The introduction of drug-eluting stent (DES) technology revolutionized the field of interventional cardiology. The main components of the DES are the stent platform, the drug, and the carrier. First-generation DES used durable polymers as the carrier to control the drug elution from the stent into the vessel wall. These polymers, however, were found to be problematic and were associated with adverse findings, which may have contributed to late stent thrombosis and the dependency on prolonged dual antiplatelet therapy (DAPT). These deficiencies motivated scientists to develop biodegradable polymers with the premise that they will completely disappear once the drug has been delivered to the tissue. Despite the availability of a wide variety of biodegradable polymers with degradation kinetics ranging from 3 months to 3 years, only a few have thus far been utilized for DES technology. Among them is polylactide-co-glycolide (PLGA). PLGA is used in the Stellium stent (DISA Vascular, Cape Town, South Africa) DES system. In this issue of the Journal, Kozuki et al report their first-in-man study results. The Stellium stent demonstrated competitive low event rates and angiographic in-stent late loss when compared historically with first-generation DES, which used durable polymers.

**Is It the Drug or the Biodegradable Polymer?**

The Stellium stent is not the first to use the combination of paclitaxel (PTX) and PLGA. The CoStar™ stent (Conor MedSystems, Menlo Park, CA, USA) had the same drug–polymer combination and although it performed well in small nonrandomized and dose finding studies it was found to be inferior in efficacy to the Taxus® stent (Boston Scientific, Natick, MA, USA) in pivotal randomized trial. The angiographic in-stent late loss at 9 months with the CoStar stent was higher when compared with Taxus, which could be explained by ineffective pharmacokinetic release, wrong PTX dosing, or lack of biocompatibility of the PLGA. PTX has repeatedly been shown to be inferior to sirolimus in suppressing neointimal hyperplasia when assessed by angiographic late lumen loss. In contrast, the Stellium stent using PLGA and PTX reports a competitive late loss of 0.19±0.54 mm, which is the lowest rate ever published using PTX, and is similar to sirolimus-based systems. Without scientific explanation, an additional confirmatory study is required to support these unexpected findings.

Biodegradable stents using sirolimus and PLGA, such as the NEVO™ stent (Cordis Corporation, Johnson & Johnson company, Miami Lakes, FL, USA), have also demonstrated superiority in terms of low late loss when compared with the Taxus stent (Table), thereby supporting the feasibility and efficacy of the PLGA polymer. Interestingly, the in-stent late loss with the Stellium stent is similar to that reported for NEVO. Because both stents use the same biodegradable polymer, the question remains whether this finding can be attributed to the polymer or to the drug.

**Recent Trials of Biodegradable Polymer Stents**

Perhaps the most important question is whether the theoretical advantage of bioabsorbable stents over durable polymers will translate into differences in clinical outcome, increasing the safety parameters with less dependency on DAPT and less stent thrombosis. The large Limus Eluted From A Durable Versus EROdable Stent Coating (LEADERS) clinical study demonstrated non-inferiority in overall cardiac event rates with similar late loss indices in a small angiographic cohort, but failed to show any benefit of the biodegradable polymer at 2 years’ clinical follow-up.

Other clinical trials such as Rapamycin-Eluting Stents With Different Polymer Coating to Reduce Restenosis (ISAR-TEST-3) and Intracoronary Stenting and Angiographic Results: Test Efficacy of 3 Limus-Eluting STents (ISAR-TEST-4), demonstrated non-inferiority of biodegradable polymer DES when compared with DES systems with durable polymers. At 2 years’ follow-up in ISAR-TEST-3, there was still no sign of a safety advantage with this novel platform over the durable polymer DES system. Because the event rate is so low, it is difficult to demonstrate the superiority of biodegradable polymers over durable polymers in a conservative clinical trial. Perhaps this will require us to look at differences over longer periods (such as 5 years’ follow-up) or to use surrogate markers, such as stent converage by endothelium, which can potentially be detected with the use of optical coherence tomography (OCT).

**OCT Assessment**

OCT has been established as a reliable tool for assessment of coronary artery disease. This technology is especially advantageous for the assessment of stent strut apposition and coverage by endothelium. In the LEADERS trial, strut

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coverage at an average follow-up of 9 months appeared to be more complete in patients allocated to the biodegradable polymer when compared with the durable polymer. These differences in stent coverage, however, did not translate into differences in clinical events during up to 2 years’ follow-up. We should carefully watch the potential of OCT to detect safety parameters such as strut coverage as a surrogate marker to differentiate between stent technologies and to find out the robustness of this surrogate to predict future clinical events.

Biodegradable Polymer Perspective

Biodegradable polymers for DES sound appealing because of the potential to shorten DAPT duration. Currently, however, there is no evidence to support that these stents will change the efficacy and safety landscape of DES or change the requirements for prolonged DAPT following DES implantation. Biodegradable polymer technology on a stent is challenging because the effect of the degradation kinetics can interfere with the drug elution kinetics and may lead to a burst of drug release at different stages of the degradation. Nevertheless, the current trend in the DES market is to move from durable polymers to biodegradable polymers, to completely biodegradable stents or polymer-free DES. Meanwhile, second-generation DES such as XIENCE V® (Abbott laboratories, Abbott Park, IL, USA), have shown excellent performance, as demonstrated in the Clinical Evaluation of the XIENCE V® Everolimus Eluting Coronary Stent System in the Treatment of Subjects With de Novo Native Coronary Artery Lesions (SPIRIT IV) trial, with low target lesion revascularization of 2.5% and a stent thrombosis rate of 0.29% at 1 year. Although second-generation DES with durable polymers, such as XIENCE V and Endeavor® Resolute (Medtronic, Minneapolis, MN, USA), demonstrate excellent safety profiles, similar to those of bare metal stents, it will be very difficult to demonstrate the superiority of DES with biodegradable polymers unless we are able to demonstrate the safety of shorter DAPT duration with such stents. Given the low event rate seen with second-generation DES and everything that goes into designing a clinical trial, we may never know whether DES with biodegradable polymers are indeed an advantage or only a perception.

| Table. Recent Trials of Biodegradable Polymer Stents

<table>
<thead>
<tr>
<th>Drug type</th>
<th>Polymer type</th>
<th>Follow-up (months)</th>
<th>TLR (%)</th>
<th>Late loss (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>STELLIUM®</td>
<td>Paclitaxel</td>
<td>PLGA</td>
<td>6</td>
<td>0.19</td>
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<tr>
<td>COSTAR II</td>
<td>Paclitaxel</td>
<td>PLGA</td>
<td>8/9*</td>
<td>8.1 (TVR)</td>
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<tr>
<td>EUROSTAR³</td>
<td>Paclitaxel</td>
<td>PLGA</td>
<td>12/6*</td>
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<tr>
<td>Res-Elution I</td>
<td>Sirolimus</td>
<td>PLGA</td>
<td>12/6*</td>
<td>3.6</td>
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<tr>
<td>LEADERS¹</td>
<td>Biolimus A9</td>
<td>PLA</td>
<td>9</td>
<td>5.4</td>
</tr>
<tr>
<td>ISAR-TEST-3²</td>
<td>Sirolimus</td>
<td>PLA</td>
<td>12/6–8*</td>
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<tr>
<td>ISAR-TEST-4²</td>
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<td>PLA</td>
<td>12</td>
<td>8.8</td>
</tr>
</tbody>
</table>

*Clinical/angiographic follow-up.

TLR target lesion revascularization; PLGA, polylactide-co-glycolic acid; TVR target vessel revascularization; PLA polyactic acid.

References