Pilot Study of the Safety and Feasibility of the Treatment of Paclitaxel Associated to a Cholesterol-Rich Nanoemulsion in Patients With Aortic Atherosclerotic Disease

Raul C Maranhao, Heart Inst, São Paulo, Brazil; Afonso A Shiozaki, Tiago Senra, Dante Pazzanese Cardiology Inst, São Paulo, Brazil; Aleksandra T Morikawa, Debora F Deus, Heart Inst, São Paulo, Brazil; Antonio T Paladino-Filho, Ibraim M Pinto, Dante Pazzanese Cardiology Inst, São Paulo, Brazil

Previously, we showed that the toxicity of chemotherapeutic agents used in cancer treatment can be drastically reduced by association to nanoemulsions (LDE) that mimic the lipid composition of low-density lipoprotein (LDL), without loss of pharmacological action. Injected into the circulation, LDE concentrates associated drugs, such as the anti-proliferative agent paclitaxel, in neoplastic tissues and in atherosclerotic lesions. In rabbits with atherosclerosis lesions were reduced by 65% by LDE-paclitaxel treatment. Tolerability and safety of high dose LDE-paclitaxel was shown in several patients with advanced cancers. Based on those findings, this pilot study was designed to test, in 9 aged patients with extensive aortic atherosclerosis, LDE-paclitaxel at 175 mg/m2 body surface dose (I.V., 3/3 weeks for 6 cycles). All were under statin treatment that was not discontinued during the 18-week treatment period. No observable clinical or laboratorial toxicity was observed. One death occurred but was unrelated with treatment toxicity. Images acquired by Multiple Detector Computer Tomography Angiography (64-slice scanner) taken before and at 2-3 month after the treatment end showed that the mean volume of the aortic artery wall was clearly reduced in 4 of the 8 patients, while in 3 it remained unchanged and in one it clearly increased. Therefore, the treatment was tolerable for patients with cardiovascular disease and these results encourage large, placebo-controlled clinical studies to ascertain the ability of LDE paclitaxel to reduce atherosclerotic lesions.