SUNDAY, NOVEMBER 13

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SCIENTIFIC SESSIONS 2016

DailyNews

NEW ORLEANS, LOUISIANA | NOV. 12-16, 2016

Houser will recall personal journey to scientific discovery

Steven R. Houser, PhD, FAHA

Steven R. Houser, PhD, FAHA, will share his personal journey as a cardiovascular scientist and long-time American Heart Association volunteer in his Presidential Address Sunday.

Houser's Presidential Address, titled "Following The Data: My Journey to Help Patients With My Dad's Disease," will kick off Sunday's Opening Session, which officially launches the AHA's 2016 Scientific Sessions. The Opening Session will be held from 1-3 p.m. in Main Event I, Hall G.

Houser will describe how his father's struggle influenced the major themes of his presidency: scientific discovery, developing the next generation of cardiovascular scientists, and preventing cardiovascular diseases and stroke.

"As a grad student, I remember sitting in my dad's hospital room and watching his PVCs, then running to the library to read about ventricular arrhythmias," said Houser, senior associate dean of research and director of the Cardiovascular Research Center at Temple University in Philadelphia. "Every change in his condition sent me in search of more reading material. … And his death changed my career."

Houser has devoted his life's work to studying heart failure secondary to myocardial infarction. His initial research focused on finding ways to make a failing heart stronger and on preventing lethal cardiac arrhythmias.

His current research explores how a heart responds to myocardial infarction and seeks to find ways to replace lost tissue, thereby improving post-MI cardiac structure and function.

"I am certain that if this field develops the new knowledge required to understand new myocyte formation in the adult heart, we can translate this knowledge into safe and effective therapeutics," he said. ▼

Study: New CPR, ECC guidelines improve survival for OHCA patients

Guidelines changes for cardiopulmonary resuscitation and emergency cardiovascular care have improved neurologically intact survival for patients suffering out-of-hospital cardiac arrest, according to research presented during Saturday's Resuscitation Science Symposium at Scientific Sessions.

The guidelines changes, which were recommended in 2005 and 2010 by the International Consensus on CPR and ECC Science with Treatment Recommendations (CoSTR), have improved the odds ratio of neurologically intact survival by 1.6 and 2.3, respectively, compared to baseline recommendations published in 2000.

"The most significant changes in the CoSTR2005 and CoSTR2010 recommendations were to increase the chest compressions delivered per minute and to reduce interruptions in chest compressions during CPR," said Ken Nagao, MD, PhD, from the cardiovascular center at Nihon University Hospital, Tokyo, Japan. "Early access to CPR, early chest compressions and early defibrillation are the most important changes in these guidelines."

Ken Nagao, MD, PhD

Nagao is lead author of the study, which was one of the "Best of the Best" oral abstract presentations at the 2016 Resuscitation Science Symposium.

The AHA and the International Liaison Committee on Resuscitation (ILCOR) published an initial set of joint guidelines for CPR and ECC in 2000.

Nagao's research team used the All-Japan Utstein Registry, a prospective, nationwide, population-based observational registry, to identify adults treated with CPR following out-of-hospital cardiac arrest between 2005 and 2014. The 1,136,283 identified cases were divided into three groups based on the guidelines in place at the time of the cardiac arrest.

In the study, 100,509 patients (8.8 percent) were treated under the 2000 guidelines. Another 549,147 patients (48.3 percent) were treated under the CoSTR2005 guidelines that were in place from 2006 to 2010, and 486,627 patients (42.8 percent) were treated under the CoSTR2010 guidelines. The primary endpoint was a favorable 30-day neurological outcome.

Each guideline change placed increased emphasis on early access, early CPR, early defibrillation and early advanced life support, Nagao said.

CPR GUIDELINES continued on page 17

ReSS Lifetime Award winners focus on need for RCT-based evidence

WINNERS OF THE 2016 LIFETIME Achievement Awards in Resuscitation Science focused on the need for building the base of randomized controlled trial evidence in resuscitation science during their acceptance speeches on Saturday. Much of the current practice in resuscitation and trauma care is based on observational evidence.

Karim Brohi, BSc, MBBS, professor of trauma sciences at Barts Hospital and the London School of Medicine, received a Lifetime Achievement Award in Trauma Resuscitation Science. Jerry Nolan, MD, consultant in anesthesia and intensive care medicine at the Royal United Hospital in Bath, England, received a Lifetime Achievement Award in Resuscitation Science.

"We have dozens of interventions on every ambulance for sudden arrest and we don't know for sure which, if any, of those interventions actually make a difference in outcomes," said Nolan, who is also editor-in-chief of the journal *Resuscitation*, vice chairman of the European Resuscitation Council and co-editor for the 2015 International Consensus on CPR Science with Treatment Recommendations. "We have a huge number of observational studies with multiple outcomes. What we really need are prospective trials."

Karim Brohi, BSc, MBBS

Jerry Nolan, MD

Nolan's research interest is airway management. Endotracheal intubation is the traditional standard for managing airway blockages, but growing numbers of observational studies support the use of external devices, generating controversy in the field. He was co-investigator for REVIVE-Airways, a feasibility study for a larger randomized controlled trial comparing intubation with newer, less invasive airway-management devices.

The follow-up trial, REVIVE-Airways 2, has already enrolled more than 5,000 of an expected 9,000 patients, Nolan said. Initial data is expected in 2017.

ReSS AWARDS continued on page 16

TODAY AT SESSIONS

Don't miss today's highlighted presentations and events. For a complete schedule, download the Mobile Meeting Guide, see the Final Program or view the online program at **scientificsessions.org.**

8-9:15 a.m.
Current Insights into Lower Extremity Peripheral Artery Disease
Rooms 255-257

8-9:40 a.m.
Cardiovascular Outcome Trials in Type 2 Diabetes Mellitus: Controversies to Consensus
Rooms 220-221

9:30-10:30 a.m.
Main Event Session: Year in Review
Great Hall A

9:45-11 a.m.
Surgical and Interventional Pathology of Cardiac Devices
Rooms 208-209

Noon-1:15 p.m.
Main Event Session: Preparing for and Executing Team Resuscitation
Great Hall A

1-3 p.m.
Opening Session
Main Event I, Hall G

2-3:15 p.m.
Obesity in CVD Risk and Prevention
Science and Technology Hall, Population Science Section

3:30-5:30 p.m.
ABIM Learning Session: Cardiovascular Disease, 2016 Update
Room 342

3:45-5 p.m.
Cardiac Regeneration – Where Are We Now?
Main Event II

3:45-5:15 p.m.
Late-Breaking Clinical Trials: Big Trials for Big Questions
Main Event I, Hall G

4-6 p.m.
Late-Breaking Basic Science Posters
Science and Technology Hall, Basic Science Section

4:30-5:45 p.m.
Main Event Session: Inhalation Therapies in Resuscitation
Great Hall A

5:30-6:45 p.m.
Heart Disease in Women
Rooms 211-213

HEARTY HUMOR by Jonny Hawkins

"Tell me about these chess pains."

Session to explore research on CV health disparities

Several investigators on Monday will review the latest data on underlying determinants of social disparities in cardiovascular health. David Siscovick, MD, MPH, senior vice president for research at the New York Academy of Medicine, will moderate the session "Cardiovascular Health Disparities: Challenges and Opportunities in Basic, Clinical, and Population Science Research" at 3:45-5 p.m. in rooms 346-347.

HIGHLIGHTS FROM THE PROGRAM CHAIR

By Frank W. Sellke, MD, FAHA, Committee on Scientific Sessions Program Chair

The Opening Session at 1 p.m. in Main Event I, Hall G, will highlight our exciting day at Scientific Sessions 2016. AHA President Steven R. Houser, PhD, FAHA, will preside and present the annual Presidential Address. The Chairman's Award and other awards also will be presented during the session. The Opening Session will conclude with the annual Lewis A. Conner Lecture, delivered by FDA commissioner and long-time AHA member Robert M. Califf, MD.

A full day of science begins at 8 a.m. This year, we have continued the use of Poster Professors for all poster sessions — optimizing interactions, networking and knowledge transfer. We have many excellent oral sessions and presentations in basic, clinical and population science. The Committee of Scientific Sessions Program has put together superb educational programs in every area. You can learn about the latest drugs and devices when the Exhibit Hall opens at 11 a.m.

This year, we have a near record number of outstanding Late-Breaking Clinical Trials that will be presented in the next four days. The first Late-Breaking Clinical Trials session — "Big Trials for Big Questions" (see description below) — begins at 3:45 p.m. today in Main Event I. Another important session — "Cardiac Regeneration — Where Are We Now?" — begins at 3:45 p.m. in Main Event II, Hall F, and will include presentations covering molecular strategies for cardiac regeneration and repair, clinical applications of induced pluripotent stem cells, stem cell therapy for ischemic and vascular disease, regenerative approaches for chronic heart failure and the future of regenerative therapies.

Joint sessions today with other domestic and international organizations — always among the highlights of Scientific Sessions — include:

- "Cardiovascular Outcome Trials in Type 2 Diabetes Mellitus: Controversies to Consensus," with ACC/CCS/ADA/ESC/EASD (8 a.m., rooms 220-221)
- "Current Insights into Lower Extremity Peripheral Artery Disease," with the Brazilian Society of Cardiology (8 a.m., rooms 255-257)
- "Classic Etiologies Meet Modern Perspectives," with the Mexican Society of Cardiology (8 a.m., rooms 260-262)
- "Tropical Heart Disease: A Growing Threat to the United States," with the Spanish Society of Cardiology and Venezuelan Society of Cardiology (8 a.m., rooms 208-209)
- "Surgical and Interventional Pathology of Cardiac Devices," with the Association for European Cardiovascular Pathology/Society of Cardiovascular Pathology (9:45 a.m., rooms 208-209)

Frank W. Sellke, MD, FAHA

- "Difficult Choices in Lipidology," with the European Atherosclerosis Society and Turkish Society of Cardiology (5:30 p.m., rooms 218-219)
- "Heart Disease in Women," with the InterAmerican Society of Cardiology (5:30 p.m., rooms 211-213)
- "Implementing Physical Activity Assessment, Counseling and Referrals in the Clinical Setting," with the American College of Sports Medicine (5:30 p.m., rooms 215-216)

Check the Final Program or Scientific Sessions Mobile Meeting Guide for the complete schedule of joint sessions.

Whatever your specialty or interests, Scientific Sessions has outstanding programs featuring cutting-edge science, new clinical techniques and procedures and results of the latest clinical trials. ▼

Late-Breaking Clinical Trials: Big Trials for Big Questions — LBCT.01
3:45-5:15 p.m. Sunday | Main Event I, Hall G

TRIAL	DESCRIPTION
Effects of Ticagrelor Compared with Clopidogrel in Patients with Peripheral Artery Disease (EUCLID)	The EUCLID trial tested if long-term monotherapy treatment with ticagrelor is superior to clopidogrel at preventing cardiovascular death, myocardial infarction or ischemic stroke in patients with symptomatic peripheral artery disease.
Cardiovascular Outcomes with Celecoxib vs. Ibuprofen or Naproxen: The Precision Trial	The large trial compared cardiovascular outcomes with three commonly used NSAIDs in high-cardiovascular-risk patients.
The Effect of Blood Pressure and Cholesterol Lowering on Cognition	HOPE-3 evaluated whether long-term cholesterol lowering or blood pressure lowering delays cognitive decline.
Short- and Long-Term Effect of Immediate Vasodilator Therapy in Acutely Decompensated Heart Failure: Results of the TRUE-AHF Trial	The TRUE-AHF trial examined a novel vasodilator therapy to treat decompensated heart failure.

FDA Commissioner to discuss revolution of 'learning health system'

Data sharing will drive the next revolution in cardiovascular care — and it must be an integral part of patient care, according to FDA Commissioner Robert M. Califf, MD, MACC.

"We have to change the model from collecting information separately for clinical trials and observational studies to a system where data are collected as part of patient care and used in research and practice," Califf said.

Califf will present the annual Lewis A. Conner Memorial Lecture during Sunday's Opening Session, which will be held from 1-3 p.m. in Main Event I, Hall G. The lecture, "Revolutionizing Cardiovascular Care Through Better Evidence," will begin at 2:14 p.m.

Gathering clinical trial evidence as part of routine clinical practice is not a new concept, said Califf, noting that you can't tell a heart attack patient to go to a research clinic.

"The only place you can conduct an acute MI trial is in real-world practice," said Califf, who was vice chancellor for clinical and translational research at Duke University Medical Center in Durham, North Carolina, and founder of the Duke Clinical Research Institute. "That's what precision medicine is all about, embedding the generation of evidence and the use of evidence in clinical practice."

Robert M. Califf, MD, MACC

LECTURE PREVIEW

Lewis A. Conner Memorial Lecture: Revolutionizing Cardiovascular Care Through Better Evidence

2:14 p.m. Sunday

Main Event I, Hall G

Embedding randomized trials in everyday practice is standard in almost every business except healthcare, Califf said. The American Heart Association, the American College of Cardiology and the FDA have created patient registries and other observational studies to collect data as a part of standard clinical practice. When those observations suggest a causal relationship, it is technically easy to randomize within that same clinical system — if the trial option has been designed into the system.

"We have explosive, exciting technology evolving in cardiology," Califf said. "Doctors and patients and payers want to know which of the technologies is best. There are compelling forces from patients, payers and the cardiology community telling us we should be generating hard evidence with every patient encounter." ▼

CAREER PROGRESSION:
Frederick A. (Fred) Masoudi, MD, MSPH, FAHA

Fred A. Masoudi always knew he wanted to be a physician, but he didn't know where a career in medicine would take him. Masoudi initially viewed the profession solely as clinical, but that changed during his fellowship training when he became involved in health services research. And a stint in a national program to measure the quality of care for Medicare beneficiaries hospitalized with heart failure and myocardial infarction helped launch his interest in quality and outcomes into a career.

"Currently, I spend half of my time on patient care activities in cardiology and the other half researching care, outcomes and populations in cardiovascular disease to assess the extent to which physicians are delivering the right care to the right person at the right time," said Masoudi, professor of medicine in the Division of Cardiology at the University of Colorado.

Clinical practice often fails to meet standards, even though data from clinical trials have been translated into authoritative practice guidelines, he said, and these gaps in care represent lost opportunities to optimize patient outcomes.

The AHA uses the tagline "Life Is Why" to answer the question: Why do we do our lifesaving work? We asked Masoudi the same question:

"Better healthcare is why."

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"All the science generated by basic scientists and trialists, and all of the work that goes into developing guidelines, is wasted if we don't build systems that help us deliver care optimally," he said. "It seemed to me like a great opportunity to make a difference, which is why I love doing it."

Masoudi is a founding member of the Colorado Cardiovascular Outcomes Research Consortium, which provides mentorship for early-career cardiovascular health services investigators at the University of Colorado. He also serves as the chief science officer and chair of the Management Board of National Cardiovascular Data Registry programs of the American College of Cardiology.

In 1999, Masoudi attended the AHA's first annual Conference on Quality of Care and Outcomes Research (QCOR) in Cardiovascular Diseases and Stroke. The AHA has since established the QCOR Scientific Council. Masoudi has served as chair of the QCOR Council and as chair of the council's nominating committee. He has also chaired the planning committee of the QCOR conference and the AHA/ACC Task Force on Performance Measures.

Masoudi supports early-career investigators because he recognizes how critical relationships and mentors were to his career progression. He said the most gratifying part of his work is seeing one of his mentees publish their research or receive a career development award.

"The AHA has been instrumental to my career by facilitating professional relationships," Masoudi said. "One of the very effective ways I've found to help foster and nurture these relationships has been in my work with the QCOR Council and by attending AHA meetings, including Scientific Sessions and the annual QCOR conference." ▼

MEMBER SPOTLIGHT

Marion Leary, RN, MSN, MPH, FAHA
Director of Innovation Research, Center for Resuscitation Science, University of Pennsylvania Philadelphia

How long have you been an AHA/ASA Professional Member?
I joined the AHA in 2007 and I became an AHA Professional Member a few years later.

Why did you join?
As a resuscitation science researcher, the AHA exemplifies my field of study. The AHA understands the needs of its members in regard to networking, mentorship and research opportunities. I joined so that I could take full advantage of the benefits a professional membership with the AHA affords.

Are you involved in AHA councils?
I am involved in the Council on Cardiopulmonary, Critical Care, Perioperative and Resuscitation and the Council on Cardiovascular and Stroke Nursing.

What do you enjoy most about these roles?
I enjoy interacting with other council members and working to improve outcomes from sudden cardiac arrest and other emergency cardiovascular care diseases. The AHA is taking the lead in innovative solutions around these areas, and these councils allow me to contribute.

How else are you involved with the AHA?
I have been fortunate to become involved with the AHA in a variety of ways, including as a member of the Emergency Cardiovascular Care Committee's Science Subcommittee and the Nursing Cardiovascular Care Communications Committee. I also was on a writing group for the 2015 ECC resuscitation guidelines, and I currently co-host the Women in Resuscitation event at Scientific Sessions.

Why is membership valuable to you?
Membership with the AHA allows me to stay connected, not only to the AHA and the work the organization is striving to perform locally and nationally, but for strong collaboration with other investigators, staff and, most importantly, the community members we serve. In addition, I appreciate that the AHA is regularly promoting early career members, helping establish these young researchers and clinicians in their respective fields.

What message would you convey to your colleagues about being an AHA member?
Becoming a member of the AHA will afford you many opportunities in mentorship, collaboration and funding in your field of study related to cardiovascular care and resuscitation science. It will also allow you to establish yourself as an expert in your field, with opportunities for presenting your research and contributing to the science and guidelines. ▼

The AHA uses the tagline "Life Is Why" to answer the question: Why do we do our lifesaving work? We asked Leary the same question:

"We know CPR, especially if performed in the first few minutes of cardiac arrest, can double or triple a person's chance of survival. However, less than half of the people who experience a sudden cardiac arrest will receive this lifesaving intervention. Why? Research plays an important role in understanding the disparities in sudden cardiac arrest care. I want to answer those questions and improve bystander response and outcomes. **Research is my why!**"

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Prehospital hypotension 'dose' associated with TBI mortality

New data from the Excellence in Prehospital Injury Care (EPIC) study indicates a direct relationship between the duration and depth of prehospital hypotension and mortality in patients with traumatic brain injury (TBI).

During an abstract oral presentation Saturday, Daniel W. Spaite, MD, reported that doubling the "dose" of hypotension as measured by depth and duration of systolic blood pressure (SBP) below 90 mm Hg increases mortality following TBI by 19 percent.

"This is the first time, to our knowledge, that anyone has been able to link detailed, timed prehospital blood pressures and comprehensive hospital data on injuries and outcomes in a large number of patients," said Spaite, the Virginia Piper Distinguished Chair of Emergency Medicine and co-director of EMS research at the University of Arizona, Phoenix. "We now have more than 16,000 patients in our database with over 500 major TBI patients who had hypotension. The largest previous study we have been able to find that has extensive, linked data only had a total of 63 hypotensive patients."

The new study's prehospital data included multiple blood pressure measurements and the time each reading was recorded. Hospital databases, even if they have EMS data, typically allow a single prehospital blood pressure entry.

While there are multiple studies of the relationship between prehospital hypotension and outcome, prior studies are almost uniformly dichotomous, Spaite explained. Small numbers of cases forced researchers to divide patients into two groups — those who had at least one prehospital SBP reading below 90 and those who didn't.

Dichotomous studies generally showed that SBP of 90 or lower during the prehospital period is associated with a doubling of the severity-adjusted likelihood of mortality, Spaite noted. Treating hypotension as a continuous, timed variable shows a more complex relationship between the depth-duration dose of hypotension and mortality in TBI.

"The response to hypotension in TBI is remarkably sensitive," Spaite said. "When you double the dose — any range from zero to more than 1,000 — you increase your likelihood of dying by 19 percent. We now have a new factor — the 'dose' of hypotension — that appears to be important in TBI outcome. You can no longer simply say that what matters is whether SBP fell below 90 or not. These early results seem to tell us that hypotension is not a single entity, but may be much more complex than the current literature has demonstrated."

Daniel W. Spaite, MD

Spaite noted that the results don't necessarily mean treating the hypotension dose will improve mortality. These results came from an observational study and mostly retrospective data.

Nevertheless, the data from EPIC are an order of magnitude larger than any previous prehospital hypotension studies in the setting of TBI. With data from thousands of patients, researchers plan future sub-analyses looking at different depths of hypotension, durations and thresholds for hypotension ranging from 120 to 90 mm Hg. There are biologically plausible reasons to believe that 90 may be too low a threshold for hypotension in TBI, but this is the first time researchers have had sufficient patients and data to realistically pose the question, Spaite said.

"The way we save patients is by being able to find the parameters that are associated with, and impact, outcomes," he said. "This is an important step forward in the science of TBI and blood flow, but it is not the big answer. Now there needs to be studies that evaluate the impact of treating various cutpoints of SBP in a way that allows the dose of hypotension to be evaluated in the setting of randomization, based upon significantly higher blood pressure treatment thresholds." ▼

Join us for our Annual Awardee Group Photo at Scientific Sessions

- Monday, November 14, at 1:40 PM
- Main Event II, Level 3 (outside of Chapin Theater)
- Participants will receive a special lapel pin!

AHA Research Awardees from Scientific Sessions 2015 in Orlando, Florida

Join Us

Multidisciplinary Management of Acute and Chronic Heart Failure: A CLINICAL WORKSHOP

Sunday, November 13, 2016
7:00 PM – 8:30 PM
Hilton New Orleans Riverside
Grand Salon A & B
New Orleans, Louisiana

Nancy Albert, PhD, CCNS, CHFN, CCRN, NE-BC, FAHA, FCCM, FHFSA, FAAN
Associate Chief Nursing Officer
Research and Innovation-Cleveland Clinic Health System
Clinical Nurse Specialist
Kaufman Center for Heart Failure, Heart and Vascular Institute
Cleveland Clinic
Cleveland, Ohio

Mary Ann Bauman, MD
Medical Director, INTEGRIS Family Care Center
Medical Director, Women's Health and Community Relations, INTEGRIS Health
Oklahoma City, Oklahoma

Zubin Eapen, MD, MHS
Associate Professor of Medicine
Medical Director, Duke Heart Failure Same Day Access
Director of Education IT Innovations, Department of Medicine
Director of Clinical Improvement, Department of Medicine
Duke University Medical Center
Durham, North Carolina

Phillip D. Levy, MD, MPH, FACEP, FAHA, FACC
Professor of Emergency Medicine
Associate Chair for Research, Department of Emergency Medicine
Director of Clinical Research Service Center
Wayne State University School of Medicine
Detroit, Michigan

Study analyzes 10-year cardiac arrest research funding

Cardiac arrest is the third-leading cause of death in the United States, but its research funding lags behind research funding for stroke, heart disease and other conditions, according to new data presented Saturday at Scientific Sessions.

"Cardiac arrest claims more than 450,000 lives annually in the U.S. and improving survival depends largely upon our ability to conduct research and the translation of research findings into clinical practice," said Ryan A. Coute, a third-year medical student at Kansas City University of Medicine and Biosciences, Missouri, who presented the findings.

Coute's findings come from an analysis of the National Institutes of Health's cardiac arrest research funding in 2007-2016. He is lead author of the study, which was recognized as a "Best of the Best" abstract at Saturday's Resuscitation Science Symposium.


Ryan A. Coute

In the study, researchers examined the NIH RePORTER database to find cardiac arrest research grants in a variety of categories, including principal investigators, newly funded grants, trainee grants, non-human subject grants, human-subject grants and pediatric grants. The team then compared NIH cardiac arrest research funding to NIH research funding for other leading causes of death in the United States.

While cardiac arrest research funding has peaks and valleys, the NIH 2016 investment has increased in both the dollar amount and the number of grants to funding levels in 2007, according to the study. The high point of the past decade was 2010, which included funding for the Resuscitation Outcomes Consortium. Coute noted that the study did not adjust annual funding levels for inflation over the research period.

The total NIH funding for cardiac arrest research represents approximately .19 percent of the 2015 NIH budget. Funding for stroke and heart disease represents 1.4 percent and 5.9 percent, respectively. On per-death basis, the NIH invests about $2,200 for stroke, about $2,100 for cardiac disease and about $91 for cardiac arrest, according to the study.

The study's findings echo the 2015 conclusions of the Institute of Medicine report, *Strategies to Improve Cardiac Arrest Survival: A Time to Act*, which identified several opportunities to improve survival rates for cardiac arrest, including increasing the impact research.

The IOM study found that federal support for resuscitation research is significantly less than for other diseases and conditions that are just as common.

"There is the possibility that the NIH may not be getting as many high-quality proposals in cardiac arrest as in stroke or heart disease. This study is another opportunity to inform the cardiac arrest community and the public of this disparity in cardiac arrest research."

Coute conducted the study during a one-year fellowship sponsored by the Sarnoff Cardiovascular Research Foundation. Sarnoff awardees take one year off during medical school to work with leading researchers at other institutions. Coute worked with Robert W. Neumar, MD, PhD, professor and chair of emergency medicine at the University of Michigan School of Medicine, Ann Arbor. Neumar is also immediate past chair of the AHA's Emergency Cardiovascular Care Committee and currently co-chair of the International Liaison Committee on Resuscitation (ILCOR). ▼

Medical student adds insight, research to ECC

Research doesn't top the agenda for most medical students, but Ryan A. Coute is an anomaly.

Coute is presenting three abstracts during the Resuscitation Science Symposium at Scientific Sessions. One of them, "NIH-Funded Cardiac Arrest Research: A 10-Year Trend Analysis," was voted a "Best of the Best" ReSS abstract (see article on page 6).

Coute, a third-year medical student at Kansas City University of Medicine and Biosciences in Missouri, entered medicine to improve care for individual cardiac arrest patients and move research forward to improve care for patient groups.

"It all goes back to a small internship I did as an undergrad in the emergency department at Baystate Medical Center in Springfield, Massachusetts," Coute said. "That's where I encountered patients in cardiac arrest and saw firsthand that outcomes are not all that great."

That short internship changed Coute's life.

Working with Timothy J. Mader, MD, director of resuscitation research in the department of emergency medicine at Baystate Medical Center and clinical professor of emergency medicine at Tufts University School of Medicine in Boston, Coute was exposed to the need for research to improve outcomes.

"It got me excited about the potential to go to medical school, become a physician and, on a day-to-day basis, impact the care of patients and hopefully improve lives," Coute said. "That is what propelled me into medical school after four years of research involvement."

His commitment to clinical research grew stronger thanks to his rigorous studies at the Kansas City University of Medicine and Biosciences, where Coute learned of the Sarnoff Cardiovascular Research Foundation.

Founded by prolific medical researcher Stanley J. Sarnoff, MD, who developed the auto-injector, the foundation helps medical students become next-generation researchers and leaders, primarily with one-year fellowships in cardiovascular research.

Coute applied and landed in one of the country's top labs devoted to cardiac arrest research with Robert W. Neumar, MD, PhD, professor and chair of emergency medicine at the University of Michigan School of Medicine. Neumar is immediate past-chair of the AHA's Emergency Cardiovascular Care Committee and currently co-chair of the International Liaison Committee on Resuscitation.

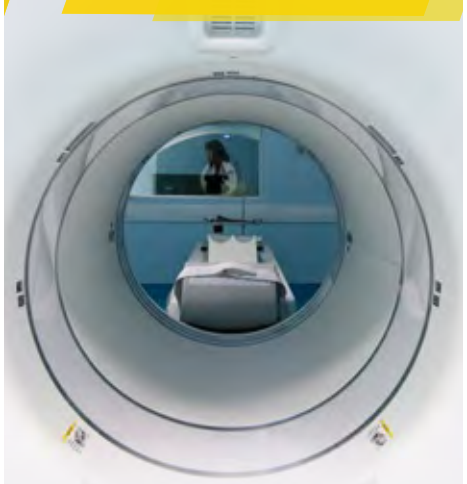
"He is particularly dedicated to delivering results," Neumar said. "It is that dedication that sets him apart. I saw it at work during his fellowship, the ReSS reviewers saw it in his abstracts and we are all seeing in at Scientific Sessions."

A Sarnoff Fellowship was also an early entrée into a world focused on the research process. Working with the ECC Committee added translational insights needed to move the research into clinical guidelines and general practice.

"Getting medical students engaged, not only in research but in the ECC Committee, is a wise investment," Neumar added. "Seeing how research gets translated into clinical guidelines and clinical practice, learning what it takes to go from a scientific discovery all the way to a guideline where practice is changed can be a career-defining opportunity. That is why we are so absolutely committed to mentoring and encouraging young researchers."

Coute presented his "Best of the Best" abstract Saturday. He will present another abstract, "Intravascular Coagulation During Prolonged Cardiac Arrest," at 8:16 a.m. Sunday in Great Hall C-D. He will present his third abstract, "Intrastate Variation in Treatment and Outcome Measures for Out-of-Hospital Cardiac Arrest," at 8:08 a.m. Monday in Great Hall C-D. ▼

PET imaging tested



In a prospective clinical study from the United Kingdom, researchers examined whether 68Ga-DOTATATE, a clinical SST2 PET tracer, outperforms 18F-FDG PET for imaging vascular inflammation in atherosclerosis.

The study results will be presented during an abstract oral session at 3:45 p.m. Sunday in rooms 343-344.

2016 Unofficial Satellite Events

SUNDAY, NOV. 13

7-8:30 p.m.
Industry-supported Symposium
Multidisciplinary Management of Acute and Chronic Heart Failure: A Clinical Workshop
Sponsored by Novartis
Supported by Novartis
Hilton New Orleans Riverside, Grand Salon A & B, First Floor

7-9 p.m.
Industry-supported Symposium
A Clinician's Guide to Using NOACs Safely and Effectively
Sponsored by Postgraduate Institute for Medicine
Supported by Medtelligence
New Orleans Downtown Marriott at the Convention Center, River Bend Ballroom
Registration: 6:30 p.m.; http://events.medtelligence.net/ha16.html

7-9 p.m.
University/Nonprofit Symposium
The Heart Brain Clinic: A Collaborative Approach to Optimize Patient Care
Sponsored by Mayo Clinic
Supported by Mayo Clinic
New Orleans Downtown Marriott at the Convention Center, Blaine Kern A-D, First Floor

7-9 p.m.
Industry-supported Symposium
Using Best Evidence to Achieve Glycemic Target and Reduce Cardiovascular Risk in Type 2 Diabetes
Sponsored by Forefront Collaborative
Supported by Boehringer Ingelheim Pharmaceuticals, Inc.
JW Marriott New Orleans
Registration: forefrontcollab.com/CV_Diabetes

7-9:15 p.m.
Industry-supported Symposium
Navigating the Complex Maze of LDL-Lowering Therapies: A Real World Roadmap for the Cardiovascular Specialist
Sponsored by CMEducation Resources
Supported by Sanofi and Regeneron Pharmaceuticals
Hilton New Orleans Riverside, Grand Ballroom C-D
Registration: www.Reg-LDL.com

7-10 p.m.
Industry-supported Symposium
Controversies in Anticoagulation Optimizing Outcome for Atrial Fibrillation
Sponsored by EMCREG-International
Supported by Janssen Scientific Affairs
The Westin New Orleans Canal Place, Grand Ballroom
Registration: www.emcreg.org

MONDAY, NOV. 14

7-9 p.m.
Industry-supported Symposium
Achieving LDL-C Goal for all Patients in the Era of PCSK9 Inhibitors
Sponsored by AcademicCME
Supported by Amgen, Inc.
New Orleans Downtown Marriott at the Convention Center, Blaine Kern Ballroom, First Floor
Registration: 6:30 p.m.; http://academiccme.com/LDL-C

7-9 p.m.
Industry-supported Symposium
The Foundational Role of IV Iron Repletion in Heart Failure and Associated Co-Morbid Conditions
Sponsored by CMEducation Resources
Supported by American Regent
Hilton New Orleans Riverside, Grand Ballroom C-D
Registration: www.Reg-IDA.com

7-9:15 p.m.
Industry-supported Symposium
Seeing Diabetes Through Heart Shaped Glasses: Multidisciplinary Perspectives on the Management of Comorbid Type 2 Diabetes and Cardiovascular Disease
Sponsored by Institute for Medical and Nursing Education, Inc
Supported by Boehringer Ingelheim Pharmaceuticals/Lilly USA
Hilton New Orleans Riverside, Salon A & B
Registration: www.caringfordiabetes.com/heart

7-9:30 p.m.
Industry-supported Symposium
Applying Guideline Recommended and Recent Evidence-based Therapies in the Treatment of Chronic Heart Failure
Sponsored by Paradigm Medical Communications
Supported by Novartis Pharmaceuticals Corporation
Hilton New Orleans Riverside, Napoleon Ballroom
Registration: www.paradigmmc.com/519

TUESDAY, NOV. 15

7-8:45 p.m.
Industry-supported Symposium
Evolving Perspectives on Intensive LDL-C Lowering and Plaque Regression: Potential Impact on Treatment Strategies
Sponsored by Amgen
Supported by PSL Group Services SARL
The Westin New Orleans Canal Place, Magnolia Ballroom (Third Floor)

7-9 p.m.
Industry-supported Symposium
Delving Deeper into the Complexities and Perplexities of Oral Anticoagulation
Sponsored by Paradigm Medical Communications, LLC
Supported by Paradigm Medical Communications, LLC
New Orleans Downtown Marriott at the Convention Center, Blaine Kern Ballroom (A-D)
Registration: 6:30 p.m.; www.paradigmmc.com/518

DailyNews

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REBOA shows survival advantage over ACC in trauma patients

New data from Japan shows a significant survival advantage for resuscitative endovascular balloon occlusion of the aorta (REBOA) compared to the more familiar aortic cross clamping (ACC) for trauma patients who suffer cardiac arrest in the hospital, according to research presented Saturday during the Resuscitation Science Symposium at Scientific Sessions.

"For patients with severe abdominal or pelvic injuries, REBOA may be the only practical intervention," said Toshikazu Abe, MD, MPH, visiting professor of health services research at the University of Tsukuba and chief of emergency and critical care medicine at Tsukuba Medical Center Hospital, Tsukuba, Japan.

Abe presented the results of the world's largest retrospective cohort study of REBOA versus ACC. No randomized controlled trials have compared the two interventions, noted Abe, adding that it would be almost impossible to design such a trial. The study was among the "Best of the Best" oral abstract presentations at the 2016 Resuscitation Science Symposium.

Researchers used the Japan Trauma Data Bank, a nationwide trauma injury registry, to construct a cohort of all adult trauma patients who underwent either REBOA or ACC in 2004-2013. They identified 903 patients — 636 who received REBOA and 267 who received ACC — from the 159,157 trauma patients in the registry. Patients with cardiopulmonary arrest before arrival at the hospital or with an Abbreviated Injury Scale (AIS) score of six or higher were excluded.

Of the patients in the analysis, 67 percent who received REBOA died compared to 90 percent of the patients who received ACC. Patients with REBOA had a higher Revised Trauma Sore (RTS) compared to those with ACC, 5.2 versus 4.2 ($p<0.001$), and a higher probability of survival, 0.43 versus 0.27 ($p<0.001$), respectively. REBOA had an odds ratio for in-hospital mortality of 0.309 after adjusting for Trauma and Injury Severity Score. There were similar results after adjusting for RTS (OR=0.224) and Injury Severity Score (OR=0.188).

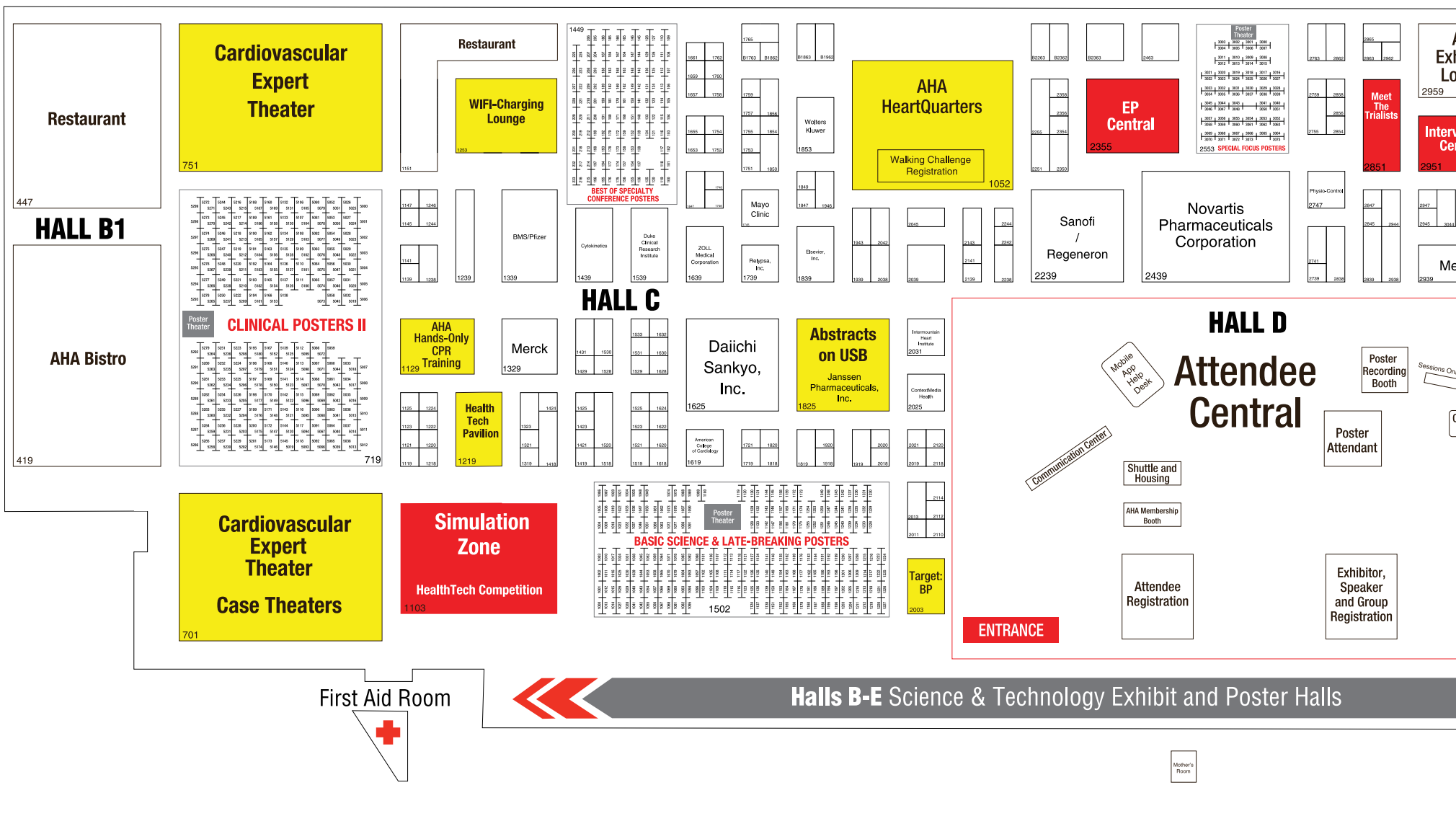
In a propensity score-matched cohort of 304 patients, REBOA was associated with lower mortality compared to ACC, OR=0.261. Patients with REBOA had less severe chest complications than those with ACC, AIS chest 3.8 versus 4.2 ($p<0.001$), even though the physiological severity and backgrounds were similar in both groups.

"I think what we are seeing is the result of REBOA being a less invasive, less traumatic procedure for these patients because it is an endovascular intervention," Abe said. "If you don't have to open the chest, it may be that patients are less likely to die." ▼

Toshikazu Abe, MD, MPH

2016 Scientific Sessions Exhibitors

Science & Technology Hall Hours		Lunch Break	
Sunday	11 a.m.-6 p.m.	Sunday	11 a.m.-1 p.m.
Monday	10 a.m.-4:30 p.m.	Monday	Noon-2 p.m.
Tuesday	10 a.m.-3 p.m.	Tuesday	Noon-2 p.m.



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SCIENTIFIC SESSIONS 2016

Sunday's Theater Demonstrations

Cardiovascular Expert Theater I

Booth 701

11:15 a.m.-Noon

Interpreting Measures of Clinical Effectiveness in Cardiovascular Outcome Trials

Amgen

Cardiovascular Expert Theater II

Booth 3661

11:15 a.m.-Noon

Thrombosis: AFib – An Exploration in Risk Reduction

Janssen Pharmaceuticals, Inc.

12:30-1:15 p.m.

Putting Guidelines into Practice: New Recommendations for Optimal Treatment of Heart Failure with Reduced Ejection Fraction (HFrEF)

Novartis

3-3:45 p.m.

Dyslipidemia and Inflammation: Emerging Strategies for Reducing Residual Risk in Patients with a History of Myocardial Infarction (MI)

Novartis

Cardiovascular Expert Theater III

Booth 751

11:15 a.m.-Noon

PRALUENT® (alirocumab) Injection: Long-term Efficacy and Safety

Sanofi Regeneron

12:30-1:15 p.m.

Repatha® (evolocumab): A Focused Clinical Review

Amgen

HeartQuarters Theater

Booth 1052

11:15-11:45 a.m.

OSO PHD, Councils JP

Noon-12:45 p.m.

***Hypertension* Journal CPC: A Case of Symptomatic Carotid Artery Stenosis in a Hypertensive Patient**

Presenter: David Calvet, MD, PhD

3-4 p.m.

Heart Science Amplified: Presented by Amgen and American Heart Association

Presenter: Steve Dentel BSN, RN, CPHQ, National Consultant, Quality and Systems Improvement

4-6 p.m.

Patient Support (AHA Patient Ambassador Program)

Distinguished Scientists to be honored during Opening Session

The American Heart Association will honor five researchers as 2016 Distinguished Scientists during the Opening Session, which begins at 1 p.m. Sunday in Main Event I, Hall G.

The annual awards recognize AHA/ASA members for significant, original and sustained scientific contributions that have advanced the AHA's mission to build healthier lives, free of cardiovascular diseases and stroke. This year's recipients join 97 past honorees. They are:

Stephen L. Archer, MD, FAHA

A renowned cardiologist and researcher, Archer is credited with many scientific discoveries in mechanism of oxygen sensing and experimental therapeutics for pulmonary hypertension and cancer.

Stephen L. Archer, MD, FAHA

Archer and his colleagues established that 02-induced changes alter H202 production, which regulates ion channels and enzymes, and thus, vascular tone. He also has shown methylation of the superoxide dismutase (SOD2) gene decreases H202 production, causing normoxic HIF-1 activation. The resulting glycolytic metabolism and mitochondrial fragmentation are amenable to therapy.

Archer and his colleagues also demonstrated that nuclear and mitochondrial division is coordinated by cyclin B-CDk1, which triggers mitosis and activates dynamin-related protein 1. This promotes the proliferative, apoptosis-resistant phenotype of pulmonary arterial hypertension and cancer, and can be therapeutically targeted. Fission also mediates cardiac ischemia-reperfusion injury.

In addition, Archer discovered that pyruvate dehydrogenase kinase (PDK)-mediated inhibition of pyruvate dehydrogenase promotes aerobic glycolysis, suppresses apoptosis and drives proliferation. PDK inhibitors regress cancer and PAH.

Archer has more than 230 publications to his name and has chaired many peer-reviewed committees and served as president of the Chicagoland AHA Board as a longstanding volunteer. He has a Tier 1 Canada Research Chair in Mitochondrial Dynamics and Translational Medicine and is head of the department of medicine at Queen's University in Kingston, Ontario.

Leon Axel, PhD, MD, FAHA

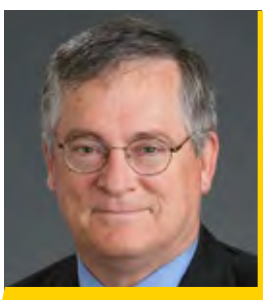
Leon Axel, PhD, MD, FAHA

Axel is a pioneer in cardiovascular magnetic resonance imaging and continues to develop MRI methods applicable to cardiovascular disease. He has sought to use imaging, particularly MRI, to quantitatively investigate cardiovascular physiology and pathophysiology. He has significantly contributed to the study of quantitative perfusion imaging, velocity imaging, surface coil imaging and magnetization tagging for regional cardiac function quantification.

Axel's current research is focused on the development of robust methods for acquiring high-quality MRI images of patients in the presence of free-breathing and arrhythmias, and for analyzing the additional physiologic information revealed in the resulting images.

Axel is professor of radiology, medicine, neuroscience and physiology at the New York University School of Medicine. He has served on the Board of Scientific Councilors of the National Institute of Biomedical Imaging and Bioengineering. He is also a fellow of the American College of Radiology, the Society for Body Computed Tomography and Magnetic Resonance, the International Society for Magnetic Resonance in Medicine and the AHA. He serves on the editorial boards of *Magnetic Resonance Imaging* and *Medical Image Analysis*, and serves as a guest editor for *Circulation: Cardiovascular Imaging*.

Gregory L. Burke, MD, MSc



Gregory L. Burke, MD, MSc

Widely recognized as a leader in population health, clinical prevention and multi-institutional studies, Burke has devoted his career to seeking a clearer understanding of the etiology of cardiovascular disease in populations and developing better strategies for chronic disease prevention.

Burke has led several observational studies and clinical trials, including the Women's Health Initiative, the Soy Estrogen Alternative Study, the CARDIA Study, the Cardiovascular Health Study, the Multi-Ethnic Study of Atherosclerosis, the MESA Family Study, the MESA Air Pollution Study, the Minnesota Heart Study, the Ginkgo Enhancing Memory Study and the Reynolds Center Sudden Cardiac Death Study.

He has written more than 350 peer-reviewed publications and has served on numerous major national committees, including as national chair of the AHA's Council on Epidemiology and Prevention; member of the National

Heart, Lung, and Blood Institute's Board of Extramural Advisors; co-chair of the NHLBI Prevention Task Force; chair of the Centers for Disease Control and Prevention's National Forum for the Prevention of Heart Disease and Stroke; and chair of numerous multicenter study monitoring boards.

Burke is professor and director of the Division of Public Health Sciences at Wake Forest School of Medicine in Winston-Salem, North Carolina.


Tiny Jaarsma, PhD, FAHA

Tiny Jaarsma, PhD, FAHA

Jaarsma aims to enhance the quality of nursing care and strengthen the healthcare delivery system for chronically ill cardiac patients through her research. She's recognized for promoting evidence-based nursing practice, specifically for heart failure patients.

Jaarsma's two current international trials focus on two areas in heart failure care. One is studying physical activity in patients with heart failure by exergaming; the other addresses communication related to palliative care in heart failure patients.

One of Jaarsma's prolific scientific achievements was the design, management and publication of COACH — a multicenter, randomized trial evaluating disease management in patients with heart failure. She also worked with colleagues from the United States and Sweden to develop the European Heart Failure Self-Care Behavior Scale, which integrates scientific knowledge in the middle range theory of self-care in chronic illness. The scale is used in clinical trials to evaluate the effect of nursing interventions and in nursing practice to improve the quality of patient education by nurses.

Jaarsma has been involved in the AHA's Council on Cardiovascular & Stroke Nursing and is a former board member of the Heart Failure Association. She is professor of nursing at the Faculty of Medical and Health Sciences of the University of Linköping, Sweden, and is editor-in-chief of the *European Journal of Cardiovascular Nursing*, the peer-reviewed journal of the Council on Cardiovascular Nursing and Allied Professionals of the European Society of Cardiology.


Klaus Ley, MD, FAHA

Klaus Ley, MD, FAHA

An internationally recognized investigator, Ley's research is focused on myeloid cells, specifically neutrophil and monocyte recruitment.

In 2007, his lab discovered a fundamental signaling mechanism in neutrophils that appears to be important in neutrophil recruitment. In 1991, Ley discovered that L-selectin was involved in leukocyte rolling *in vivo*.

For his research on neutrophils and monocytes, Ley received the 2008 Bonazinga Award, the highest honor of the Society for Leukocyte Biology. He also received the 2010 Malpighi Award, the highest award of the European Society for Microcirculation and Vascular Biology.

Ley's research in atherosclerosis began in 1997, when his lab discovered that P-selectin mediated rolling not only in venules, but also in inflamed arteries. The area of his research focuses on the role of monocyte-derived cells in atherosclerosis. In 2001, his lab discovered CCL5 and CXCL1 as monocyte arrest chemokines relevant to atherosclerosis.

Ley is professor and head of the Division of Inflammation Biology at the La Jolla Institute for Allergy and Immunology in La Jolla, California, where he runs the Ley Lab. He received his medical degree from Julius-Maximilians-Universität in Würzburg, Germany. He has a post-doctoral degree in physiology from Freie Universität Berlin, and a post-doctoral degree in biomedical engineering from the University of California San Diego. Since 1980, he has published more than 200 original papers.▼

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- Find the activity you are registered for under the "Activities in Progress" tab in the left hand navigation.
- Resume the activity.
- Complete the evaluation.
- Claim your credit(s).

International attendees can obtain their attendance verification certificate at the registration center. For a full list of conference accreditation statements and credit hours, visit **scientificsessions.org**.

Award-winning researchers to be recognized Sunday

The AHA will honor several leaders in cardiovascular disease research and care during the Opening Session, which beings at 1 p.m. Sunday in Main Event I, Hall G. The awards recognize contributions and achievements in research, mentorship and furthering the goals of the association. The 2016 awards and recipients are:

Chairman's Award

The Chairman's Award recognizes efforts to help the AHA achieve its goals. This year's honoree is Sidney C. Smith Jr., MD, FAHA, who has been involved in the AHA for nearly four decades, serving as president in 1995-1996. He served as the AHA's chief science officer from 2001-2003, when he also led the association's cooperation with the Centers for Disease Control and Prevention to develop the National Action Plan to Prevent Heart Disease and Stroke.


Sidney C. Smith Jr., MD, FAHA

Smith was instrumental in creating the AHA's Get With The Guidelines program and has worked to reduce the worldwide risk of cardiovascular diseases. He also has chaired many other AHA task forces and committees, including the Education and Community Programs Committee and the Heart Rx Implementation Advisory Group.

Smith is professor of medicine and director of the Center for Cardiovascular Science and Medicine at the University of North Carolina, Chapel Hill.

Basic Research Prize

Elizabeth M. McNally, MD, PhD, FAHA, will be awarded the Basic Research Prize in recognition of her contribution to cardiovascular science, specifically the understanding of cardiovascular genetic risks for inherited cardiovascular disorders.

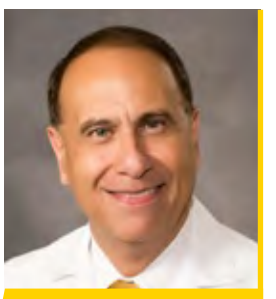
As a cardiologist and geneticist, McNally has conducted internationally acclaimed research on the genetic mechanisms responsible for heart failure, cardiomyopathy, muscular dystrophy, arrhythmias and aortic aneurysms — investigations that are leading to the identification of new therapeutic targets. Her lab also created the first genetically engineered model of cardiomyopathy and muscular dystrophy.


Elizabeth M. McNally, MD, PhD, FAHA

An active AHA volunteer, McNally serves as chair of the Louis and Arnold Katz Prize selection committee and was previously awarded the AHA's Established Investigator Award and the Basic Cardiovascular Sciences Distinguished Scientist Award. She is the Elizabeth J. Ward Professor of Genetic Medicine and professor and director of the division of cardiology at Northwestern University Feinberg School of Medicine, Chicago.

Clinical Research Prize

Joseph P. Ornato, MD, FAHA, will accept the 2016 Clinical Research Prize in recognition of his 40-year career, which has helped construct the scientific underpinnings for emergency cardiac care, cardiac arrest treatment and CPR.


Joseph P. Ornato, MD, FAHA

Ornato has published more than 350 papers on emergency cardiac care, including two landmark papers demonstrating the potential value of end-tidal CO2 monitoring during CPR, which was published in the *Journal of the American Medical Association* in 1987. His findings laid the groundwork for the widespread use of this technique as a physiologic monitor during CPR and for its inclusion in 2010 and 2015 guidelines as a key diagnostic approach during cardiac arrest.

Ornato is professor and chair of the department of emergency medicine at Virginia Commonwealth University Health System, Richmond.

Population Research Prize

Emelia Benjamin, MD, ScM, FAHA, will be awarded the Population Research Prize for her outstanding accomplishments in population research. As a Framingham Heart Study senior investigator, she has contributed to a fuller understanding of the epidemiology, genetic basis, risk factors and prognosis of cardiovascular diseases, particularly inflammation, vascular function and atrial fibrillation.


Emelia Benjamin, MD, ScM, FAHA

Benjamin has co-authored 450 original scientific reports of cardiovascular epidemiology in leading publications, including *The New England Journal of Medicine* and the *Journal of the American Medical Association*. She is chair of the AHA's Epidemiology Statistics Committee and former chair of the AHA's Functional Genomics and Translational Biology Council.

Benjamin is professor of medicine and epidemiology at Boston University School of Medicine and School of Public Health, Massachusetts.

Eugene Braunwald Academic Mentorship Award


Eric N. Olson, PhD

Eric N. Olson, PhD, will be awarded the Eugene Braunwald Academic Mentorship Award. During the past 31 years, he has trained 42 PhD students and 54 post-doctoral fellows, and he is currently training more than 30 students.

Among his protégés, 96 trained in his laboratory and 56 are now professors in major academic institutions in the U.S., Europe and Japan. Others are productive scientists, leaders in pharmaceutical, biotech industries and government agencies, or are continuing their training in basic science.

Olson is professor and chair of the department of molecular biology at the University of Texas Southwestern Medical Center, Dallas.

Research Achievement Award


Robert M. Califf, MD, MACC

Robert M. Califf, MD, MACC, Commissioner of the Food and Drug Administration, will receive the Research Achievement Award for his clinical research that has led to paradigm-changing procedures and improved the management of patients with cardiovascular diseases.

Califf was vice chancellor for clinical and translational research at Duke University Medical Center, Durham, North Carolina, and founder of the Duke Clinical Research Institute. Under his leadership, the institute has become a world leader in collecting trial results of novel therapies and strategies for managing coronary patients. Since its inception, the institute has conducted and coordinated clinical studies at more than 37,000 sites in 65 countries, enrolling more than 1.2 million patients. Many American College of Cardiology/American Heart Association guidelines are based on Califf's research results.

Joseph A. Vita Award

The AHA's newest award will be presented to Christine E. Seidman, MD, FAHA, in recognition of her laboratory's transformative achievements in identifying the molecular basis for inherited forms of heart failure, including hypertrophic and dilated cardiomyopathy.


Christine E. Seidman, MD, FAHA

In the last five years, Seidman and her colleagues identified Titin as the most common cause of inherited dilated cardiomyopathy. They also have shown that allele-specific silencing and small molecule inhibitors can suppress hypertrophic cardiomyopathy in mice. These studies, along with other ongoing work in the Seidman Lab, may lead to the development of personalized treatments of hypertrophic cardiomyopathy and inherited forms of dilated cardiomyopathy.

Seidman is the TW Smith Professor of Medicine and Genetics and director of the Brigham and Women's Cardiovascular Genetics Center in the department of genetics at Harvard Medical School, Boston, Massachusetts.

Merit Awards


Kenneth Poss, PhD, FAHA

On Friday, the AHA presented its inaugural Merit Awards to Kenneth Poss, PhD, FAHA, and William Sessa, PhD. The five-year, $1 million awards fund promising investigators — rather than specific research projects — who have the potential to move a field of science forward with creative and novel approaches.


William Sessa, PhD

Poss, the James B. Duke Professor of Cell Biology and professor of biology and medicine at Duke University School of Medicine, Durham, North Carolina, studies heart cell regeneration. Sessa, the Alfred Gilman Professor of Pharmacology and professor of medicine and vice chair of pharmacology at Yale School of Medicine, New Haven, Connecticut, is investigating triggers of coronary artery disease. ▼

Resuscitation Academy honored for efforts to improve cardiac arrest survival and advance resuscitation science

The American Heart Association on Saturday presented its Ian G. Jacobs Award for International Group Collaboration to Advance Resuscitation Science to the Resuscitation Academy.

The award — presented during the Resuscitation Science Symposium — honors Jacobs, PhD, FAHA, for his efforts to bring clinicians and researchers together from multiple disciplines worldwide to improve acute resuscitation care.

The Resuscitation Academy, which launched nine years ago to identify and disseminate best practices for treating cardiac arrest, is the U.S. base for the recently formed Global Resuscitation Alliance. The alliance is a group of international health organizations and emergency medical systems, including the AHA, that aims to increase cardiac arrest survival rates by 50 percent.

Mickey S. Eisenberg, MD, PhD

Mickey S. Eisenberg, MD, PhD, co-author of the paper that inspired the creation of the Global Resuscitation Alliance, accepted the award on behalf of the Resuscitation Academy.

"We hope to develop a road map and a set of tools that can be used by emergency medical systems in both high-resource and low-resource countries," said Eisenberg, director of medical quality improvement at King County EMS in Seattle. "We have the knowledge to increase cardiac arrest survival rates — we know how to do it. The main challenge is implementation."

For the past five years, the healthcare community in Eisenberg's region has achieved survival rates for bystander-witnessed cardiac arrest caused by ventricular fibrillation greater than 50 percent. This is in stark contrast to some areas of the country, where survival rates are in the single digits. Eisenberg said the first step to address this disparity is measuring performance at the local level.

The Global Resuscitation Alliance aims to educate EMS leaders in developed and developing countries about best practices and provide tools to help improve survival in their communities.

The Resuscitation Academy has established 10 actions as foundational steps for the integrated systems-of-care approach recommended by the AHA. They include participating in a cardiac arrest registry, dispatching first responders more rapidly, standardizing the practice of dispatcher-assisted (telephone) CPR and providing high-quality CPR for all cardiac arrest patients. ▼

ReSS AWARDS

continued from page 1

The use of epinephrine is similarly controversial, Nolan said. Multiple observational studies indicate short-term improvement with epinephrine, but poorer, longer-term outcomes. The largest randomized controlled trial of epinephrine in resuscitation, PARAMEDIC-2, has enrolled 4,000 of an expected 8,000 patient cohort. Data should be reported during the summer of 2017.

Brohi has long focused on the pathophysiology of trauma-induced coagulopathy and is the clinical director of the London Major Trauma System. Traditional trauma care focuses on reducing the time to surgery while traditional trauma resuscitation focuses on stabilizing patients long enough to get to surgery, often using massive fluid infusions to maintain perfusion which exacerbates trauma-induced coagulopathy.

"We often make them worse with our resuscitation efforts," he said. "We have to rethink trauma resuscitation."

Rethinking trauma resuscitation is a complex task, Brohi continued. New research is needed to identify new targets such as the loss of fibrinogen and seldom-recognized processes such as fibrinolysis. Addressing those new targets adds the need for new therapeutic agents and new diagnostic devices that can be used quickly and easily at the point of care. CRYOSTAT-2, a randomized controlled trial of cryoprecipitate, a concentrated source of fibrinogen, is scheduled to begin in 2017.

There is also a need for more basic research into trauma and coagulation, Brohi said. There are at least four phenotypes of trauma-induced coagulopathy. Each phenotype has distinct therapeutic needs and responses.

Trauma research is difficult, he added, but it can be tremendously effective. Research embedded in usual care for emergency medical services in London has slashed the 24-hour mortality rate by 61 percent.

A single new intervention, giving trauma victims red blood cells pre-hospital, produced the greatest benefit. In 2009, 34 percent of trauma victims in the London trauma system died of hemorrhage. In 2015, mortality from post-trauma hemorrhage was down to 18 percent. The key difference, Brohi said, was a 2012 decision to put red blood cells on every ambulance and administer them as early in the care process as possible.

"Whatever we do for these patients needs to be pushed in the pre-hospital phase, pushed to the ambulance, pushed to the very first medical team on the scene," Brohi said. "There is still a lot to be done." ▼

CPR GUIDELINES continued from page 1

"The greatest single advance was the change from the older protocol of three stacked defibrillation shocks put in place in 2000 to a one-shock scenario followed by two minutes of additional CPR," Nagao said. "When it comes to CPR, the most important changes emphasized early chest compressions with minimal interruptions to compressions, to push hard, push fast and allow for complete chest recoil between compressions."

In the study, CoSTR2005 and CoSTR2010 were independent predictors of favorable 30-day neurological outcomes for both witnessed and unwitnessed out-of-hospital cardiac arrest compared to the original 2000 guidelines. For individuals with a witnessed out-of-hospital cardiac arrest, CoSTR2005 guidelines had an odds ratio of 1.9 compared to the 2000 guidelines, and the CoSTR2010 guidelines had an odds ratio of 2.8. Individuals with an unwitnessed cardiac arrest showed similar odds ratios of 1.3 under CoSTR2005 and 1.6 under CoSTR2010.

"These changes to CPR maneuvers and protocols were helpful to save lives and improve neurological outcomes," Nagao said. "We are conducting a new study to assess the quality of CPR using new, simpler CPR methods that have been developed in recent years. Resuscitation programs must establish processes for continuous quality improvement to reduce the time to CPR and shock delivery and to improve the quality of CPR delivered." ▼

How have new guidelines affected CPR use?

Since 2010, guidelines suggest compression-only cardiopulmonary resuscitation (CO-CPR) for untrained bystanders and for trained bystanders unwilling to perform rescue breaths. Researchers in Sweden analyzed bystander-witnessed cases of out-of-hospital cardiac arrests reported to the Swedish Cardiac Arrest Registry to determine changes in the rates of bystander CPR, CO-CPR and patient survival from 2000 to 2014 after the guidelines were published.

The research will be presented during a concurrent oral session at 10:45 a.m. Sunday in rooms 206-207.

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Scientific Sessions' Wear Red Day draws attention to further women's heart health

Annabelle Santos Volgman, MD, a Chicago cardiologist, has a suggestion for her male colleagues on Wear Red Day at Scientific Sessions.

"Some of the men wear red sneakers or red jackets," she said. "I think they should wear a red dress."

She's joking, but she wants to make a point. Volgman, medical director at the Rush Heart Center for Women, believes that more male doctors need to share her zeal for raising awareness and spurring women to take control of their heart health.

Scientific Sessions' Wear Red Day, which is Monday, is part of that. It's an outgrowth of the AHA's Go Red For Women campaign. The initial effort has grown into a national movement with events around the country, ongoing awareness projects, a big online and social media presence and National Wear Red Day every February. Macy's, the national sponsor, has raised more than $55 million and counting to support the campaign and promote the red dress as its symbol.

"We want this to be like the pink ribbon for breast cancer," said Volgman, who wears red every day and had her office walls painted to match. "We'll keep plugging away until everyone understands what it means."

She points to many reasons for the misconception that heart disease is a "man's" disease — from early research focusing on men to different warning signs in women to different treatments. When statins were developed three decades ago to treat high cholesterol, they were primarily prescribed for men, while women were commonly given hormone replacement therapy — which didn't work.

Subsequent research and initiatives have improved the situation, but results are hard to quantify. Can color-coded campaigns really help?

"I'm a believer in public awareness," said Robert Harrington, MD, FAHA, FACC, FECC, an interventional cardiologist and chairman of the Department of Medicine at Stanford University. "I agree it sends an important message and I think it does make a difference."

Harrington, who produces his own podcast about cardiac health and other medical issues, embraces red in his own way.

"I'll certainly wear my red socks and my red tie," he said. "We all need to be part of this. It's particularly important because the vast majority of cardiologists are still men."

And he has his own favorite symbol: Tuesday is Wear Sneakers Day, when the same cardiologists who wore red on Monday are supposed to ditch their Rockports and Naturalizers for a comfy pair of Nikes or Skechers. The goal is to encourage physical activity and all the benefits therein.

"It does send a message to see a bunch of people in sneakers walking through the convention center to show that walking is part of a heart-healthy lifestyle," Harrington said. "My own sneakers are red," he noted.

Although he believes that sending messages has an impact, Harrington said, "I'm also a scientist, I'd like to see the data." ▼

REPATHA® (evolocumab)

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Please see package insert for full Prescribing Information

1. INDICATIONS AND USAGE

1.1 Primary Hyperlipidemia

REPATHA is indicated as an adjunct to diet and maximally tolerated statin therapy for the treatment of adults with heterozygous familial hypercholesterolemia (HeFH) or clinical atherosclerotic cardiovascular disease (CVD), who require additional lowering of low density lipoprotein cholesterol (LDL-C).

1.2 Homozygous Familial Hypercholesterolemia

REPATHA is indicated as an adjunct to diet and other LDL-lowering therapies (e.g., statins, ezetimibe, LDL apheresis) for the treatment of patients with homozygous familial hypercholesterolemia (HoFH) who require additional lowering of LDL-C.

1.3 Limitations of Use

The effect of REPATHA on cardiovascular morbidity and mortality has not been determined.

4. CONTRAINDICATIONS

REPATHA is contraindicated in patients with a history of a serious hypersensitivity reaction to REPATHA [*see Warnings and Precautions (5.1)*].

5. WARNINGS AND PRECAUTIONS

5.1 Allergic Reactions

Hypersensitivity reactions (e.g., rash, urticaria) have been reported in patients treated with REPATHA, including some that led to discontinuation of therapy. If signs or symptoms of serious allergic reactions occur, discontinue treatment with REPATHA, treat according to the standard of care, and monitor until signs and symptoms resolve.

6. ADVERSE REACTIONS

The following adverse reactions are also discussed in other sections of the label:

• Allergic Reactions [*see Warnings and Precautions (5.1)*]

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in clinical practice.

Adverse Reactions in Patients with Primary Hyperlipidemia and in Patients with Heterozygous Familial Hypercholesterolemia

REPATHA is not indicated for use in patients without familial hypercholesterolemia or atherosclerotic CVD [*see Indications and Usage (1.1)*].

The data described below reflect exposure to REPATHA in 8 placebo-controlled trials that included 2651 patients treated with REPATHA, including 557 exposed for 6 months and 515 exposed for 1 year (median treatment duration of 12 weeks). The mean age of the population was 57 years, 49% of the population were women, 85% White, 6% Black, 8% Asians, and 2% other races.

Adverse Reactions in a 52-Week Controlled Trial

In a 52-week, double-blind, randomized, placebo-controlled trial (Study 2), 599 patients received 420 mg of REPATHA subcutaneously once monthly [*see Clinical Studies (14.1)*]. The mean age was 56 years (range: 22 to 75 years), 23% were older than 65 years, 52% women, 80% White, 8% Black, 6% Asian, and 6% Hispanic. Adverse reactions reported in at least 3% of REPATHA-treated patients, and more frequently than in placebo-treated patients in Study 2, are shown in Table 1. Adverse reactions led to discontinuation of treatment in 2.2% of REPATHA-treated patients and 1% of placebo-treated patients. The most common adverse reaction that led to REPATHA treatment discontinuation and occurred at a rate greater than placebo was myalgia (0.3% versus 0% for REPATHA and placebo, respectively).

Table 1. Adverse Reactions Occurring in Greater than or Equal to 3% of REPATHA-treated Patients and More Frequently than with Placebo in Study 2

	Placebo (N=302) %	REPATHA (N=599) %
Nasopharyngitis	9.6	10.5
Upper respiratory tract infection	6.3	9.3
Influenza	6.3	7.5
Back pain	5.6	6.2
Injection site reactions†	5.0	5.7
Cough	3.6	4.5
Urinary tract infection	3.6	4.5
Sinusitis	3.0	4.2
Headache	3.6	4.0
Myalgia	3.0	4.0
Dizziness	2.6	3.7
Musculoskeletal pain	3.0	3.3
Hypertension	2.3	3.2
Diarrhea	2.6	3.0
Gastroenteritis	2.0	3.0

†includes erythema, pain, bruising

Adverse Reactions in Seven Pooled 12-Week Controlled Trials

In seven pooled 12-week, double-blind, randomized, placebo-controlled trials, 993 patients received 140 mg of REPATHA subcutaneously every 2 weeks and 1059 patients received 420 mg of REPATHA subcutaneously monthly. The mean age was 57 years (range: 18 to 80 years), 29% were older than 65 years, 49% women, 85% White, 5% Black, 9% Asian, and 5% Hispanic. Adverse reactions reported in at least 1% of REPATHA-treated patients, and more frequently than in placebo-treated patients, are shown in Table 2.

Table 2. Adverse Reactions Occurring in Greater than 1% of REPATHA-treated Patients and More Frequently than with Placebo in Pooled 12-Week Studies

	Placebo (N=1224) %	REPATHA† (N=2052) %
Nasopharyngitis	3.9	4.0
Back pain	2.2	2.3
Upper respiratory tract infection	2.0	2.1
Arthralgia	1.6	1.8
Nausea	1.2	1.8
Fatigue	1.0	1.6
Muscle spasms	1.2	1.3
Urinary tract infection	1.2	1.3
Cough	0.7	1.2
Influenza	1.1	1.2
Contusion	0.5	1.0

†140 mg every 2 weeks and 420 mg once monthly combined

Adverse Reactions in Eight Pooled Controlled Trials (Seven 12-Week Trials and One 52-Week Trial)

The adverse reactions described below are from a pool of the 52-week trial (Study 2) and seven 12-week trials. The mean and median exposure durations of REPATHA in this pool of eight trials were 20 weeks and 12 weeks, respectively.

Local Injection Site Reactions

Injection site reactions occurred in 3.2% and 3.0% of REPATHA-treated and placebo-treated patients, respectively. The most common injection site reactions were erythema, pain, and bruising. The proportions of patients who discontinued treatment due to local injection site reactions in REPATHA-treated patients and placebo-treated patients were 0.1% and 0%, respectively.

Allergic Reactions

Allergic reactions occurred in 5.1% and 4.7% of REPATHA-treated and placebo-treated patients, respectively. The most common allergic reactions were rash (1.0% versus 0.5% for REPATHA and placebo, respectively), eczema (0.4% versus 0.2%), erythema (0.4% versus 0.2%), and urticaria (0.4% versus 0.1%).

Neurocognitive Events

In placebo-controlled trials, neurocognitive events were reported in less than or equal to 0.2% in REPATHA-treated and placebo-treated patients.

Low LDL-C Levels

In a pool of placebo- and active-controlled trials, as well as open-label extension studies that followed them, a total of 1988 patients treated with REPATHA had at least one LDL-C value < 25 mg/dL. Changes to background lipid-altering therapy were not made in response to low LDL-C values, and REPATHA dosing was not modified or interrupted on this basis. Although adverse consequences of very low LDL-C were not identified in these trials, the long-term effects of very low levels of LDL-C induced by REPATHA are unknown.

Musculoskeletal Events

Musculoskeletal adverse reactions were reported in 14.3% of REPATHA-treated patients and 12.8% of placebo-treated patients. The most common adverse reactions that occurred at a rate greater than placebo were back pain (3.2% versus 2.9% for REPATHA and placebo, respectively), arthralgia (2.3% versus 2.2%), and myalgia (2.0% versus 1.8%).

Adverse Reactions in Patients with Homozygous Familial Hypercholesterolemia

In a 12-week, double-blind, randomized, placebo-controlled trial of 49 patients with HoFH (Study 4), 33 patients received 420 mg of REPATHA subcutaneously once monthly [*see Clinical Studies (14.3)*]. The mean age was 31 years (range: 13 to 57 years), 49% were women, 90% White, 4% Asian, and 6% other. The adverse reactions that occurred in at least two (6.1%) REPATHA-treated patients, and more frequently than in placebo-treated patients, included:

• Upper respiratory tract infection (9.1% versus 6.3%)
• Influenza (9.1% versus 0%)
• Gastroenteritis (6.1% versus 0%)
• Nasopharyngitis (6.1% versus 0%)

6.2 Immunogenicity

As with all therapeutic proteins, there is potential for immunogenicity. The immunogenicity of REPATHA has been evaluated using an electrochemiluminescent bridging screening immunoassay for the detection of binding anti-drug antibodies. For patients whose sera tested positive in the screening immunoassay, an in vitro biological assay was performed to detect neutralizing antibodies.

In a pool of placebo- and active-controlled clinical trials, 0.1% of patients treated with at least one dose of REPATHA tested positive for binding antibody development. Patients whose sera tested positive for binding antibodies were further evaluated for neutralizing antibodies; none of the patients tested positive for neutralizing antibodies.

There was no evidence that the presence of anti-drug binding antibodies impacted the pharmacokinetic profile, clinical response, or safety of REPATHA, but the long-term consequences of continuing REPATHA treatment in the presence of anti-drug binding antibodies are unknown.

The detection of antibody formation is highly dependent on the sensitivity and specificity of the assay. Additionally, the observed incidence of antibody positivity in an assay may be influenced by several factors including assay methodology, sample handling, timing of sample collection, concomitant medications, and underlying disease. For these reasons, comparison of the incidence of antibodies to REPATHA with the incidence of antibodies to other products may be misleading.

8. USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

There are no data available on use of REPATHA in pregnant women to inform a drug-associated risk. In animal reproduction studies, there were no effects on pregnancy or neonatal/infant development when monkeys were subcutaneously administered evolocumab from organogenesis through parturition at dose exposures up to 12 times the exposure at the maximum recommended human dose of 420 mg every month. In a similar study with another drug in the PCSK9 inhibitor antibody class, humoral immune suppression was observed in infant monkeys exposed to that drug in utero at all doses. The exposures where immune suppression occurred in infant monkeys were greater than those expected clinically. No assessment for immune suppression was conducted with evolocumab in infant monkeys. Measurable evolocumab serum concentrations were observed in the infant monkeys at birth at comparable levels to maternal serum, indicating that evolocumab, like other IgG antibodies, crosses the placental barrier. FDA's experience with monoclonal antibodies in humans indicates that they are unlikely to cross the placenta in the first trimester; however, they are likely to cross the placenta in increasing amounts in the second and third trimester. Consider the benefits and risks of REPATHA and possible risks to the fetus before prescribing REPATHA to pregnant women.

In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2-4% and 15-20%, respectively.

Data

Animal Data

In cynomolgus monkeys, no effects on embryo-fetal or postnatal development (up to 6 months of age) were observed when evolocumab was dosed during organogenesis to parturition at 50 mg/kg once every 2 weeks by the subcutaneous route at exposures 30- and 12-fold the recommended human doses of 140 mg every 2 weeks and 420 mg once monthly, respectively, based on plasma AUC. No test of humoral immunity in infant monkeys was conducted with evolocumab.

8.2 Lactation

Risk Summary

There is no information regarding the presence of evolocumab in human milk, the effects on the breastfed infant, or the effects on milk production. The development and health benefits of breastfeeding should be considered along with the mother's clinical need for REPATHA and any potential adverse effects on the breastfed infant from REPATHA or from the underlying maternal condition. Human IgG is present in human milk, but published data suggest that breast milk antibodies do not enter the neonatal and infant circulation in substantial amounts.

8.4 Pediatric Use

The safety and effectiveness of REPATHA in combination with diet and other LDL-C-lowering therapies in adolescents with HoFH who require additional lowering of LDL-C were established based on data from a 12-week, placebo-controlled trial that included 10 adolescents (ages 13 to 17 years old) with HoFH [*see Clinical Studies (14.3)*]. In this trial, 7 adolescents received REPATHA 420 mg subcutaneously once monthly and 3 adolescents received placebo. The effect of REPATHA on LDL-C was generally similar to that observed among adult patients with HoFH. Including experience from open-label, uncontrolled studies, a total of 14 adolescents with HoFH have been treated with REPATHA, with a median exposure duration of 9 months. The safety profile of REPATHA in these adolescents was similar to that described for adult patients with HoFH.

The safety and effectiveness of REPATHA have not been established in pediatric patients with HoFH who are younger than 13 years old.

The safety and effectiveness of REPATHA have not been established in pediatric patients with primary hyperlipidemia or HeFH.

8.5 Geriatric Use

In controlled studies, 1420 patients treated with REPATHA were ≥ 65 years old and 171 were ≥ 75 years old. No overall differences in safety or effectiveness were observed between these patients and younger patients, and other reported clinical experience has not identified differences in responses between the elderly and younger patients, but greater sensitivity of some older individuals cannot be ruled out.

8.6 Renal Impairment

No dose adjustment is needed in patients with mild to moderate renal impairment. No data are available in patients with severe renal impairment [*see Clinical Pharmacology (12.3)*].

8.7 Hepatic Impairment

No dose adjustment is needed in patients with mild to moderate hepatic impairment (Child-Pugh A or B). No data are available in patients with severe hepatic impairment [*see Clinical Pharmacology (12.3)*].

13. NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

The carcinogenic potential of evolocumab was evaluated in a lifetime study conducted in the hamster at dose levels of 10, 30, and 100 mg/kg administered every 2 weeks. There were no evolocumab-related tumors at the highest dose at systemic exposures up to 38- and 15-fold the recommended human doses of 140 mg every 2 weeks and 420 mg once monthly, respectively, based on plasma AUC. The mutagenic potential of evolocumab has not been evaluated; however, monoclonal antibodies are not expected to alter DNA or chromosomes.

There were no adverse effects on fertility (including estrous cycling, sperm analysis, mating performance, and embryonic development) at the highest dose in a fertility and early embryonic developmental toxicology study in hamsters when evolocumab was subcutaneously administered at 10, 30, and 100 mg/kg every 2 weeks. The highest dose tested corresponds to systemic exposures up to 30- and 12-fold the recommended human doses of 140 mg every 2 weeks and 420 mg once monthly, respectively, based on plasma AUC. In addition, there were no adverse evolocumab-related effects on surrogate markers of fertility (reproductive organ histopathology, menstrual cycling, or sperm parameters) in a 6-month chronic toxicology study in sexually mature monkeys subcutaneously administered evolocumab at 3, 30, and 300 mg/kg once weekly. The highest dose tested corresponds to 744- and 300-fold the recommended human doses of 140 mg every 2 weeks and 420 mg once monthly, respectively, based on plasma AUC.

13.2 Animal Toxicology and/or Pharmacology

During a 3-month toxicology study of 10 and 100 mg/kg once every 2 weeks evolocumab in combination with 5 mg/kg once daily rosuvastatin in adult monkeys, there were no effects of evolocumab on the humoral immune response to keyhole limpet hemocyanin (KLH) after 1 to 2 months exposure. The highest dose tested corresponds to exposures 54- and 21-fold higher than the recommended human doses of 140 mg every 2 weeks and 420 mg once monthly, respectively, based on plasma AUC. Similarly, there were no effects of evolocumab on the humoral immune response to KLH (after 3 to 4 months exposure) in a 6-month study in cynomolgus monkeys at dose levels up to 300 mg/kg once weekly evolocumab corresponding to exposures 744- and 300-fold greater than the recommended human doses of 140 mg every 2 weeks and 420 mg once monthly, respectively, based on plasma AUC.

This Brief Summary is based on the REPATHA® Prescribing Information v3, 07/16

AMGEN®

REPATHA® (evolocumab)
Manufactured by: Amgen Inc.
One Amgen Center Drive
Thousand Oaks, California 91320-1799
U.S. License Number 1080
Patent: http://pat.amgen.com/repatha/

For adults with clinical ASCVD on maximally tolerated statin therapy as an adjunct to diet who require additional lowering of LDL-C[1]

REPATHA® THE FIRST AND ONLY PCSK9 INHIBITOR WITH A SINGLE MONTHLY INJECTION[1]*

These events are not part of the official Scientific Sessions 2016 as planned by the AHA committee on Scientific Sessions Program.

Indication

- Repatha® is indicated as an adjunct to diet and maximally tolerated statin therapy for the treatment of adults with clinical atherosclerotic cardiovascular disease (CVD), who require additional lowering of low density lipoprotein cholesterol (LDL-C).
- The effect of Repatha® on cardiovascular morbidity and mortality has not been determined.

Important Safety Information

- Contraindication: Repatha® is contraindicated in patients with a history of a serious hypersensitivity reaction to Repatha®.
- Allergic reactions: Hypersensitivity reactions (e.g. rash, urticaria) have been reported in patients treated with Repatha®, including some that led to discontinuation of therapy. If signs or symptoms of serious allergic reactions occur, discontinue treatment with Repatha®, treat according to the standard of care, and monitor until signs and symptoms resolve.
- Adverse reactions: The most common adverse reactions (> 5% of Repatha®-treated patients and more common than placebo) were: nasopharyngitis, upper respiratory tract infection, influenza, back pain, and injection site reactions.

  In a 52-week trial, adverse reactions led to discontinuation of treatment in 2.2% of Repatha®-treated patients and 1% of placebo-treated patients. The most common adverse reaction that led to Repatha® treatment discontinuation and occurred at a rate greater than placebo was myalgia (0.3% versus 0% for Repatha® and placebo, respectively).
- Adverse reactions from a pool of the 52-week trial and seven 12-week trials: Local injection site reactions occurred in 3.2% and 3.0% of Repatha®-treated and placebo-treated patients, respectively. The most common injection site reactions were erythema, pain, and bruising. The proportions of patients who discontinued treatment due to local injection site reactions in Repatha®-treated and placebo-treated patients were 0.1% and 0%, respectively.

  Allergic reactions occurred in 5.1% and 4.7% of Repatha®-treated and placebo-treated patients, respectively. The most common allergic reactions were rash (1.0% versus 0.5% for Repatha® and placebo, respectively), eczema (0.4% versus 0.2%), erythema (0.4% versus 0.2%), and urticaria (0.4% versus 0.1%).

  Neurocognitive events were reported in less than or equal to 0.2% in Repatha®-treated and placebo-treated patients.

  In a pool of placebo- and active-controlled trials, as well as open-label extension studies that followed them, a total of 1,988 patients treated with Repatha® had at least one LDL-C value < 25 mg/dL. Changes to background lipid-altering therapy were not made in response to low LDL-C values, and Repatha® dosing was not modified or interrupted on this basis. Although adverse consequences of very low LDL-C were not identified in these trials, the long-term effects of very low levels of LDL-C induced by Repatha® are unknown.

  Musculoskeletal adverse reactions were reported in 14.3% of Repatha®-treated patients and 12.8% of placebo-treated patients. The most common adverse reactions that occurred at a rate greater than placebo were back pain (3.2% versus 2.9% for Repatha® and placebo, respectively), arthralgia (2.3% versus 2.2%), and myalgia (2.0% versus 1.8%).
- Immunogenicity: Repatha® is a human monoclonal antibody. As with all therapeutic proteins, there is a potential for immunogenicity with Repatha®.

Please see Brief Summary of full Prescribing Information on previous page.

*Administered subcutaneously.
ASCVD = atherosclerotic cardiovascular disease;
PCSK9 = proprotein convertase subtilisin/kexin type 9.

AMGEN® Cardiovascular

USA-145-033276 08-16

Repatha® (evolocumab) injection 140 mg/mL

BOOTH 3321