ACC.16 Daily
65TH ANNUAL SCIENTIFIC SESSION & EXPO
APRIL 4, 2016 | CHICAGO
MONDAY

EXPO DAILY & MAP INCLUDED INSIDE!

GAUSS-3 Finds Evolocumab Reduces LDL-C More Than Ezetimibe in Statin Intolerant Patients

Among patients with statin intolerance due to muscle pain, taking evolocumab resulted in a significantly greater reduction in low-density lipoprotein cholesterol (LDL-C) compared to ezetimibe, according to the GAUSS-3 study presented yesterday during the joint ACC/ *Journal of the American Medical Association* Late-Breaking Clinical Trial Session and simultaneously published in the *Journal of the American Medical Association*.

The study, led by **Steven Nissen, MD, MACC**, et al., examined 491 patients with uncontrolled LDL-C and a history of muscle pain with two or more types of statins. Patients in the trial had very high levels of LDL-C, averaging more than 120 mg/dL. During phase A of the trial, 245 patients were randomized to receive atorvastatin before placebo and 246 received statin before atorvastatin. A total of 218 patients with confirmed statin intolerance entered phase B of the trial, with 73 randomized to receive ezetimibe plus subcutaneous placebo and 145 received evolocumab plus oral placebo.

See **GAUSS-3,** page 6

"These findings provide **unique insights into the challenging clinical problem** of muscle symptoms in statin treated patients."

Steven Nissen, MD, MACC

Convocation Ceremony to Celebrate Leadership and Achievements

After three days of creating connections, igniting innovation and engaging in disruptive discussion around the latest in cardiovascular research, ACC.16 will come to a close with the time-honored tradition of Convocation.

Presided over by outgoing ACC President **Kim Allan Williams Sr., MD, FACC**, the Convocation Ceremony will usher in the newest class of ACC Fellows and Associates. In addition, recipients of ACC's Distinguished Awards, as well as recipients of ACC/Merck Research Fellowships, the ACC/William F. Keating, Esq. Endowment Award, the William W. Parmley Young Author Awards for the *Journal of the American College of Cardiology (JACC)*, the Young Author Achievement Awards for *JACC* journals, and the ACC Young Investigator Awards, will be recognized. Additionally, Convocation will honor the first class of Leadership Academy graduates.

"Convocation is an important opportunity to recognize outstanding leaders – both new and

See **CONVOCATION,** page 6

Dove Lecture Looks at Impact of Volume to Value Transition in US Health Care

The U.S. continues to move toward a health care system that is focused on quality and value versus the current volume-based fee-for-service model. Passage of the *Medicare Access and CHIP Reauthorization Act of 2015* (MACRA) last April served to further this transition and will undoubtedly have an impact on the practice of medicine.

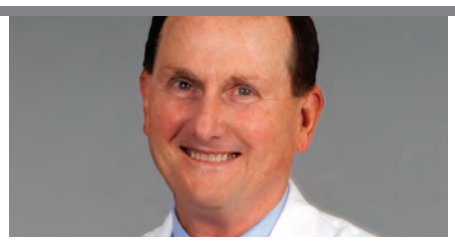
"The transformation from volume-based to value-based purchasing of health care used to be thought of by most of us as 'five years away and always will be,'" said ACC President **Kim Allan Williams Sr., MD, FACC**, during his Opening Showcase Session address. "This is certainly no longer the case."

At the broadest level, MACRA repealed the flawed sustainable growth rate formula used to calculate physician payment and established a definitive framework for moving Medicare from a volume to value-based system – a framework that private payers are already beginning to follow. As with many laws, however, MACRA is written with broad directions that will be implemented through more specific regulation by the federal agencies over the next few years.

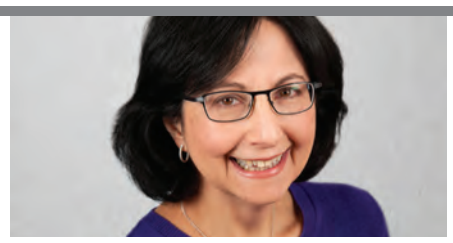
Regardless, Williams noted that practice quality improvement efforts, quality reporting and value-based reimbursement are here to stay, and will undoubtedly be a critical part of provider payment models regardless of how the details unfold. "The ACC is already at the table working to minimize challenges and take advantage of opportunities under the new

See **DOVE LECTURE,** page 24

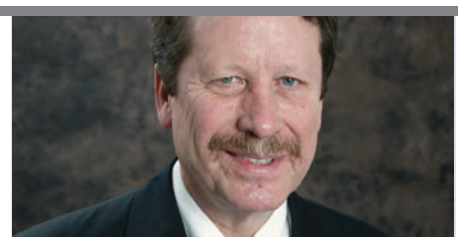
INSIDE



10 **GET TO KNOW CHAZAL**
Richard A. Chazal, MD, FACC, will become the new ACC president during today's Convocation Ceremony.



14 **McNAMARA LECTURE**
Neurological and psychosocial outcomes in congenital heart disease will be explored by Jane Newburger, MD, MPH, FACC, in today's Dan G. McNamara Lecture.



18 **BRAUNWALD LECTURE**
Robert M. Califf, MD, MACC, will present today's Eugene Braunwald Lecture on the future directions in cardiovascular medicine.

MORE

When maximally tolerated statins and diet aren't enough to get patients with clinical ASCVD or HeFH to their LDL-C goal...

ADD PRALUENT® (alirocumab): POWER LIKE NEVER BEFORE...

Larry: Has ASCVD and achieved LDL-C reduction beyond statins[1]*

INDICATIONS AND USAGE

- PRALUENT is a PCSK9 (Proprotein Convertase Subtilisin/Kexin Type 9) inhibitor antibody indicated as adjunct to diet and maximally tolerated statin therapy for the treatment of adults with heterozygous familial hypercholesterolemia or clinical atherosclerotic cardiovascular disease, who require additional lowering of LDL-C
- The effect of PRALUENT on cardiovascular morbidity and mortality has not been determined

IMPORTANT SAFETY INFORMATION

- PRALUENT is contraindicated in patients with a history of a serious hypersensitivity reaction to PRALUENT. Reactions have included hypersensitivity vasculitis and hypersensitivity reactions requiring hospitalization
- Hypersensitivity reactions (e.g., pruritus, rash, urticaria), including some serious events (e.g., hypersensitivity vasculitis and hypersensitivity reactions requiring hospitalization), have been reported with PRALUENT treatment. If signs or symptoms of serious allergic reactions occur, discontinue treatment with PRALUENT, treat according to the standard of care, and monitor until signs and symptoms resolve
- The most commonly occurring adverse reactions (≥5% of patients treated with PRALUENT and occurring more frequently than with placebo) are nasopharyngitis, injection site reactions, and influenza
- Local injection site reactions including erythema/redness, itching, swelling, and pain/tenderness were reported more frequently in patients treated with PRALUENT (7.2% versus 5.1% for PRALUENT and placebo, respectively). Few patients discontinued treatment because of these reactions (0.2% versus 0.4% for PRALUENT and placebo, respectively), but patients receiving PRALUENT had a greater number of injection site reactions, had more reports of associated symptoms, and had reactions of longer average duration than patients receiving placebo
- Neurocognitive events were reported in 0.8% of patients treated with PRALUENT and 0.7% of patients treated with placebo. Confusion or memory impairment were reported more frequently by those treated with PRALUENT (0.2% for each) than in those treated with placebo (<0.1% for each)

*Not actual patients; individual results may vary.

†Patients started on PRALUENT 75 mg Q2W in addition to existing statin therapy: Up-titration to 150 mg Q2W occurred at week 12 in 17% of patients who did not achieve their predefined target LDL-C at week 8.[1]

LDL-C = low-density lipoprotein cholesterol; **ASCVD =** atherosclerotic cardiovascular disease; **HeFH =** heterozygous familial hypercholesterolemia.

...AND MORE POWER IF YOU NEED IT

Stephanie: Has ASCVD and achieved LDL-C reduction beyond statins[1]*

PRALUENT offers 2 doses with 2 levels of efficacy[1]

In COMBO I

44% LDL-C reduction at 24 weeks on top of statins starting with **PRALUENT 75 mg**†

In the LONG TERM Study

58% LDL-C reduction at 24 weeks on top of statins with **PRALUENT 150 mg**

The recommended starting dose is 75 mg every 2 weeks[1]

CLINICAL STUDIES

COMBO I (Study 2) was a multicenter, double-blind, placebo-controlled trial that compared PRALUENT (n=209) with placebo (n=107). Patients were taking maximally tolerated doses of statins with or without other lipid-modifying therapy, and required additional LDL-C reduction. The mean age was 63 years (range 39-87), 34% were women, 82% were Caucasian, 16% were Black, and 11% were Hispanic/Latino. Mean baseline LDL-C was 102 mg/dL. The primary efficacy endpoint, measured at week 24, was the mean percent change in LDL-C from baseline.[1]

LONG TERM trial (Study 1) was a multicenter, double-blind, placebo-controlled trial that compared PRALUENT 150 mg Q2W (n=1553) with placebo (n=788). The average LDL-C at baseline was 122 mg/dL. The primary efficacy endpoint, measured at week 24, was the mean percent change in LDL-C from baseline.[1]

IMPORTANT SAFETY INFORMATION

- Liver-related disorders (primarily related to abnormalities in liver enzymes) were reported in 2.5% of patients treated with PRALUENT and 1.8% of patients treated with placebo, leading to treatment discontinuation in 0.4% and 0.2% of patients, respectively. Increases in serum transaminases to greater than 3 times the upper limit of normal occurred in 1.7% of patients treated with PRALUENT and 1.4% of patients treated with placebo
- The most common adverse reactions leading to treatment discontinuation in patients treated with PRALUENT were allergic reactions (0.6% versus 0.2% for PRALUENT and placebo, respectively) and elevated liver enzymes (0.3% versus <0.1%)
- PRALUENT is a human monoclonal antibody. As with all therapeutic proteins, there is a potential for immunogenicity with PRALUENT

Please see brief summary of Prescribing Information on next page.

Learn more at PraluentHCP.com

Praluent®
(alirocumab) Injection 75mg/mL 150mg/mL

Redefining Possible

PRALUENT® **Rx Only**

(alirocumab) injection, for subcutaneous use

Brief Summary of Prescribing Information

1 INDICATIONS AND USAGE

1.1 Primary Hyperlipidemia

PRALUENT® is indicated as an adjunct to diet and maximally tolerated statin therapy for the treatment of adults with heterozygous familial hypercholesterolemia or clinical atherosclerotic cardiovascular disease, who require additional lowering of LDL-C.

1.2 Limitations of Use

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

4 CONTRAINDICATIONS

PRALUENT is contraindicated in patients with a history of a serious hypersensitivity reaction to PRALUENT. Reactions have included hypersensitivity vasculitis and hypersensitivity reactions requiring hospitalization. [*See Warnings and Precautions (5.1)*]

5 WARNINGS AND PRECAUTIONS

5.1 Allergic Reactions

Hypersensitivity reactions (e.g., pruritus, rash, urticaria), including some serious events (e.g., hypersensitivity vasculitis and hypersensitivity reactions requiring hospitalization), have been reported with PRALUENT treatment. If signs or symptoms of serious allergic reactions occur, discontinue treatment with PRALUENT, treat according to the standard of care, and monitor until signs and symptoms resolve [*see Contraindications (4)*].

6 ADVERSE REACTIONS

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

- 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 practice.

The safety of PRALUENT was evaluated in 9 placebo-controlled trials that included 2476 patients treated with PRALUENT, including 2135 exposed for 6 months and 1999 exposed for more than 1 year (median treatment duration of 65 weeks). The mean age of the population was 59 years, 40% of the population were women, 90% were Caucasians, 4% were Black or African American, and 3% were Asians. At baseline, 37% of patients had a diagnosis of heterozygous familial hypercholesterolemia and 66% had clinical atherosclerotic cardiovascular disease.

Adverse reactions reported in at least 2% of PRALUENT-treated patients, and more frequently than in placebo-treated patients, are shown in Table 1.

Table 1 Adverse Reactions Occurring in Greater Than or Equal to 2% of PRALUENT-Treated Patients and More Frequently Than with Placebo

Adverse Reactions	Placebo (N=1276)	PRALUENT* (N=2476)
Nasopharyngitis	11.1%	11.3%
Injection site reactions†	5.1%	7.2%
Influenza	4.6%	5.7%
Urinary tract infection	4.6%	4.8%
Diarrhea	4.4%	4.7%
Bronchitis	3.8%	4.3%
Myalgia	3.4%	4.2%
Muscle spasms	2.4%	3.1%
Sinusitis	2.7%	3.0%
Cough	2.3%	2.5%
Contusion	1.3%	2.1%
Musculoskeletal pain	1.6%	2.1%

*75 mg every 2 weeks and 150 mg every 2 weeks combined
†includes erythema/redness, itching, swelling, pain/tenderness

Adverse reactions led to discontinuation of treatment in 5.3% of patients treated with PRALUENT and 5.1% of patients treated with placebo. The most common adverse reactions leading to treatment discontinuation in patients treated with PRALUENT were allergic reactions (0.6% versus 0.2% for PRALUENT and placebo, respectively) and elevated liver enzymes (0.3% versus <0.1%).

Local Injection Site Reactions

Local injection site reactions including erythema/redness, itching, swelling, and pain/tenderness were reported more frequently in patients treated with PRALUENT (7.2% versus 5.1% for PRALUENT and placebo, respectively). Few patients discontinued treatment because of these reactions (0.2% versus 0.4% for PRALUENT and placebo, respectively), but patients receiving PRALUENT had a greater number of injection site reactions, had more reports of associated symptoms, and had reactions of longer average duration than patients receiving placebo.

Allergic Reactions

Allergic reactions were reported more frequently in patients treated with PRALUENT than in those treated with placebo (8.6% versus 7.8%). The proportion of patients who discontinued treatment due to allergic reactions was higher among those treated with PRALUENT (0.6% versus 0.2%). Serious allergic reactions, such as hypersensitivity, nummular eczema, and hypersensitivity vasculitis were reported in patients using PRALUENT in controlled clinical trials [*see Warnings and Precautions (5.1)*].

Neurocognitive Events

Neurocognitive events were reported in 0.8% of patients treated with PRALUENT and 0.7% of patients treated with placebo. Confusion or memory impairment were reported more frequently by those treated with PRALUENT (0.2% for each) than in those treated with placebo (<0.1% for each).

Liver Enzyme Abnormalities

Liver-related disorders (primarily related to abnormalities in liver enzymes) were reported in 2.5% of patients treated with PRALUENT and 1.8% of patients treated with placebo, leading to treatment discontinuation in 0.4% and 0.2% of patients, respectively. Increases in serum transaminases to greater than 3 times the upper limit of normal occurred in 1.7% of patients treated with PRALUENT and 1.4% of patients treated with placebo.

Low LDL-C Values

In a pool of both placebo- and active-controlled clinical trials, 796 PRALUENT-treated patients had two consecutive calculated LDL-C values <25 mg/dL, and 288 had two consecutive calculated LDL-C values <15 mg/dL. Changes to background lipid-altering therapy (e.g., maximally tolerated statins) were not made in response to low LDL-C values, and PRALUENT 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 PRALUENT are unknown.

6.2 Immunogenicity

As with all therapeutic proteins, there is a potential for immunogenicity with PRALUENT. In a pool of ten placebo- and active-controlled trials, 4.8% of patients treated with PRALUENT had anti-drug antibodies (ADA) newly detected after initiating treatment as compared with 0.6% of patients treated with control.

Patients who developed ADA had a higher incidence of injection site reactions compared with patients who did not develop ADA (10.2% vs 5.9%).

A total of 1.2% of patients treated with PRALUENT developed neutralizing antibodies (NAb) on at least one occasion as compared with no patients treated with control, and 0.3% of patients both tested positive for NAb and exhibited transient or prolonged loss of efficacy. The long-term consequences of continuing PRALUENT treatment in the presence of persistent NAb are unknown.

Immunogenicity data are highly dependent on the sensitivity and specificity of the assay as well as other factors. Additionally, the observed incidence of antibody positivity in an assay may be influenced by several factors, including sample handling, timing of sample collection, concomitant medications, and underlying disease. For these reasons, comparison of the incidence of antibodies to PRALUENT with the incidence of antibodies to other products may be misleading.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary: There are no available data on use of PRALUENT in pregnant women to inform a drug-associated risk. In animal reproduction studies, there were no effects on embryo-fetal development when rats were subcutaneously administered alirocumab during organogenesis at dose exposures up to 12-fold the exposure at the maximum recommended human dose of 150 mg every two weeks. In monkeys, suppression of the humoral immune response was observed in infant monkeys when alirocumab was dosed during organogenesis to parturition at dose exposures 13-fold the exposure at the maximum recommended human dose of 150 mg every two weeks. No additional effects on pregnancy or neonatal/infant development were observed at dose exposures up to 81-fold the maximum recommended human dose of 150 mg every two weeks. Measurable alirocumab serum concentrations were observed in the infant monkeys at birth at comparable levels to maternal serum, indicating that alirocumab, 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 PRALUENT and possible risks to the fetus before prescribing PRALUENT 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 Sprague Dawley rats, no effects on embryo-fetal development were observed when alirocumab was dosed at up to 75 mg/kg/dose by the subcutaneous route on gestation days 6 and 12 at exposures 12-fold the maximum recommended human dose of 150 mg every two weeks, based on serum AUC.

In cynomolgus monkeys, suppression of the humoral immune response to keyhole limpet hemocyanin (KLH) antigen was observed in infant monkeys at 4 to 6 months of age when alirocumab was dosed during organogenesis to parturition at 15 mg/kg/week and 75 mg/kg/week by the subcutaneous route, corresponding to 13- and 81-fold the human exposure at the maximum recommended human dose of 150 mg every two weeks, based on serum AUC. The lowest dose tested in the monkey resulted in humoral immune suppression; therefore it is unknown if this effect would be observed at clinical exposure. No study designed to challenge the immune system of infant monkeys was conducted. No additional embryo-fetal, prenatal or postnatal effects were observed in infant monkeys, and no maternal effects were observed, when alirocumab was dosed at up to 75 mg/kg/week by the subcutaneous route, corresponding to maternal exposure of 81-fold the exposure at the maximum recommended human dose of 150 mg every two weeks, based on serum AUC.

8.2 Lactation

Risk Summary: There is no information regarding the presence of alirocumab 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 PRALUENT and any potential adverse effects on the breastfed infant from PRALUENT or from the underlying maternal condition. Human IgG is present in human milk, but published data suggest that breastmilk IgG antibodies do not enter the neonatal and infant circulation in substantial amounts.

8.4 Pediatric Use

Safety and efficacy in pediatric patients have not been established.

8.5 Geriatric Use

In controlled studies, 1158 patients treated with PRALUENT were ≥65 years of age and 241 patients treated with PRALUENT were ≥75 years of age. No overall differences in safety or effectiveness were observed between these subjects and younger subjects, 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 for patients with mild or moderately impaired renal function. No data are available in patients with severe renal impairment. [*See Clinical Pharmacology (12.3) in the full prescribing information.*]

8.7 Hepatic Impairment

No dose adjustment is needed for patients with mild or moderate hepatic impairment. No data are available in patients with severe hepatic impairment. [*See Clinical Pharmacology (12.3) in the full prescribing information.*]

Manufactured by:
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A SANOFI COMPANY
U.S. License # 1752
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and Regeneron Pharmaceuticals, Inc. (Tarrytown, NY 10591)

Revised: October 2015
ALI-BPLR-SA-OCT15

SANOFI REGENERON

01/2016 US-PRB-1513 US.ALI.16.01.008

Reference: 1. PRALUENT® (alirocumab) Prescribing Information. Sanofi/Regeneron Pharmaceuticals, 2015.

Today's Schedule:
MONDAY, APRIL 4

Joint ACC/*New England Journal of Medicine* Late-Breaking Clinical Trials
8:00 – 9:15 a.m.
Main Tent (North Hall B1)

James T. Dove Lecture
8:00 – 9:30 a.m.
Room S504

Precision Medicine Intensive
8:00 a.m. – 1:45 p.m.
Grand Ballroom S100a

International Sessions
8:00 a.m. – 1:45 p.m.
Room N427ab and N427cd

Expo Hall Open
9:30 a.m. – 2:00 p.m.

Poster Sessions
9:30 a.m. – 12:30 p.m.
South Hall A

Late-Breaking Clinical Trials
10:45 a.m. – Noon
Main Tent (North Hall B1)

Simulation Session III: Valvular Heart Disease
11:15 a.m. – 12:30 p.m.
Engage@ACC.16 Studio (Expo, #6098)

2016 Dan G. McNamara Lecture
12:30 – 1:45 p.m.
Room S403

Late-Breaking Clinical Trials: Deep Dive II
12:30 – 1:45 p.m.
Room S406a

Best of *JACC* 2015 and the Eugene Braunwald Lecture
12:30 – 1:45 p.m.
Main Tent (North Hall B1)

ACC Journal Club
1:00 – 2:00 p.m.
Engage@ACC.16 Studio (Expo #6098)

Behind the Curtain: Insights Into *JACC* and Submitting Acceptable Papers
2:00 – 3:30 p.m.
Room S101

ACC's Convocation Ceremony
6:30 – 8:00 p.m.
Main Tent (North Hall B1)

Visit the **ACC.16 App** for additional session details.

Stop by the ACC Seal in the **Lounge & Learn Pavilion** and use the hashtag **#ACC16** on social media.

DON'T MISS TODAY'S LATE-BREAKING CLINICAL TRIALS

Joint ACC/*New England Journal of Medicine* Late-Breaking Clinical Trials
- The Resuscitation Outcomes Consortium Amiodarone, Lidocaine or Placebo Study
- FIRE AND ICE
- A Randomized Trial of Rate Control vs. Rhythm Control For AFib After Cardiac Surgery
- LATITUDE-TIMI 60
- CARIN

Session 410
8:00 – 9:15 a.m.
Main Tent (North Hall B1)

Late-Breaking Clinical Trials
- ATMOSPHERE
- IxCell-DCM
- INOVATE-HF
- IMPEDANCE-HF

Session 412
10:45 a.m. – Noon
Main Tent (North Hall B1)

View complete news coverage at *ACC.org/ACC2016*

ACC.16 Daily
MONDAY

April 4, 2016

ACC.16 Daily, the official publication of ACC's 65th Annual Scientific Session, is published by the American College of Cardiology.

American College of Cardiology
2400 N St. NW
Washington, DC 20037

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ACC.org

GAUSS-3, from page 1

In total, 209 (42.6 percent) of patients who took atorvastatin had a recurrence of symptoms, but did not while taking a placebo. During the 24-week treatment period, patients given evolocumab showed a 52.8 percent reduction in LDL-C compared with a 16.7 percent reduction for patients taking ezetimibe. During weeks 22 and 24, patients taking evolocumab showed a 54.5 percent reduction in LDL-C and patients taking ezetimibe showed a reduction of 16.7 percent.

"These findings provide unique insights into the challenging clinical problem of muscle symptoms in statin treated patients," said Nissen. "Evolocumab substantially lowered LDL-C with few patients experiencing muscle symptoms. The study has important implications for both guidelines and regulatory policy, because it provides strong evidence that muscle-related statin intolerance is a real and reproducible phenomenon."

Steven Nissen, MD, MACC, presented results of the GAUSS-3 trial during yesterday's Late-Breaking Clinical Trial Session.

CONVOCATION, from page 1

old – as well as formally acknowledge all of the new Fellows and Associates who have chosen the cardiovascular profession as their life's work," says Williams. "I'm looking forward to congratulating all of the award winners, Leadership Academy graduates, and our newly inducted ACC Fellows and Associates. Their dedication and involvement reaffirm my confidence that the future of our profession, and the future of the ACC, is in good hands."

> "**Convocation** is an important opportunity to **recognize outstanding leaders** – both new and old – as well as **formally acknowledge all of the new Fellows and Associates** who have chosen the cardiovascular profession as their life's work."
>
> *Kim Allan Williams Sr., MD, FACC*

The evening also marks the official installation of new ACC leaders, including the new president. Tonight, Williams will pass the presidential chain to **Richard A. Chazal, MD, FACC** (read more about Chazal on page 10).

"This is an extraordinary opportunity to be an integral part of what I feel is the most functional and focused organization to which I've been exposed," says Chazal. "It is also a humbling experience to follow in the footsteps of talented and devoted leaders. The responsibility of helping member and staff colleagues to work toward our mission to transform cardiovascular care and improve heart health is enormous."

The **65th Annual Convocation Ceremony** will take place today from **6:30 – 8:00 p.m.** in the **Main Tent (North Hall B1)**.

Transcatheter Aortic Valve Replacement (TAVR)

This is TAVR Today

Experience TAVR Today at the Edwards Lifesciences booth #16024

- Go inside the Virtual Valve
- Sign up to receive an educational item to benefit your patients

*PARTNER II Trial high-risk and inoperable transfemoral Edwards SAPIEN 3 valve cohort 30-day results; average hospital stay is 6 days.
†PARTNER II Trial high-risk and inoperable transfemoral SAPIEN 3 valve cohort 30-day results.

See adjacent page for Important Safety Information.

CAUTION: Federal (United States) law restricts these devices to sale by or on the order of a physician.

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IMPORTANT SAFETY INFORMATION

EDWARDS SAPIEN 3 TRANSCATHETER HEART VALVE WITH THE EDWARDS COMMANDER DELIVERY SYSTEM

Indications: The Edwards SAPIEN 3 transcatheter heart valve (THV), model 9600TFX, and accessories are indicated for relief of aortic stenosis in patients with symptomatic heart disease due to severe native calcific aortic stenosis who are judged by a heart team, including a cardiac surgeon, to be at high or greater risk for open surgical therapy (i.e., Society of Thoracic Surgeons operative risk score ≥ 8% or at a ≥ 15% risk of mortality at 30 days).

Contraindications: The THV and delivery systems are contraindicated in patients who cannot tolerate an anticoagulation/antiplatelet regimen or who have active bacterial endocarditis or other active infections.

Warnings: Observation of the pacing lead throughout the procedure is essential to avoid the potential risk of pacing lead perforation. There is an increased risk of stroke in transcatheter aortic valve replacement procedures, as compared to balloon aortic valvuloplasty or other standard treatments. The devices are designed, intended, and distributed for single use only. **Do not resterilize or reuse the devices**. There are no data to support the sterility, nonpyrogenicity, and functionality of the devices after reprocessing. Incorrect sizing of the THV may lead to paravalvular leak, migration, embolization, and/or annular rupture. Accelerated deterioration of the THV may occur in patients with an altered calcium metabolism. Prior to delivery, the THV must remain hydrated at all times and cannot be exposed to solutions other than its shipping storage solution and sterile physiologic rinsing solution. THV leaflets mishandled or damaged during any part of the procedure will require replacement of the THV. Caution should be exercised in implanting a THV in patients with clinically significant coronary artery disease. Patients with pre-existing mitral valve devices should be carefully assessed prior to implantation of the THV to ensure proper THV positioning and deployment. Do not mishandle the delivery system or use it if the packaging or any components are not sterile, have been opened or are damaged (e.g., kinked or stretched), or if the expiration date has elapsed. Use of excessive contrast media may lead to renal failure. Measure the patient's creatinine level prior to the procedure. Contrast media usage should be monitored. Patient injury could occur if the delivery system is not un-flexed prior to removal. Care should be exercised in patients with hypersensitivities to cobalt, nickel, chromium, molybdenum, titanium, manganese, silicon, and/or polymeric materials. The procedure should be conducted under fluoroscopic guidance. Some fluoroscopically guided procedures are associated with a risk of radiation injury to the skin. These injuries may be painful, disfiguring, and long-lasting. THV recipients should be maintained on anticoagulant/antiplatelet therapy, except when contraindicated, as determined by their physician. This device has not been tested for use without anticoagulation.

Precautions: Long-term durability has not been established for the THV. Regular medical follow-up is advised to evaluate THV performance. Glutaraldehyde may cause irritation of the skin, eyes, nose, and throat. Avoid prolonged or repeated exposure to, or breathing of, the solution. To maintain proper valve leaflet coaptation, do not overinflate the deployment balloon. Appropriate antibiotic prophylaxis is recommended post-procedure in patients at risk for prosthetic valve infection and endocarditis. Safety, effectiveness, and durability have not been established for valve-in-valve procedures. Safety and effectiveness have not been established for patients with the following characteristics/comorbidities: non-calcified aortic annulus; severe ventricular dysfunction with ejection fraction < 20%; congenital unicuspid or congenital bicuspid aortic valve; mixed aortic valve disease (aortic stenosis and aortic regurgitation with predominant aortic regurgitation > 3+); pre-existing prosthetic heart valve or prosthetic ring in any position; severe mitral annular calcification (MAC), severe (> 3+) mitral insufficiency, or Gorlin syndrome; blood dyscrasias defined as leukopenia (WBC < 3000 cells/mL), acute anemia (Hb < 9 g/dL), thrombocytopenia (platelet count < 50,000 cells/mL), or history of bleeding diathesis or coagulopathy; hypertrophic cardiomyopathy with or without obstruction (HOCM); echocardiographic evidence of intracardiac mass, thrombus, or vegetation; a known hypersensitivity or contraindication to aspirin, heparin, ticlopidine (Ticlid), or clopidogrel (Plavix), or sensitivity to contrast media, which cannot be adequately premedicated; significant aortic disease, including abdominal aortic or thoracic aneurysm defined as maximal luminal diameter 5 cm or greater, marked tortuosity (hyperacute bend), aortic arch atheroma (especially if thick [> 5 mm], protruding, or ulcerated) or narrowing (especially with calcification and surface irregularities) of the abdominal or thoracic aorta, severe "unfolding" and tortuosity of the thoracic aorta; access characteristics that would preclude safe placement of 14F or 16F Edwards eSheath introducer set, such as severe obstructive calcification, severe tortuosity, or diameter less than 5.5 mm or 6 mm, respectively; or bulky calcified aortic valve leaflets in close proximity to coronary ostia.

Potential Adverse Events: Potential risks associated with the overall procedure including potential access complications associated with standard cardiac catheterization, balloon valvuloplasty, the potential risks of conscious sedation and/or general anesthesia, and the use of angiography: death; stroke/transient ischemic attack, clusters, or neurological deficit; paralysis; permanent disability; respiratory insufficiency or respiratory failure; hemorrhage requiring transfusion or intervention; cardiovascular injury including perforation or dissection of vessels, ventricle, myocardium, or valvular structures that may require intervention; pericardial effusion or cardiac tamponade; embolization including air, calcific valve material, or thrombus; infection including septicemia and endocarditis; heart failure; myocardial infarction; renal insufficiency or renal failure; conduction system defect which may require a permanent pacemaker; arrhythmia; retroperitoneal bleed; AV fistula or pseudoaneurysm; reoperation; ischemia or nerve injury; restenosis; pulmonary edema; pleural effusion; bleeding; anemia; abnormal lab values (including electrolyte imbalance); hypertension or hypotension; allergic reaction to anesthesia, contrast media, or device materials; hematoma; syncope; pain or changes at the access site; exercise intolerance or weakness; inflammation; angina; heart murmur; and fever. Additional potential risks associated with the use of the THV, delivery system, and/or accessories include: cardiac arrest; cardiogenic shock; emergency cardiac surgery; cardiac failure or low cardiac output; coronary flow obstruction/transvalvular flow disturbance; device thrombosis requiring intervention; valve thrombosis; device embolization; device migration or malposition requiring intervention; valve deployment in unintended location; valve stenosis; structural valve deterioration (wear, fracture, calcification, leaflet tear/tearing from the stent posts, leaflet retraction, suture line disruption of components of a prosthetic valve, thickening, stenosis); device degeneration; paravalvular or transvalvular leak; valve regurgitation; hemolysis; device explants; nonstructural dysfunction; mechanical failure of delivery system and/or accessories; and non-emergent reoperation.

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Indications: The Edwards Crimper is indicated for use in preparing the Edwards SAPIEN 3 transcatheter heart valve for implantation.

Contraindications: There are no known contraindications.

Warnings: The devices are designed, intended, and distributed for single use only. **Do not resterilize or reuse the devices**. There is no data to support the sterility, nonpyrogenicity, and functionality of the devices after reprocessing.

Precautions: For special considerations associated with the use of the Edwards Crimper prior to transcatheter heart valve implantation, refer to the Edwards SAPIEN 3 transcatheter heart valve Instructions for Use.

Potential Adverse Events: There are no known potential adverse events associated with the Edwards Crimper.

CAUTION: Federal (United States) law restricts this device to sale by or on the order of a physician.

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Edwards

Study Finds Routine Mammography May be Useful For Heart Disease Screening

Additional Studies Explore STEMI and Stress Risk Factors

Routine mammography may be a useful tool to identify women at risk for heart disease, which may lead to earlier intervention, according to a study presented yesterday and simultaneously published in *JACC: Cardiovascular Imaging*. These findings will appear in the special issue of *JACC: Cardiovascular Imaging* focused on imaging in women publishing today at 1:00 p.m. CT.

Laurie Margolies, MD, and colleagues evaluated 292 women who underwent a digital mammography and non-gated computed tomography (CT) scan to measure breast arterial calcification (BAC) and coronary artery calcification (CAC). BAC was found in 42.5 percent of women and was associated with increased age and 70 percent of these women were also found to have CAC. Half of women under 60 years of age had BAC and younger women with BAC had an 83 percent chance of also having CAC. BAC appeared to be as strong a predictor for cardiovascular risk as show by the Framingham Risk Score and the 2013 Cholesterol Guidelines Pooled Cohort Equations. The overall accuracy of BAC for the presence of CAC was 70 percent, and 63 percent of those with CAC also had BAC.

"This study suggests that we should exploit available data that may provide surrogate information about the likelihood of subclinical coronary disease," says **Jagat Narula, DM, MD, PhD, MACC**, a co-author of the study and editor-in-chief of *JACC: Cardiovascular Imaging*. "In this study, BAC was found to be equally predictive of subclinical atherosclerosis as the standard risk factors. It is important to stress that the data are not driven from the prospective study design and has inherent selection bias. Although we and others have seen a correlation between BAC and CAC, the mechanism of calcification in these vessels is different and the direct link is unresolved. However, when you have the availability of data that shows relationship to subclinical atherosclerosis, one must pay attention to it."

> "This study suggests that we should **exploit available data that may provide surrogate information** about the likelihood of subclinical coronary disease."
>
> *Jagat Narula, DM, MD, PhD, MACC*

A separate study, which will be presented today, looked at risk profiles of patients presenting with ST elevation myocardial infarction (STEMI) and found that patients are getting younger and more obese, despite increased awareness of risk factors. **Amgad G. Mentias, MD**, and colleagues found that among 3,914 patients from 1995 to 2014, the average age of STEMI decreased from 64 to 60 years and the prevalence of obesity increased from 31 to 40 percent. Rates of smoking, diabetes, high blood pressure and chronic obstructive pulmonary disease also increased significantly. Moving forward, the authors stress the importance of prevention, and note that primary care physicians and patients, not just cardiologists, should take ownership of cardiovascular health.

According to another study which will be presented today by **Amorina Ishai, MD**, et al., patients with greater activity in the stress center of the brain may also be at greater risk for cardiovascular events. Positron emission tomography/CT scans from 293 patients were evaluated. Results showed that there was a 14-fold greater risk of cardiovascular events for every unit increase in measured brain stress activity. Over five years of follow-up, 35 percent of the patients in the high-stress center activity group later suffered a cardiovascular event, compared to just 5 percent of the low-stress center activity group. According to the authors, moving forward, future studies are needed to determine if treating stress and reducing the activation of the fear center of the brain may lead to less atherosclerotic inflammation and, ultimately, reduce cardiovascular events.

Don't miss a special issue of *JACC: Cardiovascular Imaging* focused on imaging in women publishing today at 1:00 p.m. CT. Stay tuned to the *ACC in Touch Blog* for an article by **Leslee J. Shaw, PhD, FACC**, associate editor of *JACC: Cardiovascular Imaging*. Follow **@ACCinTouch** and **@JACCJournals** on Twitter and use the hashtag **#JACCIMG** to join the conversations.

Get to Know Your Leaders: Richard A. Chazal, MD, FACC

"MY family really inspires me. They know what they're passionate about and where they're headed," says **Richard A. Chazal, MD, FACC**, president-elect of the ACC, who will take the next step in his own journey as he becomes president of the ACC during today's Convocation Ceremony.

In addition to being a family man, Chazal has practiced in Fort Myers, FL, since 1983, and currently serves the Fort Myers community as senior cardiologist and the medical director of the Heart and Vascular Institute for Lee Memorial Health System, a four-hospital, not-for-profit system. An expert in echocardiography, diagnostic catheterization and coronary computerized tomography angiography, Chazal also serves as courtesy assistant professor of medicine for the University of Florida and clinical assistant professor of medicine for Florida State University.

> **"My family really inspires me.** They know what they're passionate about and where they're headed."
>
> *Richard A. Chazal, MD, FACC*

On the road to the ACC presidency, Chazal has served as councilor, treasurer and president of ACC's Florida Chapter and later was elected chair of the ACC Board of Governors. He has also served as the College's treasurer and chair of the Budget and Finance Committee, spending eight years on the ACC Board of Trustees, seven of which were spent on the executive committee. Nationally, Chazal has served as a member and/or chair of more than 50 College committees and workgroups.

Chazal didn't always know what career he wanted to pursue. Like many undergraduate students, he rotated through a series of majors during his time at the University of Florida, briefly exploring paths like engineering, economics and English, in what he says was an effort to "search for challenge and purpose." His path eventually led him to medicine, and after receiving his undergraduate degree, Chazal went on to complete medical school and internal medicine training at the University of South Florida. "Once in medical school, I was drawn to the hands-on approach, diagnostic challenges and therapeutic opportunities afforded by cardiology."

He credits many mentors for his developing passion for cardiovascular medicine and eventually the value and importance of the ACC. "ACC's Florida Chapter and its exceptional leaders provided impetus to participate," he says. "There was something really motivating about having local access to all of the benefits of the ACC and being able to engage right there in my community."

As Chazal steps into the role of ACC president for the 2016 – 2017 term, he recognizes that it is a responsibility that carries a lot of weight, and will ensure the focus is kept on both the mission and the patient. "As a clinical cardiologist, I remain convinced that the College best achieves its mission by continually focusing on what is the best for our patients, and embedding that in everything that we do as an organization," he says. "The path toward that goal is by empowering members, other physicians and society with the best translation of science to quality care."

"When I step away from work, you can find me with a fly rod in hand on the salt flats or spending time with family, including my two grandchildren, Mae and George – and of course, keeping up with my wife, Linda, who has kept me on my toes for 40 years," says Chazal.

Chazal sees many opportunities for the ACC to better help patients and cardiovascular professionals. "The College's long-range Strategic Plan calls on us to be leaders in aiding our members and others with care transformation, both on the science and delivery system sides," he says. "We also have wonderful opportunities to engage our international members bi-directionally, to both teach and learn, and thus have a positive impact on cardiovascular patients around the world." Chazal adds that the ACC must be a leader in "leveraging the strength of the entire cardiovascular care team." He notes that "it is essential as demographics expand the need for services."

Taking on the role that many of his mentors held affords Chazal the opportunity to pass along his own pieces of wisdom to the next generation of College leaders. "I have two pieces of advice: keep a focus on the patient and participate at the Chapter level; that's where the rubber really meets the road," he explains.

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References: 1. Lewis S. Value of the Terumo RUNTHROUGH® NS Coronary Guidewire. *Diagnostic & Invasive Cardiology*. March/April 2008.
2. RUNTHROUGH® NS Hypercoat™ Bench Testing Report, March 20, 2015.

TERUMO INTERVENTIONAL SYSTEMS

Intensive Session Examines the State of Precision Medicine

The rapidly-evolving field of precision medicine is poised to make a critical impact on cardiovascular care. Today, a special intensive, co-chaired by **Rhonda M. Cooper-DeHoff, PharmD, MS, FACC,** a member of ACC's Cardiovascular Team Section Leadership Council, and **Douglas L. Mann, MD, FACC**, editor-in-chief of *JACC: Basic to Translational Science*, will look at the latest developments in the field, including the U.S. Food and Drug Administration's (FDA's) efforts to lead the way in the science of precision medicine.

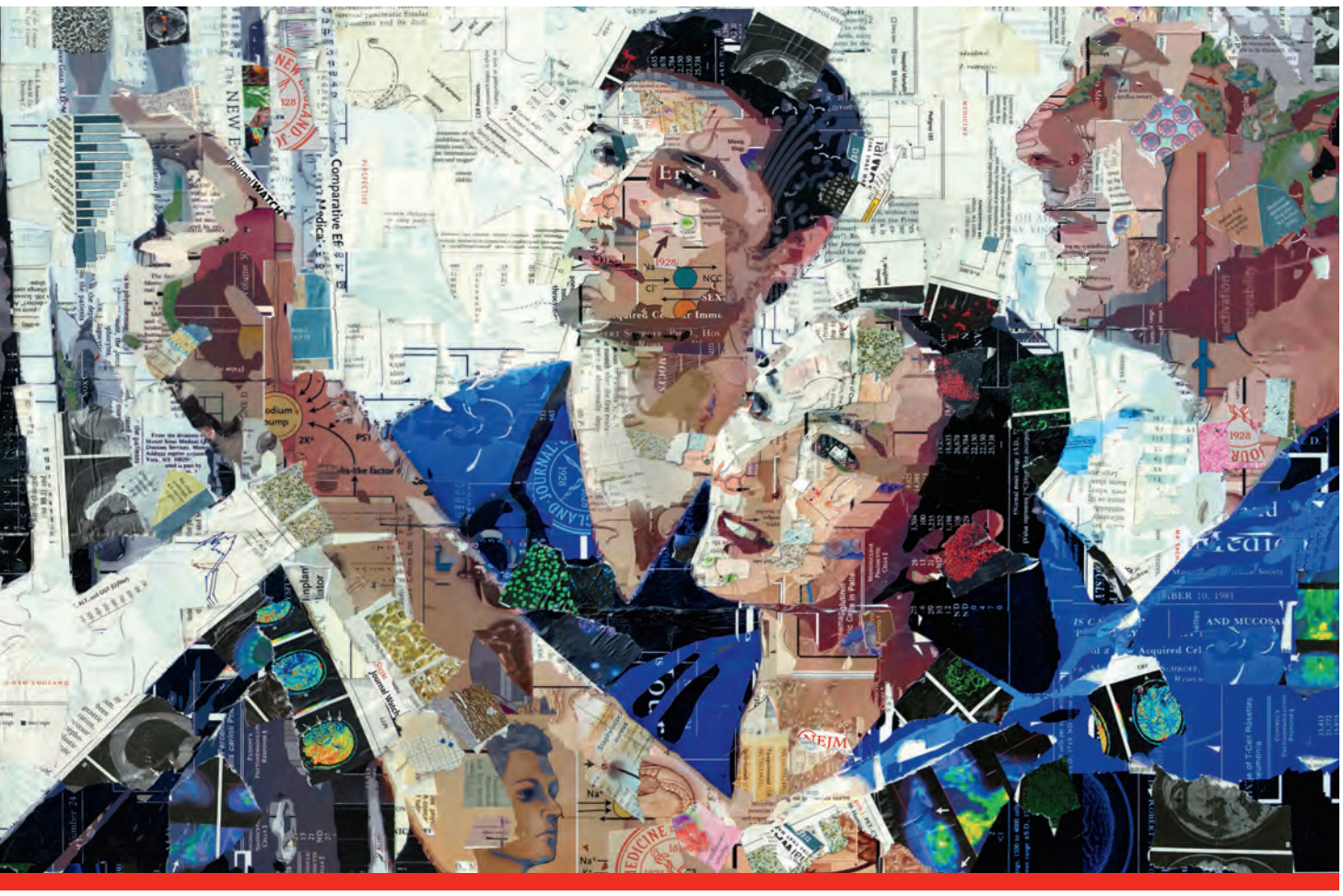
The session, the last of ACC.16's four intensives, will start with a discussion of President Obama's Precision Medicine Initiative by **Sekar Kathiresan, MD**. The initiative, which is funded with a $215 million investment in the President's 2016 budget, will "pioneer a new model of patient-powered research that promises to accelerate biomedical discoveries and provide clinicians with new tools, knowledge, and therapies to select which treatments will work best for which patients," according to the White House.

The **Precision Medicine Intensive** will take place today from **8:00 a.m. to 1:45 p.m.** in **Grand Ballroom s100a**.

For an even closer look at the present and future of precision medicine, FDA Commissioner **Robert M. Califf, MD, MACC,** will present "Precision Medicine: Where Does the FDA Stand?" In December 2015, the FDA launched precisionFDA, a web platform that allows scientists from a number of backgrounds to collaborate on the science behind a method of "reading" DNA known as next-generation.

"Precision medicine is not just a project; it is the way of the future for the FDA, optimizing the use of genetics, genomics, biological measurements, electronic health records, wearable devices and environmental data to define effective foods, drugs, devices and biologics that improve health and treat disease," explains Califf.

Attendees will also hear discussion of genotype testing and dosing of various pharmaceuticals, pharmacogenetics and genomics, and tools for clinical practice, along with several case-based discussions.



Peter Block, MD, FACC, interviews **Anand N. Ganesan, MBBS, PhD,** on the Stepathlon Cardiovascular Health Study presented yesterday and simultaneously published in the *Journal of the American College of Cardiology*. For additional video coverage, visit ***YouTube.com/ACCinTouch.*** Visit ***ACC.org/ACC2016*** for full ACC.16 meeting coverage.

Watch a video interview with **Sherry Ann Brown, MD, PhD,** a fellow in training at the Mayo Clinic, and **Ana Barac, MD, PhD, FACC,** chair of ACC's new Cardio-Oncology Section. For additional videos from the FITs on the GO, visit ***YouTube.com/FITsontheGO.***

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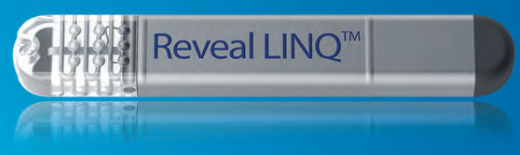

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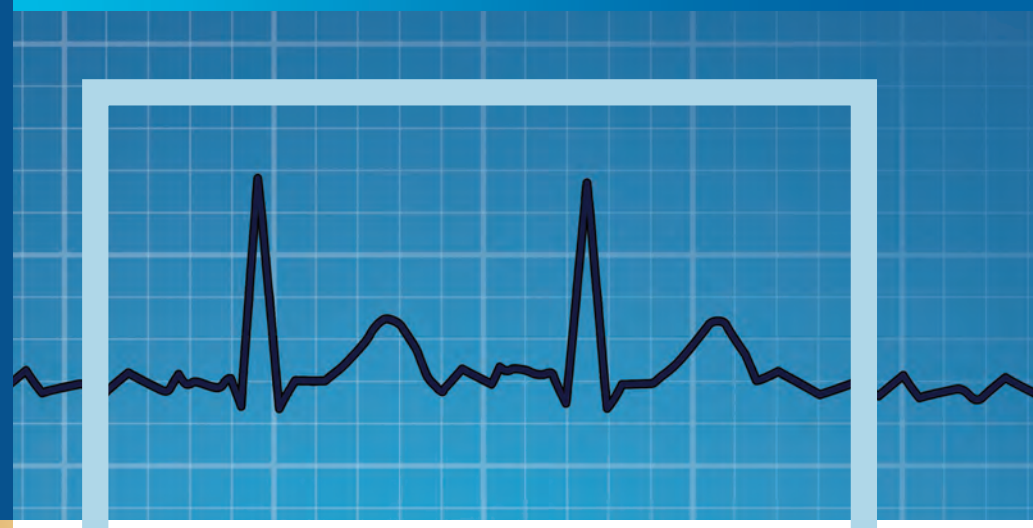

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Reference
[1] Sanna T, Diener HC, Passman RS, et al. Cryptogenic stroke and underlying atrial fibrillation. *N Engl J Med.* June 26, 2014;370(26): 2478-2486.

McNamara Lecture Explores Neurological and Psychosocial Outcomes in CHD

The neurodevelopmental outcomes associated with congenital heart disease (CHD) will be discussed today in the Dan G. McNamara Lecture. The keynote speaker, **Jane Newburger, MD, MPH, FACC**, will review research to date on the causes of neurodevelopmental impairments that occur in some individuals with CHD, considering the typical neurobehavioral signature of findings, including difficulties with attention and executive function.

"Thirty years ago, investigators were just beginning to recognize the scope of the problem of neurodevelopmental impairments in CHD patients," says Newburger who is the associate cardiologist-in-chief and director of the neurodevelopmental program at Boston Children's Hospital in Boston, MA. "In this era, primary repair of CHD in the newborn period was becoming widespread. By the mid-1990s, investigators moved beyond risk factors in the operating room to recognizing the adverse effects of pre- and post-operative hemodynamic instability. "It wasn't until a decade ago that interest began to grow in genetic and in-utero factors."

> "Today, we realize that **neurodevelopmental outcomes are best predicted by innate patient factors like genetics and socioeconomic status**, as well as global morbidity, rather than by specific cardiac surgical management techniques."
>
> *Jane Newburger, MD, MPH, FACC*

Newburger's talk, "Neurodevelopmental Outcomes in CHD: Where Have We Been and Where Are We Going?" will take place from 12:30 to 1:45 p.m. in room S403, and will forecast the translation of her findings across the lifespan of patients with CHD, additionally exploring new directions for intervention to improve the outcomes of children going forward.

"Today, we realize that neurodevelopmental outcomes are best predicted by innate patient factors like genetics and socioeconomic status, as well as global morbidity, rather than by specific cardiac surgical management techniques," she explains.

Newburger predicts that in the next decade there will be tremendous advances in the understanding of both the causes and treatments of neurocognitive comorbidities associated with CHD. "We will uncover novel genetic mutations that are associated with both CHD and neurocognitive disabilities. We will better understand the pathogenesis of in-utero factors related to abnormal fetal circulation. We will have refined therapies to preserve oxygen and substrate delivery to the brains of fetuses with forms of CHD such as hypoplastic left heart syndrome or d-transposition of the great arteries," she says.

Newburger also suggests that in the future, physicians will be able to delineate the relationship between brain structure and function using advanced brain imaging techniques. "By studying brain surface topology, quantitative T1 and T2 mapping, and structural and functional connectivity, we will be able to know so much more about how the brain is impacted in CHD patients." Additionally, Newburger projects that there will be significant findings in how neurocognitive deficits in children and adolescents, including executive dysfunction, affect the later employment, relationships and quality of life in adults with CHD.

Clinical and health psychologist **Adrienne Kovacs, PhD**, of the Oregon Health and Science University Knight Cardiovascular Institute in Portland, will follow Newburger's presentation with a discussion of the psychosocial assessment, treatment and outcomes in adult congenital heart disease (ACHD). "Through increasing collaboration between pediatric and adult providers, we now have a broader perspective of what it means to live with CHD," she says. "In addition to maximizing life expectancy, it is our collective responsibility to help patients with CHD live as rich and full as lives as possible." She adds that there is an increasing recognition that comprehensive care of patients with CHD, regardless of their age, includes attending to their quality of life and psychosocial needs. "Just like children and adolescents with CHD, adult patients face unique psychosocial challenges compared to their healthy peers," says Kovacs. According to Kovacs, some of these challenges include elevated risk of depression and anxiety among adult patients living with CHD.

The **2016 Dan G. McNamara Lecture** will take place today from **12:30 – 1:45 p.m.** in **room S403**.

Opportunity to Review, Pilot CHD Quality Metrics With ACC's ACPC QNet

ACC's Adult Congenital and Pediatric Cardiology (ACPC) Section – which recently celebrated its 10 year anniversary – has developed the ACPC Quality Network (QNet) which gives participants and practices an avenue to review and pilot sets of CHD quality metrics across several domains in pediatric cardiology and CHD. Developed with support from the College's ACPC Quality Working Group, the aggregated data are used in the production of quarterly performance reports that will display facility-level performance across a suite of quality metrics. The College will seek Maintenance of Certification Part IV accreditation for participants and will emphasize collaborative quality improvement activities and engage participants in varied learning settings aimed at identifying opportunities to measure and increase quality care in the CHD community. Learn more at ***ACC.org/ACPC***.

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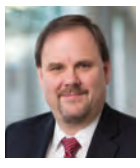
*Source: 2015–2016 US News & World Report Ranking of Top 50 Adult Cardiology & Heart Surgery Hospitals.

WakeMed Health & Hospitals: A Readmissions Success Story

Many hospitals struggle with the increased penalties for excessive readmissions for heart attack and heart failure (HF). Nearly one in five Medicare patients hospitalized with these conditions are readmitted within 30 days of discharge, often for diseases seemingly unrelated to their original diagnosis. ACC's Patient Navigator Program, which helps hospitals establish navigator teams charged with coordinating care for patients diagnosed with acute coronary syndrome, including heart attack and HF, is helping places like WakeMed Health & Hospitals navigate this challenging environment and better control their readmissions.



> "Our **Navigator care teams help minimize transition issues** and **provide personalized support to patients** during their hospital stay and in the weeks following their discharge when they are most vulnerable."
>
> *West Paul, MD, PhD*

The WakeMed Health & Hospitals campuses in Raleigh and Cary, NC, have faced some of the highest readmission penalties in the past. Despite an existing process aimed at reducing readmissions, which included a 24/7 operating cath lab, Code STEMI process, a strong outpatient HF program, cardiovascular education and cardiac rehabilitation referral, WakeMed still incurred a penalty for excessive acute myocardial infarction (AMI) 30-day readmissions.

According to **West Paul, MD, PhD**, WakeMed vice president of Quality and Patient Safety, readmissions can be related to issues ranging from the stresses of the initial hospitalization, to patient fragility at time of discharge, a lack of understanding of discharge instructions, and the inability to carry out discharge instructions. Care coordination throughout the continuum from hospital admission to recovery at home was a critical piece missing from the WakeMed process.

Over the past year, WakeMed has made concerted efforts to minimize the issues related to readmissions through participation in programs like ACC's Patient Navigator Program – and has seen results. The Raleigh campus will not face a penalty in 2016, and WakeMed Cary will only see a 0.34 percent reduction in Medicare payments.

"Once the hospital implemented the Patient Navigator Program's recommendation for multidisciplinary teams to be involved in improving care transitions, this gap in care was reduced," says Paul. "Our Navigator care teams help minimize transition issues and provide personalized support to patients during their hospital stay and in the weeks following their discharge when they are most vulnerable."

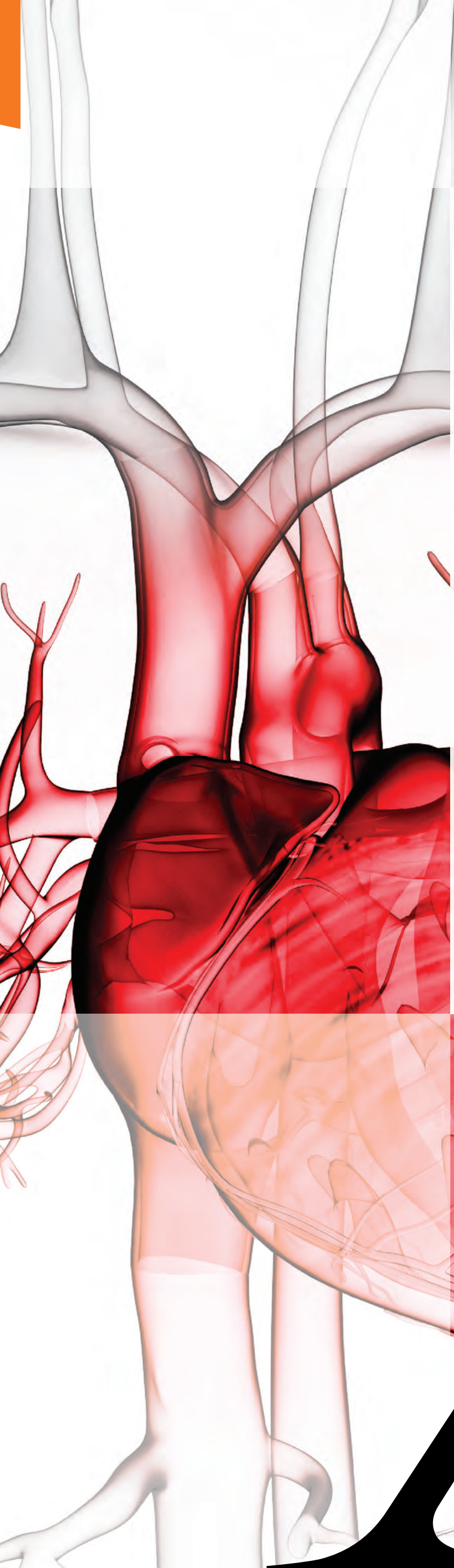
In addition to the development of Navigator teams, site visits by ACC's Patient Navigator Program representative were also crucial to the process. During these visits, WakeMed's Navigator teams were able to review the metrics used to evaluate performance improvement initiatives and ensure priorities were aligned with the overall organizational strategic plan. The hospital also received feedback on opportunities to share work occurring at other pilot sites. Based on this review and feedback, WakeMed was able to identify its target population and implement a patient-centered improvement plan focused on effective care transition.

WakeMed leaders say the focus on patients and families and using the synergy of the individuals, teams and resources within the organization, colleagues outside of the organization and partnerships with professional organizations are all reasons why the Patient Navigator Program works. They note that use of Centers for Medicare and Medicaid Services and NCDR data specific to WakeMed helped to drive change and identify risks to their hospital populations.

Over the past year, the Patient Navigator Program has allowed for an active partnership between WakeMed and the ACC in accomplishing a program for patients that not only exceeds expectations, but can be used as a model by other navigator programs at other sites, notes **Betsy Gaskins-McClaine, RN**, executive champion of the Patient Navigator Program.

"The greatest opportunity of this program is the collaborative partnership journey with our internal team, with the ACC and with the network of pilot hospitals to innovate the heart patient and family journey to better health," she adds.

Don't miss the sessions **"30 Day Readmissions"** today from **8:00 – 9:30 a.m.** in **room S406b**, and **"Hospital to Home: Risk and Opportunity"** today from **3:45 – 5:15 p.m.** in **room S401**. Visit ***CVQuality.ACC.org/PatientNavigator*** for more information about ACC's Patient Navigator program.



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From Academia to Health Policy:
Translational Cardiologist Becomes FDA Commissioner

Califf to Present Today's Eugene Braunwald Lecture on Future Directions in CV Medicine

Robert M. Califf, MD, MACC, became the commissioner of the U.S. Food and Drug Administration (FDA) in late February. Prior to this position, he served as the FDA deputy commissioner for medical products and tobacco. He has also served as the vice chancellor of clinical and translational research, director of Duke University's Translational Medicine Institute and a professor of medicine in the Division of Cardiology at Duke's Medical Center.

What kind of impact do you hope to have at the FDA?

The FDA is an amazing place, one served by talented and dedicated people. It's built on a system designed to make decisions that protect the health of Americans, but it also actively promotes health by working with patients, industry and academia to improve the ecosystem of technology development. Every week, the FDA makes hundreds of decisions that affect the well-being of American citizens and people around the world. My hope is that I can make a difference in several key areas.

I want to promote synergy across the FDA in dealing with key scientific themes that affect the whole organization. These themes cover a lot of ground: for instance, accelerating outcomes and endpoint measurement including biomarkers, surrogate endpoints, patient-reported and patient-derived data, and clinical outcomes. I am also committed to supporting efforts aimed at improving the generation of scientific evidence across a spectrum that encompasses preclinical systems biology, human phenotyping, efficient clinical trials, and "big data" drawn from "'real-world" environments and care settings. In addition, we need to consider patient-centered technology development, the globalization of biomedical research, and how scientific research interfaces with academia, other federal agencies and industry. These are broad categories, and significant work is already underway in all of these areas. My hope is that I will be able to further accelerate progress on these critical, cross-cutting issues.

In addition, I want to help the FDA team to work with Congress, patient groups and other stakeholders on pending legislation aimed at improving the environment for biomedical innovation in the U.S. We also have major user fee negotiations over the next two years involving the pharmaceutical and medical device industries. This process can lead to major innovations with the potential to advance the appropriate development and dissemination of evidence about drugs, biologics therapeutics and medical devices.

"In my new role with the FDA, I am working with colleagues from the FDA and other sister agencies within the U.S. Department of Health and Human Services to devise and implement policies that improve the system for everyone," says Califf.

What inspired you to move from clinical research in the academic setting to a policy-based leadership role?

I've always admired the work done by the FDA and have enjoyed the privilege of engaging in many policy discussions with key FDA leaders. The way in which the FDA deals fairly with individual applications concerning specific technologies and medical products is in my view outstanding and should serve as a model for other organizations. My hope is that I can contribute to small improvements that, because of the FDA's central role in the larger system, will have a big impact on science, technology development and, ultimately, human health.

From my perspective as a researcher, working to answer scientific questions through clinical research is a fun, interesting and immensely rewarding experience. But at the same time, I believe that many aspects of the current clinical research enterprise are suboptimal from both process and outcome perspectives. In my new role with the FDA, I am working with colleagues from the FDA and other sister agencies within the U.S. Department of Health and Human Services to devise and implement policies that improve the system for everyone. When my work with the FDA is done, I will certainly return to clinical research and clinical practice – having the opportunity to care for patients and to improve the knowledge base that informs that care is a real privilege.

What would you say are the biggest challenges in your role as Commissioner?

These are the key challenges that I see: first, the FDA, which has a culture marked by an extraordinary dedication to fairness, must make decisions, and often these decisions make someone unhappy. This situation is unavoidable, but a good challenge for the FDA is to do a better job of explaining its deliberations in ways that allow its many constituents to understand the factors driving these decisions. Second, the FDA is at the fulcrum of a scientific revolution that is making it possible to seriously envision treatments and even cures for diseases in ways that were simply not possible in the past. The key scientific themes provide a framework to position the FDA as a reservoir of knowledge – one that provides guidance and insight to help industry, academia and patient groups take advantage of innovation and discovery to produce more effective drugs, medical devices and biologic therapeutics. Third, there is never enough time! I really believe that we are on the verge of a major acceleration in the arena of science applied to human well-being. We just need to figure out how to "connect the dots," but this will involve a continuous evaluation of priorities. Fortunately, I have a great group of colleagues to help identify where my energy would be best directed.

Califf will present today's Eugene Braunwald Lecture during the session **"Best of *JACC* 2015: Practice Changing Research Published in the *JACC* Journals and the Eugene Braunwald Lecture on Future Directions in Cardiovascular Medicine"** from **12:30 – 1:45 p.m.** in the **Main Tent (North Hall B1)**.

Entresto™
(sacubitril/valsartan) tablets
24/26mg • 49/51mg • 97/103mg

Use ENTRESTO™ in place of ACEis and ARBs for HF*r*EF patients[1]

ENTRESTO was studied in the largest HF trial ever conducted[2]

- Trial stopped early due to finding of significantly reduced risk of CV death and the primary end point being met[3]

ENTRESTO has been proven superior to enalapril, a current standard-of-care[4] medication[1]

- Superiority vs enalapril, a standard-of-care ACEi therapy, across a range of NYHA class II–IV patients with chronic HF and reduced ejection fraction

20% REDUCED RISK OF CV DEATH OR FIRST HF HOSPITALIZATION vs ENALAPRIL[1]

P<0.0001 HR (95% CI): 0.80 (0.73, 0.87)

4.7% ABSOLUTE RISK REDUCTION[1]

REDEFINE EXPECTATIONS IN HEART FAILURE

INDICATION

ENTRESTO is indicated to reduce the risk of cardiovascular death and hospitalization for heart failure in patients with chronic heart failure (NYHA Class II-IV) and reduced ejection fraction.

ENTRESTO is usually administered in conjunction with other heart failure therapies, in place of an ACE inhibitor or other ARB.

IMPORTANT SAFETY INFORMATION

WARNING: FETAL TOXICITY
- **When pregnancy is detected, discontinue ENTRESTO as soon as possible**
- **Drugs that act directly on the renin-angiotensin system can cause injury and death to the developing fetus**

ENTRESTO is contraindicated in patients with hypersensitivity to any component. ENTRESTO is contraindicated in patients with a history of angioedema related to previous angiotensin-converting enzyme (ACE) inhibitor or angiotensin receptor blocker (ARB) therapy.

ENTRESTO is contraindicated with concomitant use of ACE inhibitors. Do not administer within 36 hours of switching from or to an ACE inhibitor. ENTRESTO is contraindicated with concomitant use of aliskiren in patients with diabetes.

Angioedema: ENTRESTO may cause angioedema. Angioedema associated with laryngeal edema may be fatal. ENTRESTO has been associated with a higher rate of angioedema in Black patients and in patients with a prior history of angioedema. If angioedema occurs, discontinue ENTRESTO immediately, provide appropriate therapy, and monitor for airway compromise. ENTRESTO must not be re-administered.

Hypotension: ENTRESTO lowers blood pressure and may cause symptomatic hypotension. Patients with an activated renin-angiotensin system, such as volume- and/or salt-depleted patients (e.g., those being treated with high doses of diuretics), are at greater risk. Correct volume or salt depletion prior to administration of ENTRESTO or start at a lower dose. If hypotension persists despite dose adjustment of diuretics, concomitant antihypertensive drugs, and treatment of other causes of hypotension (e.g., hypovolemia) reduce the dosage or temporarily discontinue ENTRESTO. Permanent discontinuation of therapy is usually not required.

Impaired Renal Function: Decreases in renal function may be anticipated in susceptible individuals treated with ENTRESTO. In patients whose renal function depends upon the activity of the renin-angiotensin-aldosterone system (e.g., patients with severe congestive heart failure), treatment with ACE inhibitors and angiotensin receptor antagonists has been associated with oliguria, progressive azotemia and, rarely, acute renal failure and death. Closely monitor serum creatinine, and down-titrate or interrupt ENTRESTO in patients who develop a clinically significant decrease in renal function.

ENTRESTO may increase blood urea and serum creatinine levels in patients with bilateral or unilateral renal artery stenosis. In patients with renal artery stenosis, monitor renal function. Avoid use with aliskiren in patients with renal impairment (eGFR <60 mL/min/1.73 m^2).

In patients who are elderly, volume-depleted (including those on diuretic therapy), or with compromised renal function, concomitant use of non-steroidal anti-inflammatory drugs (NSAIDs), including COX-2 inhibitors, with ENTRESTO may result in worsening of renal function, including possible acute renal failure. These effects are usually reversible. Monitor renal function periodically.

Hyperkalemia: Hyperkalemia may occur with ENTRESTO. Monitor serum potassium periodically and treat appropriately, especially in patients with risk factors for hyperkalemia such as severe renal impairment, diabetes, hypoaldosteronism, or a high potassium diet. Dosage reduction or interruption of ENTRESTO may be required.

Concomitant use of potassium-sparing diuretics (e.g., spironolactone, triamterene, amiloride), potassium supplements, or salt substitutes containing potassium may lead to increases in serum potassium.

ARBs: Avoid use of ENTRESTO with an ARB, because ENTRESTO contains the angiotensin II receptor blocker valsartan.

Lithium: Increases in serum lithium concentrations and lithium toxicity have been reported during concomitant administration of lithium with angiotensin II receptor antagonists. Monitor serum lithium levels during concomitant use with ENTRESTO.

Common Adverse Events: In a clinical trial, the most commonly observed adverse events with ENTRESTO vs enalapril, occurring at a frequency of at least 5% in either group, were hypotension (18%, 12%), hyperkalemia (12%, 14%), cough (9%, 13%) dizziness (6%, 5%) and renal failure/acute renal failure (5%, 5%).

Please see Brief Summary of Prescribing Information, including Boxed WARNING, on following pages.

STUDY DESIGN: PARADIGM-HF was a multinational, randomized, double-blind trial comparing ENTRESTO to enalapril in 8442 symptomatic (NYHA class II–IV) adult HF*r*EF patients (left ventricular ejection fraction ≤40%). After discontinuing their existing ACEi or ARB therapy, patients entered sequential single-blind run-in periods during which they received enalapril 10 mg twice daily, followed by ENTRESTO 100 mg (49/51 mg) twice daily, increasing to 200 mg (97/103 mg) twice daily. Patients were then randomized to receive either ENTRESTO 200 mg (97/103 mg) (n=4209) twice daily or enalapril 10 mg (n=4233) twice daily. The median follow-up duration was 27 months, and patients were treated for up to 4.3 years. The primary end point was the first event in the composite of CV death or first HF hospitalization.[1]

ACEi = angiotensin-converting enzyme inhibitor; ARB = angiotensin II receptor blocker; HF*r*EF = heart failure with reduced ejection fraction; CV = cardiovascular; NYHA = New York Heart Association; HF=heart failure.

For more information, visit **EntrestoHCP.com**

References: 1. ENTRESTO [prescribing information]. East Hanover, NJ: Novartis Pharmaceuticals Corp; August 2015. **2.** McMurray JJV, Packer M, Desai AS, et al. Baseline characteristics and treatment of patients in Prospective comparison of ARNI with ACEI to Determine Impact on Global Mortality and morbidity in Heart Failure trial (PARADIGM-HF). *Eur J Heart Fail*. 2014;16(7):817-825. **3.** McMurray JJV, Packer M, Desai AS, et al. Angiotensin–neprilysin inhibition versus enalapril in heart failure. *N Engl J Med*. 2014;371(11):993-1004. **4.** Yancy CW, Jessup M, Bozkurt B, et al. 2013 ACCF/AHA guideline for the management of heart failure: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *Circulation*. 2013;128(16):e240-e327.

NOVARTIS PHARMACEUTICALS

Novartis Pharmaceuticals Corporation
East Hanover, New Jersey 07936-1080 12/15 ETR-1321798

ENTRESTO™ (sacubitril and valsartan) tablets, for oral use
Initial U.S. Approval: 2015

BRIEF SUMMARY: Please see package insert for full prescribing information.

WARNING: FETAL TOXICITY
- **When pregnancy is detected, discontinue ENTRESTO as soon as possible (5.1)**
- **Drugs that act directly on the renin-angiotensin system can cause injury and death to the developing fetus (5.1)**

1 INDICATIONS AND USAGE

1.1 Heart Failure

ENTRESTO is indicated to reduce the risk of cardiovascular death and hospitalization for heart failure in patients with chronic heart failure (NYHA Class II-IV) and reduced ejection fraction.

ENTRESTO is usually administered in conjunction with other heart failure therapies, in place of an ACE inhibitor or other ARB.

4 CONTRAINDICATIONS

ENTRESTO is contraindicated:
- in patients with hypersensitivity to any component
- in patients with a history of angioedema related to previous ACE inhibitor or ARB therapy *[see Warnings and Precautions (5.2)]*
- with concomitant use of ACE inhibitors. Do not administer within 36 hours of switching from or to an ACE inhibitor *[see Drug Interactions (7.1)]*
- with concomitant use of aliskiren in patients with diabetes *[see Drug Interactions (7.1)]*.

5 WARNINGS AND PRECAUTIONS

5.1 Fetal Toxicity

ENTRESTO can cause fetal harm when administered to a pregnant woman. Use of drugs that act on the renin-angiotensin system during the second and third trimesters of pregnancy reduces fetal renal function and increases fetal and neonatal morbidity and death. When pregnancy is detected, consider alternative drug treatment and discontinue ENTRESTO. However, if there is no appropriate alternative to therapy with drugs affecting the renin-angiotensin system, and if the drug is considered lifesaving for the mother, advise a pregnant woman of the potential risk to the fetus *[see Use in Specific Populations (8.1)]*.

5.2 Angioedema

ENTRESTO may cause angioedema. In the double-blind period of PARADIGM-HF, 0.5% of patients treated with ENTRESTO and 0.2% of patients treated with enalapril had angioedema *[see Adverse Reactions (6.1)]*. If angioedema occurs, discontinue ENTRESTO immediately, provide appropriate therapy, and monitor for airway compromise. ENTRESTO must not be re-administered. In cases of confirmed angioedema where swelling has been confined to the face and lips, the condition has generally resolved without treatment, although antihistamines have been useful in relieving symptoms.

Angioedema associated with laryngeal edema may be fatal. Where there is involvement of the tongue, glottis or larynx, likely to cause airway obstruction, administer appropriate therapy, e.g., subcutaneous epinephrine/adrenaline solution 1:1000 (0.3 mL to 0.5 mL) and take measures necessary to ensure maintenance of a patent airway.

ENTRESTO has been associated with a higher rate of angioedema in Black than in non-Black patients.

Patients with a prior history of angioedema may be at increased risk of angioedema with ENTRESTO *[see Adverse Reactions (6.1)]*. ENTRESTO should not be used in patients with a known history of angioedema related to previous ACE inhibitor or ARB therapy *[see Contraindications (4)]*.

5.3 Hypotension

ENTRESTO lowers blood pressure and may cause symptomatic hypotension. Patients with an activated renin-angiotensin system, such as volume- and/or salt-depleted patients (e.g., those being treated with high doses of diuretics), are at greater risk. In the double-blind period of PARADIGM-HF, 18% of patients treated with ENTRESTO and 12% of patients treated with enalapril reported hypotension as an adverse event *[see Adverse Reactions (6.1)]*, with hypotension reported as a serious adverse event in approximately 1.5% of patients in both treatment arms. Correct volume or salt depletion prior to administration of ENTRESTO or start at a lower dose. If hypotension occurs, consider dose adjustment of diuretics, concomitant antihypertensive drugs, and treatment of other causes of hypotension (e.g., hypovolemia). If hypotension persists despite such measures, reduce the dosage or temporarily discontinue ENTRESTO. Permanent discontinuation of therapy is usually not required.

5.4 Impaired Renal Function

As a consequence of inhibiting the renin-angiotensin-aldosterone system (RAAS), decreases in renal function may be anticipated in susceptible individuals treated with ENTRESTO. In the double-blind period of PARADIGM-HF, 5% of patients in both the ENTRESTO and enalapril groups reported renal failure as an adverse event *[see Adverse Reactions (6.1)]*. In patients whose renal function depends upon the activity of the renin-angiotensin-aldosterone system (e.g., patients with severe congestive heart failure), treatment with ACE inhibitors and angiotensin receptor antagonists has been associated with oliguria, progressive azotemia and, rarely, acute renal failure and death. Closely monitor serum creatinine, and down-titrate or interrupt ENTRESTO in patients who develop a clinically significant decrease in renal function *[see Use in Specific Populations (8.7) and Clinical Pharmacology (12.3) in the full prescribing information]*.

As with all drugs that affect the RAAS, ENTRESTO may increase blood urea and serum creatinine levels in patients with bilateral or unilateral renal artery stenosis. In patients with renal artery stenosis, monitor renal function.

5.5 Hyperkalemia

Through its actions on the RAAS, hyperkalemia may occur with ENTRESTO. In the double-blind period of PARADIGM-HF, 12% of patients treated with ENTRESTO and 14% of patients treated with enalapril reported hyperkalemia as an adverse event *[see Adverse Reactions (6.1)]*. Monitor serum potassium periodically and treat appropriately, especially in patients with risk factors for hyperkalemia such as severe renal impairment, diabetes, hypoaldosteronism, or a high potassium diet. Dosage reduction or interruption of ENTRESTO may be required *[see Dosage and Administration (2.1) in the full prescribing information]*.

6 ADVERSE REACTIONS

Clinically significant adverse reactions that appear in other sections of the labeling include:
- Angioedema *[see Warnings and Precautions (5.2)]*
- Hypotension *[see Warnings and Precautions (5.3)]*
- Impaired Renal Function *[see Warnings and Precautions (5.4)]*
- Hyperkalemia *[see Warnings and Precautions (5.5)]*

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 practice.

In the PARADIGM-HF trial, subjects were required to complete sequential enalapril and ENTRESTO run-in periods of (median) 15 and 29 days, respectively, prior to entering the randomized double-blind period comparing ENTRESTO and enalapril. During the enalapril run-in period, 1,102 patients (10.5%) were permanently discontinued from the study, 5.6% because of an adverse event, most commonly renal dysfunction (1.7%), hyperkalemia (1.7%) and hypotension (1.4%). During the ENTRESTO run-in period, an additional 10.4% of patients permanently discontinued treatment, 5.9% because of an adverse event, most commonly renal dysfunction (1.8%), hypotension (1.7%) and hyperkalemia (1.3%). Because of this run-in design, the adverse reaction rates described below are lower than expected in practice.

In the double-blind period, safety was evaluated in 4,203 patients treated with ENTRESTO and 4,229 treated with enalapril. In PARADIGM-HF, patients randomized to ENTRESTO received treatment for up to 4.3 years, with a median duration of exposure of 24 months; 3,271 patients were treated for more than one year. Discontinuation of therapy because of an adverse event during the double-blind period occurred in 450 (10.7%) of ENTRESTO treated patients and 516 (12.2%) of patients receiving enalapril.

Adverse reactions occurring at an incidence of ≥5% in patients who were treated with ENTRESTO in the double-blind period are shown in Table 1.

Table 1: Adverse Reactions Reported in ≥5% of Patients Treated with ENTRESTO in the Double-Blind Period

	ENTRESTO (n = 4,203) %	Enalapril (n = 4,229) %
Hypotension	18	12
Hyperkalemia	12	14
Cough	9	13
Dizziness	6	5
Renal failure/acute renal failure	5	5

In the PARADIGM-HF trial, the incidence of angioedema was 0.1% in both the enalapril and ENTRESTO run-in periods. In the double-blind period, the incidence of angioedema was higher in patients treated with ENTRESTO than enalapril (0.5% and 0.2%, respectively). The incidence of angioedema in Black patients was 2.4% with ENTRESTO and 0.5% with enalapril *[see Warnings and Precautions (5.2)]*.

Orthostasis was reported in 2.1% of patients treated with ENTRESTO compared to 1.1% of patients treated with enalapril during the double-blind period of PARADIGM-HF. Falls were reported in 1.9% of patients treated with ENTRESTO compared to 1.3% of patients treated with enalapril.

Laboratory Abnormalities

Hemoglobin and Hematocrit

Decreases in hemoglobin/hematocrit of >20% were observed in approximately 5% of both ENTRESTO- and enalapril-treated patients in the double-blind period in PARADIGM-HF.

Serum Creatinine

Increases in serum creatinine of >50% were observed in 1.4% of patients in the enalapril run-in period and 2.2% of patients in the ENTRESTO run-in period. During the double-blind period, approximately 16% of both ENTRESTO- and enalapril-treated patients had increases in serum creatinine of >50%.

Serum Potassium

Potassium concentrations >5.5 mEq/L were observed in approximately 4% of patients in both the enalapril and ENTRESTO run-in periods. During the double-blind period, approximately 16% of both ENTRESTO- and enalapril-treated patients had potassium concentrations >5.5 mEq/L.

7 DRUG INTERACTIONS

7.1 Dual Blockade of the Renin-Angiotensin-Aldosterone System

Concomitant use of ENTRESTO with an ACE inhibitor is contraindicated because of the increased risk of angioedema *[see Contraindications (4)]*.

Avoid use of ENTRESTO with an ARB, because ENTRESTO contains the angiotensin II receptor blocker valsartan.

The concomitant use of ENTRESTO with aliskiren is contraindicated in patients with diabetes *[see Contraindications (4)]*. Avoid use with aliskiren in patients with renal impairment (eGFR <60 mL/min/1.73 m²).

7.2 Potassium-Sparing Diuretics

As with other drugs that block angiotensin II or its effects, concomitant use of potassium-sparing diuretics (e.g., spironolactone, triamterene, amiloride), potassium supplements, or salt substitutes containing potassium may lead to increases in serum potassium *[see Warnings and Precautions (5.5)]*.

7.3 Nonsteroidal Anti-Inflammatory Drugs (NSAIDs) Including Selective Cyclooxygenase-2 Inhibitors (COX-2 Inhibitors)

In patients who are elderly, volume-depleted (including those on diuretic therapy), or with compromised renal function, concomitant use of NSAIDs, including COX-2 inhibitors, with ENTRESTO may result in worsening of renal function, including possible acute renal failure. These effects are usually reversible. Monitor renal function periodically.

7.4 Lithium

Increases in serum lithium concentrations and lithium toxicity have been reported during concomitant administration of lithium with angiotensin II receptor antagonists. Monitor serum lithium levels during concomitant use with ENTRESTO.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

ENTRESTO can cause fetal harm when administered to a pregnant woman. Use of drugs that act on the renin-angiotensin system during the second and third trimesters of pregnancy reduces fetal renal function and increases fetal and neonatal morbidity and death. Most epidemiologic studies examining fetal abnormalities after exposure to antihypertensive use in the first trimester have not distinguished drugs affecting the renin-angiotensin system from other antihypertensive agents. In animal reproduction studies, ENTRESTO treatment during organogenesis resulted in increased embryo-fetal lethality in rats and rabbits and teratogenicity in rabbits. When pregnancy is detected, consider alternative drug treatment and discontinue ENTRESTO. However, if there is no appropriate alternative to therapy with drugs affecting the renin-angiotensin system, and if the drug is considered lifesaving for the mother, advise a pregnant woman of the potential risk to the fetus.

The estimated background risk of major birth defects and miscarriage for the indicated population is unknown. 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.

Clinical Considerations

Fetal/Neonatal Adverse Reactions

Oligohydramnios in pregnant women who use drugs affecting the renin-angiotensin system in the second and third trimesters of pregnancy can result in the following: reduced fetal renal function leading to anuria and renal failure, fetal lung hypoplasia, skeletal deformations, including skull hypoplasia, hypotension, and death.

Perform serial ultrasound examinations to assess the intra-amniotic environment. Fetal testing may be appropriate, based on the week of gestation. Patients and physicians should be aware, however, that oligohydramnios may not appear until after the fetus has sustained irreversible injury. If oligohydramnios is observed, consider alternative drug treatment. Closely observe neonates with histories of *in utero* exposure to ENTRESTO for hypotension, oliguria, and hyperkalemia. In neonates with a history of *in utero* exposure to ENTRESTO, if oliguria or hypotension occurs, support blood pressure and renal perfusion. Exchange transfusions or dialysis may be required as a means of reversing hypotension and replacing renal function.

Conundrums in CVD:
Deciphering the Role of Race/Ethnicity

By Keith Ferdinand, MD, FACC

Although health, life expectancy and overall cardiovascular care has improved dramatically for all Americans over the last several decades, the distribution of benefits has not occurred equably. There remains a persistent and disturbing mortality gap between black and white Americans which has been noted since the 1960s.

A major component of this disparity in cardiovascular disease morbidity and mortality in African Americans is due to higher risk of hypertension and heart failure, along with a unique, perhaps higher risk related to Lipoprotein(a) (Lp(a)). Cardiovascular morbidity and mortality needs to be addressed since atherosclerotic cardiovascular disease and stroke are the leading causes of death for all populations, but account for the largest proportion of inequality in life expectancy between blacks and whites.

> "Today, **a joint symposium of the ACC and the Association of Black Cardiologists** will be an opportunity to highlight contemporary concepts about the basis of and **potential solutions for cardiovascular disease disparities.**"
>
> *Keith Ferdinand, MD, FACC*

Today, a joint symposium of the ACC and the Association of Black Cardiologists will be an opportunity to highlight contemporary concepts about the basis of and potential solutions for cardiovascular disease disparities. Recognizing that race, at best, is a crude proxy for genetics, the important discussion of the impact of genomics on heart failure and cardiovascular disease in blacks will be presented by **Michael R. Bristow, MD, PhD, FACC**. Bristow will advocate for better understanding of the association between race and response to specific pharmacotherapy in heart failure. As a counterpoint, **Ivor J. Benjamin, MD, FACC**, will provide contemporary evidence on the presence or absence of underlying genetic factors. He will highlight some of the late-breaking concepts in genomics and how we can better understand which patients are at risk for cardiovascular disease based on inherited characteristics that go beyond the blunt assessment of race, which is not a scientific category at all.

Unique aspects of cardiovascular risk in blacks include high prevalence and severity of hypertension. **Kenneth A. Jamerson, MD**, will present current concepts on best approaches to hypertension in this high-risk population. He will give information on best practices or concepts in approaching high-risk African Americans with hypertension, and perhaps critique some of our current understanding in an effort to better control blood pressure, a potent risk factor, especially in the U.S. black population.

While awaiting interim results from cardiovascular outcomes trials, proprotein convertase subtilisin/kexin 9 (PCSK9) inhibition remains a potentially prominent means to reduce cardiovascular risk. The unique aspects of Lp(a) in blacks will be discussed, and the potential benefit, or lack thereof, of PCSK9 inhibition in African Americans will be highlighted by **Karol E. Watson, MD**. Our understanding of the risk of Lp(a) has been recently improving, and there may be unique means of reducing Lp(a) and cardiovascular outcomes on the horizon. PCSK9 inhibitors are now approved and their ability to approach low-density lipoprotein cholesterol and Lp(a) may offer positive opportunities, especially considering the high degree of premature atherosclerosis in African Americans.

The session will conclude with adequate time for group discussion, audience questions and debate as clinicians, public health officials and governmental agencies all strive to elucidate best practices to control the unnecessary and unacceptable disparities in cardiovascular disease. Overall, the session will be a unique opportunity to address cardiovascular disease disparities, which are persistent and significant, though hopefully modifiable.

Ferdinand is co-chair of today's joint symposium of the ACC and the Association of Black Cardiologists, **"Conundrums in Cardiovascular Disease – Deciphering the Role of Race/Ethnicity,"** from **10:45 a.m. – 12:15 p.m.** in **Grand Ballroom S100bc**.

ACC Transforms Governance Model to Better Serve Members, Meet Mission

In order to more effectively address the growing and changing needs of the more than 52,000 ACC members around the globe, the College's Board of Trustees (BOT) recently approved changes to its overarching governance process and structures. The changes, which will be phased in between now and 2018, aim to make the College more nimble, strategic, accountable, and more reflective of the diversity and breadth within the global cardiovascular community.

Scan the QR code to hear from ACC leaders about ACC's Governance Transformation.

"Our governance structure was last examined decades ago when the College – and the world of health care – was a very different place," says **Richard A. Chazal, MD, FACC**, president-elect of the ACC. "Since then the health care environment has undergone profound changes, as has the size, mission and scope of the College itself."

Following the launch of its Strategic Plan in 2013, the BOT made it a priority to review its governance and decision-making structures and processes. The resulting changes, which include a phased-in reduction in the number of BOT members from 31 to 11 between now and 2018, are based on key principles for optimal governance that center on the concepts of centralized authority and decentralized decision-making. Other changes include the creation of six Board standing committees; a reduction in BOT officers to president, president-elect, secretary and treasurer; and leadership recommendations made by a newly formed Nominating Committee.

According to **Athena Poppas, MD, FACC**, chair of ACC's Governance Committee, the new processes and structure were born out of two years of thoughtful discussion around the College's diverse needs. She also notes that the changes ensure College leaders remain strategic and focused on the mission to transform cardiovascular care and improve heart health, while also opening doors for a greater number of members to be involved in programmatic strategy at the committee level. "This is a great opportunity for Fellows in Training, Early Career professionals and our Cardiovascular Team members to get involved with the ACC," she says.

> **"Our governance structure was last examined decades ago** when the College – and the world of health care – was a very different place."
>
> *Richard A. Chazal, MD, FACC*

Large-scale transformation will take time. While many changes will start taking place this year, there are still supporting details that need to be worked out over the next two years. "We want to get this right," says **Kim Allan Williams Sr., MD, FACC**, president of the ACC. "We will course correct as necessary as we navigate these changes, and it is important that we listen to member feedback to ensure these changes are implemented in a manner that meets the needs of members and positions the College for success in the changing health care environment."

More information on the College's governance changes is available at *ACC.org/About-ACC*.

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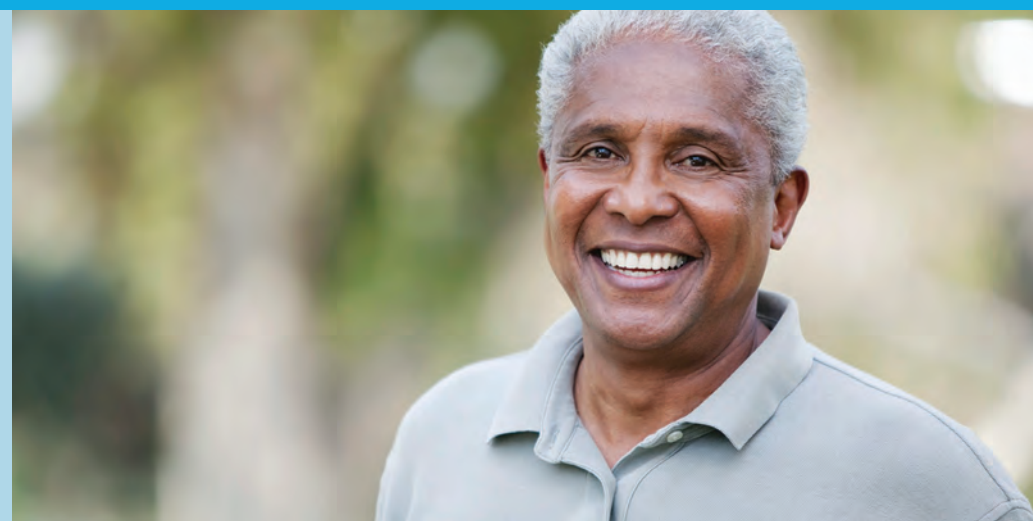

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Medtronic
Further, Together

DOVE LECTURE, from page 1

system to support policies that facilitate evidence-based, cost-effective and high quality care," he said.

Today's James T. Dove Lecture featuring **Harold D. Miller**, president and CEO of the Center for Healthcare Quality and Payment Reform, will offer a closer look at this transition from volume to value and the role physicians and other health care providers can play going forward.

"Physicians must play the lead role in creating a higher-value health care system, because only physicians can redesign the way services are delivered to reduce spending without harming quality or access for patients," says Miller. "Physicians don't need 'incentives' to deliver high-value care, they need a payment system that gives them the resources and flexibility to achieve better outcomes for their patients at lower costs for payers. Cardiologists must seize this opportunity to create a payment system that supports high-quality, affordable cardiovascular care."

> "Physicians must play the lead role in **creating a higher-value health care system**, because only physicians can redesign the way services are delivered to **reduce spending without harming quality or access for patients**."
>
> *Harold D. Miller*

The **James T. Dove Lecture** will take place today from **8:00 – 9:30 a.m.** in **room S504**. More information on MACRA is available on ACC's online MACRA hub at *ACC.org/MACRA*. Look for ACC staff and members wearing "Ask Me About MACRA" buttons in ACC Central or the ACCPAC Lounge in the Lounge & Learn Pavilion.

Check out the last interactive moderated poster session today from 9:30 a.m. to 12:30 p.m. in the new Poster Area section of the Expo Floor.

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High-risk post-PCI patients experience significant mortality during recovery from revascularization.

BOTTOM LINE

1 in 10 high-risk post-PCI patients **die in the first 3 months,**

with about

60% of this mortality due to

SUDDEN CARDIAC DEATH.[1,2]

SOURCES: 1. Halkin A et al. Prediction of Mortality After Primary Percutaneous Coronary Intervention for Acute Myocardial Infarction: CADILLAC Risk Score. JACC 2005;45:1397–1405. 2. Stone G et al. Prevention of Sudden Cardiac Arrest Post PTCA in High-Risk Patients. http://www.theheart.org/article/1202823.do (April 2011).

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Written on the Wall

WHAT IS SOMETHING YOU LEARNED AT ACC.16 THAT WILL IMMEDIATELY CHANGE YOUR CLINICAL PRACTICE?

Charles Bethea, MD, FACC

"The session on public reporting offered valuable information. I like the approach of making adjustments in the database to find innovative solutions for the challenges your patients are facing. We need public reporting. At the same time, we do not need to stifle innovation or suppress risk taking."

Brian Bethea, MD

"ACC's Annual Scientific Session has always been a great meeting and in the last few years I've noticed an increasing collaboration between cardiologists and cardiac surgeons. This year, the focus on collaboration is even more noticeable. Working together will help advance cardiovascular care."

Michele Yeadon, NP

"One particular session offered valuable information that will impact my day-to-day work: 'Recognition and Current Management of Cardiac Amyloidosis.' It shared the necessary steps for going from diagnosis to management strategies, as well as especially helpful treatment options for cardiac amyloidosis."

Stop by the **Lounge & Learn Pavilion** to answer this question and others on the interactive question walls.

INDICATIONS The Medtronic CoreValve and CoreValve Evolut R systems are indicated for use in patients with symptomatic heart disease due to either severe native calcific aortic stenosis or failure (stenosed, insufficient, or combined) of a surgical bioprosthetic aortic valve who are judged by a heart team, including a cardiac surgeon, to be at high or greater risk for open surgical therapy (ie, Society of Thoracic Surgeons predicted risk of operative mortality score ≥8% or at a ≥15% risk of mortality at 30 days).

CONTRAINDICATIONS The CoreValve and CoreValve Evolut R systems are contraindicated for patients presenting with any of the following conditions: known hypersensitivity or contraindication to aspirin, heparin (HIT/HITTS) and bivalirudin, ticlopidine, clopidogrel, Nitinol (Titanium or Nickel), or sensitivity to contrast media, which cannot be adequately premedicated; ongoing sepsis, including active endocarditis; preexisting mechanical heart valve in aortic position.

WARNINGS *General* Implantation of the CoreValve and CoreValve Evolut R systems should be performed only by physicians who have received Medtronic CoreValve training. This procedure should only be performed where emergency aortic valve surgery can be performed promptly. Mechanical failure of the delivery catheter system and/or accessories may result in patient complications. Transcatheter Aortic Valve (Bioprosthesis) Accelerated deterioration of the bioprosthesis may occur in patients presenting with an altered calcium metabolism.

PRECAUTIONS *General* The safety and effectiveness of the CoreValve and CoreValve Evolut R systems have not been evaluated in the pediatric population. The safety and effectiveness of the bioprosthesis for aortic valve replacement have not been evaluated in the following patient populations: patients who do not meet the criteria for symptomatic sever native aortic stenosis as defined: (1) symptomatic severe high gradient aortic stenosis – aortic valve area ≤1.0cm^2 or aortic valve area index ≤0.6 cm^2/m^2, a mean aortic valve gradient ≥40 mmHg; or a peak aortic-jet velocity ≥4.0 m/s, (2) symptomatic severe low-flow/low-gradient aortic stenosis – aortic valve area ≤1.0cm^2 or aortic valve area index ≤0.6 cm^2/m^2, a mean aortic valve gradient <40 mmHg; and a peak aortic-jet velocity <4.0 m/s ; who are at moderate or low surgical risk (predicted perioperative mortality risk of <15%); with untreated, clinically significant coronary artery disease requiring revascularization; with a preexisting prosthetic heart valve with a rigid support structure in either the mitral or pulmonic position if either the preexisting prosthetic heart valve could affect the implantation or function of the bioprosthesis or the implantation of the bioprosthesis could affect the function of the preexisting prosthetic heart valve; with cardiogenic shock manifested by low cardiac output, vasopressor dependence, or mechanical hemodynamic support. The safety and effectiveness of a CoreValve or CoreValve Evolut R bioprosthesis implanted within a failed preexisting transcatheter bioprosthesis has not been demonstrated. Implanting a CoreValve or CoreValve Evolut R bioprosthesis in a degenerated surgical bioprosthesis [transcatheter aortic valve in surgical aortic valve (TAV in SAV)] should be avoided in the following conditions. The degenerated surgical bioprosthesis presents with a: significant concomitant perivalvular leak (between the prosthesis and the native annulus), is not securely fixed in the native annulus, or is not structurally intact (eg, wireform frame fracture); partially detached leaflet that in the aortic position may obstruct a coronary ostium; stent frame with a manufacturer's labeled inner diameter <17 mm. The safety and effectiveness of the bioprosthesis for aortic valve replacement have not been evaluated in patient populations presenting with the following: blood dyscrasias as defined: leukopenia (WBC <1000 cells/mm^3), thrombocytopenia (platelet count <50,000 cells/mm^3), history of bleeding diathesis or coagulopathy, or hypercoagulable states; congenital bicuspid or unicuspid valve; mixed aortic valve disease (aortic stenosis and aortic regurgitation with predominant aortic regurgitation [3-4+]); moderate to severe (3-4+) or severe (4+) mitral or severe (4+) tricuspid regurgitation; hypertrophic obstructive cardiomyopathy; new or untreated echocardiographic evidence of intracardiac mass, thrombus, or vegetation; native aortic annulus size <18 mm or >29 mm for CoreValve and <18 mm or >26 mm for CoreValve Evolut R per the baseline diagnostic imaging or surgical bioprosthetic aortic annulus size <17 mm or >29 mm for CoreValve and <17 mm or >26 mm for CoreValve Evolut R; transarterial access not able to accommodate an 18-Fr sheath or the 14-Fr equivalent EnVeo R InLine sheath; sinus of valsalva anatomy that would prevent adequate coronary perfusion; moderate to severe mitral stenosis; severe ventricular dysfunction with left ventricular ejection fraction (LVEF) <20%;; symptomatic carotid or vertebral artery disease; severe basal septal hypertrophy with an outflow gradient.

Prior to Use Exposure to glutaraldehyde may cause irritation of the skin, eyes, nose, and throat. Avoid prolonged or repeated exposure to the vapors. Damage may result from forceful handling of the catheter. Prevent kinking of the catheter when removing it from the packaging. This device was designed for single patient use only. Do not reuse, reprocess, or resterilize this product. Reuse, reprocessing, or resterilization may compromise the structural integrity of the device and/or create a risk of contamination of the device, which could result in patient injury, illness, or death. The bioprosthesis size must be appropriate to fit the patient's anatomy. Proper sizing of the device is the responsibility of the physician. Refer to Instructions for Use for available sizes. Failure to implant a device within the sizing matrix could lead to adverse effects such as those listed below. Patients must present with access vessel diameters of ≥6 mm for the CoreValve system and ≥5 mm for the CoreValve Evolut R system or an ascending aortic (direct aortic) access site ≥60 mm from the basal plane for both systems. Implantation of the bioprosthesis should be avoided in patients with aortic root angulation (angle between plane of aortic valve annulus and horizontal plane/vertebrae) of >30° for right subclavian/axillary access or >70° for femoral and left subclavian/axillary access. Use caution when using the subclavian/axillary approach in patients with a patent LIMA graft or patent RIMA graft. For direct aortic access, ensure the access site and trajectory are free of patent RIMA or a preexisting patent RIMA graft.

During Use For direct aortic and subclavian access procedures, care must be exercised when using the tip-retrieval mechanism to ensure adequate clearance to avoid advancement of the catheter tip through the bioprosthesis leaflets during device closure. For direct aortic access procedures, use a separate introducer sheath; do not use the EnVeo R InLine sheath. Adequate rinsing of the bioprosthesis with sterile saline, as described in the Instructions for Use, is mandatory before implantation. During rinsing, do not touch the leaflets or squeeze the bioprosthesis. If a capsule becomes damaged during loading or the capsule fails to close, replace the entire system (bioprosthesis, catheter, and CLS). Do not use a catheter with a damaged capsule. After a bioprosthesis has been inserted into a patient, do not attempt to reload that bioprosthesis on the same or any other catheter. AccuTrak DCS Only: During implantation, if resistance to deployment is encountered (e.g., the micro knob starts clicking or is tight or stuck), apply upward pressure to the macro slider while turning the micro knob. If the bioprosthesis still does not deploy, remove it from the patient and use another system. AccuTrak DCS Only: Once deployment is initiated, retrieval of the bioprosthesis from the patient (e.g., use of the catheter) is not recommended. Retrieval of a partially deployed valve using the catheter may cause mechanical failure of the delivery catheter system, aortic root damage, coronary artery damage, myocardial damage, vascular complications, prosthetic valve dysfunction (including device malposition), embolization, stroke, and/or emergent surgery. AccuTrak DCS Only: During deployment, the bioprosthesis can be advanced or withdrawn as long as annular contact has not been made. Once annular contact is made, the bioprosthesis cannot be advanced in the retrograde direction; if necessary, and the frame has only been deployed ≤2/3 of its length, the bioprosthesis can be withdrawn (repositioned) in the antegrade direction. However, use caution when moving the bioprosthesis in the antegrade direction. EnVeo R DCS Only: If a misload is detected, unsheath the bioprosthesis and examine the bioprosthesis for damage (for example, permanent frame deformation, frayed sutures, or valve damage). Do not attempt to reload a damaged bioprosthesis. Do not load the bioprosthesis onto the catheter more than 2 times or after it has been inserted into a patient. EnVeo R DCS Only: Use the deployment knob to deploy and recapture the bioprosthesis. Do not use the trigger for deploying or recapturing because it could cause inaccurate placement of the bioprosthesis. EnVeo R DCS Only: Once the radiopaque capsule marker band reaches the distal end of the radiopaque paddle attachment (point of no recapture), retrieval of the bioprosthesis from the patient is not recommended. Retrieval after the point of no recapture may cause mechanical failure of the delivery catheter system, aortic root damage, coronary artery damage, myocardial damage, vascular complications, prosthetic valve dysfunction (including device malposition), embolization, stroke, and/or emergent surgery. EnVeo R DCS Only: During deployment, the bioprosthesis can be advanced or withdrawn as long as annular contact has not been made. Once annular contact is made, the bioprosthesis cannot be advanced in the retrograde direction; recapture until the bioprosthesis is free from annular contact, and then reposition in the retrograde direction. If necessary, and the radiopaque capsule marker band has not yet reached the distal end of the radiopaque paddle attachment, the bioprosthesis can be withdrawn (repositioned) in the antegrade direction. However, use caution when moving the bioprosthesis in the antegrade direction. While the catheter is in the patient, ensure the guidewire is extending from the tip. Do not remove the guidewire from the catheter while the catheter is inserted in the patient. Use the handle of the delivery system to reposition the bioprosthesis. Do not use the outer catheter sheath. Once deployment is complete, repositioning of the bioprosthesis (e.g., use of a snare and/or forceps) is not recommended. Repositioning of a deployed valve may cause aortic root damage, coronary artery damage, myocardial damage, vascular complications, prosthetic valve dysfunction (including device malposition), embolization, stroke, and/or emergent surgery. Do not attempt to retrieve or to recapture (EnVeo DCS only) a bioprosthesis if any one of the outflow struts is protruding from the capsule. If any one of the outflow struts has deployed from the capsule, the bioprosthesis must be released from the catheter before the catheter can be withdrawn. Ensure the capsule is closed before catheter removal. When using a separate introducer sheath, if increased resistance is encountered when removing the catheter through the introducer sheath, do not force passage. Increased resistance may indicate a problem and forced passage may result in damage to the device and/or harm to the patient. If the cause of resistance cannot be determined or corrected, remove the catheter and introducer sheath as a single unit over the guidewire, and inspect the catheter and confirm that it is complete. Clinical long-term durability has not been established for the bioprosthesis. Evaluate bioprosthesis performance as needed during patient follow-up. Postprocedure, administer appropriate antibiotic prophylaxis as needed for patients at risk for prosthetic valve infection and endocarditis. Postprocedure, administer anticoagulation and/or antiplatelet therapy per physician/clinical judgment. Excessive contrast media may cause renal failure. Preprocedure, measure the patient's creatinine level. During the procedure, monitor contrast media usage. Conduct the procedure under fluoroscopy. The safety and efficacy of a CoreValve or CoreValve Evolut R bioprosthesis implanted within the initial transcatheter bioprosthesis have not been demonstrated. However, in the event that a CoreValve or CoreValve Evolut R bioprosthesis must be implanted within the initial transcatheter bioprosthesis to improve valve function, valve size and patient anatomy must be considered before implantation of the bioprosthesis to ensure patient safety (for example, to avoid coronary obstruction). In the event that valve function or sealing is impaired due to excessive calcification or incomplete expansion, a postimplant balloon dilatation of the bioprosthesis may improve valve function and sealing. To ensure patient safety, valve size and patient anatomy must be considered when selecting the size of the balloon used for dilatation. The balloon size chosen for dilatation should not exceed the diameter of the native aortic annulus or, for surgical bioprosthetic valves, the manufacturer's labeled inner diameter. Refer to the specific balloon catheter manufacturer's labeling for proper instruction on the use of balloon catheter devices. Note: Bench testing has only been conducted to confirm compatibility with NuMED Z-MED IITM Balloon Aortic Valvuloplasty catheters where CoreValve or CoreValve Evolut R bioprosthesis device performance was maintained after dilation. Data on File.

POTENTIAL ADVERSE EVENTS Potential risks associated with the implantation of the CoreValve or CoreValve Evolut R transcatheter aortic valve may include, but are not limited to, the following: • death • myocardial infarction, cardiac arrest, cardiogenic shock, cardiac tamponade • coronary occlusion, obstruction, or vessel spasm (including acute coronary closure) • cardiovascular injury (including rupture, perforation, tissue erosion, or dissection of vessels, ascending aorta trauma, ventricle, myocardium, or valvular structures that may require intervention) • emergent surgical or transcatheter intervention (for example, coronary artery bypass, heart valve replacement, valve explant, percutaneous coronary intervention [PCI], balloon valvuloplasty) • prosthetic valve dysfunction (regurgitation or stenosis) due to fracture; bending (out-of-round configuration) of the valve frame; underexpansion of the valve frame; calcification; pannus; leaflet wear, tear, prolapse, or retraction; poor valve coaptation; suture breaks or disruption; leaks; mal-sizing (prosthesis-patient mismatch); malposition (either too high or too low)/malplacement • prosthetic valve migration/embolization • prosthetic valve endocarditis • prosthetic valve thrombosis • delivery catheter system malfunction resulting in the need for additional re-crossing of the aortic valve and prolonged procedural time • delivery catheter system component migration/embolization • stroke (ischemic or hemorrhagic), transient ischemic attack (TIA), or other neurological deficits • heart failure • cardiac failure or low cardiac output • ancillary device embolization • individual organ (for example, cardiac, respiratory, renal [including acute kidney failure]) or multi-organ insufficiency or failure • major or minor bleeding that may require transfusion or intervention (including life-threatening or disabling bleeding) • vascular access-related complications (eg, dissection, perforation, pain, bleeding, hematoma, pseudoaneurysm, irreversible nerve injury, compartment syndrome, arteriovenous fistula, stenosis) • mitral valve regurgitation or injury • conduction system disturbances (for example, atrioventricular node block, left-bundle branch block, asystole), which may require a permanent pacemaker • infection (including septicemia) • hypotension or hypertension • hemolysis • peripheral ischemia • bowel ischemia • abnormal lab values (including electrolyte imbalance) • allergic reaction to antiplatelet agents, contrast medium, or anesthesia • exposure to radiation through fluoroscopy and angiography • permanent disability.

Please reference the CoreValve and CoreValve Evolut R Instructions for Use for more information regarding indications, warnings, precautions and potential adverse events.

CAUTION Federal law (USA) restricts this device to sale by or on the order of a physician.

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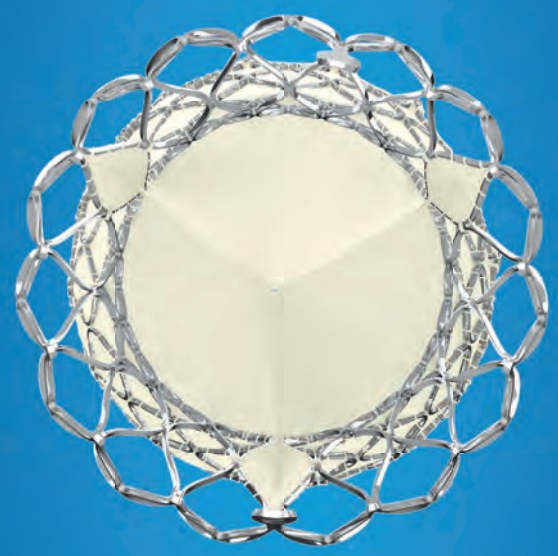

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