Editor's Note

Not Just Another Restenosis Trial

Key words: percutaneous coronary intervention, restenosis, coronary artery disease

Recently, John Douglas from Atlanta presented the results of the Cilostazol for Restenosis (CREST) trial at the late-breaking trials of the American Heart Association. This was a randomized double-blind trial of treatment with cilostazol 100 mg b.i.d.

or placebo for six months in patients receiving bare metal coronary artery stents.

As everyone knows, restenosis following stent implantation continues to occur despite concerted efforts to prevent it—and at present, it seems that stent implantation does the best job. The purpose of this particular trial as presented by Dr. Douglas, was to evaluate the drug cilostazol, which is principally used to treat peripheral vascular disease symptoms, and which it does fairly well. The CREST investigators wanted to evaluate whether cilostazol would prevent restenosis following the use of stents in those stenoses limited to coronary arteries. Thus, vein grafts were not included in this evaluation. Quantitative coronary angiography was used to assess the results of this randomized trial.

In all, 705 patients at multiple sites were randomized following an angiographically successful uncomplicated percutaneous coronary intervention (PCI).

The average age of patients was approximately 60 years. Three hundred and fifty-four patients were randomized to cilostazol, 100 mg b.i.d., and 351 received placebo following successful bare metal stent implantation. As in most studies of PCI and stent these days, all patients received aspirin and clopidogrel. Patients were assessed again at a six-month inter-

val. The primary endpoint was minimum lumen diameter assessed by quantitative coronary angiography.

The patients studied in this evaluation had patent coronary arteries with stenoses greater than 50%, and requiring a stent less than 40 mm.

Results of this investigation were fairly impressive. When the area comprising the stented segment plus 5 mm on either side of the stent was evaluated, the minimum lumen diameters were significantly larger for cilostazol-treated patients (1.77 mm) than those who received placebo (1.61 mm) ($p = 0.006$). When late lumen loss was evaluated, the cilostazol group had less late loss in stent minimum lumen diameter, in stent late loss, and lower restenosis rates than the placebo group.

Clinical endpoints such as myocardial infarction, death, target vessel revascularization, or stroke were not different in the cilostazol and placebo groups. Bleeding and rehospitalization endpoints were also similar.

These investigators concluded that cilostazol given orally after successful PCI and bare metal stent placement decreased the rate of restenosis at six months compared with placebo, and this was seen in the diabetic and in small-vessel (< 3 mm) subgroups as well.

The observations reported here may have clinical relevance, since over the last many years, multiple agents for the prevention of restenosis have been tested without much benefit. Perhaps this drug, cilostazol, which works quite well in peripheral vascular disease to relieve symptoms of intermittent claudication, may be a useful addition to our current strategies to reduce restenosis. The mechanism for this reduction in restenosis is not understood at the present time, and I suspect that these observations will be hypothesis-generating and create more clinical trials with different subsets of patients undergoing PCI with or without stents, either bare metal or drug-eluting.

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