TOP 10 CLINICAL RESEARCH ACHIEVEMENT AWARDS
PRESENTED BY CLINICAL RESEARCH FORUM
On behalf of the Board of Directors, we would like to thank everyone for submitting their achievements to the 2020 Top Ten Clinical Research Achievement Awards. These awards honor outstanding accomplishments in clinical research resulting from the nation’s investment in research to benefit the health and welfare of its citizens, and reflect the influential work conducted by investigators at research institutions and hospitals across the United States as well as at partner institutions from around the world. The level of scientific rigor, quality, and innovation of the nominations were truly outstanding. It was a very difficult decision-making process, but as a result, we can say with confidence that all of the finalists and the ten studies we are honoring are truly remarkable.

Due to the COVID-19 (coronavirus) pandemic, and the need to protect the health and safety of attendees, Clinical Research Forum is unable to host the Top Ten Awards program in person. The worldwide spread of COVID-19 demonstrates the importance and significance of the work of our member universities, clinical research scientist and doctors. We are proud to recognize your efforts and accomplishments in creating solutions that support improved health and life changing discoveries for people around the world.

Since 1996, we have put a spotlight on the importance of clinical and translational research, and have advocated for broader support from the federal government. We have also promoted “best practices” that have led to some of the most important treatment breakthroughs of our lifetimes. This is our focus, and we welcome your support with this mission.

To all of our Top Ten awardees and their colleagues in the field, doing this work every day, we salute you.

Sincerely,

Harry P. Selker, MD, MSPH
A041202: A Randomized Phase III Study of Bendamustine Plus Rituximab Versus Ibrutinib Plus Rituximab Versus Ibrutinib Alone in Untreated Older Patients (65 Years of Age) with Chronic Lymphocytic Leukemia (CLL)

**Summary:** Chronic Lymphocytic Leukemia (CLL) is the most prevalent adult leukemia, with the average age of diagnosis being 70. The A041202 Phase 3 study is one of the first trials to specifically target this older population, comparing standard chemotherapy (bendamustine plus rituximab) to two targeted treatment regimens (ibrutinib given alone or in combination with rituximab) for the initial treatment of patients age 65 or older with chronic lymphocytic leukemia (CLL).

This study was the first to compare a Bruton’s Tyrosine Kinase (BTK) inhibitor (ibrutinib) to standard of care chemoimmunotherapy for previously untreated CLL. BTK is a critical molecule regulating B cell receptor signaling, and its inhibition completely abrogates B cell receptor signaling in CLL, both in vivo and in patients. This drug has been phenomenally successful in this disease, both in terms of efficacy and safety. In this specific clinical trial, the two year progression-free survival with ibrutinib was 87 percent compared with 74 percent with chemoimmunotherapy. Significantly, even patients with very high genetic risk disease respond to ibrutinib, and in the highest-risk group of patients, those with a deletion of chromosome 17, which inhibits the TP53 tumor suppressor, two year progression-free survival was 75 percent, compared with 0 percent with chemoimmunotherapy.

The results of this study established ibrutinib as a standard of care for the initial treatment of older patients with CLL, and changed the paradigm of initial treatment away from chemotherapy and toward targeted therapy.


**Institutions:** The Ohio State University

**Funding:** The National Cancer Institute and Pharmacyclics

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Breakthrough Discovery and Development of Innovative Precision-Based Therapy in Complex Lymphatic Anomalies

**Summary:** Lymphatic vessels are part of the human body’s lymphatic system, which transports a clear fluid containing white blood cells called lymph around the body to help clear toxins and waste. Complex lymphatic anomalies, such as central conducting lymphatic anomaly (CCLA) are chronically debilitating and often life-threatening rare diseases that disrupt circulation of lymphatic fluid resulting in swelling of multiple organs. Unfortunately, for most patients, physicians can offer only palliative care (i.e., surgical and/or minimally invasive approaches) that requires multiple outpatient visits and hospital admissions for procedures that ameliorate symptoms but do not correct the underlying cause.

The study team performed whole-exome sequencing on DNA from a severe CCLA patient, a 12-year old boy, which identified a previously undiscovered mutation in the ARAF gene. The researchers then worked with zebrafish models to explore how the responsible gene mutation disrupted lymphatic channels and demonstrated that a MEK inhibitor, known to act on biological pathways affected by ARAF, rescued the structural defect in the zebrafish, causing them to develop normal lymphatic vessels. These results supported the patient’s medical team request to use a MEK inhibitor called trametinib (a chemotherapy drug) in the patient.

After three months of treatment, the patient showed significant improvements in his breathing and reduced fluid retention, and an MRI showed that his lymphatic vessels were remodeling themselves. This remodeling resulted in marked improvement of the patient’s pulmonary function tests, greatly reduced his reliance on supplemental oxygen, and enhanced his ability to return to near normal daily activities. The results are a clear example of how knowledge of a genetic mutation and its mechanisms can guide new opportunities for existing medical treatments, which in this case was life-saving.


**Institutions:** Perelman School of Medicine at the University of Pennsylvania

**Funding:** Research reported in this publication was supported in part by the Roberts Collaborative Functional Genomics Rapid Grant (to D.L.) from CHOP, Institutional Development Funds (to H.H.) from CHOP, CHOP’s Endowed Chair in Genomic Research (H.H) and donation from the Adele and Daniel Kubert family (to H.H. and CAG). The study was also funded in part through a sponsored research agreement from Aevi Genomic Medicine Inc., funding discovery and translation of rare and orphan disease genes at the CAG.
Canagliflozin and Renal Outcomes in Type 2 Diabetes and Nephropathy


**Summary:** The increasing prevalence of type 2 diabetes during recent decades is a driving factor behind the substantial global increase in end-stage kidney disease. Currently, more than 3 million people worldwide are estimated to be receiving treatment for kidney failure, with predictions that the number will increase to more than 5 million by 2035. Before this study, the only approved treatment for kidney protection in patients with type 2 diabetes was renin-angiotensin system blockade, which was first shown to be effective 18 years ago.

This landmark clinical trial involved 4,401 participants in 34 countries and showed that the approved drug, canagliflozin, lowered the risk of kidney failure by 30 percent in people with type 2 diabetes and kidney disease. In addition, the trial demonstrated that canagliflozin reduced the risk of major cardiovascular events such as death from heart causes, heart attacks and strokes, as well as hospitalization for heart failure. These results show that canagliflozin significantly reduces disability and death in patients with diabetes and kidney disease.

The FDA has already updated the label for canagliflozin to include that canagliflozin reduces kidney failure; cardiovascular death, heart attack or stroke; and hospitalization for heart failure. This will help inform clinicians caring for these patients. In addition, the American Diabetes Association, the American Heart Association with the American College of Cardiology, the European Society of Cardiology, and the European Association for the Study of Diabetes, all have issued practice guidelines or consensus documents that elevate the role of SGLT2 inhibitors in clinical care.


**Institutions:** Stanford University

**Funding:** Janssen Research and Development

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Development of CAR T-cell Therapy for Myeloma


**Summary:** Multiple myeloma is almost always an incurable cancer. While there are many treatment options available, and despite significant research efforts, in most cases the cancer will relapse and the multiple myeloma remains incurable. The discovery of novel chemotherapeutic agents such as bortezomib and lenalidomide have prolonged patient survival, but in nearly all cases relapse occurs.

This study focused on developing a new therapy for myeloma that uses the body’s own immune system to treat cancer. By reprogramming a patient’s immune cells to attack their myeloma cancer cells, patients with relapsed multiple myeloma were able to be treated.

Dr. Kochenderfer led the development of the novel Chimeric Antigen Receptor T-cell therapy bb2121 for the treatment of relapsed myeloma. In the phase I trial, it was demonstrated that 85 percent of myeloma patients treated with bb2121 had a clinical response lasting a median of almost 11 months. Importantly, complete responses were observed in patients who received larger numbers of CAR T cells and 40 percent of patients were free of progression one year after treatment. Dr. Kochenderfer demonstrated that bb2121 CART cells have a durable persistence, with CAR T cells being detectable in 57 percent of patients at six months and in 20 percent of patients at one year. Unlike other therapies for relapsing multiple myeloma, there was little evidence of minimal residual disease in bb2121-treated patients with at least a partial response. Finally, nonhematological toxic effects arising from bb2121 treatment were mostly grade two or lower. While still preliminary, bb2121 has shown tremendous promise for the treatment of relapsing multiple myeloma, and provides a new tool for doctors to use to treat myeloma patients with relapsing disease.


**Institutions:** Center for Cancer Research, National Cancer Institute

**Funding:** Bluebird Bio and Celgene
**Hematopoietic Stem Cell Transplantation for Frequently Relapsing Multiple Sclerosis**


**Summary:** Multiple sclerosis is a common and incurable chronic disease that currently affects approximately 1,575,000 women and 556,000 men in the United States alone. Current drug therapies are expensive and slow, and none of them reverse or stop the disease which takes a tremendous psychological and financial toll not only on patients but also on their families and friends.

Dr. Burt pioneered hematopoietic stem cell transplantation (HSCT) for multiple sclerosis (MS), becoming the first person to use it in pre-clinical models and the first in the US to treat MS patients with it. The goal of HSCT is to reboot a faulty immune system. Hematopoietic stem cells are taken from the patient’s blood, then the immune system is wiped clean with immune specific drugs. Next, stem cells are reintroduced to the body, where they facilitate an immune system recovery. During this process, in which there are no disease-causing immune cells or inflammation, the new immune cells reset to self-tolerance and no longer attack the body.

Dr. Burt’s randomized hematopoietic stem cell trial demonstrated that the disease can be reversed and that for more than five years after HSCT treatment, most patients show no evidence of new disease activity all at a relatively low cost compared to current MS drug regimens. In short, HSCT has changed the natural history of MS, making long-term, treatment-free remissions possible.

By analyzing patients’ immune cells before and after transplantation, researchers going forward might be able to identify MS biological markers, further subdivide different types of MS, and understand the critical pathways, cells, and cytokines that become aberrant when a patient develops the disease. HSCT might even help researchers identify the cause of MS, which, in turn, might lead to even more refined and targeted treatments.


**Institutions:** Northwestern University Feinberg School of Medicine

**Funding:** This study was made possible by financial support from the Danhakl family, the Cumming Foundation, the McNamara Purcell Foundation, Morgan Stanley, and the National Institute for Health Research Sheffield Clinical Research Facility. There was no industry support or pharmaceutical support for the study.

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**Large-Scale Assessment of a Smartwatch to Identify Atrial Fibrillation**


**Summary:** Atrial fibrillation is a condition of the heart characterized by an irregular and often very fast heartbeat. It is the most commonly recognized cause of stroke, and accounts for 130,000 deaths and 750,000 hospitalizations in the United States every year. Some people do not realize they have atrial fibrillation because they do not experience symptoms. Since wearable devices like smartwatches are becoming more widespread, this study set out to prove that technology can safely identify heart rate irregularities that subsequent testing confirmed to be atrial fibrillations.

This extraordinary study enrolled over 419,000 participants via a mobile app in only eight months, with a diverse population across 50 states. This is the first clinical study on this scale performed in a virtual manner. The test subjects were monitored with a smartwatch, linked to a virtual study doctor via their smartphone on demand, confirmed with a diagnosis via a patch ECG that was mailed, and received a follow-up through their smartphone.

Researchers found that only 0.5 percent of participants received irregular pulse notifications, an important finding given concerns about potential over-notification. Comparison between irregular pulse-detection on Apple Watch and simultaneous electrocardiography (ECG) patch recordings showed that if a participant had an irregular pulse detected on the watch 84 percent of the time, this was confirmed to be atrial fibrillation on a simultaneously worn ECG patch. One-third (34 percent) of the participants who received an initial irregular pulse notification and followed up by utilizing an ECG patch approximately two weeks later were found to have atrial fibrillation.

This study proves valuable information to clinicians with patients who present with an irregular pulse detected on a smartwatch. The researchers learned a tremendous amount about engagement, participation rates, interactions with the healthcare system, and follow up actions. More importantly, this study demonstrated the feasibility of conducting a large digital clinical trial with rapid recruitment at a relatively low cost per participant. This study, its results, and process, is a foundation on which future digital health studies can be designed.


**Institutions:** Stanford University School of Medicine

**Funding:** Apple
Prevention of Sudden Cardiac Death in High-Risk Patients with Hypertrophic Cardiomyopathy


**Summary**: Hypertrophic cardiomyopathy (HCM) is a relatively common genetic heart disease that causes the walls of the heart to abnormally thicken. HCM remains the most common cause of sudden death in young people. Implantable cardioverter defibrillators, or ICDs, are devices that can continually monitor the heart’s beating and respond to a dangerous arrhythmia by jolting the heart back to normal rhythm, essentially saving the life of the patient who otherwise would have likely suffered a sudden death event. Research supports the use of ICDs as a preventative strategy in high-risk HCM patients, but deciding which patients are the highest risk and therefore the most deserving of ICD therapy has been challenging.

This study introduces a highly sensitive risk model in a field that has lacked clear consensus on appropriate risk-assessment methods. Accurate and reliable discrimination of risk features is particularly important in light of the fact that ICD therapy is potentially life-long and not free of risk. Researchers followed more than 2,000 HCM patients treated over a 17-year period to test the risk assessment strategy. The results showed the strategy is highly effective for predicting which individuals really are at risk of sudden death. Almost all of those HCM patients who experienced a life-threatening arrhythmia after initial evaluation had been correctly identified and protected from sudden death with an ICD. Based on these results, the team created a risk assessment strategy with clear definitions and criteria that includes newer cardiac arrest risk markers. The strategy proved to be very effective and this likely saved the lives of 82 individuals who received an implanted defibrillator that responded to a serious ventricular arrhythmic event at least once during the study period.

This study provides strong evidence that will help make it easier for doctors to identify high-risk patients who are the most deserving of ICD therapy.

**Authors**: Maron MS, Rowin EJ, Wessler BS, Mooney PJ, Fatima A, Patel P, Koethe BC, Romashko M, Link MS, Maron BJ

**Institutions**: Tufts Medical Center

Skin-like Devices for Wireless Monitoring of Vital Signs in Neonatal Intensive Care


**Summary**: Each year in the United States, approximately 300,000 neonates are admitted to NICUs. Existing NICU monitoring systems require multiple electrode/sensor interfaces to the skin, with hard-wired connections to separately located base units that may be stand-alone or wall mounted, for heart rate, respiratory rate, temperature, blood oxygenation, and blood pressure. Although such technologies are essential to clinical care, the associated web of wires complicates even the most basic bedside tasks and impedes skin-to-skin contact. Up to 15 percent of a premature infant’s body surface is traumatized every single day by the adhesives that couple wired electrodes to their fragile skin, and 90 percent of patients who survive their time in the NICU will bear scars from their stay.

This study reports on the development and preliminary validation of a new NICU wireless monitoring technology that promises to replace traditional wire-based systems, allowing parents to cuddle their babies and giving healthcare personnel improved access to the infant. Dr. Rogers and his team demonstrated that the wireless system they developed—a single, skin-like sensor placed on an infant’s chest and one placed on its foot—dramatically improve medical outcomes for the most fragile patients. Dr. Rogers and his team’s sensors explicitly address the needs of the NICU because of their high mechanical compliance and noninvasive skin adhesive interface, their water resistance, and their compatibility with essential medical imaging and inspection. In addition to advanced monitoring capabilities, the sensors’ skin-like profiles and fully wireless operational modes promise to cause less harm to the delicate skin of very premature infants. Importantly, the low cost of these devices allows them to be quickly deployed to underserved sites worldwide, where improved monitoring has the capacity to dramatically improve outcomes.


**Institutions**: Northwestern University

**Funding**: Supported by Bill & Melinda Gates Foundation grants PP1182909 and OPP1193311; the Gerber Foundation; the Friends of Prentice Foundation; RIE2020 AME Programmatic Grant A18A1b0045 funded by A*STAR-SERC, Singapore; National Natural Science Foundation of China grants 11402134 and 11320101001; National Basic Research Program of China grant 2015CB351900; NSF grants 1534120 and 1635443; and Future Growth Engine Program grant 10079974 funded by the Ministry of Trade, Industry & Energy (MOTIE, South Korea).
Sustained Outcomes in Oral Immunotherapy for Peanut Allergy (POISED study): A Large, Randomized, Double-Blind, Placebo-Controlled, Phase 2 Study

Rebecca Sharon
Chinthrajah, MD


**Summary:** Food allergies affect an estimated 220 million people, including more than 9 million adults and 6 million children in the U.S. Allergy to peanut, which is often severe, is one of the most common food allergies in the United States. The management of food allergy currently focuses on avoidance of exposure to triggering foods, but oral immunotherapy (OIT) is an emerging treatment where patients gradually consume tiny doses of peanut protein until they build tolerance. Though it is not a permanent cure, by taking roughly the equivalent of one peanut every day, this oral therapy can change a patient’s and family’s quality of life.

This important clinical trial evaluated the sustained effects of peanut allergy oral immunotherapy in a randomized long-term study in adults and children. Participants in the trial ingested a dose of peanut protein each day, conditioning their immune systems to tolerate peanuts. The goal was to dampen the immune response so it would no longer be life-threatening. During a two-year study, 120 participants were randomly assigned to a no-peanut group, a 300 mg peanut-protein group, and a placebo group. The study showed that peanut oral immunotherapy can desensitize most individuals with peanut allergy to 4,000 mg of peanut protein, but discontinuation, or even a reduction to 300 mg daily, increases the likelihood of regaining clinical reactivity to peanut. Over the entire study, the most common adverse events were mild gastrointestinal symptoms, which were seen in 90 of 120 patients and skin disorders, which were seen in 50 of 120 patients. Adverse events decreased over time in all groups. Two participants in the peanut groups had serious adverse events.

This study may result in the first FDA-approved therapeutic for peanut allergy, paving the way for more food allergy treatment options and greater access. The published findings are laying the groundwork for a variety of allergy treatment options and greater access. The published findings are laying the groundwork for a variety of allergy treatment options and greater access.


**Institutions:** Sean N Parker Center for Allergy and Asthma Research, Stanford University School of Medicine

**Funding:** National Institute of Allergy and Infectious Diseases

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**Systolic Blood Pressure Intervention Trial (SPRINT) MIND Study**

Jeff Williamson, MD


**Summary:** More than 50 million people suffer from dementia worldwide, with 10 million new cases each year. Alzheimer’s Disease, the most common type of dementia, is the sixth leading cause of death in the US. Unfortunately, there are no proven interventions to prevent dementia or Mild Cognitive Impairment (MCI), an early stage of dementia. Hypertension is a strong risk factor for dementia and is one of the most common illnesses, with prevalence increasing with age and affecting 75 percent of persons older than 65. The current study was specifically designed to see if patients who were more intensely treated for high blood pressure with a goal of achieving a systolic blood pressure of 120 had a lower risk for developing dementia or MCI by 15 percent or more than patients receiving standard treatment with a goal of achieving a systolic blood pressure of 140.

The study found more intensely treated patients had a 19 percent lower risk of suffering MCI and a 15 percent lower risk of suffering either MCI or dementia. Patients who were more intensely treated also had a 17 percent lower risk of developing dementia alone, although this lower risk was not statistically significant. This is the first study to clearly identify an intervention, “intensive blood pressure control in patients with hypertension,” that can lower the risk of developing cognitive impairment.

The study’s seminal findings offer practitioners for the first time a treatment strategy for preventing or delaying the onset of cognitive decline. By more aggressively treating older adults with hypertension, practitioners can decrease patient’s risk of cognitive decline, in addition to their risk of cardiovascular events, which had been previously demonstrated by the SPRINT trial. The current study also provides compelling evidence to assure practitioners concerns about the potential adverse effects of intensive blood pressure treatment on cerebral perfusion. Lastly, the study has implications for the design of future studies by demonstrating the importance of clinical adjudication of cognitive endpoints and the longer longitudinal follow-up which may be needed to demonstrate impacts on cognitive decline, compared to follow-up periods needed for cardiovascular events.


**Institutions:** Wake Forest School of Medicine

**Funding:** SPRINT is funded with federal funds from the NIH, including the National Heart, Lung, and Blood Institute, the National Institute of Diabetes and Digestive and Kidney Diseases, the National Institute on Aging, and the National Institute of Neurological Disorders and Stroke
The Clinical Research Forum awards special honors to three studies that demonstrate excellence in clinical research and creativity and innovation in approach. We congratulate the 2020 awardees.

The Herbert Pardes Clinical Research Excellence Award

**John Rogers, PhD**, Skin-like Devices for Wireless Monitoring of Vital Signs in Neonatal Intensive Care

Named in honor of CR Forum board member Herbert Pardes for his profound impact on clinical research and academic medicine, this award, which comes with a $7,500 cash prize, is for the research study that best shows a high degree of innovation and creativity, advances science, and has an impact upon human disease.

The Distinguished Clinical Research Achievement Awards

**Kenneth W. Mahaffey, MD**, Canagliflozin and Renal Outcomes in Type 2 Diabetes and Nephropathy

**Richard Burt, MD**, Hematopoietic Stem Cell Transplantation for Frequently Relapsing Multiple Sclerosis

Presented to the top two studies that show creativity, innovation, or a novel approach that demonstrates an immediate impact on the health and well-being of patients. Each study will receive a $5,000 cash prize.

2020 TOP TEN CLINICAL RESEARCH ACHIEVEMENT AWARDS FINALISTS

- **A Phase I Evaluation of Chimeric Antigen Receptor-Modified T Cells Targeting B Cell Maturation Antigen (BCMA) in Patients with Relapsed/Refractory Multiple Myeloma**
  Michael Milone, Perelman School of Medicine at the University of Pennsylvania

- **Adjuvant Chemotherapy plus Radiation for Locally Advanced Endometrial Cancer**
  Daniela Matei, Northwestern University Feinberg School of Medicine

- **Associations of Dietary Cholesterol or Egg Consumption with Incident Cardiovascular Disease and Mortality**
  Tanuja Chitnis, MD, Massachusetts General Hospital

- **Association of Midlife to Late-Life Blood Pressure Patterns with Incident Dementia**
  Keenan Walker, John Hopkins University School of Medicine

- **Building a Better Vaccine Against Severe Respiratory Illness**
  Barney Graham, Vaccine Research Center, National Institutes of Health

- **Genomic Mismatch at LIMS1 Locus and Kidney Allograft Rejection**
  Krzysztof Kiryluk, Columbia University Irving Medical Center

- **Hidden Consciousness Following Acute Brain Injury**
  Jan Claassen, Columbia University Irving Medical Center

- **Surgical vs. Conservative Management of Cerebellar Intracerebral Hemorrhage**
  Alessandro Biffi, Massachusetts General Hospital

- **Tesamorelin as a Novel Hormonal Strategy to Treat Nonalcoholic Fatty Liver Disease**
  Steven Grinspoon, Massachusetts General Hospital/ Harvard Medical School

For full journal citations, please visit [www.clinicalresearchforum.org](http://www.clinicalresearchforum.org).
ABOUT MEMBERSHIP

As a member of Clinical Research Forum, you will join a group of unified voices that support the broader interests and needs of clinical research, and educate policymakers on the nation’s investment in clinical research to benefit the health and welfare of its citizens. Opportunities are available year-round to convene leaders at the highest levels in academic institutions, the pharmaceutical industry, information technology industry, and government to communicate and draw upon their perspectives on big issues influencing clinical research. Learn more about joining this elite community at www.clinicalresearchforum.org.

ABOUT THE CLINICAL RESEARCH FORUM

The mission of Clinical Research Forum is to provide leadership to the national and clinical translational research enterprise and promote understanding and support for clinical research and its impact on health and healthcare. Membership is open to academic health and science systems (AHASs), as well as industry partners. For more information, visit www.clinicalresearchforum.org.

TOP TEN CLINICAL RESEARCH ACHIEVEMENT AWARDS

Recognizing the need to celebrate our nation’s clinical research accomplishments that involve both innovation and impact on human disease, the Clinical Research Forum conducts an annual competition to determine the ten outstanding research accomplishments in the United States. These major research advances represent a portion of the annual return on the nation’s investment in the health and future welfare of its citizens.