Reviewer’s report

Title: A novel endothelial damage inhibitor for the treatment of vascular conduits in coronary artery bypass grafting: protocol and rationale for the European, multicentre, prospective, observational DuraGraft registry

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Reviewer: Antonio Lio

Reviewer's report:

Caliskan et al. are ongoing multicentre, prospective observational registry which enrol 3000 patients undergoing an isolated CABG procedure or a combined with at least one saphenous vein grafts or one free arterial graft. Data on baseline, clinical, and angiographic characteristics as well as procedural and clinical events will be collected.

They set primary outcome measure as the occurrence of MACE. Secondary outcome measures are the occurrence of MACCE. Events will be adjudicated by an independent clinical events committee. Finally, clinical outcome associated with DuraGraft will be examined. They mention that this European, multi-institutional registry will provide detailed insights into clinical outcome associated with the use of DuraGraft. Beyond that, and given the comprehensive data sets comprising of patient, procedural, and graft parameters that are being collected, the registry will enable for multiple subgroup analyses targeting focus groups or specific clinical questions. These may include analysis of subpopulations such as patients with diabetes or multimorbid high-risk patients (patient level), evaluation of relevance of harvesting technique including endoscopic versus open conduit harvesting (procedural level), or particular graft-specific aspects (conduit level).

I read the protocol with interest. However, the study design seems to be too rough. To evaluate the drug effect on the graft patency and effect on prevention of stenosis, 3D-CT or CAG are mandatory. MACE or MACCE does not represent DuraGraft effect directly. The patency of bypass grafts depends on not only on the graft preservation technique but also many other factors, including the runn off, proximal anastomosis device, distal anastomoses, quality of the graft, its length, and the compatibility of the diameter of the coronary artery and graft. Recently, some groups published superiority of no-touch SVGs with fat tissue. SVGs were neither stripped nor distended and exhibited a higher patency comparable to that of LITA. Among these many factors affect graft patency, I wonder how much DuraGraft short term preservation contribute to elevate the graft patency.

In contrast, similar study protocol using Dura Graft (NCT02272582/NCT02774824) reported by Ali et al. assess MD-CT angiography at 4-6 weeks, 3 months and 12 months. In their study, the primary short-term endpoint is the magnitude of change between 4-6 weeks and 3 months post-CABG surgery in mean wall thickness between the paired grafts as determined by 64-slice or better MDCT angiography. The wall thickness will be calculated every 10 mm for all grafts (varying lengths of the grafts and thus number of measurements used in creating the average for
each graft) by subtracting the lumen diameter in millimetre using contrast enhanced CT from the total vessel diameter in millimetre using non-enhanced CT and dividing by two. Each 10 mm segment is graded for quality, and the mean wall thickness for the whole graft will be computed as the average of all wall thickness measures of acceptable quality for each of the study grafts at 4-6 weeks and 3 months. The magnitude of change will be calculated per graft as the difference between the 4-6 weeks and the 3-month time points. The magnitude of these changes will then be compared between the paired grafts. The primary long-term endpoint will be the change from 4-6 weeks to 12 months following CABG surgery in lumen diameter calculated as the average of the mean lumen diameter over each graft and the lumen diameter at point of maximal stenosis within graft, using 64-slice or better MDCT angiography. Compared to their protocol, MACE and MACCE as an endpoints, study message will be weak.

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