1 in the bivalirudin treatment group (Table 1). In August 2014, upon recommendation from the Data Safety Monitoring Board, the study was permanently terminated due to excess allergic reaction rates associated with REG1 with a clear offsetting benefit to the drug.

No significant differences were observed in the primary efficacy end point with the data available; however, the exploratory end point of stent thrombosis was lower with REG1 at both days 3 and 30 (0.8% vs 0.1% with REG1; $P < .01$). Regarding the primary safety end point, major non-CABG-associated bleeding (BARC type 3 or 5) did not differ between the 2 groups (0.4% vs 0.1%; $P = .10$). Nevertheless, minor and major bleeding rates were higher in REG1, with 6.5% compared with 4.1% at day 3 ($P < .002$).

Dr Mehran concluded with a word of caution in interpreting the efficacy and bleeding data, as early termination limited the number of participants and events. She reiterated that REG1, as currently formulated, resulted an infrequent but unacceptably high rate of severe allergic reactions.

SCOT-HEART: CTCA Potential to Improve Angina Diagnosis, Treatment, and Outcomes

Written by Aimee Spevak

The SCOT-HEART trial [SCOT-HEART Investigators. *Lancet*. 2015] was conducted to determine whether rapid-access chest pain centers would benefit from the addition of computed tomography coronary angiography (CTCA) to diagnose patients presenting with suspected angina due to coronary heart disease (CHD). Use of CTCA improved the provider certainty of diagnosis, influenced changes in treatment, and showed a potential to decrease CHD-related death and nonfatal myocardial infarction (MI).

Clinicians at rapid-access chest pain centers can accurately identify patients with chest pain at high risk for CHD. However, a need remains to reduce the number of patients felt to be at lower risk who are misdiagnosed with noncardiac chest pain, as these patients compose roughly one-third of fatal and nonfatal MI cases within 6 months of presenting with chest pain [Sekhri N et al. *Heart*. 2007].

David Newby, MD, PhD, University of Edinburgh, Edinburgh, Scotland, United Kingdom, presented data from SCOT-HEART, which randomized patients presenting with suspected angina due to CHD to receive diagnosis by standard care alone or standard care plus CTCA. The primary end point of the study was the change in diagnosis of angina due to CHD when using CTCA. The study included patient groups previously excluded from angina trials, as no restrictions were put on presence of arrhythmia, obesity, or calcium score. Patients with renal failure, allergy to contrast media or other inability to undergo computed tomography scanning, pregnancy, or acute coronary syndrome within 3 months were excluded.

Data were collected at 12 centers across Scotland. A total of 4146 patients were recruited and randomized 1:1, half to standard of care and half to standard of care plus CTCA. Baseline characteristics were similar between the 2 groups.

The addition of CTCA to standard testing improved provider diagnosis certainty nearly 4-fold (RR, 3.76; 95% CI, 3.61 to 3.89), while diagnosis (angina due to CHD) frequency decreased (RR, 0.78; 95% CI, 0.70 to 0.86). At 6 weeks of follow-up, clinicians reported further increased certainty in diagnosis; during the follow-up period, CTCA use led to a significant increase in change in diagnosis (23% vs 1% in the standard care group; $P < .001$).

Use of CTCA resulted in a 14% increase in further investigations ($P < .0001$) and an 18% increase in treatment changes ($P < .0001$). Patients were followed up for a median of 1.7 years (range, 0.1 to 4.1); CTCA was associated with a 38% reduction in CHD death and nonfatal MI, which for the prespecified analysis was just under statistical significance (HR, 0.62; 95% CI, 0.38 to 1.01; $P = .0527$).

Prof Newby concluded that the use of CTCA for patients with suspected angina due to CHD was beneficial in a variety of ways: it clarified diagnosis, aided in treatment decision making, increased further testing, and increased diagnosis of CHD. Use of CTCA may improve treatment decisions, reducing fatal and nonfatal MI.

SAPIEN 3 TAVR System Produces Excellent Clinical Outcomes in PARTNER II Trial

Written by Aimee Spevak

The PARTNER II trial [NCT01314313] enrolled high-risk operable, inoperable, and intermediate-risk operable patients with symptomatic severe aortic stenosis (AS) to receive the most recently available transcatheter heart valve (THV). Both patient groups experienced lower-than-expected mortality and stroke outcomes, with low rates of adverse events (AEs) and paravalvular leak.

Since their introduction in 2003, balloon-expandable THVs have continued to evolve. The current SAPIEN 3 (S3) valve, available since 2013, is size 14 French and has several modified features in the valve and its delivery system. To investigate this new iteration of transcatheter aortic valve replacement, the PARTNER II trial was designed to evaluate safety and efficacy outcomes for

Table 1. Mortality and Stroke Outcomes at 30 Days

Outcome	S3i Group, % of Patients	S3HR Group, % of Patients
All-cause mortality	1.1	2.2
CV mortality	0.9	1.4
All stroke	2.6	1.5
Disabling stroke	1.0	0.9

CV, cardiovascular; S3HR, high-risk or inoperable patients who received the SAPIEN 3 valve; S3i, intermediate-risk, operable patients who received the SAPIEN 3 valve.

the S3 THV system for use in inoperable, high-risk, and intermediate-risk patients.

Susheel Kodali, MD, Columbia University Medical Center, New York, New York, USA, presented an as-treated analysis of 30-day data from the PARTNER II trial, which consisted of 2 single-arm, nonrandomized, historical-controlled studies, and enrolled a combined 1659 patients with symptomatic severe AS: 1076 intermediate-risk operable (S3i), and 583 high-risk operable or inoperable (S3HR). All patients received the S3 THV. Exclusion criteria were stroke or transient ischemic attack within 6 months, myocardial infarction within 1 month, untreated significant coronary artery disease, upper gastrointestinal bleed within 3 months, renal failure, prior prosthetic valve, left ventricular ejection fraction < 20%, and estimated life expectancy < 24 months. S3HR patients were enrolled at 29 sites across the United States, and S3i patients were enrolled at 51 US sites.

In both patient groups, 99.5% of patients completed follow-up visits 30 days after receiving the S3 THV. Baseline characteristics reflect the high-risk nature of both groups; the average ages were > 80 years, with average Society of Thoracic Surgeons (STS) surgery risk scores at 5.3% for S3i patients and 8.6% for S3HR patients. Between-group differences in baseline characteristics and comorbidities also reflected the risk status of each group.

Thirty-day results for the as-treated S3i and S3HR patients are summarized in Table 1. The STS risk scores were 5.3% for the S3i group and 8.6% for the S3HR group.

AEs were low for these populations, and the procedure was considered well tolerated.

Compared to previous studies, at 30-day follow-up, the S3 THV resulted in the lowest rates of all-cause mortality, stroke, and paravalvular leak of all available balloon-expandable THVs. Dr Kodali went over the excellent clinical outcomes seen in both the intermediate-risk and high-risk/inoperable groups, and cited these results as evidence that the S3 THV is an attractive alternative to surgery for all patients with AS.

BEST Trial: PCI Fails to Match CABG in Patients With Multivessel CAD

Written by Francesca Coltrera

Long-term data from the prospective open-label BEST trial found percutaneous coronary intervention (PCI) with a second-generation drug-eluting stent to be inferior to coronary artery bypass graft (CABG) surgery in patients with multivessel coronary artery disease (CAD), according to Seung-Jung Park, MD, PhD, Asan Medical Center, Seoul, Korea [Park SJ et al. *N Engl J Med*. 2015].

Recent studies have found that CABG surgery is associated with lower rates of adverse outcomes in patients with multivessel CAD when compared with PCI. The BEST trial was designed as a randomized noninferiority trial that compared optimal revascularization with PCI using everolimus-eluting stents to CABG in patients with multivessel CAD.

A total of 880 patients from 4 countries in East Asia with angina and/or objective evidence of a myocardial ischemia and multivessel CAD confirmed by angiography were enrolled in the trial. The study was terminated early because of slow enrollment.

Patients were randomly assigned to PCI (n = 438) or CABG (n = 442), although crossovers and other treatment changes occurred. The primary end point was the composite of major adverse cardiac events (all-cause death, myocardial infarction [MI], and target vessel revascularization) at 2 years. Key secondary end points included stroke, new lesion revascularization, and TIMI major bleeding.

Follow-up was performed with either a clinic visit or phone interview at 30 days; 6, 9, and 12 months; and then annually. Medications for secondary prevention (aspirin, statins) were strongly recommended, and routine angiography in the absence of ischemia was discouraged.

The composite primary end point occurred in 11.0% of PCI patients and 7.9% of CABG patients at 2 years with an absolute risk difference of 3.1 percentage points (95% CI, –0.8 to 6.9; $P_{\text{Noninferiority}} = .32$). The incidence of the primary outcome was significantly higher in the PCI group vs the CABG group at 5 years (Table 1). CABG performed better for the primary end point in all of the prespecified subgroups. As shown in Table 1, some secondary outcomes were increased at 5 years in the PCI group vs the CABG group, while TIMI major bleeding was significantly lower.

In conclusion, the BEST trial found that PCI with the second-generation everolimus-eluting stent was inferior to CABG for the primary end point of all-cause death, MI, or target vessel revascularization at 2 years. Patients randomized to PCI had an increased risk of all-cause death, MI, and target vessel revascularization that remained present at 5 years.