SUPPLEMENTARY APPENDIX

Historical Stent Platforms, Bare Metal Stents and First-generation Drug-eluting Stents

Gianturco-Roubin Stent

The Gianturco-Roubin stent, a balloon-expandable stent had a coil design manufactured from a single strand of stainless-steel wire.[1] The stent was approved in the United States in 1993 for the treatment of coronary dissections during balloon angioplasty. Similar to the Wallstent, the Gianturco-Roubin stent had a great degree of flexibility but poor radial strength resulting in increased rates of restenosis as well as stent thrombosis (ST).**[2]**

Palmaz-Schatz Stent

In the late 1980s, Julio C. Palmaz, an Argentinian radiologist - designed a vascular stent from a model taken from a piece of metal. Together with Richard A. Schatz, a cardiologist from San Antonio (Texas, USA), he modified the initial version of this prototype to bend the first tubular slotted design balloon-expandable coronary stent. In October 1987, the first peripheral Palmaz-Schatz stent was placed in Freiburg (Germany) and in December of the same year the first Palmaz-Schatz stent was implanted into a coronary artery in Sao Paolo, Brazil. The stents were manually crimped on the balloon by the interventional cardiologists, a method which resulted in frequent stent loss.

Improved Bare Metal Stents and Antiplatelet Regimen

The widespread acceptance of coronary artery stenting resulted from the results of the BElgian NEtherlands STENT (BENESTENT)[3] and the STent REStenosis Study

(STRESS)[4] trials, which showed superiority of stents compared with balloon angioplasty in terms of restenosis and need for repeat revascularization. Since then, tremendous progress has been made in improving stent material, design and processing resulting in superior deliverability and procedural success. The improved results with coronary artery stenting over time were also related to expansion of the indications for stent implantation and the discovery that dual antiplatelet therapy (DAPT) (instead of oral anticoagulation) lowered both the incidence of ST and haemorrhagic complications [5-7]. Of note, these studies also strongly suggested that platelets had a mechanistic role in the pathogenesis of ST. Based on their efficacy, coronary artery stents have emerged as the preferred tool of PCI and are currently deployed in more than 90% of procedures.[8]

Bare Metal Stents

Available stents vary in metallic composition, strut design and thickness, delivery system and coating. These different parameters play an important role in deliverability, visibility, scaffolding performance and procedural success. Some of the parameters can also influence the occurrence of adverse events during the hospital stay (peri-procedural myonecrosis, ST) and long-term follow-up (restenosis).[9]

The importance of stent design on acute vascular injury and subsequent vasculo-proliferative response is well established. In animal models, changes in stent design lead to diverse degrees of vascular injury, thrombosis, and neointimal hyperplasia.[10] Furthermore, stents which allow a circular rather than angular vessel lumen lessen neointimal proliferation.[11] However, only few randomized trials addressed the role of stent design on clinical outcome. Compared with the Palmaz-

Schatz stent, the Gianturco-Roubin II stent was found to be inferior for the prevention of restenosis.[12] Several new generation BMS have been directly compared with the Palmaz-Schatz stent in non-complex lesions without showing differences in terms of ST, restenosis, or major adverse cardiac events (MACE).[13-15] The arrival of newer generations of DESs with improved efficacy and safety and declining cost, has led to a significant fall in the use of BMS, a change supported by contemporary data. The NORSTENT study, which enrolled 9013 patients and is the largest single randomised study comparing outcomes between patients receiving BMS or contemporary DES, reported no significant between-stent differences in the primary composite outcome of all-cause death and non-fatal MI (BMS 17.1% vs. DES 16.6%, p=0.66) at a median of 5 years follow up. Rate of repeat revascularisation (19.8% vs. 16.5%, p<0.001) and definite ST (1.2% vs. 0.8%, p=0.0498) were significantly lower with the use of DES. [16]

Previously marketed BMS

Corrugated open-cell and hybrid designs dominated the market (Table 1). Technological refinements pursue the ideal balance between deliverability, strength and biocompatibility. Advances include sophisticated connectors between crowns such as J-links, quadrature-links or double-helical designs; improved coatings with the aim to increase biocompatibility and reduce platelet aggregation such as Probio® (Biotronik) and Carbofilm™ (CID Vascular); and the introduction of endothelial progenitor cells capture technology to accelerate the natural healing process (Genous, OrbusNeich, USA), among others.

Early (First) Generation Drug-Eluting Stents

Sirolimus-Eluting Stents

The first SES was the Cypher stent, developed by Cordis Corporation, Warren, NJ. It consisted of sirolimus in a concentration of 140 µg/cm^2, incorporated in an amalgam of two biostable polymers, with the polymer/drug matrix then applied onto the tubular 316L stainless steel BX Velocity stent (Table 2).[17-50]

Both fast release stents with drug release in < 15 days and slow release stents with ≥ 28 day drug release were developed and tested in the FIM study in 1999 in Sao Paulo, Brazil and Rotterdam, the Netherlands. Angiographic and IVUS results from the 45 patients who were studied showed remarkable suppression of in-stent neointimal hyperplasia, which continued out to 4 years of follow-up.[51-53] A summary of major randomized trials of the sirolimus eluting stent versus bare metal stents in different clinical settings can be found in Table 3.

The pivotal RAVEL study (RAndomised study with the sirolimus-eluting VElocity balloon-expandable stent in the treatment of patients with de novo native coronary artery Lesions) evaluated the Cypher SES by randomizing 238 patients with relatively low risk lesions to treatment with SES or BMS. At 1-year follow-up the rate of binary stenosis was 0.0% and 26.6% for patients treated with Cypher SES and BMS, respectively.[17] These results were subsequently confirmed in the larger SIRIUS trial (SIRolImUS-coated Bx Velocity balloon-expandable stent in the treatment of patients with de novo coronary artery lesions) that enrolled 1058 patients with more complex lesions than were seen in RAVEL. Significantly lower rates of target lesion revascularization (TLR) and MACE following treatment with the Cypher SES were

demonstrated when compared to BMS controls at 9-months, 2-years and 5-year follow-up.[21, 22, 54] The Cypher stent was thus the first DES to receive CE-mark in April 2002 and was subsequently approved by the FDA in 2003. A meta-analysis of data from four double-blind studies with 1,784 patients found that TLR was reduced from 23.6% with BMS to 7.8% with SES (hazard ratio [HR] 0.29, 95% CI 0.22-0.39, $p < 0.001$) at four years (Table 3)**.**[55-58] Although rates of death or MI were similar for both BMS and SES, the latter showed a somewhat higher propensity for late ST (5 vs. 0 events) between 1 and 4 years**;** efficacy remained superior with SES out to 5 years (TLR: SES 15% vs 30.1%; $p < 0.0001$).[59]

Performance of the Cypher SES has been assessed in 'off label' settings and specific subgroups of patients such as diabetics,[23, 27] and those presenting with AMI,[32, 33, 37, 60] In addition it has been assessed in patients with different lesion types including chronic total occlusions,[40, 41] SVGs,[47, 48] lesions in small coronary vessels,[44, 45] and complex lesions.[49, 50] Irrespective of clinical situation, when compared with BMS, the use of SES results in significant reductions in angiographic in-stent late loss, in-stent angiographic stenosis, and repeat revascularization at both short and long-term 5-year follow-up, with results consistent across numerous different patient and lesion types (Table 3).

Despite the wealth of data confirming the efficacy of the Cypher stent, the manufacturer ceased production at the end of 2011.

Paclitaxel-Eluting Stents

The first TAXUS PES (Boston Scientific, Natick, MA) consisted of paclitaxel contained within a polyolefin derivative biostable polymer coated on the stainless steel NIR platform. A slow release (SR) formulation with an 18 µm thick coat, a moderate release (MR) with a 7 µm coat and a fast release with 4 µm coat shed 8%, 22% and 50% of the paclitaxel within 30 days respectively. The difference in release was achieved by changing the polymer to drug ratio while maintaining the same paclitaxel concentration (1µg/mm^2).[61] The TAXUS PES has been evaluated in the TAXUS series of trials which have enrolled different patient and lesion types (Table 4): [31, 62-75]

- The TAXUS I trial, a FIM phase I feasibility study with 61 randomised patients, reported a 3% MACE rate versus 10% in BMS at one year. Patients in the PES group had no TLR or binary stenosis, proving that paclitaxel effectively inhibited neo-intimal proliferation.[62]

- The TAXUS II study randomized 536 patients to treatment with BMS or SR PES, and BMS or MR PES. The reduction in percentage neointimal hyperplasia as measured by IVUS at 6 months was, 7.8% for SR and 7.8% for MR versus 23.2% and 20.5% for control BMS.[63] These results provided the foundation for the sustained reduction in TLR of 4.5% and 10.3% for the MR PES and SR PES respectively, (BMS 18.4%, BMS vs. PES $p < 0.001$) out to 5 years.[64] Of note, the MR formulation which was not subsequently used for commercialisation showed a better anti-restenotic effect than the SR formulation at 5 years.

- TAXUS III tested the fast release PES in 28 patients with in-stent restenosis. At 6-months the in-stent late loss was 0.54 mm with a neointimal hyperplasia volume of 20.3 mm^3, and a subsequent MACE rate was 29%. Overall results suggested that PES was a potentially efficacious treatment in those with in-stent restenosis.[76]

- TAXUS IV. The PES platform was changed from the NIR platform to the less rigid Express platform (Table 2) and this combination was studied in the TAXUS IV study, which randomised 1326 patients with non-complex coronary artery disease (CAD) to treatment with the TAXUS Express stent or Express BMS. Target vessel revascularization (TVR) at 9 months was significantly lower in the PES group (12.1% vs. 4.7%; $p < 0.0001$) and this advantage was maintained through 5 years (27.4% vs. 16.9%; $p < 0.0001$), despite comparable annual TVR rates for BMS and PES between years 1 and 5 (4.1%/year vs. 3.3%/year; respectively, $p = 0.16$).[65, 66]

- TAXUS V randomized 1156 patients, over half of whom had complex coronary lesions not studied in earlier PES trials, to treatment with PES (n = 557) and BMS (n = 579). Consistent with earlier studies, use of PES lead to significantly lower rates of angiographic stenosis, TLR, and TVR at 9-months, with comparable rates of death, MI and ST. The benefit in favour of PES was maintained out to 5-year follow-up, however PES was also associated with higher rates of MI (9.3% vs. 5.6%, $p < 0.05$) and definite/probable ST (2.4% vs. 1.5%, $p < 0.05$).[67, 68]

- TAXUS VI also randomized 446 patients with long complex lesions to treatment with either PES or the Express BMS. At 9-months follow-up use of PES led to significantly lower rates of binary stenosis, TLR and TVR, whilst the overall MACE rate was similar. Subsequent 5-year follow-up demonstrated the sustained anti-restenotic effect of PES on TLR (14.6% vs. 21.4%, p = 0.03), however a significantly higher rate of non-TLR was also seen in the PES group (10.9% vs. 5.1%, p = 0.03). Rates of ST and MACE were similar. [69, 70]

Patient level meta-analysis of the initial PES approval trials have confirmed the comparable safety and superior efficacy of PES, compared to BMS out to 4-year follow-up (Table 5).[55, 57] A meta-analysis of five double-blind trials in 3,513 patients also revealed that TLR decreased from 20.0% with BMS to 10.1% with PES at 4 years (HR 0.46, 95% CI 0.38-0.55, p < 0.001).[55] Rates of death and MI were balanced among patients treated with PES and BMS at 4 years of follow up. The incidence of ST was low owing to the non-complex underlying disease and not different between PES and BMS at one year. Between 1 and 4 years, however, there was an increase in those treated with PES (0.7% vs. 0.2%, 95% CI 0.98-21.03). TAXUS II is the first trial reporting 5-year outcome data comparing PES with BMS in patients with non-complex coronary artery disease. In this analysis, both slow- and moderate-release polymer based PES were more effective than BMS to reduce TLR (PES-MR: 4.5%; PES-SR: 10.3%, BMS: 18.4%, p < 0.001).[77]

TAXUS Element

A third iteration of the TAXUS stent is the TAXUS Element stent (Ion, Boston Scientific, Natick, MA) which has a PtCr platform coated with a poly(styrene-b-

isobutylene-b-styrene) polymer, which facilitates controlled elution of paclitaxel (concentration 1µg/mm^2) in an identical pattern to that seen on the stainless steel TAXUS Liberté and Express stent (Table 2). The device was evaluated in the PERSEUS (A Prospective Evaluation in a Randomised Trial of the Safety and Efficacy of the use of the TAXUS Element Paclitaxel Eluting Coronary Stent System for the Treatment of De Novo Coronary Artery Lesions) clinical trial program, which includes: [78-80]

- The PERSEUS Workhorse trial which randomized 1262 patients, with lesions <28mm long, in vessels between 2.75-4.00 mm in diameter, to treatment with the TAXUS Element (n = 942) or the TAXUS Express PES (n = 320).[78] The study met its pre-specified criteria for non-inferiority for the primary endpoint of TVF at 12-months clinical follow-up and its secondary endpoint, per cent diameter stenosis, at 9-months angiographic follow-up. No significant differences were seen between stents with respect to late loss (Element 0.34 ± 0.55 mm vs. Express 0.26 ± 0.52 mm, p = 0.33), or other the clinical points such as MACE, mortality, MI and ST. Clinical outcomes remained similar between treatment groups through to 5-years.[81]

- The PERSEUS small vessel trial, which compared the TAXUS Element stent to historical BMS controls in patients with lesions <20 mm long, in vessels between 2.25-2.75 mm in diameter.[80] Overall the study enrolled 224 patients treated with the Element stent, who were compared to 125 lesion-matched historical controls treated with a BMS from the TAXUS IV study. Results at 9-months follow-up demonstrated a significantly lower in-stent late loss (the primary

endpoint) with the Element stent compared to the BMS stent (0.38 ± 0.51 mm vs. 0.80 ± 0.53 mm, p < 0.001). At 12-months follow-up the rates of target lesion failure (TLF) and MACE were both significantly lower with the Element stent, whilst safety endpoints and ST were comparable between both stents. At 5-year rates of MACE, and TLF were significantly lower for the Element stent following adjustment for baseline characteristics and were primarily due to lower TLR rates (Element 14.9% vs. 27.2% BMS, p=0.049).[81]

Comparative Studies of Sirolimus-Eluting and Paclitaxel-Eluting Stents

Several randomized studies, which are summarized in Table 6**[82-97]** have directly compared outcomes between patients treated with SES or PES in: (I) unselected patients populations; (II) specific patient groups such as diabetics or those with STEMI; and (III) specific lesion types such as unprotected left main stem lesions, long lesions or lesions in small vessels.[82-97] Results at short-term angiographic follow-up consistently demonstrate superior reductions in late loss with the use of SES, however long-term angiographic follow-up, indicates a greater delayed late loss with SES, such that at 5-years there was no longer a significant difference in late loss between SES and PES.[87] In terms of clinical outcomes, a meta-analysis of 16 randomized trials of SES versus PES, which included 8,695 patients and where possible patient level data, reported significant reductions in TLR (HR:0.74, 95% CI:0.63-0.87, p < 0.001) and ST (HR 0.66, 95% CI:0.46-0.94, p = 0.02) with SES, whilst no significant differences in death (HR 0.92, 95%: CI:0.74-1.13, p = 0.43), or MI (HR 0.84, 95% CI:0.69-1.03, p = 0.10) were noted at a median of 2-year follow-up.[98] The SORT-OUT II and SIRTAX studies have both reported long-term outcomes and failed to show any between-stent differences in MACE, cardiac death,

MI, clinically-indicated TLR and ST at 10-year follow-up, with attenuation of the differences in MACE noted beyond 1-year.[99, 100]

Focus Box: Early generation DES

- The stainless steel SES was the first DES to receive CE and FDA approval, shortly followed by the PES.
- Studies have confirmed consistently superior angiographic outcomes, and significantly lower rates of repeat revascularization with the use of SES or PES compared with BMS in patients with simple or complex lesions at short- and long-term follow-up.
- SES have been shown to have superior angiographic outcomes and lower rates of repeat revascularization when compared with PES.

Everolimus-eluting Stents Compared to Bare-metal or other First-generation Drug-eluting Stents

EES vs. BMS

The SPIRIT FIRST study enrolled 56 patients (EES = 27, BMS = 29) and demonstrated superior performance of EES with respect to 6-month in-stent late lumen loss (0.10 mm vs. 0.87 mm, $p < 0.001$), and angiographic binary restenosis (0.0 vs. 25.9, $p < 0.05$) (Table 7). Similarly, clinical follow-up through to 5-years demonstrated significantly lower rates of TLR with the use of EES, with comparable rates of mortality, MI and overall MACE.[101, 102]

Contemporary studies of EES versus BMS have been conducted in specific patient groups including patients with stable angina over 80 years of age (XIMA), patients undergoing primary PCI for AMI (EXAMINATION), patients requiring stents greater than 3mm in diameter (BASKET PROVE) and patients with chronic kidney disease (RENAL-DES). Results (Table 7) show superior efficacy with EES compared with BMS, and comparable safety. [46, 103-106] A meta-analysis of these studies (excluding RENAL-DES) by Valgimigli et al, which included 4896 patients followed-up for a median of 720 days, reaffirmed that compared to BMS, EES lowered MI and ST as well as cardiovascular mortality.[107]

EES vs. PES

Six randomised trials have compared EES to PES in 8,819 patients with increasingly complex lesions ranging from those with up to two relatively simple *de novo* lesions in the SPIRIT II study, to the unrestricted all-comers population in the COMPARE study (Table 7).[108-124] Irrespective of patient complexity or follow-up period, angiographic and clinical outcomes have consistently demonstrated superior outcomes in those treated with EES. Specifically in the SPIRIT II (0.11 mm vs. 0.36 mm) and SPIRIT III (0.16 mm vs. 0.30 mm) study in-stent late loss at 6- and 8-months, respectively were significantly lower with EES.[108, 114] Consistent with these results are findings of the EXECUTIVE study, which enrolled patients with multivessel disease, and reported in-stent late lumen losses at 9-months follow-up of 0.08 mm (95% CI: -0.01, 0.16) and 0.22 mm (95% CI: -0.13, 0.31) ($p = 0.018$) amongst patients randomised to EES and PES, respectively.[123] Longer angiographic follow-up is only available from the SPIRIT II study, and this demonstrated evidence of catch up in late loss with EES, such that the significant

difference in in-stent late loss between EES and PES which was observed at 6-months was no longer present at 2-years.[110] Nevertheless, clinical outcomes at 3-, 4- and 5-year follow-up in the SPIRIT II study remain consistent with those seen at 6-months and 1-year. Similarly, at 5-year follow-up in the SPIRIT III study, treatment with EES led to significantly lower rates of MACE.[115] More extensive assessment of EES took place in the SPIRIT IV trial, which randomized 3,690 patients (EES = 2,458, PES = 1,229), and the all-comers COMPARE study, which recruited 1,800 patients (EES = 897, PES = 903).[116-118, 120-122, 125] At 3- (SPIRT IV) and 5-year (COMPARE) follow-up both studies reported superior efficacy and safety with EES compared to PES. Notably rates of definite/probable ST were significantly lower with EES in both at final follow-up (SPIRIT IV 0.6% vs. 1.6%, p=0.003 and COMPARE 3.1% vs. 5.9%, p=0.005).[118, 122] The TUXEDO trial compared EES vs. PES among 1830 diabetic patients. At 2-year follow-up, EES was associated with a significant reduction in the risk of TVF (4.3% vs. 6.6%, p=0.03), mainly driven by a reduction in the risk of MI, TLR, and ST.[124]

A patient-level pooled analysis of the 6,789 patients enrolled in the SPIRIT-II, -III, -IV and COMPARE studies has confirmed the superior performance of EES compared with PES. At 12-months follow-up whilst there were no between-stent differences in mortality or cardiac death, there were significantly lower rates of MI (2.1% vs. 4.0%, $p < 0.001$), ischaemic TLR (2.3% vs. 4.7%, $p < 0.001$), MACE (4.4% vs. 7.6%), definite ST (0.4% vs. 1.2%, $p < 0.001$) and definite/probable ST (0.5% vs. 1.5%, $p < 0.001$) with EES.[126] Results were maintained even after adjustment of confounding factors. Following on from this, meta-analysis of the SPIRIT studies at 3-year follow-up have shown the emergence of a clear safety advantage with the use of EES

compared to PES. Amongst 4,989 patients, who were prospectively randomised to EES (n=3350) or PES (n=1639), significantly lower rates of all endpoints including all-cause mortality (HR 0.65, p=0.003), MI (HR 0.64, p=0.02), TLR (HR 0.72, p=0.004), MACE (HR 0.71, p=0.0002) and definite/probable ST (HR 0.45, p=0.003) were seen with EES.[127]

EES vs. SES

Several studies have reported the results from the comparison of EES with SES, which has been regarded as the most efficacious first generation DES (Table 8).[46, 128-140]

The EXCELLENT study enrolled 1,372 patients randomised 3:1 to EES (n = 1029) and SES (n = 343). The study achieved its pre-specified non-inferiority primary endpoint of in-segment late lumen loss at 9-months (EES 0.10 mm vs. SES 0.05 mm, $P_{non\text{-}inferoirty}$ = 0.023). At 12-months clinical follow-up there were no significant differences in rates of MI, TLR, and the composites of mortality/MI and MACE. Rates of ST were lower with EES (0.4% vs. 0.8%, p = 0.028).[128]

In a sub-study of the ISAR-TEST 4 trial, late loss at 6-8 months amongst the 1,304 patients randomised to treatment with EES and SES was 0.14 mm versus 0.17 mm respectively (p = NS).[129] At 2 years of follow-up with repeat angiography performed, the investigators observed a trend towards lower TLR (9.9% vs. 13.5%, HR=0.73, 0.52-1.01, p = 0.06) and a significant reduction of binary restenosis (12.7% vs. 16.9%, p = 0.03) in favour of EES in the absence of differences for safety

endpoints. At 5-year clinical follow-up both efficacy and safety remained numerically lower with EES ($p > 0.05$ for all).[130]

SORT OUT IV reported non-inferior outcomes with EES compared with SES in terms of MACE (4.9% vs. 5.2%, HR 0.94, 0.67-1.31) and TLR (1.4% vs. 1.7%, HR 0.87, 0.48-1.58) at 9 months among 2,774 patients randomly assigned treatment with EES or SES.[131] Differential outcomes occurred after the first year, and at 5-years significantly lower rates of MACE were seen in those treated with EES (14.0% vs. 17.4%, HR 0.80, p=0.02), which was larger the result of significantly lower rates of definite ST with EES (0.4% vs. 2.0%, HR 0.18).[132]

The largest randomised study of EES and SES is the RESET study which randomised 3197 all-comers patients and achieved its pre-specified non-inferiority primary clinical endpoint with rates of TLR at 12-months of 4.3% and 5.0% with EES and SES, respectively ($P_{non\text{-}inferority}<0.001$). Other safety and efficacy endpoints were comparable between the stents with similar results observed at 3-years. Of note, significant between-stent differences in favour of EES were seen in the secondary composite endpoints of TLF, TVF, MACE, and the device-orientated endpoint.

BASKET PROVE randomly assigned 2,314 patients undergoing stent implantation of large vessels (stent diameter $\geq$ 3.0 mm) to receive SES, EES or BMS. At 2 years of follow-up, TVR was lower with both EES (3.7%) and SES (4.3%) as compared with BMS (10.3%, p = 0.005 vs SES, p = 0.002 vs EES), however, the event rates were similar for EES and SES (3.7% vs 4.3%, p = 0.85).[46]

LONG-DES III assessed outcomes in 500 patients randomised to EES and SES who had a coronary lesion which required at least 28 mm of stent.[135] The study failed to meet its non-inferiority primary endpoint of in-segment late loss at 9-months follow-up (EES 0.17 mm vs. SES 0.09 mm, $P_{non\text{-}inferiority}$ = 0.96, $P_{superiority}$ = 0.04). Furthermore, in-segment binary angiographic restenosis was also significantly lower with SES (EES 7.3% vs. SES 2.7%, p = 0.046). Despite these angiographic outcomes, there were no significant between-stent differences in clinical outcomes.

ESSENCE-DIABETES study showed a similar trend in the assessment of EES versus SES in patients with diabetes.[136] Specifically the study demonstrated that EES was non-inferior to SES in terms of in-segment late loss and angiographic restenosis at 8-months, with similar clinical outcomes being seen at 12-months follow-up.

The X-AMI study[137, 138] randomised 625 patients undergoing primary PCI for acute MI in a 2:1 ratio (EES n=404, SES n=221). The study met its non-inferiority primary endpoint of MACE, a composite of cardiac death, non-fatal MI and TVR at 1-year (EES 4.0% vs. SES 7.7%, $P_{non\text{-}inferority}$=0.048); no individual endpoints were significantly different. Rates of ST were low considering the population, and no between-stent differences were observed. A further analysis at 3-years reported low overall events rates without identifying any significant differences between patients treated with EES or SES.

The RACES-MI study[139] also compared the performance of EES and SES in the setting of primary PCI for AMI randomising 500 patients in a 1:1 fashion (EES n=250, SES n=250). The study was powered for a primary endpoint of MACE, a

composite of cardiac death, reinfarction, definite or probable ST and TVR at 3-year follow-up. Results showed comparable outcomes for MACE and its components apart from ST, which was significantly lower in patients receiving EES (EES 1.6% vs. SES 5.2%, p = 0.035).

A meta-analysis of the 7,370 patients (EES = 4044, SES = 3326) enrolled in BASKET–PROVE, ESSENCE-DIABETES, EXCELLENT, SORT OUT IV and ISAR-TEST 4 has confirmed the comparable performance of EES compared with SES in terms of efficacy and safety.[141] At a median of 13.3 months follow-up rates of MACE (7.2% vs. 8.8%, p = 0.28), cardiac death (2.2% vs. 2.6%, p = 0.92), MI (1.7% vs. 1.9%, p = 0.76), repeat revascularization (3.8% vs. 4.8%, p = 0.16), and the composite of definite and probable ST (0.8% vs. 1.0%, p = 0.33) were not significantly different between EES and SES. However, this analysis did not include the most recent trial reports and therefore requires an update to include longer-term follow-up data.

A larger meta-analysis by Park *et al* which included 11 randomised trials and just under 13,000 patients followed-up for a median of 23.8 months, also confirmed comparable safety outcomes between EES and SES.[142] In contrast to the previous meta-analysis this study was able to demonstrate significantly lower rates of repeat revascularization (OR 0.85, p=0.047) and definite ST (OR 0.44, p=0.007) with EES.

EES vs. Non-EES Durable Polymer DES

A meta-analysis of 13 randomised trials enrolling a total of 17101 patients treated with either EES (n = 9764) or non-EES DES (n = 7337) has confirmed a consistent

benefit with the use EES out to a mean follow-up of 21.7 months.[143] Specifically use of EES was associated with similar cardiac mortality (1.6% vs. 1.9%, p = 0.38) and significant reductions in rates of MI (2.9% vs. 3.9%, p = 0.02), TVR (5.7% vs. 7.7%, p = 0.004) and definite/probable ST (0.7% vs. 1.5%, p = 0.001), when compared to patients receiving non-EES DES.

Consistent with this are the results of a larger comprehensive network meta-analysis of 51 randomised studies by Palmerini *et al* which included just over 51,000 patients,[144] and demonstrated that:

- EES is the only DES to show a significant reduction in all-cause mortality compared to BMS (HR 0.81, 95% CI 0.64-1.00, p<0.05), SES (HR 0.86, 95% CI 0.70-1.00, p<0.05) and PES (HR 0.81, 95% CI 0.68-1.00, p<0.05), together with offering the greatest reduction in cardiac death versus BMS (HR 0.71, 95% CI 0.54-0.91, p<0.05). No mortality reductions have been seen in the individual comparison of other DES with BMS or between DES.

- EES significantly reduces the risk of MI compared with BMS (HR 0.66, 95% CI 0.52-0.85, p<0.05), SES (HR 0.78, 95% CI 0.64-0.95, p<0.05) and PES (HR 0.64, 95% CI 0.52-0.78, p<0.05).

- EES is the only DES to significantly reduce the rate of definite ST compared to BMS (HR 0.48, 95% CI 0.29-0.82, p<0.05). Significant reductions in ST have also been seen with EES versus PES (HR 0.42, 95% CI 0.27-0.64,

p<0.05); versus SES (HR 0.41, 95% CI 0.26-0.64 p<0.05) and biolimus-eluting stents (BES, HR 0.58, 95% CI 0.31-1.00, p<0.05).

Other analyses include a mixed-treatment comparison analysis of DES (SES, PES, EES, E-ZES and R-ZES) versus BMS with 117,762 patient-years of follow-up, which reported similar findings, and concluded that EES was overall the stent with the most advantageous safety profile.[145]

A similar analysis in patients with diabetes treated with either SES, PES, EES, E-ZES, R-ZES or BMS by Bangalore *et al* also concluded that EES was the safest and most efficacious stent through 22,844 patient years of follow-up.[146] A smaller meta-analysis which only included studies using EES also reported significant reductions in ST with EES out to 2-years follow-up.[147]

Several factors that have been suggested to be behind the consistent superior performance of EES including the fact that everolimus is slightly more lipophilic than sirolimus, and therefore more rapidly absorbed into the arterial wall. In addition, pre-clinical data have suggested that the combination non-erodible, co-polymer of PVDF-HFP and PBMA, is potentially associated with less inflammation than seen with the polymers on SES and PES.[148] Finally, the fluoro-polymer has been shown to have thrombo-resistant properties,[149] which when combined with thin-struts, and the reduced polymer and drug load may contribute to the low rates of ST with EES.

E-ZES vs. BMS

The ENDEAVOR II trial enrolled 1197 patients (ZES = 598, BMS = 599) and demonstrated significantly lower rates of in-stent late loss (0.61 ± 0.46 mm vs. 1.03 ± 0.58 mm, $p < 0.001$), binary in-stent restenosis (9.4% vs. 33.5%, $p < 0.001$), TLR (4.6% vs. 11.8%, $p < 0.001$) and TVF, a composite of cardiac death, MI attributable to the target vessel, and clinically-driven TLR, (7.9% vs. 15.1%, $p < 0.001$) at 9-months follow-up, with additional clinical follow-up at 5-years indicating a sustained benefit in favour of E-ZES with respect to TLR and TVF. [150, 151] Mortality and rates of MI and ST were comparable at all time points (Table 9).

E-ZES vs. SES

The comparison of E-ZES and SES has taken place in three randomised studies - ENDEAVOR III, SORT-OUT III and PROTECT.[152-158] ENDEAVOR III compared E-ZES with SES in a non-inferiority trial with a primary angiographic endpoint (N = 436 patients).[152] E-ZES was found inferior to SES regarding late loss (in-stent: 0.60 ± 0.48 mm vs. 0.15 ± 0.34 mm, $p < 0.001$) and binary restenosis (in-segment: 11.7% vs. 4.3%, $p = 0.04$). Conversely, the incidence of late acquired stent malapposition as assessed by IVUS was lower with E-ZES than SES (0.5% vs. 5.9%, $p = 0.02$). E-ZES had a lower rate of MI than SES (SES: 3.5% vs. E-ZES: 0.6%, RR = 0.18, 95% CI 0.03-0.96, $p = 0.04$) at 9 months, which was mainly due to a lower incidence of peri-procedural myonecrosis.[152] There were no significant differences in rates of death, cardiac death, ST, repeat revascularization, MACE, and TVF. At 5-years[153] the absolute difference in TLR between E-ZES and SES was small 1.6% at 5-years (E-ZES 8.1% vs. SES 6.5%). Rates of ST remained similar

between both groups throughout follow-up, although the study was not powered for this endpoint.

In contrast, SORT-OUT III enrolled 2332 patients (E-ZES = 1162, SES = 1170) and reported significant differences in favour of SES with respect to MI, TLR and ST at both 9- and 18-months follow-up. At 3-years, rates of MI (E-ZES 3.8% vs. SES 3.3%, p = 0.44) and ST (1.1% vs. 1.4%, p = 0.61) were comparable between E-ZES and SES, whilst TLR remained significantly lower with SES (6.8% vs. 3.9%, p = 0.002).[155] This significant difference in TLR was no longer present at final 5-year follow-up (7.6% vs. 6.0%, p=0.15);[156] similarly no between-stent differences in death, MI or ST was seen. Landmark analyses showed significantly lower rates of definite ST (0.1% vs. 1.8%, p=0.003), TLR (2.4% vs. 4.8%, p=0.003) and TVR (4.1% vs. 7.0%, p=0.003) with E-ZES compared with SES between 1- and 5-years, thereby reversing the significantly higher rates of these respective endpoints with E-ZES at 1-year follow-up (definite ST 1.1% vs. 0.3%, p=0.04; TLR 5.3% vs. 1.4%, p<0.001; TVR 6.7% vs. 2.8%, p<0.001).

The much larger PROTECT study recruited 8709 all-comers patients who were randomised to treatment with SES and E-ZES.[30] Uniquely the study was powered to detect a 1% difference in definite/probable ST at 3-years follow-up, however consequent to event rates in the SES arm (1.8%) being lower than anticipated in the power calculation (2.5%), even this large study was somewhat underpowered. The study failed to identify any significant differences between E-ZES and SES with regards the primary endpoint of definite/probable ST (E-ZES 1.4% vs. SES 1.8%, HR:0.81) and secondary clinical safety endpoints such as death and MI at 3 years.

However, in the pre-specified 4-year of follow-up there was an increase in the absolute between-stent difference in definite/probable ST from 0.4% at 3-years to 1.0%, such that rates were significantly lower with E-ZES at 4-years (1.6% vs. 2.6%, p=0.003).[158] with resultant lower rates of MI as per the extended historical definition (E-ZES 4.6% vs. SES 5.8%, p=0.02). Whilst TVR was comparable at 4-years follow-up (9.0% vs. 8.6%), TLR remained significantly higher with E-ZES (5.9% vs. 4.5%, p=0.002), however there was a fall in the absolute between-stent difference (2.1% at 3-years vs. 1.4% at 4-years).

Overall these three studies confirm differential clinical outcomes over time amongst these two DES with differing abilities to suppress neointimal hyperplasia. During early follow-up E-ZES is associated with inferior outcomes compared to SES, however these differences appear to disappear or even reverse with long-term follow-up. Importantly, these contrasting short- and long-term results have implications for clinical trial design reiterating the need for long-term follow-up to fully evaluate the efficacy and safety of DES.

Endevour ZES vs. PES

ENDEAVOR IV compared E-ZES with PES in a non-inferiority, randomized trial enrolling 1,548 patients with a primary clinical endpoint of TVF (Table 9).[159, 160] In the angiographic arm of the trial, E-ZES did not achieve the pre-specified secondary endpoint of in-segment late loss (0.36 ± 47 mm vs. 0.23 ± 0.45 mm, p = 0.023). However, E-ZES met its primary clinical endpoint of non-inferiority on TVF at 9 months (E-ZES: 6.6% vs. PES: 7.2%, p = 0.685). While the rate of MI was lower at 30 days (0.8% vs. 2.3%, p = 0.02) largely related to fewer side-branch occlusions,

there were no significant differences in rates of death, cardiac death, or MI at 9 and 12 months.[159] The 5 year clinical follow-up results of ENDEAVOR IV revealed an increasing safety benefit of E-ZES over PES with a lower rate of the composite of cardiac death and MI (E-ZES=6.4%, vs. PES=9.1%, p = 0.048).[160] Rates of definite and probable ST were no different at 9 months (E-ZES=0.8% vs. PES=0.1%, P=0.12) or 5 years (E-ZES=1.4% vs. PES=1.9%, p=0.42). Of note, the incidence of very late ARC definite and probable ST between one and five years was significantly reduced in favor of patients treated with E-ZES (E-ZES=0.4% vs. PES=1.8%, p = 0.012). In terms of efficacy, differences in rates of TLR remained unchanged among E-ZES (7.7%) and PES (8.6%, p = 0.70) treated patients.

Endevour ZES vs. SES vs. PES

The ZEST trial compared outcomes amongst 2640 patients randomised to E-ZES (n = 880), PES (n = 880) and SES (n = 880).[161] The primary endpoint was MACE at 12-months, with the comparison of E-ZES with SES analysed as a non-inferiority analysis, whilst the comparison between E-ZES and PES was a superiority analysis (Table 9). At 12 months, MACE rates were non-inferior between E-ZES and SES (10.2% vs. 8.3%, $P_{\text{non-inferiority}} = 0.01$, $P_{\text{superiority}} = 0.17$) and significantly lower with E-ZES compared with PES (10.2% vs. 14.1%, p=0.01). The incidence of death or MI was similar (E-ZES 5.8% vs. SES 6.9% vs. PES 7.6%, p = 0.31), whilst the incidence of ST was significantly lower in the SES group (E-ZES 0.7% vs. SES 0.0% vs. PES 0.8%, respectively, p = 0.02). Overall at 12-months follow-up the use of E-ZES resulted in similar rates of MACE compared with SES and fewer MACE events compared with PES.

Promus EES vs. Resolute ZES

Two all-comers randomised non-inferiority studies have reported outcomes comparing treatment with the Promus EES and Resolute ZES (Table 10).[162-164]

The DUTCH PEERS[162] study enrolled 1811 patients in a 1:1 ratio (EES 905 vs. R-ZES 906) and met its non-inferiority endpoint of TVF, a composite of cardiac death, target-vessel MI, and TVR (EES 5% vs. R-ZES 6%, $P_{non\text{-}inferiority}$=0.006). All components of the primary endpoint were also comparable. Definite ST rates were low (EES 0.7% vs. R-ZES 0.3%, p=0.34). Longitudinal stent deformation was identified in 9 out of 1591 implanted EES stents, with no deformed R-ZES stents; reassuringly these deformed stents were not associated with any adverse clinical outcomes. No significant between-stent differences emerged out to 3-years of clinical follow-up.[163]

The larger HOST-ASSURE[164] study randomised 3755 patients in a 2:1 ratio to treatment with Promus EES (n=2503) or R-ZES (n=1252). The primary endpoint, which was TLF, a composite of cardiac death, target vessel MI and TLR occurred in 2.9% of patients treated with EES and R-ZES, achieving the pre-specific margin of non-inferiority ($P_{superiority}$=0.006, $P_{non\text{-}inferiority}$=0.0025). There were no differences in the components of the primary endpoint, the patient-orientated composite endpoint or definite/probable ST. As in the DUTCH PEERS study there were no stent deformations in the R-ZES arm, however 7 out of the 3500 Promus EES stents deployed were deformed with no resultant clinical sequela.

Newer-generation Drug-eluting Stents no longer commercially available

Durable-polymer DES

Myolimus-Eluting Stents With Durable Polymer

The FIM study of the myolimus-eluting stent enrolled 15-patients, and at 6-months angiographic follow-up in-stent late lumen loss, binary restenosis and percent neointimal volume obstruction were 0.15 ± 0.11mm, 0.0% and 1.4%, respectively. Clinical events out to 9-months comprised of one MI; there was no death, TLR or ST.[165]

Biodegradable-polymer DES

Nobori™ stent (Terumo, Japan)

The Nobori™ stent uses the same PLA polymer and anti-proliferative agent as the aforementioned BioMatrix stent, however, the Nobori stent uses the SS-Stent platform, which was only used on the first iteration of the BioMatrix stent. The main difference between the Biomatrix Flex and the Nobori stent is an ultra-thin non-degradable parylene coating between the stent and the polymer on the Nobori stent to enhance polymer attachment to the stent struts.[166] The Nobori stent has been compared with the Cypher SES, TAXUS PES and EES.

- The Nobori I study randomized 243 patients to treatment with either the Nobori™ stent (n = 153) or the TAXUS PES stent (n = 90).[167] Results at 9-months amongst the 86% of patients returning for follow-up demonstrated non-inferiority, and subsequent superiority, of the Nobori™ stent with respect to late loss when

compared to the TAXUS PES stent (0.11 ± 0.30 mm vs. 0.32 ± 0.50 mm, $P_{non\text{-}inferiority} < 0.001$, $P_{superiority} = 0.001$). Although the study was not powered for clinical outcomes, no differences in the composite of death and MI and TLF were reported up to 5 years. Rates of ischemia- and non-ischemia-driven TLR were higher in the TAXUS arm whereas ARC defined ST were lower in the Nobori arm (0.0% vs. 3.2%, p=0.014).[168]

- In the all-comers non-inferiority COMPARE 2 study 2707 patients were randomised 2:1 to receive either the Nobori BES (n = 1795) or EES (n = 912).[169] The study achieved its primary endpoint of MACE (a composite of cardiac death, non-fatal MI and ischaemia driven TVR at 12-months) with rates of 5.2% and 4.8% with the Nobori BES and EES, respectively ($P_{non\text{-}inferiority} < 0.0001$). All individual components of MACE were comparable as were rates of ST. At 5-years the study failed to demonstrate any reduction in very late adverse events with a biodegradable, as opposed to a durable polymer DES, following the absence of any significant between-stent differences for MACE, efficacy, safety or ST. [170]

- Similar to COMPARE 2 was the all-comers NEXT study, which randomised 3235 patients to receive either Nobori BES (n = 1617) or EES (n = 1618).[171] The study met its pre-specified non-inferiority primary endpoint of TLR at 12-months with rates of 4.2% in each group ($P_{non\text{-}inferiority} < 0.0001$). Clinical event rates for other outcome measures were low and comparable between devices. A sub-group of 528 patients underwent angiographic follow-up at 266 ± 43 days and met the primary endpoint of non-inferiority for in-segment late loss (0.03 mm vs. 0.06

mm, $P_{non\text{-}inferiority} < 0.0001$). At final three year follow-up, the study also met its non-inferior primary safety endpoint of death or MI with rates of 9.9% and 10.3% for Nobori BES and EES, respectively ($P_{non\text{-}inferiority} < 0.0001$, $P_{superiority} = 0.7$).[172]

- In the all-comers SORT OUT V study, 2468 patients were randomised to the Nobori BES (n = 1229) or the Cypher SES (n = 1239).[173] The study was powered for non-inferiority of MACE a composite of cardiac death, MI, definite ST and TVR at 9-months. Unlike previous studies of the Nobori BES, the study narrowly failed to meet this primary endpoint with rates of MACE of 4.1% with the Nobori BES and 3.1% with Cypher SES ($P_{non\text{-}inferiority} = 0.06$). This difference in MACE was driven by significantly higher rates of early definite ST (0.7% vs. 0.2%, p = 0.03), MI (1.3% vs. 0.6%, p = 0.10), and TVR (3.3% vs. 2.1%, p = 0.08) with Nobori BES. Similar to COMPARE 2, this study failed to identify any significant late clinical benefit through to 5-years from using a biodegradable polymer stent with comparable event rates between both devices (MACE, OR=0.93, p=0.53; cardiac death, OR=0.81, p=0.30; MI, OR=1.05, p=0.76; TVR, OR=0.92 p= 0.54).[174] Definite ST was also comparable at 5-years, and unlike the LEADERS trial, there was no significant difference in favour of the biodegradable polymer DES for very late ST (ST>1 year, OR=0.89, p=0.77).

- The BASKET-PROVE II trial[175] compared the performance of Nobori BES with EES and a new generation, thin strut BMS with a biocompatible coating (ProKinetik, Biotronik) in 2291 patients with stable CAD or ACS needing stenting in large vessels (≥3.0 mm in diameter) and treated with aspirin and prasugrel. The primary endpoint was a composite of cardiac death, MI and

clinically indicated TVR within 2 years. In the intention-to-treat analysis, the Nobori BES proved non-inferior compared with the EES and more effective than thin strut BMS. However, no differences in the occurrence of the secondary safety endpoint (a composite of very late ST, MI and cardiac death) were reported among the different arms challenging the concept that durable polymers are the main drivers of ST.

- The LONG-DES V study randomised 500 patients with coronary lesions >24mm to receive either Nobori BES or Promus EES.[176] The study met its non-inferiority primary endpoint of in-segment late luminal loss at 9-months angiographic follow-up (BES 0.14±0.38 vs. EES, 0.11±0.37 mm; $P_{noninferiority}$ =0.03, $P_{superiority}$ =0.45). There were no significant between-stent differences in binary restenosis and in-stent late lumen loss, together with clinical outcomes at 12-months.

Novolimus-Eluting Stents with biodegradable polymers

The FIM study of the Elixir DESyne BD biodegradable polymer NES enrolled 9-patients, and reported an in-stent late lumen loss of 0.16 ± 0.23 mm together with no binary restenosis at 6-months, and no MACE events through to 9-months.[177] In the follow-on randomized EXCELLA II BD trial 146 patients were randomised 3:1 to the Elixir DESyne BD (n=115) or the E-ZES (n=31). The study achieved its primary endpoint by demonstrating non-inferiority of the Elixir DESyn BD compared to the control stent with respect to in-stent late loss (0.12 ± 0.15 mm vs. 0.67 ± 0.47 mm, $P_{non\text{-}inferiority} < 0.001$, $P_{superiority}<0.001$). In addition significantly lower rates of binary angiographic stenosis (0.0% vs. 7.9%, p = 0.003) were seen in the Elixir DESyn

group. Clinical events remained low through to 5 years and clinically indicated TLR was lower in the DEsyne BD group compared with the E- ZES (4.5% vs. 9.7%, p=0.11). No ST was reported at 60 months.[178]

Myolimus-Eluting Stents with biodegradable polymers

The FIM study of the myolimus-eluting stent recruited 30 patients half of whom had angiographic follow-up at 6-months, whilst the remaining returned at 12-months. Late lumen loss and percent neointimal volume obstruction were 0.08±0.16mm and 3.2%, and 0.13 ± 0.27 mm and 5.4% at 6- and 12-months, respectively; there was no binary restenosis. Clinical events, assessed at 12-months, demonstrated no mortality or ST; there were however two MIs and two TLRs.[179]

Sirolimus eluting DES with biodegradable polymers

NEVO™ Stent (Cordis, Warren, NJ, USA)

The NEVO™ stent was an open-cell, cobalt chromium stent, with a PLGA biodegradable polymer which facilitated elution of sirolimus. The stent was unique in its design as the polymer and sirolimus were contained within reservoirs, which eliminate the need for a surface polymer coating, and subsequently reduce tissue-polymer contact by over 75%. This stent design was previously used on the durable polymer, paclitaxel-eluting CoStar stent (Conor MedSystems, Palo Alto, CA). Unfortunately despite promising initial results,[180-182] the CoStar stent failed to develop following disappointing results from the CoStar II study,[183] where it was shown not to be non-inferior to the TAXUS PES with respect to MACE, (CoStar 11.0% vs. PES 6.9%, p=0.005) and angiographic outcomes such as in-stent late loss (CoStar 0.49 mm vs. PES 0.18 mm, $p < 0.0001$).

The stent was evaluated in the NEVO-RES I study, which was a randomized, multi-center, non-inferiority study comparing the NEVO™ stent to the TAXUS™ Liberté PES stent in 394 patients with single *de novo* coronary artery lesions. The sirolimus-eluting NEVO stent was found not only to be non-inferior but also superior to PES for the endpoint in-stent late loss (0.13 ± 0.31 vs 0.36 ± 0.46, $P_{non\text{-}inferiority} < 0.001$ and $P_{superiority} < 0.001$) and a trend towards lower in-segment binary restenosis (3.9% vs 8.6%, p = 0.08) at 6 month of follow-up.[184]

Despite these promising initial results, two factors have led to the withdrawal of the NEVO stent. Firstly stent dislodgements were observed in three patients (all in the NEVO group) during the early phase of 'all-comers' NEVO-II study, resulting in the study being stopped. Secondly, and perhaps more importantly, the stent manufacturer, Cordis (Warren, NJ), decided to withdraw from the coronary stent industry at the end of 2011. It seems unlikely that this stent technology will develop further.

Genous™ Bio-engineered R-stent™ (OrbusNeich, Fort Lauderdale, Fl, USA)

This bare metal stainless steel stent is unique by containing on its luminal surface immobile CD34 antibodies. In pre-clinical and clinical studies these antibodies are able to bind to endothelial progenitor cells (EPC), resulting in a rapidly formed, functional endothelial covering of the stent's struts,[185] which ultimately has the potential to reduce ST and restenosis. Unfortunately, the CD34+ markers that are used to phenotype EPCs are non-specific, and are shared by other hematopoietic stem cells. Therefore, it is possible for the EPC capture stent to sequester other bone marrow cell

lines such as smooth muscle progenitor cells, which in turn can lead to neointimal proliferation.[186, 187] This is reflected in published clinical studies that have shown low rates of ST despite only one month of DAPT, however late-loss at 6-month follow-up has repeated been above 0.6mm.[188-190] Data from the TRIAS HR study, which is the only randomized trial published so far, reported a late loss as high as 1.14±0.64 mm, and an overall higher target vessel failure with the Genous stent compared to the TAXUS PES.[191] Encouragingly, preliminary data at two-year follow-up demonstrated a lower absolute increase in TLR between 1 and 2 years in those treated with EPC stent compared to PES.[192] This may reflect regression of late loss with the EPC stent, as was previously observed in the HEALING II study where late loss fell by 16.9% between 6- and 18-months, and/or late catch-up with PES.[189, 193] Additional data comes from the 5000 patients enrolled in e-HEALING registry, which reported rates of MACE, MI and ST at 1-year follow-up of 7.7%, 1.7% and 1.0% respectively.[194]

A new application of the EPC capture technology has been to combine it with DES technology in a Combo Stent.

Polymer-Free Drug-Eluting Stents

Drug Filled Stent *(Medtronic, Santa Rosa, California, U.S.)*

These polymer-free DES have 81μm struts made from a tri-layer wire:

- The outer layer is made of a cobalt alloy for radial strength
- The middle layer is made of tantalum for radio-opacity.

- The core material of the inner layer of the wire is removed to produce hollow struts which function as the reservoir for sirolimus that is present at a dose of 1.1 ug/mm^2.

Sirolimus is released through an average of six laser-drilled holes on the abluminal side of each stent, each with a minimal bore diameter of 20µm (~1,800 holes for an 18 mm stent) Drug elution commences on stent deployment and is controlled and sustained through natural diffusions via direct interaction with the vessel wall. Pre-clinical data show 68% and 93% of the sirolimus is released by 28- and 90-days respectively, with histology confirming that this drug release is effective at suppressing neointimal hyperplasia compared to BMS controls (P<0.001), with minimal inflammation. The FIM RevElution clinical trial is currently being conducted, and 9-month results from the first cohort of 50 patients are encouraging with a late loss of 0.26mm which is non-inferior to R-ZES historical controls ($P_{non-inferior}$<0.001), a 0% binary restenosis rate, and signs of rapid early healing with >98% stent strut coverage and 0% late incomplete malapposition.[195] At 12-months clinical follow-up, two patients had had experienced a cardiovascular event leading to a target vessel non-Q-wave MI, and a TLR; no ST was seen.[196]

PAX – Paclitaxel Eluting Stent (Minvasys, Genevilliers, France)

The Amazonia Pax stent is the only polymer free stent that is made of cobalt chromium, and elutes paclitaxel. The stent has an open cell design, with 73µm thick struts, which are coated with a 5µm thick abluminal coating of polymer free paclitaxel at a dose of 2.5 µg/mm^2. The pure paclitaxel is applied using a micro-drop spray crystallization process. This consistent coating ensures that 98% of the drug is eluted

within 30 days, and ensures that by 45 days all that remains is a bare metal cobalt chromium stent.

The multicenter Pax A study randomized 30 patients to treatment with either the Amazonia stent or the TAXUS PES.[197] At 4-months the respective in-stent late lumen loss and %neointimal volume obstruction for the Amazonia and PES were 0.77mm versus 0.42mm ($p = 0.20$), and 19% versus 6% ($p = 0.08$). OCT analysis demonstrated significantly more stent strut coverage with the Amazonia stent compared with PES. Clinically at 2-years there were no deaths or ST events; however four patients treated with PES had a TLR, whilst two patient in the Amazonia arm had an MI, and two had a TLR.[197]

VESTAsyn Sirolimus Eeluting Stent (MIV Therapeutics, Atlanta, GA)

The VESTAsyn SES is a polymer free stainless stent which has a nano-thin, micro-porous, hydroxyapatite surface coating impregnated with 55µg dose of sirolimus. Sirolimus is eluted over 90-days, whilst the hydroxyapatite remains stable over the first 4-months, before completely dissolving around 9-12 months after stent implantation. Pre-clinical studies indicate that the low dose of sirolimus, which is made possible by the hydroxyapatite platform, results in reduced signs of delayed vascular healing, suggesting less local toxicity, and a faster healing response.[198]

Primary evaluation of the stent took place in the 15 patients VESTAsync I FIM study.[199] At 4- and 9-months angiographic follow-up effective reductions in late loss and intimal hyperplasia were observed, with no evidence of ‘late-catch’ seen on

quantitative coronary angiography (QCA) or IVUS. Out to three year follow-up the only clinic event was a single TLR.[200]

Further assessment is on-going in the VESTAsyncII study which has randomised 75 patients in a 2:1 ration to either the VESTAsyn SES (n = 50) or the Gen X stent, a control BMS with a microporous hydroxyapatite surface coating. The in-stent late loss at 8-months follow-up was 0.39±0.20mm and 0.74±0.52mm in VESTAsyn SES and BMS respectively (p=0.03), such the study achieved its primary endpoint. In addition, IVUS demonstrated significantly less neointimal hyperplasia with the VESTAsynSES stent (15.4mm^3 vs. 29.4mm^3, p=0.01).[201] Clinical event rates out to 2-years were low, with 3 and 5 MACE events in the VESTAsyn SES group (1 death, 1 MI, 1 TLR) and BMS (2 deaths, 1 MI and 2 TLRs) respectively; there were no ST events.[202]

Covered Stents

MGuard mesh-covered stent (MGuard, InspireMD, Israel)

A SS stent covered with an ultrathin (20 µm) polyethylene terephthalate flexible micronet (MGuard, InspireMD, Israel) has been developed to immobilize thrombus and atheroma between the micronet and the vessel wall during stent expansion mitigating distal embolization. Among STEMI patients undergoing primary PCI, this device significantly increased the primary endpoint of complete (>70%) ST-segment resolution (57.8% vs. 44.7%, p=0.008) and improved TIMI 3 flow (91.7% vs. 82.9%, p=0.006) compared with standard BMS and DES in a randomized clinical trial.[203] Clinical and angiographic 1-year follow-up showed higher rates of MACE with the MGuard, driven by greater ischemia-driven TLR (8.6% vs. 0.9%, p=0.0003) and a

trend toward higher rates of definite ST (2.3% vs. 0.5%, p=0.10). Although the study was not powered for this endpoint, lower all-cause and cardiac mortality were recorded at 30 days and 1 year in the MGuard group[204].The MASTER II trial (N=1100) which was designed to compare the efficacy (ST segment resolution at 60-90 min and infarct size at 2-7 days) and safety (death or reinfarction at 30 days) of the MGuard device with BMS and DES among STEMI patients undergoing primary PCI was terminated due to poor enrolment.

Self-Expanding Stents

Self-expanding (SE) stents were the first stents to be implanted in coronary arteries,[205] being quickly followed by BE stents, such that both technologies were used with similar frequency in the early days of coronary stenting. SE stents are made from nitinol, an alloy of nickel and titanium, which is uniquely suited for this purpose given its shape memory, biocompatibility, fatigue resistance, and super-elastic qualities which allow it to withstand large amounts of recoverable strain.

In addition to comparable outcomes, SE stents offer distinct advantages over BE stents such as a lower incidence of edge dissections,[206, 207] reduced rates of side branch occlusion and no-reflow,[207] and positive remodelling.[207] Furthermore, animal data suggest that SE stents offer the ability to prevent immediate vessel wall injury, which may eventually translate into a reduction in neointimal hyperplasia, and a larger lumen area.[208] Some of the drawbacks associated with their use are related to their mechanical properties, for example precisely matching stent size to vessel size is hindered by the continued outward radial force that SE stents exert after deployment, leading to negative chronic recoil, and a subsequently larger vessel at

follow-up. In addition, SE stents are housed within a delivery catheter that ensures stent security, however, these catheters can be cumbersome to use, and have an associated learning curve. Importantly the delivery profile of these stents is dictated by strut dimensions, as opposed to the balloon profile (as in BE stents). Finally placement accuracy of SE stents is complicated by stent foreshortening on expansion, and/or forward spring movements of the stent from the delivery system once deployment commences.

The advent of DES largely led to a considerable loss of interest in pursuing the development of SE stents, and they were largely abandoned for coronary use. Recently, however there has been a resurgence of interest in this technology for niche coronary settings following new stent designs that have incorporated thinner struts, drug coatings, and improved delivery systems.

At present SE stents are being investigated for use in patients with:

Bifurcation lesions

Nitinol SE-dedicated bifurcation stents, which include the Axxess™ (Biosensors International Pte Ltd, Singapore),[209] Stentys™[209-212] (Stentys S.A., Paris, France) and Cappella Sideguard™[213] (Cappella, Inc., Auburndale, MA, USA), have been suggested to improve outcomes in the treatment of bifurcation lesions, owing to their ability to conform the angulated anatomy more optimally than a conventional BE stent.[214, 215] For a more detailed discussion on the indications for these devices please refer to Chapter 3.10.

Acute MI

Acute MI commonly results from disruption of thin-cap fibroatheromas (TCFAs).[216] It follows that pre-emptive treatment of these lesions involves preventing cap rupture, and promoting endothelialization. Understandably, BE stents are not well suited to these delicate lesions owing to the high radial forces required for their deployment, potentially causing plaque rupture, distal embolization and no-reflow. Conversely, SE stents offer the theoretical advantage of minimizing vessel injury during implantation, thereby reducing the risk of embolising necrotic material and thrombus distally. In the long-term the lack of strut penetration into the necrotic core may theoretically reduce the risk of ST, which may occur through the substantially delayed arterial healing that occurs when struts penetrate into it.[217, 218]

The STENTYS™ stent was assessed in patients having primary PCI for ST-elevation MI[219] in the APPOSITION I study. The trial enrolled 25 AMI patients and reported technical, device and procedural success rates of 100%, 96% and 96%, respectively. Notably, IVUS evaluation three days post stenting demonstrated a significant 18% increase in stent expansion, such that the stent was completely apposed to the vessel wall. At 6-months follow-up, rates of in-stent late lumen loss, binary restenosis and ischaemia-driven TLR were respectively 0.71 ± 0.71 mm, 25% and 12%. Overall the study confirmed the safety and feasibility of the use of STENTYS in AMI and resulted in its C.E. mark for this indication. Following this, the APPOSITION II study randomised 80 patients with AMI to STENTYS (n=43) or a conventional BMS (n = 37), with the aim of assessing strut malapposition 3 days after stent deployment using OCT.[220] As anticipated, results showed significantly lower rates of malapposed

struts with STENTYS (0.58% vs. 5.46%, $p < 0.001$). Clinical event rates at 6-months were comparable.

The APPOSITION III study used a sirolimus-eluting version of the device and reported low rates of MACE (11.2%) at 24-months amongst 1000 acute MI patients treated with STENTYS.[221] In the APPOSITION IV study 152 patients with AMI were randomised 3:2 to either a sirolimus-eluting STENTYS (n=90) or R-ZES (n=62). Angiographic outcomes showed lower late lumen loss at 4- and 9-months with the STENTYs device compared to R-ZES, whilst OCT demonstrated that STENTYS SES was associated with fewer malapposed struts and covered struts that R-ZES. Clinical outcomes were low and comparable between groups.[222]

The vProtect® Luminal Shield (Prescient Medical, Inc., Doylestown, PA, USA) SE stent has been shown in animal studies to promote vascular healing, and importantly, to achieve complete endothelialization of the stented vessel segment within 7 days.[223] Data from the FIM study have demonstrated that the 'shield' can induce plaque remodelling and has a positive vascular healing profile, as demonstrated on IVUS. A subsequent study in 29 patients with intermediate de novo coronary lesions treated with the device showed, at 6-months follow-up, a late loss of 0.50 ± 0.30 mm, and a binary restenosis rate of 10.3%. There was no stent malapposition. The rate of MACE was 10.3% related to three TLRs.[224]

Further evaluation of the stent took place in the prospective randomized SECRITT I pilot study, which evaluated the safety and feasibility of stenting a vulnerable plaque with the vProtect® Luminal Shield (n = 13) compared with a medically treated, non-

stented (control) group (n = 10).[225, 226] There were no device related complications or MACE events out to 6-months. The study was underpowered to detect differences in clinical events, however it did suggest that sealing these vulnerable plaques was feasible and safe, although the clinical benefit remains to be established.

Lesions in small diameter vessels

The use of BE stents in vessels with small diameters is inherently associated with a risk of edge dissection, owing to the high pressures required for optimal stent implantation. Inadequate stent strut apposition and stent underexpansion add risk for ST and restenosis. For lesions located in small-sized vessels, the use of SE stents, which can minimise baro-trauma and the risk of edge dissections, offers distinct advantages. The Cardiomind Sparrow™ (previously Cardiomind Inc, Sunnyvale, CA, USA, now Biosensors, Morges, Switzerland) is a small profile nitinol SE stent that is designed specifically for lesions in small diameter vessels (2.00-2.75mm). The stent, which has a strut thickness of 61μm, is pre-loaded on an 0.014" guidewire, with 2-3 cm of radio-opaque guidewire at the distal end, enabling positioning within the vessel. The stent is deployed through a dedicated Sparrow™ delivery system, which facilitates electrolysis of mechanical latches holding down each end of the stent. The electric current required for release of each latch is less than 0.2 mA, and release occurs within 20 seconds. The CARE I feasibility study was performed in 21 patients with de novo lesions in vessels of 2.0-2.5 mm diameter. At 6-month follow-up, a 13% rise in stent volume index was observed together with a binary restenosis rate of 20%. There was no ST at 30-days, and 2 MACE events up to 24-months follow-up.[227]

The next-generation Sparrow™ stent has a strut thickness of 67 μm, and is coated with a 4 μm-thick layer of sirolimus at a dose of 6 μg/mm and an 8 μm-thick biodegradable PLA/PGLA polymer. It was assessed in the CARE-II study that was designed to randomise 220 patients, with lesions ≤ 20mm in length, in vessels between 2.00-2.75 mm in diameter, to treatment with the bare metal Cardiomind Sparrow™, the sirolimus-eluting Cardiomind Sparrow™ or a BMS. Interim results at 8-months follow-up after enrolment of the first 100 patients (36 Cardiomind BMS, 36 Cardiomind SES and 30 BMS) demonstrated numerically lower in-stent late lumen loss with the drug coated Cardiomind stent, such that the primary endpoint of the study was met (Cardiomind SES 0.29 mm vs. Cardiomind BMS 0.86 mm [$p = 0.0001$] vs. BMS 0.94mm [$p < 0.0001$]) and enrolment was stopped. Clinical outcomes were also superior with the drug-eluting Cardiomind stent compared to the other two stents.[228]

References

1. Roubin GS, Cannon AD, Agrawal SK, Macander PJ, Dean LS, Baxley WA, et al. Intracoronary stenting for acute and threatened closure complicating percutaneous transluminal coronary angioplasty. Circulation. 1992;85(3):916-27.

2. Sutton JM, Ellis SG, Roubin GS, Pinkerton CA, King SB, 3rd, Raizner AE, et al. Major clinical events after coronary stenting. The multicenter registry of acute and elective Gianturco-Roubin stent placement. The Gianturco-Roubin Intracoronary Stent Investigator Group. Circulation. 1994;89(3):1126-37.

3. Serruys PW, de Jaegere P, Kiemeneij F, Macaya C, Rutsch W, Heyndrickx G, 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.

4. Fischman DL, Leon MB, Baim DS, Schatz RA, Savage MP, Penn I, et al. A randomized comparison of coronary-stent placement and balloon angioplasty in the treatment of coronary artery disease. Stent Restenosis Study Investigators. N Engl J Med. 1994;331(8):496-501.

5. Barragan P, Sainsous J, Silvestri M, Bouvier JL, Comet B, Siméoni JB, et al. Ticlopidine and subcutaneous heparin as an alternative regimen following coronary stenting. Catheterization and Cardiovascular Diagnosis. 1994;32(2):133-8.

6. Schomig A, Neumann FJ, Kastrati A, Schuhlen H, Blasini R, Hadamitzky M, et al. A randomized comparison of antiplatelet and anticoagulant therapy after the placement of coronary-artery stents. N Engl J Med. 1996;334(17):1084-9.

7. Cutlip DE, Leon MB, Ho KK, Gordon PC, Giambartolomei A, Diver DJ, et al. Acute and nine-month clinical outcomes after "suboptimal" coronary stenting: results from the STent Anti-thrombotic Regimen Study (STARS) registry. J Am Coll Cardiol. 1999;34(3):698-706.

8. Praz L, Cook S, Meier B. Percutaneous Coronary Interventions in Europe in 2005. Eurointervention. 2007;3:442-6.

9. Kastrati A, Schomig A, Dirschinger J, Mehilli J, von Welser N, Pache J, et al. Increased risk of restenosis after placement of gold-coated stents: results of a randomized trial comparing gold-coated with uncoated steel stents in patients with coronary artery disease. Circulation. 2000;101(21):2478-83.

10. Rogers C, Edelman ER. Endovascular stent design dictates experimental restenosis and thrombosis. Circulation. 1995;91(12):2995-3001.

11. Garasic JM, Edelman ER, Squire JC, Seifert P, Williams MS, Rogers C. Stent and artery geometry determine intimal thickening independent of arterial injury. Circulation. 2000;101(7):812-8.

12. Lansky AJ, Roubin GS, O'Shaughnessy CD, Moore PB, Dean LS, Raizner AE, et al. Randomized comparison of GR-II stent and Palmaz-Schatz stent for elective treatment of coronary stenoses. Circulation. 2000;102(12):1364-8.

13. Baim DS, Cutlip DE, Midei M, Linnemeier TJ, Schreiber T, Cox D, et al. Final results of a randomized trial comparing the MULTI-LINK stent with the Palmaz-Schatz stent for narrowings in native coronary arteries. The American journal of cardiology. 2001;87(2):157-62.

14. Baim DS, Cutlip DE, O'Shaughnessy CD, Hermiller JB, Kereiakes DJ, Giambartolomei A, et al. Final results of a randomized trial comparing the NIR stent to the Palmaz-Schatz stent for narrowings in native coronary arteries. The American journal of cardiology. 2001;87(2):152-6.

15. Kastrati A, Hall D, Schomig A. Long-term outcome after coronary stenting. Curr Control Trials Cardiovasc Med. 2000;1(1):48-54.

16. Bonaa KH, Mannsverk J, Wiseth R, Aaberge L, Myreng Y, Nygard O, et al. Drug-Eluting or Bare-Metal Stents for Coronary Artery Disease. N Engl J Med. 2016;375(13):1242-52.

17. Morice MC, Serruys PW, Sousa JE, Fajadet J, Ban Hayashi E, Perin M, et al. A randomized comparison of a sirolimus-eluting stent with a standard stent for coronary revascularization. N Engl J Med. 2002;346(23):1773-80.

18. Morice MC, Serruys PW, Barragan P, Bode C, Van Es GA, Stoll HP, et al. Long-term clinical outcomes with sirolimus-eluting coronary stents: five-year results of the RAVEL trial. J Am Coll Cardiol. 2007;50(14):1299-304.

19. Schampaert E, Cohen EA, Schluter M, Reeves F, Traboulsi M, Title LM, et al. The Canadian study of the sirolimus-eluting stent in the treatment of patients with long de novo lesions in small native coronary arteries (C-SIRIUS). J Am Coll Cardiol. 2004;43(6):1110-5.

20. Schofer J, Schluter M, Gershlick AH, Wijns W, Garcia E, Schampaert E, et al. Sirolimus-eluting stents for treatment of patients with long atherosclerotic lesions in small coronary arteries: double-blind, randomised controlled trial (E-SIRIUS). Lancet. 2003;362(9390):1093-9.

21. Moses JW, Leon MB, Popma JJ, Fitzgerald PJ, Holmes DR, O'Shaughnessy C, et al. Sirolimus-eluting stents versus standard stents in patients with stenosis in a native coronary artery. N Engl J Med. 2003;349(14):1315-23.

22. Weisz G, Leon MB, Holmes DR, Jr., Kereiakes DJ, Popma JJ, Teirstein PS, et al. Five-year follow-up after sirolimus-eluting stent implantation results of the SIRIUS (Sirolimus-Eluting Stent in De-Novo Native Coronary Lesions) Trial. J Am Coll Cardiol. 2009;53(17):1488-97.

23. Sabate M, Jimenez-Quevedo P, Angiolillo DJ, Gomez-Hospital JA, Alfonso F, Hernandez-Antolin R, et al. Randomized comparison of sirolimus-eluting stent versus standard stent for percutaneous coronary revascularization in diabetic patients: the diabetes and sirolimus-eluting stent (DIABETES) trial. Circulation. 2005;112(14):2175-83.

24. Jimenez-Quevedo P, Sabate M, Angiolillo DJ, Alfonso F, Hernandez-Antolin R, SanMartin M, et al. Long-term clinical benefit of sirolimus-eluting stent implantation in diabetic patients with de novo coronary stenoses: long-term results of the DIABETES trial. Eur Heart J. 2007;28(16):1946-52.

25. Jimenez-Quevedo P, Hernando L, Gomez-Hospital JA, Iniguez A, SanRoman A, Alfonso F, et al. Sirolimus-eluting stent versus bare metal stent in diabetic patients: the final five-year follow-up of the DIABETES trial. EuroIntervention. 2013;9(3):328-35.

26. Maresta A, Varani E, Balducelli M, Varbella F, Lettieri C, Uguccioni L, et al. Comparison of effectiveness and safety of sirolimus-eluting stents versus bare-metal stents in patients with diabetes mellitus (from the Italian Multicenter Randomized DESSERT Study). The American journal of cardiology. 2008;101(11):1560-6.

27. Baumgart D, Klauss V, Baer F, Hartmann F, Drexler H, Motz W, et al. One-year results of the SCORPIUS study: a German multicenter investigation on the effectiveness of sirolimus-eluting stents in diabetic patients. J Am Coll Cardiol. 2007;50(17):1627-34.

28. Diaz de la Llera LS, Ballesteros S, Nevado J, Fernandez M, Villa M, Sanchez A, et al. Sirolimus-eluting stents compared with standard stents in the treatment of patients with primary angioplasty. Am Heart J. 2007;154(1):164 e1-6.

29. van der Hoeven BL, Liem SS, Jukema JW, Suraphakdee N, Putter H, Dijkstra J, et al. Sirolimus-eluting stents versus bare-metal stents in patients with ST-segment elevation myocardial infarction: 9-month angiographic and intravascular ultrasound results and 12-month clinical outcome results from the MISSION! Intervention Study. J Am Coll Cardiol. 2008;51(6):618-26.

30. Boden H, van der Hoeven BL, Liem SS, Atary JZ, Cannegieter SC, Atsma DE, et al. Five-year clinical follow-up from the MISSION! Intervention Study: sirolimus-eluting stent versus bare metal stent implantation in patients with ST-segment elevation myocardial infarction, a randomised controlled trial. EuroIntervention. 2012;7(9):1021-9.

31. Di Lorenzo E, De Luca G, Sauro R, Varricchio A, Capasso M, Lanzillo T, et al. The PASEO (PaclitAxel or Sirolimus-Eluting Stent Versus Bare Metal Stent in Primary Angioplasty) Randomized Trial. JACC Cardiovasc Interv. 2009;2(6):515-23.

32. Di Lorenzo E, Sauro R, Varricchio A, Capasso M, Lanzillo T, Manganelli F, et al. Benefits of drug-eluting stents as compared to bare metal stent in ST-segment elevation myocardial infarction: four year results of the PaclitAxel or Sirolimus-Eluting stent vs bare metal stent in primary angiOplasty (PASEO) randomized trial. Am Heart J. 2009;158(4):e43-50.

33. Menichelli M, Parma A, Pucci E, Fiorilli R, De Felice F, Nazzaro M, et al. Randomized trial of Sirolimus-Eluting Stent Versus Bare-Metal Stent in Acute Myocardial Infarction (SESAMI). J Am Coll Cardiol. 2007;49(19):1924-30.

34. Musto C, Fiorilli R, De Felice F, Patti G, Nazzaro MS, Scappaticci M, et al. Long-term outcome of sirolimus-eluting vs bare-metal stent in the setting of acute myocardial infarction: 5-year results of the SESAMI trial. International journal of cardiology. 2013;166(2):399-403.

35. Valgimigli M, Percoco G, Malagutti P, Campo G, Ferrari F, Barbieri D, et al. Tirofiban and sirolimus-eluting stent vs abciximab and bare-metal stent for acute myocardial infarction: a randomized trial. JAMA. 2005;293(17):2109-17.

36. Tebaldi M, Arcozzi C, Campo G, Percoco G, Ferrari R, Valgimigli M, et al. The 5-year clinical outcomes after a randomized comparison of sirolimus-eluting versus bare-metal stent implantation in patients with ST-segment elevation myocardial infarction. J Am Coll Cardiol. 2009;54(20):1900-1.

37. Spaulding C, Henry P, Teiger E, Beatt K, Bramucci E, Carrie D, et al. Sirolimus-eluting versus uncoated stents in acute myocardial infarction. N Engl J Med. 2006;355(11):1093-104.

38. Spaulding C, Teiger E, Commeau P, Varenne O, Bramucci E, Slama M, et al. Four-year follow-up of TYPHOON (trial to assess the use of the CYPHer sirolimus-eluting coronary stent in acute myocardial infarction treated with BallOON angioplasty). JACC Cardiovasc Interv. 2011;4(1):14-23.

39. Pache J, Dibra A, Mehilli J, Dirschinger J, Schomig A, Kastrati A. Drug-eluting stents compared with thin-strut bare stents for the reduction of restenosis: a prospective, randomized trial. Eur Heart J. 2005;26(13):1262-8.

40. Suttorp MJ, Laarman GJ, Rahel BM, Kelder JC, Bosschaert MA, Kiemeneij F, et al. Primary Stenting of Totally Occluded Native Coronary Arteries II (PRISON II): a randomized comparison of bare metal stent implantation with sirolimus-eluting stent implantation for the treatment of total coronary occlusions. Circulation. 2006;114(9):921-8.

41. Van den Branden BJ, Rahel BM, Laarman GJ, Slagboom T, Kelder JC, Ten Berg JM, et al. Five-year clinical outcome after primary stenting of totally occluded native coronary arteries: a randomised comparison of bare metal stent implantation with sirolimus-eluting stent implantation for the treatment of total coronary occlusions (PRISON II study). EuroIntervention. 2012;7(10):1189-96.

42. Teeuwen K, Van den Branden BJ, Rahel BM, Laarman GJ, Tijssen JG, Kelder JC, et al. Late catch-up in lumen diameter at five-year angiography in MACE-free patients treated with sirolimus-eluting stents in the Primary Stenting of Totally Occluded Native Coronary Arteries: a randomised

comparison of bare metal stent implantation with sirolimus-eluting stent implantation for the treatment of total coronary occlusions (PRISON II). EuroIntervention. 2013;9(2):212-9.

43. Rubartelli P, Petronio AS, Guiducci V, Sganzerla P, Bolognese L, Galli M, et al. Comparison of sirolimus-eluting and bare metal stent for treatment of patients with total coronary occlusions: results of the GISSOC II-GISE multicentre randomized trial. Eur Heart J. 2010;31(16):2014-20.

44. Ardissino D, Cavallini C, Bramucci E, Indolfi C, Marzocchi A, Manari A, et al. Sirolimus-eluting vs uncoated stents for prevention of restenosis in small coronary arteries: a randomized trial. JAMA. 2004;292(22):2727-34.

45. Menozzi A, Solinas E, Ortolani P, Repetto A, Saia F, Piovaccari G, et al. Twenty-four months clinical outcomes of sirolimus-eluting stents for the treatment of small coronary arteries: the long-term SES-SMART clinical study. Eur Heart J. 2009;30(17):2095-101.

46. Kaiser C, Galatius S, Erne P, Eberli F, Alber H, Rickli H, et al. Drug-eluting versus bare-metal stents in large coronary arteries. N Engl J Med. 2010;363(24):2310-9.

47. Vermeersch P, Agostoni P, Verheye S, Van den Heuvel P, Convens C, Bruining N, et al. Randomized double-blind comparison of sirolimus-eluting stent versus bare-metal stent implantation in diseased saphenous vein grafts: six-month angiographic, intravascular ultrasound, and clinical follow-up of the RRISC Trial. J Am Coll Cardiol. 2006;48(12):2423-31.

48. Vermeersch P, Agostoni P, Verheye S, Van den Heuvel P, Convens C, Van den Branden F, et al. Increased late mortality after sirolimus-eluting stents versus bare-metal stents in diseased saphenous vein grafts: results from the randomized DELAYED RRISC Trial. J Am Coll Cardiol. 2007;50(3):261-7.

49. Kelbaek H, Thuesen L, Helqvist S, Klovgaard L, Jorgensen E, Aljabbari S, et al. The Stenting Coronary Arteries in Non-stress/benestent Disease (SCANDSTENT) trial. J Am Coll Cardiol. 2006;47(2):449-55.

50. Kelbaek H, Klovgaard L, Helqvist S, Lassen JF, Krusell LR, Engstrom T, et al. Long-term outcome in patients treated with sirolimus-eluting stents in complex coronary artery lesions: 3-year

results of the SCANDSTENT (Stenting Coronary Arteries in Non-Stress/Benestent Disease) trial. J Am Coll Cardiol. 2008;51(21):2011-6.

51. Sousa JE, Costa MA, Abizaid A, Abizaid AS, Feres F, Pinto IM, et al. Lack of neointimal proliferation after implantation of sirolimus-coated stents in human coronary arteries: a quantitative coronary angiography and three-dimensional intravascular ultrasound study. Circulation. 2001;103(2):192-5.

52. Rensing BJ, Vos J, Smits PC, Foley DP, van den Brand MJ, van der Giessen WJ, et al. Coronary restenosis elimination with a sirolimus eluting stent: first European human experience with 6-month angiographic and intravascular ultrasonic follow-up. Eur Heart J. 2001;22(22):2125-30.

53. Sousa JE, Costa MA, Abizaid AC, Rensing BJ, Abizaid AS, Tanajura LF, et al. Sustained suppression of neointimal proliferation by sirolimus-eluting stents: one-year angiographic and intravascular ultrasound follow-up. Circulation. 2001;104(17):2007-11.

54. Weisz G, Leon MB, Holmes DR, Jr., Kereiakes DJ, Clark MR, Cohen BM, et al. Two-year outcomes after sirolimus-eluting stent implantation: results from the Sirolimus-Eluting Stent in de Novo Native Coronary Lesions (SIRIUS) trial. J Am Coll Cardiol. 2006;47(7):1350-5.

55. Stone GW, Moses JW, Ellis SG, Schofer J, Dawkins KD, Morice MC, et al. Safety and efficacy of sirolimus- and paclitaxel-eluting coronary stents. N Engl J Med. 2007;356(10):998-1008.

56. Kastrati A, Mehilli J, Pache J, Kaiser C, Valgimigli M, Kelbaek H, et al. Analysis of 14 trials comparing sirolimus-eluting stents with bare-metal stents. N Engl J Med. 2007;356(10):1030-9.

57. Stettler C, Wandel S, Allemann S, Kastrati A, Morice MC, Schomig A, et al. Outcomes associated with drug-eluting and bare-metal stents: a collaborative network meta-analysis. Lancet (London, England). 2007;370(9591):937-48.

58. Kirtane AJ, Gupta A, Iyengar S, Moses JW, Leon MB, Applegate R, et al. Safety and efficacy of drug-eluting and bare metal stents: comprehensive meta-analysis of randomized trials and observational studies. Circulation. 2009;119(25):3198-206.

59. Caixeta A, Leon MB, Lansky AJ, Nikolsky E, Aoki J, Moses JW, et al. 5-year clinical outcomes after sirolimus-eluting stent implantation insights from a patient-level pooled analysis of 4 randomized trials comparing sirolimus-eluting stents with bare-metal stents. J Am Coll Cardiol. 2009;54(10):894-902.

60. Valgimigli M, Campo G, Percoco G, Bolognese L, Vassanelli C, Colangelo S, et al. Comparison of angioplasty with infusion of tirofiban or abciximab and with implantation of sirolimus-eluting or uncoated stents for acute myocardial infarction: the MULTISTRATEGY randomized trial. JAMA. 2008;299(15):1788-99.

61. Baim DS, editor. Grossman's Cardiac Catheterisation, angiography, and Intervention. 7 ed. Philadelphia: Lippincott Williams & Wilkins; 2006.

62. Grube E, Silber S, Hauptmann KE, Mueller R, Buellesfeld L, Gerckens U, et al. TAXUS I: six- and twelve-month results from a randomized, double-blind trial on a slow-release paclitaxel-eluting stent for de novo coronary lesions. Circulation. 2003;107(1):38-42.

63. Colombo A, Drzewiecki J, Banning A, Grube E, Hauptmann K, Silber S, et al. Randomized study to assess the effectiveness of slow- and moderate-release polymer-based paclitaxel-eluting stents for coronary artery lesions. Circulation. 2003;108(7):788-94.

64. Silber S, Colombo A, Banning AP, Hauptmann K, Drzewiecki J, Grube E, et al. Final 5-year results of the TAXUS II trial: a randomized study to assess the effectiveness of slow- and moderate-release polymer-based paclitaxel-eluting stents for de novo coronary artery lesions. Circulation. 2009;120(15):1498-504.

65. Stone GW, Ellis SG, Cox DA, Hermiller J, O'Shaughnessy C, Mann JT, et al. A polymer-based, paclitaxel-eluting stent in patients with coronary artery disease. N Engl J Med. 2004;350(3):221-31.

66. Ellis SG, Stone GW, Cox DA, Hermiller J, O'Shaughnessy C, Mann T, et al. Long-term safety and efficacy with paclitaxel-eluting stents: 5-year final results of the TAXUS IV clinical trial (TAXUS IV-SR: Treatment of De Novo Coronary Disease Using a Single Paclitaxel-Eluting Stent). JACC Cardiovasc Interv. 2009;2(12):1248-59.

67. Stone GW, Ellis SG, Cannon L, Mann JT, Greenberg JD, Spriggs D, et al. Comparison of a polymer-based paclitaxel-eluting stent with a bare metal stent in patients with complex coronary artery disease: a randomized controlled trial. JAMA. 2005;294(10):1215-23.

68. Ellis SG, Cannon L, Mann T, et al. Final 5-year outcomes from the TAXUS V de novo trial: Long term safety and effectiveness of the Paclitaxel-eluting TAXUS stent in complex lesions. Abstract presentation at Transcatheter Cardiovascular Therapeutics, San Francisco, 22nd September 2009. The American journal of cardiology. 2009;Vol. 104(6, Supplement):135D.

69. Dawkins KD, Grube E, Guagliumi G, Banning AP, Zmudka K, Colombo A, et al. Clinical efficacy of polymer-based paclitaxel-eluting stents in the treatment of complex, long coronary artery lesions from a multicenter, randomized trial: support for the use of drug-eluting stents in contemporary clinical practice. Circulation. 2005;112(21):3306-13.

70. Grube E, Dawkins K, Guagliumi G, Banning A, Zmudka K, Colombo A, et al. TAXUS VI final 5-year results: a multicentre, randomised trial comparing polymer-based moderate-release paclitaxel-eluting stent with a bare metal stent for treatment of long, complex coronary artery lesions. EuroIntervention. 2009;4(5):572-7.

71. Stone GW, Lansky AJ, Pocock SJ, Gersh BJ, Dangas G, Wong SC, et al. Paclitaxel-eluting stents versus bare-metal stents in acute myocardial infarction. N Engl J Med. 2009;360(19):1946-59.

72. Stone GW, Witzenbichler B, Guagliumi G, Peruga JZ, Brodie BR, Dudek D, et al. Heparin plus a glycoprotein IIb/IIIa inhibitor versus bivalirudin monotherapy and paclitaxel-eluting stents versus bare-metal stents in acute myocardial infarction (HORIZONS-AMI): final 3-year results from a multicentre, randomised controlled trial. Lancet. 2011;377(9784):2193-204.

73. Erglis A, Narbute I, Kumsars I, Jegere S, Mintale I, Zakke I, et al. A randomized comparison of paclitaxel-eluting stents versus bare-metal stents for treatment of unprotected left main coronary artery stenosis. J Am Coll Cardiol. 2007;50(6):491-7.

74. Laarman GJ, Suttorp MJ, Dirksen MT, van Heerebeek L, Kiemeneij F, Slagboom T, et al. Paclitaxel-eluting versus uncoated stents in primary percutaneous coronary intervention. N Engl J Med. 2006;355(11):1105-13.

75. Vink MA, Dirksen MT, Suttorp MJ, Tijssen JG, van Etten J, Patterson MS, et al. 5-year follow-up after primary percutaneous coronary intervention with a paclitaxel-eluting stent versus a bare-metal stent in acute ST-segment elevation myocardial infarction: a follow-up study of the PASSION (Paclitaxel-Eluting Versus Conventional Stent in Myocardial Infarction with ST-Segment Elevation) trial. JACC Cardiovasc Interv. 2011;4(1):24-9.

76. Tanabe K, Serruys PW, Grube E, Smits PC, Selbach G, van der Giessen WJ, et al. TAXUS III Trial: in-stent restenosis treated with stent-based delivery of paclitaxel incorporated in a slow-release polymer formulation. Circulation. 2003;107(4):559-64.

77. Silber S, Colombo A, Banning AP, Hauptmann K, Drzewiecki J, Grube E, et al. Final 5-Year Results of the TAXUS II Trial. A Randomized Study to Assess the Effectiveness of Slow- and Moderate-Release Polymer-Based Paclitaxel-Eluting Stents for De Novo Coronary Artery Lesions. Circulation. 2009;13

:1498-504.

78. Kereiakes DJ, Cannon LA, Feldman RL, Popma JJ, Magorien R, Whitbourn R, et al. Clinical and angiographic outcomes after treatment of de novo coronary stenoses with a novel platinum chromium thin-strut stent: primary results of the PERSEUS (Prospective Evaluation in a Randomized Trial of the Safety and Efficacy of the Use of the TAXUS Element Paclitaxel-Eluting Coronary Stent System) trial. J Am Coll Cardiol. 2010;56(4):264-71.

79. Allocco DJ, Cannon LA, Britt A, Heil JE, Nersesov A, Wehrenberg S, et al. A prospective evaluation of the safety and efficacy of the TAXUS Element paclitaxel-eluting coronary stent system for the treatment of de novo coronary artery lesions: design and statistical methods of the PERSEUS clinical program. Trials. 2010;11:1.

80. Cannon LA, Kereiakes DJ, Mann T, Popma JJ, Mooney MR, Mishkel GJ, et al. A prospective evaluation of the safety and efficacy of TAXUS Element paclitaxel-eluting coronary stent implantation for the treatment of de novo coronary artery lesions in small vessels: the PERSEUS Small Vessel trial. EuroIntervention. 2011;6(8):920-7, 1-2.

81. Kereiakes DJ, Cannon LA, Dauber I, Ball M, Bertolet B, Foster M, et al. Long-term follow-up of the platinum chromium TAXUS Element (ION) stent: The PERSEUS Workhorse and Small Vessel trial five-year results. Catheterization and cardiovascular interventions : official journal of the Society for Cardiac Angiography & Interventions. 2015;86(6):994-1001.

82. Lee SW, Park SW, Kim YH, Yun SC, Park DW, Lee CW, et al. A randomized comparison of sirolimus- versus Paclitaxel-eluting stent implantation in patients with diabetes mellitus. J Am Coll Cardiol. 2008;52(9):727-33.

83. Lee SW, Park SW, Kim YH, Yun SC, Park DW, Lee CW, et al. A randomized comparison of sirolimus- versus paclitaxel-eluting stent implantation in patients with diabetes mellitus 2-year clinical outcomes of the DES-DIABETES trial. J Am Coll Cardiol. 2009;53(9):812-3.

84. Dibra A, Kastrati A, Mehilli J, Pache J, Schuhlen H, von Beckerath N, et al. Paclitaxel-eluting or sirolimus-eluting stents to prevent restenosis in diabetic patients. N Engl J Med. 2005;353(7):663-70.

85. Morice MC, Colombo A, Meier B, Serruys P, Tamburino C, Guagliumi G, et al. Sirolimus- vs paclitaxel-eluting stents in de novo coronary artery lesions: the REALITY trial: a randomized controlled trial. JAMA. 2006;295(8):895-904.

86. Windecker S, Remondino A, Eberli FR, Juni P, Raber L, Wenaweser P, et al. Sirolimus-eluting and paclitaxel-eluting stents for coronary revascularization. N Engl J Med. 2005;353(7):653-62.

87. Raber L, Wohlwend L, Wigger M, Togni M, Wandel S, Wenaweser P, et al. Five-year clinical and angiographic outcomes of a randomized comparison of sirolimus-eluting and paclitaxel-eluting stents: results of the Sirolimus-Eluting Versus Paclitaxel-Eluting Stents for Coronary Revascularization LATE trial. Circulation. 2011;123(24):2819-28, 6 p following 28.

88. Galloe AM, Thuesen L, Kelbaek H, Thayssen P, Rasmussen K, Hansen PR, et al. Comparison of paclitaxel- and sirolimus-eluting stents in everyday clinical practice: the SORT OUT II randomized trial. JAMA. 2008;299(4):409-16.

89. Goy JJ, Stauffer JC, Siegenthaler M, Benoit A, Seydoux C. A prospective randomized comparison between paclitaxel and sirolimus stents in the real world of interventional cardiology: the TAXi trial. J Am Coll Cardiol. 2005;45(2):308-11.

90. Berger A, Stauffer JC, Seydoux C, Siegenthaler M, Benoit A, Goy JJ. Three-year follow-up of the first prospective randomized comparison between paclitaxel and sirolimus stents: the TAXi-LATE trial. Catheterization and cardiovascular interventions : official journal of the Society for Cardiac Angiography & Interventions. 2007;70(2):163-6.

91. Lee JH, Kim HS, Lee SW, Park JH, Choi SW, Jeong JO, et al. Prospective randomized comparison of sirolimus- versus paclitaxel-eluting stents for the treatment of acute ST-elevation myocardial infarction: pROSIT trial. Catheterization and cardiovascular interventions : official journal of the Society for Cardiac Angiography & Interventions. 2008;72(1):25-32.

92. Kim HS, Lee JH, Lee SW, Kim YH, Park JH, Choi SW, et al. Long-term safety and efficacy of sirolimus- vs. paclitaxel-eluting stent implantation for acute ST-elevation myocardial infarction: 3-year follow-up of the PROSIT trial. International journal of cardiology. 2011;147(2):253-7.

93. Mehilli J, Kastrati A, Byrne RA, Bruskina O, Iijima R, Schulz S, et al. Paclitaxel- versus sirolimus-eluting stents for unprotected left main coronary artery disease. J Am Coll Cardiol. 2009;53(19):1760-8.

94. Kim YH, Park SW, Lee SW, Park DW, Yun SC, Lee CW, et al. Sirolimus-eluting stent versus paclitaxel-eluting stent for patients with long coronary artery disease. Circulation. 2006;114(20):2148-53.

95. Mehilli J, Dibra A, Kastrati A, Pache J, Dirschinger J, Schomig A, et al. Randomized trial of paclitaxel- and sirolimus-eluting stents in small coronary vessels. Eur Heart J. 2006;27(3):260-6.

96. Kastrati A, Mehilli J, von Beckerath N, Dibra A, Hausleiter J, Pache J, et al. Sirolimus-eluting stent or paclitaxel-eluting stent vs balloon angioplasty for prevention of recurrences in patients with coronary in-stent restenosis: a randomized controlled trial. JAMA. 2005;293(2):165-71.

97. Mehilli J, Byrne RA, Tiroch K, Pinieck S, Schulz S, Kufner S, et al. Randomized trial of paclitaxel- versus sirolimus-eluting stents for treatment of coronary restenosis in sirolimus-eluting stents: the ISAR-DESIRE 2 (Intracoronary Stenting and Angiographic Results: Drug Eluting Stents for In-Stent Restenosis 2) study. J Am Coll Cardiol. 2010;55(24):2710-6.

98. Schomig A, Dibra A, Windecker S, Mehilli J, Suarez de Lezo J, Kaiser C, et al. A meta-analysis of 16 randomized trials of sirolimus-eluting stents versus paclitaxel-eluting stents in patients with coronary artery disease. J Am Coll Cardiol. 2007;50(14):1373-80.

99. Galloe AM, Kelbaek H, Thuesen L, Hansen HS, Ravkilde J, Hansen PR, et al. 10-Year Clinical Outcome After Randomization to Treatment by Sirolimus- or Paclitaxel-Eluting Coronary Stents. J Am Coll Cardiol. 2017;69(6):616-24.

100. Yamaji K, Raber L, Zanchin T, Spitzer E, Zanchin C, Pilgrim T, et al. Ten-year clinical outcomes of first-generation drug-eluting stents: the Sirolimus-Eluting vs. Paclitaxel-Eluting Stents for Coronary Revascularization (SIRTAX) VERY LATE trial. Eur Heart J. 2016;37(45):3386-95.

101. Serruys PW, Ong AT, Piek JJ, Neumann FJ, van der Giessen WJ, Wiemer M, et al. A randomized comparison of a durable polymer Everolimus-eluting stent with a bare metal coronary stent: The SPIRIT first trial. EuroIntervention. 2005;1(1):58-65.

102. Wiemer M, Serruys PW, Miquel-Hebert K, Neumann FJ, Piek JJ, Grube E, et al. Five-year long-term clinical follow-up of the XIENCE V everolimus eluting coronary stent system in the treatment of patients with de novo coronary artery lesions: the SPIRIT FIRST trial. Catheterization and cardiovascular interventions : official journal of the Society for Cardiac Angiography & Interventions. 2010;75(7):997-1003.

103. de Belder A, de la Torre Hernandez JM, Lopez-Palop R, O'Kane P, Hernandez Hernandez F, Strange J, et al. A prospective randomized trial of everolimus-eluting stents versus bare-metal stents in octogenarians: the XIMA Trial (Xience or Vision Stents for the Management of Angina in the Elderly). J Am Coll Cardiol. 2014;63(14):1371-5.

104. Sabate M, Cequier A, Iniguez A, Serra A, Hernandez-Antolin R, Mainar V, et al. Everolimus-eluting stent versus bare-metal stent in ST-segment elevation myocardial infarction

(EXAMINATION): 1 year results of a randomised controlled trial. Lancet (London, England). 2012;380(9852):1482-90.

105. Sabate M, Brugaletta S, Cequier A, Iniguez A, Serra A, Jimenez-Quevedo P, et al. Clinical outcomes in patients with ST-segment elevation myocardial infarction treated with everolimus-eluting stents versus bare-metal stents (EXAMINATION): 5-year results of a randomised trial. Lancet. 2016;387(10016):357-66.

106. Tomai F, Ribichini F, De Luca L, Petrolini A, Ghini AS, Weltert L, et al. Randomized Comparison of Xience V and Multi-Link Vision Coronary Stents in the Same Multivessel Patient With Chronic Kidney Disease (RENAL-DES) Study. Circulation. 2014;129(10):1104-12.

107. Valgimigli M, Sabate M, Kaiser C, Brugaletta S, de la Torre Hernandez JM, Galatius S, et al. Effects of cobalt-chromium everolimus eluting stents or bare metal stent on fatal and non-fatal cardiovascular events: patient level meta-analysis. Bmj. 2014;349:g6427.

108. Serruys PW, Ruygrok P, Neuzner J, Piek JJ, Seth A, Schofer JJ, et al. A randomised comparison of an everolimus-eluting coronary stent with a paclitaxel-eluting coronary stent:the SPIRIT II trial. EuroIntervention. 2006;2(3):286-94.

109. Ruygrok PN, Desaga M, Van Den Branden F, Rasmussen K, Suryapranata H, Dorange C, et al. One year clinical follow-up of the XIENCE V Everolimus-eluting stent system in the treatment of patients with de novo native coronary artery lesions: the SPIRIT II study. EuroIntervention. 2007;3(3):315-20.

110. Claessen BE, Beijk MA, Legrand V, Ruzyllo W, Manari A, Varenne O, et al. Two-year clinical, angiographic, and intravascular ultrasound follow-up of the XIENCE V everolimus-eluting stent in the treatment of patients with de novo native coronary artery lesions: the SPIRIT II trial. Circulation Cardiovascular interventions. 2009;2(4):339-47.

111. Garg S, Serruys PW, Onuma Y, Dorange C, Veldhof S, Miquel-Hebert K, et al. Three year clinical follow up of the XIENCE V Everolimus eluting coronary stent system in the treatment of patients with de novo coronary artery lesions. The SPIRIT II Trial. J Am Coll Cardiol Intv. 2009;2(12):1190-8.

112. Garg S, Serruys PW, Miquel-Hebert K, Investigators SI. Four-year clinical follow-up of the XIENCE V everolimus-eluting coronary stent system in the treatment of patients with de novo coronary artery lesions: the SPIRIT II trial. Catheterization and cardiovascular interventions : official journal of the Society for Cardiac Angiography & Interventions. 2011;77(7):1012-7.

113. Onuma Y, Miquel-Hebert K, Serruys PW, Investigators SI. Five-year long-term clinical follow-up of the XIENCE V everolimus-eluting coronary stent system in the treatment of patients with de novo coronary artery disease: the SPIRIT II trial. EuroIntervention. 2013;8(9):1047-51.

114. Stone GW, Midei M, Newman W, Sanz M, Hermiller JB, Williams J, et al. Comparison of an everolimus-eluting stent and a paclitaxel-eluting stent in patients with coronary artery disease: a randomized trial. JAMA. 2008;299(16):1903-13.

115. Gada H, Kirtane AJ, Newman W, Sanz M, Hermiller JB, Mahaffey KW, et al. 5-year results of a randomized comparison of XIENCE V everolimus-eluting and TAXUS paclitaxel-eluting stents: final results from the SPIRIT III trial (clinical evaluation of the XIENCE V everolimus eluting coronary stent system in the treatment of patients with de novo native coronary artery lesions). JACC Cardiovasc Interv. 2013;6(12):1263-6.

116. Stone GW, Rizvi A, Newman W, Mastali K, Wang JC, Caputo R, et al. Everolimus-eluting versus paclitaxel-eluting stents in coronary artery disease. N Engl J Med. 2010;362(18):1663-74.

117. Stone GW, Rizvi A, Sudhir K, Newman W, Applegate RJ, Cannon LA, et al. Randomized comparison of everolimus- and paclitaxel-eluting stents. 2-year follow-up from the SPIRIT (Clinical Evaluation of the XIENCE V Everolimus Eluting Coronary Stent System) IV trial. J Am Coll Cardiol. 2011;58(1):19-25.

118. Brener SJ, Kereiakes DJ, Simonton CA, Rizvi A, Newman W, Mastali K, et al. Everolimus-eluting stents in patients undergoing percutaneous coronary intervention: final 3-year results of the Clinical Evaluation of the XIENCE V Everolimus Eluting Coronary Stent System in the Treatment of Subjects With de Novo Native Coronary Artery Lesions trial. Am Heart J. 2013;166(6):1035-42.

119. Chevalier B. SPIRIT V Single Arm Study - 2 year follow-up. Presentation at EuroPCR, 25th-28th May 2010, Paris, France.

120. Kedhi E, Joesoef KS, McFadden E, Wassing J, van Mieghem C, Goedhart D, et al. Second-generation everolimus-eluting and paclitaxel-eluting stents in real-life practice (COMPARE): a randomised trial. Lancet. 2010;375(9710):201-9.

121. Smits PC, Kedhi E, Royaards KJ, Joesoef KS, Wassing J, Rademaker-Havinga TA, et al. 2-year follow-up of a randomized controlled trial of everolimus- and paclitaxel-eluting stents for coronary revascularization in daily practice. COMPARE (Comparison of the everolimus eluting XIENCE-V stent with the paclitaxel eluting TAXUS LIBERTE stent in all-comers: a randomized open label trial). J Am Coll Cardiol. 2011;58(1):11-8.

122. Smits PC, Vlachojannis GJ, McFadden EP, Royaards KJ, Wassing J, Joesoef KS, et al. Final 5-Year Follow-Up of a Randomized Controlled Trial of Everolimus- and Paclitaxel-Eluting Stents for Coronary Revascularization in Daily Practice: The COMPARE Trial (A Trial of Everolimus-Eluting Stents and Paclitaxel Stents for Coronary Revascularization in Daily Practice). JACC Cardiovasc Interv. 2015;8(9):1157-65.

123. Ribichini F, Romano M, Rosiello R, La Vecchia L, Cabianca E, Caramanno G, et al. A clinical and angiographic study of the XIENCE V everolimus-eluting coronary stent system in the treatment of patients with multivessel coronary artery disease: the EXECUTIVE trial (EXecutive RCT: evaluating XIENCE V in a multi vessel disease). JACC Cardiovasc Interv. 2013;6(10):1012-22.

124. Kaul U, Bhagwat A, Pinto B, Goel PK, Jagtap P, Sathe S, et al. Paclitaxel-eluting stents versus everolimus-eluting coronary stents in a diabetic population: two-year follow-up of the TUXEDO-India trial. EuroIntervention. 2017;13(10):1194-201.

125. Smits P. COMPARE Trial - 3 year follow-up. Presentation at Transcather Cardiovascular Therapeutics, San Francisco, November 7th 2011.

126. Stone GW, Kedhi E, Kereiakes DJ, Parise H, Fahy M, Serruys PW, et al. Differential clinical responses to everolimus-eluting and Paclitaxel-eluting coronary stents in patients with and without diabetes mellitus. Circulation. 2011;124(8):893-900.

127. Dangas GD, Serruys PW, Kereiakes DJ, Hermiller J, Rizvi A, Newman W, et al. Meta-analysis of everolimus-eluting versus paclitaxel-eluting stents in coronary artery disease: final 3-year

results of the SPIRIT clinical trials program (Clinical Evaluation of the Xience V Everolimus Eluting Coronary Stent System in the Treatment of Patients With De Novo Native Coronary Artery Lesions). JACC Cardiovasc Interv. 2013;6(9):914-22.

128. Park KW, Chae IH, Lim DS, Han KR, Yang HM, Lee HY, et al. Everolimus-eluting versus sirolimus-eluting stents in patients undergoing percutaneous coronary intervention: the EXCELLENT (Efficacy of Xience/Promus Versus Cypher to Reduce Late Loss After Stenting) randomized trial. J Am Coll Cardiol. 2011;58(18):1844-54.

129. Byrne RA, Kastrati A, Massberg S, Wieczorek A, Laugwitz KL, Hadamitzky M, 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.

130. Kufner S, Byrne RA, Valeskini M, Schulz S, Ibrahim T, Hoppmann P, 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):1372-9.

131. Jensen LO, Thayssen P, Hansen HS, Christiansen EH, Tilsted HH, Krusell LR, et al. Randomized comparison of everolimus-eluting and sirolimus-eluting stents in patients treated with percutaneous coronary intervention: the Scandinavian Organization for Randomized Trials with Clinical Outcome IV (SORT OUT IV). Circulation. 2012;125(10):1246-55.

132. Jensen LO, Thayssen P, Christiansen EH, Maeng M, Ravkilde J, Hansen KN, et al. Safety and Efficacy of Everolimus- Versus Sirolimus-Eluting Stents: 5-Year Results From SORT OUT IV. J Am Coll Cardiol. 2016;67(7):751-62.

133. Kimura T, Morimoto T, Natsuaki M, Shiomi H, Igarashi K, Kadota K, et al. Comparison of everolimus-eluting and sirolimus-eluting coronary stents: 1-year outcomes from the Randomized Evaluation of Sirolimus-eluting Versus Everolimus-eluting stent Trial (RESET). Circulation. 2012;126(10):1225-36.

134. Shiomi H, Kozuma K, Morimoto T, Igarashi K, Kadota K, Tanabe K, et al. Long-term clinical outcomes after everolimus- and sirolimus-eluting coronary stent implantation: final 3-year follow-up of the Randomized Evaluation of Sirolimus-Eluting Versus Everolimus-Eluting Stent Trial. Circulation Cardiovascular interventions. 2014;7(3):343-54.

135. Park DW, Kim YH, Song HG, Ahn JM, Kim WJ, Lee JY, et al. Comparison of everolimus- and sirolimus-eluting stents in patients with long coronary artery lesions: a randomized LONG-DES-III (Percutaneous Treatment of LONG Native Coronary Lesions With Drug-Eluting Stent-III) Trial. JACC Cardiovasc Interv. 2011;4(10):1096-103.

136. Kim WJ, Lee SW, Park SW, Kim YH, Yun SC, Lee JY, et al. Randomized comparison of everolimus-eluting stent versus sirolimus-eluting stent implantation for de novo coronary artery disease in patients with diabetes mellitus (ESSENCE-DIABETES): results from the ESSENCE-DIABETES trial. Circulation. 2011;124(8):886-92.

137. Hofma SH, Brouwer J, Velders MA, van't Hof AW, Smits PC, Quere M, et al. Second-generation everolimus-eluting stents versus first-generation sirolimus-eluting stents in acute myocardial infarction. 1-year results of the randomized XAMI (XienceV Stent vs. Cypher Stent in Primary PCI for Acute Myocardial Infarction) trial. J Am Coll Cardiol. 2012;60(5):381-7.

138. Hofma SH, Smits PC, Brouwer J, Velders MA, van 't Hof AW, Quere M, et al. Long-term follow-up of second-generation everolimus-eluting stents versus first-generation sirolimus-eluting stents in acute myocardial infarction: three-year results of the XAMI trial. EuroIntervention. 2015;10(11):1280-3.

139. Di Lorenzo E, Sauro R, Varricchio A, Capasso M, Lanzillo T, Manganelli F, et al. Randomized comparison of everolimus-eluting stents and sirolimus-eluting stents in patients with ST elevation myocardial infarction: RACES-MI trial. JACC Cardiovasc Interv. 2014;7(8):849-56.

140. Raber L, Juni P, Nuesch E, Kalesan B, Wenaweser P, Moschovitis A, et al. Long-term comparison of everolimus-eluting and sirolimus-eluting stents for coronary revascularization. J Am Coll Cardiol. 2011;57(21):2143-51.

141. de Waha A, Dibra A, Byrne RA, Ndrepepa G, Mehilli J, Fusaro M, et al. Everolimus-eluting versus sirolimus-eluting stents: a meta-analysis of randomized trials. Circulation Cardiovascular interventions. 2011;4(4):371-7.

142. Park KW, Kang SH, Velders MA, Shin DH, Hahn S, Lim WH, et al. Safety and efficacy of everolimus- versus sirolimus-eluting stents: a systematic review and meta-analysis of 11 randomized trials. Am Heart J. 2013;165(2):241-50 e4.

143. Baber U, Mehran R, Sharma SK, Brar S, Yu J, Suh JW, et al. Impact of the everolimus-eluting stent on stent thrombosis: a meta-analysis of 13 randomized trials. J Am Coll Cardiol. 2011;58(15):1569-77.

144. Palmerini T, Benedetto U, Biondi-Zoccai G, Della Riva D, Bacchi-Reggiani L, Smits PC, et al. Long-Term Safety of Drug-Eluting and Bare-Metal Stents: Evidence From a Comprehensive Network Meta-Analysis. J Am Coll Cardiol. 2015;65(23):2496-507.

145. Bangalore S, Kumar S, Fusaro M, Amoroso N, Attubato MJ, Feit F, et al. Short- and long-term outcomes with drug-eluting and bare-metal coronary stents: a mixed-treatment comparison analysis of 117 762 patient-years of follow-up from randomized trials. Circulation. 2012;125(23):2873-91.

146. Bangalore S, Kumar S, Fusaro M, Amoroso N, Kirtane AJ, Byrne RA, et al. Outcomes with various drug eluting or bare metal stents in patients with diabetes mellitus: mixed treatment comparison analysis of 22,844 patient years of follow-up from randomised trials. Bmj. 2012;345:e5170.

147. Palmerini T, Kirtane AJ, Serruys PW, Smits PC, Kedhi E, Kereiakes D, et al. Stent thrombosis with everolimus-eluting stents: meta-analysis of comparative randomized controlled trials. Circulation Cardiovascular interventions. 2012;5(3):357-64.

148. Joner M, Nakazawa G, Finn AV, Quee SC, Coleman L, Acampado E, et al. Endothelial cell recovery between comparator polymer-based drug-eluting stents. J Am Coll Cardiol. 2008;52(5):333-42.

149. Kolandaivelu K, Swaminathan R, Gibson WJ, Kolachalama VB, Nguyen-Ehrenreich KL, Giddings VL, et al. Stent thrombogenicity early in high-risk interventional settings is driven by stent design and deployment and protected by polymer-drug coatings. Circulation. 2011;123(13):1400-9.

150. Fajadet J, Wijns W, Laarman GJ, Kuck KH, Ormiston J, Munzel T, et al. Randomized, double-blind, multicenter study of the Endeavor zotarolimus-eluting phosphorylcholine-encapsulated stent for treatment of native coronary artery lesions: clinical and angiographic results of the ENDEAVOR II trial. Circulation. 2006;114(8):798-806.

151. Fajadet J, Wijns W, Laarman GJ, Kuck KH, Ormiston J, Baldus S, et al. Long-term follow-up of the randomised controlled trial to evaluate the safety and efficacy of the zotarolimus-eluting driver coronary stent in de novo native coronary artery lesions: five year outcomes in the ENDEAVOR II study. EuroIntervention. 2010;6(5):562-7.

152. Kandzari DE, Leon MB, Popma JJ, Fitzgerald PJ, O'Shaughnessy C, Ball MW, et al. Comparison of zotarolimus-eluting and sirolimus-eluting stents in patients with native coronary artery disease: a randomized controlled trial. J Am Coll Cardiol. 2006;48(12):2440-7.

153. Kandzari DE, Mauri L, Popma JJ, Turco MA, Gurbel PA, Fitzgerald PJ, et al. Late-term clinical outcomes with zotarolimus- and sirolimus-eluting stents. 5-year follow-up of the ENDEAVOR III (A Randomized Controlled Trial of the Medtronic Endeavor Drug [ABT-578] Eluting Coronary Stent System Versus the Cypher Sirolimus-Eluting Coronary Stent System in De Novo Native Coronary Artery Lesions). JACC Cardiovasc Interv. 2011;4(5):543-50.

154. Rasmussen K, Maeng M, Kaltoft A, Thayssen P, Kelbaek H, Tilsted HH, et al. Efficacy and safety of zotarolimus-eluting and sirolimus-eluting coronary stents in routine clinical care (SORT OUT III): a randomised controlled superiority trial. Lancet. 2010;375(9720):1090-9.

155. Maeng M, Tilsted HH, Jensen LO, Kaltoft A, Kelbaek H, Abildgaard U, et al. 3-Year clinical outcomes in the randomized SORT OUT III superiority trial comparing zotarolimus- and sirolimus-eluting coronary stents. JACC Cardiovasc Interv. 2012;5(8):812-8.

156. Maeng M, Tilsted HH, Jensen LO, Krusell LR, Kaltoft A, Kelbaek H, et al. Differential clinical outcomes after 1 year versus 5 years in a randomised comparison of zotarolimus-eluting and

sirolimus-eluting coronary stents (the SORT OUT III study): a multicentre, open-label, randomised superiority trial. Lancet. 2014;383(9934):2047-56.

157. Camenzind E, Wijns W, Mauri L, Kurowski V, Parikh K, Gao R, et al. Stent thrombosis and major clinical events at 3 years after zotarolimus-eluting or sirolimus-eluting coronary stent implantation: a randomised, multicentre, open-label, controlled trial. Lancet. 2012;380(9851):1396-405.

158. Wijns W, Steg PG, Mauri L, Kurowski V, Parikh K, Gao R, et al. Endeavour zotarolimus-eluting stent reduces stent thrombosis and improves clinical outcomes compared with cypher sirolimus-eluting stent: 4-year results of the PROTECT randomized trial. Eur Heart J. 2014;35(40):2812-20.

159. Leon MB, Mauri L, Popma JJ, Cutlip DE, Nikolsky E, O'Shaughnessy C, et al. A randomised comparison of the Endeavor Zotarolimus-eluting stent versus the TAXUS Paclitaxel-eluting stent in de novo native coronary lesions: 12-Month outcomes from the ENDEAVOR IV Trial. J Am Coll Cardiol. 2010;55(6):543-54.

160. Kirtane AJ, Leon MB, Ball MW, Bajwa HS, Sketch MH, Jr., Coleman PS, et al. The "final" 5-year follow-up from the ENDEAVOR IV trial comparing a zotarolimus-eluting stent with a paclitaxel-eluting stent. JACC Cardiovasc Interv. 2013;6(4):325-33.

161. Park DW, Kim YH, Yun SC, Kang SJ, Lee SW, Lee CW, et al. Comparison of zotarolimus-eluting stents with sirolimus- and paclitaxel-eluting stents for coronary revascularization: the ZEST (comparison of the efficacy and safety of zotarolimus-eluting stent with sirolimus-eluting and paclitaxel-eluting stent for coronary lesions) randomized trial. J Am Coll Cardiol. 2010;56(15):1187-95.

162. von Birgelen C, Sen H, Lam MK, Danse PW, Jessurun GA, Hautvast RW, et al. Third-generation zotarolimus-eluting and everolimus-eluting stents in all-comer patients requiring a percutaneous coronary intervention (DUTCH PEERS): a randomised, single-blind, multicentre, non-inferiority trial. Lancet. 2014;383(9915):413-23.

163. van der Heijden LC, Kok MM, Lowik MM, Danse PW, Jessurun GAJ, Hautvast RWM, et al. Three-year safety and efficacy of treating all-comers with newer-generation Resolute Integrity or

PROMUS Element stents in the randomised DUTCH PEERS (TWENTE II) trial. EuroIntervention. 2017;12(17):2128-31.

164. Park KW, Kang SH, Kang HJ, Koo BK, Park BE, Cha KS, et al. A randomized comparison of platinum chromium-based everolimus-eluting stents versus cobalt chromium-based Zotarolimus-Eluting stents in all-comers receiving percutaneous coronary intervention: HOST-ASSURE (harmonizing optimal strategy for treatment of coronary artery stenosis-safety & effectiveness of drug-eluting stents & anti-platelet regimen), a randomized, controlled, noninferiority trial. J Am Coll Cardiol. 2014;63(25 Pt A):2805-16.

165. Rutsch W. Multi-center First-In-Man Study With the Lowest Known Limus Dose on the Elixir Medical Myolimus Eluting Coronary Stent System With a Durable Polymer: Nine Month Clinical and Six Month Angiographic and IVUS Follow-up. Presentation at EuroPCR 19th-22nd May 2009, Barcelona, Spain.

166. Schurtz G, Delhaye C, Hurt C, Thieuleux H, Lemesle G. Biodegradable polymer Biolimus-eluting stent (Nobori(R)) for the treatment of coronary artery lesions: review of concept and clinical results. Med Devices (Auckl). 2014;7:35-43.

167. Chevalier B, Silber S, Park SJ, Garcia E, Schuler G, Suryapranata H, et al. Randomized comparison of the Nobori Biolimus A9-eluting coronary stent with the Taxus Liberte paclitaxel-eluting coronary stent in patients with stenosis in native coronary arteries: the NOBORI 1 trial--Phase 2. Circulation Cardiovascular interventions. 2009;2(3):188-95.

168. Chevalier B, Wijns W, Silber S, Garcia E, Serra A, Paunovic D, 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 1 trial. EuroIntervention. 2015;11(5):549-54.

169. Smits PC, Hofma S, Togni M, Vazquez N, Valdes M, Voudris V, 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.

170. Vlachojannis GJ, Smits PC, Hofma SH, Togni M, Vazquez N, Valdes M, et al. Biodegradable Polymer Biolimus-Eluting Stents Versus Durable Polymer Everolimus-Eluting Stents in Patients With

Coronary Artery Disease: Final 5-Year Report From the COMPARE II Trial (Abluminal Biodegradable Polymer Biolimus-Eluting Stent Versus Durable Polymer Everolimus-Eluting Stent). JACC Cardiovasc Interv. 2017;10(12):1215-21.

171. Natsuaki M, Kozuma K, Morimoto T, Kadota K, Muramatsu T, Nakagawa Y, et al. Biodegradable polymer biolimus-eluting stent versus durable polymer everolimus-eluting stent: a randomized, controlled, noninferiority trial. J Am Coll Cardiol. 2013;62(3):181-90.

172. Natsuaki M, Kozuma K, Morimoto T, Kadota K, Muramatsu T, Nakagawa Y, et al. Final 3-Year Outcome of a Randomized Trial Comparing Second-Generation Drug-Eluting Stents Using Either Biodegradable Polymer or Durable Polymer: NOBORI Biolimus-Eluting Versus XIENCE/PROMUS Everolimus-Eluting Stent Trial. Circulation Cardiovascular interventions. 2015;8(10).

173. Christiansen EH, Jensen LO, Thayssen P, Tilsted HH, Krusell LR, Hansen KN, et al. Biolimus-eluting 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.

174. Christiansen E. 5-year outcomes after implantation of biodegradable polymer-coated biolimus-eluting stents versus durable polymer-coated sirolimus-eluting stents in unselected patients. Presentation at ESC 2016, Rome. 2016.

175. Kaiser C, Galatius S, Jeger R, Gilgen N, Skov Jensen J, Naber C, et al. Long-term efficacy and safety of biodegradable-polymer biolimus-eluting stents: main results of the Basel Stent Kosten-Effektivitats Trial-PROspective Validation Examination II (BASKET-PROVE II), a randomized, controlled noninferiority 2-year outcome trial. Circulation. 2015;131(1):74-81.

176. Lee JY, Park DW, Kim YH, Ahn JM, Kim WJ, Kang SJ, 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. Circulation Cardiovascular interventions. 2014;7(3):322-9.

177. Verheye S. Overview of novolimus eluting and myolimus elution from durable and bioabsorbable polymers. Presentation at Transcatheter Cardiovascular Interventions, Washington, USA, 22nd September 2010.

178. Costa R. Device specifications and clinical program update - Desyne BD. Presentation at TCT 2016. . 2016.

179. Schofer J. Multicentre, first-in-man study on the Elixir Myolimus-eluting coronary stent system with bioabsorbable polymer: 12-month clinical and angiographic/IVUS results. Presentation EuroPCR, 25th-28th May 2010, Paris, France. Available [online] www.pcronline.com/Lectures/2010/Multicentre-first-in-man-study-on-the-Elixir-Myolimus-eluting-coronary-stent-system-with-bioabsorbable-polymer-12-month-clinical-and-angiographic-IVUS-results. [Accessed 29th May 2010].

180. Serruys PW, Sianos G, Abizaid A, Aoki J, den Heijer P, Bonnier H, et al. The effect of variable dose and release kinetics on neointimal hyperplasia using a novel paclitaxel-eluting stent platform: the Paclitaxel In-Stent Controlled Elution Study (PISCES). J Am Coll Cardiol. 2005;46(2):253-60.

181. Kaul U, Gupta RK, Mathur A, Dani S, Sapra R, Nayak PR, et al. Cobalt chromium stent with antiproliferative for restenosis trial in India (COSTAR I). Indian Heart J. 2007;59(2):165-72.

182. Dawkins KD, Verheye S, Schuhlen H, Dens J, Mudra H, Rutsch W, et al. The European cobalt STent with Antiproliferative for Restenosis trial (EuroSTAR): 12 month results. EuroIntervention. 2007;3(1):82-8.

183. Krucoff MW, Kereiakes DJ, Petersen JL, Mehran R, Hasselblad V, Lansky AJ, et al. A novel bioresorbable polymer paclitaxel-eluting stent for the treatment of single and multivessel coronary disease: primary results of the COSTAR (Cobalt Chromium Stent With Antiproliferative for Restenosis) II study. J Am Coll Cardiol. 2008;51(16):1543-52.

184. Ormiston JA, Abizaid A, Spertus J, Fajadet J, Mauri L, Schofer J, et al. Six-month results of the NEVO Res-Elution I (NEVO RES-I) trial: a randomized, multicenter comparison of the NEVO

sirolimus-eluting coronary stent with the TAXUS Liberte paclitaxel-eluting stent in de novo native coronary artery lesions. Circulation Cardiovascular interventions. 2010;3(6):556-64.

185. Larsen K, Cheng C, Tempel D, Parker S, Yazdani S, den Dekker WK, et al. Capture of circulatory endothelial progenitor cells and accelerated re-endothelialization of a bio-engineered stent in human ex vivo shunt and rabbit denudation model. Eur Heart J. 2012;33(1):120-8.

186. Inoue T, Sata M, Hikichi Y, Sohma R, Fukuda D, Uchida T, et al. Mobilization of CD34-positive bone marrow-derived cells after coronary stent implantation: impact on restenosis. Circulation. 2007;115(5):553-61.

187. Garg S, Duckers HJ, Serruys PW. Endothelial progenitor cell capture stents: will this technology find its niche in contemporary practice? Eur Heart J. 2010;31(9):1032-5.

188. Aoki J, Serruys PW, van Beusekom H, Ong AT, McFadden EP, Sianos G, et al. Endothelial progenitor cell capture by stents coated with antibody against CD34: the HEALING-FIM (Healthy Endothelial Accelerated Lining Inhibits Neointimal Growth-First In Man) Registry. J Am Coll Cardiol. 2005;45(10):1574-9.

189. Duckers HJ, Silber S, de Winter R, den Heijer P, Rensing B, Rau M, et al. Circulating endothelial progenitor cells predict angiographic and intravascular ultrasound outcome following percutaneous coronary interventions in the HEALING-II trial: evaluation of an endothelial progenitor cell capturing stent. EuroIntervention. 2007;3(1):67-75.

190. den Dekker WK, Houtgraaf JH, Onuma Y, Benit E, de Winter RJ, Wijns W, et al. Final results of the HEALING IIB trial to evaluate a bio-engineered CD34 antibody coated stent (GenousStent) designed to promote vascular healing by capture of circulating endothelial progenitor cells in CAD patients. Atherosclerosis. 2011;219(1):245-52.

191. Beijk MA, Klomp M, Verouden N, Van Geloven N, Koch K, Henriques JP, et al. Genous Endothelial progenitor cell capturing stent versus the Taxus Liberte stent in patients with de novo coronary lesions with a high-risk of coronary restenosis: a randomised, single-centre, pilot study. Eur Heart J. 2009;31(9):1055-64.

192. Beijk M. Two year follow-up of the endothelial progenitor cell capturing stent versus a Paclitaxel-eluting stent in patients with de novo coronary lesions with a high-risk of coronary restenosis: the single-centre randomised TRIAS study. Presented at EuroPCR 2009 19th-22nd May 2009.

193. Aoki J, Abizaid AC, Ong AT, Tsuchida K, Serruys PW. Serial assessment of tissue growth inside and outside the stent after implantation of drug-eluting stent in clinical trials. - Does delayed neointimal growth exist? EuroIntervention. 2005;1(3):235-55.

194. Silber S, Damman P, Klomp M, Beijk MA, Grisold M, Ribeiro EE, et al. Clinical results after coronary stenting with the Genous Bio-engineered R stent: 12-month outcomes of the e-HEALING (Healthy Endothelial Accelerated Lining Inhibits Neointimal Growth) worldwide registry. EuroIntervention. 2011;6(7):819-25.

195. Worthley SG, Abizaid A, Kirtane AJ, Simon DI, Windecker S, Brar S, et al. First-in-Human Evaluation of a Novel Polymer-Free Drug-Filled Stent: Angiographic, IVUS, OCT, and Clinical Outcomes From the RevElution Study. JACC Cardiovasc Interv. 2017;10(2):147-56.

196. Worthley S. RevElution: 12-months clinical outcomes with a novel polymer-free drug-filled stent. Presentation at EuroPCR 2017, Paris. 2017.

197. Costa R. Amazonia PAX (Minvasys) Programme Update. Presentation at Transcatheter Therapeutics, Oct 23 2012, Miami, USA. Available at tctmd.com.

198. Tector AJ, Schmahl TM, Janson B, Kallies JR, Johnson G. The internal mammary artery graft. Its longevity after coronary bypass. JAMA. 1981;246(19):2181-3.

199. Dimas AP, Arora RR, Whitlow PL, Hollman JL, Franco I, Raymond RE, et al. Percutaneous transluminal angioplasty involving internal mammary artery grafts. Am Heart J. 1991;122(2):423-9.

200. Abizaid A. The MIV VESTASYNC Polymer-Free Sirolimus-Eluting Stent Program (Micorporous Hydroxyapatite Surface). Presentation at Transcatheter Cardiovascular Therapeutics, San Francisco, September 21st 2009. Available online:

http://www.tctmd.com/txshow.aspx?tid=939088&id=84036&trid=938634. [Accessed October 10th 2009]. 2009.

201. Costa JR, Jr., Oliveira BA, Abizaid A, Costa R, Perin M, Abizaid A, et al. Clinical, angiographic, and intravascular ultrasound results of the VestSaync II trial. Catheterization and cardiovascular interventions : official journal of the Society for Cardiac Angiography & Interventions. 2014;84(7):1073-9.

202. Abizaid A. Two-year results form the VESTASync II randomized trial with a hydroxyapatite polymer-free sirollimus eluting stent. Presentation at Transcatheter Cardiovascular Therapeutics, San Francisco, November 8th 2011.

203. Stone GW, Abizaid A, Silber S, Dizon JM, Merkely B, Costa RA, et al. Prospective, Randomized, Multicenter Evaluation of a Polyethylene Terephthalate Micronet Mesh-Covered Stent (MGuard) in ST-Segment Elevation Myocardial Infarction: The MASTER Trial. J Am Coll Cardiol. 2012;60(19):1975-84.

204. Dudek D, Dziewierz A, Brener SJ, Abizaid A, Merkely B, Costa RA, et al. Mesh-covered embolic protection stent implantation in ST-segment-elevation myocardial infarction: final 1-year clinical and angiographic results from the MGUARD for acute ST elevation reperfusion trial. Circulation Cardiovascular interventions. 2015;8(2):e001484.

205. Sigwart U, Puel J, Mirkovitch V, Joffre F, Kappenberger L. Intravascular stents to prevent occlusion and restenosis after transluminal angioplasty. N Engl J Med. 1987;316(12):701-6.

206. Hirayama A, Kodama K, Adachi T, Nanto S, Ohara T, Tamai H, et al. Angiographic and clinical outcome of a new self-expanding intracoronary stent (RADIUS): results from multicenter experience in Japan. Catheterization and cardiovascular interventions : official journal of the Society for Cardiac Angiography & Interventions. 2000;49(4):401-7.

207. Konig A, Schiele TM, Rieber J, Theisen K, Mudra H, Klauss V. Stent design-related coronary artery remodeling and patterns of neointima formation following self-expanding and balloon-expandable stent implantation. Catheterization and cardiovascular interventions : official journal of the Society for Cardiac Angiography & Interventions. 2002;56(4):478-86.

208. Joner M, Nakazawa G, Bonsignore C, Acampado E, Steigerwald K, Merl S, et al. Histopathologic evaluation of nitinol self-expanding stents in an animal model of advanced atherosclerotic lesions. EuroIntervention. 2010;5(6):737-44.

209. Verheye S, Grube E, Ramcharitar S, Schofer JJ, Witzenbichler B, Kovac J, et al. First-in-man (FIM) study of the Stentys bifurcation stent--30 days results. EuroIntervention. 2009;4(5):566-71.

210. Laborde JC, Borenstein N, Behr L, Ramcharitar S. Stentys coronary bifurcation stent. EuroIntervention. 2007;3(1):162-5.

211. Ramcharitar S, Verheye S. The STENTYS(R) self-apposing stent in bifurcation lesions. EuroIntervention. 2010;6 Suppl J:J151-4.

212. Verheye S, Ramcharitar S, Grube E, Schofer JJ, Witzenbichler B, Kovac J, et al. Six-month clinical and angiographic results of the STENTYS(R) self-apposing stent in bifurcation lesions. EuroIntervention. 2011;7(5):580-7.

213. Latib A, Chieffo A. The Cappella Sideguard stent. EuroIntervention. 2010;6 Suppl J:J143-6.

214. Tanaka N, Martin JB, Tokunaga K, Abe T, Uchiyama Y, Hayabuchi N, et al. Conformity of carotid stents with vascular anatomy: evaluation in carotid models. AJNR Am J Neuroradiol. 2004;25(4):604-7.

215. Kaneda H, Ikeno F, Lyons J, Rezaee M, Yeung AC, Fitzgerald PJ. Long-term histopathologic and IVUS evaluations of a novel coiled sheet stent in porcine carotid arteries. Cardiovasc Intervent Radiol. 2006;29(3):413-9.

216. Virmani R, Kolodgie FD, Burke AP, Farb A, Schwartz SM. Lessons from sudden coronary death: a comprehensive morphological classification scheme for atherosclerotic lesions. Arterioscler Thromb Vasc Biol. 2000;20(5):1262-75.

217. Farb A, Burke AP, Kolodgie FD, Virmani R. Pathological mechanisms of fatal late coronary stent thrombosis in humans. Circulation. 2003;108(14):1701-6.

218. Joner M, Finn AV, Farb A, Mont EK, Kolodgie FD, Ladich E, et al. Pathology of drug-eluting stents in humans: delayed healing and late thrombotic risk. J Am Coll Cardiol. 2006;48(1):193-202.

219. Amoroso G, van Geuns RJ, Spaulding C, Manzo-Silberman S, Hauptmann KE, Spaargaren R, et al. Assessment of the safety and performance of the STENTYS self-expanding coronary stent in acute myocardial infarction: results from the APPOSITION I study. EuroIntervention. 2011;7(4):428-36.

220. van Geuns RJ, Tamburino C, Fajadet J, Vrolix M, Witzenbichler B, Eeckhout E, et al. Self-expanding versus balloon-expandable stents in acute myocardial infarction: results from the APPOSITION II study: self-expanding stents in ST-segment elevation myocardial infarction. JACC Cardiovasc Interv. 2012;5(12):1209-19.

221. Lu H, Grundeken MJ, Vos NS, AJJ IJ, van Geuns RJ, Wessely R, et al. Clinical outcomes with the STENTYS self-apposing coronary stent in patients presenting with ST-segment elevation myocardial infarction: two-year insights from the APPOSITION III (A Post-Market registry to assess the STENTYS self-exPanding COronary Stent In AcuTe MyocardIal InfarctiON) registry. EuroIntervention. 2017;13(5):e572-e7.

222. van Geuns RJ, Yetgin T, La Manna A, Tamburino C, Souteyrand G, Motreff P, et al. STENTYS Self-Apposing sirolimus-eluting stent in ST-segment elevation myocardial infarction: results from the randomised APPOSITION IV trial. EuroIntervention. 2016;11(11):e1267-74.

223. Granada JF, Pomeranz M, Heringes J, Odess I. vProtect luminal shield system. EuroIntervention. 2007;3(3):416-9.

224. Granada JF, Milewski K, Uribe MP, Moncada M, Fernandez A, Blanco G, et al. First clinical evaluation of a luminal self-expanding shield in patients with intermediate coronary lesions. EuroIntervention. 2011;7(7):780-8.

225. Ramcharitar S, Gonzalo N, van Geuns RJ, Garcia-Garcia HM, Wykrzykowska JJ, Ligthart JM, et al. First case of stenting of a vulnerable plaque in the SECRITT I trial-the dawn of a new era? Nat Rev Cardiol. 2009;6(5):374-8.

226. Wykrzykowska JJ, Diletti R, Gutierrez-Chico JL, van Geuns RJ, van der Giessen WJ, Ramcharitar S, et al. Plaque sealing and passivation with a mechanical self-expanding low outward force nitinol vShield device for the treatment of IVUS and OCT-derived thin cap fibroatheromas (TCFAs) in native coronary arteries: report of the pilot study vShield Evaluated at Cardiac hospital in Rotterdam for Investigation and Treatment of TCFA (SECRITT). EuroIntervention. 2012;8(8):945-54.

227. Abizaid A. CardioMind Stent. Presentation at Transcatheter Cardiovascular Therapeutics, San Francisco, 24th September 2009. Available online www.tctmd.com/txshow.aspx?tid=939038&id=81898&trid=938634. [Accessed 26th Jan 2010]. 2009.

228. Abizaid A. First Report of the Randomized CARE II Trial with a PLA-Based Sirolimus-Eluting "Micro-Stent". Presentation at Transcatheter Cardiovascular Therapeutics, Washington, USA, 22nd September 2010 2010.

229. Brener SJ, Murphy SA, Gibson CM, DiBattiste PM, Demopoulos LA, Cannon CP, et al. Efficacy and safety of multivessel percutaneous revascularization and tirofiban therapy in patients with acute coronary syndromes. The American journal of cardiology. 2002;90(6):631-3.

230. Byrne RA, Kastrati A, Massberg S, Wieczorek A, Laugwitz KL, Hadamitzky M, 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.

231. Jensen LO, Thayssen P, Hansen HS, Christiansen EH, Tilsted HH, Krusell LR, et al. Randomized comparison of everolimus-eluting and sirolimus-eluting stents in patients treated with percutaneous coronary intervention: the Scandinavian Organization for Randomized Trials with Clinical Outcome IV (SORT OUT IV). Circulation. 2012;125(10):1246-55.

232. Kaiser C, Galatius S, Erne P, Eberli F, Alber H, Rickli H, et al. Drug-eluting versus bare-metal stents in large coronary arteries. N Engl J Med. 2010;363(24):2310-9.

233. Kimura T, Morimoto T, Natsuaki M, Shiomi H, Igarashi K, Kadota K, et al. Comparison of everolimus-eluting and sirolimus-eluting coronary stents: 1-year outcomes from the Randomized

Evaluation of Sirolimus-eluting Versus Everolimus-eluting stent Trial (RESET). Circulation. 2012;126(10):1225-36.

234. Kim WJ, Lee SW, Park SW, Kim YH, Yun SC, Lee JY, et al. Randomized Comparison of Everolimus-Eluting Stent Versus Sirolimus-Eluting Stent Implantation for De Novo Coronary Artery Disease in Patients With Diabetes Mellitus (ESSENCE-DIABETES): Results From the ESSENCE-DIABETES Trial. Circulation. 2011;124(8):886-92.

235. Hofma SH, Brouwer J, Velders MA, Van't Hof AW, Smits PC, Quere M, et al. Second-Generation Everolimus-Eluting Stents Versus First-Generation Sirolimus-Eluting Stents in Acute Myocardial Infarction: 1-Year Results of the Randomized XAMI (XienceV Stent vs. Cypher Stent in Primary PCI for Acute Myocardial Infarction) Trial. J Am Coll Cardiol. 2012;60(5):381-7.

236. Hofma SH, Smits PC, Brouwer J, Velders MA, van 't Hof AW, Quere M, et al. Long-term follow-up of second-generation everolimus-eluting stents versus first-generation sirolimus-eluting stents in acute myocardial infarction: three-year results of the XAMI trial. EuroIntervention. 2015.

237. Meredith IT, Ormiston J, Whitbourn R, Kay IP, Muller D, Bonan R, et al. First-in-human study of the Endeavor ABT-578-eluting phosphorylcholine-encapsulated stent system in de novo native coronary artery lesions: Endeavor I Trial. EuroIntervention. 2005;1(2):157-64.

238. Meredith IT, Ormiston J, Whitbourn R, Kay IP, Muller D, Cutlip DE. Five-year clinical follow-up after implantation of the endeavor zotarolimus-eluting stent: ENDEAVOR I, first-in-human study. Catheter Cardiovasc Interv. 2009;74(7):989-95.

239. Fajadet J, Wijns W, Laarman GJ, Kuck KH, Ormiston J, Munzel T, et al. Randomized, double-blind, multicenter study of the Endeavor zotarolimus-eluting phosphorylcholine-encapsulated stent for treatment of native coronary artery lesions: clinical and angiographic results of the ENDEAVOR II trial. Circulation. 2006;114(8):798-806.

240. Fajadet J, Wijns W, Laarman GJ, Kuck KH, Ormiston J, Baldus S, et al. Long-term follow-up of the randomised controlled trial to evaluate the safety and efficacy of the zotarolimus-eluting driver coronary stent in de novo native coronary artery lesions: five year outcomes in the ENDEAVOR II study. Eurointervention.6(5):562-7.

241. Kandzari DE, Leon MB, Popma JJ, Fitzgerald PJ, O'Shaughnessy C, Ball MW, et al. Comparison of zotarolimus-eluting and sirolimus-eluting stents in patients with native coronary artery disease: a randomized controlled trial. J Am Coll Cardiol. 2006;48(12):2440-7.

242. Kirtane AJ, Leon MB, Ball MW, Bajwa HS, Sketch MH, Jr., Coleman PS, et al. The "final" 5-year follow-up from the ENDEAVOR IV trial comparing a zotarolimus-eluting stent with a paclitaxel-eluting stent. JACC Cardiovasc Interv. 2013;6(4):325-33.

243. Park DW, Kim YH, Yun SC, Kang SJ, Lee SW, Lee CW, et al. Comparison of zotarolimus-eluting stents with sirolimus- and paclitaxel-eluting stents for coronary revascularization: the ZEST (comparison of the efficacy and safety of zotarolimus-eluting stent with sirolimus-eluting and paclitaxel-eluting stent for coronary lesions) randomized trial. J Am Coll Cardiol. 2010;56(15):1187-95.

244. Camenzind E, Wijns W, Mauri L, Kurowski V, Parikh K, Gao R, et al. Stent thrombosis and major clinical events at 3 years after zotarolimus-eluting or sirolimus-eluting coronary stent implantation: a randomised, multicentre, open-label, controlled trial. Lancet. 2012;380(9851):1396-405.

245. Rasmussen K, Maeng M, Kaltoft A, Thayssen P, Kelbaek H, Tilsted HH, et al. Efficacy and safety of zotarolimus-eluting and sirolimus-eluting coronary stents in routine clinical care (SORT OUT III): a randomised controlled superiority trial. Lancet. 2010;375(9720):1090-9.

246. Maeng M, Tilsted HH, Jensen LO, Krusell LR, Kaltoft A, Kelbaek H, et al. Differential clinical outcomes after 1 year versus 5 years in a randomised comparison of zotarolimus-eluting and sirolimus-eluting coronary stents (the SORT OUT III study): a multicentre, open-label, randomised superiority trial. Lancet. 2014;383(9934):2047-56.

247. Meredith IT, Worthley S, Whitbourn R, Walters DL, McClean D, Horrigan M, et al. Clinical and Angiographic Results With the Next-Generation Resolute Stent System A Prospective, Multicenter, First-in-Human Trial. JACC Cardiovasc Interv. 2009;2(10):977-85.

248. Leon MB. Zotarolimus-eluting (RESOLUTE) stents 2011/2012: Emerging data from randomised trials and registries. Presentation at Transcatheter Cardiovascular Therapeutics, 7th

November 2011. Available online at http://www.tctmd.com/txshow.aspx?tid=1087388&id=109713&trid=1086298. [Accessed 20th November 2011].

249. Serruys PW, Silber S, Garg S, van Geuns RJ, Richardt G, Buszman PE, et al. Comparison of Zotarolimus-Eluting and Everolimus-Eluting Coronary Stents. N Engl J Med. 2010;363:123-35.

250. Serruys P, Silber S, Windecker S. Final 5-year outcomes from the randomised comparison of Zotarolimus-eluting stents with Everolimus-eluting stents in the RESOLUTE All Comers Trial. Presentation at EuroPCR 2014, Paris, France. 2014.

251. Yeung AC, Leon MB, Jain A, Tolleson TR, Spriggs DJ, Mc Laurin BT, et al. Clinical evaluation of the Resolute zotarolimus-eluting coronary stent system in the treatment of de novo lesions in native coronary arteries: the RESOLUTE US clinical trial. J Am Coll Cardiol. 2011;57(17):1778-83.

252. Massberg S, Byrne RA, Kastrati A, Schulz S, Pache J, Hausleiter J, et al. Polymer-Free Sirolimus- and Probucol-Eluting Versus New Generation Zotarolimus-Eluting Stents in Coronary Artery Disease: The Intracoronary Stenting and Angiographic Results: Test Efficacy of Sirolimus- and Probucol-Eluting Versus Zotarolimus-Eluting Stents (ISAR-TEST 5) Trial. Circulation. 2011;124(5):624-32.

253. Kufner S, Sorges J, Mehilli J, Cassese S, Repp J, Wiebe J, et al. Randomized Trial of Polymer-Free Sirolimus- and Probucol-Eluting Stents Versus Durable Polymer Zotarolimus-Eluting Stents: 5-Year Results of the ISAR-TEST-5 Trial. JACC Cardiovasc Interv. 2016;9(8):784-92.

254. von Birgelen C, Basalus MW, Tandjung K, van Houwelingen KG, Stoel MG, Louwerenburg JH, et al. A randomized controlled trial in second-generation zotarolimus-eluting Resolute stents versus everolimus-eluting Xience V stents in real-world patients: the TWENTE trial. J Am Coll Cardiol. 2012;59(15):1350-61.

255. von Birgelen C, van der Heijden LC, Basalus MW, Kok MM, Sen H, Louwerenburg HW, et al. Five-Year Outcome After Implantation of Zotarolimus- and Everolimus-Eluting Stents in

Randomized Trial Participants and Nonenrolled Eligible Patients: A Secondary Analysis of a Randomized Clinical Trial. JAMA Cardiol. 2017;2(3):268-76.

256. Ahn JM, Park DW, Kim YH, Song H, Cho YR, Kim WJ, et al. Comparison of resolute zotarolimus-eluting stents and sirolimus-eluting stents in patients with de novo long coronary artery lesions: a randomized LONG-DES IV trial. Circulation Cardiovascular interventions. 2012;5(5):633-40.

Table 1. Bare Metal Stents.

Company	Name	Stent material	Stent coating	Strut thickness (μm)
Abbott	Multi-link Vision	Cobalt Chromium, L605	None	81
Abbott	Multi-link Mini Vision	Cobalt Chromium, L605	None	81
Abbott	Multi-link Ultra	Stainless Steel, 316L	None	140
Alvimedica	Ephesos II	Stainless Steel, 316L	None	80
AMG	Arthos Pico	Cobalt Chromium, L605	None	65
B. Braun	Coroflex ® Blue Ultra	Cobalt Chromium, L605	None	50
B. Braun	Coroflex ® Blue Neo	Cobalt Chromium, L605	None	60
Biosensors	Gazelle	Stainless Steel, 316L	None	112

Biotronik	PRO-Kinetic Energy	Cobalt Chromium, L605	PROBIO (Amorphous Silicon Carbide Coating)	60
Boston Scientific	OMEGA	Platinum Chromium	None	81
CeloNova	Cobra PzF	Cobalt Chromium, L605	Polyzene®-F (“PzF™”)	71
CeloNova	Catania™	Cobalt Chromium, L605	Polyzene®-F (“PzF™”)	74
CID	Avantgarde	Cobalt Chromium, L605	Carbofilm	70
CID	Chrono	Cobalt Chromium, L605	Carbofilm	78
Clearstream	ClearFlex-X	Stainless Steel, 316L	No coating, surgace polishing	100
COMED (Lepu Medical)	Deimos	Stainless Steel, 316L	None	85
Elixir Medical	Core	Cobalt Chromium, L605	None	81
Eucatech	CC-flex ProActive	Cobalt Chromium, L605	Camouflage®	65

Eucatech	CC Flex	Cobalt Chromium, L605	None	65
Eucatech	Euca STSflex	Stainless Steel, 316L	Electropolished surface.	85
EuroCor	Genius MAGIC	Cobalt Chromium, L605	None	63.5
Hexacath	Titan2	Stainless Steel, 316L	Titanox™ - Titanium-Nitride-Oxide (TiNO).	70
Medtronic	Integrity	Cobalt Chromium, L605	None	91
Meril Life Science	Nexgen	Cobalt Chromium, L605	None	65
Minvasys	AmazoniaCroCo®	Cobalt Chromium, L605	None	73
MicroPort Medical	Mustang	Stainless Steel, 316L	None	102
MicroPort Medical	Tango	Cobalt Chromium, L605	None	86
MIV Therapeutics	Protea	Cobalt Chromium, L605	None	65

MIV Therapeutics	VestaCor	Cobalt Chromium, L605	Micro Porous Hydroxyapatite	65
OrbusNeich Medical	Azule	Cobalt Chromium, L605	None	81
OrbusNeich Medical	R stent	Stainless Steel, 316L	None	102
OrbusNeich Medical	Genous CoCr	Cobalt Chromium, L605	Anti-hCD34 antibody	81
OrbusNeich Medical	Genous	Stainless Steel, 316L	Anti-hCD34 antibody	102
Sahajanand Medical	Coronnium	Cobalt Chromium, L605	None	60
Sahajanand Medical	Millennium Matrix	Stainless Steel, 316L	None	80
Sino Medical	SUN	Stainless Steel, 316L	None	100
Svelte Medical	Acrobat	Cobalt Chromium, L605	None	81
Terumo	Tsunami	Stainless Steel, 316L	None	80
Terumo	Kaname	Cobalt Chromium, L605	None	80

Translumina	Yukon Choice 4	Stainless Steel, 316L	None	87
Translumina	Yukon CC	Cobalt Chromium, L605	None	79
Vascular Concepts	ProLink LP	Stainless Steel, 316L	None	95
Vascular Concepts	ProPass	Stainless Steel, 316L	Platinum coating	60-120

Table 2. Specificications or prior iterations of FDA approved DES

Stent	Drug (concentration)	Drug mechanism	Polymer	Polymer thickness (µm)	Release Kinetics (Days)	Metal	Geometry	Strut thickness (µm)
CYPHER	Sirolimus (140µg/cm^2)	Inhibits mTOR Cytostatic	Polyethelyne co-vinyl acetate & PBMA	12.6	80% (28)	SS	Closed cell	140
TAXUS Express	Paclitaxel (100µg/cm^2)	Microtubule inhibitor Cell cycle arrest in G0/G1 and G2/M	Poly(styrene-b-isobutylene-b-styrene)	16	<10% (28)	SS	Open cell	132

TAXUS Liberté	Paclitaxel (100µg/cm^2)	Microtubule inhibitor Cell cycle arrest in G0/G1 and G2/M	Poly(styrene-b-isobutylene-b-styrene)	16	<10% (28)	SS	Hybrid	97
TAXUS Element	Paclitaxel (100µg/cm^2)	Microtubule inhibitor Cell cycle arrest in G0/G1 and G2/M	Poly(styrene-b-isobutylene-b-styrene)	15	<10% (90)	PtCr	Open cell	81
Endeavor	Zotarolimus (100µg/cm^2)	Inhibits mTOR Cytostatic	Phosphorylcholine	4.1	95% (14)	CoCr	Open cell	91
Endeavor RESOLUTE	Zotarolimus (10µg/mm)	Inhibits mTOR Cytostatic	Biolinx	4.1	85% (60)	CoCr	Open cell	91

RESOLUTE Integrity	Zotarolimus (10µg/mm)	Inhibits mTOR Cytostatic	Biolinx	4.1	85% (60)	CoCr	Open cell	91
Xience V	Everolimus (100µg/cm^2)	Inhibits mTOR Cytostatic	PBMA & PVDF-HFP	7	80% (90)	CoCr	Open cell	81
PROMUS Element	Everolimus (100µg/cm^2)	Inhibits mTOR Cytostatic	PBMA & PVDF-HFP	7	80% (90)	PtCr	Open cell	81

SS, stainless steel; CoCr, cobalt chromium; PtCr, platinum chromium

PBMA, poly (n-butyl methacrylate) (PBMA); PVDF-HFP, poly (vinylidene fluoride-co-hexafluoropropylene)

Table 3. Summary of major randomized trials of the sirolimus eluting stent versus bare metal stents in different clinical settings.

Differences are non-significant unless indicated. Stent thrombosis defined per ARC definitions, unless indicated.

Trial/ Author	No. Of Patients	Clinical Setting	Follow-up Period (months)	In-stent late loss (SES vs.) (mm)	Binary in-stent restenosis (SES vs.) (%)	MACE (SES vs.) (%)	Death (SES vs.) (%)	MI (SES vs.) (%)	TLR (SES vs.) (%)	Definite/ Probable ST (SES vs.) (%)
RAVEL [17, 18]	SES (n=120) vs. BMS (n=118)	Elective Simple lesions	6*/12†	-0.01 vs. 0.80‡	0.0 vs. 26.6‡	5.8 vs. 28.8‡	1.7 vs. 1.7	3.3 vs.4.2	0.0 vs. 23.7§	0.0 vs. 1.7
			60	NA	NA	25.8 vs. 35.2§	12.1 vs. 7.1	8.9 vs. 6.9	10.3 vs. 26.0‡	1.7 vs. 2.5

C-SIRIUS [19]	SES (n=50) vs. BMS (n=50)	Canadian approval trial	8*/9†	0.12 1.02‡	vs.	0.0 vs. 45.5‡	4.0 vs. 18.0	0.0 vs. 0.0	2.0 vs. 4.0	4.0 vs. 18.0‖	2.0 vs. 2.0
E-SIRIUS [20]	SES (n=175) vs. BMS (n=177)	Elective Long lesions Small vessels Overlapped stents	8*/9†	0.20 1.05‡	vs.	3.9 vs. 41.7‡	8.0 vs. 22.6‡	1.1 vs. 0.6	4.6 vs. 2.3	4.0 vs. 20.9 ‡	1.1 vs. 0.0
SIRIUS [21, 22]	SES (n=163)	US Pivotal approval	8*/12†	0.17 1.00‡	vs.	3.2 vs. 35.4‡	8.3 vs. 23.2‡	1.3 vs. 0.8	3.0 vs. 4.2	4.9 vs. 20.2‡‖	0.4 vs. 1.1

	vs. BMS (n=159)	trial	60	NA	NA	20.3 vs. 33.5‡	8.4 vs. 8.4	6.2 vs. 6.5	9.4 vs. 24.2‡‖	1.2 vs. 1.8
DIABETES [23-25]	SES (n=80) vs. BMS (n=80)	Diabetes	9*/24†	0.09 vs.0.67‡	3.9 vs. 31.7‡	12.8 vs. 41.3‡§§	2.6 vs. 3.8§§	3.8 vs. 8.8	7.7 vs. 35.0‡‖	0.0 vs. 2.6
			60	NA	NA	15.6 vs. 45.5‡§§	3.9 vs. 5.2§§	5.2 vs. 10.4	7.8 vs. 37.7‡	2.6 vs. 3.9
DESSERT [26]	SES (n=75) vs. BMS (n=75)	Diabetes	8*/12†	0.14 vs. 0.96‡	3.6 vs. 38.8‡	22.1 vs. 44.0§	4.4 vs. 2.9	16.2 vs. 20.0	5.9 vs. 30.0‡	1.4 vs. 1.5

SCORPIUS [27]	SES (n=98) vs. BMS (n=102)	Diabetes	8*/12†	0.22 0.99‡	vs.	8.8 vs. 42.1‡	NA	5.3 vs. 4.1	4.3 vs. 5.2	5.3 vs. 21.1‡	2.1 vs. 2.1
Luis-S Díaz [28]	SES (n=60) vs. BMS (n=60)	STEMI	12	NA		NA	6.7 vs. 11.1	5.0 vs. 3.6	6.7 vs. 5.4 (Death + MI)	0.0 vs. 5.7#	3.4 vs. 1.8††
MISSION! [29, 30]	SES (n=158) vs. BMS (n=152)	STEMI	9*/12†	0.19 0.95‡	vs.	2.3 vs. 22.6‡	NA	1.3 vs. 2.6	5.7 vs. 9.2	3.2 vs. 11.2§	1.3 vs. 2.0
			60	NA		NA	NA	5.7 vs. 7.2	10.6 vs. 13.7	7.2 vs. 12.9	4.1 vs. 2.0

PASEO [31, 32]	SES (n=90) vs. BMS (n=90)	STEMI	12	NA	NA	11.1 vs.24.4§	3.3 vs. 6.7	4.4 vs. 6.7	3.3 vs. 14.4§	0.0 vs. 1.1**	
			48	NA	NA	36.7 vs. 21.1§	7.8 vs. 12.2	8.9 vs.13.3	5.6 vs. 21.1§	1.1 vs. 2.2**	
SESAMI [33, 34]	SES (n=160) vs. BMS (n=160)	STEMI	12	0.18 vs. 0.85§	9.3 vs. 21.3§	6.8 vs. 16.8§	1.8 vs. 4.3	1.8 vs. 1.8	4.3 vs. 11.2§‖	1.2 vs. 0.6**	
			60	NA	NA	19.0 vs. 26.0	7.0 vs. 8.0	3.9 vs. 3.2	8.0 vs. 15.0§‖	2.0 vs. 1.3**	
STRATEGY [35, 36]	SES (n=87) vs. BMS (n=88)	STEMI	8	0.22 vs. 0.60‡	7.5 vs. 28§	18.4 vs. 31.8§	8.0 vs. 9.1	6.9 vs. 9.1	5.7 vs. 20.5§	0.0 vs. 2.3††	
			60	NA	NA	29.9 vs. 43.2	18 vs. 16	22 vs. 25 (Death + MI)	10.3 vs. 26.1§#	7 vs. 8‡‡	

TYPHOON [37, 38]	SES (n=355) vs. BMS (n=357)	STEMI	8*/12†	0.14 vs. 0.83‡	3.5 vs. 20.3§	5.9 vs. 14.6‡	2.3 vs. 2.2	1.1 vs. 1.4	5.6 vs. 13.4‖‡	2.4 vs. 3.6	
			48	NA	NA	NA	4.0 vs. 6.4	4.8 vs. 4.0	7.2 vs. 15.2§	4.4 vs. 4.8	
Pache *et al* [39]	SES (n=250) vs. BMS (n=250)	Elective all-comers	6*/12†	0.14 vs. 0.94‡	8.3 vs. 25.5‡	13.6 vs. 22.4§#	2.8 vs. 2.0	4.6 vs. 2.8	7.2 vs. 18.8‡#	0.8 vs. 0.4	
PRISON II [40-42]	SES (n=100) vs. BMS (n=100)	Chronic Total Occlusion	6*/12†	0.05 vs. 1.09‡	7.0 vs. 36.0‡	5.0 vs. 24.0‡	0.0 vs. 1.0	2.0 vs. 3.0	5.0 vs. 21.0§	2.0 vs. 0.0‡‡	
			60	0.19 vs. 0.51	NA	12.0 vs. 36.0‡	5.0 vs. 5.0	8.0 vs. 7.0	12.0 vs. 30.0§	8.0 vs. 3.0‡‡	

GISSOC II-GISE [43]	SES (n=78) vs. BMS (n=74)	Chronic Total Occlusion	8*/24†	0.20 vs. 1.57‡		8.2 vs. 67.7‡	17.6 vs. 50.0‡	2.7 vs. 1.3	2.7 vs. 5.1	8.1 vs. 44.9‡	1.4 vs. 1.3
SES-SMART [44, 45]	SES (n=129) vs. BMS (n=128)	Small vessels	8	0.16 vs. 0.90‡		4.9 vs. 49.1‡	9.3 vs. 31.3‡ ¶‖	0.0 vs. 1.6	1.6 vs. 7.8§	7.0 vs. 21.1§‖	0.8 vs. 3.1††
			24	NA		NA	12.6 vs. 33.1‡¶‖	0.8 vs. 3.9	1.6 vs. 10.2§	7.9 vs. 29.9‡‖	0.8 vs. 3.1††
SCANDSTENT [49, 50]	SES (n=163) vs. BMS (n=159)	Complex disease	6*/7†	0.02 vs. 1.01‡		2.0 vs. 30.6‡	4.3 vs. 29.9‡	0.6 vs. 0.6	1.2 vs. 3.1	2.5 vs. 29.3‡‖	0.6 vs. 3.8
			36	NA		NA	12.3 vs..37.6‡	5.6 vs. 1.9	3.7 vs. 9.6	4.9 vs. 33.8‡‖	1.2 vs. 4.4

RRISC [47, 48]	SES (n=38) vs. BMS (n=37)	Saphenous vein grafts	6	0.38 vs. 0.79§	11.3 vs. 30.6§	15.8 vs. 29.7	2.6 vs. 0.0	2.6 vs. 0.0	5.3 vs. 21.6§	0.0 vs. 0.0
			32	NA	NA	57.9 vs. 40.5	28.9 vs. 0.0‡	18.4 vs. 5.4	23.7 vs. 29.7	5.0 vs. 0.0**
BASKET PROVE [46]	SES (n=775) vs. BMS (765)	Large vessels	24	-	-	7.9 vs. 12.9‡#	3.6 vs. 4.4	0.9 vs. 2.6	4.3 vs. 10.3#‡	0.8 vs. 1.2

*Angiographic follow-up; †Clinical follow-up

‡ P<0.001; § P<0.05

‖Ischemia driven ¶ Major Adverse Cardiovascular and Cerebrovascular events

Target vessel revascularization

** Definite ST only, †† Protocol defined ST, ‡‡ Definite, probable and possible, §§ Cardiac

STEMI, ST-elevation MI; ST, stent thrombosis; MACE, major adverse cardiovascular events (a composite of death, MI and target lesion revascularization); BMS, bare metal stent; SES, sirolimus-eluting stent; NA, not available;

Table 4. Summary of major randomized trials of paclitaxel eluting stent versus bare metal stents in different clinical settings. Differences are non-significant unless stated.

Stent thrombosis as per ARC definition, unless indicated.

Trial/ Author	No. Of Patients	Clinical Setting	Follow-up Period (months)	In-stent late loss (PES vs.) (mm)	Binary in-stent restenosis (PES vs.) (%)	MACE (PES vs.) (%)	Death (PES vs.) (%)	MI (PES vs.) (%)	TLR (PES vs.) (%)	Definite/ Probable ST (PES vs.) (%)
TAXUS-I [62]	PES (n=31) vs. BMS (n=30)	Simple lesions	6*/12†	0.36vs. 0.71	0.0 vs. 10.4	3.3 vs. 10.0§§	0.0 vs. 0.0	0.0 vs. 0.0 (Q-wave only)	0.0 vs. 10.0#	0.0 vs. 0.0
TAXUS-II Slow release	PES (n=131)	Simple lesions	6*/12†	0.31 vs.0.79‡	2.3 vs. 17.9‡	10.9 vs. 22.0§‡‡	0.0 vs. 1.5	2.4 vs. 5.3	4.7 vs. 12.9§	0.7 vs. 0.0††

[63, 64]	vs. BMS (n=136)		60	NA	NA	20.4 vs. 27.6¶§§	2.4 vs. 1.5¶	4.7 vs. 7.1	10.3 vs. 18.4§	2.7 vs. 0.8††		
TAXUS-II Moderate release [63, 64]	PES (n=135) vs. BMS (n=134)	Simple lesions	6*/12†	0.30 vs. 0.77‡	4.7 vs. 20.2‡	9.9 vs. 21.4§‡‡	0.0 vs. 0.0	3.8 vs. 5.4	3.8 vs. 16.0§	0.7 vs. 0.0††		
			60	NA	NA	15.1 vs. 27.6§¶§§	1.6 vs. 1.5¶	5.3 vs. 7.1	4.5 vs. 18.4‡	1.7 vs. 0.8††		
TAXUS-IV [65, 66]	PES (n=662) vs. BMS (n=652)	Pivotal approval trial	9	0.39 vs. 0.92‡	5.5 vs. 24.4‡	8.5 vs. 15.0‡‖¶	2.4 vs. 2.2	3.5 vs. 3.7	3.0 vs. 11.3‡‖	0.8 vs. 1.1		
			60	NA	NA	24.0 vs. 32.0‡¶§§	10.0 vs. 11.2	7.2 vs. 7.4	9.1 vs. 20.5‡‖	2.1 vs. 2.3		

TAXUS-V [67, 68]	PES (n=577) vs. BMS (n=579)	Complex lesions	9	0.49 vs. 0.90‡		13.7 vs. 31.9‡	15.0 vs. 21.2§‖¶		0.5 vs. 0.9¶		5.4 vs. 4.6	8.6 vs. 15.7§‖		0.7 vs. 0.7††
			60	NA		NA	NA		10.2 vs. 8.5		9.3 vs. 5.6§	17.0 vs. 23.2§‖		2.4 vs. 1.5§
TAXUS-VI [69, 70]	PES (n=219) vs. BMS (n=227)	Long complex lesions	9	0.39 vs. 0.99‡		9.1 vs. 32.9‡	16.4 vs. 22.5		0.0 vs. 0.9¶		8.2 vs. 6.2	6.8 vs. 18.9‡		0.5 vs. 0.9††
			60	NA		NA	31.3 vs. 27.8¶‡‡		2.8 vs. 3.2¶		11.2 vs. 8.2	14.6 vs. 21.4§		0.9 vs. 0.9††
HORIZONS-AMI [71, 72]	PES (n=2257) vs. BMS (n=749)	STEMI	13*/12†	0.41 vs. 0.82‡		8.2 vs. 21.0‡	8.0 vs. 7.9‖‖		3.5 vs. 3.5		3.6 vs. 4.4	4.3 vs. 7.2‖§		3.1 vs. 3.3
			36	NA		NA	13.6 vs. 12.9‖‖		5.6 vs. 6.6		7.0 vs. 6.6	9.4 vs. 15.1‖‡		4.8 vs. 4.3

PASEO [31, 32]	PES (n=90) vs. BMS (n=90)	STEMI	12	NA	NA	11.1 vs. 24.4§	4.4 vs. 6.7	3.3 vs. 6.7	4.4 vs. 14.4§	1.1 vs. 1.1**
			48	NA	NA	21.1 vs. 36.7§	8.9 vs. 12.2	7.8 vs. 13.3	6.7 vs. 21.1§	1.1 vs. 2.2**
PASSION [74, 75]	PES (n=310) vs. BMS (n=309)	STEMI	12	NA	NA	8.8 vs. 12.8¶‖	4.6 vs. 6.5	1.7 vs. 2.0	5.3 vs. 7.8	1.4 vs. 2.3
			60	NA	NA	18.3 vs. 22.0¶‖	8.9 vs. 11.5¶	6.5 vs. 4.3	7.3 vs. 10.5	3.9 vs. 3.4
Erglis *et al* [73]	PES (n=53) vs. BMS (n=50)	UPLMS	6	0.22 vs. 0.60‡	5.7 vs. 22.0§	13.2 vs. 30.0	1.9 vs. 2.0	9.4 vs. 14.0	1.9 vs. 16.0§	0.0 vs. 0.0

*Angiographic follow-up, †Clinical follow-up, ‡ P<0.001, § P<0.05, ‖Ischemia driven, ¶ Cardiac death, #Percutaneous revascularization only, **Definite ST only, ††Protocol defined ST, ‡‡ Major adverse cardiovascular events a composite of death, MI and target vessel revascularization, §§ Major adverse cardiovascular events a composite of death, MI, target vessel revascularization and stent thrombosis, ‖‖Major adverse cardiovascular events a composite of death, MI, stroke and stent thrombosis

UPLMS, unprotected left main stem; STEMI, ST-elevation MI; ST, stent thrombosis; MACE, major adverse cardiovascular events (a composite of death, MI and target lesion revascularization) BMS, bare metal stent; PES, paclitaxel-eluting stent; NA, not available; TVR, target vessel revascularization

Table 5: Rates of death, myocardial infarction and target lesion revascularization from meta-analyses of drug eluting stents compared to bare metal stents. Differences non-significant unless indicated.

Reference	Number of patients	Longest Follow-up (years)	Death (DES vs. BMS)	MI (DES vs. BMS)	TLR (DES vs. BMS)
SES vs. BMS					
Stettler et al[57]	8,646 (4,643 SES, 4,003 BMS)	4	HR 1.0	HR 0.81*****	HR 0.3†
Stone *et al*[55]	1,748 (878 SES, 870 BMS)	4	6.7% vs. 5.3%	6.4% vs. 6.2%	7.8% vs. 23.6%†
Kastrati et al[229]	4,958 (2,486 SES, 2,472 BMS)	5	6.0% vs. 5.9%	9.7% vs. 10.2%‡	HR 0.43§†
PES vs. BMS					

Stettler et al[57]	8,330 (4,327 PES, 4,003 BMS)	4	HR 1.03	HR 1.0	HR 0.42†
Stone *et al*[55]	3,513 (1,755 PES, 1,758 BMS)	4	6.1% vs. 6.6%	7.0% vs. 6.3%	10.1% vs. 20.0%†
Other					
Stettler et al[57]	8,970 (4,643 SES, 4,327 PES)	4	HR 0.96	HR 0.83*****	HR 0.70*****
Kirtane et al[58] [on-label]	9,470 (4867 DES, 4603 BMS)	5	HR 1.05	HR 1.03	HR 0.54†
Kirtane et al[58] [off-label]			HR 0.84	HR 0.83	HR 0.42†

*****p<0.05 †p<0.001 ‡Combined death or MI **§**Combined death, MI or TVR

MI, myocardial infarction; BMS, bare metal stent; SES, sirolimus eluting stent; PES, paclitaxel eluting stent; DES, drug eluting stent; HR, hazard ratio; TLR, target lesion revascularization; TVR, target vessel revascularization

Table 6. Summary of major randomized trials (>100 patients in each group) comparing the sirolimus-eluting stent to the paclitaxel eluting stents in different clinical settings. Differences are non-significant unless indicated. Stent thrombosis ARC definition unless indicated.

Trial/ Author	No. Of Patients	Clinical Setting	Follow-up Period (months)	In-stent late loss (SES vs. PES) (mm)	Angiographic in-stent restenosis (SES vs. PES) (%)	MACE (SES vs. PES) (%)	Death (SES vs. PES) (%)	MI (SES vs. PES) (%)	TLR (SES vs. PES) (%)	Definite/ Probable ST (SES vs. PES) (%)
DES-DIABETES	SES (n=200)	Diabetics	9	0.13 vs. 0.53‡	3.4 vs. 18.2‡	2.0 vs. 8.0§	0.0 vs. 0.5	0.5 vs. 0.5	2.0 vs. 7.5§	0.5 vs. 0.0

[82, 83]	vs. PES (n=200)		24	NA	NA	3.5 vs. 12.5§	0.0 vs. 1.5	0.5 vs. 1.0	3.5 vs. 11.0§	1.0 vs. 0.0
ISAR-DIABETES [84]	SES (n=125) vs. PES (n=125)	Diabetics	9	0.19 vs. 0.46‡	4.9 vs. 13.6§	NA	3.2 vs. 4.8	4.0 vs. 2.4	6.4 vs. 12.0	0.0 vs. 0.1
REALITY [85]	SES (n=701) vs. PES (n=685)	Unselected	8*/12†	0.09 vs. 0.31‡	7.0 vs. 8.3	10.7 vs. 11.4‖	2.3 vs. 1.3	5.1 vs. 6.0	6.0 vs. 6.1	0.7 vs. 1.9**

SIRTAX [86, 87, 100]	SES (N=503) vs. PES (N=509)	Unselected	8*/9†	0.12 vs. 0.25‡	3.2 vs. 7.5§	6.2 vs. 10.8§¶‖ –	1.0 vs. 2.2	2.8 vs. 3.5	4.8 vs. 8.3§¶	2.0 vs. 1.8
			60	0.30 vs. 0.37	NA	21.3 vs. 24.2	10.9 vs. 9.4	6.6 vs. 6.9	14.9 vs. 17.9	4.6 vs. 4.1
			120	NA	NA	33.7 vs. 33.8	25.0 vs. 23.4	9.0 vs. 10.4	19.2 vs. 22.8	5.6 vs. 5.6††
SORT-OUT II [88, 99]	SES (n=1065) vs. PES (n=1065)	Unselected	18	NA	NA	10.0 vs. 11.6‖#	3.8 vs. 3.9	4.2 vs. 5.1	4.5 vs. 5.9	2.6 vs. 2.8
			120	NA	NA	32.5 vs. 33.1‖#	27.4 vs. 26.3	18.1 vs. 18.1	14.8 vs. 16.4	5.3 vs. 6.0††
TAXI [89, 90]	SES (n=102)	Unselected	6	NA	NA	6.0 vs. 4.0	0.0 vs. 0.0	2.0 vs. 3.0	2.0 vs. 1.0	1.0 vs. 0.0**

	vs. PES (n=100)		36	NA	NA	17 vs. 11	7.0 vs. 3.0	3.0 vs. 6.9	5.0 vs. 1.0	2.0 vs. 2.0**
PROSIT [91, 92]	SES (n=154) vs. PES (n=154)	STEMI	6*/12†	0.19 vs. 0.43§	5.0 vs. 12.0	5.8 vs. 11.7 (+ST)	3.2 vs. 5.8	0.0 vs. 1.9	2.6 vs. 6.5	0.0 vs. 1.3**
			36	NA	NA	12.3 vs. 18.8# (+ST)	6.5 vs. 10.4	2.6 vs. 3.9	3.9 vs. 8.4#	0.6 vs. 1.9
ISAR-LEFT MAIN [93]	SES (n=305) vs. PES (n=302)	UPLMS	6-8*/24†	NA	19.4 vs. 16.0	20.6 vs. 21.3	8.7 vs. 10.4	4.6 vs. 5.4	10.7 vs. 9.2	1.0 vs. 0.3

LONG-DES II [94]	SES (n=250) vs. PES (n=250)	Long lesions	6	0.09 vs. 0.45‡	2.9 vs. 11.7§	12.0 vs. 17.2	0.8 vs. 0.0	8.8 vs. 10.8	2.4 vs. 7.2§	0.8 vs. 0.0**
ISAR-SMART 3 [95]	SES (n=180) vs. PES (n=180)	Small vessels, non-diabetic	6-8*/12†	0.25 vs. 0.56‡	8.0 vs. 14.9§	5.0 vs. 5.6 (death/MI)	1.7 vs. 2.2	3.9 vs. 3.3	6.6 vs. 14.7§	0.0 vs. 0.0 (30 days)

ISAR-DESIRE [96]	SES (n=100) vs. PES (n=100)	In-stent restenosis	6	0.10 vs. 0.26§	11.0 vs. 18.5	NA	2.0 vs. 1.0	1.0 vs. 2.0	8.0 vs. 19.0#§	NA	
ISAR-DESIRE 2 [97]	SES (n=225) vs. PES (n=225)	SES In-stent restenosis	6-8*/12†	0.40 vs. 0.38	19.0 vs. 20.6	20.4 vs. 19.6	3.4 vs. 4.5	2.7 vs. 1.8	16.6 vs. 14.6	0.4 vs. 0.4††	

*Angiographic follow-up

†Clinical follow-up

‡ P<0.001

§ P<0.05

‖Cardiac death

¶ Ischemia driven

Target vessel revascularization

**Protocol defined ST

††Definite only

UPLMS, unprotected left main stem; STEMI, ST-elevation MI; ST, stent thrombosis; MACE, major adverse cardiovascular events (a composite of death, MI and target lesion revascularization) BMS, bare metal stent; PES, paclitaxel-eluting stent; SES, sirolimus eluting stent; NA, not available

Table 7. The most prominent randomized trials comparing the 2nd generation everolimus-eluting stent to the bare-metal stent and to the paclitaxel-eluting stent. Differences non-significant unless indicated.

Study	No. of Patients	Follow-up (months)	In-stent late lumen loss (EES vs.) (mm)	Angiographic in-stent restenosis (EES vs.) (%)	Death (EES vs.) (%)	Myocardial infarction (EES vs.) (%)	Target lesion revascularization (EES vs.) (%)	MACE (EES vs.) (%)	Definite/ Probable ST (EES vs.) (%)
SPIRIT I [101, 102]	EES (n=27) vs. BMS (n=29)	6	0.10 vs.0.87‡	0.0 vs. 25.9§	0.0 vs. 0.0	3.8 vs. 0.0	3.8 vs. 21.4‖	7.7 vs. 21.4	0.0 vs. 0.0
		60	-	-	0.0 vs. 7.4	8.3 vs. 0.0	8.3 vs. 28.0‖	16.7 vs. 28.0	0.0 vs. 0.0
SPIRIT II [108, 113]	EES (n=223) vs.	6	0.11 vs. 0.36‡	1.3 vs. 3.5	0.0 vs. 1.3	0.9 vs. 3.9	2.7 vs. 6.5	2.7 vs. 6.5	0.5 vs. 1.3

	PES (n=77)	60	-	-	1.5 vs. 7.3§¶	4.8 vs. 11.4 (cardiac death +MI)	4.7 vs. 9.4‖	8.0 vs. 18.1‖§	0.9 vs. 2.8
SPIRIT III [114, 115]	EES (n=669) vs.	8* / 12†	0.16 vs. 0.30§	2.3 vs. 5.7	1.2 vs. 1.2	2.8 vs. 4.1	3.4 vs. 5.6	6.0 vs. 10.3§	1.1 vs. 0.6
	PES (n=333)	60	-	-	5.9 vs. 10.1§	4.4 vs. 6.3	8.7 vs. 12.3‖	13.7 vs. 20.2§	1.4 vs. 1.6
SPIRIT IV [116, 118]	EES (n=2458) vs. PES (n=1229)	12	-	-	1.0 vs. 1.3	1.9 vs. 3.1§	2.5 vs. 4.6‖‡	4.2 vs. 6.9‡‖	0.3 vs. 1.1§
		36	-	-	3.2 vs. 5.1§	3.0 vs. 4.6§	6.2 vs. 7.8‖	-	0.6 vs. 1.6§
SPIRIT V [119]	EES (n=2663)	12	-	-	1.7	3.5	1.9	5.3	0.65
		24	-	-	3.0	4.4	3.0	7.5	0.79

COMPARE [120, 122]	EES (n=897) vs. PES (n=903)	12	-	-		2.0 vs. 1.6	2.8 vs. 5.3§	2.0 vs. 5.3‡	6.2 vs. 9.1§	0.7 vs. 2.6§
		60	-	-		9.0 vs. 10.3	7.0 vs. 11.5‡	5.0 vs. 8.3‖§	18.4 vs. 25.1‡	3.1 vs. 5.9‡
EXECUTIVE [123]	EES (n=91) vs. PES (n=77)	9*	0.01 vs. 0.22§	-		-	-	-	-	-
EXAMINATION [104, 105]	EES (n=737) vs. BMS (n=732)	12				3.2 vs. 2.8¶	1.4 vs. 2.1	2.2 vs. 5.1‡	12.0 vs. 14.4	0.9 vs. 2.6§
		60			–	6.3 vs. 7.4¶	4.7 vs. 3.6	4.3 vs. 7.2‡	21.2 vs. 25.7§	2.0 vs. 3.1
XIMA[103]	EES (n=399) vs. BMS (n=401)	12	-	-		8.5 vs. 7.2	4.3 vs. 8.7‡	2.0 vs. 7.0‡#	14.3 vs. 18.7$	-
BASKET PROVE[46]	EES (n=774) vs.	24	-	-		3.2 vs. 4.4	1.7 vs. 2.6	3.7 vs. 10.3‡#	7.6 vs. 12.9‡#	0.6 vs. 1.2

	BMS (n=765)										
RENAL-DES[106]	EES (n=257) vs. BMS (n=255)	12	-	-	-	-	2.7 vs. 11.4‡‖#	-	-		
TUXEDO[124]	EES (n=914) vs. PES (n=916)	24	-	-	3.2% vs. 3.4%	1.6% vs. 3.5%§	1.9% vs. 3.7%§	4.9% vs. 7.0%	0.2% vs. 2.2%‡		

*Angiographic follow-up

†Clinical follow-up

‡ P<0.001

§ P<0.05

‖Ischemia driven

¶ Cardiac death

Target vessel revascularization

$ MACE, a composite of death, MI, stroke, target vessel revascularization and major haemorrhage

ST, stent thrombosis; MACE, major adverse cardiovascular events (a composite of death, MI and target lesion revascularization)

BMS, bare metal stent; PES, paclitaxel-eluting stent

Table 8. The most prominent randomized trials and registries comparing the 2nd generation everolimus eluting stent to the sirolimus-eluting stent. Differences non-significant unless indicated.

Study	No. of Patients	Follow-up – (months)	In-stent late lumen loss (EES vs.) (mm)	Angiographic in-stent restenosis (EES vs.) (%)	Death (EES vs.) (%)	Myocardial infarction (EES vs.) (%)	Target lesion revascularization (EES vs.) (%)	MACE (EES vs.) (%)	Definite/ Probable ST (EES vs.) (%)
EXCELLENT [128]	EES (n=1029) vs. SES (n=343)	9*/12†	0.19 vs. 0.15	1.9 vs. 1.1	-	1.3 vs. 1.4	2.4 vs. 1.7	-	0.4 vs. 0.8
ISAR-TEST 4	EES (n=652)	6-8*/12†	0.14 vs. 0.17	10.1 vs. 13.4	4.5 vs. 5.0	-	8.1 vs. 10.7	13.6 vs. 15.2¶	1.4 vs. 1.6

[130, 230]	vs. SES (n=652)	24*/60†	0.29 vs. 0.31	12.7 vs. 16.9§	14.8 vs. 17.9	4.1 vs. 5.1#	12.6 vs. 15.9	28.4 vs. 33.1	1.4 vs. 2.4
SORT OUT IV[132, 231]	EES (n=1390) vs.	9	-	-	1.9 vs. 1.4¶	1.1 vs. 1.4	1.4 vs. 1.7	4.9 vs. 5.2**††§	0.9 vs. 0.9
	SES (n=1384)	60	-	-	4.6 vs. 4.7¶	4.1 vs. 5.6	4.8 vs. 7.0§	14.0 vs. 17.4††§	0.9 vs. 2.3§
BASKET PROVE[232]	EES (n=774) vs. SES (n=774)	24	-	-	3.2 vs. 3.6	1.7 vs. 0.9	3.7 vs. 4.3#	7.6 vs. 7.9#	0.6 vs. 0.8
RESET[134, 233]	EES (n=1597) vs.	8-12*/12†	0.16 vs. 0.14	-	1.9 vs. 2.5	3.0 vs. 3.5	4.3 vs. 5.0		0.39 vs. 0.38
	SES (n=1600)	36	-	-	7.0 vs. 7.8	4.2 vs. 4.5	6.6 vs. 7.9	26.4 vs. 28.6	0.7 vs. 0.8

LONG-DES III[135]	EES (n=225) vs. SES (n=225)	9*/12†	0.22 vs. 0.18	3.9 vs. 2.7	0.4 vs. 0.0	9.8 vs. 8.0	3.1 vs. 2.2	14.3 vs. 10.2	0.4 vs. 0.0
ESSENCE-DIABETES[234]	EES (n=149) vs. SES (n=151)	8*/12†	0.11 vs. 0.20	0.0 vs. 4.7§	1.3 vs. 3.3	0 vs. 1.3	0.7 vs. 2.6‖	2.0 vs. 5.3	0.7 vs. 0.7
LESSON[140]	EES (n=1342) vs. SES (n=1342)	36	-	-	6.0 vs. 6.5	3.3 vs. 5.0§	4.6 vs. 6.0	14.9 vs. 18#	2.5 vs. 4.0§
X-AMI[235, 236]	EES (n=404) vs.	12	-	-	2.0 vs. 3.2	0.5 vs. 1.4	1.2 vs. 0.9	4.0 vs. 7.7¶#**§	1.2 vs. 2.7
	SES (n=221)	36	-	-	3.8 vs. 5.5	2.5 vs. 3.2	2.5 vs. 1.8	8.0 vs. 10.5¶#	2.3 vs. 3.2

RACES-MI[139]	EES (n=250) vs. SES (n=250)	36	-	-	4.4 vs. 5.6¶	6.4 vs. 10	4.8 vs. 4.8#	16 vs. 20.8‡‡	1.6 vs. 5.2§

*Angiographic follow-up

†Clinical follow-up

‡ P<0.001

§ P<0.05

‖Ischemia driven

¶ Cardiac death; # Target vessel

**Non-inferiority

†† MACE, a composite of cardiac death, myocardial infarction, definite stent thrombosis and target vessel revascularization

‡‡ MACE, a composite of cardiac death, myocardial infarction, definite/probable stent thrombosis and target vessel revascularization

ST, stent thrombosis; MACE, major adverse cardiovascular events (a composite of death, MI and target lesion revascularization)

SES, sirolimus-eluting stent

Table 9. The most prominent randomized trials and registries of the 2nd generation Endeavor zotarolimus eluting stent. Differences non-significant unless indicated.

Study	No. of Patients	Follow up (months)	In-stent late lumen loss (E-ZES vs.) (mm)	Angiographic in-stent restenosis (E-ZES vs.) (%)	Death (E-ZES vs.) (%)	Myocardial infarction (E-ZES vs.) (%)	Target lesion revascularization (E-ZES vs.) (%)	TVF (E-ZES vs.) (%)	Definite/ Probable ST (E-ZES vs.) (%)
Randomized Trials									
Endeavor I [237, 238]	E-ZES N=100	12	0.61	5.4	0	1.0	2.0	2.0	1.0
		60	-	-	4.1	1.0	3.1	5.2	1.0
Endeavor II [239, 240]	E-ZES (n=598)	9	0.61 vs. 1.03‡	9.4 vs. 33.5‡	1.2 vs.0.5	2.7 vs. 3.9	4.6 vs. 11.8‡‖	7.9 vs. 15.1‡	0.5 vs. 1.2

Study	No. of Patients	Follow up (months)	In-stent late lumen loss (E-ZES vs.) (mm)	Angiographic in-stent restenosis (E-ZES vs.) (%)	Death (E-ZES vs.) (%)	Myocardial infarction (E-ZES vs.) (%)	Target lesion revascularization (E-ZES vs.) (%)	TVF (E-ZES vs.) (%)	Definite/ Probable ST (E-ZES vs.) (%)
	vs. BMS (n=599)	60	-	-	6.2 vs. 7.6	3.8 vs. 4.8	7.5 vs. 16.3‡‖	15.4 vs. 24.4‡	0.9 vs.1.7
Endeavor III [153, 241]	E-ZES (n=323)	8* / 9†	0.60 vs.0.15‡	9.2 vs. 2.1§	0.6 vs. 0.0	0.6 vs. 3.5§	6.3 vs. 3.5‖	12.0 vs. 11.5	0.0 vs. 0.0
	vs. SES (n=113)	60	-	-	5.2 vs. 13.0§	1.0 vs. 4.6§	8.1 vs. 6.5‖	17.9 vs. 18.5	0.7 vs. 0.9
Endeavor IV [159, 242]	E-ZES (n=773) vs. PES (n=775)	8* / 12†	0.67 vs.0.42‡	13.3 vs. 6.7	1.1 vs. 1.1	1.6 vs. 2.7	4.5 vs. 3.2‖	6.6 vs. 7.2#	0.9 vs. 0.1
		60	-	-	10.0 vs. 9.1	2.6 vs. 6.0§	7.7 vs. 8.6‖	17.2 vs. 21.1	1.4 vs. 1.9

Study	No. of Patients	Follow up (months)	In-stent late lumen loss (E-ZES vs.) (mm)	Angiographic in-stent restenosis (E-ZES vs.) (%)	Death (E-ZES vs.) (%)	Myocardial infarction (E-ZES vs.) (%)	Target lesion revascularization (E-ZES vs.) (%)	TVF (E-ZES vs.) (%)	Definite/ Probable ST (E-ZES vs.) (%)
ZEST[243]	E-ZES (n=880) vs. SES (n=880) vs. PES (n=880)	9* / 12†	0.53 vs. 0.15 vs. 0.46	9.6 vs. 1.8 vs. 10.9	0.7 vs. 0.8 vs. 1.1	5.3 vs. 6.3 vs. 7.0	4.9 vs. 1.4 vs. 7.5‡‖	-	0.7 vs. 0.0 vs. 0.8§

Study	No. of Patients	Follow up (months)	In-stent late lumen loss (E-ZES vs.) (mm)	Angiographic in-stent restenosis (E-ZES vs.) (%)	Death (E-ZES vs.) (%)	Myocardial infarction (E-ZES vs.) (%)	Target lesion revascularization (E-ZES vs.) (%)	TVF (E-ZES vs.) (%)	Definite/ Probable ST (E-ZES vs.) (%)
PROTECT[244]	E-ZES (n=4357) vs. SES (n=4352)	36			4.2 vs. 4.4	4.2 vs. 4.8	5.6 vs. 3.5‡	-	1.4 vs.. 1.8
SORT-OUT	E-ZES	9	-	-	2.0 vs. 2.0	1.4 vs. 0.5§	4.0 vs. 1.0‡‖	-	1.1 vs. 0.2§¶

Study	No. of Patients	Follow up (months)	In-stent late lumen loss (E-ZES vs.) (mm)	Angiographic in-stent restenosis (E-ZES vs.) (%)	Death (E-ZES vs.) (%)	Myocardial infarction (E-ZES vs.) (%)	Target lesion revascularization (E-ZES vs.) (%)	TVF (E-ZES vs.) (%)	Definite/ Probable ST (E-ZES vs.) (%)
III[245] [246]	(n=1162) vs. SES (n=1170)	60	-	-	13.2 vs. 11.8	5.5 vs. 5.7	7.6 vs. 6.0‖	-	1.2 vs. 2.1¶

*Angiographic follow-up

†Clinical follow-up

‡ P<0.001

§ P<0.05

‖Ischemia-driven

#P<0.001 for non-inferiority

¶ Definite only

ST, stent thrombosis; TVF, target vessel failure (a composite of cardiac death, myocardial infarction, or target vessel revascularization).

ZES, zotarolimus-eluting stent; BMS, bare metal stent; SES, sirolimus-eluting stent; PES, paclitaxel-eluting stent

Table 10. The most prominent randomized trials and registries of the 2nd generation RESOLUTE zotarolimus-eluting stent. Differences non-significant unless indicated.

Study	No. of Patients	Follow-up (months)	In-stent late lumen loss (R-ZES vs.) (mm)	Angiographic in-stent restenosis (R-ZES vs.) (%)	Death (R-ZES vs.) (%)	Myocardial infarction (R-ZES vs.) (%)	Target lesion revascularization (R-ZES vs.) (%)	MACE (R-ZES vs.) (%)	Definite/ Probable ST (R-ZES vs.) (%)
RESOLUTE[247, 248]	R-ZES (n=139)	9*/12†	0.22	1.0	2.3	5.4	0.8	8.5‖	0
		60†	-	-	7.1	6.3	3.1	16.5‖	0
RESOLUTE	R-ZES	13*/12†	0.27 vs. 0.19	4.2 vs. 3.8	1.6 vs. 2.8	4.2 vs. 4.1#	3.9 vs. 3.4‖	8.7 vs. 9.7	1.6 vs. 0.7

All-Comers[249, 250]	(n=1140) vs. EES (n=1152)	60†	-	-	6.5 vs. 5.7¶	5.7 vs. 5.7#	7.8 vs. 7.1‖	17.1 vs. 16.3††	2.4 vs. 1.7
RESOLUTE US[251]	R-ZES (n=1402)	12	-	-	1.3	1.4	2.8‖	-	0.1
ISAR-TEST 5[252, 253]	R-ZES (n=1000) vs. SES+Probucol (n=2002)	6-8*/12†	0.30 vs. 0.31	13.4 vs. 13.3 (In-segment)	4.7 vs. 3.6	3.8 vs. 3.9	10.4 vs. 10.3	13.5 vs. 13.1¶#	1.2 vs. 1.1
		60†	-	-	19.4 vs. 17.0	4.8 vs. 4.3	14.7 vs. 14.7	24.2 vs. 23.8¶#	1.6 vs. 1.3
TWENTE[254, 255]	R-ZES (n=690) vs. EES (n=690)	12†	-	-	1.0 vs. 1.4¶	4.6 vs. 4.6#	3.3 vs. 2.7#‖	11.2 vs. 10.5	0.9 vs. 1.2
		60†	-	-	3.7 vs. 5.2¶	6.8 vs. 6.2#	8.9 vs. 10.5#‖	16.1 vs. 18.1	1.9 vs. 2.1

LONG DES IV[256]	R-ZES (n=250) vs. SES (n=250)	9*/12†	0.26 vs. 0.24	4.0 vs. 6.0	0.8 vs. 1.6	11.6 vs. 13.6	1.6 vs. 2.4‖	14.4 vs. 16.0	0.0 vs. 0.8
TWENTE II – Dutch Peers[162, 163]	R-ZES (n=906) vs. PROMUS EES (n=905)	12†	-	-	2.4 vs.	2.2 vs. 1.3#	2.2 vs. 2.2‖	6.4 vs. 4.9	0.6 vs. 0.9
		36†	-	-	5.3 vs. 4.8	2.8 vs. 2.2#	4.7 vs. 4.4‖	11.7 vs. 11.4	1.4 vs. 1.1

*Angiographic follow-up

†Clinical follow-up

‡ P<0.001

§ P<0.05

‖Ischemia driven

¶ Cardiac death

Target vessel

**Non-inferiority

††MACE, a composite of cardiac death, target vessel MI and clinically indicated TLR

ST, stent thrombosis; MACE, major adverse cardiovascular events (a composite of death, MI and target lesion revascularization)

SES, sirolimus-eluting stent