should be collected, stored, protected, and shared with others. Once the plan is created, communicate it with your team to discuss if any update is needed as per applicable regulations guidelines and MHC's policies. All responsible staff should review and reach a consensus with the plan to ensure consistency of the process.

Data management takes time and costs money in terms of software, hardware, and personnel. Review your plan and make sure that there are lines in the

budget to support all these requirements.

A well prepared DMP will clearly mention the roles and responsibilities of every named individual and organization associated with the research project. Roles may include data collection, data entry, Quality Assurance/ Quality Improvement (QA/QI), backup, data preparation and submission to an archive. Consider the time and levels of expertise required by the staff. For small to medium size research projects, a single person may easily manage most, or all the data management tasks. In contrast, large, multi-investigator/site projects may require dedicated staff person(s) assigned to different data management tasks.

Treat your DMP as a living document and reevaluate it frequently for any new changes in protocols and policies. Ensure that before you implement those changes, you submit the modification application to MHC's IRB for their review and approval.

Do I really need to collect this identifiable data?

To justify your requirements, make a list of identifiers you are collecting and describe why you need each and how it will be used. This information will be helpful for creating Inform consent forms. This will guide you in what needs to be included in the consent form, if HIPAA authorization is needed, or the need to ask for waiver of authorization.

What tools should I use to collect data safely and securely?

When multiple people are conducting research, you often end up with multiple tools and multiple ways in which data is stored. Teams need to decide which tools to use before data collection, to avoid having data stored in multiple places and, thus, manage the risk associated with a data breach.

During and after data collection maintain participant anonymity while taking notes, while cleaning data and preparing it for storage, or while sharing results. Ask only for information which you really need from participants for your research project.

Quality Assurance/ Quality Improvement (QA/QI) analysis of collected data:

Once the data is generated, validate the data in accordance with the protocol specifications. Consider implementing edit check programs to identify the discrepancies in the entered data, to catch the data discrepancies and ensure data validity. Discrepancy may be due to inconsistent data, missing data, range checks, and deviations from the protocol.

When working with sensitive data, subject identifiers should be removed or destroyed as soon as is feasible for the research.

If, despite precautions, a video or audio recording does include identifying information, make sure to delete that part of the recording or blur it as soon as possible.

Data Storage/Disposal

If the data are being collected to undertake a given study, then personal identifier data should not be retained longer than necessary to complete the research and publish the results. It is good practice to regularly review personal data holdings to determine whether they need to be retained or can be safely destroyed.

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If personal data will be retained in the long term after the completion of the research, planning should take into consideration where and under whose authority they will be held, and what provision is made for transfer of ownership should the original owner leave the institution.

Federal regulations require human subjects' records be retained for at least three years after completion of the research. MHC IRB policy holds that human-subjects research data must be retained for a minimum of seven years after the study is closed by the MHC IRB. In accordance with Federal HIPAA privacy regulations, IRB records pertaining to those containing protected health information (PHI) are retained for at least six years after the completion of the research. Investigators must be familiar with these requirements and maintain all research records for the period which meets the requirements of all parties. It is MHC IRB's policy to retain records for the greatest amount of mandated time. See policy MHC_RP0114 IRB Documentation and Research Record Retention.

Plan a consistent way of storing data so it can be found easily in case it needs to be retrieved in an immediate situation. Researchers shouldn't be searching for places where the data files could be. They should already know where it is. Personal devices, such as laptops, cell phones, or digital recorders that are owned by the researcher or member of the study team are not an acceptable method to collect identifiable or MHC's Confidential data due to inherent risk of loss of confidentiality.

If a server is used for data storage, research subject's personal identifying information should be kept separate from the data. It is recommended that competent data destruction services be used to ensure that no data can be recovered from obsolete electronic media.

You should use a locked storage container such as a filing cabinet in a locked office for paper-based personal data; for digital data use the password-protected or, preferably, encrypted storage. Sensitive personal data should be encrypted, and not stored or shared by means of cloud services other than a MHC secured drive.

Using the online available data collection instruments like survey tools have their own challenges and issues. Any third-party service provider collecting personal survey data on your behalf is acting in the capacity of a data processor as defined under the Data Protection Act. Whenever a data controller uses a data processor, a written contract must be in place between the MHC and the third party, so that both parties understand their responsibilities and liabilities. See policy MHC's Corporate Compliance policy MHC_CC0139 Contract Management and Authorizations.

Data Sharing

Research done under the National Institutes of Health guidelines focus largely on data sharing and are found in a document entitled "NIH Data Sharing Policy and Implementation Guidance" (http://grants.nih.gov/grants/policy/data_sharing/data_sharing_guidance.htm).

Transmitting identifiable datasets by email is not a good practice due to the inherent risk of compromise. When planning for the management of data collected from research participants, you have an ethical and legal responsibility to ensure that you store and share confidential and personal data securely and do not disclose them to unauthorized persons.

Collecting and sharing the data via cloud-storage services like Google Drive, Dropbox, and One Drive could make your life easy but same time it puts the data at risk since you don't have complete control over data. For example, if cloud services are down or hacked, you don't have the control to fix the issue. Also, it further exposes research participants to data breaches and cyber threats. Instead, researchers should consider using an external drive to store encrypted data and find more-secure ways to share data.

Research done at MHC shall enter into the Data Use Agreements (DUAs) to permit the use or disclosure of the limited data set. When a DUA is required, it must be study specific. DUAs details the terms and conditions of the transfer.

If you will be processing personal data in your research, you are advised to review MHC's guidance on Data protection. You should familiarize yourself with the MHC's Data Protection, Encryption and Remote Working policies, which can be found under corporate compliance policy on SharePoint. Understand your responsibilities in reporting data breaches. If the applicable regulations do not require you to report a data breach, consider whether you are required to do so by your obligations to your institutional IRB and research participants.

Summary

A strong Research Data Management plan is critical in clinical research, which leads to generation of high-quality, reliable, and statistically sound data from clinical trials. Various components of data management plans including designing data collection tools, data-entry, data validation, discrepancy management, data storage and sharing are assessed for quality at regular intervals during a trial.

Research Data Management planning has evolved in response to the ever-increasing demand from pharmaceutical company drug development processes and from the regulatory authorities to put the quality systems in place to ensure research participant's privacy and confidentiality are maintained. To meet the expectations, there is a gradual shift from the paper-based to the electronic systems of data management. Developments on the technological front have positively impacted the process.

In the present scenario, there is an increased demand to improve the data management standards to meet the regulatory requirements and stay ahead of the competition by means of providing good quality, reliable data.

UPCOMING RESEARCH EDUCATION

SOCRA
Clinical Research Professional Certification Preparation and GCP Virtual Review Course
February 23 - 24, 2023

Clinical Research Monitoring and GCP Virtual Workshop
February 28 - March 3, 2023

Advanced Site Management: Finance and Productivity Virtual Workshop
January 24 -26, 2023

Pediatric Clinical Trials Conference
February 16- 17, 2023
Miami Beach, FL
Holiday Inn Miami Beach Hotel Oceanfront
4333 Collins Avenue
Miami Beach, FL 33140

Oncology Clinical Trials Conference
March 30 & 31, 2023
San Diego, CA
Hilton Garden Inn San Diego Downtown/Bayside
2137 Pacific Hwy
San Diego, CA 92101

ACRP 2022
2023 Annual Conference
Dallas, Texas
April 28 - May 1, 2023

WCG Center Watch
Run More Efficient, More Diverse Decentralized Clinical Trials:
How Mobile Nursing Can Transform Your Research
Jan 24, 2023

MAGI EAST 2023
Philadelphia, PA
May 21-24, 2023

OHRP Research Community Forum
Research in the Age of Technology:
The Impact of Innovative and Emerging Technologies on Human Subjects Research
March 29 - 30, 2023

FACULTY, FELLOWS & RESIDENTS

SCHOLARLY ACTIVITY NEWS

Carlos F. Rios-Bedoya, ScD

REVISITING THE HUMAN SUBJECTS RESEARCH PRE-DETERMINATION PROCESS FOR GRADUATE MEDICAL EDUCATION SCHOLARLY ACTIVITY PROJECTS

By Carlos F. Rios-Bedoya, ScD, MPH

The Division of Scholarly Activity decided to establish a separate process for the Human Subjects Research Pre-Determination (HSRPD) for scholarly activity projects. This new HSRPD process was implemented by McLaren Graduate Medical Education effective February 1, 2022. All scholarly activity projects, except case reports/case series and systematic literature reviews (without meta-analysis), must follow this new process. The new HSRPD does NOT require using the IRB iRIS submission system. However, if the scholarly project is determined to be human subjects research by the new process, an IRB application must be completed and submitted using the iRIS submission system. The new process uses two new PDF fillable forms (HSRPD form and checklist) and a supporting template. These forms and supporting template are available through “new innovation”, which is the scholarly activity website, and the PhDs.

The forms have instructions on completion and signature requirements. Please read and follow them carefully. The PhDs know how to complete and submit these forms and should be contacted first for guidance. An incomplete form will delay the review and the pre-determination decision.

Briefly, the process is as follows:

- Answer ALL the questions to the best of your knowledge.
- Consult a PhD if you are not sure on how to answer specific questions.
- Provide as much detail as possible when answering open-ended questions to assist the reviewers in making a valid and accurate pre-determination.

- Make sure you gather the required signatures and initialize the appendix.
- Complete the required checklist.
- Complete the supporting work template. Please, provide as much details as possible when completing the template to expedite the process. Specific supporting templates for secondary data analysis and meta-analysis projects are also available. Consult with a PhD before using any of these project specific templates. Selecting the wrong supporting template might cause delays in the review process.

Send the completed documents to **mhc.sarc@mclarenmeded.org**.

Please pay attention to the email address as it is similar to the Scholarly Activity Review Committee (SARC) email. Sending the pre-determination forms to the wrong email could substantially delay the pre-determination of your scholarly activity project. The estimated/ expected turnaround time for a properly completed and submitted application is 5 business days.

After receiving the pre-determination letter, you still CANNOT start your scholarly activity project. The next step is to either submit a SARC application if your project was determined to be non-human subjects research OR submit an IRB application if your project was determined to be human subjects research. Your scholarly activity project can start after receiving either a SARC or IRB letter of approval. Once again, if you have questions or need guidance consult a PhD.

The Division of Scholarly Inquiry is committed to support and facilitate scholarly activity for McLaren residents, fellows, and faculty. For additional information contact Dr. Carlos F. Ríos-Bedoya at **carlos.rios@mclaren.org**.

ANNOUNCEMENTS AND WHAT'S NEW

Regina Miyauchi

The McLaren Center for Research and Innovation (MCRI) is pleased to announce the addition of **Regina Miyauchi** to the team. She is a Clinical Research Nurse at McLaren St. Luke's. Regina is a long-time registered nurse with a varied background that includes ambulatory family practice, obstetrics, comprehensive care, pre-op / PACU and Clinical Research. Regina's first love is Clinical Research. She previously coordinated many trials of well-known medications. We look forward to watching her grow the program at St. Luke's.

Susmita Jain

Research Integrity is pleased to announce the addition of **Susmita Jain** to the team. She is the new Research Compliance QI and Education Specialist for McLaren Health Care. Susmita holds a master's degree in clinical research administration from Eastern Michigan University. She comes with more than 10 years of the clinical research management experience in various fields such as infectious disease, radiation oncology, cosmetics and dermatology. Susmita is looking forward to learning more and utilizing her knowledge & skills to help strengthen our research Program.

Kiona Graham

The McLaren Center for Research and Innovation (MCRI) is pleased to announce the addition of **Kiona Graham** to the team. She is a Clinical Research Coordinator at McLaren Bay Region. Kiona previously served as a Sergeant for the Genesee County Sherriff's department, as well as working as a licensed paramedic. In addition, she is currently attending Delta College pursuing a degree in nursing. Kiona aspires to continue work with MCRI as a Clinical Research Nurse once she completes her education. With 14 years of public service, Kiona proves to be a motivated professional and consented her first research participant after 1 month on the team. We look forward to watching her grow in her research role.

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