Long-term effectiveness and safety of sirolimus drug-eluting stents

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Abstract: The root cause of coronary artery disease is atherosclerosis, ie, intraluminal narrowing (stenosis) of the arteries that supply blood to tissues of the heart. The introduction of the drug-eluting stent over the past decade has revolutionized the field of interventional cardiology. It is used extensively in clinical practice for the treatment of coronary artery disease. The first drug-eluting stent to receive US Food and Drug Administration approval was the sirolimus-eluting stent. Recently, two other stent analogs of sirolimus were approved, ie, the zotarolimus-eluting stent and the everolimus-eluting stent. However, concern has arisen in recent years about the long-term safety and efficacy of drug-eluting stents, due to the occurrence of late adverse clinical events, such as stent thrombosis. This review focuses on clinical studies that have been performed with the sirolimus-eluting stent or its analogs. We discuss the pharmacology, safety, and various therapeutic options that exist when choosing stents for coronary artery disease. Our aim is to provide a thorough review of the long-term efficacy and safety of sirolimus drug-eluting stents, and also to discuss currently approved and promising investigational drug-eluting stents, in an effort to provide insight into how these stents are currently evolving and generate further investigation in this area.

Keywords: drug-eluting stent, long-term safety, sirolimus

Introduction
In 1977, Andreas Grünztig introduced percutaneous transluminal coronary angioplasty, whereby a catheter was introduced through a peripheral artery and a balloon expanded to dilate the narrowed segment of artery.1 Since then, the explosion in percutaneous techniques and research has been astonishing. In the mid-1980s, Dotter and Judkins were among the first to suggest using prosthetic devices inside arteries to maintain blood flow after dilation.2 In 1986, Puel and Sigwart implanted the first coronary stent in a human patient.3 This would eliminate two of the main problems associated with angioplasty, ie, elastic recoil and neointimal hyperplasia.4 Multiple trials have demonstrated the superiority of stents versus balloon angioplasty. Stents nonetheless remained vulnerable to restenosis, even though this occurred with less frequency than with balloon angioplasty.

To address the issue of restenosis, developers of drug-eluting stents were using the devices themselves as a platform for delivery of antiproliferative drugs by 2001. This drug delivery method involved applying high concentrations locally and directly at the target lesion, with minimal systemic side effects. Drug-eluting stents, as a group, are superior to bare metal stents in reducing the incidence of restenosis, intimal hyperplasia, and repeat interventions.5 They have antiproliferative and antimigratory properties,
which prevent restenosis via smooth muscle inhibition.\textsuperscript{6–8} The different drug mechanisms and delivery platforms have been found to have different clinical outcomes.

**Pharmacology**

The ideal drug-eluting stent should have three components:

- A design that allows for uniform scaffolding and drug distribution.
- A polymer that is biocompatible, and maintains and provides consistent controlled release of a therapeutic level of the drug into the tissue; the drug must not wash off during the most time-intensive procedures and must provide durability, ensuring drug retention during stent delivery and deployment (Figure 1).
- A drug that safely and effectively prevents neointimal hyperplasia while allowing natural healing to occur.

The Cypher\textsuperscript{8} is designed to be a closed-cell drug delivery platform. The closed-cell design ensures optimal drug delivery in two ways, ie, circumferentially via a consistent metal-to-artery ratio, and longitudinally via consistent uniform lesion coverage in the most tortuous vessels.

Sirolimus is the alternative name for rapamycin, a rarely used antibiotic. Sirolimus is highly lipophilic and has two mechanisms of action, ie, antiproliferation of the intima and reduction of inflammatory cell activity. The selectivity for proliferating cells and preferential targeting of smooth muscle cells occurs via target of rapamycin (TOR). It also has a cytostatic mode of action whereby it acts before the critical checkpoint in the G1 phase of the cell cycle. Sirolimus also has the ability to stop the proliferation of smooth muscle cells effectively. The mechanism of action is shown in Figures 2–5.

The typical dose of sirolimus in each Cypher stent is 140 $\mu$g/cm\textsuperscript{2}. The high lipid solubility of sirolimus allows it to pass easily through cell membranes and contributes to

**Figure 1** [CYPHER\textsuperscript{8} sirolimus-eluting coronary stent. © Cordis Corporation 2010.]

**Figure 2** Diffusion of sirolimus into smooth muscle cells. © Cordis Corporation 2010.

**Abbreviations:** CDK, Cyclin-dependent kinase; FKBP, FK binding protein; TOR, Target of Rapamycin.

**Figure 3** Sirolimus binds to FKBP to form a sirolimus-FKBP complex. © Cordis Corporation 2010.

**Abbreviations:** CDK, Cyclin-dependent kinase; FKBP, FK binding protein; TOR, Target of Rapamycin.

**Figure 4** The sirolimus-FKBP complex binds to TOR, p27 levels increase, and cyclin/CDKp27 is inhibited. © Cordis Corporation 2010.

**Abbreviations:** CDK, Cyclin-dependent kinase; FKBP, FK binding protein; TOR, Target of Rapamycin.
its retention in arterial tissue. Its half-life is approximately 62 hours, allowing it to diffuse readily into tissue and remain there long enough to exert a beneficial effect. During clinical trials, patients received up to six stents totaling 54 mm in length without untoward effects. Furthermore, doses six times greater than those used in clinical trials also exhibited no toxicity in 30-day animal studies. The dose response curve illustrates its broad safety window (see Figure 6). Normal re-endothelialization is a key factor in preventing thrombosis. Preclinical data for the Cypher stent showed complete re-endothelialization at 30 days, and this was demonstrated in clinical trials as well.

**Efficacy of drug-eluting stents**

Drug-eluting stents have been used extensively since the Cypher stent was first approved in 2003. The indications for their use have expanded over the years. Traditionally approved (on-label) indications for using drug-eluting stents have included discrete, previously untreated lesions in native coronary vessels. These are the types of lesions that have been extensively studied in early clinical trials involving drug-eluting stents. Over time, these stents has also been used to treat complex coronary artery disease states, including left main lesions, multivessel coronary artery disease, acute myocardial infarction, bifurcation lesions, moderate to heavily calcified lesions, chronic total occlusions, and saphenous vein graft stenosis.

The sirolimus-eluting stent showed significant promise for the prevention of neointimal proliferation, restenosis, and major cardiovascular events in an early French study published in 2002. Numerous studies have unequivocally shown the effectiveness of drug-eluting stents in discrete single-vessel coronary lesions. Drug-eluting stents in ST segment elevation myocardial infarction (STEMI) patients have consistently been shown to decrease the risk of repeat revascularization, without increasing the incidence of stent thrombosis or recurrent myocardial infarction. However, a recent study concluded that drug-eluting stents used in STEMI have a higher rate of cardiac death not attributable to myocardial infarction or stent thrombosis. Drug-eluting stent use in STEMI also showed a significantly higher three-year survival rate free from major adverse cardiovascular events and a lower rate of target vessel revascularization and target vessel failure when compared with bare-metal stents (Table 1). A similar result was obtained in another study, with benefits observed for up to four years. Similarly, Table 2 shows event rates for all stents at five years. A meta-analysis of 13 clinical trials comparing drug-eluting stents and bare-metal stents concluded that drug-eluting stents significantly reduced target vessel revascularization without

**Figure 5** Elevated p27 levels inhibit cyclin/CDK activity, turning off the cell cycle in G1 (at the G1 checkpoint).

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**Abbreviations:** CDK, Cyclin-dependent kinase; FKBP, FK binding protein; TOR, Target of Rapamycin.

**Figure 6** Dose-response curve for Cypher® stent.

**Note:** Drug-eluting stents versus bare metal stents for angina or acute coronary syndromes.

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**Table 1** Clinical outcome at three years

<table>
<thead>
<tr>
<th></th>
<th>SES group</th>
<th>BMS group</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>157</td>
<td>156</td>
<td></td>
</tr>
<tr>
<td>Death</td>
<td>5 (3.2) (1–7.2)</td>
<td>8 (5) (2.2–10)</td>
<td>0.38</td>
</tr>
<tr>
<td>Reinfarction</td>
<td>4 (2.5) (0.7–6.3)</td>
<td>4 (2.5) (0.7–6.4)</td>
<td>NS</td>
</tr>
<tr>
<td><strong>Stent thrombosis</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Definite</td>
<td>3 (1.9) (0.4–5.4)</td>
<td>2 (1.3) (0.1–4.5)</td>
<td>NS</td>
</tr>
<tr>
<td>Probable/possible</td>
<td>5  (3.2) (1–7.2)</td>
<td>6  (3.8) (1.4–8.1)</td>
<td>NS</td>
</tr>
<tr>
<td>MACE</td>
<td>20 (12.7) (8–18)</td>
<td>33 (21) (15–28)</td>
<td>0.034</td>
</tr>
<tr>
<td>TLR</td>
<td>11 (7) (3.5–12)</td>
<td>21 (13.5) (8.3–19)</td>
<td>0.048</td>
</tr>
<tr>
<td>TVR</td>
<td>13 (8.3) (4–13)</td>
<td>25 (16) (10–22)</td>
<td>0.027</td>
</tr>
<tr>
<td>TVF</td>
<td>18 (11.5) (7–17)</td>
<td>32 (20.5) (14–27)</td>
<td>0.028</td>
</tr>
</tbody>
</table>

**Note:** Values are n (%) and (95% confidence interval).

**Abbreviations:** MACE, major adverse cardiovascular event; TLR, target lesion revascularization; TVF, target vessel failure; TVR, target vessel revascularization; NS, not significant.
increasing rates of thrombosis, death, or myocardial infarction.

The drug-eluting stent has been used in the treatment of unprotected left main coronary artery lesions. The drug-eluting stent was compared with coronary artery bypass grafting in the treatment of unprotected left main coronary artery lesions, and the conclusion was that the drug-eluting stent showed similar rates of mortality, but higher rates of target vessel revascularization when compared with coronary artery bypass grafting.\(^\text{15}\)

The drug-eluting stent has been compared with coronary artery bypass grafting in the treatment of multivessel coronary artery disease in diabetic patients. There was no significant difference in rates of death and myocardial infarction between the two groups. Compared with coronary artery bypass grafting, the drug-eluting stent was associated with a higher risk of major cardiovascular events (odds ratio [OR] 0.18, 95% confidence interval [CI] 0.11–0.30, \(P = 0.30\)) and a lower risk of cerebrovascular events (OR 2.15, 95% CI 0.99–4.68, \(P = 0.80\)).\(^\text{16}\) The Arterial Revascularization Therapies Study II compared the sirolimus-eluting stent, the bare-metal stent, and coronary artery bypass grafting in patients with de novo multivessel coronary artery disease. The percentage of percutaneous three-vessel treatment was 46.6% for the sirolimus-eluting stent versus 18.0% for the bare-metal stent \((P < 0.001)\). The mean (standard deviation) number of significant lesions per patient was 3.6 ± 1.3 for the sirolimus-eluting stent versus 2.8 ± 1.0 for coronary artery bypass grafting \((P < 0.001)\) and 2.8 ± 1.0 for bare-metal stents. Patients allocated to the sirolimus-eluting stent group received a mean of 3.7 ± 1.5 stents, with an average total stented length of 72 ± 32 mm, compared with 2.8 ± 1.3 stents and a stented length of 48 ± 22 mm in bare-metal stented patients \((P < 0.001)\). The conclusions of this study were that the drug-eluting stent was comparable with coronary artery bypass grafting and superior to bare-metal stents for reducing the risks of major adverse cardiovascular and cerebrovascular events.\(^\text{17}\) The SPIRIT-II trial tested everolimus-eluting stents in patients with calcified coronary artery lesions. This study concluded that the calcified group had higher instant restenosis and major adverse cardiovascular events rates when compared with the noncalcified group (7.4% versus 0%, \(P = 0.08\)).\(^\text{18}\) Drug-eluting stents were also studied in the treatment of very long segment diffuse de novo coronary artery lesions and were found to be effective in this subset as well.\(^\text{19}\) The mean follow-up duration in this study was 26.5 months.

Chronic total occlusions are another group of patients in whom the drug-eluting stent has been studied. In a meta-analysis involving 14 studies and more than 4000 patients, the drug-eluting stent was found to be more effective than bare-metal stents in reducing the risk of major adverse cardiovascular events (relative risk [RR] 0.45, 95% CI 0.34–0.60, \(P < 0.001\)) and target vessel revascularization for up to three years (RR 0.40, 95% CI 0.28–0.58, \(P < 0.001\)).\(^\text{20}\)

Finally, the drug-eluting stent has been studied in degenerative saphenous vein graft stenosis. A meta-analysis published in early 2010 of observational studies concluded that the drug-eluting stent was associated with a lower risk of death, myocardial infarction, and a lower risk of cerebrovascular events (odds ratio 2.15, 95% confidence interval 1.00–4.64, \(P = 0.050\)).\(^\text{21}\)
that the drug-eluting stent used for vein graft stenosis needs larger multicenter, randomized, controlled trials to confirm its effectiveness and to address safety issues.21

Safety issues with sirolimus

Initial approval of the sirolimus-eluting stent was based on two randomized, controlled trials involving more than 1000 patients, each showing reduced rates of target vessel revascularization and target vessel failure when compared with bare-metal stents. Initial enthusiasm led to rapid acceptance of the use of the drug-eluting stent, and soon approximately 80% of all stents used in the US were drug-eluting stents. Safety concerns about the drug-eluting stent surfaced in 2006 when late thrombosis, death, and myocardial infarction were reported to be higher in patients receiving drug-eluting stents than in those receiving bare-metal stents. DESIRE (Drug-Eluting Stents in the Real World) was a prospective, nonrandomized, single-center registry trial22 that reported on the incidence and predictors of stent thrombosis and major adverse cardiovascular events. In this study, patients were followed up for a median period of five years. The incidence of stent thrombosis was 1.7% in this study (hazards ratio [HR] 3.02, 95% CI 1.27–7.19, \( P = 0.012 \)). Multiple studies have reported an increased incidence of stent thrombosis and nonfatal myocardial infarction when drug-eluting stents are used for off-label indications.22–24

The incidence of stent thrombosis within the first year was identical between sirolimus-eluting stents and bare-metal stents, as well as between paclitaxel-eluting stents and bare-metal stents. No significant differences in the cumulative four-year rates of death or myocardial infarction were observed between the drug-eluting stent and bare-metal stent groups (\( P = 0.20 \)).25 Between one and four years after stent implantation, the incidence of stent thrombosis was higher in the drug-eluting stent group than in the bare-metal stent group (\( P = 0.025 \)).25,26

In another meta-analysis of randomized controlled trials and observational studies, no significant differences were observed in the long-term rates of myocardial infarction (HR 0.95, 95% CI 0.79–1.13, \( P = 0.54 \)) or death (HR 0.97, 95% CI 0.81–1.15, \( P = 0.72 \)) after drug-eluting stent or bare-metal stent use for either on-label or off-label indications,27 and the conclusion was that sirolimus is safe in both on-label and off-label indications. Another comprehensive meta-analysis of 28 trials comparing drug-eluting stents with bare-metal stents reached the conclusions that there was no excess mortality with the drug-eluting stent (5.9% versus 5.7%, \( P = 0.79 \)), that the drug-eluting stent appears to be safe and effective within one year, with possibly decreased rates of non-Q wave myocardial infarction and significantly decreased target vessel revascularization (\( P = 0.001 \)) compared with bare-metal stents, and similar mortality between the drug-eluting stent and bare-metal stent after one year, despite an increased rate of stent thrombosis (0.7% versus 0.3%, \( P = 0.006 \)).28

In DESIRE, 2084 patients treated with the drug-eluting stent were followed for a mean duration of 2.6 ± 1.2 years. The results of this study showed a target vessel revascularization rate of 3.3%, non-Q wave myocardial infarction 0.7%, and stent thrombosis 1.6%. This study concluded that use of the drug-eluting stent in an unselected population is associated with long-term safety and effectiveness, with acceptable low rates of clinically significant adverse events.29

Comparison of various drug-eluting stents

The first-generation drug-eluting stents are the sirolimus-eluting (Cypher) stent and the paclitaxel-eluting (TAXUS®) stent. The second-generation stents are the zotarolimus-eluting (ENDEAVOR®) stent and the everolimus-eluting (XIENCE®) stents.

The TAXUS IV trial compared the paclitaxel-eluting stent with the bare-metal stent in single- vessel de novo coronary lesions. The paclitaxel-eluting stent showed better long-term efficacy with regard to target vessel revascularization at five years (27.4% versus 16.9%, \( P < 0.0001 \)) and safety with regard to major adverse cardiovascular events at five years (24% versus 32.8%, \( P = 0.001 \)) and stent thrombosis at five years (2.2% versus 2.1%, \( P = 0.87 \)).30

The ENDEAVOR II trial compared the zotarolimus-eluting stent and the bare-metal stent over a four-year follow-up period. The zotarolimus-eluting stent was shown to be effective in reducing target vessel revascularization (10.4% versus 21.5%, \( P < 0.001 \)) during four years of follow-up without any significant difference in rates of death (5% versus 5.2%, \( P = 0.29 \)) or nonfatal myocardial infarction (3.2% versus 4.4%, \( P = 0.29 \)).31 Multiple studies comparing various drug-eluting stents with bare-metal stents have reached similar conclusions as the above studies.32,33

All the four drug-eluting stents have definitely proved superior to bare-metal stents in head-to-head studies. In a meta-analysis of 14 trials comparing the sirolimus-eluting stent with the bare-metal stent, use of the sirolimus-eluting stent did not have a significant effect on overall long-term survival free of myocardial infarction when compared with the bare-metal stent (\( P = 0.56 \)). However, there was a significant reduction in need for reintervention after use of the sirolimus-eluting stent. There was evidence of a slight increase in overall risk of stent
thrombosis with the sirolimus-eluting stent when compared with the bare-metal stent after the first year ($P = 0.49$).\textsuperscript{34}

The SORT-OUT III trial compared the sirolimus-eluting stent with the zotarolimus-eluting stent, and concluded that the sirolimus-eluting stent was superior to the zotarolimus-eluting stent for patients receiving routine clinical care (major adverse cardiovascular events 3\% versus 6\%, $P = 0.0002$) and for all-cause mortality (4\% versus 3\%, $P = 0.035$).\textsuperscript{35} The ENDEAVOR IV trial compared the zotarolimus-eluting stent and the paclitaxel-eluting stent. The conclusions of this study were that the zotarolimus-eluting stent has similar clinical safety and efficacy to the paclitaxel-eluting stent (target vessel failure 6.6\% versus 7.1\%, respectively, target vessel revascularization at 12 months 4.5\% versus 3.2\%, $P = 0.228$) in simple and medium complexity single de novo coronary lesions.

A single-center registry study from Singapore evaluated the safety and efficacy of the sirolimus-eluting, paclitaxel-eluting, and zotarolimus-eluting stents in diabetic patients with complex coronary lesions. At 18 months, the rates of major adverse cardiovascular events were 12.7\%, 8.7\%, and 12.7\%, respectively. Stent thrombosis was found in one patient each in the sirolimus-eluting stent and zotarolimus-eluting stent groups and in two patients in the paclitaxel-eluting stent group. The conclusion was that there was no significant difference in efficacy between the three stent groups ($P = 0.228$).\textsuperscript{36} The zotarolimus-eluting stent was compared with the everolimus-eluting stent in a recently published study with a follow-up duration of 13 months. The conclusions of the study were that the zotarolimus-eluting stent was noninferior to the everolimus-eluting stent with regard to major adverse cardiovascular events (8.2\% versus 8.3\%) and stent thrombosis (2.3\% versus 1.5\%, $P < 0.001$ for noninferiority).\textsuperscript{37}

In a prospective, multicenter German drug-eluting stent registry, the sirolimus-eluting stent was compared with the paclitaxel-eluting stent in diabetic patients. Target vessel revascularization was achieved in 12\% versus 11.3\%. The rate of major adverse cardiovascular events was 11.4\% versus 10.3\% and the rate of stent thrombosis was 5.6\% versus 4.6\%. It was concluded that the sirolimus-eluting and paclitaxel-eluting stents were similar with regard to outcome in diabetics ($P < 0.05$).\textsuperscript{38} The everolimus-eluting stent and the paclitaxel-eluting stent were compared in the SPIRIT II and III trials. The conclusion was that the everolimus-eluting stent was superior to the paclitaxel-eluting stent in patients with small coronary vessel disease, with major adverse cardiovascular event rates of 5.2\% versus 10.7\%, $P = 0.037$.\textsuperscript{39}

Patients who have received the sirolimus-eluting stent have shown better clinical outcomes than those who have received the paclitaxel-eluting stent.\textsuperscript{26,40–42} In one study, two-dimensional intravascular ultrasound showed an overall intimal hyperplasia rate of 2.8\% with the sirolimus-eluting stent versus 13.8\% for the paclitaxel-eluting stent.\textsuperscript{43,44} In another study, the sirolimus-eluting stent were compared with the paclitaxel-eluting stent, and after 24 months of follow-up, patients who received the paclitaxel-eluting stent had significantly higher rates of non-Q wave myocardial infarction (5.9\% versus 1.9\%, $P = 0.002$), target vessel revascularization (4.9\% versus 1.9\%, $P = 0.002$), and coronary artery bypass graft surgery (6.9\% versus 1.9\%, $P = 0.002$).

In a meta-analysis of randomized trials, the sirolimus-eluting stent was compared with the paclitaxel-eluting stent in patients who had suffered a STEMI. It was found that the sirolimus-eluting stent was superior to the paclitaxel-eluting stent for reducing the incidence of restenosis (4\% versus 9.6\%, $P = 0.004$) in patients undergoing primary percutaneous coronary intervention for STEMI, without any significant differences in death, myocardial infarction, target vessel revascularization, or stent thrombosis.\textsuperscript{45} However, the deliverability of the sirolimus-eluting stent in tortuous and calcified vessels remains more difficult than with the paclitaxel-eluting and zotarolimus-eluting stents.

**Patient satisfaction**

Patient satisfaction is always directly proportional to the least number of interventions needed to make them feel better. During this era of the Internet, many patients and/or their relatives have access to the results of the clinical trials described here. In the light of current knowledge, a longer-lasting stent, ie, the sirolimus-eluting stent, generates more confidence in the patient as well as in the physician performing the procedure.

**Future advances**

While there are good clinical data for the drug-eluting stent, several safer drug-eluting stents with biodegradable polymers are available commercially in Europe. These include the SUPRALIMUS\textsuperscript{®} stent, the EXCEL\textsuperscript{®} stent, and the NEVO\textsuperscript{®} stent, with several others presently undergoing clinical investigation. Interest has focused on these stents because after implantation, in theory they may offer the initial antirestenotic benefits of a standard drug-eluting stent, as well as the safety benefits of the bare-metal stent after the polymer has biodegraded. The important remaining question is whether this new technology will lead to improved clinical outcomes. Unfortunately, present studies of these stents are limited by short-term follow-up.
The NEVO stent is well studied compared with the others, but has only been evaluated in the NEVO RES-ELUTION study, which was a randomized, multicenter, noninferiority study comparing the NEVO stent with the TAXUS Liberté® paclitaxel-eluting stent in 394 patients with single de novo coronary artery lesions. At six-month angiographic follow-up, the primary endpoint of instent late lumen loss was significantly lower in patients treated with the NEVO stent. Future trials of this promising stent technology are planned for 2011. In particular, the NEVO II study has commenced, and will randomize 2500 “all-comers” to treatment with either the NEVO stent or the Xience V® everolimus-eluting stent, with clinical follow-up planned annually out to five years.

**Conclusion**

There would be very few areas in modern medicine that have generated as much debate as coronary drug-eluting stent implantation. Evidence for the efficacy of drug-eluting stents in reducing clinical restenosis is consistent. In our interpretation of the available data, we conclude that the benefit of drug-eluting stent therapy when compared with the bare-metal stents in reducing restenosis is of the order of 35%–70%, and is seen across a broad spectrum of lesions, encompassing both on-label and off-label indications.

Percutaneous coronary intervention by its very nature produces severe coronary endothelial injury and an increased risk of thrombosis. After stent placement, platelet activation is usually reduced by the use of two platelet inhibitors with differing modes of action (aspirin and clopidogrel). The selection criteria for dual antiplatelet therapy is for future review, because there have been concerns regarding a higher risk of thrombotic occlusion and patient mortality in the short to medium term. These complications following sirolimus implantation have not been fully studied by systematic data analysis. Analysis of the available benefit and risk data has shown that drug-eluting stent implantation should be the preferred approach for treating patients with obstructive coronary disease and who require percutaneous coronary intervention. The sirolimus-eluting stent has been shown to be safe and effective in percutaneous coronary intervention since 2003. Many studies have published long-term safety data, and these devices have proven to be valuable assets in treating coronary artery disease. It is clear that no single stent design and polymer type will be suitable for all patients and lesion types. Therefore, a more individualized choice of stent should take into account individual patient characteristics.

**Disclosure**

The authors report no conflicts of interest in this work.

**References**


