RESEARCH Matters

Winter 2024

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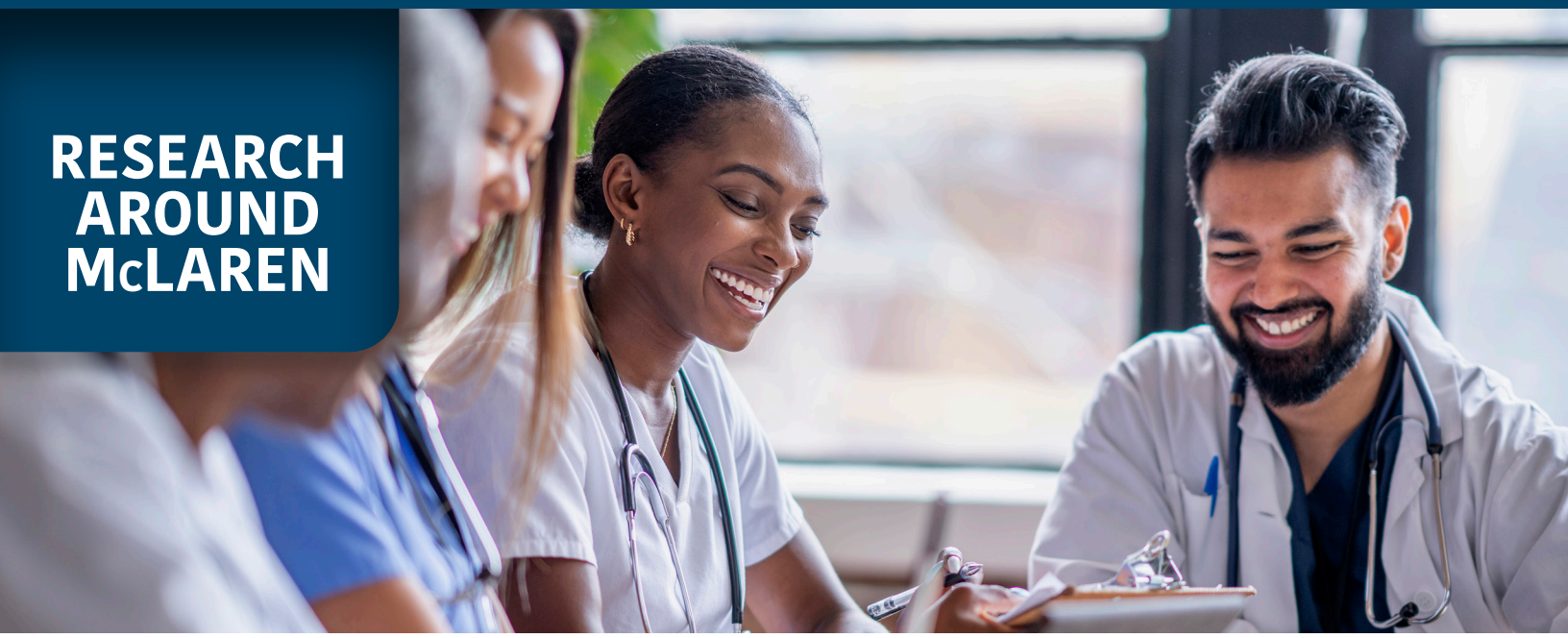
Association for the Accreditation of Human Research Protection Programs, Inc.
Full Accreditation

McLaren

RESEARCH AROUND McLAREN



CLINICAL RESEARCH NAVIGATOR

The McLaren Center for Research and Innovation (MCRI) is pleased to announce the addition of a Clinical Research Navigator to our team. The creation of this role was prompted by the increasing interest across the McLaren system from non-oncology investigators in conducting their research. From projects that do not involve human subjects, to chart reviews, to full-blown multi-site clinical trials, the Clinical Research Navigator will be the first point of contact for those investigators interested in pursuing any non-industry sponsored research and help guide the investigator through the life of the study.

MCRI's vision for this new role is to have a single person assigned to work with an investigator from start to finish, guiding them through the research process and connecting them with relevant resources and colleagues to make their project successful at McLaren. This process will start with an initial consultation to identify what the investigator's idea or project consists of and to develop and execute an action plan. Using a "concierge-style" service, the clinical research navigator will work with the investigator to identify the tools, resources and services needed to make their idea come to fruition. The navigator will be available to the investigators from start to finish, guiding them through each step of the research process.

The idea of initiating a study from conception can seem even more daunting and challenging, and most have no idea where to begin. This new role provides investigators with that starting point and a guide to take them through the complexities of the research process.

"What we were finding was the whole research process was overwhelming for those that had not participated in writing their own research before," Chandan Gupte, VP of Clinical Excellence and Research, reports. "The concept of the clinical research navigator is to identify one person who can help navigate the entire process of investigator-initiated research at McLaren."

As any investigator on a sponsored clinical trial knows, there are numerous extra responsibilities and requirements that add to an already busy workload. The idea of initiating a study from conception can seem even more daunting and challenging, and most have no idea where to begin. This new role provides investigators with that starting point and a guide to take them through the complexities of the research process.

"When looking at the steps required to develop and implement a clinical research study, it can seem burdensome. The clinical research navigator will break down the steps and assist with each, thereby making the process much simpler for our investigators," states Pam Wills-Mertz, Director of Corporate Research Administration.

A "start to finish" approach can look different for each project, but may consist of things like: guidance on FDA regulations, protocol development support, funding procurement, drug or device procurement, project feasibility and scientific review, grant and contract management, investigator education and training, consent and source document development, IRB submission, recruitment and enrollment support, and promotion of institutional policies and best practices.

As we begin to develop this position and support service, we look forward to connecting with investigators and working together to forge new pathways for the conduct of research at McLaren. If you are a non-oncology investigator with a potential project you'd like to discuss, please email **MCRI@mclaren.org** with "IIT" in the subject line, and we will be in touch to start your action plan. Please note, this service is not applicable to Graduate Medical Education researchers, if you would like to conduct GME-related projects, please reach out to your GME leaders.

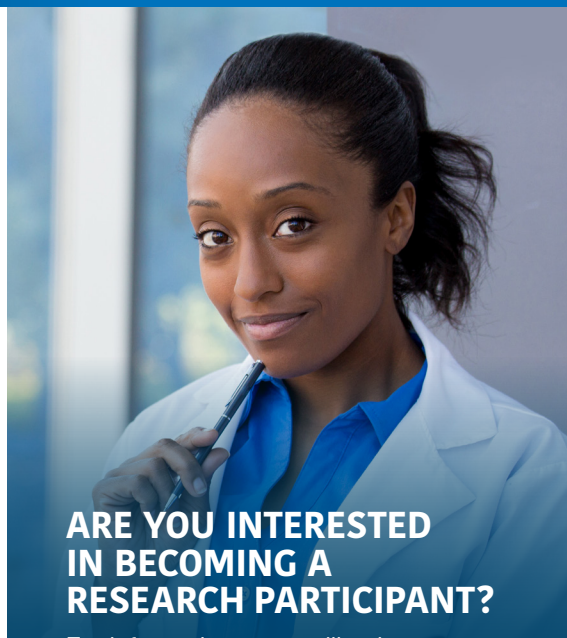
"When looking at the steps required to develop and implement a clinical research study, it can seem burdensome. The clinical research navigator will break down the steps and assist with each, thereby making the process much simpler for our investigators."

– Pam Wills-Mertz
Director of Corporate Research Administration

MEET THE NAVIGATOR

Jocelyn Contesti, MSA

Jocelyn Contesti, MSA, comes to McLaren Center for Research and Innovation with 10 years of clinical trials experience, holding advanced roles in research coordination and administration in a private ophthalmology practice. Jocelyn received her bachelor's degree in counseling psychology from Rochester College and her master's degree in health service administration from Central Michigan University. "I enjoy being a part of the research community and using my skills to contribute to the exciting medical advances that clinical trials can offer," she explains. Jocelyn's new role as Clinical Research Navigator with MCRI will provide support for investigators who wish to conduct their own non-industry sponsored research. We are currently working to develop Jocelyn's toolbox for this exciting new program, and collecting resources she can use to provide this support to our investigators. MCRI is excited to bring Jocelyn into this new role and see what the future holds for investigator-initiated research at McLaren!



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

INVESTIGATOR INITIATED TRIALS

Also referred to as an Investigator Initiated Study (IIS), Investigator Initiated Trials (IITs) are clinical research trials in which the Principal Investigator conceives of the research question, develops the study protocol and serves as the "sponsor-investigator." The FDA defines a "sponsor-investigator" as an investigator who both initiates and conducts an investigation, and under whose immediate direction the investigational drug or device is administered or dispensed. In such trials, the sponsor-investigator assumes the responsibilities of, and must comply with, FDA regulations applicable to both a sponsor and an investigator. The sponsor-investigator takes on the responsibility of initiating the clinical trial and acting as the coordinating center, and often times takes on a dual role of an investigator conducting the trial as well.

In many aspects, IITs are the same as an industry sponsored trial and need to follow the same pathways for study feasibility, start-up and regulatory approvals as a sponsored clinical trial. As a sponsor, an IIT investigator's responsibilities include:

All investigators taking part in a sponsored clinical trial or considering an IIT should ensure their knowledge of ethical and scientific standards as well as human subject protection is up to date and documented. Getting started with the basic training requirements is an essential first step.

- Selection and training of qualified investigators
- Obtaining executed FDA Form 1572 and financial disclosures from each PI
- Assuring the protection and safety of human subjects at all study locations
- Providing the investigators and their study staff with information to conduct the study properly
- Monitoring the progress of the investigation
- Controlling and documenting disposition of the investigational agent

An investigator invited to participate in an IIT, or planning on conducting their own IIT, has the same responsibilities as they would conducting a sponsored clinical trial. Those responsibilities include:

- Ensuring the investigation is conducted according to the investigational plan (protocol)
- Maintaining case histories on each patient
- Providing reports to various vested entities including regulatory entities like the FDA or IRB and the sponsor or funding agency
- Submitting progress reports, safety reports, final reports, and other regulatory documents like financial disclosures and FDA Form 1572
- Protecting the rights and safety of subjects under the investigator's care
- Obtaining and properly documenting informed consent from each patient
- Assuring review by a responsible IRB and complying with its requirements
- Permit FDA inspections of the study records and site

A common question amongst investigators interested in conducting their own IIT is what regulations apply and which rules need to be followed? This is dictated by the funding agency as well as the products employed in the trial. For FDA-regulated products, drugs (FDA 21 CFR 312) or devices (FDA 21 CFR 812) the Code of Federal Regulations (CFR) apply and dictate the conduct of the study. If another federal agency funds the research, Health and Human Services rules may apply (FDA 45 CFR 46). If a study is federally funded by an agency other than HHS, but involves an FDA-regulated product, both sets of rules may apply. There are many FDA guidance documents and HHS guidance documents available online for review prior to initiating an IIT, so an investigator can be aware of what rules might apply given the particular drug or device they wish to study.

Some protocols may require the sponsor-investigator to submit an Investigational New Drug (IND) or Investigational Device Exemption (IDE) application to the FDA. Criteria for this requirement are outlined in the FDA regulations at 21 CFR 312.2(b) or 21 CFR 812. If a sponsor-investigator is unsure what applies to their particular protocol, they should seek counsel from the FDA to be sure they are following all applicable rules and regulations, as well as submitting the proper applications, if required.

All investigators taking part in a sponsored clinical trial or considering an IIT should ensure their knowledge of ethical and scientific standards as well as human subject protection is up to date and documented. Getting started with the basic training requirements is an essential first step. Biomedical Research Training, Conflict of Interest training and Good Clinical Practice training are all made available to McLaren investigators and research staff at **www.citiprogram.org**. You will need to affiliate with McLaren Health Care to access the required courses. To participate in clinical trials or initiate an IIT, these training courses are an institutional requirement.

If you want to increase your knowledge base and take your research education to the next level, consider becoming a member of one of the accredited Clinical Research Associations, SOCRA (Society of Clinical Research Associates) or ACRP (Association of Clinical Research Professionals). Both associations have a wealth of educational opportunities, articles, webinars and courses available to members and non-members. For those who want to certify their knowledge, ACRP offers a Certified Principal Investigator exam to earn the "CPI" credentials. Experienced investigators may also wish to consider attending or speaking at one of the national conferences held yearly by ACRP or SOCRA.

As an investigator at McLaren, if you wish to discuss your ideas for an IIT or becoming an investigator on a clinical trial, your first step is to contact the administrative offices of the McLaren Center for Research and Innovation. The MCRI administrative team can meet with you to discuss the resources available to you for protocol writing assistance or statistical analysis, how to create a budget and apply for funding for your project, data collection tools, coordinator and regulatory support options, and work with you to create a project plan and timeline for initiation of your trial. MCRI can also be your resource for listing your trial on **www.ClinicalTrials.gov**, a federal requirement for qualifying clinical trials.

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INVESTIGATOR RESOURCES

McLaren Research Administration and Research Integrity
www.mclaren.org/main/research

CITI Training, Biomedical, GCP
www.citiprogram.org

SOCRA
www.socra.org

ACRP
www.acrp.org

Health and Human Services
www.hhs.gov/programs/research

FDA Guidance for Industry: Investigator Responsibilities
www.fda.gov/media/77765/download

FDA Guidance for Sponsor-Investigators
www.fda.gov/media/92604/download

GCP Regulations
www.fda.gov/science-research/clinical-trials-and-human-subject-protection/regulations-good-clinical-practice-and-clinical-trials

Code of Federal Regulations
www.ecfr.gov/current/title-21

- 21 CFR 312 – Investigational New Drug Application
- 21 CFR 812 – Investigational Device Exemptions
- 45 CFR 46 – Protection of Human Subjects

Clinical Trials.gov
www.clinicaltrials.gov

RESEARCH AROUND McLAREN

INVESTIGATOR INITIATED TRIALS

CONTINUED FROM PAGE 5

Investigator initiated trials are important to medical science because they drive translational research, taking data and applying it to day-to-day, real world practices. IITs demonstrate the commitment of a health care institution to growth and learning, as well as the dedication of a physician to their patients by initiating change in standard practices and innovation in treatment options. They are an important piece of any institution's research portfolio and McLaren strives to support their investigators in such endeavors. Developing and conducting an IIT as a sponsor-investigator is a significant investment of your time and a great deal of effort, but well worth the outcome for you and your patients.

For more information or to start a discussion about your research interests, please contact the administrative offices of MCRI at **MCRI@mclaren.org** or (248) 484-4960.

RESEARCH FUNDING AVAILABLE

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. These funds are to be used for conducting research studies and will be awarded on a quarterly basis.

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/investigators.

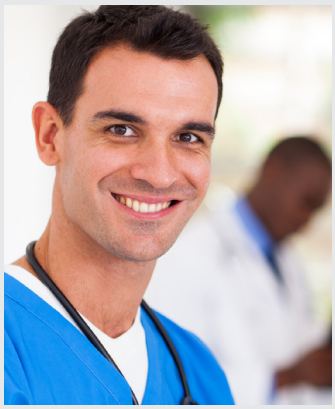
Due dates for application submissions are January 1st, April 1st, July 1st, and October 1st of each year.

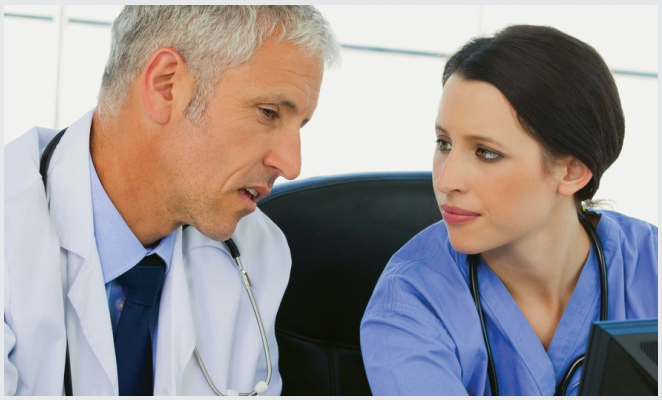
Required information for the application includes a detailed description of the research project, as well as a proposed budget. Incomplete applications will be returned to the applicant. Please email **MCRI@mclaren.org** with any questions.

Application link:
www.mclaren.org/FundingApplication

** Excluded from this funding program:*

- Travel
- Computer Equipment
- Conference Fees
- Indirect Costs





LED BY KARMANOS RESEARCHERS

STUDY REPORTS PROGRESS IN LONG-TERM PROTECTION AGAINST OVARIAN CANCER TUMORS

Gil Mor, MD, PhD

Ayesha Alvero, MD

Karmanos investigators who are part of the Wayne State University C.S. Mott Center for Human Growth and Development, reported in Cancer Immunology Research the characterization of a novel therapeutic approach capable of restoring immune surveillance and providing long-term protection against ovarian cancer tumors.

The study, "Immune modulation of innate and adaptive responses restores immune surveillance and establishes anti-tumor immunological memory," used an immune modulatory platform called CARG-2020 in collaboration with CaroGen Corp. CARG-2020, an onco-immunomodulatory vesicle, is capable of inducing in situ vaccination and activation of both arms of the immune system, leading to the development of a long-term antitumoral immune memory capable of preventing recurrence in animal models of ovarian cancer.

The team of investigators led by Gil Mor, MD, PhD, Tumor Biology and Microenvironment (TBM) Research Program member at Karmanos and scientific director of the C.S Mott Center, and Ayesha Alvero, MD, MS, Molecular Therapeutics (MT) Research Program member, director of the Ovarian Cancer Program at the C.S. Mott Center, characterized the efficacy of CARG-2020s.

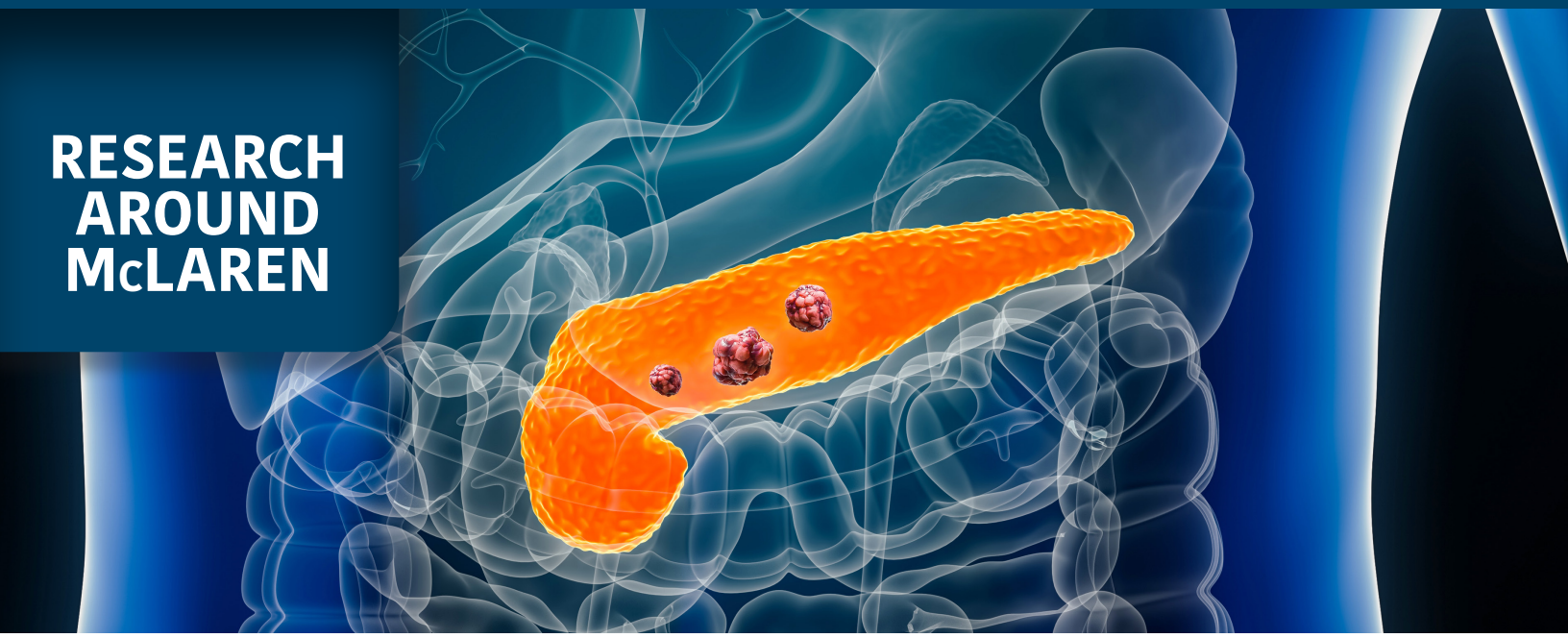
"The ability of CARG-2020 to modulate the two arms of the immune system and to restore immune surveillance provides a unique protection that eliminates the existing tumor, prevents tumor recurrence and provides 100% survival benefit over a long period. These findings make CARG-2020 a promising candidate for further development for human cancer immunotherapy," Dr. Mor said.

CaroGen is finalizing a protocol to advance CARG-2020 into Phase 1 clinical trials for ovarian cancer patients. This novel approach may prove more effective than existing immunotherapies, which had limited results in patients with ovarian cancer.

"More than 13,000 women die of ovarian cancer in the United States each year, and CARG-2020 could be a breakthrough immunotherapy in helping them to live longer," Dr. Alvero said. "CARG-2020 preclinical results are impressive and could potentially help to prolong and save lives in patients with ovarian cancer."

A phase 1 clinical trial is being prepared in collaboration with investigators from the University of South Florida and CaroGen Corp. *(Originally published at Today@Wayne.)*

RESEARCH AROUND McLAREN



KARMANOS SCIENTISTS DISCOVER TREATMENT COMBINATION

AVOIDS KRAS^{G12C} INHIBITOR DRUG RESISTANCE

Husain Yar Khan, PhD

Scientists at Karmanos have found a combination to continue treating patients who have developed drug resistance to KRAS^{G12C} inhibitors. "Anticancer efficacy of KRAS^{G12C} inhibitors is potentiated by PAK4 inhibitor KPT9274 in preclinical models of KRAS^{G12C}-mutant pancreatic and lung cancers" was published in Molecular Cancer Therapeutics in December 2023. For more than 30 years, the KRAS mutation often found in many cancers, especially pancreatic ductal adenocarcinoma (PDAC) and non-small lung cancers (NSCLC), was labeled as undruggable. A few years back, scientists developed a molecule that can bind the KRAS^{G12C} protein to stop cancer cells from dividing. And now, Karmanos scientists are addressing the issue of cancer cells becoming resistant to KRAS^{G12C} inhibitors as a monotherapy, a common problem with most cancer drugs used over time.

Husain Yar Khan, PhD, research scientist at Karmanos, under the supervision of Asfar Azmi, PhD, leader of the Molecular Therapeutics Research Program, director of pancreatic cancer research, and associate professor of oncology at Wayne State University (WSU) School of Medicine, began focusing on resistance mechanisms in patients who receive a KRAS^{G12C} inhibitor, such as sotorasib and adagrasib, as their only line of treatment. The team specifically studied the role of the protein p21 activated kinase 4 (PAK4), a hub molecule that links several major signaling pathways in KRAS cancers. The results in KRAS^{G12C} inhibitor resistant cellular models indicated that PAK4 can bypass KRAS inhibition, thereby promoting tumor growth making KRAS targeted therapy ineffective. When they blocked PAK4 using a drug KPT-9274, there was sufficient and continuous inhibition of KRAS leading to reduced tumor growth.

"We found that both NSCLC and PDAC tumor cells were responding to the addition of KPT-9274 with the KRAS^{G12C} inhibitors," said Dr. Khan. "The combination effectively suppressed the KRAS pathway and resulted in antitumor effects."

Asfar Azmi, PhD

The study results suggest the combination therapy for patients who have developed resistance to single-agent KRAS^{G12C} inhibitor treatment.

"This is a huge step toward the treatment of patients who may not respond or have developed a resistance to KRAS^{G12C} targeted monotherapy. We're also looking further into novel combinations to address resistance to KRAS^{G12D} inhibitors," Dr. Azmi adds.

Co-authors of this study included Karmanos and WSU School of Medicine research program members Md. Hafiz Uddin, PhD; Najeeb Al Hallak, MD, MS; Eliza Beal, MD; Miguel Tobon, MD; Rafic Beydoun, MD; Steve Kim, MD, FACS; Ramzi Mohammad, PhD; and Anthony Shields, MD, PhD.

STAGE IV LUNG CANCER SURVIVOR, DISPARITIES CANCER RESEARCHER, AND FAMILY PHYSICIAN

APPOINTED AS KARMANOS' NEW ASSOCIATE CENTER DIRECTOR

Dr. Morhaf Al Achkar joins Team Karmanos as the associate center director for Education

The Barbara Ann Karmanos Cancer Institute welcomed Morhaf Al Achkar, MD, PhD, MSCR, FAAFP, as the new associate center director for Education in September. Dr. Al Achkar brings over 10 years of experience in education and teaching, research, and clinical family care. One of his investigational focuses is disparities in cancer research. He also brings valuable personal experience to his new role as a seven-year stage IV lung cancer survivor.

Morhaf Al Achkar, MD

"It has been a pleasure and an exciting transition moving from Seattle to Detroit to join the team here at Karmanos," said Dr. Al Achkar. "I have begun building relationships and connecting with colleagues and community members. My responsibilities at Karmanos center around advancing education and training initiatives for the cancer center community. Additionally, I am deeply passionate about enhancing the cancer care experience for our patients and addressing health disparities."

Dr. Al Achkar refuses to be defined or stopped by his incurable condition. He was diagnosed in 2016 following episodes of shortness of breath. His tests revealed the anaplastic lymphoma kinase (ALK) rearrangement, or ALK fusion, a genetic alteration linked to lung cancer. Advances in treatment have enabled him to live with lung cancer as a chronic condition.

His diagnosis also significantly shaped his research, driving him to investigate cancer patients' experiences and needs. He delved into patient-provider communication, aiming to improve access to second opinions and specialist oncologists, and disparities in lung cancer diagnoses. His latest study delves into the systemic issues and access challenges that contribute to the later-mentioned issue. Dr. Al Achkar is dedicated to examining how discrimination and racism affect experiences, collaborating with BIPOC (Black, Indigenous, and other people of color) communities, especially African American, Arabic-speaking Middle Eastern, and North African communities. He recently co-authored "Factors leading to disparity in lung cancer diagnosis among black/African American

CONTINUED ON PAGE 17

"The addition of Dr. Al Achkar furthers our research and expands research training and education."

– Boris Pasche, MD

RESEARCH AROUND McLAREN

REVOLUTIONIZING CANCER TREATMENT

ADVANCED RADIOPHARMACEUTICALS SUCCESSFULLY TARGETING PROSTATE CANCER AND NEUROENDOCRINE TUMORS

Radiopharmaceutical therapy (RPT) is a revolutionary treatment that targets metastasized tumors at the cellular level, reducing radiation exposure to normal, healthy tissue and reducing significant side effects – a possibility that occurs with conventional external radiation therapies.

Nitin Vaishampayan, MD

"RPT uses radioisotope therapy in the process of delivering the radiation intravenously to cancer cells by adding radioactive material, or radionuclides, to proteins that bind with the receptors on the cancer cells, destroying those cells," explained Nitin Vaishampayan, MD, radiation oncologist, physician lead for radiopharmaceuticals at Karmanos Cancer Institute, and member of the Gastrointestinal and Neuroendocrine Oncology and Genitourinary Oncology Multidisciplinary Teams, among others.

Medical and radiation oncologists often see RPT as an option for patients who have failed previous lines of treatment, such as androgen deprivation therapy for prostate cancer, and lanereotide and octreotide used to treat neuroendocrine cancer. RPT is non-invasive and does not require daily visits; patients receive infusions at a small number of appointments spread out over months. RPT is also painless, and most patients tolerate the treatment well. However, before this therapy is suggested, clinicians must investigate whether the compound can find the patient's tumor cells.

"Each patient recommended for this treatment must undergo pre-imaging with a PET scan," said Dr. Vaishampayan. "During this initial part of the process, we use an imaging version of the compound. We must see on the PET scan that the imaging compound is expressed on the surface of the cancer cells to move forward with radiopharmaceutical therapy. This ensures that the radioisotope is delivered accurately to the target cells with less uptake by normal tissues. If the PET scan does not show avidity for the target molecules, then we have other treatment options that we can recommend."

Karmanos has been a pioneer in Michigan, using radiopharmaceuticals since 2017, with over 650 infusions completed to date. The latest FDA-approved radiopharmaceuticals are available to Karmanos patients, including Lutathera™ (177Lu-DOTA0-Tyr3-octreotate), used to treat neuroendocrine tumors that have spread throughout the body. The targeted agent is given to patients as an intravenous line (IV) treatment. Lutathera™ targets the somatostatin receptors found within neuroendocrine cancers.

"Patients who are getting Lutathera™ receive four- or five-hour treatments every two months – a total of four infusions," said Dr. Vaishampayan.

FDA-approved metastatic prostate cancer treatments, Pluvicto™ (177Lu vipivotide tetraxetan) and Xofigo® (radium Ra 223 dichloride), are also available at Karmanos. Dr. Vaishampayan was a co-investigator in the nationwide VISION phase 3 clinical trials that used the PSMA-targeted radioligand 177Lu-PSMA-617 for patients with prostate-specific membrane antigen (PSMA)-positive metastatic castration-resistant prostate cancer (mCRPC). The study was published in *The New England Journal of Medicine* in 2021 and led to the FDA approval of Pluvicto™.

"When treating with Pluvicto™, patients receive outpatient treatment every six weeks for a maximum of six infusions. Appointment times are usually less than one hour," Dr. Vaishampayan explained.

Xofigo® is an FDA-approved treatment for bone metastatic prostate cancer that is no longer responding to androgen deprivation therapy. This treatment is given with an intravenous injection once every four weeks for a total of six injections. Xofigo® is also being investigated at Karmanos in a current clinical phase II trial of radium-223 dichloride in combination with paclitaxel in patients with bone metastatic breast cancer.

"Randomized studies have shown a modest survival advantage for the use of Xofigo®, Pluvicto™, and Lutathera™ for patients who meet the treatment criteria," added Dr. Vaishampayan. "We're excited that these new lines of treatment at Karmanos have been well tolerated, and we look forward to the additional tumor sites we are investigating to expand this treatment to more patients."

Along with Dr. Vaishampayan, radiation oncologists Steven Miller, MD, and Michael Dominello, DO, treat patients with Lutathera™, Pluvicto™ and Xofigo®. Faheem Ahmad, MD (Maumee, Ohio), Arthur Frazier, MD, FACRO (Mount Clemens), Hesham Gayar, MD (Flint), and Isaac Kaufman, MD (Petoskey), provide Xofigo® treatments for patients within the Karmanos Cancer Network.

RPT is non-invasive and does not require daily visits; patients receive infusions at a small number of appointments spread out over months. RPT is also painless, and most patients tolerate the treatment well.

CONGRATULATIONS!

Congratulations to Dr. Srinivas Chakravarthi for his recent publication in the book *Principles of Neuro-Oncology Brain & Skull Base*. His published chapter is titled "360° Surgical Management of the Orbit and Its Exo-orbital Projections." Dr. Chakravarthi is a neurosurgeon at McLaren Bay Region.

Srinivas Chakravarthi, MD

RESEARCH AROUND McLAREN

KARMANOS CANCER INSTITUTE FIRST TO RECEIVE NEW FDA-APPROVED TREATMENT FOR ADVANCED LIVER CANCER

Innovative treatment uses radio frequency to target and reduce cancerous tumors

Karmanos Cancer Institute announced in November that it will be the first provider in the country to offer patients the new FDA-approved TheraBionic P1 device for the treatment of advanced hepatocellular carcinoma (HCC), the most common type of liver cancer. HCC accounts for approximately 90% of all liver cancers, with average survival rates between 6 and 20 months. The innovative TheraBionic P1 device is a novel at-home treatment that emits low levels of radio-frequency electromagnetic fields that block the growth of tumor cells without affecting healthy tissue. The device is approved for treating patients 18 years of age or older who fail first- and second-line therapies.

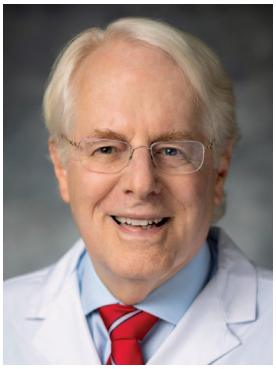
"Advanced hepatocellular carcinoma is an incurable cancer, so the FDA's approval of this non-invasive treatment option is transformative as physicians across the country will now have access to this revolutionary treatment that has proven to prolong the life of those battling the disease."

– Boris Pasche, MD

Boris Pasche, MD

"Twenty years ago, I hypothesized that radio frequencies might block tumor growth and hoped one day it could make a meaningful difference and become the future of cancer treatment, so it's incredibly rewarding to see the TheraBionic P1 device finally come to market starting with Karmanos," said Boris Pasche, MD, PhD, FACP, president and CEO of the Barbara Ann Karmanos Cancer Institute, CEO of TheraBionic, Inc. and co-inventor of the TheraBionic P1 device. "Advanced hepatocellular carcinoma is an incurable cancer, so the FDA's approval of this non-invasive treatment option is transformative as physicians across the country will now have access to this revolutionary treatment that has proven to prolong the life of those battling the disease."

TheraBionic P1 is a hand-held device that produces low levels of 27.12 MHz radiofrequency electromagnetic fields, which are amplitude-modulated at tumor-specific frequencies. The device, which is fully portable for in-home use, is coupled with a spoon-shaped antenna placed on the patient's tongue during treatment administered in three one-hour sessions per day, delivering low levels of radiofrequency electromagnetic



Anthony Shields, MD

fields throughout the patient's body. The radiofrequency levels delivered during treatment are lower than those generated by cellular phones when held close to the body.

Watch Dr. Pasche describe the benefits of the TheraBionic P1 device and how to use it here, **https://youtu.be/35EEz0GZQAA**.

"Often, patients with advanced hepatocellular carcinoma who fail first- and second-line therapies have severely impaired liver function, so additional treatment options are limited or nonexistent. We are very pleased that the TheraBionic P1 device will provide our patients with an effective alternative treatment option," said Anthony Shields, MD, PhD, medical oncologist and leader of the Gastrointestinal and Neuroendocrine Multidisciplinary Team at Karmanos. "We're excited to be the first cancer hospital in the United States to offer this innovative therapy that is safe, well tolerated, and has the clinical benefit of reducing tumor growth."

"The TheraBionic P1 device has a proven response rate that is comparable to the best treatment options available for advanced hepatocellular carcinoma, so it is immensely gratifying to provide patients access to this easy-to-use, at-home solution that can critically impact their quality of life," said Dr. Pasche.

No serious adverse events have been reported with the use of the TheraBionic P1 device, even after more than six years of continuous use. Physicians treating patients who meet the criteria of TheraBionic P1 device can prescribe treatment, and TheraBionic will ship the device to the practice.

Multiple clinical trials are underway studying the TheraBionic P1 device's impact on various other cancers such as breast, brain, ovarian, gallbladder, pancreatic and prostate.

TheraBionic P1 is a hand-held device that produces low levels of 27.12 MHz radiofrequency electromagnetic fields, which are amplitude-modulated at tumor-specific frequencies.

The radiofrequency levels delivered during treatment are lower than those generated by cellular phones when held close to the body.

EQuIP CORNER

DIVERSITY, EQUITY, AND INCLUSION IN CLINICAL TRIALS MATTERS

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

Research Population

Participants in clinical trials should represent the patients affected by a particular disease, condition, or behavior. Ideally, the research population should include a diverse group of people. This is often not the case as marginalized racial and ethnic minorities, women, and other historically disenfranchised populations are often underrepresented in clinical trials. This should be of great concern to researchers and health care providers.

Susmita Jain, MS

Why does diversity in clinical trial matter?

Promoting diversity and inclusion falls within ethical human actions involving research with human subjects as outlined in the Belmont Report, specifically the ethical principle of justice. Injustice may appear in the selection of subjects, even if individual subjects are selected fairly by investigators and treated fairly in the course of research. Per the Belmont Report injustice arises from social, racial, sexual and cultural biases institutionalized in society. Thus, even if individual researchers are treating their research subjects fairly, and even if IRBs are taking care to assure that subjects are selected fairly within a particular institution, unjust social patterns may nevertheless appear in the overall distribution of the burdens and benefits of research. Although individual institutions or investigators may not be able to resolve a problem that is pervasive in their social setting, they can consider distributive justice in selecting research subjects.

Enrolling participants with a wide range of baseline characteristics creates a study population that more accurately reflects the patients likely to use the medical product if approved. People of different ages, races, and ethnicities may react differently to certain medical products. Underrepresentation of patient populations in clinical trials undermines health equity for patients around the world; introduces lower efficacy rates and unacceptable safety risks that new therapies entering the market may cause in different patient cohorts; and can leave billions of dollars of investment hanging in the balance.

A recent example of including diversity in clinical trials is during the COVID-19 clinical trials, researchers have engaged diverse populations in planning and implementing the trial to reflect the disproportionate impact of the pandemic. It also helped in building public trust and confidence in the vaccine product.

What can we do to recruit a more diverse population?

Organizations need to create a framework that consists of commitment, partnerships, accountability, and resources to encourage diversity, equity, and inclusion (DEI) in clinical trials. Below are a few promising

practices for researchers to adopt when engaging in new clinical trials to encourage the diversity, equity, and inclusion.

Getting Commitment from Senior Leadership – Leadership commitment is the key to the success of clinical trial diversity initiatives, particularly the dedication of senior-level leaders as they hold the decision-making power and drive the organization's mission. It can be a matter of allocating resources, investing in staffing, providing staff education and training on DEI in research, creating infrastructure, policy development, and encouraging community or patient initiatives.

Development of Diversity, Equity, and Inclusion (DEI)-based study design and goal setting – One of the challenges that can limit diversity in clinical trials includes the use of narrow eligibility criteria. A review of eligibility criteria should ensure that under-studied populations are not unnecessarily excluded and that criteria are only as restrictive as necessary for safety and to minimize harm. Some eligibility criteria have become commonly accepted and used across trials over time, excluding certain populations from trials without clinical or scientific justification. The trial may then underrepresent certain groups in the study and make the results less applicable to groups that may benefit the most from the findings.

One of the ways to overcome this challenge is to evaluate eligibility criteria specific to the benefits and risks of each trial and to ensure that there is strong clinical or scientific justification for excluding populations from a trial. For example, when laboratory values serve as the basis for eligibility criteria, they should be adapted to reflect known sex-, age- or race-specific normal values when failure to do so would unnecessarily decrease the eligibility of some individuals.

Another area of development is the research data tool. Researchers should use or develop appropriate data collection tools to ensure the inclusion and representation of participants across different socioeconomic statuses in clinical trials. Some potential participants will not have access to computers or Internet for self-assessment tools.

Improve Community Engagement – Incorporating tailored innovative techniques to expand outreach can diversify participants enrolled in the study. Research teams can partner with patients and their families, advocacy groups, and community representatives to be effective in informing recruitment and retention strategies as well as in providing input on study questions and participant-relevant endpoints, study conduct, and culturally and linguistically appropriate communications. Also consider fostering community engagement through medical societies, focus groups, community advisory boards, disease registries, and community-based participatory research.

Improve patient participation and retention – Research participants often have busy schedules. Researchers should consider challenges due to planned visit schedules and accessibility to the clinical trial sites. Some examples are: considering the use of electronic informed consent,

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DIVERSITY, EQUITY, AND INCLUSION IN CLINICAL TRIALS MATTERS

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reducing the frequency of visits, adding flexibility in visit windows, offering childcare services, offering transportation, providing the option of telemedicine, and providing alternative study sites available that are closer to where participants live.

Another option is decentralizing study procedures and adopting innovative technology for more flexible data collection, and self-surveillance to identify and prevent biases.

The financial impact of clinical trials on participants is a challenge for those who may have to travel to distant clinical trial sites. Sponsors may offer financial reimbursements for expenses incurred by participants in clinical trials, such as for travel and lodging.

It is essential to provide trial resources and documents in multiple languages. This can be achieved by hiring multilingual research staff and/or interpreters to encourage the participation and retention of individuals with limited English comprehension. If it is anticipated that participants will be recruited that are not English-speakers, IRB approval of documents and consent forms in the native language must be sought.

Finally, the use of digital health technologies, and real-world data collection tools could promote more efficient recruitment of a diverse population. Online and social media recruitment strategies may also be used to identify participants for whom a traditional referral center is not accessible.

Identify practices that suppress recruitment – Researchers should identify common practices like using overly subjective criteria "investigator discretion" that limit enrollment of immigrant or minority communities and introduce bias in participant selection.

As a part of the oversight and continuing monitoring of ongoing clinical trials, the researcher should periodically review the demographic breakdown of the accrued participants by age, race, ethnicity, sex, and social determinants of health where applicable to the research. There should be further strategies and approaches in study design if the researcher finds any diversion from the recruitment plan.

What are the available regulation guidelines?

Numerous efforts to increase the diversity of trial participants have been implemented in the United States. The US Food and Drug Administration (FDA) and the National Institutes of Health (NIH) have issued several policies and guidance that encourage diversity and inclusion in clinical trials.

- https://www.fda.gov/regulatory-information/search-fda-guidance-documents/diversity-plans-improve-enrollment-participants-underrepresented-racial-and-ethnic-populations
- https://www.fda.gov/regulatory-information/search-fda-guidance-documents/enhancing-diversity-clinical-trial-populations-eligibility-criteria-enrollment-practices-and-trial
- https://www.fda.gov/regulatory-information/search-fda-guidance-documents/collection-race-and-ethnicity-data-clinical-trials
- https://www.fda.gov/media/89307/download?attachment
- NIH guidelines on Inclusion of Women and Minorities as Participants in Research Involving Human Subjects https://grants.nih.gov/policy/inclusion/women-and-minorities.htm

Conclusion

It is well known that people may experience the same disease differently. Clinical trials must include people with a variety of lived experiences and living conditions, as well as demographic characteristics so that all communities can benefit from scientific advances. Being inclusive and making the products of research available, accessible, and affordable to volunteers and their loved ones can promote trust and support for research in communities. Although some progress has been made to improve clinical trial diversity, more work is needed.

KARMANOS' NEW ASSOCIATE CENTER DIRECTOR

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communities in the USA: A qualitative study," which was published in *BMJ Open*.

As the associate center director for Education at Karmanos, Dr. Al Achkar oversees the Office of Cancer Research Training and Education Coordination (CRTEC), and is responsible for establishing a vision for the cancer center's education efforts. He also leads professional development across the training continuum from high school students to tenured faculty and health care professionals, throughout the Karmanos catchment area (46 Michigan counties) and beyond. Moreover, he oversees the integration of education and training into the scientific research programs, assesses a broad range of active training programs, catalogs cancer education activities through the Wayne State University (WSU) School of Medicine, and advocates for and initiates new research training and development opportunities to enrich the educational environment for the cancer center community.

"The addition of Dr. Al Achkar furthers our research and expands research training and education," said Boris Pasche, MD, PhD, FACP, president and CEO of Karmanos. "His broad experience in research, teaching, and practice provides a wonderful base for Dr. Al Achkar to build and develop our scientific research initiatives."

Dr. Al Achkar joins Karmanos following a six-year tenure at the University of Washington in Seattle. During his time there, he served as an associate professor in the Department of Family Medicine, an adjunct associate professor in the Department of Health Services School of Public Health, and a core faculty member at the AIMS Center within the Department of Psychiatry. Additionally, Dr. Al Achkar has spent five years as an attending family medicine physician and assistant professor at Indiana University.

Dr. Al Achkar has authored close to 50 peer-reviewed publications, covering a wide array of topics, including medical education, curriculum design, community engagement, integration of mental health in primary care, care for people experiencing homelessness, the cancer care continuum, and faculty development, among others. He has secured several grants, including a notable grant from ALK Positive, a lung cancer community foundation, for a three-year survey project. He also participated in initiatives funded by organizations such as the CDC, Premera Foundation and CanTest UK.

In 2018, Dr. Al Achkar received the Pearls Award from the North America Practice Care Research Network for a research study that will impact clinical practice.

"His broad experience in research, teaching, and practice provides a wonderful base for Dr. Al Achkar to build and develop our scientific research initiatives."

– Boris Pasche, MD

He has also received the Family Medicine Residency Program's Faculty of the Year Award at Indiana University and multiple recognitions from the Society of Teachers of Family Medicine.

A Syrian immigrant, Dr. Al Achkar completed his medical degree at Aleppo University in Syria. He completed his residency training at Florida Hospital in Orlando and Winter Park, Florida, where he also served as a chief resident. Dr. Al Achkar holds a Master of Science in Clinical Research from Indiana University-Purdue University Indianapolis and a Doctorate of Philosophy in Inquiry Methodology and Education from Indiana University in Bloomington. His extensive teaching experience includes leading training in evidence-based medicine and research methodology coursework, focusing on qualitive research. He's also board-certified with the American Board of Family Medicine and is involved with the North America Practice Care Research Network, the Society of Teachers of Family Medicine, and the American Academy of Family Physicians.

FACULTY, FELLOWS & RESIDENTS

SCHOLARLY ACTIVITY NEWS

McLAREN SCHOLARLY ACTIVITY GRADUATION REQUIREMENTS: REVISED

By Carlos F. Rios-Bedoya, ScD, MPH

In December of 2023, McLaren Graduate Medical Education approved a revision to the McLaren Health Care Corporation Policy Manual Article II Section 2.04-2.06.

The revision clarifies and specifies promotion and graduation requirements for all residency training programs. The scholarly activity requirements of the residency training programs were revised for two important purposes. First, it standardizes and specifies the minimum scholarly activity graduation requirements across the system for ALL residency training programs. Second, it raises the bar for McLaren residents on what should be completed to meet scholarly activity graduation requirements.

McLaren HEALTH CARE		**Policy Title: Promotion and Graduation** **Subject: Graduate Medical Education** **Scope:**	
Effective Date	9/27/2019	**Policy Number**	GME 105
Review Date		**Department**	Graduate Medical Education
Revised Date	12/15/2023	**Oversight Level**	Corporate
Supersedes: MHCC Policy Manual Article II Section 2.04 -2.06			
Administrative Responsibility	Chief Academic Officer		

As the Sponsor institution of the residency programs, McLaren can establish graduation requirements above and beyond the minimum criteria recommended by the American College for Graduate Medical Education (ACGME). Also, if ACGME requirements are greater than the McLaren requirements, the ACGME requirements should be followed.

Carlos F. Rios-Bedoya, ScD

GME Policy 105 states that McLaren graduation requirements, among others, include completion of at least one (1) research or quality improvement project (additional or specific projects may be required per ACGME and/or the specialty specific board):

- a quality improvement project requires at least one PDSA cycle to be completed
- residents in one year training programs may complete at least one (1) case report in lieu of the research or quality improvement project unless otherwise required by the ACGME or the specialty specific board

We wanted to use this space as another way to disseminate this important revision to graduation requirements. Residents with questions, concerns, or who need further clarification please contact your Program Director as soon as possible. Those residents who currently might not meet these revised graduation requirements, please contact the PhD assigned to your program as soon as possible to determine the best approach to comply with these requirements. The Division of Scholarly Inquiry is committed to supporting and facilitating scholarly activity for McLaren residents, fellows, and faculty. For additional information contact Dr. Carlos F. Ríos-Bedoya at **carlos.rios@mclaren.org**.

UPCOMING RESEARCH EDUCATION

MHC Research Integrity Brown Bag Session
Mindful Approach to Stress
March 5, 2024
12:00 pm - 1:00 pm

Speaker:
Barbara Wolf, PhD
Corporate Director, Behavioral Health Education and Physician Well-Being McLaren Health Care
Associate Professor, Family Medicine and Psychiatry Departments – Michigan State University Colleges of Human and Osteopathic Medicine

To register, contact:
susmita.jain@mclaren.org

ACRP
ACRP 2024 is Where Clinical Researchers go for Inspiration, Education and Connection
Anaheim Marriott
May 3 - 6, 2024

To register follow the link:
https://2024.acrpnet.org/

OHRP
Curating Connection Objectives: Research Community Forum with University of Miami
April 10 - 11, 2024
Coral Gables, FL

To register follow the link:
https://web.cvent.com/event/bfa81286-5b7f-45ec-8cb8-d8d83f9f0878/summary?i=VyFfJei_i0SVPkpBqjg9Lw&locale=en-US

SOCRA
Clinical Research Monitoring and GCP Virtual Workshop for Monitors, Site Coordinators and Auditors
February 13 - 16, 2024
11:00 am to 3:00 pm ET

To register follow the link:
https://www.socra.org/conferences-and-education/live-webinars/clinical-research-monitoring-and-gcp-virtual-workshop/register/

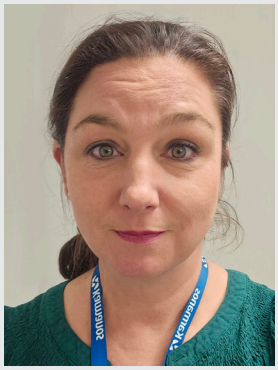
FDA Clinical Trial Requirements, Regulations, Compliance and GCP Conference
March 20 and 21, 2024
Anaheim, CA

To register follow the link:
https://www.socra.org/conferences-and-education/training-conferences-workshops-courses/fda-clinical-trial-requirements-regulations-compliance-and-gcp-conference/register/

ANNOUNCEMENTS AND WHAT'S NEW

Jocelyn Contesti

We are pleased to announce **Jocelyn Contesti**, Clinical Research Navigator has joined the McLaren Center for Research and Innovation on January 8, 2024. She has 10 years of clinical research administration experience and has joined MCRI to support Investigator Initiated Research. Jocelyn received her Bachelor's Degree in Counseling Psychology from Rochester College and her Master's Degree in Health Service Administration from Central Michigan University.



Billie Jo (BJ) Hardesty

We are pleased to announce **Billie Jo (BJ) Hardesty**, Clinical Research Coordinator II has joined the Karmanos Cancer Institute Clinical Trials Office on December 4, 2023. BJ has more than 20 years of clinical research experience and is providing clinical research support at Karmanos Cancer Institute at McLaren Greater Lansing. BJ has a Bachelor of Science in Anthropology/Zoology with a Minor in Biology/ Medicine Prerequisites from University of Michigan and a Master of Science in Health Sciences and Clinical Research Administration from George Washington University.

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