Shot May Be Alternative to Drug-Eluting Stents

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VANCOUVER, B.C. — Injection of nanoparticle albumin-bound paclitaxel after bare-metal stent implantation may have a future as a lower-cost alternative to drug-eluting stents for prevention of in-stent restenosis, John E. McDonald, M.D., said at a meeting sponsored by the International Academy of Cardiology.

He presented the results of the Systemic Nanoparticle Albumin-Bound Paclitaxel for Prevention of In-Stent Restenosis Trial (SNAPIST-1), a multicenter dose-ranging and safety study involving 23 patients.

Within half an hour after successful implantation of a single bare-metal stent for a de novo coronary lesion, SNAPIST-1 participants received a single intravenous injection of nanoparticle albumin-bound paclitaxel (Coroxane) at 10, 30, 70, or 100 mg/m^2. Paclitaxel is a poorly soluble drug that traditionally has been mixed with the emulsifying agent Cremophor and alcohol, a formulation having extensive side effects. Coroxane is a novel agent that uses nanotechnology to bind paclitaxel to albumin.

In cancer studies, Coroxane can be prescribed in higher doses than conventional paclitaxel with less toxicity and improved responses. And in animal studies, Coroxane is selectively uptaken by injured vascular endothelium, said Dr. McDonald of the Victoria Heart Institute Foundation.

Follow-up in SNAPIST-1, including coronary angiography at 6 months, showed there were essentially no adverse events associated with the 10-mg/m^2 dose of Coroxane—but no suggestion of efficacy in preventing angiographic restenosis or repeat revascularization, either.

At the other extreme, the 100-mg/m^2 dose had lots of unacceptable side effects—neutropenia, neuropathy, and alopecia, all reversible—but again, no evidence of efficacy. "That may be too high a dose to permit healing," he observed.

In contrast, there appeared to be significant suppression of neointimal hyperplasia at the 30- and 70-mg/m^2 doses. Since neutropenia and alopecia occurred in patients on 70 mg/m^2 but not lesser doses, investigators selected the dose of 35 mg/m^2 IV for further studies.

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Indeed, in the larger SNAPIST-2 study, which recently completed enrollment, patients get a second 35-mg/m^2 injection 2 months after bare-metal stent implantation. Animal studies have suggested a second injection would contribute to greater reduction in restenosis.

If the results of SNAPIST-2 are favorable, the logical next step will be a randomized trial comparing outcomes in patients treated with a bare-metal stent plus Coroxane versus a drug-eluting stent.

Session cochair Henning Kelbaek, M.D., of Skejby Hospital, Denmark, questioned the point of trying to develop a systemic therapy that appears to be laden with so many problematic side effects, all of which are avoidable by using drug-eluting stents.

"Any further studies will have to look at doses where we don't get those adverse events," Dr. McDonald conceded. "But clearly, there are some benefits of systemic therapy, particularly in patients with multivessel disease, or in patients unsuitable for stenting."

Moreover, a systemic therapy such as Coroxane used in conjunction with a bare metal stent would be far less expensive than a drug-eluting stent, a fact of considerable interest to financially strapped health care systems, he continued.

Besides, drug-eluting stents are not nearly as targeted and efficient as they're often portrayed. "A lot of the drug administered in drug-eluting stents becomes entombed within the stent and doesn't have any effect," said Dr. McDonald.

He said there is also interest, albeit not yet at the clinical stage, in the possibility of using Coroxane in the setting of acute coronary syndromes because of the drug's anti-inflammatory effect.

The SNAPIST trials are sponsored by American BioScience Inc. ■