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ACC.07 and i2 Summit Highlights: A Conversation With the Experts

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Introduction

As always, the 56th Annual Scientific Session of the American College of Cardiology (ACC) set out to present the latest innovations, medical updates, and new technologies in cardiovascular medicine, but the 2007 meeting also sought to present this information in more innovative ways that would be more useful to cardiologists. Consequently, the annual meeting included more video case studies, live presentations from leading medical centers around the world, and e-posters that allowed imbedded multimedia images. The e-posters remain available for viewing at Cardiosource, along with other online coverage of the annual meeting.

As part of the effort to make new information applicable to the day-to-day problems of cardiologists, there was a change in the format of the closing symposium that reviews the meeting's most important and interesting presentations. This supplement to the *Journal of the American College of Cardiology* (*JACC*) presents the Highlights of the Annual Scientific Session, which for the first time were presented as a *Conversation With the Experts*. Rather than a comprehensive examination of all major presentations, short summaries of individual presentations were reviewed in an effort to provide the most important insights and bullet points of the meeting, followed by a spirited discussion from a panel of experts.

The Highlights Session was chaired by E. Murat Tuzcu, MD, FACC, Chair of the 2007 Annual Scientific Session Program Committee. He was joined on the panel by his committee co-chairs, Randall C. Starling, MD, MPH, FACC, and James D. Thomas, MD, FACC. Summaries of original research and structured sessions were prepared and presented by the coordinators of the topic working groups from the Program Planning Committee.

James H. Stein, MD, FACC, led off the ACC.07 and i2 Summit Highlights covering Vascular Disease, Hypertension, and Prevention. This topic attracted 22.2% of the abstract submissions for ACC.07, which was the highest percentage of overall submissions for any topic in more than a decade. Robert A. Harrington, MD, FACC, was the topic coordinator who summarized key themes and important messages to emerge from the sessions on Myocardial Ischemia and Infarction. William D. Knopf, MD, FACC, prepared the highlights of the Innovation in Intervention: i2 Summit, along with his co-chairs, David Holmes, Jr., MD, FACC, FSCAI, and Barry Uretsky, MD, FACC, FSCAI. Valvular Heart Disease was addressed by Samir R. Kapadia, MD, FACC, and highlights relating to Cardiac Function and Heart Failure were summarized by Lynne E. Wagoner, MD, FACC. Steven Markowitz, MD, FACC, reviewed Cardiac Arrhythmias and Flordeliza Villanueva, MD, FACC, presented the highlights related to Imaging and Diagnostic Testing. According to Dr. Tuzcu, John Rhodes, Jr., MD, FACC, probably created the largest, most diverse congenital heart disease track of any previous ACC sessions, and he presented highlights in Pediatric Cardiology and Adult Congenital Heart Disease. JoAnne Foody, MD, FACC, had 1 of the toughest tasks because Special Topics encompasses a broad range of investigations that may be hard to classify but are of great importance. Special Topics include subjects as diverse as assessing and improving cardiovascular health care quality and the measurement of the impact of cardiovascular informatics. Finally, the discussants included 2 of the College's leading editors: Anthony N. DeMaria, MD, FACC, Editor-in-Chief of *JACC*, and C. Richard Conti, MD, MACC, Editor-in-Chief of *ACCEL*.

This supplement to *JACC* presents the highlights of this *Conversation With the Experts* and features more detailed summaries of the individual presentations covered during the final session; plus, there is additional artwork and references that can be used to find the many sessions with full audio and video that are available online at ACC's Cardiosource. After the session highlights are summarized, the panelists provide important perspectives on the topics discussed and help discern what the data mean for clinical practice.

Vascular Disease, Hypertension, and Prevention

There were 424 presentations related to vascular disease, hypertension, and prevention at the ACC.07 Scientific Session, including disappointing results from trials targeting high-density lipoprotein (HDL) cholesterol. However, the news was decidedly better for drugs that lower low-density lipoprotein (LDL) cholesterol and for studies evaluating

Abbreviations and Acronyms

ACHD	=	adult congenital heart disease
ACS	=	acute coronary syndrome
ADHF	=	acute decompensated heart failure
AF	=	atrial fibrillation
AMI	=	acute myocardial infarction
AS	=	aortic stenosis
BMS	=	bare-metal stent(s)
CAD	=	coronary artery disease
CHD	=	coronary heart disease
CI	=	confidence interval
CIMT	=	carotid intima-media thickness
CMR	=	cardiac magnetic resonance
CRT	=	cardiac resynchronization therapy
CT	=	computed tomography
CTA	=	computed tomography angiography
DES	=	drug-eluting stent(s)
FDG	=	fluorodeoxyglucose
HDL	=	high-density lipoprotein
ICD	=	implantable cardioverter-defibrillator
LDL	=	low-density lipoprotein
LV	=	left ventricular
LVAD	=	left ventricular assist device
LVEF	=	left ventricular ejection fraction
MACE	=	major adverse cardiac events
MI	=	myocardial infarction
MPI	=	myocardial perfusion imaging
MR	=	mitral regurgitation
MV	=	mitral valve
MVR	=	mitral valve replacement
NNT	=	number needed to treat
NYHA	=	New York Heart Association
ox-LDL	=	oxidized low-density lipoprotein
PCI	=	percutaneous coronary intervention
PET	=	positron emission tomography
PHV	=	percutaneous heart valve
PPAR	=	peroxisome proliferator-activated receptors
PPM	=	patient prosthesis mismatch
PVAD	=	percutaneously placed continuous-flow left ventricular assist device
SES	=	sirolimus-eluting stent(s)
STEMI	=	ST-segment elevation myocardial infarction
TIMI	=	Thrombolysis In Myocardial Infarction
TRA	=	thrombin receptor antagonist
TWA	=	T-wave alternans

screening tests used to assess cardiac risk. These presentations were selected from a total of 1,181 abstracts on these specific topics that were submitted to the Program Planning Committee.

High-density lipoprotein cholesterol is an attractive target for reducing cardiovascular risk because of epidemiologic evidence demonstrating a strong inverse relationship between HDL cholesterol levels and cardiovascular risk. The rationale for increasing HDL cholesterol levels as a therapeutic strategy is further supported by evidence of the lipoprotein's anti-inflammatory properties, antioxidant effects, and ability to promote reverse cholesterol transport. Dr. Stein began by noting the abundance of bad news relating to drugs in development for raising HDL cholesterol levels. Torcetrapib, a cholesterol-ester transfer protein inhibitor, was tested versus atorvastatin in the ILLUSTRATE (Investigation of Lipid Level Management to Understand Its Impact in Atherosclerotic Events) trial (1) and the RADIANCE 1 and RADIANCE 2 (Rating Atherosclerotic Disease Change by Imaging with a New Cholesteryl Ester Transfer Protein [CETP] Inhibitor) trials (2–4). In these studies, there were large increases in HDL cholesterol levels (~60%) and a substantial decrease in levels of LDL cholesterol (~20%) (Table 1), yet there was no significant decrease in the progression of coronary atherosclerosis. Indeed, one secondary end point of RADIANCE 1 suggested progression of disease in torcetrapib-treated patients based on measurement of carotid intima-media thickness (CIMT) studies.

One issue still to be resolved is whether the failure of torcetrapib is due to the molecule or the mechanism (5). Whether that question gets answered or not, the data safety and monitoring board for the ILLUSTRATE trial recommended that the study be terminated. Pfizer subsequently halted its torcetrapib research program. (In the interest of patient safety, Pfizer stopped all torcetrapib clinical trials.) (6).

In the ERASE (Effects of Reconstituted HDL on Atherosclerosis) trial, treatment with CSL-111, which chemically and biologically resembles native HDL, was not superior to placebo in the primary efficacy end point of percent change in coronary atheroma volume (7). However, CSL-111 did lead to significant differences in 3 secondary efficacy end points: change in atheroma volume versus baseline, change in plaque characterization indexes, and change in coronary score on quantitative coronary angiography.

Another approach under study uses peroxisome proliferator-activated receptors (PPARs). Although the results of early trials were disappointing, a series of PPAR agonists have been described, leading to the discovery of LY518674, a highly potent and selective PPAR agonist. However, in data presented at ACC.07, LY518674 proved to be no better than fenofibrate (Table 2); plus, it increased the level of serum creatinine compared with placebo ($p < 0.001$), with many patients experiencing serum creatinine values exceeding the upper limits of normal (8). Also, the PPAR agonist was associated with what Dr. Stein called "a very odd dose response." Specifically, there were unusual dose-response curves; for example, the greatest elevation of HDL was found with the intermediate LY518674 dose (25 μg), whereas the 100-μg dose produced almost no effect on these lipids. Furthermore, the study drug had a significantly unfavorable effect on LDL compared with fenofibrate, increasing LDL by 18.3% (50 μg) and 19.5% (100 μg), versus 2.3% with fenofibrate ($p = 0.002$ for both comparisons). The results of this study were published simultaneously in *JAMA* (9). "Overall there was not very good news for raising HDL cholesterol at this meeting," said Dr. Stein,