832 Radiation for In-Stent Restenosis: Current Issues

Monday, March 18, 2002, 4:00 p.m.-5:30 p.m.
Georgia World Congress Center, Hall D1

3:00 p.m.

832-1 Predictors of Radiation Failure After Treatment of In-Stent Restenosis With Gamma Vascular Brachytherapy: Pooled Analysis From GAMMA I, II, and SCRIPP III Studies

Toshaool Limajandji, A. Abizaid, R. Mehran, A. A. Lansky, G. Dangas, N. Kipshidze, G. W. Stone, M. B. Collins, J. W. Moses, M. B. Leon, P. S. Teirstein, Cardiovascular Research Foundation, New York, New York; Lenox Hill Heart & Vascular Institute, New York, New York; Stanford University School of Medicine, Stanford, California; New York University, New York, New York; University of Virginia Health System, Charlottesville, Virginia; and the University of Maryland School of Medicine, Baltimore, Maryland.

Background: Vascular Brachytherapy (VBT) is the only current effective therapy for treatment of in-stent restenosis. Despite its success, there is a failure rate of 15-30% depending on lesion/patient substrate.

Methods: Using the combined GAMMA-I and -II and SCRIPP-III database, we sought to identify predictors of radiation failure following gamma-VBT (r=192) for ISR. Radiation failure was defined as composite of death, target vessel revascularization (TVR), myocardial infarction, late thrombosis or total occlusion at 6 months follow-up.

Results: A total of 727 consecutive patients who enrolled in the active treatment arm of the GAMMA-I and II and SCRIPP-III trials had complete follow-up at 6-months. Univariate predictors of radiation failure are shown in the table. Most failures resulted in restenosis (80%), while others had either death, MI, thrombosis, or total occlusion.

Conclusion: The predictors of radiation failure after gamma-VBT treatment are persistent at 24 months. No additional clinical sequelae occurred in patients who underwent radiation failure compared to placebo (up to 80%).

<table>
<thead>
<tr>
<th>Radiation Failure</th>
<th>No Radiation Failure</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td></td>
<td>0.06</td>
</tr>
<tr>
<td>Male Gender</td>
<td>75.2%</td>
<td>74.9%</td>
</tr>
<tr>
<td>History of MI</td>
<td>49.3%</td>
<td>36.2%</td>
</tr>
<tr>
<td>Diabetes Mellitus</td>
<td>29.6%</td>
<td>35.0%</td>
</tr>
<tr>
<td>Prior PTCA</td>
<td>7.9%</td>
<td>2.9%</td>
</tr>
<tr>
<td>Subject Gender</td>
<td>3.1±0.3</td>
<td>3.3±1.5</td>
</tr>
<tr>
<td>New Stent Implantation</td>
<td>53.5%</td>
<td>36.5%</td>
</tr>
</tbody>
</table>

4:15 p.m.

832-2 Efficacy of Sr-90 Beta Radiation for the Treatment of In-Stent Restenosis: 24-Month Clinical Outcomes From the STents And Radiation Therapy Trial (START)

Warren K. Laskey, Mohan Sutharasingam, Jeffrey Popma, Richard Heuser, Barry Rutherford, Paul Teirstein, Alexandra Lansky, Richard Kuntz, Raoul Bonan, University of Maryland School of Medicine, Baltimore, Maryland.

Background: The STents and Radiation Therapy Trial (START), the first and largest triple-blind multi-center randomized trial investigating the use of Sr-90 beta radiation for the treatment of in-stent restenosis, demonstrated a 31% to 66% reduction in angiographic and clinical outcome parameters for those patients receiving radiation vs. placebo at a 9 month endpoint. The objective of this study is to report clinical outcomes of patients enrolled in this trial at the 24 month (2 year) endpoint.

Methods: 476 patients were enrolled in the START trial. 244 patients received Sr-90 beta radiation; 232 patients received placebo. There were no significant differences in baseline parameters between the two groups.

Results: At 24 months, patients receiving Sr-90 demonstrated a 26% reduction in major adverse cardiac event (MACE) rates, defined by death, MI, emergent CABG and target vessel revascularization, compared to patients receiving placebo (31.1% vs. 41.8%, p = 0.0156). Target vessel failure (TVF) was reduced by 26% (31.1% vs. 41.8%, p = 0.0156), target vessel revascularization (TVR) was reduced by 43% (27.5% vs. 39.2%, p = 0.0064) and target lesion revascularization was reduced by 33% (23.4% vs. 35.6%, p = 0.0030) in patients receiving Sr-90 vs. patients receiving placebo, respectively. One patient presented with late site thrombosis in the Sr-90 group (0.4%), which occurred at day 244; this was not statistically significant compared to placebo (0.4% vs. 0.0%, p = 0.329). There were no other reported late site thrombus events identified at the 24-month time period.

Conclusion: The early (9-month) clinical benefits of Sr-90 for the treatment of in-stent restenosis are persistent at 24 months. No additional clinical sequelae occurred in patients receiving Sr-90. This data suggests that vascular brachytherapy using Sr-90 beta radiation for the treatment of in-stent restenosis is clinically effective and safe with no unexpected deleterious effects at 24 months.

4:45 p.m.

832-3 Vascular Brachytherapy for Osial In-Stent Restenotic Lesions


Background: In-stent restenosis in the ostial location remains a disease with high recurrence after percutaneous re-intervention. The impact of vascular brachytherapy (VBT) on ostial lesion remains unknown. Methods: We evaluated the angiographic results of 133 pts treated with osial in-stent restenosis selected from a pooled database of 990 pts enrolled in VBT randomized trials. Independent angiographic analyses (QCA) were performed at baseline and follow-up in 45 Gamma, 27 Beta, and 81 placebo pts. Results: Baseline lesion characteristics are similar in all groups with ACC/AHA lesion complexity >61 in 82% of lesions. Baseline compared to follow-up total occlusions were present in 8.9 vs. 4.4% of gamma, 0% vs 3.7% of Beta, and 3.3% vs 8.2% of placebo pts (p=NS for all comparisons). By pairwise comparison differences in binary angiographic restenosis reached significance between gamma vs. placebo (p=0.001) and beta vs. placebo (p=0.0001), however no difference was found between both radiation strategies (p=0.64).

Conclusion: Conventional treatment of osial in-stent restenosis is associated with a malignant recurrence rate. VBT with either a Gamma or a Beta sources result in similar significant reductions in restenosis compared to placebo (up to 80%). In addition, among pts with treatment failures after VBT, lesions are significantly more focal compared to placebo. The observed benefits of VBT do not occur at the expense of higher total occlusion rates.

4:54 p.m.

832-4 Wrist 12 Versus Wrist Plus: Twelve Versus Six Months of Clopidogrel for Prevention of Late Total Occlusion After Gamma Radiation Therapy for In-Stent Restenosis

Ron Weisman, Andrew E. Ajan, Dong-Hun Cha, Danielle Claus, Regina Deible, Ellen Pinnock, Honggang Wu, Augusto D. Picard, Lowell F. Sattler, Kenneth M. Kent, Joseph Lindsay, Washington Hospital Center, Washington, District of Columbia.

Background: An extended duration of antiplatelet therapy (6 months) for patients (pts) treated with intracoronary radiation therapy (IRT) utilizing a gamma emitter for the prevention of recurrent in-stent restenosis (ISR) reduces late thrombosis (LT). The aim of this study is to determine whether additional Clopidogrel therapy (6 months), further reduces the rate of LT and late total occlusion (LTO). Methods: WRIST 12 (Washington Radiation for In-stent Restenosis Trial with 12 months of Clopidogrel) is a registry of 120 pts with diffuse ISR in native coronaries and vein grafts with lesions ≤30 mm in length, treated with IRT (192-Ir). Pts were discharged on 12 months of Clopidogrel (75 mg QD) and scheduled for angiographic follow-up at 15 months. The clinical events of this cohort were compared with 120 pts from the WRIST PLUS registry (6 months of Clopidogrel after IRT). Results: Radiation was delivered successfully to all pts. Clopidogrel was tolerated well and there was no report of leukopenia. Baseline clinical and angiographic characteristics were similar to the WRIST PLUS cohort. The clinical events in pts who had completed 12 months of Clopidogrel were lower than those treated with 6 months (Table). Conclusion: Twelve months of Clopidogrel for pts with ISR treated with gamma radiation is well tolerated and is associated with a reduction in the late total occlusion and revascularization rates compared to 6 months of Clopidogrel. Complete analysis will be available at presentation.

<table>
<thead>
<tr>
<th>Event</th>
<th>WRIST 12 (N=120)</th>
<th>WRIST PLUS (N=111)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>TLR, %</td>
<td>17</td>
<td>31</td>
<td>0.04</td>
</tr>
<tr>
<td>TVR, %</td>
<td>20</td>
<td>35</td>
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</tr>
<tr>
<td>MACE, %</td>
<td>21</td>
<td>36</td>
<td>0.32</td>
</tr>
<tr>
<td>Late Thrombosis, %</td>
<td>1</td>
<td>3</td>
<td>0.52</td>
</tr>
<tr>
<td>Late Total Occlusion, %</td>
<td>3</td>
<td>10</td>
<td>0.06</td>
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