Embargoed until Wednesday, September 13, 9:15 AM PST (12:15 PM EST)

Late-Breaking Trials

HIGHLIGHTS FROM WEDNESDAY MORNING'S TRIAL PRESENTATIONS.

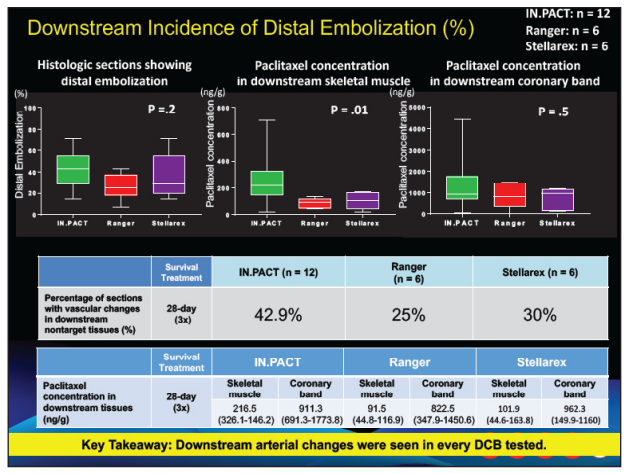
COMPARISON OF PARTICULATE EMBOLIZATION AFTER FEMORAL ARTERY TREATMENT WITH THE IN.PACT ADMIRAL, RANGER, AND STELLAREX PACLITAXEL-COATED BALLOONS IN HEALTHY SWINE

Presenter: Aloke Finn, MD

Femoropopliteal disease treated by endovascular therapy with adjunctive local drug delivery via drug-coated balloons (DCBs) has led to further improvements in early clinical outcomes. However, limitations unique to each of these drug delivery platforms may impair their long-term clinical effectiveness. Different combinations of carrier excipients and drug crystallinity unique to individual DCBs may influence embolic safety characteristics in peripheral vascular territories through embolization of released particulates. This has the potential to cause damage to nontarget tissues downstream of the treated area. A comparator study of the In.Pact Admiral (Medtronic) versus Stellarex (Spectranetics Corporation) versus Ranger (Boston Scientific Corporation) balloons (3x dosing) in healthy swine was therefore performed to assess the vascular response of the treated vessel and nontarget tissues (embolic effects) at 28 days.

Histomorphometry showed no differences in area measurements of external elastic lamina, internal elastic lamina, lumen, media, or neointima among the groups. Likewise, measures of vessel healing and injury were not different between groups. Examination of left and right skeletal muscle and coronary bands for embolic effects showed evidence of downstream embolization in all animals. Vascular changes due to emboli were mainly confined to arterioles. Downstream vascular changes in arterioles were greatest for In.Pact Admiral > Stellarex > Ranger. Paclitaxel was detected in downstream tissues for all DCBs and followed a similar trend.

In summary, there were no differences in target tissue paclitaxel-induced injury and healing between the three balloons tested. All exhibited evidence of downstream embolization to nontarget tissues. The potential for downstream embolic effects with certain DCBs may present a concern that may influence the selection of DCBs for clinical use.

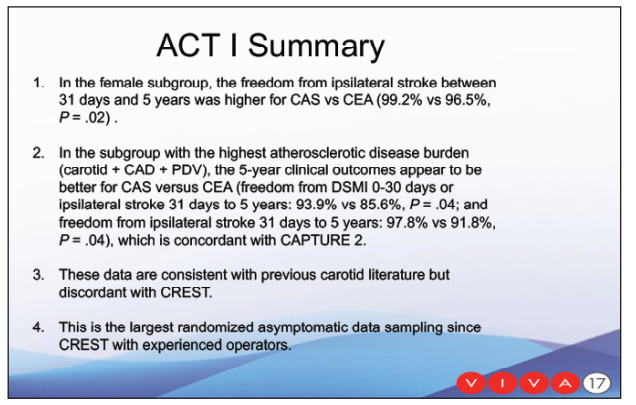


CAS BENEFIT: SUBGROUP ANALYSIS OF ACT 1

Presenter: Gary Ansel, MD

The ACT I clinical trial was a prospective, multicenter, randomized (carotid artery stenting [CAS]: carotid endarterectomy [CEA], 3:1) study to support the approval of the Xact rapid exchange carotid stent system (Abbott Vascular) in conjunction with Emboshield embolic protection systems (Emboshield EPSs) (Abbott Vascular) in the treatment of standard CEA risk, asymptomatic extracranial carotid atherosclerotic disease subjects. The trial represents the largest randomized trial of its kind with asymptomatic patients. The primary endpoint was the composite of death, stroke (ipsilateral or contralateral, major or minor), or myocardial infarction (DSMI) within 30 days or ipsilateral stroke from 31 days to 365 days postprocedure. The trial enrolled 1,453 patients, in which at 1 year, CAS and CEA were found to be noninferior (P = .01), and at 5 years there was no difference between the two treatment groups in any stroke or survival.

The purpose of the current analysis is to evaluate the performance of CAS versus CEA out to 5 years in the subgroups of gender (212 women and 278 men) and different atherosclerotic disease burdens (carotid only [n = 161]; carotid plus coronary artery disease [CAD] [n = 141]; carotid plus CAD plus peripheral artery disease [PAD] [n = 65]; and carotid plus CAD plus PAD [n = 109]). Additional Kaplan-Meier comparison out to 5 years was conducted in these subgroups. Freedom from ipsilateral stroke from 31 days to 5 years was 99.2% in CAS versus 96.5% in CEA (P = .02) in women. This difference was not found in men (96.9% vs 97.9%, P = .54). Across the atherosclerotic disease burden subgroups, carotid plus CAD plus PAD was the only subgroup in which patients treated with CAS versus CEA had a higher freedom from DSMI within 30 days or ipsilateral stroke between 31 days and 5 years (93.9% vs 85.6%, P = .04) and a higher freedom from ipsilateral stroke between 31 days and 5 years (97.8% vs 91.8%, P = .04). In select subgroups of ACT I, CAS treatment resulted in fewer long-term clinical events at 5 years compared to CEA.



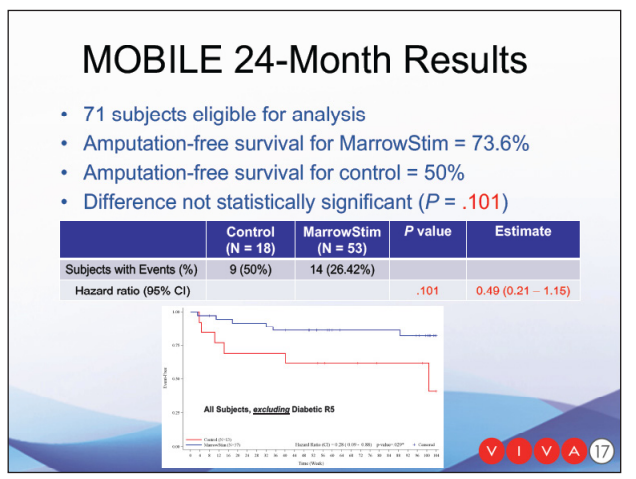
MARROWSTIM PAD KIT FOR THE TREATMENT OF CLI IN SUBJECTS WITH SEVERE PERIPHERAL ARTERY DISEASE: 24-MONTH RESULTS FROM THE MOBILE TRIAL

Presenter: John Laird, MD

The phase 3 MOBILE (MarrowStim Treatment of Limb Ischemia in Subjects With Severe Peripheral Arterial Disease) clinical trial is a prospective, double-blinded, randomized, multicenter study that sought to determine if autologous bone marrow–derived progenitor cells (MarrowStim, Zimmer Biomet) could decrease major amputation in patients with critical limb ischemia (CLI). The primary efficacy endpoint was assessment of treatment-related adverse events, defined as time to major amputation or all-cause mortality (amputation-free survival).

This is the first phase 3 trial in the United States to study bone marrow cell therapy for CLI. There were 152 patients (155 limbs treated) enrolled at 24 sites. The rationale and design of this trial was based on a previous phase 1 trial and used a 3:1 treatment-to-placebo randomization scheme.

At 24 months, 71 patients were eligible for analysis. Amputation-free survival was 73.6% in the MarrowStim arm and 50% in the control arm (not statistically significant, P = .101). Cell therapy appears to be durable through 24 months and improved amputation-free survival rates compared to placebo, although analysis is limited by sample size.



Late-Breaking Trials

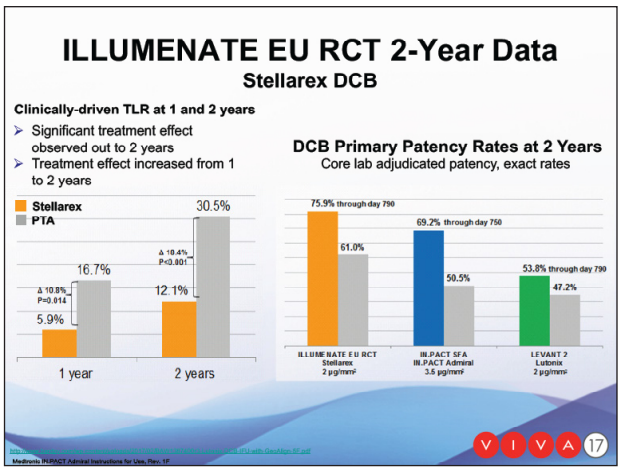
HIGHLIGHTS FROM WEDNESDAY MORNING'S TRIAL PRESENTATIONS.

ILLUMENATE EUROPEAN RANDOMIZED TRIAL: 2-YEAR RESULTS

Presenter: Prof. Marianne Brodmann, MD

The purpose of the ILLUMENATE European randomized controlled trial (EU RCT) was to demonstrate the safety and effectiveness of the 0.035-inch Stellarex drug-coated balloon (DCB) (Spectranetics Corporation) for femoropopliteal revascularization. Stellarex is a low-dose (2 µg/mm^2 surface concentration of paclitaxel) next-generation DCB, recently approved by the US Food and Drug Administration for commercialization in the United States. The ILLUMENATE EU RCT is a prospective, randomized, multicenter trial. Patients were randomized (3:1) to treatment with the Stellarex DCB or an uncoated percutaneous transluminal angioplasty (PTA) balloon. The trial included independent oversight by a clinical events committee and data safety monitoring board. Blinded core laboratories analyzed angiographic and duplex ultrasound images to ensure data were unbiased and accurate.

In total, 294 patients (339 lesions) were randomized to treatment with the Stellarex DCB (n = 222 patients, 254 lesions) or an uncoated PTA balloon (n = 72 patients, 79 lesions) at 18 sites in Europe. A significant treatment effect was observed out to 2 years. Patients treated with the DCB maintained a significantly higher primary patency rate of 75.9% (145/191) versus 61% (36/59) (P = .025). In conjunction with the higher patency rate, the rate of clinically driven target lesion revascularization (CD-TLR) was significantly lower in the DCB group (12.1% vs 30.5%; P < .001). Functional outcomes, such as walking impairment questionnaire scores and walking distance, were similar between groups despite the fact that there were 60% fewer revascularizations in the DCB group. These outcomes have important implications for patients' quality of life and bolster the value proposition of this DCB. The 2-year outcomes from the ILLUMENATE EU RCT show a significantly higher primary patency rate and lower CD-TLR rate in the DCB cohort as compared to the PTA cohort. The results demonstrate a significant and durable treatment effect of the Stellarex DCB for treatment of symptomatic femoropopliteal disease.



FIVE-YEAR EVAR OUTCOMES ARE EQUIVALENT BETWEEN GENDERS: RESULTS FROM THE ENGAGE REGISTRY

Presenter: Marc L. Schermerhorn, MD

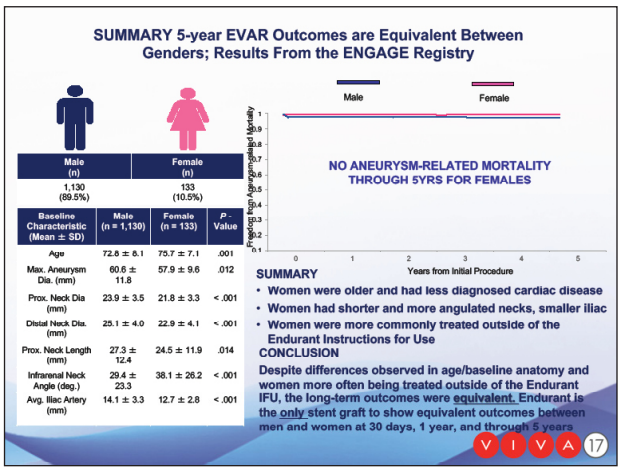
The purpose of this study was to compare gender-specific outcomes and report the 5-year results after endovascular aneurysm repair (EVAR) from a large global registry.

There were 1,263 patients (133 women,10.5%; 1,130 men, 89.5%) with infrarenal aneurysms treated with the Endurant stent graft (Medtronic) prospectively enrolled in the ENGAGE registry and followed clinically and radiographically. Gender outcomes were analyzed and compared.

Women in the registry were older (75.7 ± 7.1 years vs 72.8 ± 8.1 years; P < .001) and had smaller aneurysms (57.9 ± 9.6 mm vs 60.6 ± 11.8 mm; P = .012). Women had narrower proximal aortic neck diameters (21.8 ± 3.3 mm vs 23.9 ± 3.5 mm; P < .001), shorter nonaneurysmal aortic neck lengths (24.5 ± 11.9 mm vs 27.3 ± 12.4 mm; P = .014), greater infrarenal angulation (38.1° ± 26.2° vs 29.4° ± 23.3°; P < .001), and smaller bilateral iliac artery diameters. When evaluating challenging proximal aortic necks (lengths < 15 mm or infrarenal neck angulation > 60°), women had more nonaneurysmal proximal aortic necks < 15 mm (16.5% vs 11.5%; P = .088) and more angulated necks > 60° (19.7% vs 9%; P < .001).

Successful delivery and deployment of the Endurant stent graft was achieved in equal numbers of women and men (99.2% vs 99.5%; P = .746). Through 5 years, there were no aneurysm-related mortalities or ruptures in women. Through 5 years, the rate of freedom from secondary endovascular procedures was similar between the two genders (women, 85.6%; men, 84.1%; P = .5150). At 5 years, the combined rate of abdominal aortic aneurysm diameter stability and shrinkage was similar between genders (women, 89.6%; men, 89.4%).

Within ENGAGE, women had more challenging baseline characteristics and anatomies and were more often treated outside of the instructions for use. However, despite these challenges, 5-year long-term outcomes were equivalent between the genders when treated with the Endurant stent graft. Endurant has now demonstrated equivalent outcomes between genders at 30 days, 1 year, and through 5 years between genders.



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Late-Breaking Trials

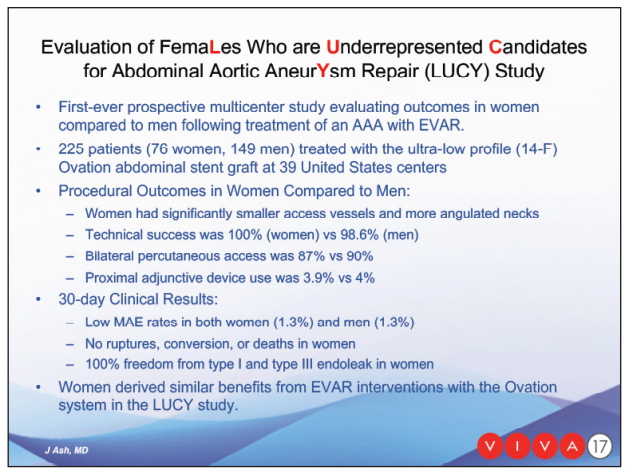
HIGHLIGHTS FROM WEDNESDAY AFTERNOON'S TRIAL PRESENTATIONS.

FIRST PROSPECTIVE MULTICENTER STUDY EVALUATING OUTCOMES FOLLOWING EVAR IN WOMEN VERSUS MEN: EARLY RESULTS FROM THE LUCY STUDY

Presenter: Jennifer Ash, MD

Historically, women have had greater morbidity and mortality from traditional endovascular aneurysm repair (EVAR). The LUCY study is the first prospective multicenter study designed to assess outcomes in women compared to men treated with the Ovation stent graft system (Endologix) for elective abdominal aortic aneurysm (AAA) repair. The primary endpoint is major adverse events (MAEs) at 30 days, and the secondary endpoints evaluate the effectiveness of the Ovation system in both arms through 1 year.

The 30-day results of the 225 patients (76 women and 149 men) enrolled across 39 United States study centers show that compared to men, women had smaller neck diameters (women, 22 ± 3.6 mm; men, 23.1 ± 3.1 mm, $P = .01$), greater juxtarenal angle (women, 26.6° ± 19.2°; men, 18.3° ± 18.1°; $P < .01$), and smaller access vessels (women, 6.5 ± 1.3 mm; men, 8.1 ± 2.2 mm; $P < .01$). Technical success was achieved in 100% of the women and 98.6% of the men ($P = .55$). There was no significant difference in the use of general anesthesia (women, 77.6%; men, 73.8%; $P = .75$) nor in vascular access technique, with the majority of patients having percutaneous access (women, 86.8%; men, 89.9%, $P = .55$). At 30-day follow-up, there were no type Ia endoleaks in the female arm compared to three in the male arm. There was no significant difference in MAEs between the female and male arms (women, 1.3%; men, 1.3%; $P = 1.00$), and there were no deaths, conversions, or ruptures in either cohort. No women underwent a secondary intervention for endoleak, occlusion/stenosis, or migration compared to two reinterventions in the male arm for type Ia endoleak. Despite having more complex anatomy at baseline, the early results of the LUCY study show that women derive similar benefits with the Ovation system through the 30-day endpoint compared to men.



SAFETY AND FUNCTIONALITY OF THE SURVEIL DRUG-COATED BALLOON FOR TREATMENT OF DE NOVO FEMOROPOPLITEAL LESIONS: 6-MONTH RESULTS FROM THE PREVEIL EARLY FEASIBILITY STUDY

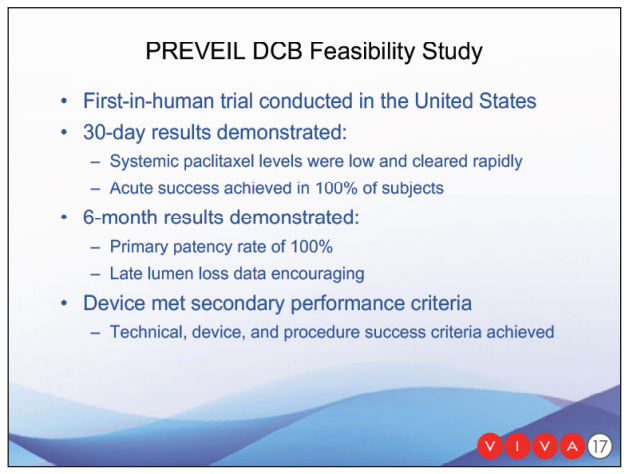
Presenter: Gary M. Ansel, MD

PREVEIL is a prospective, United States, multicenter, single-arm trial to assess the safety and feasibility of the SurVeil drug-coated balloon (DCB) (Surmodics) in the treatment of subjects with de novo lesions of the femoropopliteal artery. The PREVEIL trial is the product of the US Food and Drug Administration's efforts to bring first-in-human trials back to the United States.

The study enrolled 13 patients at three clinical sites with symptomatic (Rutherford 2–4) femoropopliteal lesions ≤ 90 mm in length. Study assessments included primary patency and late lumen loss through 6 months, plasma paclitaxel levels, and changes in Rutherford classification, resting ankle-brachial index/toe-brachial index (ABI/TBI), 6-minute walk test, and walking impairment questionnaire (WIQ) at 1, 6, 12, 24, and 36 months. Key secondary safety endpoints included freedom from evidence of paclitaxel toxicity, major vascular complications, or thrombolysis in myocardial infarction.

Acute success measures of safety were achieved in 100% of subjects. At 6 months, subjects treated with the SurVeil DCB demonstrated primary patency of 100% and mean late lumen loss of 0.27 ± 0.54 mm. Subjects experienced significant improvement in Rutherford classification, ABI/TBI, 6-minute walk test, and WIQ at 30 days and 6 months. Median plasma concentration peaked immediately postprocedure (Cmax 1.07 ng/mL) and was undetectable at 30 days. Secondary technical, device, and procedural success criteria were achieved.

Ongoing positive results of the PREVEIL study demonstrate that the SurVeil DCB has the potential to be a next-generation DCB given the improved efficacy of drug transfer and drug effect within the arterial wall with reduced risk of emboli reaching downstream tissue beds, as demonstrated in preclinical studies against benchmark DCBs.



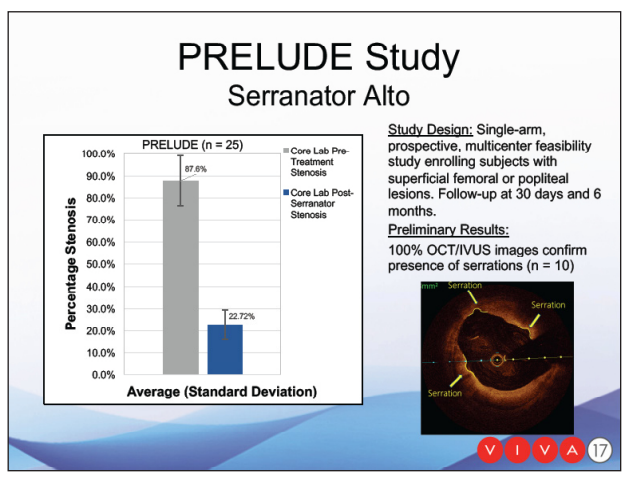
THE PRELUDE STUDY: PROSPECTIVE STUDY FOR THE TREATMENT OF ATHEROSCLEROTIC LESIONS IN THE SUPERFICIAL FEMORAL AND/OR POPLITEAL ARTERIES USING THE SERRANATOR DEVICE

Presenter: Prof. Marianne Brodmann, MD

The purpose of the PRELUDE study is to evaluate the safety and efficacy of the Serranator Alto percutaneous transluminal angioplasty serration balloon catheter (Cagent Vascular) in subjects with atherosclerotic disease of the superficial femoral and popliteal arteries. The Serranator device has four external metal serrated strips embedded on a semicompliant balloon to create multiple longitudinal lines of interrupted microserrations to aid arterial expansion. The device received US Food and Drug Administration 510(k) clearance in 2017. The PRELUDE study is a single-arm, prospective, multicenter feasibility study.

Subjects with stenosis > 70%, lesion length ≤ 10 cm, and reference vessel diameters of 4 to 6 mm were included. Occlusions were allowed up to 6 cm in length. The primary safety endpoint was a composite of major adverse events plus perioperative death 30-days post-procedure. The primary efficacy endpoint is defined by device success with a final diameter stenosis < 50%. A secondary objective is to confirm the presence of serrations across the lesions using optical coherence tomography (OCT) and/or intravascular ultrasound (IVUS) in a subset of 10 subjects. Acute angiographic data comparing the pre-Serranator inflation versus postinflation effects were evaluated by an independent core lab, with follow-up at 30 days and 6 months.

Twenty-five patients were enrolled at four study centers. Moderate or severe calcification was present in 56% (n = 14) of subjects, and 32% of subjects (n = 8) had chronic total occlusions. The average pretreatment stenosis was 88% with a posttreatment stenosis of 23%. Only one stent was placed (4%) post-Serranator. There were no major adverse events or perioperative deaths at 30 days. Serration effect was confirmed by an independent core lab in all OCT or IVUS images (n = 10). Acute results show that the Serranator can safely achieve low residual stenosis. Final study results with 6-month follow-up are expected at the end of the year.



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Late-Breaking Trials

HIGHLIGHTS FROM WEDNESDAY AFTERNOON'S TRIAL PRESENTATIONS.

USE OF A PACLITAXEL-COATED BALLOON TO TREAT OBSTRUCTIVE LESIONS IN THE SUPERFICIAL FEMORAL AND POPLITEAL ARTERIES: PRELIMINARY RESULTS FROM THE SAFE-DCB REGISTRY

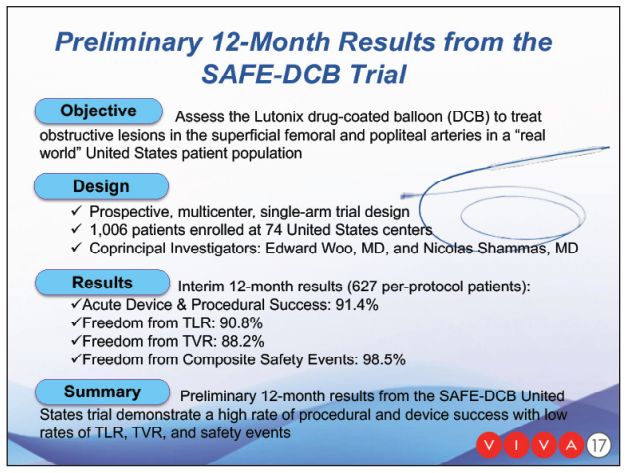
Presenters: Edward Y. Woo, MD

SAFE-DCB is a prospective, United States multicenter study designed to assess the on-label use of the Lutonix 035 drug coated balloon (DCB) catheter (Bard Peripheral Vascular) for the treatment of de novo or restenotic lesions in the native superficial femoral or popliteal arteries in a real-world patient population. A total of 1,006 patients were enrolled at 74 centers in the United States, while 968 patients fulfilled all of the study requirements (per-protocol population). The per-protocol group had symptoms of intermittent claudication or critical limb ischemia, obstructive lesions up to 150 mm in length, and reference vessel diameters of 4 to 7 mm.

The Lutonix 035 DCB is coated with a nonpolymer-based formulation that includes the antiproliferative drug, paclitaxel, with a surface concentration of 2 µg/mm^2. The primary endpoints are freedom from target lesion revascularization (TLR) at 12 months and a safety composite at 30 days of device- and/or procedure-related perioperative death, target limb major amputation, and target vessel revascularization (TVR).

Patients were on average aged 69 years, 57% were male, 42% had lifestyle-limiting claudication, and 34% suffered from ischemic rest pain or had critical limb ischemia with tissue loss (Rutherford categories 4–6). The mean lesion length was 73.9 ± 42.8 mm. To date, 627 per-protocol patients have reached the 12-month follow-up (365 days), and all evaluable 12-month data are included in this analysis. An early look at the primary endpoints revealed that the 30-day freedom from safety events was 98.5% (611/620), while 12-month freedom from TLR was 90.8% (514/566). Secondarily, acute device and procedure success was 92.4% (572/626), while the freedom from TVR was 88.2% at 12 months.

Preliminary 12-month results from the SAFE-DCB United States trial demonstrate a high rate of procedural and device success with low rates of TLR, TVR, and safety events. The trial is ongoing with follow-up planned through 3 years.



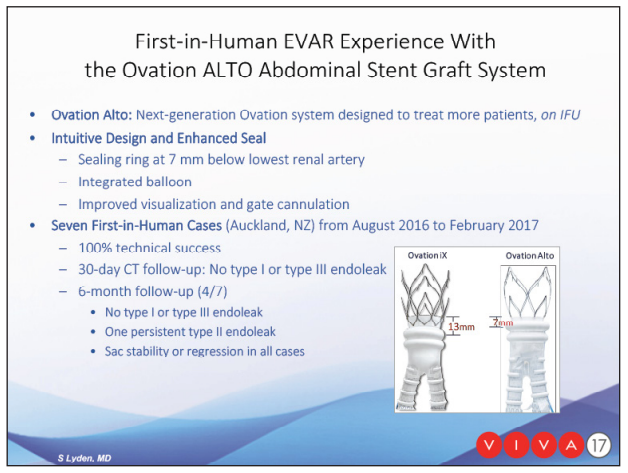
FIRST-IN-HUMAN EXPERIENCE WITH ENDOVASCULAR ANEURYSM REPAIR USING THE OVATION ALTO STENT GRAFT

Presenter: Sean Lyden, MD

This case review evaluated the first-in-human experience with the newest-generation Ovation stent graft, the Ovation Alto (Endologix), intended to accommodate the widest range of anatomies for on-label endovascular aneurysm repair (EVAR) compared to other commercially available devices.

This review describes the first seven patients treated with the Ovation Alto stent graft at a single center (Auckland City Hospital in Auckland, New Zealand) from August 2016 to February 2017. The ability of the Ovation Alto to fundamentally expand EVAR indications mainly relate to the unique sealing mechanism and the delivery system. Key features of this device include a low-profile, 15-F outer-diameter delivery system and ability to achieve seal at the level of the proximal sealing ring, which is 7-mm distal to the top of the fabric. Relative to the commercially available Ovation iX (Endologix), where sealing occurs at 13 mm, this is the most significant design change because sealing occurs in aortic tissue closer to the renal arteries. The polymer sealing technology in the Alto is the same technology used in the Ovation stent graft, where neck dilatation was not observed through 5 years.

Ovation Alto was successfully delivered and deployed in all patients with 100% technical success. At 30-day follow-up, no type I or III endoleaks, stent graft migrations, abdominal aortic aneurysm (AAA) rupture, abdominal aortic aneurysm–related mortality, or secondary intervention were reported. Although limited to only seven patients, early experience with the Ovation Alto was promising and suggests the device may safely expand EVAR indications beyond that of other available devices.



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