Update on Interventional Cardiology for the Internist

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DISCLOSURES

• none
Topics to be Discussed

- Update on dual anti-platelet therapy
- Surgery and stents
- Proton pump inhibitors and coronary intervention
- New anti-platelet drugs (Prasugrel)
- Left atrial appendage occluder devices
- Percutaneous aortic valve therapies
Off-label or Investigational Drugs and Devices to be discussed:

- Prasugrel
- Investigational drug-eluting stents
- Left atrial appendage occluder devices
- Percutaneous aortic valve therapies
Abbreviations Interventional Cardiologists like to use:

- PCI = Percutaneous coronary intervention
- BMS = Bare metal stent
- DES = Drug-eluting stent
Important topics I won’t be talking about:

- The COURAGE trial
- Fractional flow reserve and the FAME trial
- The SYNTAX trial: PCI versus CABG
- Percutaneous mitral valve therapies
Case: Surgery with recent stents

• You are seeing a 63 year old man prior to elective total knee replacement. 4 months earlier, he had an MI and underwent placement of a Cypher drug-eluting stent in his LAD. The orthopedic surgeon insists on stopping the clopidogrel prior to surgery.

• You recommend:
Case continued

What should you recommend?

A. You recall that the Cypher stent requires only 3 months of dual-antiplatelet therapy (versus 6 for Taxus). Stop the clopidogrel but continue aspirin peri-operatively.

B. Stop both aspirin and clopidogrel prior to surgery.

C. Tell the surgeon the operation must be done on aspirin and clopidogrel

D. Delay the operation until at least 12 months post-stent.
## Restenosis versus Thrombosis

<table>
<thead>
<tr>
<th>Stent Restenosis</th>
<th>Stent Thrombosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Is a cellular proliferative response of the vessel wall to trauma of angioplasty</td>
<td>• Is the development of clot within the stent</td>
</tr>
<tr>
<td>• Largely composed of smooth muscle cells and extra-cellular matrix.</td>
<td>• Is caused by activated platelets</td>
</tr>
<tr>
<td>• Usually leads to gradual reduction in lumen size</td>
<td>• Is relatively rare: 0.4 – 1.7% <em>(Mauri et al. NEJM 2007)</em></td>
</tr>
<tr>
<td>• Is common – 10-15% clinical restenosis with bare metal stents</td>
<td>• Is catastrophic:</td>
</tr>
<tr>
<td>• Drug-eluting stents reduce restenosis</td>
<td>– 66-100% have MI</td>
</tr>
<tr>
<td></td>
<td>– Up to 45% mortality <em>(Deamen et al. Lancet 2007)</em></td>
</tr>
</tbody>
</table>
In-Stent Restenosis

Gradual (over weeks to months) proliferation of vessel wall cells
Stent Thrombosis

Sudden formation of clot within the stent lumen
Vessel Healing: DES vs. BMS

- Dual anti-platelet therapy (ASA + Plavix) is required until the vessel heals and the stented segment is endothelialized.
- The drug and polymer in DES delay vessel healing.
- Therefore, while BMS require 4 weeks of dual anti-platelet therapy, DES require a much longer period of treatment.
Millions face risk from drug-coated stents

Potentially lethal heart devices a frightening problem for patients, doctors

By Robert Bazell
Chief science and health correspondent
NBC News
updated 6:38 a.m. PT, Thurs., March 1, 2007

Millions of Americans could be walking around with tiny time bombs in their hearts.

The concern centers on devices called drug-eluting stents. Doctors implant them in the hearts of about a million Americans a year to treat coronary artery disease. They generate some $5 billion a year in sales for the two companies that make them. But they may be doing more harm than good.
FDA Panel Conclusions

• On-label DES use compared to BMS use is not associated with an increased incidence of death or MI.
• On-label DES use compared to BMS use is associated with an increased incidence of very late stent thrombosis that is of uncertain magnitude and clinical significance.
• Benefits of on-label DES use (reduced restenosis) appear to outweigh the risks.

Pinto Slottow et al Cath Cardiovasc Interven 2007:69;1064-1074
FDA Panel Conclusions

• Dual anti-platelet therapy should be continued for **at least 12 months** following DES PCI, especially in the off-label setting, for patients at low risk for bleeding.

Pinto Slottow et al Cath Cardiovasc Interven 2007:69;1064-1074
Case follow up

- The patient waited another 9 months, and ultimately underwent his knee operation safely, on aspirin alone.
Alternate ending…

• While waiting for his knee surgery, the patient falls and breaks his hip. He needs surgery relatively urgently to avoid long-term disability. What will happen if he has hip surgery now?
What happens when patients with recent coronary stents undergo surgery?

Things we know:

• The peri-operative period represents a pro-thrombotic state.
• Patients with stents are at increased risk of stent thrombosis.
• Stent thrombosis is always bad, but can be especially catastrophic in the peri-operative period.
Stents and Surgery: data

- Retrospective analysis of 207 patients undergoing early surgery (within 2 months) after bare-metal stent implantation.
- 8 patients died or suffered MI – all 8 underwent surgery in the 6 weeks after stenting.
- No events after 6 weeks.

Mayo Clinic database
Early surgery after stents is dangerous:

Stents and Surgery: more data

- Study of 192 patients having surgery after stenting (both BMS and DES)
- Among patients having surgery before the end of the required period of ASA + Plavix:
  - 30.6% death or MI if both ASA and Plavix were stopped
- Only 0.6% death or MI in patients having “late” surgery -- after completing the course of anti-platelet therapy
- No difference in transfusion (20% vs 24%) in patients left on anti-platelet drugs vs those taken off.

Schouten O et al JACC 2007;49:122-4
Pre-operative coronary revascularization is generally not beneficial: CARP

McFalls, E. et al. NEJM 2004;351:2795-2804
Stents and Surgery: Take-home points

- Whenever possible, avoid coronary revascularization prior to surgery
- If surgery is necessary, try to delay until > 6 weeks for BMS and > 1 year for DES.
- If surgery cannot wait, try to continue ASA and/or clopidogrel peri-operatively.
- Good communication with surgeons and cardiologists is essential
Case: Stents and PPIs

• Your patient is a 52 year old man with a history of peptic ulcer disease and upper GI bleeding 3 months ago who presented recently with NSTEMI. Drug eluting stents were placed in the mid LAD and mid LCX. You are seeing him several weeks later in follow-up.
Case: Stents and PPIs (cont)

- His medications include aspirin 325 mg, clopidogrel 75 mg, and omeprazole 40 mg daily. His CBC is normal. You have read the recent studies suggesting that omeprazole decreases the antiplatelet activity of clopidogrel, and may be a risk factor for recurrent coronary events after stenting. What do you do?
Stents and PPIs

What should you do?

A. Make no changes to his medications.
B. Stop the omeprazole. He no longer needs it.
C. Change the omeprazole to pantoprazole.
D. Double the clopidogrel dose.
E. How should I know?? Better let the cardiologists and gastroenterologists fight it out.
The ACC, ACG, and AHA publish joint recommendations in October 2008.
ACCF/ACG/AHA Expert Consensus Document: Antiplatelets, NSAIDs, and GI Risk

- **Recommendation**: PPIs are the preferred agents for the therapy and prophylaxis of NSAID- and ASA-associated GI injury.
- **Traditional doses of H2-receptor antagonists (H2RAs) do not prevent most NSAID-related gastric ulcers (although high doses may be better).**

• “To date…there has been relatively little evidence of any clinically significant interaction between clopidogrel and PPIs. The ongoing COGENT-1 (Clopidogrel and the Optimization of Gastrointestinal Events) study…should provide further evidence to help address these issues.”

Why should there be an interaction between clopidogrel and PPIs?

Conversion to the active metabolite can be absent or impaired by:

- Genetic variants
- Interacting drugs
Association between Status as a Carrier of a CYP2C19 Reduced-Function Allele and the Primary Efficacy Outcome or Stent Thrombosis in Subjects Receiving Clopidogrel in TRITON TIMI 38

CONCLUSION:
Patients with reduced function of CYP2C19 derive less benefit from clopidogrel, and have worse outcomes.

FAST-MI
Do PPIs interact with Clopidogrel?

Most PPIs interact with CYP2C19, potentially leading to less conversion of clopidogrel to the active metabolite.

One study reported that pantoprazole, alone among PPIs, does not interact.
Do PPIs interact with Clopidogrel?

*In vitro* studies

  - Patients on omeprazole have diminished platelet aggregation response to clopidogrel
- OCLA study JACC 2008; 51:256-260
  - Omeprazole significantly decreased clopidogrel inhibitory effect in a randomized trial (207 pts)
  - Omeprazole, but not esomeprazole or pantoprazole, decreased clopidogrel effect
Retrospective Clinical Studies: AHA meeting 2008

2 Conflicting Studies:

• CREDO trial
  – clopidogrel reduced adverse events at one year to an approximately similar degree whether or not patients were on a PPI

• Clopidogrel Medco outcomes study:
  – 16,700 patients post-stenting
  – Cardiovascular events increased in patients taking PPIs along with clopidogrel
Retrospective Clinical Studies, continued:

Juurlink et al, CMAJ 2009;180(7).

• 13,636 patients receiving clopidogrel post-MI in Canada
• Current use of PPI was associated with an increased risk of reinfarction (OR 1.27, 95% CI 1.03–1.57)
• Pantoprazole (which does not inhibit CYP2C19) did not show this effect.
Retrospective Clinical Studies, continued:

Ho et al, JAMA. 2009 Mar 4;301(9):937-44

- 8205 patients discharged from VA hospitals on clopidogrel for acute coronary syndromes
Just to make it more confusing...

- MACE rates by PPI, from the Clopidogrel Medco outcomes study:

<table>
<thead>
<tr>
<th>PPI</th>
<th>MACE rate (%)</th>
<th>Hazard ratio</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Omeprazole</td>
<td>25.1</td>
<td>1.39</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Esomeprazole</td>
<td>24.9</td>
<td>1.57</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Pantoprazole</td>
<td>29.2</td>
<td>1.61</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Lansoprazole</td>
<td>24.3</td>
<td>1.39</td>
<td>&lt;0.0004</td>
</tr>
</tbody>
</table>

Differs from the Canadian study, which did not show an effect of pantoprazole.
And…Patients on PPIs are sicker!
Can we really adjust for all variables??

Table 1. Baseline Characteristics of Patients Taking Clopidogrel After Hospital Discharge\(^a\)

<table>
<thead>
<tr>
<th></th>
<th>Clopidogrel Without PPI (n = 2961)</th>
<th>Clopidogrel With PPI (n = 5244)</th>
<th>(P) Value</th>
<th>Clopidogrel With PPI During Follow-up (n = 1953)</th>
<th>At Discharge (n = 3291)</th>
<th>(P) Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (SD), y</td>
<td>65.7 (11.7)</td>
<td>67.7 (11.4)</td>
<td>(&lt; .001)</td>
<td>67.4 (11.4)</td>
<td>67.8 (11.3)</td>
<td>(.21)</td>
</tr>
<tr>
<td>Male sex</td>
<td>2928 (98.9)</td>
<td>5162 (98.4)</td>
<td>(.10)</td>
<td>1921 (68.4)</td>
<td>3241 (98.5)</td>
<td>(.74)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>1126 (38.0)</td>
<td>2386 (45.5)</td>
<td>(&lt; .001)</td>
<td>900 (46.1)</td>
<td>1486 (45.1)</td>
<td>(.51)</td>
</tr>
<tr>
<td>Prior myocardial infarction</td>
<td>564 (20.1)</td>
<td>1383 (26.4)</td>
<td>(&lt; .001)</td>
<td>517 (26.5)</td>
<td>868 (26.3)</td>
<td>(.90)</td>
</tr>
<tr>
<td>PCI within last 6 mo</td>
<td>209 (7.1)</td>
<td>395 (7.5)</td>
<td>(.59)</td>
<td>148 (7.6)</td>
<td>247 (7.5)</td>
<td>(.92)</td>
</tr>
<tr>
<td>CABG surgery</td>
<td>587 (19.8)</td>
<td>1377 (26.3)</td>
<td>(&lt; .001)</td>
<td>503 (25.6)</td>
<td>874 (26.8)</td>
<td>(.52)</td>
</tr>
<tr>
<td>Heart failure</td>
<td>477 (18.1)</td>
<td>1372 (26.2)</td>
<td>(&lt; .001)</td>
<td>498 (25.5)</td>
<td>874 (26.8)</td>
<td>(.40)</td>
</tr>
<tr>
<td>Cerebrovascular disease</td>
<td>225 (7.6)</td>
<td>478 (9.1)</td>
<td>(.02)</td>
<td>195 (10.0)</td>
<td>283 (8.5)</td>
<td>(.09)</td>
</tr>
<tr>
<td>Peripheral vascular disease</td>
<td>451 (16.2)</td>
<td>1345 (25.6)</td>
<td>(&lt; .001)</td>
<td>483 (24.7)</td>
<td>662 (26.2)</td>
<td>(.24)</td>
</tr>
<tr>
<td>Prior clopidogrel use</td>
<td>519 (17.5)</td>
<td>1379 (26.3)</td>
<td>(&lt; .001)</td>
<td>474 (24.3)</td>
<td>905 (27.5)</td>
<td>(.01)</td>
</tr>
<tr>
<td>Cancer</td>
<td>166 (5.6)</td>
<td>382 (7.3)</td>
<td>(&lt; .1)</td>
<td>135 (6.9)</td>
<td>247 (7.5)</td>
<td>(.42)</td>
</tr>
<tr>
<td>COPD</td>
<td>503 (17.0)</td>
<td>1346 (25.7)</td>
<td>(&lt; .001)</td>
<td>454 (23.2)</td>
<td>892 (27.1)</td>
<td>(.002)</td>
</tr>
<tr>
<td>Renal disease</td>
<td>294 (9.9)</td>
<td>914 (17.4)</td>
<td>(&lt; .001)</td>
<td>323 (16.5)</td>
<td>591 (18.0)</td>
<td>(.19)</td>
</tr>
<tr>
<td>Liver disease</td>
<td>70 (2.4)</td>
<td>181 (3.5)</td>
<td>(&lt; .1)</td>
<td>64 (3.3)</td>
<td>117 (3.6)</td>
<td>(.59)</td>
</tr>
<tr>
<td>Dementia</td>
<td>301 (10.2)</td>
<td>726 (13.8)</td>
<td>(&lt; .001)</td>
<td>261 (13.4)</td>
<td>466 (14.1)</td>
<td>(.44)</td>
</tr>
<tr>
<td>TIMI risk score, mean (SD)</td>
<td>2.8 (1.2)</td>
<td>2.9 (1.2)</td>
<td>(&lt; .001)</td>
<td>2.9 (1.2)</td>
<td>2.9 (1.3)</td>
<td>(.79)</td>
</tr>
<tr>
<td>LVEF &lt;40%</td>
<td>719 (24.3)</td>
<td>1395 (26.6)</td>
<td>(.02)</td>
<td>535 (27.4)</td>
<td>860 (26.1)</td>
<td>(.32)</td>
</tr>
<tr>
<td>ACS presentation</td>
<td></td>
<td></td>
<td>(&lt; .001)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>STEMI</td>
<td>644 (21.7)</td>
<td>876 (16.7)</td>
<td>(&lt; .001)</td>
<td>331 (16.9)</td>
<td>545 (16.6)</td>
<td>(.43)</td>
</tr>
<tr>
<td>NSTEMI</td>
<td>2036 (68.8)</td>
<td>3696 (70.5)</td>
<td>(_)</td>
<td>1358 (69.5)</td>
<td>2338 (71.0)</td>
<td>(_)</td>
</tr>
<tr>
<td>PCI performed</td>
<td>1644 (55.5)</td>
<td>2427 (46.3)</td>
<td>(&lt; .001)</td>
<td>902 (46.2)</td>
<td>1525 (46.3)</td>
<td>(.91)</td>
</tr>
<tr>
<td>CABG performed</td>
<td>75 (2.5)</td>
<td>137 (2.6)</td>
<td>(.88)</td>
<td>44 (2.3)</td>
<td>93 (2.8)</td>
<td>(.21)</td>
</tr>
<tr>
<td>Discharge medications</td>
<td></td>
<td></td>
<td>(_)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aspirin</td>
<td>2700 (91.2)</td>
<td>4657 (89.4)</td>
<td>(.01)</td>
<td>1736 (68.9)</td>
<td>2961 (89.7)</td>
<td>(.57)</td>
</tr>
<tr>
<td>β-Blocker</td>
<td>2747 (92.8)</td>
<td>4892 (93.3)</td>
<td>(.64)</td>
<td>1818 (93.1)</td>
<td>3074 (93.4)</td>
<td>(.21)</td>
</tr>
<tr>
<td>ACE inhibitor</td>
<td>2340 (79.0)</td>
<td>4114 (78.4)</td>
<td>(.89)</td>
<td>1531 (78.4)</td>
<td>2583 (78.5)</td>
<td>(.84)</td>
</tr>
<tr>
<td>Statin</td>
<td>2825 (95.4)</td>
<td>5031 (95.9)</td>
<td>(.25)</td>
<td>1875 (66.0)</td>
<td>3156 (95.9)</td>
<td>(.85)</td>
</tr>
</tbody>
</table>

Abbreviations: ACE, angiotensin-converting enzyme; ACS, acute coronary syndrome; CABG, coronary artery bypass graft; COPD, chronic obstructive pulmonary disease; LVEF, left ventricular ejection fraction; NSTEMI, non-ST elevation myocardial infarction; PCI, percutaneous coronary intervention; PPI, proton pump inhibitors; STEMI, ST-elevation myocardial infarction; TIMI, Thrombolysis in Myocardial Infarction.

\(^a\)Values are expressed as number (percentage) unless otherwise indicated.

Randomized trials to the rescue!

- **AHA statement**, Nov 11, 2008: “The ongoing COGENT-1 study should help answer some of these questions – this trial is randomizing patients with coronary artery disease to ASA plus clopidogrel in combination with 20 mg of omeprazole (a PPI) or placebo.”

- **SCAI statement**, Nov 25, 2008: “SCAI is eager for the findings of ongoing studies, including the large, randomized study COGENT-1…”
COGENT 1 trial scrapped, sponsor declares bankruptcy

JANUARY 22, 2009 | Shelley Wood

Palo Alto, CA - The sponsor of what was intended to be a 4000-patient trial testing a single-pill combination of clopidogrel and omeprazole to reduce the incidence of GI side effects has pulled the plug on the study and is filing for bankruptcy.

Investigators for the trial say the study has been shut down so abruptly that study sites have been left with no support for patients and staff to close down the study in a safe and timely way.

"We're going to do the best we can for patients, but this has been a pretty big shock for everybody to be left sort of holding the bag," Dr Ian C Gilchrist, a principal investigator for the study at the Heart & Vascular Institute, in Hershey, PA, told heartwire. "I've been doing this for 20 years and some of the companies have not survived, but the question of whether a site was going to be properly reimbursed and the study properly concluded has never been an issue."

The COGENT 1 study, sponsored by Cogentus Pharmaceuticals (Palo Alto, CA), was a phase 3 trial testing its combination product, known as CGT-2168, in patients requiring clopidogrel for at least 12 months, typically following non-ST-segment-elevation ACS, STEMI, or stent implantation. CGT-2168 is a once-daily pill that combines 75-mg clopidogrel with 20 mg of the gastroprotectant omeprazole.
Stents and PPIs: bottom line

• Patients requiring clopidogrel should only be on PPIs for solid indications. Consider H2 blockers or antacids when appropriate.

• Plenty of patients still require PPIs. These patients should not be deprived of PPIs regardless of their cardiac status.
Some PPIs may have lesser interactions with clopidogrel (e.g. pantoprazole), but this has not been borne out in all studies.

The clinical data available to date, while compelling, is not conclusive.

Newer drugs (such as Prasugrel) may offer a partial solution to this problem.
Which of the following is not true about the new thienopyridine Prasugrel?

A. Like clopidogrel, prasugrel is a prodrug.
B. In the TIMI 38 trial, prasugrel was more effective than clopidogrel at preventing a composite of death, MI, and stroke.
C. Prasugrel causes less bleeding than clopidogrel.
D. Prasugrel (compared with clopidogrel) appears to be less subject to interactions with drugs like PPIs.
Prasugrel vs Clopidogrel: TIMI 38

Fewer ischemic events, but...

More bleeding compared with clopidogrel

More on Prasugrel

• Prasugrel metabolism is less affected by P450 polymorphisms, and appears to have less interaction with PPIs.
• Prasugrel may turn out to be a good alternative for clopidogrel non-responders, or for patients who require medications like PPIs.
Genetics

Cytochrome P450 Genetic Polymorphisms and the Response to Prasugrel
Relationship to Pharmacokinetic, Pharmacodynamic, and Clinical Outcomes

Jessica L. Mega, MD, MPH; Sandra L. Close, PhD; Stephen D. Wiviott, MD; Lei Shen, PhD; Richard D. Hockett, MD; John T. Brandt, MD; Joseph R. Walker, PharmD; Elliott M. Antman, MD; William L. Macias, MD, PhD; Eugene Braunwald, MD; Marc S. Sabatine, MD, MPH

Background—Both clopidogrel and prasugrel require biotransformation to active metabolites by cytochrome P450 (CYP) enzymes. Among persons treated with clopidogrel, carriers of reduced-function CYP2C19 alleles have significantly lower levels of active metabolite, diminished platelet inhibition, and higher rates of adverse cardiovascular events. The effect of CYP polymorphisms on the clinical outcomes in patients treated with prasugrel remains unknown.

Methods and Results—The associations between functional variants in CYP genes, plasma concentrations of active drug metabolite, and platelet inhibition in response to prasugrel were tested in 238 healthy subjects. We then examined the association of these genetic variants with cardiovascular outcomes in a cohort of 1466 patients with acute coronary syndromes allocated to treatment with prasugrel in the Trial to Assess Improvement in Therapeutic Outcomes by Optimizing Platelet Inhibition With Prasugrel–Thrombolysis in Myocardial Infarction 38 trial. Among the healthy subjects, no significant attenuation of the pharmacokinetic or the pharmacodynamic response to prasugrel was observed in carriers versus noncarriers of at least 1 reduced-function allele for any of the CYP genes tested (CYP2C19, CYP2C9, CYP2B6, CYP3A5, and CYP1A2). Consistent with these findings, in subjects with acute coronary syndromes treated with prasugrel, no significant associations were found between any of the tested CYP genotypes and risk of cardiovascular death, myocardial infarction, or stroke.

Conclusions—Common functional CYP genetic variants do not affect active drug metabolite levels, inhibition of platelet aggregation, or clinical cardiovascular event rates in persons treated with prasugrel. These pharmacogenetic findings are in contrast to observations with clopidogrel, which may explain, in part, the different pharmacological and clinical responses to the 2 medications. (Circulation. 2009;119:000-000.)

Circulation, May 4, 2009
What’s to come with DES?

Minimize what’s left in the vessel in order to reduce stent thrombosis and limit long-term effects on endothelial function

• DES with no polymer
• DES with bioabsorbable polymers
• Bioabsorbable stents!
New developments in drug-eluting stents

- The original DES:
  - Cypher: sirolimus
  - Taxus: paclitaxel

- Recent additions to the DES world:
  - Xience/Promus: everolimus
  - Endeavor: zotarolimus
  - Taxus Liberte: same paclitaxel coating on a newer stent design.

- All are incremental improvements in usability
- All involve metallic stents with a durable polymer
EDITORIAL COMMENT

The Excel Stent: A Good DES, But Can We Really Stop Clopidogrel After 6 Months?

James R. Margolis, MD

Miami, Florida

In their report of the CREATE (Multi-Center Registry of Excel Biodegradable Polymer Drug-Eluting Stents) study in this issue of *JACC: Cardiovascular Interventions*, Han et al. (1) suggest that the Excel stent (JW Medical System, Weihai, China)—a sirolimus-eluting stent with biodegradable polymer—has equal or superior major adverse cardiac event (MACE) rates to presently available drug-eluting stents (DES). Because the biodegradable polymer precludes late stent thrombosis (LST), only 6 months of clopidogrel are required. This is a well-designed study performed in a scientific manner. The data are reported objectively, and the authors recognize the deficiencies of a registry. Upon first reading, the results are impressive. On closer inspection, it is necessary to ask what the study actually showed, and is there any solid evidence that Excel is superior to presently available DES?
A bioabsorbable everolimus-eluting coronary stent system (ABSORB): 2-year outcomes and results from multiple imaging methods

Patrick W Serruys, John A Ormiston, Yoshinobu Onuma, Evelyn Regar, Nieves Gonzalo, Hector M Garcia-Garcia, Koen Nieman, Nico Bruining, Cécile Dornage, Karine Miquel-Hébert, Susan Veldhof, Mark Webster, Leif Thuesen, Dariusz Dudek

Summary
Background Drug-eluting metallic coronary stents predispose to late stent thrombosis, prevent late lumen vessel enlargement, hinder surgical revascularisation, and impair imaging with multislice CT. We assessed the safety of the bioabsorbable everolimus-eluting stent (BVS).

Methods 30 patients with a single de-novo coronary artery lesion were followed up for 2 years clinically and with multiple imaging methods: multislice CT, angiography, intravascular ultrasound, derived morphology parameters (virtual histology, palmpography, and echogenicity), and optical coherence tomography (OCT).

Findings Clinical data were obtained from 29 of 30 patients. At 2 years, the device was safe with no cardiac deaths, ischaemia-driven target lesion revascularisations, or stent thromboses recorded, and only one myocardial infarction (non-Q wave). 18-month multislice CT (assessed in 25 patients) showed a mean diameter stenosis of 19% (SD 9). At 2-year angiography, the in-stent late loss of 0·48 mm (SD 0·28) and the diameter stenosis of 27% (11) did not differ from the findings at 6 months. The luminal area enlargement on OCT and intravascular ultrasound between 6 months and 2 years was due to a decrease in plaque size without change in vessel size. At 2 years, 34·5% of strut locations presented no discernible features by OCT, confirming decreases in echogenicity and in radiofrequency backscattering; the remaining apparent struts were fully apposed. Additionally, vasomotion occurred at the stented site and adjacent coronary artery in response to vasoactive agents.

Interpretation At 2 years after implantation the stent was bioabsorbed, had vasomotion restored and restenosis prevented, and was clinically safe, suggesting freedom from late thrombosis. Late luminal enlargement due to plaque reduction without vessel remodelling needs confirmation.

Funding Abbott Vascular (USA).
Case: Atrial fibrillation

• Your 76 year old patient with atrial fibrillation and a CHADS2 score of 4 is unable to take warfarin. You are looking for alternatives.

• You have seen the results of the ACTIVE study (N Engl J Med. 2009 Apr 3) showing a benefit to aspirin + clopidogrel.

• You have also heard about an implantable device that prevents thrombus formation in the atrial appendage...
Left Atrial Appendage Occluder Devices

Watchman

PLAATO
PROTECT AF Trial

• Randomized trial of the Watchman LAA occluder in patients with atrial fibrillation.

• 707 patients randomized to device placement or warfarin (2:1 randomization).

• Patients followed bi-annually for up to 5 years.
PROTECT AF Results

- CV death, stroke, or systemic embolism: 3.4 events per 100 pt-yrs with closure vs. 5.0 events per 100 pt-yrs with control (p for non-inferiority < 0.05)
- Hemorrhagic stroke: 1 vs. 6 (p for superiority < 0.05)
- Composite safety outcome: 8.7 events per 100 pt-yrs vs. 4.2 events per 100 pt-yrs (p < 0.05)
PROTECT AF Conclusions

- In patients with non-valvular AF, use of Watchman for LA appendage closure is feasible
- The device was:
  - Non-inferior to warfarin for all stroke
  - Superior to warfarin for hemorrhagic stroke
  - Inferior with respect to composite safety, due to pericardial effusion
Case: Aortic Stenosis

Your patient is a 45-year-old man with bicuspid aortic valve and progressive aortic stenosis. He was an avid cyclist, but over the past 2 years he has been tiring more rapidly, and has more recently had to give up exercise altogether because of exertional dyspnea and chest pain. The echo shows: normal LV systolic function, mild LVH, heavily calcified aortic valve, peak gradient 79 mmHg, mean gradient 51 mmHg, valve area 0.6 mm2. The coronary arteries are free of disease. When you bring up aortic valve replacement, he asks: What about this procedure I’ve been reading about where they can replace the valve without cutting open the chest?
Aortic Stenosis Case

What do you tell your patient?

A. That’s just Star Wars stuff. It’s not possible.
B. Maybe we can get you into a trial of percutaneous aortic valve replacement (AVR)
C. Percutaneous AVR will be generally available soon. Let’s wait.
D. You are not a good candidate for percutaneous AVR. You need surgery.
Percutaneous AVR: an update

- Initial implantation in a patient with severe AS and cardiogenic shock in April 2002.
- Multiple systems and approaches have been tried with varying success.
- Two different valve models have progressed to large-scale trials.
  - Edwards SAPIEN balloon-expandable valve
  - CoreValve Revalving system
CoreValve

- Self-expanding, stent-mounted porcine tissue valve
- 18F catheter delivery system
- By October 2008, over 1800 high-risk patients had been treated internationally with this device.
- Not yet in trials in the US
Edwards SAPIEN valve

- Balloon-expandable, stent-mounted bovine pericardial prosthesis.
- 22F and 24F delivery systems.
- The only percutaneous valve currently in trials in the US.
What the valves have in common

Both valves:

- can be inserted via the femoral artery or trans-apically via a small surgical incision.
- are tissue valves (not mechanical), with expected limitations on valve life similar to surgically-implanted valves.
- are currently in international trials for high-risk surgical patients with severe AS.

The number of patients worldwide who have undergone treatment with these devices is currently around 4000.
Summary: Percutaneous AVR

- PAVR is coming
- PAVR may be restricted to patients who are at high risk for surgery, at least at first
- Current PAVR devices are tissue valves, and therefore have limited lifespan – not great for younger patients!
- PAVR may not be good for bicuspid aortic valves, due to trouble fitting the round prosthesis in an elliptical space.
Update on Interventional Cardiology for the Internist

Thanks for your attention!