**Current State of Bioabsorbable Polymer-Coated Drug-Eluting Stents**

Abhilash Akinapelli¹, Jack P. Chen², Kristine Roy³, Joseph Donnelly³, Keith Dawkins³, Barbara Huibregtse³ and Dongming Hou³,*

¹Creighton University Medical Center, Omaha, NE, USA; ²Northside Hospital, Atlanta, GA, USA; ³Boston Scientific, Marlborough, MA, USA

**Abstract:** Drug-eluting stents (DES) have been shown to significantly reduce clinical and angiographic restenosis compared to bare metal stents (BMS). The polymer coatings on DES elute antiproliferative drugs to inhibit intimal proliferation and prevent restenosis after stent implantation. Permanent polymers which do not degrade in vivo may increase the likelihood of stent-related delayed arterial healing or polymer hypersensitivity. In turn, these limitations may contribute to an increased risk of late clinical events. Intuitively, a polymer which degrades after completion of drug release, leaving an inert metal scaffold in place, may improve arterial healing by removing a chronic source of inflammation, neoatherosclerosis, and/or late thrombosis. In this way, a biodegradable polymer may reduce late ischemic events. Additionally, improved healing after stent implantation could reduce the requirement for long-term dual antiplatelet therapy and the associated risk of bleeding and cost. This review will focus on bioabsorbable polymer-coated DES currently being evaluated in clinical trials.

**Keywords:** Bioabsorbable polymer, drug-eluting stent, abluminal coating, BMS, clinical trials.

**INTRODUCTION**

Percutaneous coronary intervention (PCI) is a mainstay in the treatment of acute coronary syndromes and stable coronary artery disease. Since the invention of balloon angioplasty, the field of PCI has progressed significantly over the last three decades. The use of balloon-expandable metallic stents has decreased, but not eliminated, the risk of restenosis as compared to simple balloon angioplasty [1]. Permanent polymer-coated drug-eluting stents (DES) elute drugs that inhibit intimal proliferation and prevent restenosis after stent implantation. Compared to bare-metal stents (BMS), DES have similar rates of death and myocardial infarction (MI), but lower rates of clinical and angiographic restenosis [2].

DES consist of three components: a permanent metallic scaffold, the polymer, and an antiproliferative drug. First-generation stents were made of nitinol and then stainless steel; later generation metallic stent scaffolds have used cobalt chromium or platinum chromium alloys which allow thinner stent struts, whilst maintaining radial strength. Coronary scaffolds which fully degrade (for example Absorb Bioresorbable Vascular Scaffold System, Abbott Vascular, Santa Clara, USA) have been introduced in the past decade and are beyond the scope of this review [3]. Antiproliferative drugs used in current DES (for example, sirolimus, everolimus, biolimus, novolimus) generally inhibit the mammalian target of rapamycin (mTOR) pathway but have different pharmacological profiles [4].

The purpose of the polymer is to store and modulate the elution of the drug into the arterial tissue/site of the lesion. Permanent polymers used in first- and second-generation DES do not degrade; first-generation polymers included polyethylene-co-vinyl acetate (PEVA) and polybutyl methacrylate (PBMA), whereas the current best-in-class DES use polyvinylidene fluoride- hexafluoropropylene (PVDF-HFP) or phosphorylcholine [5, 6]. Animal models of arterial healing have shown that first-generation DES are associated with delayed healing, hypersensitivity, and an increased incidence of vascular inflammatory reactions compared with BMS and second-generation DES [7-11]. These observations are supported by findings in human autopsy [12, 13] and optical coherence studies [14, 15]. Second-generation DES have shown improvements in biocompatibility and clinical outcomes [8, 16] but may still lead to neoatherosclerosis and thrombosis [7, 17].

Delayed endothelialization and chronic inflammation associated with DES may be attributed to the drug, the permanent polymer, or both; however, persistent hypersensitivity reactions (beyond the period of drug delivery) support a role for permanent polymers in the inflammatory reaction [18, 19]. As such, efforts have been made to develop bioabsorbable polymers which, after completion of drug release, degrade leaving a bare metal scaffold in place and potentially facilitate endothelialization and reduce the risk of an in-
flammatory reaction. The vast majority of biodegradable polymers developed are synthetic polymers from the poly (α-hydroxy acid) family including polyactic acid and polyglycolic acid and their co-polymer polyactic-co-glycolic acid. The potential clinical benefits of a polymer which degrades include a reduction in stent-related ischemic events and/or the potential to reduce the required duration of dual antiplatelet therapy (DAPT) after stent implantation. The recent large-scale DAPT study by Mauri et al. (2014) demonstrated that a long-term (30-month) DAPT regimen resulted in significantly lower rates of thrombosis compared to a shorter (12-month) DAPT regimen, but was associated with a significantly increased risk of bleeding [20]. Permanent polymer DES were used exclusively in this study; the potential for improved healing associated with bioabsorbable polymer-coated DES (BP-DES) may permit shorter DAPT duration following PCI with DES and, consequently, reduce the risk of bleeding without increasing the risk of stent thrombosis (ST).

This review will focus on permanent metallic stents releasing ‘olimus drugs from bioabsorbable polymers. A list of bioabsorbable-polymer coated DES currently being tested in clinical trials is shown in Table 1. The time course of drug release and polymer absorption is shown in Fig. 1.

Preclinical Trials Comparing Bioabsorbable Polymer DES to Permanent Polymer DES

Multiple animal models have demonstrated that BP-DES induce similar levels of inflammation as BMS [12-14]. Comparable vascular responses were observed after BP-DES, BMS, or a polymer-only control stent implantation in a porcine coronary artery model and endothelialization with BP-DES was complete by 28 days [21-24]. Koppara et al. showed that BP-DES were associated with significantly less inflammation and neointimal growth when compared to permanent polymer DES at 28 days after implantation [25]. Likewise, a reduction in the inflammatory response to stent implantation and rapid neointimal coverage was observed with BP-DES compared to a permanent polymer DES in pigs and in rabbits [26, 27].

In humans, optical coherence tomography (OCT)-based studies have demonstrated equivocal results in relation to endothelialization after implantation of BP-DES compared to permanent polymer DES, with either favorable results [18-20] or negative or neutral effects when earlier, thicker strut BP-DES were tested [21-23]. More recent BP-DES studies have found that an everolimus-eluting BP-DES displayed complete and smooth coverage over all struts by 2 months [28-34]. An evaluation of coronary lesions by OCT five years after biolimus-eluting BP-DES implantation demonstrated fewer uncovered stent struts compared to sirolimus-eluting permanent polymer stents [35]. In a study performed by Hamilos and colleagues, endothelial dependent vasomotor function was preserved in patients with BP-DES, but not in patients who received a permanent polymer DES [36]. However, Puricel et al. demonstrated that endothelium-dependent and independent vasomotor responses were similar between biolimus-eluting BP-DES and everolimus-eluting permanent polymer DES [37].

![Fig. (1). Time Course For Polymer Bioabsorption.](image)

Drug release (yellow) and polymer absorption (blue) arranged by length of polymer absorption.
**Table 1.** Current bioabsorbable-polymer coated drug-eluting stents tested in clinical trials.

| Name          | Company             | Platform                  | Thickness (µm) | Polymer                          | Polymer Distribution/ Thickness | Drug        | Drug Release/ Polymer Absorption |
|---------------|---------------------|---------------------------|----------------|----------------------------------|---------------------------------|-------------|---------------------------------|
| Biomatrix [49]| Biosensors          | Stainless Steel           | 120            | Polylactic acid                  | Abluminal/10 µm                 | Biolimus A9 | 6 mo/9 mo                      |
| Nobori [53]   | Terumo              | Stainless Steel           | 125            | Polylactic acid                  | Abluminal/20 µm                 | Biolimus A9 | 6 mo/9 mo                      |
| Ultimaster [65]| Terumo             | Cobalt Chromium           | 80             | Poly (DL-lactide-co-caprolactone)| Abluminal/15 µm                 | Sirolimus   | For both 3-4 mo                 |
| SYNERGY [41]  | Boston Scientific   | Platinum chromium        | 74             | Polylactic co-glycolic acid      | Abluminal/4 µm                  | Everolimus  | 3 mo/4 mo                       |
| Orsiro [114]  | Biotronik           | Cobalt chromium           | 61             | Poly L lactic acid               | Conformal/up to 7.5µm           | Sirolimus   | 3 mo/15 mo                      |
| MiStent [75]  | Micell              | Cobalt Chromium           | 64             | Polylactic co-glycolic acid      | Conformal/Not reported          | Crystalline sirolimus | 9 mo/3 mo |
| DESyne BD [78]| Elixir Medical      | Cobalt chromium           | 81             | Poly L Lactide (PLLA)-based polymer | Conformal/<3 µm              | Novolimus  | 3 mo/9 mo                       |
| TIVOLI [81]   | Essen Tech          | Cobalt chromium           | 80             | Polylactic co-glycolic acid      | 5.5 µm                         | Sirolimus   | 80% by 1 mo/3-6 mo             |
| EXCEL [82]    | JW Medical Systems  | Stainless steel           | 119            | Polylactic acid                  | 10-15 µm                       | Sirolimus   | 6 mo/6-9 mo                     |
| EXCEL II [85]| JW Medical Systems  | Cobalt chromium           | 88             | Polylactic acid                  | 4 µm                           | Sirolimus   | NR/6-9 mo                      |
| Inspiron [86] | Scitech             | Cobalt chromium           | 75             | Polylactic acid + Polylactic co-glycolic acid | Abluminal/5 µm            | Sirolimus   | 80% by 1 mo/6-9 mo             |
| Firehawk [95] | Microport Medical   | Cobalt chromium           | 86             | Polylactic acid                  | Abluminal                      | Sirolimus   | 3 mo/9 mo                       |
| Yukon Choice Flex [100]| Translumina GmbH  | Stainless Steel           | 79             | Polylactic acid                  | Abluminal/Not reported          | Sirolimus   | 4 wk/ 6-9 mo                   |
| BuMA [102]    | Sino Medical        | Stainless Steel           | 100-110        | Polylactic co-glycolic acid      | Conformal/10 µm                 | Sirolimus   | 30 d/2-3 mo                    |
| Svelte [105]  | Svelte Medical      | Cobalt chromium           | 81             | Poly(ester amide)                | Conformal/6 µm                  | Sirolimus   | 2 mo/12 mo                     |
| BioMime [106] | Meril Life Sciences | Cobalt chromium           | 65             | PLLA+PLGA                        | Conformal/2 µm                  | Sirolimus   | 75% in 15 d/60 d               |

**Table 2.** Summary of clinical trials for the SYNERGY everolimus-eluting bioabsorbable polymer stent.

| Trial         | Control       | # of patients/study design | Results                                                                                                                                                                                                 |
|---------------|---------------|----------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| EVOLVE 6-months [39] | EES           | N=291; Prospective, multi-site, randomized (1:1:1), single-blind, noninferiority; 29 sites (Europe, Australia, New Zealand) Single target lesion ≤28mm, ≥2.25 to ≤3.5 mm RVD | Clinical 1st endpoint: 30-d TLF EES 0 (0%), SYNERGY 1 (1.1%), and SYNERGY ½ Dose 3 (3.1%); SYNERGY vs EES P=0.49 and SYNERGY ½ dose vs EES P=0.25, respectively |
| EVOLVE 5-year [40] | EES           | N=291; Prospective, multi-site, randomized (1:1:1), single-blind, noninferiority; 29 sites (Europe, Australia, New Zealand) Single target lesion ≤28mm, ≥2.25 to ≤3.5 mm RVD | Angiographic 1st Endpoint: 6 m in-stent late loss in EES 0.15±0.34 mm; SYNERGY (0.10±0.25 mm) and SYNERGY ½ Dose group (0.13±0.26 mm) were both noninferior to EES; P<0.001 |
| NCT01135225  | EES           | N=291; Prospective, multi-site, randomized (1:1:1), single-blind, noninferiority; 29 sites (Europe, Australia, New Zealand) Single target lesion ≤28mm, ≥2.25 to ≤3.5 mm RVD | 2nd endpoints: • At 5 years, rates of cardiac death, MI, TVR, TLR, TLF, and TVF remained low and not significantly different between treatment groups; no incidence of definite/probable ST in any treatment group |
(Table 2) Contd.….  

| Trial               | Control       | # of patients/study design                                                                 | Results                                                                                   |
|---------------------|---------------|------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------|
| EVOLVE II 1 year [41] | EES           | N=1684; Prospective, multisite, single-blind, randomized (1:1) noninferiority; 125 sites (US, Canada, Europe, Australia, New Zealand, Singapore, and Japan); ≤3 target lesions ≤34mm, ≥2.25 to ≤4.0 mm RVD | 1° endpoint: 12 m TLF was 6.5% of EES and 6.7% SYNERGY treated subjects (ITT: 97.5% upper confidence bound=2.68%; Pnoninferiority=0.0005; Per Protocol: TLF EES 6.4%, 6.4% SYNERGY, 97.5% upper confidence bound=2.51%; Pnoninferiority=0.0003) |
|                     |                |                                                                                          | 2° endpoints:                                                                            |
|                     |                |                                                                                          | At 2 years, cardiac death (EES 1.5% vs SYNERGY 1.0%; P=0.35), MI (5.4% vs 5.5% based on 3x CK-MB ULN; P=0.89), TLR (3.1% vs 4.3%; P=0.17), or ST (0.8% vs 0.4%; P=0.31). |
| EVOLVE II Diabetes [43, 44] NCT01665053 |                |                                                                                          | Diabetes Substudy:                                                                 |
|                     |                |                                                                                          | 1° endpoint: 12 m TLF occurred in 7.5% of SYNERGY-treated patients with diabetes, significantly less than the performance goal (P<0.0001). The 2-year rate of TLF was 11.2% and definite/probable ST occurred in 1.1% of patients. |
| EVOLVE II QCA 12-month [45] NCT01787799 | N/A           | N=100; Prospective, multisite, single-arm: 12 sites (Australia, New Zealand, Singapore, and Japan); ≤3 target lesions ≤34mm, ≥2.25 to ≤4.0 mm RVD | 1° endpoint: 9 m in-stent late loss 0.23 mm (1-sided 97.5% upper confidence bound 0.40 mm), and was significantly below the prespecified performance goal of 0.4 mm (P<0.0001). Post-procedure incomplete stent apposition was also low (2.1%), and 9-month % volume obstruction by IVUS was 5.2%. At 12 m follow-up, there were no deaths or ST. Five patients had peri-procedural non-Q wave MI (based on CK-MB>3x upper limit of normal), and 1 TLR. |
| EVOLVE China 12-month [115] NCT01966159 | EES           | N=412; Prospective, multisite, single-blind, randomized (1:1) noninferiority: 14 sites in China; ≤2 target lesions ≤34mm, ≥2.25 to ≤4.0 mm RVD | 1° endpoint: 9 m in stent late loss (SYNERGY 0.20mm±0.33mm vs EES 0.17mm±0.37mm). The upper 1-sided 97.3% confidence interval of the difference (0.10 mm) was significantly less than the noninferiority margin of 0.15 mm (P>0.0008). Clinical adverse event rates were low and not significantly different at 12 months (all P>0.05). |

Abbreviations: CAD = coronary artery disease; EES = everolimus-eluting stents; IVUS = intravascular ultrasound; MI = myocardial infarction; RVD = reference vessel diameter; TLF = target lesion failure; TLR = target lesion revascularization; TVR = target-vessel revascularization; ST = stent thrombosis.

CLINICAL TRIALS OF BIOABSORBABLE POLYMER-COATED DES

SYNERGY Stent

The SYNERGY stent (Boston Scientific, Marlborough, USA) is the only BP-DES approved by the United States Food and Drug Administration for commercial use. SYNERGY is a thin-strut (74 µm) platinum chromium stent that delivers everolimus from a 4 µm ultrathin bioabsorbable poly (DL-lactide-co-glycolide) (PLGA) polymer applied to the abluminal surface (no drug/polymer are present on the luminal side; Table 1). The platinum chromium platform which remains after complete degradation of the polymer has been shown to be less pro-inflammatory compared to gold, cobalt chromium, or cobalt nickel alloy platforms in cell assay, and may enhance endothelial cell stent coverage while and reducing platelet adhesion when compared with a stent coated with a PVDF permanent polymer in vitro [38]. Animal studies have demonstrated that PLGA absorption is complete shortly after drug release (Fig. 2; <4 months) [24].

The EVOLVE first-human-use trial compared the safety and efficacy of SYNERGY to the permanent polymer everolimus-eluting PROMUS Element™ stent (Boston Scientific, Marlborough, USA); 2 dose formulations of everolimus were used ("SYNERGY" had an equivalent dose to PROMUS Element; "SYNERGY ½ dose" had half the dose of PROMUS Element) [39]. A total of 291 patients with de novo native coronary lesions were enrolled in a 1:1:1 ratio (Table 2). The primary clinical endpoint was 30-day target lesion failure (TLF: defined as cardiac death, target-vessel related myocardial infarction [TV-MI], or target vessel revascularization [TVR]) and the primary angiographic endpoint was 6-month in-stent late loss. The 30-day TLF rates
were 0%, 1.1%, and 3.1% for patients in the PROMUS Element, SYNERGY, and SYNERGY ½ dose groups, respectively (Table 2). The 6-month rates of in-stent late loss in both SYNERGY arms were noninferior to PROMUS Element (Table 2) [39]. After 5 years of follow-up, subjects enrolled in the study continued to have low mortality and MI rates. There were no stent thromboses (ST) reported for any group at 5 years [40].

EVOLVE II was a global, single-blind, randomized, multicenter, noninferiority pivotal trial comparing SYNERGY to the PROMUS Element Plus everolimus-eluting stent (Boston Scientific, Marlborough, USA). A total of 1,684 ‘more-comer’ patients with non-ST elevation MI or stable coronary artery disease were randomized 1:1 to receive SYNERGY or PROMUS Element Plus. At 12 months, the SYNERGY stent was noninferior to PROMUS Element Plus for the primary endpoint of TLF (Table 2). There were no significant differences in clinically- indicated TVR or definite/probable ST between SYNERGY and PROMUS Element Plus at 1 year [41]. At 2 years, TLF occurred in 8.5% of PROMUS Element Plus patients compared to 9.4% of SYNERGY patients (P=0.66) [42]. Definite/probable ST was infrequent with SYNERGY and, beyond 24 hours, only 1 probable and no definite ST occurred on day 6 in the SYNERGY arm (cumulative rates at 2 years: PROMUS Element 0.8% vs SYNERGY 0.4%; P=0.31) [41, 42].

In the EVOLVE II Diabetes Substudy, patients with diabetes randomized to the SYNERGY arm in the EVOLVE II RCT (263 subjects) were pooled with diabetic subjects enrolled in a single-arm Diabetes study [43]. The primary endpoint of the EVOLVE II Diabetes Substudy, 12-month TLF, was 7.5% (34/451) in SYNERGY-treated patients with diabetes which was significantly less than the performance goal (14.5%; P<0.0001; Table 2). At 2 years, clinical outcomes were similar to the overall population [44].

SYNERGY has also been tested in an angiographic cohort of patients in EVOLVE II QCA, a prospective, single-arm, multicenter study (N=100; Table 2) [45]. The primary endpoint, in-stent late loss at 9 months, was 0.23±0.34 mm which was significantly less than the performance goal of 0.40 mm (P<0.0001). There were no deaths; 5 subjects had periprocedural non-Q-wave MI based on the conservative protocol definition (based on CK-MB >3x URL). No patient experienced a definite or probable ST through 12 months [45].

Finally, EVOLVE China assessed SYNERGY versus PROMUS Element Plus in a randomized controlled trial at 12 sites in China (N=412; Table 2) [46]. The primary endpoint of 9-month in-stent late loss in SYNERGY was found to be noninferior to PROMUS Element Plus. Clinical outcomes at 12 months were similar between arms [46].

Two studies are in progress to test the safety of a shorter duration of DAPT. SENIOR (NCT02099617) will compare outcomes in elderly patients receiving either SYNERGY or BMS with DAPT for 1 or 6 months depending on clinical presentation [47]. The primary endpoint is major adverse cardiac and cerebrovascular events at 12 months. EVOLVE Short DAPT study is a prospective, multicenter, single-arm post-approval study designed to assess the safety of 3-month dual antiplatelet therapy in PCI patients at high risk of bleeding (NCT02605447). The study has 2 powered co-primary endpoints assessed between 3 and 15 months post index procedure: the rate of death or MI, and definite/probable ST.

**Biomatrix™ Stent**

Biomatrix (Biosensors Europe SA, Morges, Switzerland) is one of the first BP-DES developed and tested clinically. The Biomatrix stent elutes biolimus A9 (a sirolimus analogue) from a tubular, laser-cut, stainless steel stent (137µm strut thickness; Table 1). Biomatrix delivers the antiproliferative drug via a bioabsorbable poly lactic acid polymer (PLA; 120 µm thick) coated on the abluminal surface of the stent (Table 1). The PLA coating is fully absorbed within 6-9 months.

The Biomatrix stent was first tested in humans in the STEALTH trial (STent Eluting A9 BioLimus Trial in Humans), a randomized (2:1), multicenter study of 120 patients comparing Biomatrix to a BMS control. Six-month results from STEALTH demonstrated that for the primary endpoint of in-segment late lumen loss, Biomatrix had significantly less lumen loss compared to BMS (Table 3). Event-free survival at 6 months was similar between arms (Biomatrix 96.3% vs S-Stent 97.5%; P=0.72) [48].

The STEALTH trial was followed by the larger LEADERS multicenter, noninferiority trial (Limus Eluted from A Durable Versus ERodable Stent Coating) comparing the Biomatrix stent to a sirolimus-eluting permanent polymer DES (SES: Cypher SELECT™, Cordis, Miami Lakes, USA) in 1,707 randomized patients with chronic stable coronary artery disease or acute coronary syndromes. The LEADERS trial demonstrated noninferiority of Biomatrix to SES for the composite primary endpoint of major adverse cardiac events (MACE: cardiac death, MI, or clinically- indicated TVR) at nine months (Table 3) [49]. Five-year follow-up of the LEADERS trial demonstrated that Biomatrix remained noninferior to SES for MACE and that late ST and associated clinical events were significantly reduced with Biomatrix compared to SES (P=0.005; Table 3) [50].

The Biomatrix stent has also been tested in the COMFORTABLE trial (Comparison of Biolimus Eluted from an Erodible Stent Coating with Bare Metal Stents in Acute ST-Elevation Myocardial Infarction) which examined outcomes in 1,161 patients with ST-elevation myocardial infarction (STEMI) treated with either Biomatrix or the Gazelle™ BMS (Biosensors Europe SA, Morges, Switzerland). The primary endpoint for this randomized, multicenter study was MACE (cardiac death, TV-MI, and ischemia-driven TVR) at one year and was significantly lower with Biomatrix compared to BMS (Table 3). Biomatrix also demonstrated significantly less definite ST compared to BMS at 1 year [51]. MACE rates at 2 years were significantly lower with Biomatrix than with BMS (5.8% vs 11.9%; P<0.001) [52].

**Nobori and Ultimaster™ Stents**

**Nobori Stent**

The Nobori stent (Terumo Corporation, Tokyo, Japan) is a biolimus A9-eluting stent made of 316L stainless steel with
A strut thickness of 120 μm. The stent is coated only on the abluminal surface with a 20 μm thick bioabsorbable PLA polymer layer that fully dissolves in 6–9 months (Table 1).

The Nobori biolimus-eluting stent (Terumo Corporation, Tokyo, Japan) has been tested extensively (summarized in Table 4).

Ostojic et al. performed the first feasibility study (Nobori Core) comparing Nobori to a SES (Cypher) in 107 patients. The study showed lower MACE in the Nobori group at 12 months [53]. In the NOBORI 1 trial (phases 1 and 2), Nobori was compared to a paclitaxel-eluting stent (PES; TAXUS™ Express and TAXUS Liberté™, Boston Scientific, Marlborough, MA) and was noninferior to PES for the primary endpoint of 9-month in-stent late loss [54]. Five-year follow-up data revealed no differences between the Nobori stent and PES for the death/MI or TLF (Table 4) [55]. However, ischemia-driven and non-ischemia-driven TLR were lower in the Nobori group compared to PES. The rates of ST (ARC definite and probable) were also lower in the Nobori group (Nobori 0.0% vs PES 3.2%, P=0.014) [55].

Additional randomized studies with Nobori have demonstrated favorable outcomes in patients with de novo lesions (NOBORI Japan [56], NEXT [57]), acute or stable angina (COMPARE II [58] and BASKET-PROVE II [59]), an all-comer patient population (SORT OUT V [60]), patients with graft lesions (NEXT [57]) and in patients with long lesions (LONG-DES V [61]) (Table 4).

A meta-analysis of randomized trials which evaluated the Nobori stent was performed and demonstrated comparable efficacy and safety of the Nobori stent to other tested DES [62]. A total of 9,114 patients randomized to receive the Nobori BP-DES (n=5,080) were compared to control DES (n=4,034: everolimus-eluting stents [EES] n=2,533; SES

| Table 3. Summary of clinical trials for the Biomatrix biolimus-eluting bioabsorbable polymer stent. |
| --- |
| Trial | Control | θ of patients/study design | Results |
| STEALTH 6-month results (2005) [116] | BMS | De novo coronary lesions <24 mm in length, diameter 2.7 mm to 3.7 mm. 120 patients randomized 2:1; double-blind; multicenter | 1° endpoint: LLL at 6 months: Biomatrix 0.14±0.45 mm vs BMS 0.40±0.41 mm; P=0.004 2° endpoint: Similar event free survival (Biomatrix 96.3% vs BMS 97.5%; P=0.72) and TLR (Biomatrix 3.9% vs BMS 7.7%; P=NS) in both groups |
| LEADERS 9-month results (2008) [49] | SES | Patients with chronic, stable CAD or ACS; RVD 2.25 mm to 3.5 mm. 1,707 patients randomized 1:1; multicenter; noninferiority | 1° endpoint: MACE at 9 months: Biomatrix 9% vs SES 11%; P noninferiority =0.003, P superiority =0.39 2° endpoints: 9-month in-stent %DS Biomatrix 20.9% vs SES 23.3%; P noninferiority =0.001, P superiority =0.26 5-year MACE Biomatrix 22.3% vs SES 26.1%; P noninferiority<0.0001, P superiority=0.07 |
| LEADERS 5-year results (2013) [50] | | | |
| NCT00389220 | | | |
| COMFORTABLE 1-year results (2012) [51]; 2-year follow-up (2014) [52] | BMS | 1,161 patients with STEMI randomized 1:1; multicenter | 1° endpoint: 1-year MACE: Biomatrix 4.3% vs BMS 8.7%; P=0.004 2° endpoints: 1-year Definite ST with Biomatrix 0.9% vs BMS 2.1%; P=0.10 13-month in-stent %DS Biomatrix 12.0±7.2 mm vs BMS 39.6±25.2 mm; P<0.001 2-year MACE Biomatrix 5.8% vs BMS 11.9%; P<0.001 |
|| N/A | Consists of 2 registries: e-BioMatrix PMS N= 1,106 patients; and e-BioMatrix PMR N=4,453 patients | 1° endpoint: 12-month MACE was 4.5% 2° endpoints: 2-year MACE was 6.8% (cardiac death 1.5%, MI 2.4%, TVR 4.3%). ST occurred in 0.8% of patients |
| e-Biomatrix Registry [117] | | | |
| NCT01289002 and NCT01254487 | | | |

Abbreviations: BMS = bare metal stents; LLL = late lumen loss; TLR = target lesion revascularization; NS = non-significant; RVD = reference vessel diameter; CAD = coronary artery disease; ACS = acute coronary syndrome; SES = sirolimus-eluting stent; ST = stent thrombosis; %DS = percent diameter stenosis; MACE = major adverse coronary event; TV-MI = target-vessel myocardial infarction; TVR = target-vessel restenosis.
Table 4. Summary of clinical trials for the Nobori and Ultimaster biolimus-eluting bioabsorbable polymer stent.

| Trial                                      | Control                        | # of patients/study design               | Key Results                                                                                                                                                                                                 |
|--------------------------------------------|--------------------------------|----------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| NOBORI CORE 9-month results (2008) [53]    | SES                            | 107 patients with de novo CAD, randomized 1:1, 5 centers | 1° endpoint: 9-month in-stent LLL Nobori 0.10mm±0.26mm vs SES 0.13mm±0.44mm; \( P=0.660 \)                                                                                                             |
|                                            |                                |                                        | 2° endpoints:                                                                                                                                                                                               |
|                                            |                                |                                        | 12-month MACE Nobori 1.9% vs SES 4.1%                                                                                                                                                                       |
|                                            |                                |                                        | 9-month in-stent % diameter stenosis for Nobori 13%±10% vs SES 20%±12%; \( P=0.002 \)                                                                                                                        |
| NOBORI 1 Trial – Phase 1 9-month results (2007) [54] | PES (TAXUS Express)            | 120 patients with native CAD, prospective, controlled, noninferiority, randomized 2:1, 29 centers | 1° endpoint: 9-month in-stent LLL with 0.15mm±0.27mm vs PES 0.32mm±0.33mm; \( P=0.006 \)                                                                                                          |
|                                            |                                |                                        | 0% ST for both groups                                                                                                                                                                                      |
| NOBORI 1 Trial - Phase 2 9-month results (2009) [118] | PES (TAXUS Liberté)           | 243 patients with native CAD, prospective, controlled, noninferiority, randomized 2:1, 29 centers | 1° endpoint: 9-month in-stent LLL Nobori 0.11mm±0.30mm vs PES 0.32mm±0.50mm; \( P\text{noninferiority}<0.001 \), \( P\text{superiority}=0.001 \)              |
|                                            |                                |                                        | 2° endpoints:                                                                                                                                                                                               |
|                                            |                                |                                        | 9-month MACE Nobori 4.6% vs PES 5.6%                                                                                                                                                                       |
|                                            |                                |                                        | ST rate Nobori 0% vs PES 4.4%                                                                                                                                                                              |
| NOBORI 1 Trial – Phases 1 & 2 5-year results (2015) [55] | PES                            | 363 patients with native CAD, prospective, controlled, noninferiority, randomized 2:1, 29 centers | 1° endpoint: 5-year TLF Nobori 9.2% vs PES 10.4%                                                                                                                                                         |
|                                            |                                |                                        | 2° endpoints:                                                                                                                                                                                               |
|                                            |                                |                                        | TLR Nobri 6.3% vs PES 16.0%                                                                                                                                                                               |
|                                            |                                |                                        | Def/prob ST Nobori 0.0% vs PES 3.2%; \( P=0.014 \)                                                                                                                                                        |
| NOBORI Japan 9-month results (2012) [56]    | SES                            | 335 patients with de novo lesions in up to 2 native coronary arteries, controlled, randomized 3:2, 15 centers in Japan | 1° endpoint: Freedom from TVF Nobori 92.6% vs SES 93.8%; \( P\text{noninferiority}<0.001 \)                                                                                                          |
|                                            |                                |                                        | 2° endpoints:                                                                                                                                                                                               |
|                                            |                                |                                        | 9-month in-stent LLL Nobori 0.12mm±0.30mm vs SES 0.14mm±0.34mm                                                                                                                                              |
|                                            |                                |                                        | 9-month TLR Nobri 0.5% vs 3.9%; \( P=0.04 \)                                                                                                                                                              |
|                                            |                                |                                        | 0% def/prob ST for both groups                                                                                                                                                                            |
| SORT OUT V 9-month results (2013) [60]     | SES                            | 1,229, all-comers, noninferiority, randomized 1:1, 3 sites | 1° endpoint: 9-month MACE Nobori 4.1% vs SES 3.1%; \( P\text{noninferiority}=0.06 \)                                                                                                                     |
|                                            |                                |                                        | 2° endpoint: 9-month definite ST Nobri 0.7% vs SES 0.2%; \( P=0.03 \)                                                                                                                                    |
| NEXT trial 1-year results (2013) [57]      | EES                            | 2,707 patients with RVD between 2.0mm and 4.0mm, prospective, controlled, noninferiority, randomized 2:1, 12 sites | 1° endpoint: 1-year MACE Nobori 5.2% vs EES 4.8%; \( P\text{noninferiority}<0.0001 \)                                                                                                                   |
|                                            |                                |                                        | 2° endpoints:                                                                                                                                                                                               |
|                                            |                                |                                        | 1-year def/prob ST Nobori 0.8% vs EES 1.0%; \( P=0.58 \)                                                                                                                                                 |
|                                            |                                |                                        | 3-year MACE Nobori 11.9% vs EES 11.1%; \( P=0.57 \)                                                                                                                                                     |
|                                            |                                |                                        | 3-year ST Nobri 1.2% vs EES 0.8%; \( P=0.33 \)                                                                                                                                                           |
|                                            |                                |                                        | 9-month in-segment LLL Nobori 0.03mm±0.39mm vs EES 0.06mm±0.45mm; \( P\text{noninferiority}<0.0001 \), \( P\text{superiority}=0.52 \) (266±43 days after stent implantation) |
| COMPARE II 1-year results (2013) [119]; 3-year results (2015) [58] | EES                            | 3,235 patients with native and graft vessel disease scheduled for PCI, prospective, noninferiority, randomized 1:1, multicenter | 1° endpoint: 1-year TLR Nobri 4.2% vs EES 4.2%; \( P\text{noninferiority}<0.0001 \), \( P\text{superiority}=0.93 \)                                                                  |
and coated with a 15 µm thick poly (DL-lactide-co-caprolactone) on the abluminal surface (without coating on hinges) (Table 1). Both drug release and polymer degradation occur within 3-4 months.

The Ultimaster stent has been tested in the small, single-arm CENTURY I (n=105) and the larger, randomized CENTURY II studies. The primary endpoint of the CENTURY I study, angiographic late loss at 6 months, was 0.04±0.35 mm and was significantly lower than late loss in the control arm (Table 4) [65]. Through 4 years of follow-up, the rate of TLF was 6.7% and ARC definite/probable ST was 0.9% [66]. CENTURY II was a larger-scale, prospective, multicenter, randomized noninferiority trial comparing Ultimaster (N=551) to the XIENCE™ everolimus-eluting permanent polymer stent (EES; Abbott Vascular, Santa Clara, USA; n=550) [67]. The primary endpoint, freedom from TLF at 9 months, was 95.6% with Ultimaster compared to 95.1% with EES (Pnoninferiority<0.0001). At 2 years, TLF occurred in 6.5% and ARC definite/probable ST was 0.9% [66].

Ultimaster Stent

The Ultimaster stent, the next generation BP-DES from Terumo, is an 80 µm cobalt chromium stent eluting sirolimus and coated with a 15 µm thick poly (DL-lactide-co-caprolactone) on the abluminal surface (without coating on
L.605 struts covered with an 7.5 µm thick amorphous silicon carbide layer. Sirolimus is released from a biodegradable poly-L-lactic acid (PLLA) polymer, which completely degrades during a period of 12 to 24 months. Preclinical studies have shown similar suppression of neointimal proliferation for Orsiro as compared to the Cypher SES and low inflammatory scores compared to BMS [68].

The Orsiro stent was first tested in 30 patients with single de novo lesions [69]. The primary endpoint was 9-month in stent late loss (0.05 ± 0.22 mm). At 1 year, MACE was 10% with no MI or ST [69]. Following the initial feasibility study, the larger BIOFLOW-II trial compared the Orsiro stent with XIENCE Prime™, a permanent polymer EES [70]. A total of 452 patients were randomly assigned 2:1 to treatment with Orsiro (n=298) or EES (n=154 patients). Orsiro was noninferior to EES for the primary endpoint of in-stent late lumen loss at 9 months [70]. TLF was similar at 1 year with no cases of ST in either arm.

BIOSCIENCE was a large randomized, noninferiority trial with minimal exclusion criteria comparing Orsiro with a permanent polymer EES (XIENCE Prime/Xpedition, Abbott Vascular, Santa Clara, USA); 19% of enrolled patients had STEMI [71]. The primary endpoint, 12-month TLF, was a composite of cardiac death, TV-MI, and clinically-indicated TVR. A total of 2,119 patients were randomized to receive the Orsiro stent (N=1,063 patients) or an EES (N=1,056). Orsiro was found to be noninferior to EES for the primary endpoint of in-stent late lumen loss at 9 months [70]. TLF was similar at 1 year with no cases of ST in either arm. The Orsiro stent was found to be noninferior to EES (0.12±0.15 mm vs E-ZES 0.63±0.47 mm; P<0.001). In addition, the Orsiro stent was superior to E-ZES for the primary endpoint of TLF at 12 months. The rates of definite TVR. A total of 2,119 patients were randomized to receive the Orsiro stent (N=1,063 patients) or an EES (N=1,056). Orsiro was found to be noninferior to EES for the primary endpoint of in-stent late lumen loss at 9 months [70]. TLF was similar at 1 year with no cases of ST in either arm.

The BIOFLOW-III registry was designed to evaluate Orsiro in ‘real-world’ patients (N=1,356) [72]. The primary endpoint, 12-month TLF occurred in 5.1% of patients in the overall population and in 7.7% of patients with diabetes, 5.8% of patients with small vessels, 1.8% of patients with chronic total occlusion, and 7.2% of patients with acute MI [72].

The Orsiro stent is currently being tested in more complex patient groups.

MiStent™

MiStent (Micell Technologies, Durham, USA) is a thin-strut (64µm) cobalt-chromium stent covered with a bioabsorbable polymer and crystalline sirolimus which controls drug release through 6 months post-implantation without an initial burst (Table 1). The polymer is completely absorbed by the tissue within 90 days in an animal model [73]. This stent was initially evaluated in the DESSOLVE I Trial (DES with Sirolimus and a Bioabsorbable Polymer for the Treatment of Patients with De Novo Lesion in the Native Coronary Arteries; NCT01247428) which included 30 patients [73]. DESSOLVE I demonstrated low and stable in-stent lumen late loss and complete strut coverage at 18 months [73]. No ST was observed through 5 years [74].

The subsequent, larger DESSOLVE II trial (NCT01294748) compared the efficacy and safety of the MiStent with a first generation Zotarolimus-eluting stent, Endeavor™ (E-ZES; Medtronic, Santa Rosa, USA) [75]. A total of 184 patients were randomized in a 2:1 fashion with MiStent (n=123) versus E-ZES (n=61). MiStent was superior to E-ZES for the primary endpoint of 9-month in stent late lumen loss (MiStent 0.27±0.46mm vs E-ZES 0.58±0.41mm; P<0.001). The proportion of uncovered stent struts assessed by OCT was very low and similar in both groups. Mean neointimal thickness (P=0.002) and percent net volume obstruction (P=0.003) were significantly lower in the MiStent group at 9 months [75]. Major adverse cardiac events and ST rates were low and comparable between groups through 4 years [74].

A pooled analysis of the DESSOLVE I/II and ISAR-TEST-4 studies examined the performance of MiStent in a propensity-matched comparison (n=102 each arm) versus a permanent polymer EES [76]. In this small post hoc analysis, MiStent exhibited lower TLF and TLR through 3 years compared to EES (TLF: MiStent 5.0% vs EES 12.5%, P=0.07; TLR: 2.0% vs 8.4%, P=0.04) [76].

Longer-term follow-up and larger trials in ‘real-world’ patients with MiStent are in progress.

Elixir DESyne BD™ Stent

Elixir DESyne BD (Elixir Medical Corporation, Sunnyvale, USA) is an 81 µm thick cobalt-chromium stent eluting novelimus (an active metabolite of sirolimus) from an ultrathin (<3 µm) polylactide-based bioabsorbable polymer which degrades within 6-9 months (Table 1).

This stent was first tested in the Excella BD trial (NCT0200956) which compared the Elixir DESyne BD Stent to the Endeavor ZES (E-ZES). A total of 146 patients were randomized in a 3:1 fashion. The study met the primary endpoint (angiographic in-stent late lumen loss at 6 months) demonstrating both noninferiority and superiority of Elixir DESyne BD as compared to E-ZES (Elixir DESyne 0.12±0.15 mm vs E-ZES 0.67±0.47 mm; P noninferiority<0.001). Additionally, in-stent binary restenosis was significantly lower with Elixir DESyne BD compared to E-ZES (0% vs 7.9%; P=0.003). At 3 years, the device-oriented composite endpoint (DoCE: cardiac death, TV-MI, and clinically-indicated TLR) was similar in the Elixir DESyne BD and control groups [77].

This initial study was followed by the small ExcelLA II study randomizing Elixir DESyne to E-ZES in a 2:1 fashion (NCT00792753) [78]. The primary endpoint was in stent late lumen loss at 9 months and Elixir DESyne was superior to E-ZES (Elixir DESyne 0.11 ± 0.32 mm vs E-ZES 0.63 ± 0.42 mm, P noninferiority<0.0001 and P superiority=0.0001) [78]. Neither DoCE nor its individual components were significantly different between the bioabsorbable and permanent polymer coated stents. The rate of DoCE at 5 years was significantly lower in the Elixir DESyne cohort compared to E-ZES (HR 0.38 [0.17, 0.83], P=0.01) [79]. No differences between groups were found for cardiac death (2.9% vs 4.2%, P=0.69), TV-MI (2.9% vs 7.0%, P=0.17), or ST (5.0% vs 7.0%, P=0.54). Revascularization was significantly reduced with Elixir DESyne BD compared to E-ZES at 5 years (18.7% vs 32.4%, P=0.04) [78].
TIVOLI™ Stent

TIVOLI (Essen Technology Beijing Co. Ltd., Beijing, China) is a bioabsorbable polylactic-co-glycolic acid (PLGA) polymer-coated sirolimus-eluting stent with a strut thickness of 80 µm (Table 1).

Xu and colleagues evaluated Tivoli in a 324 patient RCT (TIVOLI n=168 vs E-ZES n=156) [80]. The primary end-point, in-stent late lumen loss at 8 months, was superior in Tivoli compared to E-ZES (TIVOLI 0.25 ±0.33 mm vs E-ZES 0.57 ±0.55 mm; \( P_{\text{noninferiority}}<0.0001 \)). The 8-month rate of in-stent binary restenosis was also significantly reduced with TIVOLI (2.9% vs 8.6%; \( P=0.02 \)). At 2 years, TLR was significantly reduced in patients receiving the TIVOLI stent compared to E-ZES (4.2% vs 9.6%; \( P=0.0495 \)) with no significant difference in MACE (cardiac death, MI or TVR) rates between groups (6.6% vs 10.9%; \( P=0.16 \)) [80].

The TIVOLI stent has also been evaluated in the I-LOVE-IT 2 trial; a prospective, multicenter, noninferiority study based in China (NCT01681381) which included 2,737 patients randomized 2:1 to TIVOLI (n=1,829) compared to the Firebird stent, a durable polymer SES (MicroPort, Shanghai, China; n=908) at 32 centers [81]. The primary endpoint, 12-month TLF, occurred in 6.3% of Tivoli patients vs 6.1% of SES patients (\( P_{\text{noninferiority}}=0.0002 \)). The individual components of TLF were not significantly different between groups including cardiac death (0.7% vs 0.6%, \( P=0.62 \)), TV-MI (3.6% vs 4.3%, \( P=0.39 \)), and TLR (2.6% vs 2.2%, \( P=0.50 \)). The rates of ST were also similar between cohorts (0.4% vs 0.6%, \( P=0.55 \)).

EXCEL™ Stent

The EXCEL Stent (JW Medical System Ltd., WeiHai, Shandong, China) is a sirolimus-eluting stent coated with a bioabsorbable polylactic acid polymer. The stent platform is a laser cut, 316L stainless steel with a strut thickness of 119 µm (Table 1). The 10-15 µm thick coating is absorbed completely in 6–9 months in animal models.

The RESOLVE study (NCT00713557) demonstrated noninferiority of the EXCEL stent to its comparator Firebird or Firebird II, a durable polymer coated SES (Microport Co Ltd., Shanghai, China) for the primary endpoint of MACE (all death, MI, TLR at 1 year) in STEMI patients [82]. A total of 1,192 STEMI patients were randomized 1:1 to receive the EXCEL stent (n=596) or the SES (n=596). MACE at 1-year was 12.4% in the EXCEL group as compared to 13.3% in the control group (\( P_{\text{noninferiority}}=0.001 \)). Late ST (oc-
curing >30 days) was lower in EXCEL-treated patients versus SES (0.7% vs 2.2%, \( P = 0.03 \)) [82].

The ‘real-world’ CREATE registry (NCT00331578) enrolled 2,077 patients treated with the EXCEL stent [83]. At 5 years, clinical outcomes were low: cardiac death 3.0%, nonfatal MI 1.5%, TLR 3.7%, and overall MACE 7.4%. The 5-year rates of definite/probable ST at and definite ST from 1 to 5 years were 1.1% and 0.3%, respectively. Patients with or without clopidogrel treatment after six months had similar clinical outcomes in a landmark analysis of a propensity score-matched cohort [83].

Additionally, the EXCEL stent was found to be superior to the polymer-free sirolimus-eluting (PF) and drug-eluting stents (Real Dual drug-eluting stents; Dual DES) in the DKPLUS-Wave 1 randomized trial [84]. A total of 1,346 patients with de novo CAD were randomized to either the EXCEL or Dual DES. The rate of the primary endpoint, TVR at 12 months, was 3.5% in the EXCEL group and 13.9% in the Dual DES group (\( P = 0.001 \)). ST at 12 months was 0% in the Dual DES group and 1.2% in the EXCEL group (EXCEL vs Dual DES, \( P = 0.50 \)) [84].

The next generation of the EXCEL stent, EXCEL II, is a thinner strut (88 µm) cobalt chromium PLA-coated sirolimus-eluting stent was tested in the first-human-use CREDIT-I study [85]. A total of 45 patients were enrolled and evaluated up to 12 months post implantation. No MACE events (cardiac death, MI or TLR) occurred within the year [85].

**Inspiron™ Stent**

The Inspiron sirolimus-eluting stent (Scitech Medical, Aparecida de Goiânia, Goiás, Brazil) consists of a L-605 cobalt-chromium alloy platform with a 75 µm strut thickness and a Xµm thick abluminal, bioabsorbable coating which dissolves within 30 days (Table 1) [86]. The INSPIRON-I trial (NCT01093391) compared the Inspiron Stent with a BMS in 57 patients, randomized in a 2:1 fashion. The primary endpoint was in-segment late loss at 6 months and was reduced in the Inspiron group compared to BMS (0.19 ± 0.16 mm vs. 0.58 ± 0.4 mm, respectively; \( P < 0.001 \)) [87]. After 4 years, MACE was lower with Inspiron (7.9% vs. 23.5%, \( P = 0.11 \)), the rates of death and MI were similar between groups but the rate of TLR was lower with the Inspiron Stent as compared to BMS (0.0% vs. 23.5% respectively, \( P = 0.02 \)) [86].

The DESTINY trial (NCT01856088) is a prospective, multicenter, randomized study comparing Inspiron with Biomatrix Flex [88]. A total of 170 patients with 1 or 2 de novo lesions were randomized in a 2:1 fashion (Inspiron Stent+Biomatrix Stent). The Inspiron Stent demonstrated noninferiority with regards to in-stent late loss at 9 months compared to the Biomatrix Stent (Inspiron 0.20 ± 0.29 mm vs Biomatrix 0.15 ± 0.20 mm; \( P_{\text{noninferiority}} < 0.001 \)). At one year, the rates of death (0.9% vs 0.0%), MI (4.4% vs 7.4%), and TVR (2.7% vs 3.7%) were low and similar between groups [88]. An additional all-comers single-arm registry (Inspiron Registry) enrolled 470 patients who exhibited a 300 day MACE rate of 8.1%, TLR of 5.4%, and ST of 0.4% with no cases after 30 days [89]. Long-term follow-up of the DESTINY trial and enrollment in a ‘real-world’ registry are in progress.

**FIREHAWK™ Stent**

The FIREHAWK stent (Microport Medical, Shanghai, China) is an 86 µm thick, cobalt chromium, biodegradable polylactic acid polymer coated DES releasing sirolimus. Drug and polymer are poured into abluminal grooves located on the outer surface of the struts (average rapamycin dosage 3 µg/mm stent) [90]. FIREHAWK was first tested in the 21 patient FIREHAWK trial. The primary endpoint was MACE at 30 days (cardiac death, MI, TLR); there were no MACE or ST events through 13 months of follow-up.

The Target I trial compared FIREHAWK to a permanent polymer EES (XIENCE V) [91]. A total of 458 patients were randomized. Nine-month in-stent late lumen loss, the primary endpoint, was found to be noninferior in FIREHAWK stents compared to EES (0.13 ± 0.24 mm vs 0.13 ± 0.18 mm, \( P_{\text{noninferiority}} < 0.0001 \)). At 12 months, cardiac death (0.4% vs 0.0%), TV-MI (1.3% vs 1.7%), TLR (0.4% vs 0.4%), and TLF (2.2% vs 2.2%) were similar between groups; no ST were reported in either arm [91]. Three-year in-stent late lumen loss and vascular healing (as assessed by OCT) were similar between groups [92]. The long lesion subgroup of TARGET I enrolled an additional 50 patients receiving either a 33 or 38 mm stent. The primary endpoint, 9-month in-stent late loss was 0.16 ± 0.16 mm with no death or ST within a year and 2 patients experiencing a MI [93]. Similar results were found in the Target II trial which was a prospective single-arm registry enrolling 730 patients. At one year, TLF was 4.4% and only 1 definite/probable ST was observed in Firehawk-treated patients [94]. Long-term follow-up of the Target II registry is in progress.

Combining the TARGET I and II trials, Gao et al evaluated 12-month TLF compared to a performance goal [95]. A total of 1,007 patients were included in this analysis and TLF at 1 year was 3.9% which was significantly lower than the prespecified performance goal of 9.0%. At 2 years, TLF was 4.6% which was composed of cardiac death 0.8%, TV-MI 2.9%, and clinically-indicated TLR 1.2% and definite/probable ST rate 0.1% [95].

**Yukon Choice PC™ Stent**

The Yukon Choice PC stent scaffold (Translumina GmbH, Hechingen, Germany) consists of a microporous stainless steel stent surface abuminally coated with sirolimus and a PLA biodegradable polymer. Mehilli et al. first compared this sirolimus-eluting BP-DES with a polymer-free (PF) stents and a permanent polymer sirolimus-eluting stent (SES; Cypher) in the ISAR-TEST 3 study (NCT00350454) [96]. More than 600 patients were randomized to BP-SES (n=202), SES (n=202), and PF (n=201). The primary endpoint was mean late lumen loss at 6 to 8-months and was 0.17±0.45mm in the Yukon Choice PC stent group, 0.23±0.46mm with SES, and 0.47±0.56mm in PF stent-treated patients. As such, Yukon Choice PC met the noninferiority criteria compared to SES (\( P_{\text{noninferiority}} < 0.001 \)); however, the PF stent did not (\( P_{\text{noninferiority}} < 0.94 \)) [96]. At 1 year, death occurred in 2.0% of patients in each group and ST oc-
curred in 1.0%, 2.0%, and 1.5% of Yukon Choice PC, SES, and PF patients, respectively [96].

The Yukon Choice PC stent (N=1,299) was then evaluated against a permanent polymer EES (XIENCE V; n=652) or SES (Cypher; n=652) in ISAR-TEST-4 (Intracoronary Stenting and Angiographic Results: Test Efficacy of 3 Limus-Eluting Stents; NCT00598676) a prospective, randomized, open-label trial [97]. The primary endpoint was the composite of cardiac death, TV-MI, and TLR; the Yukon Choice PC Stent was noninferior to the combined permanent polymer DES group for the primary endpoint at 12 months (BP-DES 13.8 vs DES 14.4%; P noninferiority=0.005) [97]. Cardiac death, TV-MI, TLR, and ST were similar in both groups at 12 months [97]. Between 6 and 8 months, angiographic outcomes were similar (in-stent late lumen loss BP-DES 0.24±0.6mm vs DES 0.26±0.5mm, P=0.49; in-segment binary restenosis (11.6% vs 11.8%, P=0.85) [98]. Three-year outcomes were not significantly different between the BP-DES and permanent polymer DES with regard to the primary endpoint (BP-DES 20.1% vs 20.9% DES, P=0.59). Rates of definite/probable ST were also similar in both groups at 3 years (1.2% vs 1.7%, P=0.32) [99]. While not statistically significant, the SES group displayed numerically higher rates of device-related adverse events as compared to the Yukon Choice PC arm or the EES arm at 5 years [100].

BuMATM

The BuMA stent (SINOMED, Beijing, China) is a stainless steel 100 µm thick stent coated conformally with 2 layers: an electro-grafting base layer (poly [n-butyl methacrylate] coating) and a biodegradable PLGA drug carrier [101]. The BuMA stent was compared to the EXCEL stent in the randomized (1:1) 80 patient single-center BuMA OCT non-inferiority RCT study (NCT01752582) [101]. The primary endpoint was OCT-evaluated stent strut coverage at 3 months. Compared to the EXCEL stent, stent strut coverage was higher in the BuMA arm compared to EXCEL (94.2% vs 90%, P noninferiority<0.0001). The proportion of malapposed struts and neointimal thickness were similar between stents. At 3 months, there were no cardiac deaths or STs but TV-MI was 7.5% in each group [101].

The BuMA and EXCEL stents were then compared in the larger, all-comers multicenter PANDA III trial (NCT02017725) [102]. A total of 2,348 patients were enrolled and randomized (1:1, n=1,174 in each arm); the primary endpoint of 1 year TLF (cardiac death, TV-MI, ID-TLR) with BuMA was noninferior to the EXCEL stent (6.4% in each group, P noninferiority=0.0003). The individual components of TLF were similar between arms. The rate of 1-year definite/probable ST was significantly reduced in the BuMA arm (0.5% vs 1.3%, P=0.048); this difference may be influenced by the difference in polymer degradation time (EXCEL 9 months vs BuMA 3 months, Table 1).

The second generation BuMA stent, BuMA Supreme, is currently being tested in the PIONEER global clinical program including the PIONEER, PIONEER II, and PIONEER US-Japan studies.

SvelteTM

The Svelte stent (Svelte Medical Systems, New Providence, USA) is integrated with its delivery system and is made of an 81 µm cobalt chromium platform and coated with a 6 µm thick bioabsorbable amino acid drug carrier which elutes sirolimus [103]. The Svelte stent was designed to facilitate direct stenting using a transradial approach. The Svelte stent was first tested in the Direct study, a single-arm multicenter study with a primary angiographic endpoint of 6-month in stent late lumen loss and an efficacy endpoint of 6-month TVF (cardiac death, TV-MI, clinically-indicated TVR). At 6 months, in stent late lumen loss was 0.22 ± 0.27 mm; TVF (non-TLR TVR) occurred in 2 patients [103]. The SPEED registry assessed experienced compared to inexperienced operators and showed that experience demonstrably improved in device success [104].

Direct II was a small randomized study comparing Svelte (n=108) to Resolute Integrity (R-ZES; n=51) [105]. The primary endpoint of in stent late lumen loss at 6 months in the Svelte stent was noninferior to R-ZES (0.09 ± 0.31 mm vs 0.13 ± 0.27 mm, P noninferiority<0.001) (105). TVF at 1 year was 6.5% vs 9.8% (P=0.52) [105].

The Svelte stent is currently being tested in the OPTIMIZE pivotal randomized clinical trial (compared to currently available DES).

BioMimeTM

The BioMime stent (Meril Life Science, Vapi, India) is an 65 µm thick cobalt-chromium stent eluting sirolimus from an ultrathin (2 µm) Poly L Lactide/ Polylactic co-glycolic acid -based bioabsorbable polymer of which three-quarters degrades within 2 months (Table 1).

This stent was evaluated in the first-human-use meriT-1 study (NCT01507519) which included 30 patients [106]. The study demonstrated median 8-month in-stent late lumen loss was 0.15 mm [0.09, 0.33]. At 12 months, no cardiac deaths, MI, TLR, or ST [106].

Currently, the BioMime stent is being tested in the single-arm MeriT-II (NCT02406326) study, the larger randomized meriT-V trial (compared to an everolimus-eluting permanent polymer DES; NCT02112981) and an all-comers registry (NCT02398955).

META-ANALYSES

There have been multiple meta-analyses comparing BP-DES to permanent polymer-coated DES. The most comprehensive meta-analysis performed by Lupi et al included 20 studies and 20,005 patients [107]. The durable polymer DES control groups included both the first- and second-generation DES. Median clinical follow-up of the included studies was 1 year, with 7,142 coronary lesions having angiographic follow-up at 6-9 months. Compared with the DES group, the BP-DES treated patients had significantly lower in-stent and in-segment late loss (P<0.001). BP-DES nearly halved the rate of late ST rate in comparison to DES. When the comparators were grouped into first- and second-generation DES, late ST occurred less often with BP-DES compared to
first-generation DES (OR 0.43 [0.24, 0.79], P=0.006); whereas the risk of late ST was similar between BP-DES and second-generation DES (0.95 [0.30, 3.02], P=0.95). There were no significant differences between BP-DES and either first- or second-generation DES for overall death, MI, or acute/subacute ST. Other meta-analyses have found similar results [62, 107-112]; three meta-analyses have shown significant benefits for BP-DES in terms of late, and especially very late, ST. In all of these meta-analyses, newer BP-DES (SYNERGY, Ultimaster, Tivoli, Svelte) were not included.

Newer BP-DES with thinner struts and reduced polymer load have the potential to show even greater benefits with regards to clinical outcomes including late and very late ST [107]. This is supported by recent ‘real-world’ experience in the Swedish Coronary Angiography and Angioplasty Registry (SCAAR) where SYNERGY reported the lowest rate of definite ST compared to all other DES analyzed [113].

CONCLUSION
Aboluminal, BP-DES appear noninferior to the first- and second-generation permanent polymer-coated DES. Studies with long-term follow up suggest that there may be less ST for BP-DES as compared to permanent polymer DES. Additional trials and longer follow-up is needed to fully elucidate the respective clinical indications of these devices in comparison to their permanent polymer counterparts. The ability to safely reduce or interrupt DAPT with BP-DES may reduce bleeding risk and cost if confirmed in adequately powered clinical studies.

ABBREVIATIONS
ACS = Acute coronary syndrome
BMS = Bare metal stents
BP = Bioabsorbable polymer
BP-DES = Bioabsorbable polymer drug-eluting stents
CAD = Coronary artery disease
DES = Drug-eluting stents
EES = Everolimus-eluting stent
MI = Myocardial infarction
PCI = Percutaneous coronary intervention
PES = Paclitaxel-eluting stent
PF = Polymer free
SES = Sirolimus-eluting stent
STEMI = Stent thrombosis elevation myocardial infarction
TLF = Target lesion failure
TLR = Target lesion revascularization
TVF = Target vessel failure
TVR = Target vessel revascularization

CONFLICT OF INTEREST
Dawkins K, Huibregtse B, Hou D, & Roy K are full-time employees of Boston Scientific.

ACKNOWLEDGEMENTS
Declared none.

REFERENCES
[1] Serruys PW, de Jaegere P, Kiemeneij F, et al. A comparison of balloon-expandable-stent implantation with balloon angioplasty in patients with coronary artery disease. Benestent Study Group. N Engl J Med 1994; 331(8): 489-95.
[2] Goldstein LB, Bushnell CD, Adams RJ, et al. Guidelines for the primary prevention of stroke: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. Stroke 2011; 42(2): 517-84.
[3] Indolfi C, De Rosa S, Colombo A. Bioreosorbable vascular scaffolds — basic concepts and clinical outcome. Nat Rev Cardiol 2016; 13: 719-29.
[4] Ramcharitar S, Vaina S, Serruys PW. The next generation of drug-eluting stents: what’s on the horizon? Am J Cardiovasc Drugs Devices Interv 2007; 7(2): 81-93.
[5] Busch R, Strohbach A, Peterson S, Sternberg K, Felix S. Parameters of endothelial function are dependent on polymeric surface material. Biomed Tech 2013; [Epub ahead of print].
[6] Busch R, Strohbach A, Rethfeldt S, et al. New stent surface materials: The impact of polymer-dependent interactions of human endothelial cells, smooth muscle cells, and platelets. Acta Biomater 2014; 10(2): 688-700.
[7] Nakazawa G, Nakano M, Otsuka F, et al. Evaluation of polymer-based comparator drug-eluting stents using a rabbit model of iliac artery ath erosclerosis. Circ Cardiovasc Inter 2011; 4(1): 38-46.
[8] Hiranuma N, Shinke T, Nakazawa G, et al. Optical coherence tomography and histopathology assessment after implantation of first- and second-generation drug-eluting stents in a porcine coronary model. Circ J 2014; 78(11): 2665-73.
[9] Yeh JS, Oh SJ, Hsee CM. Frequency of Vascular Inflammation and Impact on Neointimal Proliferation of Drug Eluting Stents in Porcine Coronary Arteries. Acta Cardiol Sin 2016; 32(5): 570-7.
[10] Finn AV, Nakazawa G, Joner M, et al. Vascular responses to drug-eluting stents: importance of delayed healing. Arterioscler Thromb Vase Biol 2007; 27(7): 1500-10.
[11] Virmani R, Guagliumi G, Farb A, et al. Localized hypersensitivity and late coronary thrombosis secondary to a sirolimus-eluting stent: should we be cautious? Circulation 2004; 109(6): 701-5.
[12] Joner M, Finn AV, Farb A, et al. Pathology of Drug-Eluting Stents in Humans: Delayed Healing and Late Thrombotic Risk. J Am Coll Cardiol 2006; 48(1): 193-202.
[13] Lee S-Y, Shin D-H, Mintz GS, et al. Optical coherence tomography-based evaluation of in-stent neatherosclerosis in lesions with more than 50% neointimal cross-sectional area stenosis. EuroIntervention 2013; 9(8): 945-51.
[14] Won H, Kim J-S, Shin D-H, et al. Relationship between endothelial vasomotor function and strut coverage after implantation of drug-eluting stent assessed by optical coherence tomography. Int J Cardiovasc Imaging 2014; 30(2): 263-70.
[15] Otsuka F, Vorpahl M, Nakano M, et al. Pathology of second-generation everolimus-eluting stents versus first-generation sirolimus- and paclitaxel-eluting stents in humans clinical perspective. Circulation 2014; 129(2): 211-23.
[16] Byrne RA, Joner M, Kastrati A. Polymer coatings and delayed arterial healing following drug-eluting stent implantation. Minerva Cardioangiol 2009; 57(5): 567-84.
[17] Finn AV, Nakazawa G, Joner M, et al. Vascular responses to drug-eluting stents: Importance of delayed healing. Arterioscler Thromb Vasc Biol 2007; 27(7): 1500-10.
[18] Chen JP, Hou D, Pandyala L, Goudevenos JA, Kounis NG. Drug-eluting stent thrombosis: the Kounis hypersensitivity-associated
acute coronary syndrome revisited. JACC Cardiovasc Interv 2009; 2(7): 583-93.
[20] Mauri L, Kereiakes DJ, Yeh RW, et al. Twelve or 30 months of dual antiplatelet therapy after drug-eluting stents. N Engl J Med 2014; 371(23): 2155-66.
[21] Chen M, Wang X, Zheng B, et al. Investigation of long-term implantation of BuMA stent in a porcine coronary model. Chin Med J (Engl) 2012; 125(22): 4083-7.
[22] Hagihara H, Hiraiishi Y, Terao H, et al. Vascular responses to a biodegradable polymer (polylactic acid) based biolimus A9-eluting stent in porcine models. EuroIntervention 2012; 8(6): 743-51.
[23] Takamura CK, Campos CAHM, Melo PHMC, et al. Preclinical Study of a Novel Biodegradable Polymer-Based Stent with Abliminal Sirolimus Release. Arq Bras Cardiol 2014; 102(5): 432-40.
[24] Wilson GJ, Marks A, Berg KJ, et al. The SYNERGY biodegradable polymer everolimus eluting coronary stent: Porcine vascular compatibility and polymer safety study. Catheterization Cardiovasc Interv 2015; 86(6): E247-57.
[25] Koppara T, Joner M, Bayer G, Steigerwald K, Dierer T, Witzhoub E. Histopathological comparison of biodegradable polymer and permanent polymer based sirolimus eluting stents in a porcine model of coronary stent implantation. Thromb Haemost 2012; 107(6): 1161-71.
[26] Pendyala K, Matsumoto D, Shinke T, et al. Nobori stent shows left vessel inflammation and early recovery of endothelial function compared with Cypher stent. JACC Cardiovasc Interv 2012; 5(4): 436-44.
[27] Nakazawa G, Torii S, Ijichi T, et al. Comparison of vascular responses following new-generation biodegradable and durable polymer-based drug-eluting stent implantation in an athersclerotic rabbit iliac artery model. J Am Heart Assoc 2016; 5(10): e003803.
[28] Gutiérrez-Chico JL, Jüni P, García-García HM, et al. Long-term tissue coverage of a biodegradable polylactide polymer-coated biolimus-eluting stent: comparative sequential assessment with optical coherence tomography until complete resorption of the polymer. Am Heart J 2011; 162(5): 922-31.
[29] Barlis P, Regar E, Serruys PW, et al. An optical coherence tomography study of a biodegradable vs. durable polymer-coated limus-eluting stent: a LEADERS trial sub-study. Eur Heart J 2010; 31(2): 165-76.
[30] Karjalainen PP, Varho V, Nammans W, et al. Early neointimal coverage and vasodilator response following biodegradable polymer sirolimus-eluting vs. durable polymer zotarolimus-eluting stents in patients with acute coronary syndrome –HATTRICK-OCT trial. Circ J Off J Jpn Circ Soc 2015; 79(2): 360-7.
[31] Davlouros PA, Mavronasiou E, Xanthopoulou I, et al. An optical coherence tomography study of two new generation stents with biodegradable polymer carrier, eluting paclitaxel vs. biolimus-A9. Int J Cardiol 2017; 231(1): 436-43.
[32] Guagliumi G, Sirbu V, Musumeci G, et al. Strut coverage and vessel wall response to a new-generation paclitaxel-eluting stent with an ultrathin biodegradable abluminal polymer: Optical Coherence Tomography Drug-Eluting Stent Investigation (OCTDESII). Circ Cardiovasc Interv 2010; 3(4): 367-75.
[33] Kuro T, Akasaka T, Koizumi K, et al. Vascular Response to Drug-Eluting Stent With Biodegradable vs. Durable Polymer. Circ J 2014; 78(10): 2408-14.
[34] de la Torre Hernández JM, Tejedor P, Camarero TG, et al. Early healing assessment with optical coherence tomography of everolimus-eluting stents with bioabsorbable polymer (SYNERGY) at 3 and 6 months after implantation. Catheterization Cardiovasc Interv 2016; 88(3): E67-73.
[35] Kuramitsu S, Sonoda S, Yokoi H, et al. Long-term coronary arterial response to biodegradable polymer biosilimus-eluting stents in comparison with durable polymer sirolimus-eluting stents and bare-metal stents: five-year follow-up optical coherence tomography study. Atherosclerosis 2014; 237(1): 23-9.
[36] Hamilos MI, Ostojic M, Belisien B, et al. Differential effects of drug-eluting stents on local endothelium-dependent coronary vasmotion. J Am Coll Cardiol 2008; 51(22): 2123-9.
[37] Puricel S, Kallinikou Z, Espanola J, et al. Comparison of endothelium-dependent and -independent vasmotor response after abluminal biodegradable polymer biosilimus-eluting stent and persistent polymer everolimus-eluting stent implantation (COMPARE-IT). Int J Cardiol 2016; 202: 525-31.
[38] Eppighainer MJ, Sushkova N, Grimsby JL, et al. Impact of Stent Surface on Thrombogenicity and Vascular Healing: A Comparative Analysis of Metallic and Polymeric Surfaces. Circ Cardiovasc Interv 2013; 6(4): 370-7.
[39] Meredith IT, Verheyse S, Dubois CL, et al. Primary endpoint results of the EVOLVE trial: A randomized evaluation of a novel biodegradable polymer-coated, everolimus-eluting coronary stent. J Am Coll Cardiol 2012; 59(15): 1362-70.
[40] Meredith I. Final five-year clinical outcomes in the EVOLVE trial: A randomized evaluation of a novel biodegradable polymer-coated, everolimus-eluting stent. Presented at EuroPCR; 2016.
[41] Kereiakes DJ, Meredith IT, Windecker S, et al. Efficacy and safety of biodegradable polymer everolimus-eluting coronary stent: the EVOLVE II Randomized Trial. Circ Cardiovasc Interv 2015; 8(4): pii: e002372.
[42] Kereiakes DJ. Late Clinical Outcomes after Bioresorbable or Permanent Polymer Everolimus-Eluting Stents: 2-Year Results from the EVOLVE II Randomized Trial. J Am Coll Cardiol 2016; 67(13): 17.
[43] Windecker S, Kereiakes DJ, Meredith IT, et al. Primary clinical outcomes of the EVOLVE II diabetes substudy evaluating a novel biodegradable polymer-coated, everolimus-eluting coronary stent in diabetic patients. EuroIntervention 2015; 10:540.
[44] Meredith IT. Two-Year Clinical Outcomes of a Biodegradable Polymer-Covered, Everolimus-Eluting Coronary Stent in Patients with Diabetes. Presented at EuroPCR; 2016.
[45] Meredith I, Jaffe W, El-Jack S, et al. Nine-month primary endpoint results of the EVOLVE II QCA study: a prospective, multicenter trial assessing clinical, angiographic, and intravascular ultrasound outcomes with the novel platinum-chromium ablyuniformly-coated biodegradable polymer synergy everolimus-eluting stent in de novo coronary stenoses. J Am Coll Cardiol 2015; 65(10): A1789.
[46] Han Y. EVOLVE China: A Randomized Comparison of Biodegradable Polymer- and Permanent Polymer-coated Platinum Chromium Everolimus-Eluting Coronary Stents in China. Presented at CIT; 2016.
[47] Varenna D, Cuisset T, Chab A, et al. The SYNERGY II Everolimus eluting Stent In Patients Older than 75 years undergoing coronary Revascularisation associated with a short dual antplatelet therapy (SENIOR) trial: rationale and design of a large-scale randomised multicentre study. EuroIntervention 2015; 11(8): pii: 20150220-08.
[48] Grube E, Hauptmann K-E, Buesselfeld L, Lim V, Abizaid A. Six-month results of a randomized study to evaluate safety and efficacy of a Biosilimus A9 eluting stent with a biodegradable polymer coating. EuroIntervention 2005; 1(1): 53-7.
[49] Windecker S, Serruys PW, Wandel S, et al. Biolimus-eluting stent with biodegradable polymer versus sirolimus-eluting stent with durable polymer for coronary revascularisation (LEADERS): a randomised non-inferiority trial. Lancet 2008; 372(9644): 1163-73.
[50] Serruys PW, Farooq V, Kalesan B, et al. Improved safety and reduced in stent thrombosis associated with biodegradable polymer-based biolimus-eluting stents versus durable polymer-based sirolimus-eluting stents in patients with coronary artery disease: final 5-year report of the LEADERS (limus Eluted From A Durable Versus Erodable Stent Coating) randomized, noninferiority trial. JACC Cardiovasc Interv 2013; 6(5): 777-89.
[51] Räber L, Kelbah K, Ostojic M, et al. Effect of biolimus-eluting stents with biodegradable polymer vs bare-metal stents on cardiovascular events among patients with acute myocardial infarction: The comfortable ami randomized trial. J Am Med Assoc 2012; 308(8): 777-87.
[52] Räber L, Kelbah K, Tanwani M, et al. Biolimus-Eluting Stents With Biodegradable Polymer Versus Bare-Metal Stents in Acute Myocardial Infarction Two-Year Clinical Results of the COMFORTABLE AMI Trial. Circ Cardiovasc Interv 2014; 7(3): 355-64.
[53] Ostojic M, Sagic D, Belisien B, et al. First clinical comparison of Nobori-Biolimus A9 eluting stents with Cypher-Sirolimus eluting stents: NOBORI CORE nine months angiographic and one year clinical outcomes. EuroIntervention 2008; 3(5): 574-9.
[54] Chevalier B, Serruys PW, Silber S, et al. Randomised comparison of Nobori, biolimus A9-eluting coronary stent with a Taxus(R), paclitaxel-eluting coronary stent in patients with stenosis in native coronary arteries: the Nobori I trial. EuroIntervention 2007; 2(4): 426-34.
[55] Chevalier B, Wijns W, Silber S, et al. Five-year clinical outcome of the Nobori drug-eluting coronary stent system in the treatment of patients with coronary artery disease: final results of the NOBORI I trial. EuroIntervention 2015; 11(5): 549-54.

[56] Kadota K, Muramatsu T, Iwabuchi M, et al. Randomized comparison of the nobori biolimus A9-eluting stent with the sirolimus-eluting stent in patients with stenosis in native coronary arteries. Catheter Cardiovasc Interv 2012; 80(5): 789-96.

[57] Natsuki M, Kozuma K, Morimoto T, et al. Biodegradable polymer biolimus-eluting stent versus durable polymer everolimus-eluting stent: a randomized, controlled, noninferiority trial. J Am Coll Cardiol 2013; 62(2): 181-90.

[58] Vlachoannis GJ, Smits PC, Hofma SH, et al. Long-term clinical outcomes of biodegradable polymer biolimus-eluting stents versus durable polymer everolimus-eluting stents in patients with coronary artery disease: three-year follow-up of the COMPARE II (Abuminal biodegradable polymer biolimus-eluting stent versus durable polymer everolimus-eluting stent) trial. EuroIntervention 2015; 11(3): 272-9.

[59] Kaiser C, Galatius S, Jeger R, et al. Long-term efficacy and safety of biodegradable-polymer biolimus-eluting stents main results of the baseline stent kosten-effektivitäts trial—PROSpective validation examination II (BASKET-PROVE II), a randomized, controlled non-inferiority 2-year outcome trial. Circulation 2015; 131(1): 74-81.

[60] Christiansen EH, Jensen LO, Thayssen P, et al. Bio-Mimic biodegradable polymer-coated stent versus durable polymer coated sirolimus-eluting stent in unselected patients receiving percutaneous coronary intervention (SORT OUT V): a randomised non-inferiority trial. Lancet 2013; 381(9867): 661-9.

[61] Lee J-Y, Park D-W, Kim Y-H, et al. Comparison of biolimus A9-eluting (Nobori) and everolimus-eluting (Promus Element) stents in patients with de novo native long coronary artery lesions: a randomized long drug-eluting stent V trial. Circ Cardiovasc Interv 2014; 7(3): 322-9.

[62] Cassese S, Fusaro M, Byrne RA, et al. Clinical outcomes of patients treated with Nobori biolimus-eluting stent: Meta-analysis of randomized trials. Int J Cardiol 2014; 175(2): 464-91.

[63] Dangir GB, Chevalier B, Urban P, et al. Clinical performance of a drug-eluting stent with a biodegradable polymer in an unselected patient population: the NOBORI 2 study. EuroIntervention 2012; 8(1): 109-16.

[64] Godino C, Parenti DZ, Regazzoli D, et al. One-year outcome of biolimus eluting stent with biodegradable polymer in all comers: the Italian Nobori Stent Prospective Registry. Int J Cardiol 2014; 177(1): 11-6.

[65] Barbato E, Salinger-Martinovic S, Sicag D, et al. A first-in-man clinical evaluation of Ultimaster, a new drug-eluting coronary stent system: CENTURY study. EuroIntervention 2015; 11(5): 541-8.

[66] Beleslin B. Long-term clinical outcomes of coronary DES with biodegradable coating: results of the CENTURY study. Presented at EuroPCR 2016.

[67] Saito S, Valdes-Chavarri M, Richard G, et al. A randomized, prospective, intercontinental evaluation of a biodegradable polymer sirolimus-eluting coronary stent system: the CENTURY II (Clinical Evaluation of New Terumo Drug-Eluting Coronary Stent System in the Treatment of Patients with Coronary Artery Disease) trial. Eur Heart J 2014; 35(30): 2021-31.

[68] Koppara T, Joner M, Bayer G, Steigervald K, Diener T, Wittchow E. Histopathological comparison of biodegradable polymer and permanent polymer based sirolimus eluting stents in a porcine model of coronary stent implantation. Thromb Haemost 2012; 107(6): 1161-71.

[69] Hamon M, Nicolas R, Deleau D, Dorobantu M, Weissman NJ, Waksman R. Clinical and angiographic experience with a third-generation drug-eluting Orion stent in the treatment of single de novo coronary artery lesions (BIOFLOW-I): a prospective, first-in-man study. EuroIntervention 2013; 9(9): 1006-11.

[70] Windecker S, Haude M, Neumann F-J, et al. Comparison of a novel biodegradable polymer sirolimus-eluting stent with a durable polymer everolimus-eluting stent: results of the randomized BIOFLOW-II trial. Circ Cardiovasc Interv 2015; 8(2): e004141.

[71] Pilgrim T, Heg D, Roffi M, et al. Ultihrin strut biodegradable polymer sirolimus-eluting stent versus durable polymer everolimus-eluting stent for percutaneous coronary revascularisation (BIOSCIENCE): a randomised, single-blind, non-inferiority trial. Lancet 2014; 384(9960): 2111-22.

[72] Waltenberger J, Brachmann J, van der Heyden J, et al. Real-world experience with a novel biodegradable polymer sirolimus-eluting stent: twelve-month results of the BIOFLOW-III registry. EuroIntervention 2015; 10(11): 1106-10.

[73] Ormiston J, Webster M, Stewart J, et al. First-in-human evaluation of a bioabsorbable polymer-coated sirolimus-eluting stent: imaging and clinical results of the DESSOLVE I Trial (DES with sirolimus and a bioabsorbable polymer for the treatment of patients with de novo lesion in the native coronary. JACC Cardiovasc Interv 2013; 6(10): 1026-34.

[74] Vrolix M. An update on the DESSOLVE programme. Presented at EuroPCR; 2016.

[75] Wijns W, Vrolix M, Verheyse S, et al. Randomised study of a bio-absorbable polymer-coated sirolimus-eluting stent: results of the DESSOLVE II trial. EuroIntervention 2015; 10(12): 1383-90.

[76] Lansky AJ, Kastrati A, Edelman ER, et al. Comparison of the Absorbable Polymuir-Sirolimus-Eluting Stent (MiStent) to the Durable Polymer Everolimus-Eluting Stent (Xience) (from the DESOLVE I and ISAR-TEST-IV Studies). Am J Cardiol 2016; 117(4): 532-8.

[77] Verheyse S. Novolimus Elution from a Biodegradable Polymer: Latest Update from EXCELLA II BD. Presented at TCT; 2014.

[78] Serruys PW, Garg S, Abizaid A, et al. A randomised comparison of sirolimus-eluting and zotarolimus-eluting coronary stents: 9-month follow-up of the EXCEL IIa study. EuroIntervention 2010; 2(2): 195-205.

[79] Iqbal J, Verheyse S, Abizaid A, et al. DESyne novolimus-eluting coronary stent is superior to Endeavor zotarolimus-eluting coronary stent at five-year follow-up: final results of the multicentre EXCELLA II randomised controlled trial. EuroIntervention 2016; 12(11): e1336-e1342.

[80] Xu B, Dou K, Han Y, et al. A prospective multicenter parallel-controlled trial of TIVOli biodegradable-polymer-based sirolimus-eluting stent compared to ENDEAVOR zotarolimus-eluting stent for the treatment of coronary artery disease: 8-month angiographic and 2-year clinical follow-up. Chin Med J (Engl) 2011; 124(6): 1146-52.

[81] Han Y, Xu B, Jing Q, et al. A randomized comparison of novel biodegradable polymer- and durable polymer-coated cobalt-chromium sirolimus-eluting stents. JACC Cardiovasc Interv 2014; 7(12): 1352-60.

[82] Zhang Q, Qiu JP, Kirtane AJ, et al. Comparison of biodegradable polymer versus durable polymer sirolimus-eluting stenting in patients with acute st-elevation myocardial infarction undergoing primary percutaneous coronary intervention: results of the RE-SOLVE study. J Intervent Cardiol 2014; 27(2): 131-41.

[83] Han Y-L, Zhang L, Yang L-X, et al. A new generation of biodegradable polymer-coated sirolimus-eluting stents for the treatment of coronary artery disease: final 5-year clinical outcomes from the CREATE study. EuroIntervention 2012; 8(7): 815-22.

[84] Chen S-L, Ye F, Zhang J-L, et al. Real polymer-free sirolimus- and probucol-eluting versus biodegradable polymer sirolimus-eluting stents for obstructive coronary artery disease: DKPLUS-Wave I, a multicenter, randomized, prospective trial. Cardiovasc Ther 2013; 31(4): 193-200.

[85] Wang G, Sun Z, Jin Q, et al. First-in-man study evaluating the safety and efficacy of a second generation biodegradable polymer sirolimus-eluting stent in the treatment of patients with de novo coronary lesions: Clinical, Angiographic, and OCT outcomes of CREDIT-1. Catheter Cardiovasc Interv 2015; 85(S1): 744-51.

[86] Oliveira MDP, Ribeiro EE, Campos CM, et al. Four-year clinical follow-up of the first-in-man randomized comparison of a novel sirolimus eluting stent with abluminal biodegradable polymer and ultra-thin strut cobalt-chromium alloy: the INSPIRON-I trial. Cardiovasc Diagn Ther 2015; 5(4): 264-70.

[87] Ribeiro EE, Campos CM, Ribeiro HB, et al. First-in-man randomised comparison of a novel sirolimus-eluting stent with abluminal biodegradable polymer and thin strut cobalt-chromium alloy: INSPIRON-II trial. EuroIntervention 2014; 9(12): 1380-4.

[88] Lemos PA, Abizaid AAC, Meireles GC, et al. Metallic limus-eluting stents abuminally coated with biodegradable polymers: angiographic and clinical comparison of a novel ultra-thin sirolimus stent versus sirolimus stent in the destiny randomised trial. Cardiovasc Ther 2015; 33(6): 367-71.

[89] Prado GFA, Ribeiro EE, Melo PHMC, et al. Clinical performance of a novel ultrathin strut, low-dose, sirolimus-eluting stent with ab-
luminal-only biodegradable polymeric coating for patients undergoing percutaneous coronary intervention in the daily practice. Cardiovasc Diagn Ther 2015; 5(6): 414-9.

[90] Qian J, Xu B, Lansky AJ, et al. First report of a novel abluminal groove filled biodegradable polymer rapamycin-eluting stent in de novo coronary artery disease: results of the first in man FIREHAWK trial. Chin Med J (Engl) 2012; 125(6): 970-6.

[91] Gao R-L, Xu B, Lansky AJ, et al. A randomised comparison of a novel abluminal groove-filled biodegradable polymer sirolimus-eluting stent with a durable polymer everolimus-eluting stent: clinical and angiographic follow-up of the TARGET I trial. EuroIntervention 2013; 9(1): 75-83.

[92] Xu B, Zhang Y-J, Sun Z-W, et al. Comparison of long-term instent vascular response between abluminal groove-filled biodegradable polymer sirolimus-eluting stent and durable polymer everolimus-eluting stent: 3-year OCT follow-up from the TARGET I trial. Int J Cardiovasc Imaging 2015; 31(8): 1489-96.

[93] Xu B, Gao R-L, Zhang R-Y, et al. Efficacy and safety of FIREHAWK® abluminal groove filled biodegradable polymer sirolimus-eluting stents for the treatment of long coronary lesions: nine-month angiographic and one-year clinical results from TARGET I trial long cohort. Chin Med J (Engl) 2013; 126(6): 1026-32.

[94] Xu B, Zhao Y, Yang Y, et al. Safety and efficacy of a novel abluminal groove-filled biodegradable polymer sirolimus-eluting stent for the treatment of de novo coronary lesions: 12-month results from the TARGET II trial. Chin Med J (Engl) 2014; 127(6): 1027-32.

[95] Gao Z, Zhang R, Xu B, et al. Safety and efficacy of a novel abluminal groove-filled biodegradable polymer sirolimus-eluting stent for the treatment of de novo coronary lesions: Two-year results from a prospective patient-level pooled analysis of TARGET trials. Catheter Cardiovasc Interv 2015; 85(S1): 734-43.

[96] Mehili J, Byrne RA, Wiczkorek A, et al. Randomized trial of three rapamycin-eluting stents with different coating strategies for the reduction of coronary restenosis. Eur Heart J 2008; 29(16): 1975-82.

[97] Byrne RA, Kastrati A, Kufner S, et al. Randomized, non-inferiority trial of three limus agent-eluting stents with different polymer coatings: the Intracoronary Stenting and Angiographic Results: Test Efficacy of 3 Limus-Eluting Stents (ISAR-TEST-4) Trial. Eur Heart J 2009; 30(20): 2441-9.

[98] Kufner S, Massberg S, Dommasch M, et al. Angiographic outcomes with (bio)degradable polymer and permanent polymer drug-eluting stents. Catheter Cardiovasc Interv Off J Soc Card Angiogr Interv 2011; 78(2): 161-6.

[99] Byrne RA, Kastrati A, Massberg S, et al. Biodegradable polymer versus permanent polymer drug-eluting stents and everolimus- versus sirolimus-eluting stents in patients with coronary artery disease: 3-year outcomes from a randomized clinical trial. J Am Coll Cardiol 2011; 58(13): 1325-31.

[100] Kufner S, Byrne RA, Valeskini M, et al. Five-year outcomes from a trial of three limus-eluting stents with different polymer coatings in patients with coronary artery disease: final results from the ISAR-TEST 4 randomised trial. EuroIntervention 2016; 11(12): 1372-3.

[101] Qian J, Zhang Y-J, Xu B, et al. Optical coherence tomography assessment of a PLGA-polymer with electro-grafting base layer versus a PLA-polymer sirolimus-eluting stent at three-month follow-up: the BuMA-OCT randomised trial. EuroIntervention 2014; 10(7): 806-14.

[102] Xu B, Gao R, Yang Y, et al. Biodegradable Polymer-Based Sirolimus-Eluting Stents With Differing Elution and Absorption Kinetics: The PANDA III Trial. J Am Coll Cardiol 2016; 67(19): 2249-58.

[103] Webster M, Harding S, McClean D, et al. First-in-human evaluation of a sirolimus-eluting coronary stent on an integrated delivery system: the DIRECT study. EuroIntervention 2013; 9(1): 46-53.

[104] Khattab AA, Nijhoff F, Schofer J, et al. Svelte integrated delivery system performance examined through diagnostic catheter delivery: The SPEED registry. Catheter Cardiovasc Interv 2015; 85(1): E23-31.

[105] Verheye S, Khattab AA, Carrie D, et al. Direct implantation of rapamycin-eluting stents with bioreosorbable drug carrier technology utilising the Svelte coronary stent-on-a-wire: the DIRECT II study. EuroIntervention 2016; 12(5): 615-22.

[106] Dani S, Costa RA, Joshi H, et al. First-in-human evaluation of the novel BioMime sirolimus-eluting coronary stent with biodegradable polymer for the treatment of single de novo lesions located in native coronary vessels - results from the merIT-I trial. EuroIntervention 2013; 9(4): 493-500.

[107] Lupi A, Gabrio Secco G, Rognoni A, et al. Meta-analysis of biodegradable versus durable polymer drug-eluting stents in 20,005 patients with coronary artery disease: An update. Catheter Cardiovasc Interv 2014; 83(6): E193-206.

[108] Navarese EP, Kubica J, Castriota F, et al. Safety and efficacy of biodegradable versus durable polymer drug-eluting stents: evidence from a meta-analysis of randomised trials. EuroIntervention 2011; 7(8): 985-94.

[109] Wang Y, Dong P, Li L, et al. Biodegradable Polymer Drug-Eluting Stents Versus Second-Generation Drug-Eluting Stents for Patients With Coronary Artery Disease: An Update Meta-Analysis. Cardiovasc Drugs Ther 2014; 28(4): 379-85.

[110] Wang Y, Liu S, Luo Y, et al. Safety and efficacy of degradable vs. permanent polymer drug-eluting stents: A meta-analysis of 18,395 patients from randomized trials. Int J Cardiol 2014; 173(1): 100-9.

[111] Zhang J. Stent thrombosis in patients with coronary artery disease treated with biodegradable polymer drug-eluting stents. Int Heart J 2014; 55(3): 213-8.

[112] Sun L-X, Zhang J. Biodegradable polymer DES versus durable polymer everolimus-eluting stents for patients undergoing PCI: a meta-analysis. Heart Lung Circ 2014; 23(6): 496-502.

[113] Sarno G. Real-world clinical experience with an everolimus eluting platinum chromium stent with an abluminal biodegradable polymer – a report from the Swedish Coronary Angiography and Angioplasty Registry (SCAAR). Presented at CRT; 2016.

[114] Pilgrim T, Roffi M, Tüller D, et al. Randomized comparison of biodegradable polymer sirolimus-eluting stents versus durable polymer everolimus-eluting stents for percutaneous coronary revascularization: Rationale and design of the BIOSCIENCE trial. Am Heart J 2014; 168(3): 256-61.

[115] Han Y, Xu B, Xu K, et al. Six versus 12 months of dual antiplatelet therapy after implantation of biodegradable polymer sirolimus-eluting stent randomized substudy of the I-LOVE-IT 2 Trial. Circ Cardiovasc Interv 2016; 9(2): e003145.

[116] Grube E, Hauptmann K, Buellesfeld L, Lim V, Abizaid A. Six-month results of a randomized study to evaluate safety and efficacy of a Biolimus A9 eluting stent with a biodegradable polymer coating. EuroIntervention 2005; 1(1): 53-7.

[117] Urban P, Valdés M, Herrmann J, et al. Outcomes following implantation of the biolimus A9-eluting BioMatrix coronary stent: Primary analysis of the eBioMatrix registry. Catheter Cardiovasc Interv 2015; 1151-60.

[118] Chevalier B, Silber S, Park S-J, et al. Randomized comparison of the nobori biolimus A9-eluting coronary stent with the taxis liberté paclitaxel-eluting coronary stent in patients with stenosis in native coronary arteries: the NOBORI I trial—phase 2. Circ Cardiovasc Interv 2009; 2(3): 188-95.

[119] Smits PC, Hofma S, Togni M, et al. Abluminal biodegradable polymer biolimus-eluting stent versus durable polymer everolimus-eluting stent (COMPARE II): a randomised, controlled, non-inferiority trial. Lancet 2013; 381(9867): 651-60.

[120] Saito S. CENTURY II: a prospective randomized trial of a biodegradable polymer biolimus-eluting stent versus a durable polymer everolimus-eluting stent in patients with coronary Artery. Presented at TCT; 2015.

[121] Bennett J, Dubois C. A novel platinum chromium everolimus-eluting stent for the treatment of coronary artery disease. Biol Targets Ther 2013; 7: 149-59.