PARIS, France—Early data on a handful of new, second-generation bioresorbable scaffold (BRS) devices presented at the EuroPCR 2017 meeting seem to be exciting engineers and clinicians alike, but questions remain with regard to the proper trajectory for research in this field.

Following the unexpectedly negative 3-year results seen with the first-generation Absorb GT1 bioresorbable vascular scaffold (BVS) compared with the Xience everolimus-eluting metallic stent (both Abbott Vascular) presented last fall, BRS researchers have been scrambling to justify further investigation in the field—when the safety and efficacy of permanent coronary stents is at an all-time high—without repeating what the same mistakes.

Panel co-chair Elazer Edelman, MD, PhD (Massachusetts Institute of Technology, Cambridge), kicked off the forward-looking BRS session with excitement. “Those of us who have been in technology for a very long time . . . understand that when technologies stumble, they provide the greatest opportunity to learn and to advance. [This] is precisely where we are today in this realm. The stumbling that has occurred, as you will see, will lead to greater and greater science and greater and greater advances,” he said.

DREAMS-2G

First up, Michael Haude, MD, PhD (Städtische Kliniken Neuss, Germany), presented combined 6-month results from the BIOSOLVE-II and BIOSOLVE-III trials of 184 patients treated with the sirolimus-eluting DREAMS-2G scaffold (Biotronik). The device, which gained CE Mark approval in June 2016, is constructed from magnesium and a poly-L-lactic acid (PLLA)-based polymer and features 150 µm thick struts.

At 6 months, there were no instances of definite or probable scaffold thrombosis, three deaths, one target-vessel MI, and three instances of TLR. Twenty-four month data from the BIOSOLVE-II trial alone confirm no additional scaffold thromboses beyond 6 months. These numbers are “low and comparable to other absorbable scaffolds and permanent drug-eluting stents out to 24 months when the DREAMS-2G is already fully absorbed,” Haude said.

Further, “in-segment and in-scaffold late lumen loss remained stable between 6-and 12-month follow-up in 42 patients with serial angiographic assessment in BIOSOLVE-II,” he reported.

Aptitude

Next Antonio Colombo, MD (Columbus Hospital/San Raffaele Hospital, Milan, Italy), presented 9-month clinical and imaging results from the RENASCENT II study of a scaffold with even thinner struts (115 µm) in 60 patients. The Aptitude sirolimus-eluting BRS (Amaranth Medical) is also made from a PLLA-based polymer and is a second-generation device as well.

The study showed high clinical success (98.3%), a low MACE rate (3.4%), and no angiographic restenosis or scaffold thrombosis. Scaffold stability as assessed by optical coherence tomography was maintained at 9 months, as were a high level of strut coverage and low rate of malapposition.

The company’s “proprietary ultra-high-molecular-weight PLLA and unique polymer-processing technology has led to a further thinning of the BRS wall,” Colombo explained, adding that the third-generation Magnitude BRS is currently being evaluated. “These next-generation BRS show the potential of matching the performance of current metallic DES.”

DESolve Cx and Nx

Another thin-strut scaffold (120 µm), the DESolve Cx novolimus-eluting device (Elixir Medical), which degrades by 6 months with full absorption by 1 year, is also showing promise, according to presenter Alexandre Abizaid, MD PhD (Dante Pazzanese, Sao Paulo, Brazil). There were no instances of MACE or scaffold thrombosis at 6 months, and the late lumen loss observed (0.19 mm) was similar to that seen in a comparable earlier-generation device, the DESolve Nx BRS, according to Abizaid.

Indeed, looking at 5-year clinical and imaging results in 122 patients treated with the DESolve Nx, presenter Stefan Verheye, MD PhD (ZNA Middelheim, Antwerp, Belgium), concluded that this device “achieves early degradation and resorption while achieving excellent efficacy by maintaining the functional integrity of the scaffold in the early critical period. Long-term angiographic results confirmed sustained efficacy well beyond the resorption of the scaffold.”

Additionally, Verheye said these results confirm the long-term safety of the device with no late or very late stent thrombosis.

FANTOM

In a second presentation, Abizaid also discussed 12-month results of the FANTOM II study. This scaffold (REVA Medical) is made from a desaminotyrosine polycarbonate, elutes sirolimus, features 125 µm-thick stent struts, and is designed to degrade within 1 year. Six-month results of the 240-patient study were presented at TCT 2016, and the 12-month outcomes are in line with a MACE rate of 4.2%, including two cardiac deaths, three target-vessel MIs, and six instances of clinically driven TLR. There was one instance of definite scaffold thrombosis in which the target lesion was not fully covered with the scaffold, but no occurrences of late thrombosis.

MesRes100

Also following up on a presentation he made at TCT 2016, Ashok Seth, MBBS (Fortis Escorts Heart Institute, New Delhi, India), showed 1-year data from the MeRes-1 study of the MeRes100 sirolimus-eluting bioresorbable scaffold (Meril Life Sciences), which features a hybrid cell design, optimal side-branch access, and 100 µm-thick struts and is designed to degrade in 2-3 years. Among 108 patients with single de novo lesions treated in India, there was one instance of MACE (ischemia-driven TLR) but no scaffold thrombosis.

“Multimodality vascular imaging are consistent in demonstrating high efficacy of MeRes100 BRS up to 1 year [with] low late lumen loss, virtually complete strut coverage, sustained mean flow area and very low percent volume obstruction, and low mean area stenosis,” Seth concluded. The results are encouraging, he added, and “provide the basis for further studies using a wider range of lengths and sizes in more complex and larger patient populations.”

Firesorb

Lastly, Bo Xu, MBBS (Fu Wai Hospital, Beijing, China), presented the 1-year results from the first-in-human FUTURE-1 study of the Firesorb device (Shanghai MicroPort Medical), which also elutes sirolimus but at a dosage that is lower than Absorb’s, with a strut thickness of 100-125 µm. Among 45 patients, there was one MI and one revascularization but no deaths or scaffold thromboses.

Imaging analyses “demonstrated the feasibility, preliminary safety and efficacy of the thin-strut

PLLA-based sirolimus-eluting Firesorb BRS in the treatment of patients with single de novo coronary lesions," Xu said. "Long-term imaging follow-ups at different time points will provide more information and a pivotal randomized controlled trial (FUTURE-II) will be initiated soon."

'Philosophical' Questions

Following the FANTOM II presentation, one attendee asked panel members how to reconcile the worrisome late outcomes from many—but not all—of the ABSORB studies against some of the more promising data shown in the session. "People now perceive all BRS [as] the same, and most people are sort of refraining from using BRS," he said. As such, how can experts explain the differences in outcomes viewed in this session as compared with those of Absorb BVS? "Is it related to the design of the material," he asked, "the design of the stent, or the operator technique?"

Calling this "a philosophical question," Abizaid replied that, in general, operators have overcome the BRS learning curve. Now that they are using so-called PSP technique, "we cannot blame the operator anymore," he said. Instead, he suggested, the main components of a bioresorbable device's success today likely relate to strut thickness, degradation time, and capacity to avoid negative remodeling.

However, because all of the studies so far are fairly small, only "when the companies invest a little bit more in larger randomized trials, [will we] be more and more convinced that these [elements], together with good deployment technique, will prevail," Abizaid observed. "I'm not saying that it's going to 100% replace metallic scaffolds. We've been working and developing metallic stents for the past 20 years, so [BRS are] still in the teenage phase, but I think that there is a future."

Audience member Roxana Mehran, MD (Icahn School of Medicine at Mount Sinai, New York, NY), congratulated the presenters on their work on the next generation of BRS, but emphasized that despite the exciting data, hard outcomes are still lacking. "What we're seeing is a hope for the future of good clinical outcomes and improvement, and hopefully this time the technique won't be an issue," she said. "But I do not believe that we're out of the woods yet at all in understanding the thrombosis. All these zeros look good, but we all know that we need clinical outcomes."

Best Comparator?

Panelist Stefan James, MD (Uppsala University, Sweden), also urged caution, posing some tough questions for investigators in this field. “Have we actually unequivocally shown that all of these seven devices are substantially different than the [Absorb] BVS? Should we in fact be pursuing a different route for how we evaluate technologies and registries and single-arm trials? What should be the next multicenter trials that match technologies? Should they be against BVS or bare-metal stents or drug-eluting stents, and are we in fact in danger of recapitulating history?”

There is still a danger of repeating past mistakes, he added, but adopting an engineering point of view, the ultimate focus needs to be on “what is the device doing to the artery, not what is the artery doing to the device.”

Colombo echoed the concern that BRS will continue to struggle against permanent drug-eluting stents, suggesting that “we still don’t have the gold standard BRS to go against metallic stents” in a head-to-head clinical trial. With BRS, the best duration of dual antiplatelet therapy isn’t yet known, and “we don't know if it's better [to take] 1 year or 3 years to resorb,” he added. “Before going into the battlefield, we need to refine more this technology and answer some questions. I think it’s crazy to go against the best metal stent with primordial devices.”

The suggestion that a technology already on the market around the world—albeit one with new limitations—not be studied against a cheaper, high-performing device is a provocative one, but several experts attending the EuroPCR session appeared to support this option.

It may be, James said, that rather than first designing a new technology and then asking questions of its performance, better questions should be asked at the outset.

“Perhaps what we should do is take a step back and ask: why did this happen given that we really don't know but we think we understand? And then we can evaluate whether new technologies have in fact addressed the issues,” he suggested. “I think the fear all of us have is to be disappointed again and then to drag down promising technologies.”

Agreeing to a degree, Colombo said that scaffold design still needs to be refined. The Absorb BVS was “an uneducated child” that was thrown into “an aggressive business community,” he analogized. “I mean, it’s really amazing how this poor Absorb was able to survive.”

It will be important for the community to “continue to probe especially in the face of challenge and lack of success,” James concluded. “I'm, however, casting a warning though that if we don’t continue to ask the questions but only continue to revise designs, we run a much higher risk of being disappointed.”

Note: Abizaid is a faculty member of the Cardiovascular Research Foundation, the publisher of TCTMD.

Source:

- Haude M. Short and midterm safety, clinical performance and multi modality imaging results of the drug-eluting absorbable metal scaffold: combined data of the BIOSOLVE-II and BIOSOLVE-III trials. Presented at: EuroPCR 2017. May 16, 2017.
- Colombo A. Nine-month clinical and imaging outcomes of a novel ultra-high molecular weight poly-L-lactide BRS. A prospective multicenter international investigation: The RENASCENT II study. Presented at: EuroPCR 2017. May 16, 2017.
- Abizaid A. Multicentre evaluation of a novel 120µm DeSolve CX BRS: first report of six-month clinical and imaging endpoints. Presented at: EuroPCR 2017. May 16, 2017.
- Verheye S. Prospective, multicentre evaluation of the DESolve Novolimus-Eluting coronary BRS: imaging outcomes and four-year clinical and imaging results. Presented at: EuroPCR 2017. May 16, 2017.
- Abizaid A. The FANTOM II study: first report for the 12-month clinical outcomes of the Fantom sirolimus eluting bioresorbable scaffold. Presented at: EuroPCR 2017. May 16, 2017.
- Seth A. One-year clinical and multi-slice computed tomography results with a thin-strut poly-L-lactic acid based sirolimus eluting BRS in patients with coronary artery disease: the MERES - 1 study. Presented at: EuroPCR 2017. May 16, 2017.
- Xu B. A first-in-man study of the Firesorb sirolimus target eluting BRS in patients with coronary artery disease (FUTURE-I): one-year clinical and imaging outcomes. Presented at: EuroPCR 2017. May 16, 2017.

Disclosures:

- Haude reports receiving institutional grant/research support from Biotronik AG, Abbott Vascular, Cardiac Dimensions, Medtronic, Volcano, and Lilly and serving as a consultant to Biotronik AG, Abbott Vascular, and Cardiac Dimensions.
- Abizaid reports serving as a consultant to and receiving research grants from Elixir Medical and serving as a consultant to REVA Medical.
- Verheye reports serving as a consultant to Elixir.
- Seth reports receiving honorarium from and serving as a consultant to Abbott Vascular and Meril Life Sciences.
- Colombo and Xu report no relevant conflicts of interest.