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E-SIRIUS: Direct stenting vs predilatation in patients with long lesions

ESC news **Vienna, Austria** - The final results of the second European study investigating the Cypher™ sirolimus-eluting stent were presented today at the **European Society of Cardiology Congress 2003** and confirm the benefit seen in previous SIRIUS trials, as well as the clinical benefit the study demonstrated in preliminary results reported at eight months.

The European arm of the Cordis/Johnson & Johnson-sponsored trial of its sirolimus-eluting stent—the **E-SIRIUS** trial—showed that patients treated with the sirolimus-eluting stent had lower rates of restenosis and major adverse cardiac events than patients treated with bare-metal stents.

Equally important, however, say investigators, E-SIRIUS is the first study to investigate the effect of direct stenting vs predilatation in patients with long lesions, and the results appear to be positive.

"Direct stenting saves costs by foregoing the extra balloon catheter needed for predilatation and also appears to be as safe and effective as predilatation plus stenting," said lead investigator **Dr Joachim Schofer** (Center for Cardiology and Vascular Interventions, Hamburg, Germany).

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Reduced restenosis and MACE with CYPHER

The E-SIRIUS study is a multicenter, randomized, double-blind trial conducted at 35 hospitals throughout Europe. The study enrolled 352 patients with de novo native coronary lesions and was designed for patients with a reference vessel diameter of 2.5 mm to 3.0 mm and a lesion length of 15 mm to 32 mm. Of the 352 patients enrolled in the study, 175 patients were randomized to receive the sirolimus-eluting stent and 177 patients to receive an uncoated metal stent (control group).

Eight-month angiographic results—previously reported by **heartwire**—showed that 43.6% of all patients who received the conventional bare-metal stent exhibited restenosis, defined as a greater than 50% renarrowing of the coronary artery lumen at the treatment site. In contrast, only 5.8% of patients treated with the sirolimus-eluting stent experienced restenosis, corresponding to a reduction of 86%.

Schofer presented data showing event-free survival rate at 270 days to be 92% in patients treated with a sirolimus-eluting stent, compared with 77% in the



Dr Joachim Schofer

conventional bare-metal-stent arm ($p < 0.001$). This benefit was maintained at 12 months, according to the E-SIRIUS investigators, who noted the clinical benefit of the sirolimus-eluting stent at 12 months is consistent with the findings of the previous SIRIUS trials. The one-year MACE rate with the sirolimus-eluting stent was 8.6%, compared with 26.6% in the control group.

Schofer also reported that the primary end point of in-stent mean luminal diameter (MLD) was significantly increased at eight months in patients who received the sirolimus stent compared with those who received the bare-metal stent. The mean late loss for the bare-metal stent group was 1.05 mm compared with 0.2 mm for the sirolimus-eluting stent patients, a highly significant difference of treatment effect of 81%, said Schofer. This benefit was also maintained at 12 months.

Direct stenting vs predilatation

In a nonrandomized manner, the E-SIRIUS investigators sought to compare direct stenting with predilatation of the coronary lesion. There were no significant differences in clinical characteristics between patients included in the subanalysis.

Of the 352 patients enrolled in the E-SIRIUS study, 26% of patients ($n=92$) were included in the direct stenting vs predilatation analyses. In total, 45 patients in the sirolimus-eluting stent group were directly stented and 47 patients in the control group were directly stented.

While there were no significant differences between directly stenting and predilatating in either the sirolimus-eluting stent or control group, the investigators found trends toward reduced restenosis and MACE in the sirolimus subgroup undergoing direct stenting.

Rates of restenosis and MACE in the different subgroups

Outcome	Predilatation (%)	Direct stenting (%)
Restenosis	7.2	2.4
MACE	9.2	4.4

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Schofer noted that as a consequence of operator selection in the nonrandomized substudy of E-SIRIUS, directly stented lesions had, on average, lower preprocedure diameter stenosis than predilatated lesions. However, he concluded that direct stenting appears to be as effective as predilatation plus stenting in these patients.

"In patients who receive a directly implanted sirolimus-eluting stent, late loss tended to be lower than in patients who underwent predilatation," said Schofer. "Also, in contrast with predilatated sirolimus-eluting stent implantation and directly implanted bare-metal stents, no restenotic lesions were observed at the stent margins."

Issue of randomization

In a discussion following the presentation of the E-SIRIUS data, **Dr Sigmund Silber** (University of Munich, Germany) addressed the small sample size of the E-SIRIUS subanalysis, a limitation in interpreting the results. The lack of randomization in the study arms, said Silber, may also contribute to the favorable outcomes seen in patients who were stented without predilatation.

“ I'm not really interested in reducing in-stent MLD or late lumen loss. What I want is to improve the patient's outcome.”

"One of the most important parameters in the success of direct stenting is the degree of calcification in the lesions," said Silber. Based on operator bias, Silber said patients with less calcified coronary lesions might be more likely to be treated by direct stenting in nonrandomized trials.

However, the largest difficulty with the study is the primary end point, said Silber, noting the primary end point of the study was luminal diameter. Secondary end points, including MACE, were insufficiently powered to detect significant differences between the sirolimus-eluting stent and control groups.

"What is our goal?" asked Silber rhetorically. "If we are physicians, it is to treat the patient and our goal is not to improve angiographic parameters. I'm going to be a little provocative and tell you I'm not really interested in reducing restenosis. I'm not really interested in reducing in-stent MLD or late lumen loss. What I want is to improve the patient's outcome."

New SIRIUS: Combined data from European and Canadian sirolimus-eluting stent studies

In addition to presenting 12-month data of the European arm of the SIRIUS study, Schofer also presented pooled data from the European and Canadian study arms involving the Cypher sirolimus-eluting stent. According to Schofer, the results of the analysis—dubbed **New SIRIUS**—should alleviate concerns of possible in-stent restenosis at the proximal margin found in earlier studies with Cypher stent.

"Analysis of the old SIRIUS data revealed a lack of suppression of neointimal hyperplasia at the proximal stent margin," said Schofer. "This lack of efficacy stimulated debate about whether this was device-specific or the result of suboptimal stenting implantation techniques."

While noting the rate of in-stent restenosis was slightly lower in the new SIRIUS study compared with the original US-based SIRIUS trial, the major difference between the two was the rate of in-stent restenosis at the margins.

"When we compare the rate of in-stent restenosis of the proximal stent margins of old SIRIUS with new SIRIUS, the results turn out be statistically significant," said Schofer. "This device effectively suppresses neointimal hyperplasia not only within the stent but also at the proximal and distal stent margins."

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