Involving a bifurcation site, restenotic lesions (including in-stent restenosis), two-vessel disease (a maximum of 2 lesions located in 2 different epicardial vessels), long lesions (≥ 25 mm).

Methods: The primary endpoint of the study is the Target Lesion Revascularization (TLR) rate at 180 days after stent implantation. Secondary endpoints are Target Vessel Failure (TVF) at 180 days, Major Adverse Cardiac Events (MACE) at 30 days and 180 days, and MACCE at 1-year, 2-years and 3-years in a subset of 500 patients, device success, procedure success and resource utilization.

Results: As of abstract submission, data about 1526 patients enrolled at 67 investigational sites were available for analysis, for a total of 1435 lesions treated. Among these, 374 (34%) were restenotic lesions.

Conclusions: The patient recruitment in the DELIVER II study was completed on 9th of September 2002. Thirty-day safety results from the restenotic lesions subgroup will be available for presentation and will be compared with the outcome of other lesion subgroups. Multivariate analysis combining restenosis with other complicating factors will be presented as well.

* Manufactured by Cook Incorporated. DELIVER II is conducted by Guidant Corporation on behalf of Cook Incorporated.

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1198-182 Oral Rapamycin for the Prevention of In-Stent Restenosis

Ronak Mehran, Steven Marx, Srinivas Kesana-Kurthy, Yuia Adamian, Ally Aboufahes, Issam Moussa, Sigmund Kokols, Michael Collins, Gauthiel New, Sotir Polena, Josep Coscito, Alexandra J. Lansky, Jeffrey W. Moses, Wugong Ge, Mihong Ge, Leon, George Dangas, Lenox Hill Heart and Vascular Institute, Cardiovascular Research Foundation, New York, NY; Columbia University, New York, NY.

Background: Rapamycin, a macrolide antibiotic, inhibits SMC proliferation in vitro and in vivo by blocking cell cycle progression at the G1/S transition. Given the anti-proliferative and anti-migratory properties of rapamycin, it may have anti-restenosis properties after PTCA and placement of coronary stents. Recently, implantation of rapamycin eluting stents in de novo lesions was shown to be safe and effective in inhibiting neointimal formation. The safety and efficacy of oral rapamycin in reducing the incidence of intimal hyperplasia and restenosis is not known.

Methods: Thirty Patients with stable exertional angina will receive standard therapy (ASA + Clopidogrel) plus rapamycin (loading dose 6 mg on the day of the procedure, followed by 2 mg/day for either 2 (phase 1, n = 15) or 4 (phase II, n = 15) weeks after stent implantation for denovo lesions. Blood will be obtained for rapamycin levels, CBC, renal function and lipid profiles. Quantitative coronary angiography (QCA) and IVUS imaging will be performed immediately after the procedure and at 6 months follow-up in all patients for evaluation of the primary endpoint of neointimal volume and binary restenosis. Results: To date, 15 (completed study-phase one) patients (mean age 60±10 years, 70% males, 27% diabetics, 40% prior MI) have been enrolled. All patients tolerated the loading dose plus two week course of oral Rapamycin without any significant side effects or laboratory abnormalities. There was one episode of recurrent in-hospital ischemia (few hours after the procedure) for adjuunctive angiographic revascularization which required further stenting. Angiographic and IVUS follow-up is ongoing and will be presented for these patients as well as the full safety data on all 30 patients.

1198-183 Oral Rapamune to Inhibit Restenosis in Patients With Multi De-Novo Coronary Lesions Requiring Stenting

Ron Waxman, Andrew C. Alani, Augusto D. Pichard, Ellen Pinnow, Lowell F. Saeter, Kenneth M. Kent, Philip W.H. Weisman, Rebecca M. Ahnott, Peter Linskaya, Joseph I. Inbar, Washington Hospital Center, Washington, DC.

Background: Dual-antiplatelet therapy using aspirin and clopidogrel is the standard of care for patients undergoing coronary arterial stenting. However, despite this, restenosis rates remain high.

Methods: The Oral Rapamune to Inhibit Restenosis (ORBIT) is an open label study of 60 patients (pts) with multi-coronary lesion anatomy treated with stent implantation in up to 2 vessels. The first 30 pts received R 2 mg/day for 30 days. The loading dose for both regimens was 5 mg given either immediately prior to or after the intervention. Patients underwent clinical and vessel revascularization was 15.6%. Conclusions: Oral Rapamune administration were observed with a dose of 2 mg/day. Complete 6-month follow-up for the R 5mg/d group will be available at presentation.

1198-184 Stent Release of a Rapamycin Analogue: Tissue Pharmacokinetics of Rapid Versus Delayed Release

Frederick G. Waller, Elazer R. Edelman, Neda Vukmirovic, Campbell Rogers, Harvard-MIT, Cambridge, MA, Brigham and Women’s Hospital, Boston, MA.

Background: The effect of drug release rates from stents on tissue uptake and biological effect is poorly understood. We investigated tissue distribution under varied release conditions of a stent-delivered rapamycin analogue. Methods and Results: Rabbits underwent iliac artery stenting with a stent coated with a phosphoethanolamine polymer loaded with 14C drug (100 μg/stent). We compared 2 formulations: formulation 1- rapid release, and formulation 2- slow release. Animals were harvested at 1, 3, 7, 14, and 28 days and stent and tissue drug concentration determined through liquid scintillation counting. In vivo drug release from formulation 1 was >90% at 3 days. Release from formulation 2 did not reach >90% until 14 days (P = 0.05 by ANOVA). Arterial deposition at 1 day with formulation 1 (75.9±14.5 μg tissue) and at 3 days in formulation 2 (1339.6±418.8 μg tissue). When plotted against percent of drug released from stent, efficiency of deposition (μg drug/g tissue) vs. drug released from formulation 2 was best fit by a polynomial equation (R² = 0.94, p < 0.001) and was greater (R² = 0.94 by ANOVA) then efficiency from formulation 1 which was best fit by a linear equation (R² = 0.58, p < 0.001). Conclusion: Delayed release enhances the efficiency of delivery of a rapamycin analogue to the vessel wall. Modulating release may offer a more effective method of enhancing stent-based drug delivery than increasing dose.

1198-185 Can Sirolimus-Eluting Stents Tolerate Some Degree of Geographic Miss? A Prospective Multicenter Study

Chengkaiqiang Zhang, Yves Louvard, Marie-Claude Monic, Mario di Carlo, Marlen Leon, Jeffrey Moses, Judith Jaeger, Josto Ludeck, David Holmes, Antonio Colombo, Institut Cardiovasculaire Paris Sud, Massy, France, Cento Cuore Columbus, Milan, Italy.

Background. Sirolimus-eluting stents have proven their ability to almost completely suppress 6-month neointimal proliferation in the stented segment. However, little is known on the efficacy in the segments adjacent to the stent, dilated but not stented.

Methods and Results: In a multicenter randomised bifurcation trial, between June 2001 and April 2002, 80 pts with a significant stenosis at a bifurcation were randomised. The efficacy of sirolimus-eluting stents in these lesions has been evaluated. Pts were randomised into 3 groups of 43 each to receive either 2 stents (main vessel and branch) or 1 stent (main vessel only). At this operator's discretion 20 patients in the single stent arm have crossed over to the 2 stent arm. Baseline characteristics were comparable in both groups: mean age 63±10 years, males 82.5%, diabetes 22%, and unstable angina 17.6%.

By means of QCA, films of 47 pts were analyzed before and after intervention and at 6 months for the presence of geographic miss and its effect on restenosis. 5 patients who had acute procedural failure were excluded from the analysis. Geographic miss has been defined as any balloon inflation to the non-stented segment. The segments proximal and distal to the stent in the main vessel as well as the side branch have been examined for geographic miss. Conclusion. Even in the era of drug-eluting stents, the process of restenosis is multifactorial and the presence of geographic miss does not seem to influence the restenosis rates in bifurcations lesions.

Study Group

<table>
<thead>
<tr>
<th>Restenosis</th>
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<tr>
<td>No geographic miss (47/42)</td>
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<tr>
<td>Geographic miss (25/42)</td>
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Main vessel (10)

Proximal to stent (4) | 0
Distal to stent (9) | 1
Side branch (19) | 3

1198-186 Association Between Progression of Untreated Coronary Lesions and In-Stent Restenosis

Dirk Strosbach, Joosthien Veenstra, Alexander Jatso, Mariel Andrehlc, Berndt Lỏiwe, Dmitriy Burtk6, University of Bonn, Bonn, Germany.

Background: Progression of coronary artery disease is not completely understood, neither for de novo stenoses nor for in-stent restenosis (ISR) as accelerated arteriosclerosis. The objective of this angiographic study was to assess an association between presence of ISR and the progression of untreated coronary lesions.

Methods: A series of 212 high-grade native coronary stenoses (mean stenotic degree 88%) of 150 patients was treated by stent implantation; 12 additional lesions with mild to moderate stenoses (<30%) remained untreated. Quantitative coronary angiography analysis was performed after 6±2 months regarding ISR (stenosis ≥50%), coronary progression (increase in stenoses ≥20%) and regression (decrease ≥20%), resp. Angiographic, procedural and clinical characteristics were assessed for a possible association to ISR and coronary progression.