NEW APPROACHES IN THE TREATMENT OF CORONARY ARTERY DISEASE

Evolution of Coronary Artery Stents and Scaffolding Devices

A CME-CERTIFIED ACTIVITY

FACULTY TRAINING TRANSCRIPT

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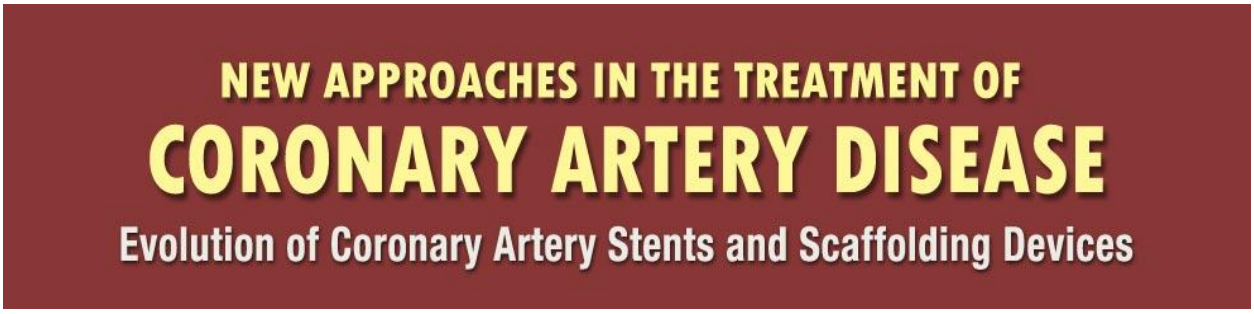

Slide 1 – Title Slide

James B. Hermiller, MD, FSCAI: Hello, this is Jim Hermiller. I'm from St. Vincent Medical Group, St. Vincent Hospital in Indianapolis, and it's a real pleasure to talk today about this slide deck which is a CME-certified Grand Rounds Program really targeted at new approaches in the treatment of coronary disease and, really, evaluating the evolution of coronary stents and scaffolding device. It's provided by Society for Cardiovascular Angiography and Intervention, the activity is supported through an educational grant from Abbott Vascular.

Slide 2 – Please Help Us with the Following

Slide 3 – CME Information

Slide 4 – Polling Question 1

Slide 5 -Educational Objectives

With respect to the educational objectives, what we're really trying to do with this slide set is: first of all, help those in the audience understand when PCI is appropriate, and how is it a management choice to help improve clinical outcomes of our patients; and then implement strategies based on that understanding to use the appropriate, stents and scaffolding technologies we have; and then to look to the future and really dig into the emerging stent and scaffolding technologies and see how we might best use these technologies to improve our patients' outcomes.

Slide 6 – How and When Should PCI Be Used

Slide 7 – Appropriate Use Criteria: Key Variables

First of all, let's talk about appropriate use and appropriate-use criteria. I think, as we look at what determines is something appropriate or not, there's about, really, five fields that we always use in the calculus to decide that:

What's the clinical presentation? Stable angina all the way up to a STEMI.

What is the symptomatic state of the patient? Do they have a Class I angina? Do they have Class IV angina?

Thirdly, what's the ischemic risk? Very low, low stress tests, prognosis, and all the way up to a very high-risk patient. Medical therapy – have they had none, are they on maximum medical therapy? And then what's the anatomic disease? Is it single-vessel not involving the proximal LAD, all the way up to somebody that's got left main and three-vessel coronary disease.

And then, I think, probably all of you have the SCAI application to look at all of your patients and really decide is it appropriate or rarely appropriate, and then those in the middle area where it may be appropriate.

I think, as we talk to the audience, it's important for them to understand, how far we've come, I think, with, really, choosing our patients correctly and having this on the front of the plate when we decide whether to do stenting or not.

Slide 8 - Appropriate Use Criteria for Revascularization
Might just take this slide a second to demonstrate how these different metrics are used to decide is it appropriate care, sort of, the intermediate yellow zone may be appropriate care, and then in red, rarely appropriate. And you might talk to a few examples of this so the audience understands. You might also say that the appropriate-use criterion and those guidelines are going to be coming out later this year with an update, so stay tuned for that.

Slide 9 - Appropriate Use Criteria 2012: In a Nutshell
I think, in a nutshell, the criterion we have right now, essentially using transcatheter revascularization with acute coronary syndromes is almost always appropriate. Revascularization in asymptomatic patients, those at low risk on medical therapy are much less frequently appropriate. We all are doctors and we have to really weigh all the factors in these individual patients, and, although it may add up on the application to be rarely appropriate or yellow, may be appropriate, we need to justify why we're going to do a PCI in this particular patient and why these patient's characteristics really mitigate against using the criteria.

Slide 10 – Polling Question 2

Slide 11 - Percutaneous Coronary Interventions (PCI): Timeline of Development
We're going to move now from appropriate use and really talk, then, about PCI. This is just a slide looking at the history of PCI and balloon angioplasty, bare-metal stents, DES, and then, talk to improvements in DES, and we're going to really follow this as we go along the rest of the lecture.

Slide 12 – Polling Question 3

Slide 13 - Early Bare-metal Stent Trials
We go back to the early bare-metal stent trials, and what led to approval of the pulmonary shunt stent, the STRESS Trial, the BENESTENT Trial, you can see restenosis, TLR last, or MACE last. And I think, more than anything besides the restenosis issues with bare-metal stents, it was the ability to put a stent home, go home, to bed, and you knew you were going to be called because of abrupt closure that we so often saw after ballooning angioplasty. So not only was this reduction of restenosis of bare-metal stents complete, compared to balloon angioplasty, it was the ability to take care of dissections and not have abrupt vessel closure.

Slide 14 - Stents Improve Acute Gain But Cause Late Loss: Neointimal Proliferation
Now, stents, really, were associated with two differences compared to balloon angioplasty in terms of restenosis question. One, they allowed for a much bigger acute gain. But unlike restenosis with PTCA, neointimal proliferation was what leads to restenosis with bare-metal stents. And with a balloon angioplasty, it's more frequently negative remodeling. It's really negative remodeling and abrupt recoil. And despite them being much better than balloon angioplasties, bare-metal stents were associated with a 20% to 30% restenosis and a stent thrombosis for very vanilla, easy lesions of 1% or more.

Slide 15 - First-generation Drug-eluting Stents

This then led to drug-eluting devices to inhibit that intimal hyperplasia, which was at the foundation of bare-metal stent restenosis. And, as we all know, the first generation were the Cypher with sirolimus-eluting stent. It had PEVA and PBMA blend for polymer; these are both durable polymers, and this was a closed-cell design stent. And then, the paclitaxel-eluting TAXUS stent that had a polyolefin derivative, durable polymer, as well.

Slide 16 - SIRIUS Trial: SES Reduced Restenosis and TVR compared to BMS at 1 Year

These first-generation devices did what they were supposed to do. They really did reduce intimal hyperplasia and led to lower restenosis rate. These are just some data from the SIRIUS Trial, looking at TVR compared to bare-metal stent at a year, and restenosis in segment was about four-fold lower; TLR – about a quarter as much; target vessel failure -- more than half as, low; and then MACE –about a third lower. So, in terms of what they were meant to do, and that was prevent restenosis, prevent repeat target- lesion revascularization the first-generation devices were quite effective.

Slide 17 – Polling Question 4

Slide 18 - Late Thrombosis Increased with DES vs BMS: Meta-analysis of Randomized Clinical Trials

What we all found out about them, however, was that there was this risk of late stent thrombosis, particularly very late stent thrombosis compared to bare-metal stents. And these are some classic data from Bavry, a meta-analysis of randomized clinical trials, looking at DES, vs BMS, whether that be, sirolimus-eluting or paclitaxel-eluting. The time to stent thrombosis significantly longer compared to bare-metal stent. Not much happened with bare-metal stents particularly very late, but not so for drug-eluting stents, which were associated with a significantly higher rate of very late stent thrombosis. Although, if you looked at *overall* stent thrombosis, particularly with Cypher, it was hard to show that the overall stent thrombosis rate was higher with these platforms because bare-metal stents, because of the restenosis issue and 10% of restenosis have an acute MI. They have a higher stent thrombosis rate, particularly within that first six months.

Slide 19 – Polling Question 5

Slide 20 - Limitation of Early Generation of DES: Pathological Healing Response to Stent Implantation

This issue, though, of very late stent thrombosis came to the forefront and it led to the second-generation devices, which, importantly, really were designed to get over these pathologic healing responses of these first-generation devices, and that's shown here. And this included, really, we think, a reaction to the polymer; although, we're all uncertain, exactly. Is it the polymer? Is it the late drug effect? But, it's probably the polymer led to eosinophilic infiltrates, a delayed healing. The velocity with which the struts were covered with endothelium were so much slower compared to bare-metal stents, and there was an incompleteness of how those struts were covered, and that often led to late positive remodeling and late malapposition. Furthermore, there was evidence of neoatherosclerosis, and, really, neoatherosclerosis associated with very unstable lesions, and that neoatherosclerosis, likely resulting in stent thrombosis related to plaque underneath the struts and not necessarily just uncovered struts themselves.

Slide 21 - Comparative Efficacy and Safety of Contemporary Stent Options

Slide 22 - BMS vs 1st-gen DES vs 2nd-gen DES

Now, as we get into the *second*-generation devices, however, one sees that this very late stent thrombosis issue essentially went away. And these are some data from the SCAAR Registry: 94,000 patients, 64,000 patients with BMS, 19,000 patients with first-generation DES, and then 10,000-plus patients with *second*-generation DES. And if we look at restenosis, not surprisingly, the risk of having restenosis with bare-metal stent compared to either the first- or second-generation devices was *substantially* less, about a third of that compared to bare-metal stents. And the restenosis rate of the second-generation stents was *significantly* less with a hazard ratio of about 0.62, compared to the first-generation with respect to restenosis, on the left.

For definite stent thrombosis, as you can see, BMS, over time, associated with a higher stent thrombosis out to two years, the first-generation devices a stent thrombosis rate that was 40% lower than bare-metal stents. I think that's particularly true of Cypher and SES, probably less so for PES. Certainly, the risk of very late stent thrombosis is higher for PES than it is for the first-generation Cypher SES.

And then, if we look at the *second*-generation devices on the bottom, again, much lower, and the rate of stent thrombosis after a year is really no different than bare-metal stents, a substantial improvement in this stent thrombosis issue, particularly, very late stent thrombosis for the second-generation devices. Really came a long way, both with respect to efficacy and restenosis and then the safety issue and the stent thrombosis.

Slide 23 - Definite Stent Thrombosis

This is a classic study from Bangalore, a network meta-analysis, over 258,000 patient-year follow-up, 126 RCTs, and this looked at DES, and BMS, with respect to the question of definite stent thrombosis. And, really, no difference, overall, for SES and PES, the first-generation devices. Cobalt-chromium EES was significantly lower, but, really, all the second-generation devices fell to the left, suggesting at least either no *increase* in definite stent thrombosis or a favorable effect on stent thrombosis. And some of that, not being statistically significant, may, in part, be a consequence of how powered those different subsets were.

Slide 24 - New Stenting Technologies: DES with Bioresorbable Polymer

Slide 25 - Multiple Studies Examining Safety of Biodegradable Polymer Metallic DES in the First Year

Now, I think the question with the second-generation devices, whether that's EES cobalt-chromium, EES platinum-chromium, or, Resolute, is what if we don't leave a polymer on there. Although, these polymers are much more biocompatible than the first-generation polymers, what if we were to just get rid of them and what are some of the data related to biodegradable polymer metallic DES? These are some data from the LEADERS Trial, SORT OUT V, COMPARE II, and NEXT. In blue, biodegradable polymer DES, and, in purple, everolimus, eluting stent, and then sirolimus in gray, and you can see that, it was difficult to show with the LEADERS Study as well as the others that, really, this biodegradable polymer added a lot in terms of ARC definite stent thrombosis. So, although, I think, intuitively, having a biodegradable polymer is a favorable aspect to a stent in the long-term, we intuitively think that would make difference. It's been a bit hard to show that it's better than these very good second generation DES devices.

Slide 26 - EVOLVE II Trial: Patient Flow and Disposition

I think the most recent platform which was studied in the EVOLVE II Trial looked at EES platinum-chromium with a biodegradable polymer. It's an abluminal polymer from Boston

Scientific, and that was randomized, against a EES platinum-chromium with a durable polymer. And 1684 patients randomized.

Slide 27 - EVOLVE II Trial: Primary Safety Endpoint: Target Lesion Failure (TLF) at 1 year
And if we look at target-lesion failure for either the durable polymer or compared to the biodegradable polymer, clearly, the biodegradable polymer was non-inferior; although, it was hard to show superiority.

Slide 28 - Emerging Stent/Scaffolding Technologies

Slide 29 - Drug-filled Stent (DFS) Technology: Polymer Free Drug Delivery
I think we all want to see longer-term data maybe not having that polymer in the long-term and just a bare-metal platform may result in potentially less catch-up in the long-term. We all know, with DES there does seem to be late catch-up, and restenosis, it occurs anywhere from 3% to 4%, over time, and maybe having a bare-metal platform without a polymer, that we may see less catch-up. But I think that's to be proven.

Another way to get at not having a polymer on these drug-losing devices is just not to have it biodegrade but simply not have a polymer. And there's a number of technologies aimed at this. Polymer-free drug delivery –this is a Medtronic design and they're basically drug-filled stents with a hollow core, and then the drug exits through these holes, without having any polymer. And, actually, this is coming to trial, late this year and next year.

The other idea is to just have a surface which the drug is imbedded in, and so, sort of a complex structure to the stent itself that allows the polymer to be housed there and then eluted over time. But it's really not based on any polymer; it's based on this structure of the surface itself.

Slide 30 - LEADERS FREE Clinical Trial
I think this was an exceptionally exciting trial, the LEADERS FREE Trial, but 2500 patients were randomized to either the LEADERS polymer-free drug coated stent vs a bare-metal stent, and these were in patients who were at a very high risk for bleeding. And patients were treated with DAP for 30 days in both groups. And what was found was, I think, very surprising. The first shown here – efficacy – and this is target-lesion revascularization; this part wasn't surprising. So, out to a year, bare-metal stents had twice the need for target-lesion revascularization.

Slide 31 - LEADERS FREE Clinical Trial: Primary Safety Endpoint: Composite of Cardiac Death, MI or ST
But, what I think *was* surprising was, in fact, the biolimus-coated stent, had a superior *safety* profile, so it was really superior with respect to safety, and that was a composite to cardiac death, MI, or stent thrombosis compared to bare-metal stent. So I think this was a very exciting study, and I think we're going to hear more about this.

Slide 32 – Polling Question 6

Slide 33 - Limitations of Durable Metallic Stents
So that's it for, sort of, the metallic platforms. And we're really getting, I think, towards the end of what we can do with metallic platforms. I think the question is, "What are some of the limitations that are going to lead to non-metallic platforms?"

Well, one, you have uncovered stent struts, with or without late malapposition, and that may lead to late stent thrombosis. There is chronic inflammation due to late foreign-body reactions

and potentially polymer hypersensitivity. No matter what the platform is strut factures over time can occur. Inability to place bypass grafts into stented segments, you stent a big, full metal jacket in the LAD and now down the road the LIMA option is excluded. You permanently "jail" a side branch – there's *multiple* layers of metal stent sandwich in these patients that restenose, and that can reduce the lumen vessel. Neoatherosclerosis, which we've already talked about. There's lack of vasomotion. Certainly, some of the angina that patients who have metallic stenting is a result of an inability to dilate the vessel in response to physiologic response to exercise.

Slide 34 - Bioresorbable Vascular Scaffolds: "Top Ten" Potential Physiological Advantages

So what might be the top 10 potential reasons for a bioresorbable vascular scaffold? What, sort of, intuitively, would a scaffold that goes away – why would that be something that we'd all like? Well, it preserves a capacity for adaptive remodeling, so the Glagov phenomenon, and we can accommodate atherosclerosis, potentially, something that can't be done when the vessel is "jailed." Preserve auto-regulation, physiologic recovery. Improve microcirculation, endothelial function. Eliminate that nidus for neoatherosclerosis and that ongoing injury related to that metallic platform. Enhance flexibility and conformability – we know the more that we distort the vessel architecture, the more we take bends out of arteries, the higher the risk of both chronic injury, leading to restenosis, but also an increased risk of a stent fracture. Restore physiologic strain, pulsatile flow, all of which is important in normal vascular biology. Plaque regression.

Vulnerable plaque sealing with a neomedia – we'll talk a little bit about this, but, if you already have a scaffold that goes away, and what it leaves behind is a relatively inert neomedia that is at low risk for abrupt events down the road; this would be very exciting. Eliminate impediments to future revascularization –and so, non-invasive imaging, particularly with the advanced CT with flow reserve these days being able to do that without having a vascular metallic scaffold interfering with that analysis would be very useful. And then, there are many cultural and other reasons that people don't want permanent implants in their bodies.

Slide 35 - Bioresorbable Coronary Scaffolds

Let's talk now about bioresorbable scaffolds. What's the history? It goes all the way back to 1996. Then I think the most famous picture with respect to bioresorbable technology is the Tamai, *Circulation* article. Dr. Tamai was the first to implant a fully biodegradable non drug-eluting stent scaffold. And then there's been steady progress across time with a variety of different platforms, and we're going to see an explosion in these platforms over time.

Slide 36 - ABSORB BVS

The ABSORB bioresorbable scaffold, or BDS, is the first to get to market and, certainly, now is approved and, is far down the road with respect to the other technologies, so it's going to be the bioresorbable scaffold platform that we're going to have for some time.

The device itself – fully resorbable. It's made up of a backbone of lactide chains. And lactide, which is probably acetic acid, comes in two varieties. There's an L and there's a right-handed chain, and the everolus is in a matrix, so the actual everolimus the drug, is in a combination of a L and the right- configured chain, or PDLLA, and so this is a matrix coating. And, really, the drug release is very similar to what we have with cobalt-chromium EES today.

Now, PLLA, which is the backbone, is just the left-handed chains of the lactide and, it's semi-crystalline, in contradistinction to the matrix coating, the PDLLA, which is very amorphous. There is circumferential sinusoidal rings connected by linear links. There's three rings per link. Strut thickness is thick; it's 150 microns, OK, so this is a little bit *Back to the Future.* And then

there are platinum markers on each end to see where the end of the device is. You cannot see these devices radiographically.

Slide 37 - Phases of ABSORB Functionality

What are the phases of ABSORB functionality? There's really three parts to this. One is the revascularization itself. You put the stent in; you open up the vessel. It turns out that you need scaffolding of the vessel to get over the initial recoil, and the negative remodeling, you need a scaffold there for about three to four months, maybe a little bit longer, and that's the time that the ABSORB scaffold is really structurally in place, and it doesn't lose any of its radial strength during that time.

And then out after six months, you start to have some loss of mechanical support -- you really don't need that -- and, during that time, the vessel starts to react physiologically to those stresses as the mechanical source is lost. And then, after 24, 36 months, there's actually resorption of the entire device and, you no longer have any of the implant in place.

Slide 38 - BVS: Serial imaging of matched cross-sections at 6, 24 and 60 months post procedure

This is just serial studies both with OCT angiography and IVUS, post procedure, six months, two years, and five years. And you can see, on OCT, what happens over time. You can see the lucent boxes on the OCT. They're nicely endothelialized and covered with neointima at six months. At two years, you can see, there's neointima.

One can still see the struts of the device. And then, out to five years, the device is completely gone. You're left with this kind of golden ring or this, kind of smooth neovascular covering. And what's interesting, also, is to see, between the two-year and the five-year, there's actually an *increase* in the size of the lumen. And if one looked at the plaque area, it's also reduced. So there's some very interesting biology and remodeling that occurs that seems to be favorable.

Slide 39 - ABSORB BVS: Unjailing of Side Branches

One of the other aspects is that "jailed" side branches don't remain "jailed," so, post procedure, one year, three year, and five years, and you can see that that ostium in the side branch increases with time as the struts are lost.

Slide 40 - ABSORB III Study Design

Now, what are the clinical data? ABSORB III – large randomized trial, 2,000 patients, 2:1, EES bioresorbable vascular scaffold vs EES durable metallic, Xience platform. Primary endpoint was non-inferiority; secondary endpoints were superiority.

Slide 41 - ABSORB III: 1-Year Target Lesion Failure (TLF): Components

It was published back in 2015, and these are the one-year target-lesion failure data with the components. In blue, as the metallic platform, in gold, the BVS. No difference in TLF cardiac death, TVMI, ischemic-driven TLR.

Slide 42 - ABSORB III Device Thrombosis to 1 Year

This looks at the critical issue of stent thrombosis. Overall, there's no statistical difference; although, numerically, it was twice as high for the bio- revascular scaffold, and, you can see here that there was, numerically, a higher stent thrombosis across the timeframe. It was interesting – who was it that was having the stent thrombosis with the BVS? And it turns out they're very small vessels really, were, I think, the culprit.

Slide 43 - ABSORB III: Very Small Vessel Analysis

The study itself was to include reference vessel diameters between 2.5 and 3.75. And, if you think of 150-micron strutted stent, you get down to small vessels, less than 2.5; the struts are taking up a lot of the vessel. And, as such, there was a subgroup analysis, performed in the small vessel and, overall 19% of the patients had target lesions with reference vessel diameters less than 2.2 5 by QCA.

Slide 44 – ABSORB III: Outcomes by QCA RVD 2.25 mm

And if you look at those reference vessel diameter vessels less than 2.25 vs those greater than 2.25, you can see a dramatic difference in target-lesion failure, target-vessel MI stent thrombosis. So stent thrombosis in these less than 2.25-millimeter vessels was almost 5% vs 1.5%, and that's what primarily drove those numeric differences in stent thrombosis. If you look at the 2.25 or greater, really not much going on here at stent thrombosis 0.9 vs 0.6. So, it *seemed* as though a lot of the action, with respect to the higher stent thrombosis, was in these smaller vessels.

Slide 45 - ABSORB III Clinical Trial: Summary and Conclusions

As you talk to the audience about the summary and conclusions: BVS was not inferior and it met its primary endpoint. TLF components were not significantly different between the metallic and the BVS devices. Angina, all revascularization ischemia-driven TVR was similar, and there was no significant difference in the device thrombosis.

Slide 46 - Bioresorbable Vascular Stent vs CoCr-EES: A Meta-analysis of 4 Randomized Trials Totaling 3,389 Patients

Greg Stone did a nice meta-analysis, looking at BVS vs cobalt-chromium EES -- death, MI, or revascularization. And this was a patient-oriented composite. All-cause mortality, all MI or all revascularization. And, again, this is what the patient sees. They get revascularized; they don't care whether it was an in-stent restenosis or someplace else.

Slide 47 – Bioresorbable Vascular Scaffold vs Durable Metallic CoCr-EES

But there was no difference in these patient-oriented composites, and this is device-oriented, which was cardiac death, target vessel-related MI, or ischemia-driven target-lesion revascularization. No statistically significant difference here, as well.

Slide 48 - ABSORB IV

ABSORB IV Trial, is going to be a 3,000-patient trial, 1:1 EES, BVS vs EES, durable metallic stent, and, it's so really get 5,000 total patients between ABSORB III and ABSORB IV, and there's going to be follow-up out to five years. And what we really want to see is what happens with this TLF between one and five years? Does the promise of not having a scaffold around, down the road, with those issues that come along with a metallic implant, does it really translate into what we think are going to be advantages?

Slide 49 - BVS Technically Challenging to Deliver

Now, this is, I think, very exciting technology but it isn't as easy to put these devices in. And, it's *really* important to emphasize the technical challenges and the importance of putting this BVS in correctly. Again, it's 150 micron. The scaffold is not as flexible as a thin, strutted metallic stent. It's got a 1.4-millimeter crossing profile. Since French guides can be tight, GuideLiner can be used, and, actually, this says 8 French, but you can use a 7 French GuideLiner. And you may, use all those tricks that you learned in trying to put in the old bare-metal stents, the pulmonary shaft, you need good guide support; you need good predilatation and vessel preparation 'til you get the device where it needs to go.

Also, very different than bare-metal stents, there's a limit expansion capability. You don't want to go beyond 0.5 millimeters, beyond the nominal. Got a 2.5 BVS. You don't want to take it more than 3; you'll crack the rings and you'll crack the device itself.

Slide 50 - Angiographic Exclusions in Absorb Protocols

Some of the angiographic exclusion in the ABSORB Trial – excessive tortuosity, moderate calcification, and then longer lesions. So that's in ABSORB. And I think the way to use this device, and like anything new, kind of start out in fairly straightforward lesions, and then, as you get comfort and confidence, you can take on more complex disease.

Slide 51 - Vessel Preparation for Absorb

You need to treat the vessel differently in terms of its preparation. You really need to prep it. Remember, this is unlike a stent. Where you put a stent in, there's that metallic platform which scores the artery and helps with dilation. There isn't anything like that with the BVS, and so mandatory to dilate and really see that your balloon has expanded appropriately. If necessary, use a cutting or scoring balloon, and atherectomy, if necessary. Again, full balloon expansion before you attempt scaffold delivery. *Very* different than, a metallic device where it's a 3.0 vessel; you put in a 2.5 balloon; yeah, it looks pretty good; and then you jump in with the stent -- that is not the way to implant a BVS.

If you've got a vessel that you think may be small, it's on the 2.5 border, or it's big and you think it may be more than 4.0, it's useful to do IVUS or OCT early on to get a better idea of how big this vessel is, because you don't want to get caught with sticking this in something less than 2.5; or you put it in a vessel that's really over 4 millimeters, and you're not going to be able to dilate the device safely.

The BVS won't track across: recommend additional lesion preparation, buddy wire, et cetera, and this is a little different than when we first started out putting BVS in – you need to come back and hit it hard with a non-compliant balloon, and I think high pressures with a non-compliant balloon that's not more than 0.5 millimeters bigger than the nominal size of the device.

So that is sort of how to treat the BVS. And how to implant it – very important: if one looks at how outcomes have changed, compared to the early days of implantation compared to now, with contemporary placement of the device, the outcomes are *far* superior, and that is really due to preparation of the lesion, sizing it correctly, and then post-dilating it.

Slide 52 – Dual Antiplatelet Therapy: An Approach to Reduce Post-PCI Complications

Finally, we're going to just end with a discussion of dual antiplatelet therapy and, how long to use dual antiplatelet therapy.

Slide 53 - DAPT Trial

These are some data from the DAPT Trial, which looked at prolonged DAPT after 12 to 30 months vs just 12 months, in patients who, during the first year after their stent placement, they had no bleeding and no ischemic events, and there was a reduction in stent thrombosis – about a 30% reduction in stent thrombosis, and also overall MACCE, with respect to myocardial infarction reduced. There was a trade-off with mortality being higher, which was thought to be potentially a play of chance with higher mortality due to excess cancer deaths in the prolonged-treatment group.

Slide 54 - Clinical and Procedural Factors Associated with Increased Ischemic Risk (Including Stent Thrombosis) or Increased Bleeding Risk

As you look at your patients and try and decide, “Should I keep them on prolonged DAPT or not?” These are some of the important factors to consider. Increased risk of bleeding, it really favors a shorter duration of DAPT. Increased ischemic risk – whether that be because the patient is at high risk for ischemic events because of their clinical profile, or because they’re at high risk of stent thrombosis, because of the nature of the stent that they had placed, and then there are underlying risk factors for stent thrombosis. It’s really a decision trying to integrate both of these and come up with a decision.

There’s a very nice description from the most recent update on the DAPT Guidelines that just came out, from the ACC/AHA, from Levine and colleagues. And, the scoring system, to help decide should somebody on DAPT or not is nicely reviewed there and, I think it’s something to bring up during this discussion. I think the other thing that can be said, in patients that have not presented with acute coronary syndrome, the minimum duration of DAPT, at least for metallic second-generation DES, that there’s nothing technically complicated about their stent placement -- it’s only six months now, not 12 months.

Slide 55 - Summary

So I think, to summarize how and when a stent should be used the AUC Guidelines are very helpful but they’re a guide; they’re not the end-all, say-all, and we need to use clinical judgment, to really treat patients the appropriate way. But we know the more unstable the presentation, the more angina that the patient has, the higher the risk profile is, the more complex the disease, and the more aggressive the medical therapy the more likely they’re going to be appropriate for revascularization.

PCI has radically changed, and we’re sort of now in the fourth revolution, that being bioresorbable scaffolds. It started with balloon angioplasty, which was limited by abrupt closure and restenosis. BMS really *helped* with abrupt closure, in particular, did restenosis. Drug-eluting stents came along, *further* reduced restenosis by reducing intimal hyperplasia, but these first-generation devices had the assured very late stent thrombosis, which led to the second-generation devices that are much more favorable, very low stent thrombosis rates that are no different than bare-metal stents.

But the trouble is having a metallic platform with or without a polymer in there, over time, leads to continued target-lesion failure. Whether that’s due to neoatherosclerosis, or late stent thrombosis, just intimal hyperplasia that occurs over time because of the mechanical implant causing injury, whatever the mechanism is, there is this catch-up with these devices over time with ongoing events.

So this has led to, sort of, these next-generation devices. There are DES with the bioresorbable polymers and no polymer, which, if part of the reason there is late catch-up is due to the polymer, these help to solve that.

And then, the Holy Grail, are bioresorbable scaffolds. We’re really in the first-generation of this with the ABSORB BRS. And, being first-generation, its thick struts, it takes a lot of care to put this in. And because of those thick struts, it’s just absolutely necessary to be *very compulsive* about the implant, to make sure it is as perfect as can be.

And then, finally, we end with a brief discussion – dual antiplatelet therapy, which, comes up all the time. Not only for interventional cardiologists but, in particular with general cardiologists,

there is not a great understanding right now. I know you think, there should be, at the end of the presentation, lots of questions about DAPT because this is a question that, so often arises in clinical practice.

Slide 56 - CME Credit

And then, final slide is just a bit of housekeeping and the CME credit. Good luck. Thanks so much.