Physician HealthCare Network

MPR DEVELOPMENT GROUP
ONE WORLD, ONE TEAM: A MISSION FOR A CURE

Detroit Clinical Research Center

**Issue 1 Spring 2014**

# Physician HealthCare Network Partners With Detroit Clinical Research Center for Research

Physician HealthCare Network is proud to announce our partnership with MPR Development Group, a full service Michigan-based Clinical Research and Development Organization, and Detroit Clinical Research Center (DCRC), a health research institution that supports clinical research studies across hospitals and medical facilities in Southeast and Mid Michigan.

MPR has been serving the health and bio-pharmaceutical industries for more than thirty years to efficiently bring new therapies to people who need them by consolidating therapeutic, operational, and scientific capabilities of organizations and individuals. DCRC was founded to meet important needs in research by addressing major and critical operational bottlenecks in the conduct of clinical trials, as well as providing process and resourcing solutions.

The Detroit Clinical Research Center will serve as the medium to promote our involvement in clinical research studies. Several studies have already been launched (see pages 3-4 for details), and many more will be opening soon. We encourage the involvement of our physicians in these studies, which will deliver the latest medical advancements and treatment options to St. Clair County and residents of the surrounding areas.

NATIONAL® CANCER INSTITUTE

*One of the many benefits of this partnership is the opportunity to join DCRC's NCI Consortium. For this effort, PHCN is lead by Dr. Michael Basha & Karen Basha.* ***See page 2 for details.***

# PHCN JOINS DUKE UNIVERSITY'S PEDIATRIC TRIALS NETWORK VIA DCRC

Through our partnership with the Detroit Clinical Research Center, Physician HealthCare Network has joined Duke University's Pediatric Trials Network (PTN), sponsored by the Eunice Kennedy Shriver National Institute of Child Health and Development; This has offered several excellent opportunities for PHCN, DCRC, and health care as a whole. Upcoming studies that are sponsored by the PTN are featured on page 6.

Dr. Nandamudi is currently leading a Prospective Study of the Pharmacokinetics of Understudied Drugs Administered to Children Per Standard of Care. For this study, drugs of interest include but are not limited to the following: Clindamycin, Doxycycline, Griseofulvin, HCTZ, Ketamine, Methadone, Metoclopramide, SMZ-TMP, Hydroxycycobalamin, Epinephrine, Amiodarone, Simvastatin, Pravastatin, Furosemide, Ondasterone, Clonidine, Fentanyl, Granisetron.

If you have patients whom are being prescribed any of the above listed drugs, or if you would like to pursue a research project proposal, please contact Kimberly Rooker (see contact info on page 8).

## Working Research Committee



## Inside this issue:

# National Cancer Institute Consortium

This project assists the National Cancer Institute's Community Oncology Research Program to accomplish its goal of accruing a larger minority patient population. It also aims to address and reduce the cancer care disparities that minorities in Michigan face. It intends to promote cancer research within groups historically underrepresented in research, specifically in racial and ethnic minorities. The program will participate in a broad range of research, e.g.: clinical trials focused on prevention, control and treatment of cancer, as well as research focused on cancer care delivery.

> ***"It aims to address and reduce the cancer care disparities that minorities in Michigan face."***

The project plans to set up a Minority Based Community Consortium in Michigan to support the NCI Cancer Oncology Research Program. The component sites of this Consortium are two community hospitals, two large medical groups, one research organization, one lead Native American Health Care and Community center, and one medical practice. There has been an established working relationship between component sites for years, which supports clinical trials; therefore, this Consortium is a natural move.

The Consortium will be lead by multiple principle investigators and/or project directors, all with minority or special ethnic group backgrounds, including two women. The component sites serve large and diverse minority populations covering almost all sectors, although the African American population is largest in cities such as Detroit, Flint, and Lansing. Michigan has one of the largest, most diverse minority populations in the nation, and this Consortium proves to benefit the NCI's goal to expand cancer research to these minority groups.

The project is planned for five years, renewable each year, with the first year's efforts divided into 90% clinical trial support and 10% cancer care delivery research. The funding will be used mainly for incremental efforts to support NCI clinical studies, and limited funds will be spent on fixed costs or infrastructure costs because the consortium components sites have already established the infrastructure for clinical trials and research, namely facilities, equipment, processes, and training. As such, the NCI grant will be an efficient and productive investment to produce results.

The Consortium plans to expand the current two affiliations with NCI Research Bases to additional ones in an effort to expand its ability to bring a larger number of studies to minority patients. The Consortium will cover these three major population areas: East Michigan, Metro-Detroit, and Mid Michigan; Thereby covering over 60% of Michigan's population with over 70% of Michigan's minority population. Throughout the following years (years two through five), the plan is to expand to Southeastern, Western, and Upper Michigan to serve an even larger minority patient population.

The latest financial crisis has had a strong impact on Michigan and its minority population; This program will have a significant and positive role on reducing disparities in the access to leading cancer clinical trials.

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## Consortium Partners

Physician HealthCare Network, Mid-Michigan Physicians, Mid-Michigan Physicians Hematology Oncology, American Indian Health and Family Services, Botsford Hospital Cancer Center, Clinical Oncology Associates, Christyne Lawson, M.D., P.C., Memorial Healthcare Cancer Center, Bingham Farms Dermatology, Cancer and Leukemia Group B (CALGB), NRG Oncology

# CURRENT STUDIES

## Ulcerative Colitis

**Sponsored by: HUMIRA®**

**Study Title:** A Long-Term Non-Interventional Registry to Assess Safety and Effectiveness of HUMIRA® (Adalimumab) in Patients with Moderately to Severely Active Ulcerative Colitis (UC)

**Principle Investigator:** Bassam Nasr, M.D.

**Inclusion:** Must be 18+ y/o male or female with moderately to severely active UC and has received HUMIRA® for at least six weeks OR an IMM therapy (6-mercaptopurine, azathioprine) for at least twelve weeks

**Exclusion:** Patients should not be enrolled into the IMM treatment group if they require ongoing treatment with approved biologic agents including HUMIRA® (adalimumab) or any investigational agents or if they are being treated with any investigational agents.

## COPD/Pulmonary Hypertension

**Sponsored by: IKARIA**

**Study Title:** A Placebo-Controlled, Double-Blind, Parallel, Randomized, Two-Part Clinical Dose-Confirming Study of Pulsed, Inhaled Nitric Oxide (iNO) in Subjects With World Health Organization (WHO) Group 3 Pulmonary Hypertension (PH) Associated With Chronic Obstructive Pulmonary (COPD) on Long-Term Oxygen Therapy (LTOT)

**Principle Investigator:** Michael Basha, D.O.

**Inclusion:** Subjects, male or female, ages ≥ 40 years, ≤ 80 years, with a confirmed diagnosis of COPD who are receiving LTOT and have PH (defined echocardiographically by a measured TRV ≥ 2.9 m/s)

**Exclusion:** Positive urine cotinine test; currently using, or having used within the past month, a nicotine patch; experienced an exacerbation requiring the start of or increase in systemic oral corticosteroid therapy and/or hospitalization during the last month

PTN
Pediatric Trials Network
Leading the Way

## Understudied Drugs in Pediatrics

**Sponsored by: Pediatric Trials Network (PTN) of Duke University & National Institute of Child Health and Development (NICHD)**

**Study Title:** Pharmacokinetics of Understudied Drugs Administered to Children Per Standard of Care

**Principle Investigator:** Dev Nandamudi, M.D.

**Inclusion:** Male or female children (< 21 years of age) who are receiving understudied drugs of interest per standard of care as prescribed by their treating caregiver

**Exclusion:** Failure to obtain consent/assent (as indicated); known pregnancy as determined via interview or testing if available.

# CURRENT STUDIES CONTINUED;

## Asthma, controlled

**Sponsored by: AstraZeneca**

**Study Title:** A 26 week, randomized, double-blind, parallel-group, active controlled, multicenter, multi-national safety study evaluating the risk of serious asthma-related events during treatment with Symbicort®, a fixed combination of inhaled corticosteroid (ICS) (budesonide) and a long acting β2-agonist (LABA) (formoterol) as compared to treatment with ICS (budesonide) alone in adult and adolescent (≥12 years of age) patients with asthma

**Principle Investigator:** Michael Basha, D.O.

**Sub- Investigator:** Dev Nandamudi, M.D.

**Inclusion:** Male or female ≥12 y/o; clinical diagnosis of asthma for at least one year with history of at least one asthma exacerbation

**Exclusion:** Life-threatening asthma; systemic corticosteroid treatment within last four weeks; unstable asthma status; COPD diagnosis; requires or has required use of any oral or ophthalmic β-blocker during the last month

## Asthma, uncontrolled

**Sponsored by: AstraZeneca**

**Study Title:** A Multicentre, Randomized, Double-blind, Parallel Group, Placebo-controlled, Phase III Efficacy and Safety Study of Benralizumab (MEDI-563) Added to High-dose Inhaled Corticosteroid Plus Long-acting β2 Agonist in Patients with Uncontrolled Asthma (SIROCCO)

**Principle Investigator:** Michael Basha, D.O.

**Inclusion:** Male or female, ages 18-75 inclusively; history of asthma requiring treatment with medium-to-high dose ICS; minimum two exacerbations within last year that required use of a systemic corticosteroid

**Exclusion:** History of anaphylaxis to any biologic therapy; history of alcohol or drug abuse within 12 months prior to the date informed consent is obtained; current smokers or former smokers with a smoking history of > 10 pack-years; current use of any oral or ophthalmic β-adrenergic antagonist

# UPCOMING STUDIES— GASTROENTEROLOGY

A Phase 3 Randomized, Double Blind, Placebo-controlled, Multicenter, Parallel Group Study to Assess the Efficacy and Safety of Fixed-dose Combination RHB-104 in Subjects With Moderately to Severely Active Crohn's Disease

A Phase 1 Double-blind, Randomized, Placebo-Controlled, Single and Multiple Dose Ranging Study Evaluating the Safety, Tolerability, Pharmacokinetics and Efficacy of GS-5745 in Subjects with Moderate to Severe Ulcerative Colitis

An Observational Study Evaluating Detection of Advanced Colorectal Neoplasia by Stool DNA in Inflammatory Bowel Disease: OCEANIA Study

A Phase 2, Randomized, Double-blind, Placebo-controlled Study to Evaluate the Safety and Efficacy of RM-131 Administered to Patients With Diabetic Gastroparesis

# UPCOMING STUDIES– ONCOLOGY

Open-label, uncontrolled Phase II trial of intravenous PI3K inhibitor BAY 80-6946 in patients with relapsed, indolent or aggressive Non-Hodgkin's lymphomas

A Phase I, open-label, multiple ascending dose trial to investigate the safety, tolerability, pharmacokinetics, biological and clinical activity of MSB0010718C in subjects with metastatic or locally advanced solid tumors and expansion to selected indications

A multicenter, randomized, double-blind, placebo controlled phase III trial of tecemotide versus placebo in subjects with completed concurrent chemo-radiotherapy for unresectable stage III non-small cell lung cancer (NSCLC)

A Phase 3, Multicenter, Randomized, Open-label Study to Compare the Efficacy and Safety of Pomalidomide (POM), Bortezomib (BTZ) and Low-Dose Dexamethasone (LD-DEX) versus Bortezomib and Low-Dose Dexamethasone in Subjects with Relapsed or Refractory Multiple Myeloma (MM)

Connect MDS and AML: The Myelodysplastic Dyndromes (MDS) and Acute Myeloid Leukemia (AML) Disease Registry

A Randomized, Placebo Controlled , Multicenter Phase 2 Study of Etodolac and Propranolol in Patients with Clinically Progressive Prostate Cancer

A Phase III, Randomized, Double-Blind, Double-Dummy, Multicenter Trial Comparing the Efficacy and Safety of 2 Doses of Daily Oral ONO-4641 (0.05 mg and 0.1 mg) versus Interferon-β-1a 30 µg IM Weekly in Subjects with Relapsing-Remitting Multiple Sclerosis

# UPCOMING STUDIES– CARDIOLOGY

A Phase 2 Prospective Randomized Double Blind Placebo Controlled Trial of Intra-coronary Infusion of AMR-001, a Bone Marrow Derived Autologous CD34+ Selected Cell Product, in Patients With Acute Myocardial Infarction

A Phase 3 Randomized, Double Blind, Vehicle Controlled Study Investigating the Safety and Efficacy of HP802-247 in the Treatment of Venous Leg Ulcers >12 cm2 to ≤ 36 cm2

A Phase 4 Randomized, Double Blind, Assessment of Aspirin in Reducing Events in the Elderly

A Phase 3 Randomized, Open-Label, Study of Safety and Efficacy of AngelMed for Early Recognition and Treatment of STEMI

A Phase 2 A Randomized, Parallel, Placebo-controlled, Double-blind Study of Efficacy and Safety of Recombinant Human Neuregulin-1 (Neucardin) in Subjects With Stable Chronic Heart Failure

# UPCOMING STUDIES— NEUROLOGY

A Phase 3 Randomized, Double-Blind, Double-Dummy, Multicenter Trial Comparing the Efficacy and Safety of 2 Doses of Daily Oral ONO-4641 (0.05 mg and 0.1 mg) versus Interferon-β-1a 30 µg IM Weekly in Subjects with Relapsing Multiple Sclerosis

A Phase 3 Randomized, Double-Blind, Double-Dummy, Multicenter Trial Comparing the Efficacy and Safety of 2 Doses of Daily Oral ONO-4641 (0.05 mg and 0.1 mg) versus Interferon-β-1a 30 µg IM Weekly in Subjects with Relapsing-Remitting Multiple Sclerosis

A Phase 2 Multicenter, Randomized, Double-Blind, Placebo-Controlled, Parallel-Group Study to Evaluate the Efficacy, Safety, and Pharmacokinetics of SUN13837 Injection in Adult Subjects With Acute Spinal Cord Injury

A 12-month, Randomized, Rater- and Dose-blinded Study to Compare the Efficacy and Safety of Fingolimod 0.25 mg and 0.5 mg Administered Orally Once Daily With Glatiramer Acetate 20 mg Administered Subcutaneously Once Daily in Patients With Relapsing-Remitting Multiple Sclerosis

# UPCOMING STUDIES— PEDIATRICS

## THE PTN POST, ISSUE 7

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### The Effect of Obesity on the Pharmacokinetics of Pantoprazole in Children and Adolescents

The World Health Organization has called childhood obesity "one of the most serious public health challenges of the 21st century." The alarming childhood obesity epidemic brings with it increasing need for pediatricians to treat obesity-related diseases (e.g., type II diabetes mellitus, hypertension, hyperlipidemia, gastroesophageal reflux disease [GERD]) that traditionally have not had origins in childhood or adolescence. Given that obese participants are often excluded from clinical trials during the drug development process, little to no information exists regarding the impact of obesity on drug disposition and action or the appropriate dosing of drugs in obese pediatric patients.

Obese children are more frequently diagnosed with GERD than children of normal weight. Proton pump inhibitors, such as pantoprazole, have become key components in the pharmacologic management of GERD in pediatrics. In this multi-center, open-label, single-dose study of pantoprazole, the PTN will examine the pharmacokinetics of the drug in obese children who require treatment with an acid-modifying agent. The data collected in this study will be compared to existing pharmacokinetic data in non-obese subjects.

The study population will comprise obese male and female children and adolescents, ranging in age from 6–17 years (inclusive) with the diagnosis of GERD. Approximately 40 participants will be enrolled at up to 3 sites.

## Antibiotic Safety in Infants with Complicated Intra-abdominal Infections (SCAMP)

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Complicated intra-abdominal infections are common and often fatal in premature infants. These infections often occur as a result of necrotizing enterocolitis (NEC), the pathogenesis of which involves intestinal mucosal injury, usually associated with intestinal ischemia and bacterial overgrowth. NEC has a high overall mortality (15%) and, in extremely-low-birth-weight infants (≤1000 grams), mortality for surgical NEC is nearly 50%. Survivors often suffer from complications, including stricture formation, and life-long morbidities such as short bowel syndrome. Infants who have had NEC are also at increased risk of poor neurodevelopmental outcomes.

Recommended antibiotics for complicated intra-abdominal infections in infants include combinations of ampicillin, piperacillin-tazobactam, meropenem, metronidazole, clindamycin, or gentamicin. In spite of their frequent use, however, the safety and efficacy of these antibiotics in infants with complicated intra-abdominal infections have not been established.

The PTN is seeking to fill this information gap with SCAMP, a randomized, multicenter, open-label safety study of clindamycin, ampicillin, metronidazole, and piperacillin-tazobactam in infants with complicated intra-abdominal infections. The primary objective of this study is to determine the safety of these drug regimens in this specialized context; secondary objectives include determining the drugs' effectiveness, their pharmacokinetics in this unique population, biomarker association with disease severity and antibiotic exposure, and diversity or shift of intestinal microbiota. Approximately 350 infants will be enrolled at approximately 50 sites. Total length of study participation is 100 days, including 10 days of treatment and up to 90 days of follow-up assessments.

## Extremely-low-birth-weight Infants Exposed to Furosemide or Bumetanide in the Neonatal Intensive Care Unit

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The most common serious disease associated with premature birth is bronchopulmonary dysplasia (BPD). More than 60,000 infants are born ≤29 weeks gestational age each year in the United States, and nearly 40% of those develop BPD.

Premature infants with BPD are challenging to treat and frequently suffer from multiple morbidities such as pulmonary hypertension, prolonged hospitalization, and life-long neurodevelopmental problems. Because the consequences of BPD can be catastrophic, neonatologists frequently use diuretics such as furosemide and bumetanide to reduce pulmonary edema, improve pulmonary mechanics, minimize exposure to mechanical ventilation, and, ultimately, to prevent BPD.

The understanding of the safety profile of furosemide and bumetanide in premature infants, however, is limited. This is due, in part, to concerns about exposing premature infants to the risks of prospective drug studies. Fortunately, retrospective observational studies carry no risk for participants.

We will conduct an observational, retrospective study using medical records from approximately 700 extremely-low-birth-weight infants admitted to neonatal intensive care units. The data analyzed will provide valuable safety information for the use of these drugs in premature infants and will facilitate the design of future clinical trials.

# Pharmacokinetics of Multiple-dose Methadone in Children

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Critically ill children routinely receive opioids for analgesia and sedation with the goals of reducing pain and stress, facilitating ventilation, and avoiding secondary complications. Continuous infusions of opioids can induce tolerance, however, sometimes resulting in withdrawal symptoms if the drugs are discontinued abruptly. In fact, opioid withdrawal is a major problem in the pediatric intensive care unit, where it is estimated to occur in up to 57% of patients. Withdrawal symptoms are not only unpleasant but can be life-threatening and may prolong the need for hospitalization.

Fortunately, gradual opioid tapering is possible with drugs such as methadone, which can be substituted for narcotic infusions during the weaning process to prevent withdrawal symptoms. Methadone is an opiate commonly prescribed to hospitalized children, particularly in younger age groups. We know that methadone levels in the blood vary dramatically in adults, especially after oral administration. That is likely to be the case in children, but there are virtually no studies to guide dosing in children. The methadone product label currently states that safety and effectiveness in patients below the age of 18 years have not been established, and no dosing information is provided.

The primary objective of this prospective, multi-center, open-label, multiple-dose study is to determine the pharmacokinetics of enteral methadone in children treated for opiate withdrawal. The study population will include children aged >90 days to <18 years of age prescribed methadone per routine care. As many as 36 participants will be enrolled at up to 5 sites. Participation in the study will last up to 10 days (up to 5-day treatment period, up to 5-day observation period after study drug administration to monitor for adverse events and collect elimination samples).

## Find a current or upcoming study you would like to be a part of?

Contact:

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As always, we welcome your input about topics of interest for future studies. Please contact Kimberly Rooker with your suggestions.

## Your Other Research Contacts

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