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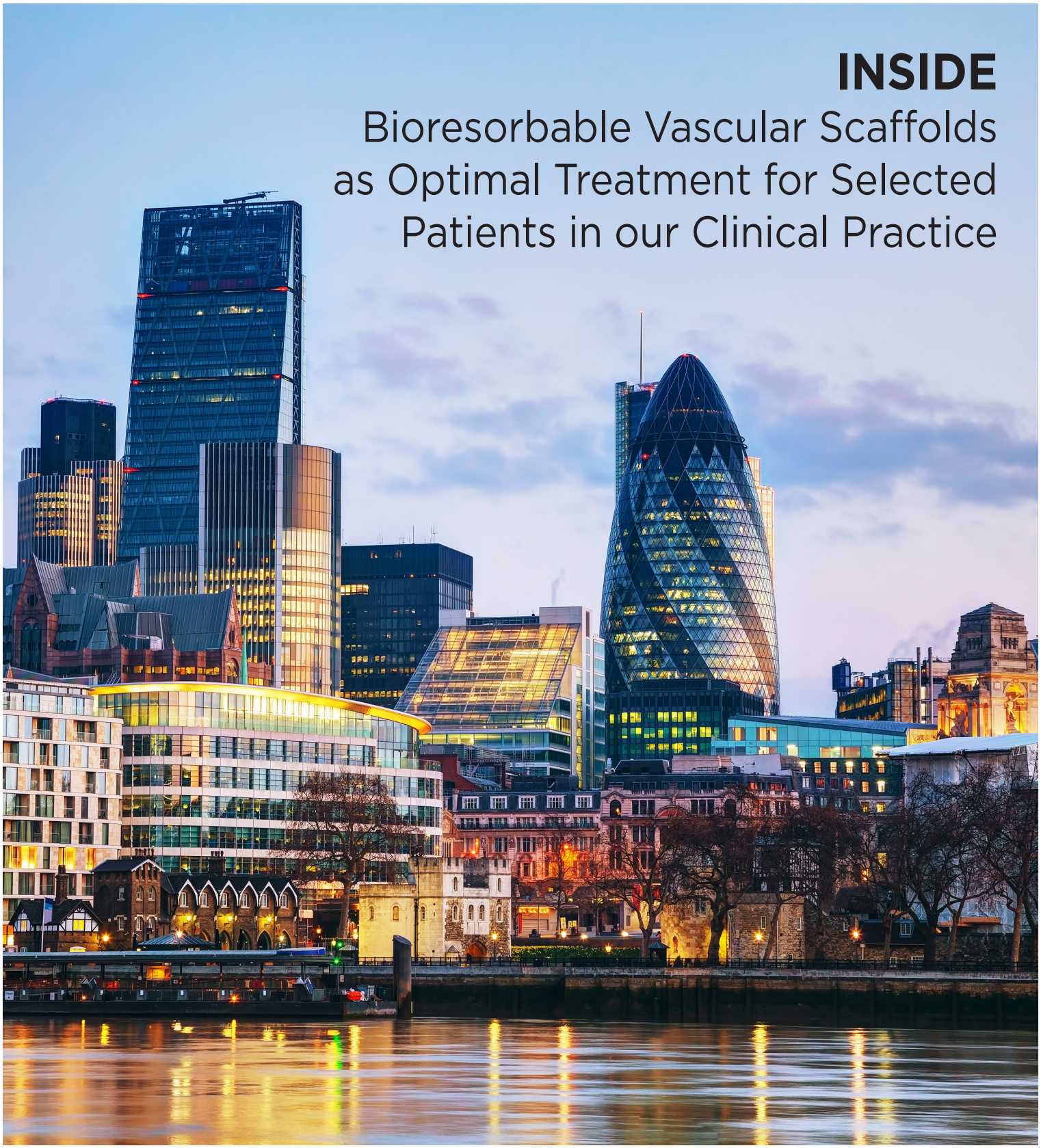

INSIDE

Bioresorbable Vascular Scaffolds as Optimal Treatment for Selected Patients in our Clinical Practice

BIORESORBABLE VASCULAR SCAFFOLDS AS OPTIMAL TREATMENT FOR SELECTED PATIENTS IN OUR CLINICAL PRACTICE

Four Experts Translate Clinical Trial Evidence to the Real World

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ABSTRACT

Bioresorbable vascular scaffolds (BRS)/bioabsorbable stents are a new and promising generation of intravascular devices that may potentially circumvent many of the problems associated with permanent metallic stents for coronary artery bypass graft surgery. The ABSORB™ BRS (Abbott Vascular, Santa Clara, California, USA) received Conformité Européenne (CE) mark approval in 2011 and has been implanted in over 150,000 patients over the globe.

New ABSORB data was presented at the 2016 EuroPCR Congress held in Paris, France, from 17th–20th May 2016. EuroPCR is the official congress of the European Association of Percutaneous Cardiovascular Interventions (EAPCI), with the goal of reducing the burden of cardiovascular disease.

We conducted an interview with four leading interventional cardiologists to discuss the prospective implications and advantages to patients generated by the development of such a technology, and how their experience in daily surgical practice is reflective of the device characteristics and features, which are interesting for select patient subsets.

Keywords: Bioresorbable vascular scaffolds (BRS), drug-eluting stents (DES), coronary angioplasty, coronary artery disease, interventional cardiology.

INTRODUCTION

Bioresorbable vascular scaffolds (BRS)/bioabsorbable stents are a new and promising generation of intravascular devices that may potentially circumvent many of the problems associated with permanent metallic stents for coronary artery bypass graft surgery.

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DOCTOR NICK WEST'S INTERVIEW

Q: Could you explain why and when do you consider bioresorbable vascular scaffolds for your patients?

A: This technology potentially offers all the advantages of contemporary metallic drug-eluting

stents (DES) in terms of reduced acute recoil and vessel occlusion, as well as reduction of restenosis (and possibly stent thrombosis), but without a permanent implant.

The lack of vessel 'caging' and the potential of this technology to allow restoration of vascular function to any degree is highly likely, from a physiological standpoint, to be beneficial to patients (and to translate into clinical benefit) in the longer-term.

Data from the plain old balloon angioplasty era suggest that if the early hazards of vessel occlusion and mid-term restenosis can be avoided, accrued patient event rates in the longer-term are lower than the steady year-on-year attrition observed in patients treated with metallic stents of any form (including metallic DES).

Although long-term randomised data are not yet available, the lack of early hazard for BRS is reassuring, and the favourable outcomes seen in the long-term follow-up of the ABSORB Cohort B study are encouraging.[1-3]

Late lumen stabilisation, as observed in the 5-year follow-up of the Cohort B patients,[3] is clearly likely to be important in reducing adverse events. This may in part be directly related to the restoration of vascular function observed at earlier time points in this study. Indeed, the return of endothelium-dependent vasomotor responses is like a barometer on vascular health and homeostasis, and reflects not only the disappearance of the scaffold itself and loss of caging, but also the likelihood (as extrapolated from animal models of disease) that the vascular environment will become less prothrombotic, more anti-inflammatory, and less proatherogenic: all features, again, that favour improved long-term outcomes.

Regarding plaque capping, the pre-emptive treatment of so-called 'vulnerable plaques' with the aim of avoiding patients suffering myocardial infarction is an attractive concept, but also a controversial one.

First, the issue of how to clearly define a vulnerable plaque is a thorny one, as natural history atherosclerosis studies have as yet failed to determine the optimum imaging modality to define such targets. Secondly, the debate of vulnerable plaque versus vulnerable patient continues to rage: should we be treating plaques locally or applying pharmacological therapies to a more systemic disease?

Such debate aside, the PROSPECT II study,[4] currently enrolling in Scandinavia, will further inform whether such a strategy will be of utility. However, it should be emphasised that if in such a situation, BRS implant technique is absolutely paramount; we should not be swapping the future risk of an ischaemic event for the risks of any device-related complications.

Q: Are the 6-year multislice computed tomography Cohort B results important to you? Why? And what do you think will be the outcome?

A: The late multislice computed tomography (MSCT) follow-up results presented at EuroPCR are very important as they provide correlation with the invasive studies performed in this study. Whilst repeat imaging of stented vessels is not routinely performed in UK practice, the possibility of following implanted BRS with non-invasive (and therefore less risky) imaging is attractive.

In particular, MSCT replicates the intravascular ultrasound (IVUS)/optical coherence tomography (OCT) data in this study: this could confirm the utility of such a strategy that overcomes the issue of 'blooming' artefacts that render MSCT follow-up of metallic stents problematic.[3,5,6]

PROFESSOR TOMMASO GORI'S INTERVIEW

Q: Could you explain why and when you consider bioresorbable vascular scaffolds for your patients?

A: Because I believe that coronary physiology is just as important as structure or anatomy. The regulation of blood flow, and in general vascular homeostasis (including platelet aggregation and coagulation), are far more complex than the function of a 'tube' that simply carries blood. A metallic stent is a mechanical therapy for a problem that is biological, namely the loss of vascular homeostasis. There is enough evidence to suggest that vascular homeostasis can be improved or that it can return to normal once it was disturbed. A metal stent does nothing to help it and possibly actually impairs it.

Three and a half years into our BRS experience, I can state that we do not have inclusion criteria, only exclusion ones. That is, we use BRS as the default strategy, unless the patient has contraindications. The main contraindications include a limited life expectancy, contraindication to dual antiplatelet therapy (DAPT), left main

disease, bifurcation lesions with two-stent strategies, ostial lesion (right circumflex artery and right coronary artery), and failure to properly prepare the lesion.

Q: A lot of huge national registry results were presented at EuroPCR. What are your thoughts on these?

A: There are a number of national registries that gave us more insight on real-world practices and complex settings. None of these studies showed an incidence of device-oriented endpoints, including scaffold thrombosis, not higher than that known from DES. Practice with BRS and safety endpoints have radically changed (and improved) in the last 1–2 years and the implantation technique refinement is responsible for this change.

Q: Can ST-elevation myocardial infarction patients benefit from bioresorbable vascular scaffolds?

A: Sure. Our data,[7] those of the Serruys group,[8] and those of the TROFI II trial[9,10] show that plaque sealing and regeneration actually do exist. Ruptured or eroded plaques, which cause thrombosis and vessel occlusion, only need structural support for a limited amount of time. What they need is biological stabilisation, which is the formation of a fibrotic, stable, adluminal layer that seals the plaque and prevents the interaction of prothrombotic components of the vessel wall with platelets. I believe that sealing or stabilisation have not much to do with the BRS itself, it is more the effect of time. What is true, however, is that at that point a permanent implant is not necessary. And what is not necessary is harmful.

Q: Can you describe the main results available on this subpopulation?

A: There are a number of registry studies and some more data from randomised trials that absolutely prove the safety of BRS implantation in acute coronary syndromes (ACSs). The results of our own registry and those of the TROFI II trial, which used a slightly different approach, substantiate the concept of plaque healing, that is the formation of a (likely fibrotic) stable layer capping the previously thrombotic plaque.[7,9] Clinically this is confirmed by series, which have already been published, for instance the POLAR-ACS and the STEMI-FIRST, and by two late breaking clinical trials presented at EuroPCR and published in the last issue of EuroIntervention. This is very important. What is also meaningful is that the general rules for BRS implantation appear to apply to the ACS setting. With metal stents, it is believed that the mechanisms of stent failure differ according to the clinical presentation: in non-ACS patients, the major reason for stent failure is believed to be incomplete vessel expansion.[11] In ACSs, malapposition is thought to be the major factor: due to intravascular thrombus and spasm, if one does not pay attention stents can be easily undersized (too small stent for the vessel), causing incomplete strut apposition. With BRS, scaffold under-expansion appears to be a common mechanism of failure for both clinical settings.[12,13]

Q: What is the proportion of patients with ST-elevation myocardial infarction that you choose to treat with bioresorbable vascular scaffolds?

A: I would say about 60%, based on the contraindications cited above.

Q: What are the key recommendations you would give to peers for a successful use of bioresorbable vascular scaffolds?

A: Strictly respect the instruction for use and the 'PSP' guidelines for implantation (Figure 1). Sizing is particularly important: with metal stents 'the bigger the better' might be true. For scaffolds, this is definitely not the case, at least, not in this generation of devices. In preparing the lesion, use the predilation balloon to size the vessel, never use a predilation balloon smaller than the vessel or smaller than the BRS you intend to implant. Confirm balloon expansion in two angiographic planes. Also, read the papers that focus on implantation technique very carefully. A correct use saves lives. It makes no sense to risk the life of patients (and the whole concept of scaffolds) just for the sake of pushing the envelope. About 20–30% of patients can be treated safely with BRS, we should focus on these ones.

PROFESSOR MACIEJ LESIAK'S INTERVIEW

Q: Could you explain why and when you consider bioresorbable vascular scaffolds for your patients?

A: I'm not the average percutaneous coronary intervention (PCI) surgeon because I challenge the device: in my first series of 300 patients, I had 30% bifurcations and 30% chronic total occlusion (CTO) lesions. So I go further than what the indications comprise. Of course, this was done

following bench testing and model testing to apprehend how the device behaves, before moving on to patients, with great results. While I do not recommend this to the average doctor, and advise that they start with simple *de novo* lesions (as in Cohort B), the switch to complex cases was relatively quick and the learning curve was short. Moreover, the general performance of the device was further improved by the new delivery system, and the procedure is even easier now. This is why I go beyond the indications.

Q: Which patients could benefit the most from bioresorbable vascular scaffold therapy? What are the main principles for lesion selection?

A: I think that the indications comprise life expectancy around 5 years or more (because the benefits will appear after the device would disappear, which takes a couple of years) in patients with lesions in vessels that may be the subsequent target for bypass grafts, namely young people in whom we expect a progression of the disease. In such patients, it is very beneficial that the stent disappears, because it allows for another procedure later on: these are the ideal candidates for me.

We have now treated about 100 CTO patients with BRS, and the data from the first 40 CTO patients with 1-year follow-up will be published in June in EuroIntervention. Out of these 40 patients, only one developed scaffold thrombosis. But that was a difficult case of clopidogrel resistance, in which the patient developed scaffold thrombosis twice; first, 5 days after implantation when his clopidogrel regimen was switched to prasugrel; after 4 months, he was switched back to clopidogrel and he thrombosed again. We also had one case of scaffold restenosis. As of now, more than 80% of these patients were evaluated angiographically and we only had one case of scaffold restenosis, so generally the results are comparable to those of new-generation DES. However, there was some selection bias because we did not choose the more difficult CTO cases, with an average Japan-CTO score of 1.6. With these results in mind, we believe the indications of BRS could be expanded.

In general, when starting a programme:
1) Consider your target patients and lesions carefully
Do not save up the most complex cases for this novel technology.
2) Start with simple cases
Focus on optimal implant technique before gaining confidence to expand indications in your practice.
3) Critically appraise, analyse, and learn from each case
Intravascular imaging can provide very useful feedback on sizing and deployment. Our data[12] suggest that a learning curve of only 25 cases or so is sufficient to achieve good results.[7]
4) Consider carefully what you are trying to do in any case
Will the patient benefit? Is this technology appropriate for this particular patient or lesion? • Take into account the learning curve, with a possible more liberal usage of invasive imaging. • The 'PSP' for optimal implantation technique: ✓ **Prepare** the lesion: Non-compliant balloons, cutting/scoring balloons, rotablation needed? Is this the right case for BRS? ✓ **Size** appropriately: Liberal use of intravascular imaging when a programme starts; QCA if your lab has the expertise; if not, 'poor-man's IVUS' with non-compliant balloon expanded at nominal pressure in two orthogonal views. ✓ **Post-dilate** with a non-compliant balloon (ensure complete expansion) while keeping in mind the expansion limits. Always post-dilate to high pressure (>14–16 atm) after deploying scaffold at more modest pressures (10–12 atm); use non-compliant balloon of +0.25 – +0.5 mm above scaffold size. ✓ Prescribe DAPT: Some physicians prefer the newer antiplatelet agents. However, more potent antiplatelet therapy will not mitigate a poor/suboptimal percutaneous coronary intervention (PCI) result with BRS: concentrate on technique and apply DAPT as normal practice. Personally, I only use the novel agents for STEMI/NSTEMI cases as guidelines suggest.

Figure 1: Dr West's key recommendations to peers for a successful use of bioresorbable vascular scaffold. BRS: bioresorbable vascular scaffold; QCA: quantitative coronary angiography; IVUS: intravascular ultrasound; DAPT: dual antiplatelet therapy; STEMI: ST-segment elevation myocardial infarction; NSTEMI: Non-STEMI.

Another setting in which I use BRS is diffuse disease, in which the vessels are reconstructed and stents are placed in multiple lesions.

Q: Do you ever use non-invasive follow-up, such as multislice computed tomography, in your ABSORB patients? If so, what are the advantages? If not, would you consider it, and where do you see advantages?

A: No, sometimes, but not very often. For all the complex procedures including OCT, we try to use intravascular imaging. We do not routinely follow all patients with computerised tomography scan although of course it is possible to do so and it would be interesting as it is non-invasive. But if it is not needed, we do not do it.

Q: What are the key recommendations you would give to peers for a successful use of bioresorbable vascular scaffold?

A: My key recommendation would be to prepare the lesion well: use a properly sized balloon and preferably a non-compliant one. If the lesion is undilatable (i.e. if it is not possible to fully open the balloon in the lesion) do not implant a BRS, and actually, do not use a stent (because the risk is under-expansion).

Then, really pay attention to expansion limits to look for strut rupture that cannot be seen with angiography, unless you use intravascular imaging.

If you pre-dilate well and you size the scaffold properly, post-dilating is not really necessary but we try to post-dilate in almost all cases. Finally, since March 2009, in all BRS patients, we switch patients undergoing stent procedures from clopidogrel to prasugrel therapy.

DOCTOR FLAVIO RIBICHINI'S INTERVIEW

Q: First of all, could you explain why and when do you consider bioresorbable vascular scaffold for your patients?

A: The driving indication, in my opinion, is patients of a relatively young age. Then of course we can discuss about what is 'young', but for sure, any patient <50 years old could be eligible to receive BRS. Between 50 years and 60 years of age, it would be subject to the patient's characteristics (general condition, comorbidities, biological parameters).

The healthier/younger the patient, the more I am prone to implant a BRS, because of the long to very long-term benefits that are expected with BRS, versus metallic stents. You can implant the device in other situations but this is what I believe the most medically adequate way of considering a BRS in a patient.

Regarding diffuse disease, we know that surgery has limitations related to the poor run-off of the small vessels, associated with a high incidence of bypass graft occlusion in the short to mid-term. Moreover, stent implantation with conventional PCI devices is associated to high restenosis rates and a risk for thrombosis, and in such cases, I am against implanting many metallic stents permanently. In such patients, which represent an unmet need, for which bioresorbable technology could become an option, compared to what we have today.

Q: Why one should consider bioresorbable vascular scaffold use in long lesions?

A: Long lesions are theoretically an interesting subset of patients in which to implant a BRS, in order to avoid a full-metal jacket (high-risk of restenosis, long-term risk of stent thrombosis, and maybe a problem for long-term surgery).

Q: What are the respective proportions of patients with multivessel disease/long lesions that you choose to treat with bioresorbable vascular scaffold?

A: I treat all my patients <50 years old with a BRS. In patients between 50 years and 60 years of age, I try to implant most of them with a BRS too. But of course, over the workload of a full year, BRS implantation in young patients does not represent a lot of patients.

Q: Is there any other clinical situation for which you would consider bioresorbable vascular scaffold implantation?

A: There is a subset of patients that I treat with BRS, if possible, regardless of age: single-culprit lesion in patients with an empty cardiovascular history, with no comorbidities, and who are admitted to the hospital for an acute myocardial infarction or an ACS. In such patients, if they have beautiful coronary arteries with only an occlusion in a proximal large vessel due to unstable plaque rupture. This is a perfect situation to heal a patient forever, because he/she has normal arteries, and we can intervene and fix this part of the vessel with a single scaffold and this patient will likely

have a complete coronary circulation over the long-term after the reabsorption of the scaffold.

Q: Is the non-invasive follow-up with ABSORB an added value? Do you use multislice computed tomography?

A: We do not use MSCT in our centre, because after 2–3 years, our experience shows that the scaffold is still there and we like to see the complete reabsorption of the scaffold and this is expected to happen in between 4–5 years.

What we do now at 5 years is full imaging data with IVUS and OCT but in the meantime, we suggest non-invasive imaging (computerised tomography scan between 1 year and 2 years or even in the first year following surgery) to exclude the possibility of severe restenosis and silent occlusion in very important vessels.

Q: What are the key recommendations you would give to peers for a successful use of the bioresorbable vascular scaffold?

A: Three main points: first, it is patient selection that most likely drives the real advantages of this technology. I would not implant it in patients without thinking over the long-term follow-up perspectives and advantages for complete healing. Secondly, in the technical performance of the PCI, remember that it is very important to prepare the lesion well, and properly size the scaffold. My third piece of advice is very important and relates to long-term adherence to DAPT: it is very important in avoiding late scaffold thrombosis to ensure that the patient is properly receiving DAPT, for the appropriate amount of time (at least 1 year). I would also advise shifting from clopidogrel to prasugrel to maximise scaffold thrombosis prevention.

Click here to view the full webcast.

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