Preclinical Evaluation of Vasomotion at 12 Months in a Bioresorbable Vascular Scaffold Implanted in Porcine Coronary Arteries

Authors: **Traci T. Goodchild[2], James J. Benham[1], Steve H. Hsu[1], Deepal K. Panchal[2], Shashi F. Bhushan[3], David J. Lefer[3], Laura E.L. Perkins[1], Alexander J. Sheehy[1], Byron J. Lambert[1], Daniel L. Cox[1], Richard J. Rapoza[1]**

1 Abbott Vascular, Santa Clara, CA, USA 2 Saint Joseph's Translational Research Institute, Atlanta, GA, USA
3 Emory University. Atlanta, GA, USA

Introduction

The principle components responsible for vasomotion are the smooth muscle cells (SMC) and endothelial cells (EC). ECs influence SMCs by producing nitric oxide for vaso-dilation and endothelin-1 for the maintenance of basal tone. Arterial SMCs phenotypically change, in response to injury, from a non-proliferative, contractile phenotype to a synthetic proliferative and non-contractile phenotype. Absorb™ BVS is a bioresorbable vascular scaffold with three functional phases: revascularization, restoration, and resorption. It is hypothesized that during *restoration*, Absorb BVS is expected to allow SMCs to restore their native contractile phenotype and allow restoration of arterial vasomotion. The purpose of the study was to evaluate vasomotion in porcine coronary arteries implanted with Absorb BVS during and beyond this restoration phase at 12, 24, 30 and 36 months by evaluating SMC and EC function *in vivo, ex vivo* and *in vitro* (gene expression). The results from the 12 month time point are available and described below.

Materials and Methods

Porcine coronary arteries were implanted with Absorb BVS (n = 8) for *in vivo*, *ex vivo* and *in vitro* vasomotion evaluation at 12 months. *In vivo* vasomotion was measured after the administration of acetylcholine (Ach) and nitroglycerin (NTG) using quantitative coronary angiography (QCA). Explanted treated and untreated arteries were sectioned and segments for *ex vivo* analysis were suspended in individual organ chambers. Various agents known to induce vasomotion were used to evaluate the EC and SMC specific responses in the implanted and untreated regions. Gene expression of functional EC and SMC specific pathways in the implanted and untreated regions were determined using a porcine DNA microarray and real time reverse transcription polymerase chain reaction (RT-PCR).

Results

The Absorb BVS implanted region demonstrates an attenuated dose dependent constriction to Ach and dilation response to NTG compared to the control regions when evaluated by QCA. As with the Absorb BVS implanted arteries assessed *in vivo*, Absorb BVS implanted arteries demonstrated less contractility *ex vivo* compared to untreated control arteries ($p<0.01$). Microarray gene expression revealed that multiple early markers of SMC differentiation have been recovered while several late markers have not recovered ($p<0.05$ and $\geq$ 2-fold change from control) in the implanted region. Absorb BVS exhibited similar endothelial cell membrane and signaling marker gene expression compared to the untreated proximal control. All microarray data was verified using RT-PCR.

Discussion and Conclusions

At 12 months, Absorb BVS treated arteries demonstrated a small contractile and dilatory response both *in vivo* as assessed by angiography as well as *ex vivo*. In both settings, the response was significantly less than that seen in the untreated arterial region (*in vivo*) and in untreated control arteries (*ex vivo*). Planned *in vivo* and *ex vivo* assessments at later time points of 24, 30 and 36 months will determine whether 12 months represents a transitional stage with Absorb BVS treated arteries regaining full capability of responding to vasomotive stimuli at later follow-ups.

References

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Disclosures

This study was funded by Abbott Vascular. All of the authors above that are affiliated with Abbott Vascular are full-time employees of Abbott Vascular.