SPOTLIGHT ON CLINICAL RESEARCH

Clinical Studies at LG Health

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This Spotlight on Research highlights the currently enrolling research studies being conducted by the LG Health Research Institute. To learn more about all research studies at Penn Medicine Lancaster General Health, visit iConnect by scanning the QR code at right.

ALZ-NET

Alzheimer's Association / "Alzheimer's Network for Treatment and Diagnostics (ALZ-NET)" registry: aims to collect data from individuals who are evaluated for, or receive treatment with, novel (or new) FDA-approved therapies for Alzheimer's disease (AD) — *Sponsor: Alzheimer's Association · Principal Investigator: Matthew Beelen, MD · Sub-Investigator: Connie Metzler, RN · Study Coordinators: Natalie Maston, Annmarie Blair, LouAnne Kruse*

The research team at LG Health is enrolling in the Alzheimer's Network for Treatment and Diagnostics (ALZ-NET) Registry sponsored by the Alzheimer's Association. This registry explores long-term safety, along with clinical use and outcomes for patients being evaluated for or treated with novel FDA-approved therapies for Alzheimer's disease. Enrollment in this registry has been highly successful due to the strong efforts of the investigators and study coordinators. Patients and their legally authorized representatives have expressed great interest in this registry as it will contribute to the advancement of treatments for Alzheimer's disease that may benefit their children, grandchildren, and all future generations.

BACKBEAT

BradycArdia paCemaker with AV interval modulation for Blood prEssure treAtmenT — *Sponsor: Orchestra Biomed · Principal Investigator: Jeffrey Arkles, MD · Sub-Investigators: Sandeep Bansal, MD; Matthew Bernabei, MD; R. Ward Pulliam, MD; Stacy Eshleman, CRNP; Laura Koonce, CRNP; Nicole Newman, CRNP; Jill Schaeffer, CRNP · Study Coordinators: Sarah Stuart, Andy Hershey*

This is a prospective, multinational, randomized, double-blind, clinical trial evaluating the safety and effectiveness of a novel atrioventricular interval modulation (AVIM) algorithm downloaded into a dual-chamber Medtronic Astra/Azure pacemaker. Patients scheduled to undergo implantation of a de novo Astra/Azure pacemaker system — and those who already have one implanted — may be screened for inclusion into this study if they also have uncontrolled hypertension. All eligible subjects will receive the AVIM RAMware and be randomized 1:1 to either have AVIM therapy turned On or turned Off. All subjects will continue to receive antihypertensive drug therapy.

The study team has experienced some challenges with enrollment due to the study's strict eligibility criteria. This makes it difficult to find patients who qualify for the study. The current blood pressure treatments used are effective and well managed, which also limits the number of eligible patients.

CARDIO-TTRansform OLE

An Open-Label Extension Study to Assess the Long-Term Safety of Eplontersen (ION-682884) in Patients with Transthyretin-Mediated Amyloid Cardiomyopathy (ATTR-CM) — *Sponsor: Ionis Pharmaceuticals · Principal Investigator: Tareck Nossuli, MD · Sub-Investigators: Arpan Patel, DO; Roy Small, MD; Amit Varma, MD; Michael Viray, MD · Study Coordinators: LouAnne Kruse, Kay Knepper*

Ionis Pharmaceuticals, in collaboration with Akcea Therapeutics, is sponsoring a multicenter, double-blind study, referred to as CARDIO-TTRansform, to evaluate the efficacy of AKCEA-TTR-LRx. This drug is a second-generation RNA-targeted therapy designed to inhibit TTR production. The study randomized participants to receive subcutaneous injections of either the study drug, AKCEA-TTR-LRx, or placebo. In early 2024, the study

sponsor invited sites to join the open-label extension (OLE) study, which is open to people who participated in the CARDIO-TTRansform study. The two participants enrolled in CARDIO-TTRansform at Lancaster General Hospital (LGH) were invited to join the OLE. Participation in the OLE begins after participants have completed their end-of-study visit for CARDIO-TTRansform and extends for up to 3.7 years. All participants in the OLE receive the study drug eplontersen and go through a screening period (up to 10 weeks), treatment period (up to 36 months after screening period), and post-treatment period (six months after end-of-treatment period).

DCM-DETECT

Dilated Cardiomyopathy Detection using AI and screening with mobile Technology — *Sponsor: Investigator-Initiated Study · Principal Investigator: Roy Small, MD · Sub-Investigators: Tareck Nossuli, MD; Arpan Patel, DO; Amit Varma, MD; Michael Viray, MD; Douglas Gohn, MD · Study Coordinators: Natalie Maston, Brianna Triplett*

The DCM-DETECT study utilizes an AI-enhanced mobile 6-lead EKG to detect undiagnosed dilated cardiomyopathies (DCM) in family members of patients with DCM. In this study, probands (the first family member identified with a non-ischemic DCM) will be recruited and asked to provide family medical history, complete a 6-Lead EKG using a mobile EKG device, contact their first-degree relatives (FDRs) to invite them to join the study, and complete a survey. FDRs who choose to participate will also complete the mobile 6-Lead EKG and survey. In addition, they will be encouraged to obtain a transthoracic echocardiogram (TTE) through their health care provider. The primary objective of the study is the uptake of screening TTEs in FDRs of patients with DCM compared to historical controls. The study is also recruiting at the Central Pennsylvania Clinic (CPC), which cares for Amish and Old Order Mennonite populations. At this site the added goal is to study the application of advanced technology in a rural, underserved population.

Enrollment at LG Health has been successful, with 28 probands enrolled. Of these, 10 have successfully recruited some or all their FDRs, resulting in a total of 11 FDRs enrolled at LG Health. At CPC, five probands have been enrolled, all of whom have successfully recruited their FDRs, contributing to a total of 20 FDRs enrolled, with still more expected to enroll. Due to the larger family sizes within the Amish and Old Order Mennonite populations seen there, the proband-to-FDR ratio at CPC is significantly higher than at LG Health.

EMPOWER

Assessment of the Carillon Mitral Contour System® in Treating Heart Failure with Functional Mitral Regurgitation — *Sponsor: Cardiac Dimensions · Principal Investigator: Rupal Dumasia, MD · Sub-Investigators: T. Raymond Foley, MD; Rahul Jhaveri, MD; Arpan Patel, DO · Study Coordinators: Andy Hershey, LouAnne Kruse*

The objective of this prospective, randomized, blinded clinical trial is to assess the safety and efficacy of the Carillon Mitral Contour System® in treating heart failure with functional regurgitation (FMR). Eligible patients must have symptomatic heart failure with functional mitral regurgitation; be NYHA class II, III, or IV; have left ventricular EF ≤50%; and meet the study's six-minute walk test requirements. Participants are randomized to either the study group and receive the study device or to the control group, whose members receive no device.

The study team follows the participants at set intervals until 24 months post-randomization, at which point everyone is unblinded. All participants will continue to be followed annually for three years after unblinding. The enrollments for this study had a slower start due to the effectiveness of current heart failure therapy. Enrollment is improving as practitioners recognize the potential benefits of this heart failure modifying treatment.

LeAAPS

Left Atrial Appendage Exclusion for Prophylactic Stroke Reduction Trial — *Sponsor: AtriCure · Principal Investigator: Jeremy McGarvey, MD · Sub-Investigators: Mark Epler, MD; Alexander Bridges, MD; Robert Wenger, MD · Study Coordinators: Lynsey Jones, Andy Hershey, Sarah Stuart, Molly Clifford*

The objective of this trial is to evaluate the effectiveness of left atrial appendage exclusion (LAAE) for the prevention of ischemic stroke or systemic arterial embolism in subjects undergoing cardiac surgery who have risk factors for atrial fibrillation (AF) and ischemic stroke. The AtriClip is FDA approved for use in patients with AF, but the use of it in patients without diagnosed AF is investigational. Participants can expect their participation to last for about five years from enrollment to study end.

Enrollment at LGH for this study continues to be successful. The study team exceeded its initial enrollment goal of 100 patients and has consistently ranked within the top 10 enrolling sites study-wide since study initiation.

Left vs. Left RCT

Cardiac Resynchronization Therapy Using His/Left Bundle Branch Pacing vs. Biventricular Pacing with a Left Ventricular Epicardial Lead in Patients with Heart Failure with Left Ventricular Ejection Fraction ≤50% and with either a Wide QRS Complex (>130 ms) or with/anticipated >40% Pacing Randomized Clinical Trial — *Sponsor: Baylor College of Medicine · Principal Investigator: Matthew Bernabei, MD · Sub-Investigators: Sandeep Bansal, MD; Jeffrey Arkles, MD; R. Ward Pulliam, MD · Study Coordinators: Andy Hershey, Sarah Stuart*

This trial compares the effects of His or left bundle branch pacing (LBBP) to biventricular pacing (BiVP) on quality of life, exercise capacity, hospitalization for heart failure, and mortality in patients with heart failure and conduction system disease. Patients are randomized 1:1 to one of two pacing therapy arms: His/LBBP or BiVP using any commercially available leads and devices.

The enrollment goal at our site was 34 participants. Challenges to enrollment center around LBBP being the preferred treatment option among most patients and physicians. As a result, many patients are hesitant to join the study since there is a chance they may be randomized to receive BiVP instead of LBBP. For many physicians, LBBP is seen as preferrable due to the lower cost, shorter procedure time, and perceived lower risks. However, enrollment efforts remain ongoing as this is the seminal randomized clinical trial comparing LBBP to traditional BiVP to determine which therapy is most effective.

Lp(a) EZEF – ACCLAIM

A Phase 3, Randomized, Double-Blind, Placebo-Controlled Study to Investigate the Effect of Lepodisiran on the Reduction of Major Adverse Cardiovascular Events in Adults with Elevated Lipoprotein(a) who have Established Atherosclerotic Cardiovascular Disease or Are at Risk for a First Cardiovascular Event — *Sponsor: Eli Lilly · Principal Investigator: Marjan Mujib, MD · Sub-Investigator: Joette Hughes, CRNP · Study Coordinator: Kay Knepper*

The purpose of this study is to evaluate the efficacy of lepodisiran, a small interfering RNA, in reducing cardiovascular risk in participants with high lipoprotein(a) who have cardiovascular disease or are at risk of a heart attack or stroke. Study participants are randomized to receive either the study drug or a placebo. Participation lasts about five years and includes a Screening Period, Study Treatment Period, and Final Visit. Although one study arm closed to enrollment shortly after our site was activated to begin the study, the study team has enrolled 12 of the 20 participants set as the enrollment goal. The success in enrollment can be attributed to the pre-existing relationships between the study investigators and the patient population.

PACeS

Anticoagulation for New-Onset Post-Operative Atrial Fibrillation (POAF) after CABG — *Sponsors: CT Surgical Trials Network Research Group; National Heart, Lung, and Blood Institute (NHLBI) · Principal Investigator: Mark Epler, MD · Sub-Investigators: Alexander Bridges, MD; Jeremy McGarvey, MD; Robert Wenger, MD · Study Coordinators: Lynsey Jones, Andy Hershey*

The primary objective of this prospective, open-label, randomized study is to evaluate the effectiveness (prevention of thromboembolic events) and safety (major bleeding) of adding oral anticoagulation (OAC) to background antiplatelet therapy in patients who develop new-onset POAF after isolated coronary artery bypass graft (CABG) surgery. This trial randomizes participants (1:1 ratio) to receive OAC (intervention arm) or no OAC (control arm). Eligible patients who choose not to participate may enroll in a parallel registry instead.

The study team successfully enrolled 14 participants into this study. They continue to screen, but many patients do not develop AF post-operatively at LGH. The study coordinators have a strong relationship with the Lancaster General Health Physicians Cardiothoracic Surgery team, from the physicians and advance practice providers to schedulers and administrative staff. The team is dedicated to the success of this study and will continue to screen for eligible patients while the study remains open.

PSR-APV

Product Surveillance Registry — *Sponsor: Medtronic · Principal Investigator: Meghan Dermody, MD · Sub-Investigator: John Affuso, MD · Study Coordinators: Brianna Triplett, Jordan Lapp*

The Product Surveillance Registry (PSR) collects data about the safety and effectiveness of Medtronic products on the market. The original registry has been active for many years, but there are multiple cohorts under the PSR umbrella. LG Health received approval to enroll participants in two of the cohorts: Aortic and Arteriovenous (AV) Access. The AV Access cohort of the study has been closed to enrollment by the sponsor. The study team at LG Health enrolled 37 participants into this cohort and was recognized as the top enrolling site in the Fall of 2023, prior to enrollment closure. The Aortic cohort remains open to enrollment.

REAL-AF Registry

Real-world Experience of Catheter Ablation for the Treatment of Symptomatic Paroxysmal and Persistent Atrial Fibrillation Using Novel Contact Force Technologies — *Sponsors: Biosense Webster; Heart Rhythm Clinical and Research Solutions, LLC (HRCRS) · Principal Investigator: Sandeep Bansal, MD · Sub-Investigators: Jeffrey Arkles, MD; Matthew Bernabei, MD; Stacy Eshleman, CRNP; Jill Martin, CRNP; Nicole Newman, CRNP; Jill Schaeffer, CRNP · Study Coordinators: Andy Hershey, Jordan Lapp*

This registry aims to collect real-world clinical experience of Paroxysmal (PAF) and Persistent (PsAF) Atrial Fibrillation ablation radiofrequency technologies. The study team collects data at pre-ablation, during the procedure, and at 10-12 weeks, six months, and one year post-ablation. Data from the registry will be used to assess the effectiveness and long-term safety of the technologies.

Enrollment at LG Health was very successful for the first two years. Any patient who was scheduled for a standard of care (SOC) pulmonary vein isolation (PVI) was screened for the registry. In September 2024, there was a change in SOC — radiofrequency PVI procedures were largely replaced with pulsed field ablations. The sponsor updated the registry protocol to include these procedures using their equipment, however the LG Health team had adopted equipment from an alternative device company. In June 2025, however, Biosense Webster equipment was approved for use at LG Health. The investigators will use this equipment and determine if they will continue using it or return to the equipment previously in use.

ROADSTER 3

Post-Approval Study of Transcarotid Artery Revascularization in Standard-Risk Patients with Significant Carotid Artery Disease and ROADSTER 3 Extended Follow-up Sub-Study — *Sponsor: Boston Scientific · Principal Investigator: Meghan Dermody, MD · Sub-Investigators: John Affuso, MD; Thomas O'Connor, MD; Todd Wood, MD · Study Coordinators: Kay Knepper, LouAnne Kruse*

This open-label, multicenter, single-arm, prospective post-approval study evaluates the ENROUTE Transcarotid Stent System when used with the ENROUTE Transcarotid Neuroprotection System. The study will explore the treatment of patients at standard risk for adverse events from carotid endarterectomy who require carotid revascularization and meet the study eligibility criteria.

The sponsor planned to enroll a maximum of 400 patients at up to 65 U.S. and EU sites. At LG Health, the study team enrolled eight participants, five of whom have consented to participate in the ROADSTER 3 Extended Follow-up Sub-Study, which extends long-term follow-up from one year post-procedure to five years post-procedure. The remaining three participants are anticipated to join the Follow-Up Sub-Study when they complete their participation in the main study. This extended follow-up period is expected to provide long-term outcomes for these participants who were treated with the ENROUTE Transcarotid Stent System and ENROUTE Transcarotid Neuroprotection System.

THRIVE

A Pivotal, Prospective, Multicenter, 2:1 Randomized, Double-Blind, Controlled Study Comparing the THerapeutIc IntraVasculaR Ultrasound (TIVUS™) REnal Denervation System vs. Sham for the Adjunctive Treatment of Hypertension — *Sponsor: SoniVie · Principal Investigator: Rupal Dumasia, MD · Sub-Investigators: Jian Shan, MD; Dean Campbell, MD; David Somerman, DO · Study Coordinators: Lynsey Jones, Sarah Stuart, Kay Knepper, LouAnne Kruse, Brianna Triplett*

The primary objective of the THRIVE Pivotal study is to demonstrate the adjunctive effectiveness and safety of the TIVUS™ renal denervation system in people with hypertension. THRIVE is a double-blind, sham-controlled study in which participants are randomized 2:1 to the treatment group using the TIVUS™ system or to the sham group. Patients who may be eligible will go through multiple eligibility visits to ensure they qualify for the study after signing the consent form. If they are still eligible after the screening period, they will be randomized. In order to maintain the double-blind, all patients will undergo a procedure. However, the sham procedure will be minimally invasive so participants are not put at increased risk.

All participants will stop taking any blood pressure medications during the screening period through two months post-procedure. After that, participants with uncontrolled hypertension will be put back on antihypertensive medication. Participants will be unblinded at the six-month study visit. At that time, any participants who are in the sham group who have uncontrolled blood pressure can cross over to have the renal denervation procedure performed.

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