INTERVENTION

More MACE with zotarolimus-eluting stents than with sirolimus-eluting stents

First-generation drug-eluting stents have been associated with increased risk of late and very late stent thrombosis, and early reports suggested that the second-generation zotarolimus-eluting stent was a safer alternative in low-risk patients. However, in a study that included patients with complex lesions and those with acute coronary syndromes, the SORT OUT III investigators have shown reduced efficacy and safety of a zotarolimus-eluting stent, compared with that of the first-generation sirolimus-eluting stent.

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The SORT OUT study group uses an all-comer, clinically driven event detection method that requires access to existing population-based health-care databases. According to SORT OUT investigator Dr Jens Flensted Lassen, this method “may enable large randomized clinical

studies to cover a broad range of patients, facilitate prolonged and completely unbiased follow-up, and thus better reflect everyday clinical practice.”

The SORT OUT III investigators randomly assigned patients who had chronic stable coronary artery disease or acute coronary syndromes, and had at least one lesion requiring treatment with a drug-eluting stent, to receive the sirolimus-eluting stent (Cypher® or Cypher Select® Plus, Cordis Corporation, Warren, NJ; $n = 1,170$) or the zotarolimus-eluting stent (Endeavor®, Medtronic Inc., Santa Rosa, CA; $n = 1,162$). All-cause mortality, cardiac death, myocardial infarction (MI), target vessel revascularization, and target lesion revascularization were assessed 30 days, as well as 9 and 18 months after stent implantation. The primary end point of the study was the composite of all these events at the 9-month follow-up.

No differences in the number of events were observed for the treatment groups at the 30-day follow-up. After 9 months, however, the primary composite end point was twofold higher in the patients who received the zotarolimus-eluting stent than in those who received the sirolimus-eluting stent, owing to higher occurrences of MI and target vessel and lesion revascularization in the zotarolimus group. These observations were sustained

to the 18-month follow-up, when all-cause mortality was also found to be higher in the patients who received the zotarolimus-eluting stent.

Definite stent thrombosis also occurred more often in the zotarolimus group at the 9-month follow-up, but not at 18 months. The higher incidence of stent thrombosis was, at least in part, responsible for the observed difference in occurrence of MI.

Compared with the sirolimus-eluting stent, the zotarolimus-eluting stent was also associated with increased occurrence of symptom-driven restenosis at the 9-month and 18-month follow-ups, and this restenosis was the most common cause of target lesion revascularization.

The SORT OUT study group have now finalized SORT OUT IV, which compares sirolimus-eluting stents with those eluting everolimus, and are currently enrolling patients in SORT OUT V, which compares sirolimus-eluting stents with those eluting biolimus-A9. Plans for a sixth SORT OUT study are also underway; SORT OUT VI is expected to begin enrollment later this year.

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Original article Rasmussen, K. *et al.* Efficacy and safety of zotarolimus-eluting and sirolimus-eluting coronary stents in routine clinical care (SORT OUT III): a randomised controlled superiority trial. *Lancet* doi:10.1016/S0140-6736(10)60208-5