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Outside Start Cilostazol Bridge Study (Outpatient peri-Surgical Interruption of Drug Eluting Stent Antiplatelet Regimen Testing A Cilostazol Bridge Study): A 6 year experience

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BACKGROUND Dual antiplatelet therapy (DAPT) with a P2Y12 inhibitor + aspirin (ASA) decreases drug-eluting stent (DES) thrombosis. Annually 5%-10% of DES patients (pts) are advised DAPT interruption to reduce peri-operative (peri-op) bleeding. Premature DAPT stoppage especially early during the first year after (post) 1st generation (F-Gen) DES leads to high stent thrombosis (ST) rates of 10-20%. Of all DES, paclitaxel eluting DES have highest ST rates off DAPT with recent studies showing associated major adverse cardiac event (MACE) rates persist for at least 30 months post DES placement. There is no consensus as to the best bridging in DES patients taken off DAPT preoperatively. The feasibility of outpatient cilostazol bridging of DES off DAPT peri-op has not been formally tested. We report our 6 year experience with cilostazol bridging during peri-op DAPT stoppage mostly in F-Gen paclitaxel DES during periods of proven high ST/MACE risk.

METHODS From 2005 to 2010 we tested cilostazol bridging of DES in consecutive pts advised to stop both DAPT peri-op. 2 dosing regimen intervals were tailored to reduce risk and degree of expected peri-op bleeding. Initially DAPT was only advised for 6 months post DES and later extended to 1 year, thus early bridging was in urgent unavoidable surgeries during the high risk first 6-12 month post DES. When DAPT was later advised long-term due to late ST reports, peri-op cilostazol bridging was extended to all procedures up to 5 years post DES placement. MACE was felt related to bridging if it occurred while off DAPT peri-op or within 30 days post-op. We hereby report results for peri-op cilostazol bridging off DAPT from 2 weeks to 60 months post latest DES.

DAPT was stopped after last doses on 8th day pre-op and cilostazol 100mg po bid started on the 7th pre-op day: for low risk bleeding surgeries, cilostazol was stopped 24-30 hours (hrs) pre-op and DAPT resumption advised at 12-24 hrs post-op. For moderate-high bleeding risk surgeries (epidurals; back & urology surgery, coronary bypass) cilostazol was stopped 54-60 hrs pre-op after 1000 mg and DAPT resumed 24-36 hrs post-op. For those who didn't tolerate cilostazol 100mg, dose was reduced to 50mg po bid. Pts were deemed adequately bridged if they took at least 600 mg of cilostazol pre-op and resumed DAPT within 48 hrs post-op.

RESULTS A total of 95 pts with DES's underwent 167 consecutive surgeries advising DAPT stoppage utilizing the cilostazol bridging and DAPT resumption protocols. 95% of patients had 1 or more high ST risk paclitaxel DES. Pts were adequately bridged during 157/167 surgeries with optimal dosing of 100mg bid (or 50mg if intolerant) and DAPT resumed within 48 hrs. None of the 157 fully bridged experienced peri or post-op MACE giving observed respective 100% compliant, and 94% intention to treat, success rates for cilostazol DES bridging. In the remaining 10 patients that were cilostazol intolerant, non-compliant and/or who failed DAPT resumption within 48 hrs post-op, 3 had MACE (Table) perioperatively or in the follow up period. Overall, a very low MACE rate of 2% (ie. 1/48 bridged surgeries) was observed with cilostazol off DAPT in the highest risk first 12 months post DES when compared to historical MACE rates of 10-20% with paclitaxel DES in the first year post DES when DAPT stopped prematurely without planned bridging. No significant bleeding other than nuisance bleeding occurred, none altering surgery success or requiring additional transfusions over that typical of surgery type.

CONCLUSION Our study suggests that outpatient cilostazol peri-op bridging of DES off DAPT is feasible and results in low bleeding and low MACE rates as seen in patients with first generation DES when bridged off DAPT. Bridging success requires strict adherence to the cilostazol regimen and DAPT resumption schedules. As new generation DES have reported less ST risk & most surgeries don't stop both DAPT, the value of cilostazol bridging needs further confirmation in current generation DES and in those continuing ASA peri-op.

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Clinical Outcomes Of The BIOFLEX-I Study: Utilization Of Self Expanding Stents In The Iliac Arteries

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BACKGROUND Percutaneous transluminal angioplasty has historically been the standard in minimally invasive treatment of peripheral artery disease (PAD). In iliac arteries, self-expanding, nitinol stent technology has evolved as an effective treatment of atherosclerotic lesions. BIOFLEX-I evaluates the safety and efficacy of the Astron stent in the iliac arteries.

METHODS The BIOFLEX-I study was a prospective, multicenter, non-randomized, single arm, investigational device exemption (IDE) study performed in the United States, Canada, and Europe. Thirty (30) study centers enrolled 161 evaluable study subjects for treatment of de novo or restenotic lesions (≤140mm length) or occlusions (≤100mm length) in common and/or external iliac arteries with reference vessel diameters from 6 to 9mm. The primary endpoint was the composite rate of procedure or stent related major adverse events (MAEs) at 12 months post index procedure. MAEs were defined as 30-day mortality, clinically-indicated target lesion revascularization (TLR) and index limb amputation at 12 months. Results were compared to a pre-specified performance goal based on prior prospective, multicenter studies utilizing nitinol-based, self-expanding stents for the treatment of iliac lesions similar to those in this study. Core laboratories were utilized for independent confirmation of angiography and duplex ultrasound findings. All site reported MAEs were adjudicated by an independent Clinical Events Committee.

RESULTS For the BIOFLEX-I study of patients with iliac disease treated with the Astron stent, the primary endpoint was met. The 12-month composite endpoint of MAE was 2.1% (3/146) ($p<0.001$) 95 % CI [0.4%, 5.9%]. The 30 day mortality rate was 0.7% (1/146) 95 % CI [0.0%, 3.8%]. Target lesion revascularization (TLR) rates at 12 months were 1.4% (2/146) 95 % CI [0.2%, 4.5%], and 12-month index limb amputation was 0.0% (0/146) 95 % CI [0.0%, 2.5%]. The secondary endpoint of primary patency was 89.8% (115/128) 95 % CI [83.3%, 94.5%] at 12 months.

CONCLUSION The 12-month outcomes of the BIOFLEX-I study for the Astron stent in iliac indications demonstrate a low MAE rate, high primary patency, and a low rate of TLR. This supports the safety and efficacy of the self-expanding, nitinol stent for treatment of atherosclerotic lesions in the iliac arteries.

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Passeo-18 Lux Drug Releasing Balloon: 12-month Update From The Biolux P-I And Biolux P-II Studies And The Biolux P-III All-comers Study Design

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PURPOSE Drug releasing balloon (DRB) angioplasty has evolved to a paradigm-shift in the endovascular treatment of peripheral artery disease (PAD). The current evidence base has been fuelled mostly by clinical trials with restrictive eligibility criteria, excluding most patients treated in daily practice.

METHODS BIOLUX P-I and BIOLUX P-II were prospective, international, multicentre, first-in-human, randomized controlled trials investigating the safety and efficacy of the Passeo-18 Lux DRB in the femoropopliteal and infrapopliteal arteries, respectively. BIOLUX P-III is a global, prospective, international, multicentre, all-comers study to enroll at least 700 patients with infrainguinal artery lesions treated with the Passeo-18 Lux DRB. The clinical and performance primary endpoints are major adverse events at 6 months and freedom from clinically-driven target lesion revascularization at 12 months, respectively. Pre-specified analysis subgroups include: Age≥65; Diabetes; Renal Insufficiency; Rutherford Category≥3; Popliteal, Infrapopliteal, TASC C&D and heavily calcified lesions.

RESULTS BIOLUX P-III will build and expand on safety and performance outcomes from the BIOLUX P-I and BIOLUX P-II studies: BIOLUX P-I demonstrated significant differences in late lumen loss, TLR and binary restenosis in favour of the Passeo-18 Lux compared to control PTA in femoropopliteal lesions. In BIOLUX P-II, Rutherford Class 5 patients with infrapopliteal lesions demonstrated significant clinical improvement at 6 months. Updated 12 month results from both studies will be presented.

CONCLUSION With inclusion and exclusion criteria that reflect complex, 'real-world' clinical practice, BIOLUX P-III will further illuminate the role of DRB, alone or in combination with other treatment modalities, in the contemporary management of patients with infrainguinal PAD (ClinicalTrials.gov Identifier: NCT02276313).

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Long Term Clinical Data Of The BIOSOLVE-I Study With The Paclitaxel-eluting Absorbable Magnesium Scaffold (DREAMS) And Multi-modality Imaging Analysis

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OBJECTIVES In order to assess the long term safety, clinical performance and the bioabsorption process of the paclitaxel-eluting absorbable magnesium Scaffold (DREAMS) 3-year clinical data and multi-modality imaging outcomes are reported.

METHOD Forty-six subjects were enrolled in the first-in-man BIOSOLVE-I study in two different cohorts with clinical follow-up at 1, 6, 12, 24 and 36 months; angiographic and IVUS follow-up for cohort 1 at 6-month and for cohort 2 at 12-month. A subgroup of patients underwent OCT and vasomotion testing. The primary endpoint

is Target Lesion Failure (TLF) at 6-month for cohort 1 and at 12-month for cohort 2. For some patients also 18-month and 24-month imaging data are available.

RESULTS TLF rate at 36-month was 6.8% including 2 TLRs and 1 peri-procedural MI occurring at the 12-month follow-up angiography; no events emerged from 12- to 36-month. No cardiac death or scaffold thrombosis was observed.

Vasoconstriction after acetylcholine at 6-month (delta=-10.04%; p=0.0008 versus baseline) followed by vasodilatation after nitroglycerine(delta=8.69%; p<0.0001 versus baseline) demonstrates the uncaging aspect of the absorption process with no further change at the 12-month follow-up. Six-month virtual histology (VH) data showed a significant decrease in the dense calcium by 39.5% (p=0.0015) remaining stable from 6- to 12-month follow-up. This decrease is interpreted as a surrogate assessment for the bioabsorption process of the scaffold material.

Echogenicity data using the decrease in intensity of the ultrasound signal to quantify the change in strut structure demonstrate a continuous decrease in % hyperechogenicity over the follow-up period, with the most pronounced changes within the first 6 months (22 to 16% p<0.001).

CONCLUSION DREAMS shows excellent safety and efficacy data with no death and no scaffold thrombosis up to 3 years in the BIOSOLVE-I trial. Multi-modality imaging documented the absorption process and the uncaging aspect of this device already at 6 months.

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Six-month Revascularization Outcome Of Jetstream Atherectomy In Treating In-stent Restenosis Of Femoropopliteal Arteries: Results Of The Jetstream-ISR Study

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BACKGROUND Treatment of in-stent restenosis (ISR) of the femoropopliteal (FP) artery is complex and is associated with high rate of restenosis. Debulking of FP ISR lesions have been attempted to reduce restenotic tissue burden and improve patency or target lesion revascularization (TLR). Recently laser atherectomy of FP ISR was shown to reduce target lesion revascularization at 6 months when compared to plain old balloon angioplasty (POBA) alone.

JetStream Atherectomy (JS) is a rotational cutter with aspiration capacity that has been shown to cut and remove atherosclerotic and restenotic tissue. Its application within a stented FP artery is off label. In this study, JS Navitus L or XC was applied prospectively in a cohort of FP ISR from 2 centers to evaluate acute procedural and 6-month outcomes and stent-device interaction. Data on 40 infrainguinal ISR lesions treated with the older generation Pathway PV atherectomy system were previously reported from Europe and no safety concerns were raised. The primary patency rate, however, was low at 33 % after 12 months. Since then, the device was upgraded to the JetStream Navitus with enhanced cutting ability and aspiration. This is the first prospective report on the off label use of the Jetstream Navitus XC atherectomy device in treating FP ISR (clinicaltrials.gov identifier NCT01722877).

METHODS 29 patients (32 limbs) with FP ISR were treated at 2 medical centers by 2 operators from October 2012 to August 2014. Patients were consented prior to the procedure and were included in the study only if they were found to have an in-stent restenotic lesion in the FP segment. The Jetstream device was used as a first modality of treatment. No other debulking devices, cutting/scoring balloons or cryogenic balloons were allowed. Adjunctive treatment was limited to POBA using a semi or non-compliant peripheral vascular balloon or stenting only if significant residual narrowing (>30%) remained or a significant dissection (type C or higher) was seen. It was recommended that the Jetstream be used to maximize debulking until the residual stenosis ≤ 50% prior to adjunctive therapy. The study was approved by the Institutional Review Board (IRB) at both institutions. Demographics, clinical, procedural and angiographic variables were prospectively collected. Quantitative vascular angiography was performed on lesions at baseline, post atherectomy alone and post adjunctive treatment. Six-month follow up was achieved on all patients (except 3 at the time of this writing). In-hospital and 6-month major adverse events were recorded. The primary effectiveness endpoint was acute procedural success defined as obtaining angiographically ≤ 30% residual narrowing with no serious adverse events at the end of the procedure. The primary safety endpoint was major adverse events in-hospital and at 6 months which included device-induced vascular injury as reported by the operator, amputation (major and minor unplanned), death, significant distal embolization requiring the use of pharmacologic or mechanical means to treat (other than a vasodilator), perforation, major bleeding, myocardial infarction as defined by ACC criteria, stroke, access complications (AV fistula and pseudoaneurysm), acute renal failure and acute (≤ 24 hours) or subacute (than 24 hours) vessel closure. Secondary endpoints included acute device success defined as a residual narrowing of ≤ 50% by the JetStream device alone and before adjunctive treatment and with no serious adverse events, distal embolization, clinically driven TLR and TVR at 6-month follow up based on symptom recurrence, ankle brachial indices (ABI), Rutherford- Becker class at one month and 6 month, death, and amputation. Device-stent untoward interaction was evaluated by an independent angiographic core laboratory. Descriptive analysis was done on all variables. Continuous variables were presented as mean ± SD and dichotomous variables as percentages. Kaplan-Meier survival curve for TLR was plotted.

RESULTS 29 consecutive patients (32 limbs) (mean age 72.5 ± 11.1 years, 34.5% males) were included in the study. One patient withdrew from the study. Six-month follow-up was completed on 25 patients. Adjunctive balloon angioplasty was performed in 100% at a mean pressure of 12.2 ± 3.2 atm. Lesion length was 16.6 ± 12 cm and total treated length 23.7 ± 18.8 cm. Acute procedural success occurred in 100% of patients. Acute device success was 75.8%. Embolic filter protection (EFP) was used in 16/32 (50.0%) of limbs. Macrodebris was noted in 2/16 (12.5%) of filters and distal embolization (DE) requiring treatment was 9.4% (2 with no EFP (one after adjunctive PTA), 1 with Spider EFP, 0 with Nav-6 EFP). There were no new stent fractures (n=24) post JS as reported by Core Lab analysis. On 6-month follow-up TLR occurred in 14.3% (Figure 1), patency rate (PSVR<2.4) 16/23 (70%), total death 4% (1/25), vascular related death 0%, major bleeding 0%.

CONCLUSION JS atherectomy using the Navitus device has favorable acute results in treating in-stent restenosis of the FP arteries with no device-stent interaction and high procedural success. At 6-month follow-up TLR compares favorably to historic controls from balloon angioplasty or other atherectomy devices. A multicenter randomized trial is needed to confirm these results.

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Early In Vivo Evaluation of Strut Healing Following Bioresorbable Polymer Everolimus Eluting Stent Implantation in Humans: The TIMELESS Study

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Bioresorbable polymer DES technologies promise to enhance vascular healing by reducing the polymer exposure to the vessel wall potentially allowing the earlier discontinuation of dual anti-platelet therapy. At the present time, the in vivo early vascular healing response to this type of technologies is still unclear. The TIMELESS study is a multi-center, prospective, single arm study enrolling real world patients undergoing PCI. All patients underwent Synergy stent implantation (Boston Scientific Corp, MA, USA) using the Element Platinum-chromium platform coated with an ultra-thin abluminal bioabsorbable PLGA polymer eluting Everolimus. At 3 months, all patients underwent OCT imaging and Clopidogrel was stopped regardless of the OCT findings. A total of 37 patients were included in the study. The majority of the patients underwent PCI due to acute coronary syndromes (~65%). The mean vessel reference diameter was 2.63 ± 0.40 mm and 67.5% of the cases received stents longer than 20 mm in length. At 3 months, angiographic follow up showed a percentage diameter of stenosis of 8.1% ± 7.5% and an angiographic late loss of 0.03 ± 0.24 mm. A total of 7,761 struts (209.9 ± 45.8 struts per stent) were analyzed using OCT imaging. Full OCT analysis will be available at the time of the presentation.