

Evaluation of a Novel Slow-Release Paclitaxel-Eluting Stent with a Bioabsorbable Polymeric Surface Coating

Refat Jabara^{1,2}, Nicolas Chronos², Damian Conway³, Warner Molema³, Keith Robinson²

¹ Heart Institute, Hadassah-Hebrew University Medical Center, Jerusalem, Israel,

² Cardiovascular Research Institute, Saint Joseph's Hospital, Atlanta, GA, USA, ³ DISA Vascular Ltd, Cape Town, South Africa

Objectives: To evaluate a new second-generation drug-eluting stent (DES) comprising a slow-release biodegradable PLGA polymer (polylactide/polyglycolide) and low-dose paclitaxel on a thin-strut cobalt chromium stent platform, in a clinically relevant animal model.

Background: Our previous work demonstrated sub-acute vascular toxicity and necrosis triggering late excess neointima in pig coronaries, with a moderate paclitaxel dose eluted from an erodible polymer. The use of slower-releasing absorbable polymers with lower doses of paclitaxel is expected to minimize such adverse outcomes.

Methods: Three types of stents were implanted in pig coronary arteries using QCA to optimize stent apposition: Bare metal stents (BMS); absorbable, slow-release polymer-coated-only stents (POLY); and absorbable polymer-based paclitaxel-eluting stents (PACL). The dose density of paclitaxel was 0.15 $\mu\text{g}/\text{mm}^2$ with *in-vitro* studies demonstrating a gradual elution over 12-16 weeks. Animals underwent angiographic restudy and were terminated at one and three months for complete histopathologic and histomorphometric analyses.

Results: At one month, intimal thickness varied significantly according to stent type with the lowest level for the PACL group compared to BMS and POLY (0.06mm \pm 0.02 vs. 0.17mm \pm 0.07, 0.17mm \pm 0.08, respectively, $P < 0.001$); histological % area stenosis was 18% \pm 4 for PACL compared to 27% \pm 7 for BMS and 30% \pm 12 for POLY, respectively ($P = 0.001$). At three months, PACL showed similar neointimal thickness as BMS and POLY (0.09mm \pm 0.05 vs. 0.13mm \pm 0.10 and 0.11mm \pm 0.03 respectively, $P = 0.582$). Histological % area stenosis was 23% \pm 8 for PACL vs. 23% \pm 11 for BMS and 23% \pm 2 for POLY, respectively ($P = 1.000$).

Conclusions: This study shows favorable vascular compatibility and efficacy for a novel DES eluting paclitaxel, in porcine coronary arteries. These results support the notion that slowing the release rate and lowering the dose of paclitaxel favorably influences the vascular biological response to DES implant, decreasing early toxicity and promoting stable healing while still suppressing neointima formation.