

Review Article



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Bioresorbable Scaffolds in Coronary Intervention: Unmet Needs and Evolution

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ABSTRACT

Bioresorbable scaffolds (BRS) represent a novel paradigm in the 40-year history of interventional cardiology. Restoration of cyclic pulsatility and physiologic vasomotion, adaptive vascular remodeling, plaque regression, and removal of the trigger for late adverse events are expected BRS benefits over current metallic drug-eluting stents. However, first-generation BRS devices have significant manufacturing limitations and rely on optimal implantation technique to avoid experiencing an excess of clinical events. There are currently at least 22 BRS devices in different stages of development, including many trials of device iterations with thinner (<150 μm) struts than first-generation BRS. This article reviews the outcomes of commercially available and potentially upcoming BRS, focusing on the most recent stages of clinical development and future directions for each scaffold type.

Keywords: Bioresorbable scaffolds; ABSORB; Biodegradable stents; Angioplasty; Coronary stents

INTRODUCTION

The rationale for implanting permanent stents in the coronary arteries is based on 2 principles — counteracting vessel recoil and sealing dissections after balloon angioplasty. These benefits are achieved relatively early following percutaneous coronary intervention. After the initial period, the presence of a scaffolding platform in the coronary artery becomes unnecessary and acts as a potential trigger for undesirable events.

Drug-eluting stents (DES) have significantly reduced the rates of angiographic restenosis and target lesion revascularization (TLR) compared with bare metal stents, and second-generation DES have further reduced the rates of stent thrombosis compared with both earlier generation DES and bare metal stents.¹⁾ Current DES are sophisticated platforms featuring biocompatible or biodegradable polymers that reduce the long-term risk of vascular inflammation and stent thrombosis. In this context, the impetus for manufacturing and developing bioresorbable scaffolds (BRS) stems from the notion that even current generation DES are not immune from late complications attributable to the permanent presence of metal in the coronary wall, which are estimated at a rate of about 2% per year.²⁾

Enthusiasm for the introduction of BRS in the clinical market has been mitigated by criticism of initial results in the near and long-term. Clinical evidence for BRS has been so far dominated by studies of the ABSORB scaffold (Abbott Vascular, Santa Clara, CA, USA), with thousands of patients treated in the setting of clinical registries and randomized trials. Literature on other BRS technologies, including devices available for clinical use in some geographical realities, is limited.

One clear barrier to the penetration of BRS in clinical practice is the practical challenge of improving the good outcomes of second-generation DES. Indeed, BRS cannot be expected to perform better than DES in the early period where vessel scaffold properties are necessary, particularly because the manufacturing characteristics that allow for bioresorption require scaffold struts to be substantially thicker than the current DES platform in order to maintain an acceptable radial strength. Miniaturizing strut thickness while preserving radial strength is a key requisite to improve the current outcomes of BRS (Figure 1) since thicker struts have procedural limitations and impaired vascular healing.³⁾ On the other hand, in comparison with DES, BRS benefits are expected to accrue from the point in time when the device has disappeared due to anticipated reductions in clinical events triggered by permanent metal. This implies a substantial challenge in trial design because demonstrating superiority vs. current DES requires long-term follow-up, complicating the organization, conduction, and clinical applicability of BRS studies. As such, the BRS field is moving slower than at its start, with some companies around the globe conducting small studies of their first-generation device with the objective of regulatory approval and other companies seeking manufacturing improvements to advance their products to the next phase.⁴⁾

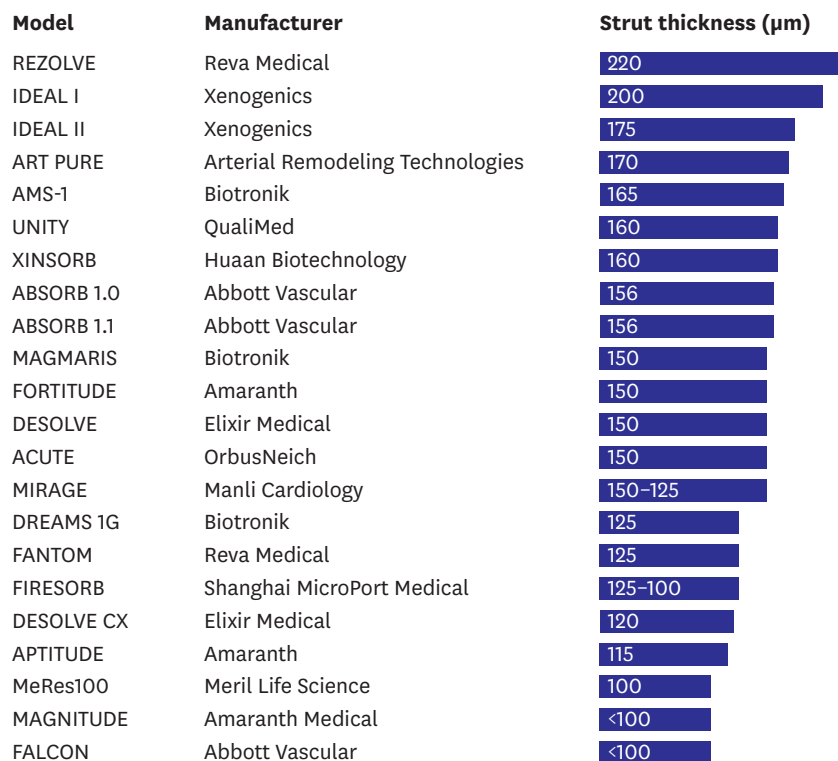


Figure 1. Strut thickness of early and current generation BRS. BRS = bioresorbable scaffolds.

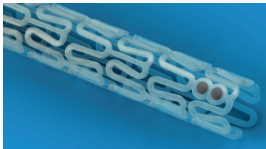
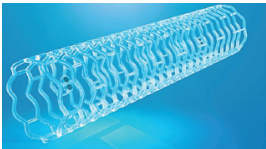
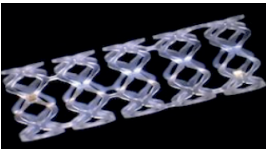

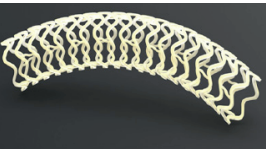
ABSORB	DESOLVE	ART Pure	MAGMARIS	FANTOM
				
PLLA, everolimus-eluting Strut thickness 150 µm, coat thickness 3 µm/side Full mass loss at approximately 3 years CE mark in January 2011	PLLA, novolimus-eluting Strut thickness 150 µm, coat thickness <3 µm/side Full mass loss at approximately 1 year CE mark in May 2014	PDLA, drug-free Strut thickness 170 µm, uncoated Full mass loss at approximately 1 year CE mark in May 2015	Mg, sirolimus-eluting Strut thickness 150 µm, coat thickness 8 µm/side Full mass loss at approximately 1 year CE mark in June 2016	TP, sirolimus-eluting Strut thickness 125 µm, uncoated Full mass loss at approximately 1 year CE mark in April 2017

Figure 2. Key features of BRS currently approved by the CE. BRS = bioresorbable scaffolds; CE = European Conformity; Mg = magnesium; PDLA = poly-d,l-lactic acid; PLLA = poly-l-lactic acid; TP = tyrosine polycarbonate.

This article reviews the outcomes of commercially available and potentially upcoming BRS, focusing on the most recent stages of clinical development and future directions for each scaffold type. In Europe, at the time of writing, scaffolds with European Conformity (CE) approval are the polymeric ABSORB (Abbott Vascular), DESOLVE (Elixir Medical, Sunnyvale, CA, USA), ART Pure (Arterial Remodeling Technologies [Paris, France] and Terumo [Franklin Township, NJ, USA]), FANTOM (Reva Medical, San Diego, CA, USA), and the magnesium-based MAGMARIS (Biotronik, Bülach, Switzerland), whose key characteristics are summarized in **Figure 2**. The only device currently approved in the United States is the ABSORB BRS. Clinical development status and evolution of other devices manufactured in the United States (MAGNITUDE [Amaranth Medical, Mountain View, CA, USA] and IDEAL BIOSTENT [Xenogenics, Canton, MA, USA]) and in Asia (MeRes100 [Meril Life Science, Vapi, India], MIRAGE [Manli Cardiology, Singapore, Singapore], and NeoVas [Lepu Medical, Beijing, China]) are also reviewed.

ABSORB

The story of the poly-l-lactic acid (PLLA) everolimus-eluting ABSORB 1.1 (Abbott Vascular), the most investigated BRS to date, has included several rounds of enthusiasm and disappointment (**Figure 3**). The device was approved for clinical use in Europe in January 2011, in the United States in July 2016, and in Japan in December 2016. Early small investigations of the ABSORB device in selected populations with multimodality imaging and long-term serial assessments have built and sustained the rationale for BRS use over DES.²⁾

The first large study reporting disturbing signals of “non-negligible” 6-month scaffold thrombosis with the ABSORB BRS was a multicenter European collaboration named Gauging coronary Healing with bioresorbable Scaffolding platforms in Europe (GHOST-EU).⁵⁾ Still, the 1-year results of pivotal sponsored studies and the corresponding meta-analyses were acceptable overall, with a lack of statistically significant differences for key regulatory endpoints.⁶⁻¹¹⁾ Problems again emerged with the accrual of adverse events on longer follow-up. This was particularly the case for ABSORB 2, a phase II randomized study of the ABSORB BRS and everolimus-eluting stent (EES). Outcomes between 1 and 3 years showed 6 more cases of thrombosis in the ABSORB BRS group compared with the EES group, raising important doubts on device performance beyond the initial period.¹²⁾

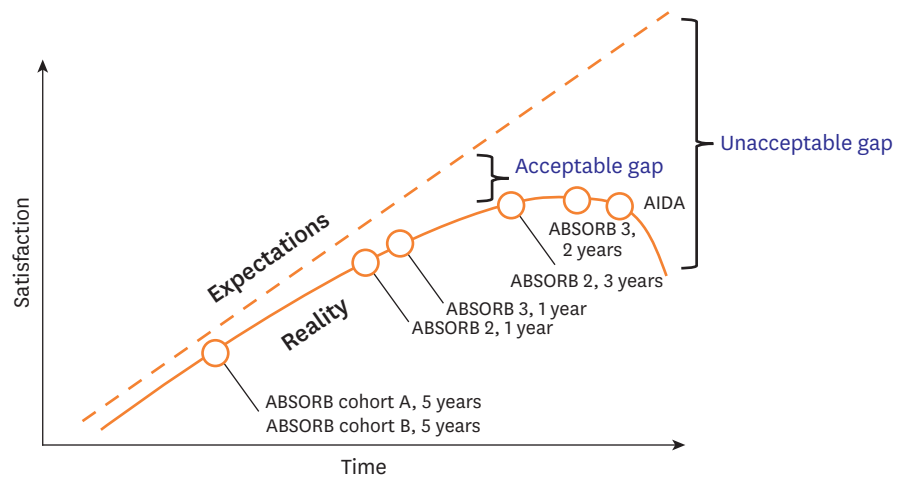


Figure 3. Schematic representation of the parabolic trajectory of the first-generation ABSORB BRS. After presentation of 3-year follow-up results of the ABSORB 2 trial, the gap between expectations and reality appears unacceptable. This has been corroborated by 2-year follow-up results of the ABSORB 3 trial, the AIDA trial, and subsequent meta-analyses. Technological refinements and adherence to strict implantation protocol are necessary to bring this technology to the next phase. AIDA = Amsterdam Investigator-initiated Absorb Strategy All-comers Trial; BRS = bioresorbable scaffolds.

ABSORB 3, the regulatory randomized trial of ABSORB BRS for approval in the United States, reported significantly increased rates of target lesion failure (TLF) at 2 years compared with EES (11.0% vs. 7.9%; $p=0.03$), driven by significantly more target vessel myocardial infarction (MI) (7.3% vs. 4.9%; $p=0.04$) and a numerical but nonsignificant increase in cardiac death and ischemia-driven TLR (Ellis S, unpublished). In parallel with reporting of these results, the Food and Drug Administration sent a letter to healthcare providers recommending strict adherence to the instructions for vessel size selection and optimal device implantation specified by the ABSORB BRS labeling. In an almost simultaneous press release, the manufacturer emphasized some positive highlights of the trial, including the nonsignificant difference in TLF at 2 years in vessels ≥ 2.25 mm by quantitative coronary angiography (QCA), the fact that the recommended pre-dilate, size, and post-dilate (PSP) implantation protocol was not followed adequately at the time of the index procedure in the 4 patients with new scaffold thrombosis reported between 1 and 2 years, and the observation that full PSP was undertaken in only about 8% of patients included in ABSORB 3 who experienced the same event rates as patients in the EES control group (Abbott Vascular, press release). In aggregate, these remarks imply that the outcomes of the ABSORB BRS in ABSORB 3 were affected by imperfect technique at implantation in addition to limitations of the current device generation (150 μ m strut thickness). In line with this reasoning, blinded, pooled, interim results from the ongoing ABSORB 4 trial were also disclosed, with device thrombosis rates reassuringly at 0.4% at 30 days and 0.5% in the context of better vessel selection (only 4% of patients had vessels < 2.25 mm by QCA) and implantation technique (post-dilation was undertaken in 84% of ABSORB BRS cases) than in prior ABSORB trials (Stone GW, unpublished). The ABSORB 3 and ABSORB 4 trials combined, encompassing about 5,000 patients, will enable a powered landmark pooled analysis aimed at demonstrating the superiority of ABSORB BRS vs. EES with respect to TLF between 1 and 7–10 years. Interestingly, the protocol of the ABSORB 3/4 program initially anticipated a landmark analysis of TLF between 1 and 5 years. The amendment extending the follow-up duration reflects the growing understanding that the benefits of the device, if any, will not emerge before bioresorption is complete.

A few weeks after the report of the 2-year results of ABSORB 3, the AIDA investigators published an interim analysis of their ongoing trial comparing ABSORB BRS and EES in a

more real-world scenario.¹³⁾ The stimulus to publish the Amsterdam Investigator-initiated Absorb Strategy All-comers Trial (AIDA) results prematurely (2-year follow-up completion is ongoing) was a recommendation of the trial data safety monitoring board reacting to the unexpectedly and significantly higher rates of device thrombosis observed in the ABSORB BRS arm (3.5% vs. 0.9%; $p < 0.001$), which might have also contributed to significantly higher rates of target-vessel MI compared with EES (5.5% vs. 3.2%; $p = 0.04$). Bad news for the ABSORB BRS also came from the European regulatory agency, which restricted device use for only clinical registries effective May 2017.

Indeed, evidence against the use of the ABSORB BRS in routine clinical practice at one point in time became overwhelming. A recent meta-analysis of 5,583 patients from 7 randomized trials of ABSORB BRS vs. EES from Ali et al.¹⁴⁾, including ABSORB 3 and AIDA, reported that the risk of TLF with the ABSORB BRS increases significantly by 29%, the risk of the device-oriented composite endpoint (death, MI, or revascularization) by 14%, the risk of target-vessel MI by 68%, and the risk of clinically driven TLR by 40%. Even more worrisome, the risk of device thrombosis is significantly higher not only in the early-(2.16-fold), but also in the late-(5.77-fold) and very late-terms (9.67-fold) based on Academic Research Consortium criteria. It should be noted that all ABSORB trials and AIDA have so far reported higher rates of device thrombosis in the ABSORB BRS than in the EES arms at the longest follow-up available at the time of writing this article (3 years for ABSORB 2, ABSORB China, and ABSORB Japan; 2 years for ABSORB 3 and AIDA), which makes a safety concern poorly arguable. The meta-analysis of Ali et al.¹⁴⁾ also reported individual patient data at 2 years from 3,389 relatively low-risk patients enrolled in the 4 sponsored ABSORB trials, confirming the results of the larger study level meta-analysis. Between 1 and 2 years after device implantation, more events accrued in patients treated with the ABSORB BRS than in those treated with EES, especially target vessel-related MI and device thrombosis. In an attempt to generate hypotheses for future studies, the authors reported that scaffold thrombosis did not occur in 226 patients undergoing post-dilatation with a balloon larger than the nominal scaffold diameter of 18 atmospheres or more compared with 11 events in 1,773 patients treated otherwise. The TLF difference between ABSORB BRS and EES was no longer significant when patients experiencing device thrombosis were excluded. On multivariable analyses not corrected for multiplicity testing, significant interactions were found for 2-year TLF between device type and pre-procedural variables such as American College of Cardiology/American Heart Association lesion classification, target vessel, and degree of calcification. A vessel diameter < 2.25 mm was reported as an independent predictor of multiple study outcomes, including scaffold thrombosis.¹⁴⁾

The bulk of data coming from the ABSORB experience, with about 6,000 patients randomized and follow-up available up to 2–3 years, shows that the current device requires adjustment to comply with strict implantation rules, as well as technological improvement. On September 2017, the manufacturer stopped production of the first-generation ABSORB scaffold due to low sales. Clinical development of a thin-strut 100 μ m version is underway.

DESOLVE

Similar to the ABSORB BRS, the novolimus-eluting DESOLVE scaffold (Elixir Medical) (Figure 2), CE-marked in May 2014, has a PLLA backbone; however, the biodegradation and resorption process are quicker than those of ABSORB BRS, and intrinsic self-correcting deployment properties and relative greater elasticity and ductility have been advocated.¹⁵⁾ In the

first-in-man study of 15 patients, a previous iteration of a device eluting the drug myolimus was associated with acceptable 0.19 ± 0.19 mm late lumen loss at 6 months, low neointimal volume by intravascular ultrasound (IVUS), and optical coherence tomography (OCT) confirmation of thin neointimal coverage.¹⁶⁾ At 12 months, there was no clinical event directly attributable to the scaffold, and vessel patency was documented by multi-scan computed tomography.

A 150- μ m-thick version of the device was refined with a new drug (novolimus) and its performance tested in a multicenter international registry of 126 patients called DESOLVE Nx.¹⁷⁾ The primary efficacy endpoint of late lumen loss at 6 months confirmed the results of the first-in-man study (0.20 ± 0.32). Paired IVUS and OCT assessments showed significant increase in vessel, lumen, and scaffold dimensions between post-procedure and 6-month follow-up. Major adverse cardiac events were low at 6 months (3.3%) and at 2 years (7.4%), including 1 probable stent thrombosis within the first month. Outcomes at 5 years have recently been presented at a large international meeting documenting that, long after complete bioresorption of the DESOLVE BRS, the event rate remains low (9.0%) with no additional clinically indicated TLRs from years 2 through 5 and no definite scaffold thrombosis through 5 years (Verheye S, unpublished data).

A second-generation DESOLVE scaffold with a strut thickness of 120 μ m has been tested in the DESOLVE Cx study, promisingly reporting late lumen loss of 0.18 ± 0.29 mm at 6 months and no clinical events (Abizaid A, unpublished data). Another iteration named DESOLVE NXT has recently been manufactured, featuring contoured struts for improved embeddedness in the vessel wall and an accompanying balloon with enhanced force transmission at the center of the scaffold. A clinical multicenter study of 100 patients treated with the DESOLVE NXT BRS is underway.

Together, the above findings indicate that the DESOLVE scaffold is a promising device in the early stage of clinical development, albeit with neither randomized data nor robust registries yet available to support its theoretical premises and initial results in small trial cohorts.

ART PURE

The second-generation non-drug-eluting and polymeric ART Pure BRS (Arterial Remodeling Technologies and Terumo) (**Figure 2**) was approved in Europe in May 2015, following the results of the Arterial Remodeling Transient Dismantling Vascular Angioplasty (ARTDIVA) first-in-man study (n=30) that reported 1 case of ischemic-driven TLR at 6 months (Lafont A, unpublished data). No further clinical results are available, although the clinical development of a sirolimus-eluting version of the device is in process.

MAGMARIS

The sirolimus-eluting magnesium drug-eluting absorbable metal scaffold (DREAMS 2G) (**Figure 2**), CE-approved in June 2016 and currently marketed as MAGMARIS (Biotronik), is built on the experience gained from its 2 previous iterations, the bare absorbable metal scaffold (AMS-1) and the paclitaxel-eluting DREAMS 1G tested in the PROGRESS and BIOSOLVE-I studies, respectively.¹⁸⁾¹⁹⁾ The late lumen loss of these first-generation devices was deemed unacceptable, suggesting the need for a new drug-eluting version with prolonged scaffolding time.

MAGMARIS, which is heralded with the good radial strength expected with metallic devices, is currently being tested in several registries within the BIOSOLVE program.²⁰⁾ BIOSOLVE-II was a first-in-man study of 123 patients with angiographic follow-up at 6 months and intravascular imaging with IVUS and OCT planned in a subgroup of 30 patients.²¹⁾ The primary endpoint of 6-month late lumen loss was reported at 0.27 ± 0.37 mm. IVUS documented preservation of the scaffold area with low neointimal area, and OCT did not detect intraluminal masses. TLF was recorded in 3.3%, with one cardiac death, one periprocedural MI, and 2 clinically-driven TLR. Further angiographic follow-up of 42 patients was confirmatory at 12 months.²²⁾ Clinical outcomes at 12- and 24-month follow-up are available, displaying no substantial catch-up in clinical events after 6 months.²²⁾²³⁾

BIOSOLVE-III (NCT02716220) is a registry currently enrolling a total of 61 patients with angiographic follow-up mandated at 12 months. The primary endpoint is procedure success during hospital stay. Six-month outcomes of BIOSOLVE-III have been pooled with those of BIOSOLVE-II, reporting TLF at 3.3%.²³⁾ In further clinical development of the MAGMARIS device, BIOSOLVE-IV has been designed as a post-marketing registry of 1,065 patients, with a focus on TLF at 12 months.

These initial results of the current generation MAGMARIS scaffold, obtained in small series, are encouraging (i.e., low TLF up to 24 months and no case of scaffold thrombosis detected to date), but randomized comparisons vs. DES or other BRS are lacking. This prevents clear understanding of the safety and efficacy of the device compared with other available options.

FANTOM

FANTOM (Reva Medical) is a sirolimus-eluting BRS made of tyrosine polycarbonate and designed to degrade within 1 year (**Figure 2**). CE-mark approval was granted in April 2017. This device represents the evolution of the former ReZolve and ReZolve-2 BRS, formerly tested in the RESTORE and RESTORE-II studies (Abizaid A, unpublished). Key differentiating features of FANTOM compared with other BRS technologies include its 125 μ m thickness, DES-like radiographic visibility, single-step inflation, good expansion range, and no special storage or handling requirements.

The FANTOM II trial (n=240) reported major adverse cardiac events in 2.1% of patients at 6 months (unpublished data), including one cardiac death, 3 target vessel MIs, and 2 clinically driven TLRs. Scaffold thrombosis occurred in one patient (0.4%) subacutely. On QCA, late lumen loss at 6 months was 0.25 ± 0.40 mm, and OCT showed 98.1% struts coverage. Twelve-month results of the FANTOM II study have recently been presented, with major adverse cardiac events in 4.2% of patients including one additional cardiac death and 4 additional instances of clinically driven TLR between 6 and 12 months (Abizaid A, unpublished data). The company is currently pursuing private financing to support the commercial launch of the device, including follow-on clinical trials and new product feasibility work.

MAGNITUDE

The Amaranth Medical polymer technology possesses special manufacturing properties that display superior elongation at break compared with other PLLA-based BRS. A scaffold

miniaturization process that preserves radial strength and over-expansion capabilities has been developed over time, spanning from the 150 μm (FORTITUDE) to the 115 μm (APTITUDE) and <100 μm (MAGNITUDE) iterations of the device.

In the FORTITUDE first-in-man study of 63 patients, encompassing 42 patients from the MEND II study and 21 patients from the RENASCENT I study, late lumen loss by QCA at 9 months was 0.27 ± 0.41 mm with the FORTITUDE BRS, and the rate of TLF was 4.9%, with 2 cases of target vessel MIs and 1 case of clinically-driven TLR (Granada JF, unpublished data). The RENASCENT II study of the APTITUDE BRS has also recently reported angiographic and clinical outcomes at 9 months in 60 patients, with late lumen loss at 0.34 ± 0.36 mm, major adverse cardiac events in 3.4%, and no scaffold thrombosis (Colombo A, unpublished data). The RENASCENT III study (n=70) is ongoing to further investigate the MAGNITUDE BRS, the thinnest BRS device in clinical testing.

IDEAL BIOSTENT

The sirolimus-eluting IDEAL BIOSTENT (Xenogenics) is synthesized entirely from salicylic acid polymer. The scaffold, which is radiopaque and requires 9-12 months for complete biodegradation, also elutes approximately 10 μg of salicylic acid, thus implying both anti-inflammatory and anti-proliferative properties. In the first-in-man trial of the IDEAL BIOSTENT BRS, named WHISPER (n=11), IVUS and OCT showed negligible neointimal suppression and a significant reduction in lumen area, which were attributed to inadequate drug dose and fast drug elution (Jabara R, unpublished data). The new generation IDEAL BIOSTENT with improved drug kinetics and improved platform has been designed and is currently undergoing preclinical evaluation.

MERES100

The 100- μm -thick MeRes100 PLLA sirolimus-eluting scaffold (Meril Life Science) is designed to degrade in 2–3 years. The scaffold has been preliminary tested in the first-in-man MeRes-1 study (n=108).²⁴⁾ At 6 months, late lumen loss was 0.15 ± 0.23 with no binary restenosis. IVUS demonstrated a neointimal hyperplasia area of 0.14 ± 0.16 mm², while OCT showed a minimum scaffold area of 6.86 ± 1.73 mm² and 99.3% strut coverage. At 12 months, major adverse cardiac events occurred in only one patient (0.93%) with no scaffold thrombosis, and all scaffolds were shown to be patent on multi-scan computed tomography. These results provide the basis for further studies in a larger patient population of this relatively thin BRS in more complex and larger patient populations. The ambitious clinical program of MeRes100 now includes a large all-comers multicenter registry of about 2,000 patients (MeRes100 Global) and randomized trials vs. EES (MeRes-Evolve) and ABSORB (MeRes100-China and MeRes100 US/JP).

MIRAGE

The MIRAGE PLLA sirolimus-eluting scaffold (Manli Cardiology), featuring strong mechanical properties related to a special manufacturing process and round-shaped struts for less protrusion into the lumen, was compared with the ABSORB BRS in a study of 60

patients with angiographic and OCT imaging.²⁵ At 12 months, angiographic late lumen loss was not statistically different between the MIRAGE (0.37 mm) and ABSORB BRS (0.23 mm, $p=0.2$), although the diameter of stenosis on angiography and on OCT was significantly higher with the MIRAGE scaffold. Clinical outcomes were comparable between the 2 study groups. The authors reported suboptimal technique in both arms of the study, warranting OCT guidance for implantation in future studies of the MIRAGE BRS.

NEOVAS

The NeoVas PLLA sirolimus-eluting scaffold (Lepu Medical) has been investigated only in a first-in-man study of 31 patients.²⁶ The primary endpoint of TLF occurred in 3.2% of patients at 6 months, with only one patient having clinically driven TLR, and no scaffold thrombosis cases were documented. Late lumen loss was 0.26 ± 0.32 mm, while the minimal scaffold area measured by IVUS was 6.74 ± 1.38 mm². By OCT, the neointimal hyperplasia area was low, and strut coverage was 95.7%. A randomized clinical trial comparing the clinical safety and efficacy of the NeoVas scaffold with EES (n=560) and a multicenter registry of 825 patients have been launched.

FIRESORB

The FIRESORB PLLA sirolimus-eluting BRS (Shanghai MicroPort Medical, Shanghai, China) features a strut thickness of 100–125 μ m depending on the scaffold size. In the FUTURE-I trial (n=45), 6-month QCA demonstrated late lumen loss of 0.15 ± 0.11 mm and no binary restenosis. On OCT, covered struts were observed in 93% of patients (Xu B, unpublished data). One-year outcomes have also been presented, with one MI and one revascularization but no deaths or scaffold thrombosis (Xu B, unpublished data). A pivotal randomized controlled trial of the FIRESORB BRS (FUTURE-II) has been planned.

XINSORB

The XINSORB PLLA sirolimus-eluting BRS (Huaan Biotechnology, Laiwu, China) has been investigated in a first-in-man study of 30 patients. At 6 months, late lumen loss was 0.17 ± 0.12 mm, with one case of TLF at 18 months (3.7%), attributable to a nonfatal definite thrombosis.²⁷ The manufacturer has started a randomized study vs. a biodegradable-polymer DES and a single-arm registry of about 800 patients.

OTHER SCAFFOLDS AT PRECLINICAL OR EARLY CLINICAL DEVELOPMENT STAGE

Other announced scaffolds in their infancy include the polymeric ACUTE (OrbusNeich, Fort Lauderdale, FL, USA), ARTERIOSORB (Arterius Ltd., Bradford, United Kingdom), AVATAR (S3V Vascular Technologies, Bangalore, India), SAHAJANAND (Sahajanand Medical Technologies, Surat, India), STANZA (480 Biomedical, Watertown, MA, USA), MICROPORT (Shanghai MicroPort Medical), the magnesium FADES (Zorion Medical, Indianapolis, IN, USA), IMBIBE (Envision Scientific, Hazira, India), UNITY (QualiMed, Winsen, Germany),

and the iron-based LIFETECH (Lifetech, Carlsbad, CA, USA). Boston Scientific has recently announced the strategic termination of its RENUVIA FAST BRS development program.

BRS: UNMET NEEDS AND EVOLUTION

Restoration of cyclic pulsatility and physiologic vasomotion, adaptive vascular remodeling, plaque regression, and removal of the trigger for late adverse events are expected BRS benefits over current generation metallic DES. However, first-generation BRS devices have significant manufacturing limitations and rely on optimal implantation to minimize clinical events. In addition, the clinical benefits of BRS after bioresorption compared to DES are not fully known. This is a crucial investigational point because future device improvements are expected to match but not necessarily improve the early and mid-term performance of best-in-class DES. The ABSORB BRS is not currently associated with tangible long-term advantages over DES (i.e., angina reduction, vasomotion, TLF). For successful clinical adoption, the BRS technology must meet this standard of evidence.

Current issues identified by histopathological evaluation of BRS at the preclinical level include mild increases in inflammation during bioresorption, greater acute thrombogenicity, delayed re-endothelialization of thicker stent struts, and ultimately a higher risk of device thrombosis and other clinical events than DES. There is a clear need for technological refinement and progress in manufacturing to improve mechanical integrity (i.e., better ductility, higher tensile strength and stiffness, better elongation-at-break). Clinical concerns can be resolved only from well conducted and large randomized trials that embrace late-generation devices and optimal implantation practices. With at least 22 BRS devices in different stages of development, including trials of device iterations with thinner (<150 μm) struts than the ABSORB BRS, the development journey of BRS in interventional cardiology continues.

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