Caution: Federal (USA) law restricts this device to sale by or on the order of a physician.

STERILE. Sterilized with electron beam radiation. Nonpyrogenic. For one use only. Do not resterilize. Store in a cool, dark, dry place.

Cordis EXOSEAL™ Vascular Closure Device
INSTRUCTIONS FOR USE

I. Device Name

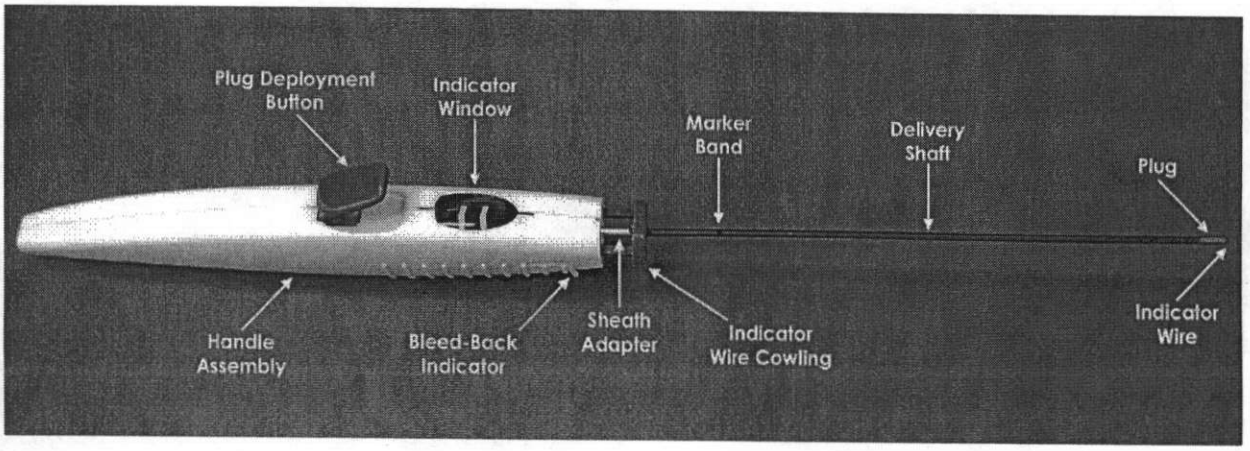
The device brand name is the Cordis **EXOSEAL™ Vascular Closure Device (VCD).**

II. Description

The **EXOSEAL Vascular Closure Device (VCD)** consists of a Plug Applier and an absorbable Plug. The Plug Applier consists of a Handle Assembly and a Delivery Shaft (See Figure 1). The absorbable Plug is fully enclosed in the distal portion of the Delivery Shaft. The Plug Applier positions and deploys the absorbable Plug to the extravascular surface of the femoral artery access site through the existing French (F) size-specific procedural Vascular Sheath Introducer with a working length of up to 12cm without the need for a Vascular Sheath Introducer exchange before device deployment. Hemostasis is achieved when the absorbable Plug is deposited on top of the arteriotomy site. The Plug exhibits partial to advanced absorption at 30 days, with complete absorption between 60 and 90 days post-implant. The components of the **EXOSEAL VCD** are not made from natural rubber latex. The **EXOSEAL** closure Plug is MRI compatible.

NOTE: The indwelling vascular sheath introducer must allow the Bleed-Back Port to extend beyond the distal tip of the sheath. The French size of the **EXOSEAL VCD** must correspond to the French size of the sheath introducer in use. For a listing of compatible vascular sheath introducers, please refer to the **"Sheath Introducer Compatible with EXOSEAL Vascular Closure Device (VCD)" section.**

Figure 1: Components of the EXOSEAL™ Vascular Closure Device



III. Indications for Use

The **EXOSEAL Vascular Closure Device** is indicated for femoral artery puncture site closure, reducing times to hemostasis and ambulation in patients who have undergone diagnostic or interventional catheterization procedures using a standard 5F, 6F, or 7F vascular sheath introducer with up to 12 cm working length. Additionally, the **EXOSEAL Vascular Closure Device** is indicated to reduce times to hemostasis and ambulation in patients who have undergone interventional catheterization procedures, using a standard 6F vascular sheath introducer up to a 12 cm working length, who have received preprocedural and/or intraprocedural glycoprotein (GP) IIb/IIIa inhibitor therapy.

IV. Contraindications

There are no contraindications to the use of this device. Attention is drawn to the Warnings, Precautions, and Special Patient Populations.

V. Warnings

- Do not use the **EXOSEAL VCD** if the package is damaged or any portion of the package has been previously opened.
- Do not use the **EXOSEAL VCD** if the device appears damaged or defective in any way.
- Do not use the **EXOSEAL VCD** if the sterile field has been broken where bacterial contamination of the sheath or surrounding tissues may have occurred; a broken sterile field may result in infection.
- For SINGLE USE ONLY. Do not resterilize or reuse. Reuse, reprocessing, or resterilization may compromise the structural integrity of the device and/or lead to device failure, which in turn, may result in patient injury, illness, or death. Use aseptic technique when handling the product.
- Do not use the **EXOSEAL VCD** in patients with known allergy to polyglycolic acid.

VI. Precautions

- Serious adverse events might result with the use of the **EXOSEAL VCD** in vessels not suitable for the use of the device. Avoid the use of EXOSEAL VCD in patients with arteriotomies created in areas of calcified plaque or in vessels with diameters < 5 mm.
- With antegrade puncture (restricted to peripheral vascular catheterization procedures), the ability to accurately assess vessel size or extraluminal device position may be limited.
- The **EXOSEAL Vascular Closure Device** procedure should be performed by physicians who have expertise in the techniques of vascular catheterization (or other healthcare professionals authorized by, or under the direction of, such physicians) and possess adequate training in the use of the device, e.g., participation in an **EXOSEAL VCD** training program.
- Observe sterile technique at all times when using the **EXOSEAL VCD**. Employ proper groin management post-procedure and post-hospital discharge to prevent infection.
- The vascular sheath introducer and/or **EXOSEAL VCD** should not be advanced or withdrawn when resistance is met without first determining the cause by fluoroscopic

examination. Using excessive force to advance or torque the **EXOSEAL VCD** may lead to arterial damage and/or breakage of the device, which may necessitate interventional and/or surgical removal of the device and arterial repair.

- If for any reason it is desired to abort the procedure once the **EXOSEAL VCD** has been introduced into the bloodstream, remove the **EXOSEAL VCD** and vascular sheath introducer as a unit. Do not attempt to withdraw the **EXOSEAL VCD** from the vascular sheath introducer, as Plug dislodgement may occur.
- Pulsatile flow is necessary for proper positioning. If pulsatile flow is not observed from the Bleed-Back Indicator, discontinue the procedure.
- Do not remove the **EXOSEAL VCD** from the vascular sheath introducer after removal from the patient; discard the **EXOSEAL VCD** with the Delivery Shaft still locked inside the vascular sheath introducer.
- In patients undergoing interventional endovascular procedures, ambulation less than 2 hours after **EXOSEAL VCD** use increases the risk of oozing or rebleeding after initial hemostasis, and should be done only after all clinical factors have been considered.

VII. Special Patient Populations

The safety and effectiveness of the **EXOSEAL VCD** has not been established in the following patient populations:

- Patients with acute ST-elevation myocardial infarction ≤ 48 hours prior to the cardiac or peripheral catheterization procedure
- Patients with uncontrolled hypertension at time of closure (BP $\geq$ 180/110 mmHg)
- Patients who bruise or bleed easily or with a history of significant bleeding or platelet disorders, such as thrombocytopenia (with < 100,000 platelet count), Von Willebrand's disease, anemia (Hgb < 10 g/dL, Hct < 30%), thrombasthenia, decreased fibrinogen (< 200 mg/dL), and Factor V deficiency
- Patients with prior femoral vascular surgery or vascular graft in region of access site
- Patients with pre-existing systemic or cutaneous infection
- Patients who are known to be pregnant or who are lactating
- Patients on thrombolytic therapy (e.g. streptokinase, urokinase, t-PA) ≤ 24 hours prior to the catheterization procedure
- Patients on Angiomax (bivalirudin) or other thrombin-specific anticoagulants or low molecular weight heparin ≤ 24 hours prior to the cardiac or peripheral catheterization procedure
- Patients with a BMI > 40 kg/m^2
- Patients with symptomatic leg ischemia in the target vessel limb including severe claudication (< 30.48 meters / < 100 feet) or weak/absent pulse
- Patients with planned arterial access at the same access site ≤ 30 days following the femoral artery closure procedure
- Patients undergoing arterial puncture in the femoral artery of both legs
- Patients with prior target artery closure with any closure device, or closure with manual compression ≤ 30 days prior to the cardiac or peripheral catheterization procedure
- Patients with prior or recent use of an intra-aortic balloon pump through the arterial access site

- Patients with evidence of a preexisting hematoma, arteriovenous fistula, or pseudoaneurysm at the access site prior to start of femoral artery closure procedure
- Patients with a tortuous targeted femoral artery
- Patients who within ≤ 1 cm of the puncture site have fluoroscopically visible calcium, atherosclerotic disease, or a stent
- Patients with a targeted femoral artery diameter stenosis ≥ 50%
- Patients with arteriotomies in vessels with diameters < 5 mm
- Patients where there is difficulty in obtaining vascular access resulting in multiple arterial punctures and/or posterior arterial puncture
- Patients with antegrade puncture
- Heparinized patients with elevated pre-closure ACT level: > 250 seconds with GP IIb/IIIa inhibitor, > 300 seconds without GP IIb/IIIa inhibitor
- Patients experiencing cardiogenic shock (hemodynamic instability requiring intravenous medications or mechanical support) during or immediately post-catheterization

VIII. Adverse Events

The 6F **EXOSEAL VCD** was evaluated in a prospective, multi-center, randomized (2:1) clinical trial (the ECLIPSE Trial) in the United States comparing the 6F **EXOSEAL VCD** to Manual Compression (MC) and involving 401 total patients undergoing diagnostic angiography (n=200) or interventional procedures (n=201).

The 7F **EXOSEAL VCD** was evaluated in 2 small, non-randomized clinical studies, which were a multi-center study in Germany and a single-center study in Mexico, whose data were pooled and compared to the MC control group from the 6F ECLIPSE Trial. The pooled German/Mexican 7F VCD data were from 88 total patients undergoing diagnostic angiography (n = 43) or interventional procedures (n = 45).

Tables 1 – 3 show the major and secondary complications data for the 6F ECLIPSE Trial and for the 7F VCD group versus 6F MC group comparison.

Table 1 Safety Results - All Patients (ITT) Treated

Description of Event (Event Based)	6F ECLIPSE Trial					Pooled 7F VCD Data Compared to 6F MC Data			
	VCD (n=267patients)	MC (n=134patients)	Difference VCD-MC[1]	Upper Bound[2]	P-Values[3]	Pooled 7F VCD (n=88 patients)	Difference VCD-MC[4]	Upper Bound[5]	P-values[6]
Major Adverse Events (Combined Event Rate) at 30-days	0/267 (0.00%)	0/134 (0.00%)	0.00%	1.14%	0.0006	0/88 (0.00%)	0.00%	3.35%	0.0276
Vascular Repair	0/267 (0.00%)	0/134 (0.00%)	0.00%	1.14%	0.0006	0/88 (0.00%)	0.00%	3.35%	0.0276
Access site-related bleeding requiring transfusion	0/267 (0.00%)	0/134 (0.00%)	0.00%	1.14%	0.0006	0/88 (0.00%)	0.00%	3.35%	0.0276
Access site-related infection requiring treatment	0/267 (0.00%)	0/134 (0.00%)	0.00%	1.14%	0.0006	0/88 (0.00%)	0.00%	3.35%	0.0276
Any new documented ipsilateral lower extremity ischemia	0/267 (0.00%)	0/134 (0.00%)	0.00%	1.14%	0.0006	0/88 (0.00%)	0.00%	3.35%	0.0276
Surgery for access site-related nerve injury	0/267 (0.00%)	0/134 (0.00%)	0.00%	1.14%	0.0006	0/88 (0.00%)	0.00%	3.35%	0.0276
Permanent(>30 days) access site-related nerve injury	0/267 (0.00%)	0/134 (0.00%)	0.00%	1.14%	0.0006	0/88 (0.00%)	0.00%	3.35%	0.0276
Secondary Adverse Events (Combined Event Rate) at 30-days	24/267 (8.99%)	6/134 (4.48%)	4.51%	8.66%	-	3/88 (3.41%)	-1.07%	4.18%	-
Rebleeding Following Initial Hemostasis	14/267 (5.24%)	3/134 (2.24%)	3.00%	6.17%	-	0/88 (0.00%)	-2.24%	0.70%	-
Pseudoaneurysm not Requiring Treatment	0/267 (0.00%)	0/134 (0.00%)	0.00%	1.14%	-	0/88 (0.00%)	0.00%	3.35%	-
Treated Pseudoaneurysm	0/267 (0.00%)	0/134 (0.00%)	0.00%	1.14%	-	0/88 (0.00%)	0.00%	3.35%	-
Documented Arteriovenous Fistula	0/267 (0.00%)	0/134 (0.00%)	0.00%	1.14%	-	0/88 (0.00%)	0.00%	3.35%	-
Access Site Hematoma >= 6cm	6/267 (2.25%)	1/134 (0.75%)	1.50%	3.72%	-	3/88 (3.41%)	2.66%	7.47%	-
Access Site-Related Bleeding Requiring > 30 min for Hemostasis	1/267 (0.37%)	1/134 (0.75%)	-0.37%	1.16%	-	0/88 (0.00%)	-0.75%	2.20%	-
Post-Hospital Discharge Access Site-Related Bleeding	0/267 (0.00%)	0/134 (0.00%)	0.00%	1.14%	-	0/88 (0.00%)	0.00%	3.35%	-
Ipsilateral Lower Extremity Arterial Emboli	0/267 (0.00%)	0/134 (0.00%)	0.00%	1.14%	-	0/88 (0.00%)	0.00%	3.35%	-
Transient Loss of Ipsilateral Lower Extremity Pulse	0/267 (0.00%)	0/134 (0.00%)	0.00%	1.14%	-	0/88 (0.00%)	0.00%	3.35%	-
Ipsilateral Deep Vein Thrombosis	0/267 (0.00%)	0/134 (0.00%)	0.00%	1.14%	-	0/88 (0.00%)	0.00%	3.35%	-
Access Site-Related Vessel Laceration	0/267 (0.00%)	0/134 (0.00%)	0.00%	1.14%	-	0/88 (0.00%)	0.00%	3.35%	-
Transient Access Site-Related Nerve Injury	1/267 (0.37%)	0/134 (0.00%)	0.37%	1.81%	-	0/88 (0.00%)	0.00%	3.35%	-
Access Site Wound Dehiscence	0/267 (0.00%)	0/134 (0.00%)	0.00%	1.14%	-	0/88 (0.00%)	0.00%	3.35%	-
Treated, Localized Access Site Infection	0/267 (0.00%)	0/134 (0.00%)	0.00%	1.14%	-	0/88 (0.00%)	0.00%	3.35%	-
Retroperitoneal Bleeding	2/267 (0.75%)	0/134 (0.00%)	0.75%	2.34%	-	0/88 (0.00%)	0.00%	3.35%	-
Ipsilateral Peripheral Artery Total Occlusion	0/267 (0.00%)	0/134 (0.00%)	0.00%	1.14%	-	0/88 (0.00%)	0.00%	3.35%	-
Ecchymosis >= 6cm	0/267 (0.00%)	1/134 (0.75%)	-0.75%	0.43%	-	0/88 (0.00%)	-0.75%	2.20%	-
Intraluminal Plug Delivery Not Requiring Surgical Intervention	0/267 (0.00%)	0/134 (0.00%)	0.00%	1.14%	-	0/88 (0.00%)	0.00%	3.35%	-
Decrease in Pedal Pulse	0/267 (0.00%)	0/134 (0.00%)	0.00%	1.14%	-	0/88 (0.00%)	0.00%	3.35%	-
Death	0/267 (0.00%)	0/134 (0.00%)	0.00%	1.14%	-	0/88 (0.00%)	0.00%	3.35%	-

Numbers are % (counts/sample size)

[1] Proportion differences between 6F VCD group and 6F MC group ($P_{VCD} - P_{MC}$)

[2] One-sided upper bound of 95% Confidence Intervals (CI) of the difference of two binomial proportions: between 6F VCD group and 6F MC group ($P_{VCD} - P_{MC}$). It was calculated using unconditional exact method

[3] P-values were calculated using unconditional exact test of non-inferiority using difference of two binomial proportions (6F VCD group vs. 6F MC group) with the pre-specified margin of 4.0%. The calculation was performed using StatXact.

[4] Proportion differences between pooled 7F VCD group and 6F MC group ($P_{VCD} - P_{MC}$)

[5] One-sided upper bound of 95% Confidence Intervals (CI) of the difference of two binomial proportions: between pooled 7F VCD group and 6F MC group ($P_{VCD} - P_{MC}$). It was calculated using unconditional exact method

[6] P-values were calculated using unconditional exact test of non-inferiority using difference of two binomial proportions (7F VCD group vs. 6F MC group) with the pre-specified margin of 4.0%. The calculation was performed using StatXact.

Table 2 Safety Results – Diagnostic ITT Patients

Description of Event (Event Based)	6F ECLIPSE Trial					Pooled 7F VCD Data Compared to 6F MC Data			
	VCD (n=134patients)	MC (n=66patients)	Difference VCD-MC[1]	Upper Bound[2]	P-Values[3]	Pooled 7F VCD (n=43 patients)	Difference VCD-MC[4]	Upper Bound[5]	P-values[6]
Major Adverse Events (Combined Event Rate) at 30-days	0/134 (0.00%)	0/66 (0.00%)	0.00%	2.34%	0.0129	0/43 (0.00%)	0.00%	6.73%	0.1728
Vascular Repair	0/134 (0.00%)	0/66 (0.00%)	0.00%	2.34%	0.0129	0/43 (0.00%)	0.00%	6.73%	0.1728
Access site-related bleeding requiring transfusion	0/134 (0.00%)	0/66 (0.00%)	0.00%	2.34%	0.0129	0/43 (0.00%)	0.00%	6.73%	0.1728
Access site-related infection requiring treatment	0/134 (0.00%)	0/66 (0.00%)	0.00%	2.34%	0.0129	0/43 (0.00%)	0.00%	6.73%	0.1728
Any new documented ipsilateral lower extremity ischemia	0/134 (0.00%)	0/66 (0.00%)	0.00%	2.34%	0.0129	0/43 (0.00%)	0.00%	6.73%	0.1728
Surgery for access site-related nerve injury	0/134 (0.00%)	0/66 (0.00%)	0.00%	2.34%	0.0129	0/43 (0.00%)	0.00%	6.73%	0.1728
Permanent(>30 days) access site-related nerve injury	0/134 (0.00%)	0/66 (0.00%)	0.00%	2.34%	0.0129	0/43 (0.00%)	0.00%	6.73%	0.1728
Secondary Adverse Events (Combined Event Rate) at 30-days	4/134 (2.99%)	1/66 (1.52%)	1.47%	5.42%	-	1/43 (2.33%)	0.81%	8.55%	-
Rebleeding Following Initial Hemostasis	2/134 (1.49%)	1/66 (1.52%)	-0.02%	3.46%	-	0/43 (0.00%)	-1.52%	4.78%	-
Pseudoaneurysm not Requiring Treatment	0/134 (0.00%)	0/66 (0.00%)	0.00%	2.34%	-	0/43 (0.00%)	0.00%	6.73%	-
Treated Pseudoaneurysm	0/134 (0.00%)	0/66 (0.00%)	0.00%	2.34%	-	0/43 (0.00%)	0.00%	6.73%	-
Documented Arteriovenous Fistula	0/134 (0.00%)	0/66 (0.00%)	0.00%	2.34%	-	0/43 (0.00%)	0.00%	6.73%	-
Access Site Hematoma >= 6cm	1/134 (0.75%)	0/66 (0.00%)	0.75%	3.55%	-	1/43 (2.33%)	2.33%	10.56%	-
Access Site-Related Bleeding Requiring > 30 min for Hemostasis	1/134 (0.75%)	0/66 (0.00%)	0.75%	3.55%	-	0/43 (0.00%)	0.00%	6.73%	-
Post-Hospital Discharge Access Site-Related Bleeding	0/134 (0.00%)	0/66 (0.00%)	0.00%	2.34%	-	0/43 (0.00%)	0.00%	6.73%	-
Ipsilateral Lower Extremity Arterial Emboli	0/134 (0.00%)	0/66 (0.00%)	0.00%	2.34%	-	0/43 (0.00%)	0.00%	6.73%	-
Transient Loss of Ipsilateral Lower Extremity Pulse	0/134 (0.00%)	0/66 (0.00%)	0.00%	2.34%	-	0/43 (0.00%)	0.00%	6.73%	-
Ipsilateral Deep Vein Thrombosis	0/134 (0.00%)	0/66 (0.00%)	0.00%	2.34%	-	0/43 (0.00%)	0.00%	6.73%	-
Access Site-Related Vessel Laceration	0/134 (0.00%)	0/66 (0.00%)	0.00%	2.34%	-	0/43 (0.00%)	0.00%	6.73%	-
Transient Access Site-Related Nerve Injury	0/134 (0.00%)	0/66 (0.00%)	0.00%	2.34%	-	0/43 (0.00%)	0.00%	6.73%	-
Access Site Wound Dehiscence	0/134 (0.00%)	0/66 (0.00%)	0.00%	2.34%	-	0/43 (0.00%)	0.00%	6.73%	-
Treated, Localized Access Site Infection	0/134 (0.00%)	0/66 (0.00%)	0.00%	2.34%	-	0/43 (0.00%)	0.00%	6.73%	-
Retroperitoneal Bleeding	0/134 (0.00%)	0/66 (0.00%)	0.00%	2.34%	-	0/43 (0.00%)	0.00%	6.73%	-
Ipsilateral Peripheral Artery Total Occlusion	0/134 (0.00%)	0/66 (0.00%)	0.00%	2.34%	-	0/43 (0.00%)	0.00%	6.73%	-
Ecchymosis >= 6cm	0/134 (0.00%)	0/66 (0.00%)	0.00%	2.34%	-	0/43 (0.00%)	0.00%	6.73%	-
Intraluminal Plug Delivery Not Requiring Surgical Intervention	0/134 (0.00%)	0/66 (0.00%)	0.00%	2.34%	-	0/43 (0.00%)	0.00%	6.73%	-
Decrease in Pedal Pulse	0/134 (0.00%)	0/66 (0.00%)	0.00%	2.34%	-	0/43 (0.00%)	0.00%	6.73%	-
Death	0/134 (0.00%)	0/66 (0.00%)	0.00%	2.34%	-	0/43 (0.00%)	0.00%	6.73%	-

Numbers are % (counts/sample size)

[1] Proportion differences between 6F VCD group and 6F MC group ($P_{VCD} - P_{MC}$)

[2] One-sided upper bound of 95% Confidence Intervals (CI) of the difference of two binomial proportions: between 6F VCD group and 6F MC group ($P_{VCD} - P_{MC}$). It was calculated using unconditional exact method

[3] P-values were calculated using unconditional exact test of non-inferiority using difference of two binomial proportions (6F VCD group vs. 6F MC group) with the pre-specified margin of 4.0%. The calculation was performed using StatXact.

[4] Proportion differences between pooled 7F VCD group and 6F MC group ($P_{VCD} - P_{MC}$)

[5] One-sided upper bound of 95% Confidence Intervals (CI) of the difference of two binomial proportions: between pooled 7F VCD group and 6F MC group ($P_{VCD} - P_{MC}$). It was calculated using unconditional exact method

[6] P-values were calculated using unconditional exact test of non-inferiority using difference of two binomial proportions (7F VCD group vs. 6F MC group) with the pre-specified margin of 4.0%. The calculation was performed using StatXact.

Table 3 Safety Results – Interventional ITT Patients

Description of Event (Event Based)	6F ECLIPSE Trial					Pooled 7F VCD Data Compared to 6F MC Data			
	VCD (n=133patients)	MC (n=68patients)	Difference VCD-MC[1]	Upper Bound[2]	P-Values[3]	Pooled 7F VCD (n=45 patients)	Difference VCD-MC[4]	Upper Bound[5]	P-values[6]
Major Adverse Events (Combined Event Rate) at 30-days	0/133 (0.00%)	0/68 (0.00%)	0.00%	2.23%	0.0119	0/45 (0.00%)	0.00%	6.44%	0.1593
Vascular Repair	0/133 (0.00%)	0/68 (0.00%)	0.00%	2.23%	0.0119	0/45 (0.00%)	0.00%	6.44%	0.1593
Access site-related bleeding requiring transfusion	0/133 (0.00%)	0/68 (0.00%)	0.00%	2.23%	0.0119	0/45 (0.00%)	0.00%	6.44%	0.1593
Access site-related infection requiring treatment	0/133 (0.00%)	0/68 (0.00%)	0.00%	2.23%	0.0119	0/45 (0.00%)	0.00%	6.44%	0.1593
Any new documented ipsilateral lower extremity ischemia	0/133 (0.00%)	0/68 (0.00%)	0.00%	2.23%	0.0119	0/45 (0.00%)	0.00%	6.44%	0.1593
Surgery for access site-related nerve injury	0/133 (0.00%)	0/68 (0.00%)	0.00%	2.23%	0.0119	0/45 (0.00%)	0.00%	6.44%	0.1593
Permanent(>30 days) access site-related nerve injury	0/133 (0.00%)	0/68 (0.00%)	0.00%	2.23%	0.0119	0/45 (0.00%)	0.00%	6.44%	0.1593
Secondary Adverse Events (Combined Event Rate) at 30-days	20/133 (15.04%)	5/68 (7.35%)	7.68%	14.93%	-	2/45 (4.44%)	-2.91%	6.44%	-
Rebleeding Following Initial Hemostasis	12/133 (9.02%)	2/68 (2.94%)	6.08%	11.75%	-	0/45 (0.00%)	-2.94%	3.04%	-
Pseudoaneurysm not Requiring Treatment	0/133 (0.00%)	0/68 (0.00%)	0.00%	2.23%	-	0/45 (0.00%)	0.00%	6.44%	-
Treated Pseudoaneurysm	0/133 (0.00%)	0/68 (0.00%)	0.00%	2.23%	-	0/45 (0.00%)	0.00%	6.44%	-
Documented Arteriovenous Fistula	0/133 (0.00%)	0/68 (0.00%)	0.00%	2.23%	-	0/45 (0.00%)	0.00%	6.44%	-
Access Site Hematoma >= 6cm	5/133 (3.76%)	1/68 (1.47%)	2.29%	6.47%	-	2/45 (4.44%)	2.97%	11.29%	-
Access Site-Related Bleeding Requiring > 30 min for Hemostasis	0/133 (0.00%)	1/68 (1.47%)	-1.47%	0.87%	-	0/45 (0.00%)	-1.47%	4.38%	-
Post-Hospital Discharge Access Site-Related Bleeding	0/133 (0.00%)	0/68 (0.00%)	0.00%	2.23%	-	0/45 (0.00%)	0.00%	6.44%	-
Ipsilateral Lower Extremity Arterial Emboli	0/133 (0.00%)	0/68 (0.00%)	0.00%	2.23%	-	0/45 (0.00%)	0.00%	6.44%	-
Transient Loss of Ipsilateral Lower Extremity Pulse	0/133 (0.00%)	0/68 (0.00%)	0.00%	2.23%	-	0/45 (0.00%)	0.00%	6.44%	-
Ipsilateral Deep Vein Thrombosis	0/133 (0.00%)	0/68 (0.00%)	0.00%	2.23%	-	0/45 (0.00%)	0.00%	6.44%	-
Access Site-Related Vessel Laceration	0/133 (0.00%)	0/68 (0.00%)	0.00%	2.23%	-	0/45 (0.00%)	0.00%	6.44%	-
Transient Access Site-Related Nerve Injury	1/133 (0.75%)	0/68 (0.00%)	0.75%	3.61%	-	0/45 (0.00%)	0.00%	6.44%	-
Access Site Wound Dehiscence	0/133 (0.00%)	0/68 (0.00%)	0.00%	2.23%	-	0/45 (0.00%)	0.00%	6.44%	-
Treated, Localized Access Site Infection	0/133 (0.00%)	0/68 (0.00%)	0.00%	2.23%	-	0/45 (0.00%)	0.00%	6.44%	-
Retroperitoneal Bleeding	2/133 (1.50%)	0/68 (0.00%)	1.50%	4.67%	-	0/45 (0.00%)	0.00%	6.44%	-
Ipsilateral Peripheral Artery Total Occlusion	0/133 (0.00%)	0/68 (0.00%)	0.00%	2.23%	-	0/45 (0.00%)	0.00%	6.44%	-
Ecchymosis >= 6cm	0/133 (0.00%)	1/68 (1.47%)	-1.47%	0.87%	-	0/45 (0.00%)	-1.47%	4.38%	-
Intraluminal Plug Delivery Not Requiring Surgical Intervention	0/133 (0.00%)	0/68 (0.00%)	0.00%	2.23%	-	0/45 (0.00%)	0.00%	6.44%	-
Decrease in Pedal Pulse	0/133 (0.00%)	0/68 (0.00%)	0.00%	2.23%	-	0/45 (0.00%)	0.00%	6.44%	-
Death	0/133 (0.00%)	0/68 (0.00%)	0.00%	2.23%	-	0/45 (0.00%)	0.00%	6.44%	-

Numbers are % (counts/sample size)

[1] Proportion differences between 6F VCD group and 6F MC group ($P_{VCD} - P_{MC}$)

[2] One-sided upper bound of 95% Confidence Intervals (CI) of the difference of two binomial proportions: between 6F VCD group and 6F MC group ($P_{VCD} - P_{MC}$). It was calculated using unconditional exact method

[3] P-values were calculated using unconditional exact test of non-inferiority using difference of two binomial proportions (6F VCD group vs. 6F MC group) with the pre-specified margin of 4.0%. The calculation was performed using StatXact.

[4] Proportion differences between pooled 7F VCD group and 6F MC group ($P_{VCD} - P_{MC}$)

[5] One-sided upper bound of 95% Confidence Intervals (CI) of the difference of two binomial proportions: between pooled 7F VCD group and 6F MC group ($P_{VCD} - P_{MC}$). It was calculated using unconditional exact method

[6] P-values were calculated using unconditional exact test of non-inferiority using difference of two binomial proportions (7F VCD group vs. 6F MC group) with the pre-specified margin of 4.0%. The calculation was performed using StatXact.

Among the 6F ECLIPSE Trial patients, 1 diagnostic VCD patient, 1 diagnostic MC patient, 37 interventional VCD patients, and 14 interventional MC patients received glycoprotein (GP) IIb/IIIa inhibitor therapy before and/or during the catheterization procedure. Table 4 shows the major and secondary complication data for the interventional patients receiving IIb/IIIa inhibitor therapy in the 6F ECLIPSE Trial.

Table 4 Safety Results – Interventional ITT Patients who have received GP IIb/IIIa inhibitor in 6F ECLIPSE Trial

Description of Event (Event Based)	6F VCD (n=37 patients)	6F MC (n=14 patients)	Difference VCD-MC[1]	Upper Bound[2]	P-values[3]
Major Adverse Events (Combined Event Rate) at 30-days	0/37 (0.00%)	0/14 (0.00%)	0.00%	7.83%	0.2208
Vascular Repair	0/37 (0.00%)	0/14 (0.00%)	0.00%	7.83%	0.2208
Access site-related bleeding requiring transfusion	0/37 (0.00%)	0/14 (0.00%)	0.00%	7.83%	0.2208
Access site-related infection requiring treatment	0/37 (0.00%)	0/14 (0.00%)	0.00%	7.83%	0.2208
Any new documented ipsilateral lower extremity ischemia	0/37 (0.00%)	0/14 (0.00%)	0.00%	7.83%	0.2208
Surgery for access site-related nerve injury	0/37 (0.00%)	0/14 (0.00%)	0.00%	7.83%	0.2208
Permanent (>30 days) access site-related nerve injury	0/37 (0.00%)	0/14 (0.00%)	0.00%	7.83%	0.2208
Secondary Adverse Events (Combined Event Rate) at 30-days	4/37 (10.81%)	2/14 (14.29%)	-3.47%	12.76%	-
Rebleeding Following Initial Hemostasis	2/37 (5.41%)	0/14 (0.00%)	5.41%	16.05%	-
Pseudoaneurysm not Requiring Treatment	0/37 (0.00%)	0/14 (0.00%)	0.00%	7.83%	-
Treated Pseudoaneurysm	0/37 (0.00%)	0/14 (0.00%)	0.00%	7.83%	-
Documented Arteriovenous Fistula	0/37 (0.00%)	0/14 (0.00%)	0.00%	7.83%	-
Access Site Hematoma >= 6cm	0/37 (0.00%)	1/14 (7.14%)	-7.14%	2.36%	-
Access Site-Related Bleeding Requiring > 30 min for Hemostasis	0/37 (0.00%)	1/14 (7.14%)	-7.14%	2.36%	-
Post-Hospital Discharge Access Site-Related Bleeding	0/37 (0.00%)	0/14 (0.00%)	0.00%	7.83%	-
Ipsilateral Lower Extremity Arterial Emboli	0/37 (0.00%)	0/14 (0.00%)	0.00%	7.83%	-
Transient Loss of Ipsilateral Lower Extremity Pulse	0/37 (0.00%)	0/14 (0.00%)	0.00%	7.83%	-
Ipsilateral Deep Vein Thrombosis	0/37 (0.00%)	0/14 (0.00%)	0.00%	7.83%	-
Access Site-Related Vessel Laceration	0/37 (0.00%)	0/14 (0.00%)	0.00%	7.83%	-
Transient Access Site-Related Nerve Injury	1/37 (2.70%)	0/14 (0.00%)	2.70%	12.48%	-
Access Site Wound Dehiscence	0/37 (0.00%)	0/14 (0.00%)	0.00%	7.83%	-
Treated, Localized Access Site Infection	0/37 (0.00%)	0/14 (0.00%)	0.00%	7.83%	-
Retroperitoneal Bleeding	1/37 (2.70%)	0/14 (0.00%)	2.70%	12.48%	-
Ipsilateral Peripheral Artery Total Occlusion	0/37 (0.00%)	0/14 (0.00%)	0.00%	7.83%	-
Ecchymosis >= 6cm	0/37 (0.00%)	0/14 (0.00%)	0.00%	7.83%	-
Intraluminal Plug Delivery Not Requiring Surgical Intervention	0/37 (0.00%)	0/14 (0.00%)	0.00%	7.83%	-
Decrease in Pedal Pulse	0/37 (0.00%)	0/14 (0.00%)	0.00%	7.83%	-
Death	0/37 (0.00%)	0/14 (0.00%)	0.00%	7.83%	-

Numbers are % (counts/sample size)

[1] Proportion differences between 6F VCD group and 6F MC group ($P_{VCD} - P_{MC}$).

[2] One-sided upper bound of 95% Confidence Intervals (CI) of the difference of two binomial proportions: between 6F VCD group and 6F MC group ($P_{VCD} - P_{MC}$). It was calculated using unconditional exact method

[3] P-values were calculated using unconditional exact test of non-inferiority using difference of two binomial proportions (6F VCD group vs. 6F MC group) with the pre-specified margin of 4.0%. The calculation was performed using StatXact.

IX. Clinical Studies

ECLIPSE TRIAL

The purpose of the ECLIPSE Trial was to evaluate the safety and effectiveness of the 6F **EXOSEAL VCD** to facilitate hemostasis, ambulation, eligibility for hospital discharge, and hospital discharge in comparison to manual compression (MC). The study population was defined as patients undergoing cardiac or peripheral diagnostic or interventional catheterization procedures via the femoral artery approach when using a standard 6F sheath introducer with an 11 cm working length.

This was a multi-center, prospective, randomized, non-blinded controlled trial conducted at 17 sites in the United States. To be eligible, a patient was required to be at least 18 years of age and

have signed an Informed Consent Form. Additionally, he or she was to be scheduled for a cardiac or peripheral diagnostic or interventional catheterization procedure utilizing a 6F arterial puncture in the common femoral artery with a target vessel lumen diameter ≥ 5 mm. The primary protocol exclusions were: acute ST-elevation myocardial infarction ≤ 48 hours prior to the catheterization procedure, prior femoral vascular surgery or vascular graft at the target site, treatment with thrombin-specific anticoagulant or low molecular weight heparin ≤ 24 hours prior to the catheterization procedure, arterial puncture in the femoral artery of both legs, prior target artery closure with any closure devices, or closure with manual compression ≤ 30 days prior to the catheterization procedure.

Eighty-seven (87) roll-in patients and 401 randomized patients (267 6F **EXOSEAL VCD** and 134 MC patients in a 2:1 randomization ratio) entered the study across 17 investigative sites for a total of 488 patients. Of the 401 randomized patients, 50% (n=200) were diagnostic patients and the remaining 50% (n=201) were interventional patients. Among the 200 diagnostic patients, 134 patients were 6F **EXOSEAL VCD** patients and 66 patients were MC patients and among the 201 interventional patients, 133 patients were 6F **EXOSEAL VCD** patients and 68 patients were MC patients. Patient demographic characteristics at baseline, such as gender, age, and BMI were comparable between the two randomized groups. The majority of patients were male in both treatment groups, which is a reflection of the general referral pattern for patients undergoing diagnostic and interventional procedures. The percentages of males were similarly distributed in the 6F **EXOSEAL VCD** and MC treatment group of 68.2% and 61.9% respectively. The mean age for the 6F **EXOSEAL VCD** patient was 63.3 ± 11.13 years, and in the MC group the mean age was 61.4 ± 10.47 years. BMI in the 6F **EXOSEAL VCD** group averaged 28.9 ± 4.99 kg/m^2 and in the MC group averaged 29.5 ± 5.40 kg/m^2.

Among the 6F ECLIPSE Trial patients, 1 diagnostic 6F **EXOSEAL VCD** patient, 1 diagnostic MC patient, 37 interventional 6F **EXOSEAL VCD** patients, and 14 interventional MC patients received glycoprotein (GP) IIb/IIIa inhibitor therapy before and/or during the catheterization procedure.

The primary safety endpoint was the combined rate of major complications within 30 ± 7 days following the catheterization procedure. The secondary safety endpoint was the combined rate of secondary complications within 30 ± 7 days following the procedure. The primary effectiveness endpoints were time to hemostasis and time to ambulation. The secondary effectiveness endpoints were time to eligibility for hospital discharge, time to hospital discharge, time to device deployment, procedure success, and device success.

German and Mexican Studies

The purpose of the German and Mexican studies was to evaluate the safety and effectiveness of the 7F **EXOSEAL VCD** to facilitate hemostasis, ambulation, eligibility for hospital discharge, and hospital discharge. The study population was defined as patients undergoing cardiac or peripheral diagnostic or interventional catheterization procedures via the femoral artery approach when using a standard 7F sheath introducer with an 11 cm working length.

The studies were a multi-center (German), single-center (Mexican), prospective, non-randomized, non-blinded, single treatment trials conducted at six sites in Germany and one site in Mexico. To be eligible, a patient was required to be at least 18 years of age and have signed an Informed Consent Form. Additionally, he or she was to be scheduled for a cardiac or peripheral diagnostic or interventional catheterization procedure utilizing a 7F arterial puncture in the common femoral artery with a target vessel lumen diameter ≥ 5 mm. The primary protocol exclusions were: acute ST-elevation myocardial infarction ≤ 48 hours prior to the catheterization procedure, prior femoral vascular surgery or vascular graft at the target site, treatment with thrombin-specific anticoagulant or low molecular weight heparin ≤ 24 hours prior to the catheterization procedure, arterial puncture in the femoral artery of both legs, prior target artery closure with any closure devices, or closure with manual compression ≤ 30 days prior to the catheterization procedure.

The data from the German and Mexican studies were pooled and compared to the manual compression control group data (134 MC patients) from the 6F ECLIPSE Trial. Patient demographic characteristics at baseline, such as gender, age, and BMI were comparable between the German and Mexican studies. Thirty-Five (35) roll-in patients and 88 study patients entered the study across seven investigative sites for a total of 123 patients. Of the 88 study patients, 49% (n=43) were diagnostic patients and the remaining 51% (n=45) were interventional patients.

Patient demographic characteristics for gender and age were comparable between the 7F **EXOSEAL VCD** pooled studies and the 6F MC control group, while BMI was lower in the 7F **EXOSEAL VCD** pooled studies. The percentages of males were similarly distributed in the 7F **EXOSEAL VCD** pooled studies and 6F MC control group of 71.6% and 61.9% respectively. The mean age in the 7F **EXOSEAL VCD** pooled studies was 62.7 ± 10.85 years, and in the 6F MC group the mean age was 61.4 ± 10.47 years. BMI in the 7F **EXOSEAL VCD** pooled studies averaged 27.9 ± 3.77 kg/m^2 and in the MC group averaged 29.5 ± 5.40 kg/m^2.

The primary safety endpoint was the combined rate of major complications within 30 ± 7 days following the catheterization procedure. The secondary safety endpoint was the combined rate of secondary complications within 30 ± 7 days following the catheterization procedure. The primary effectiveness endpoints were time to hemostasis and time to ambulation. The secondary effectiveness endpoints were time to eligibility for hospital discharge, time to hospital discharge, time to device deployment, procedure success, and device success.

Effectiveness Results from ECLIPSE Trial and German and Mexican Studies

All 401 enrolled subjects in the ECLIPSE Trial were evaluable for effectiveness. Time to hemostasis was defined as time from when the introducer sheath was removed to the time that hemostasis (no or minimal subcutaneous oozing and the absence of expanding or developing hematoma) was achieved.

Hemostasis was achieved in significantly less time with the 6F **EXOSEAL VCD** device as compared to manual compression. The mean time to hemostasis was 4.38 ± 11.59 minutes compared with 20.05 ± 22.54 minutes for 6F **EXOSEAL VCD** and MC respectively, with the -15.68 minute difference 95% CI: [-19.04, -12.31] P<0.0001.

Time to ambulation was defined as the time from when the introducer sheath was removed to the time when ambulation was achieved (patient standing and walking at least 20 feet without rebleeding).

Time to ambulation was also significantly favorable to the 6F **EXOSEAL VCD** group over MC with a mean time to ambulation of 2.54 ± 5.02 hours compared with 6.24 ± 13.34 hours in the MC group, with the -3.70 hour difference 95% CI: [-5.53, -1.87] *P*=0.0028.

All 88 study subjects in the German and Mexican Studies were evaluable for effectiveness. Time to hemostasis and time to ambulation were defined the same as in the ECLIPSE Trial. Hemostasis was achieved in significantly less time with the 7F **EXOSEAL VCD** device as compared to manual compression. The mean time to hemostasis was 3.25 ± 4.25 minutes compared with 20.05 ± 22.54 minutes for 7F **EXOSEAL VCD** and MC respectively, with the –16.80 minute difference 95% CI: [-21.60, -12.01] *P*<0.0001.

Time to ambulation was also significantly favorable to the 7F **EXOSEAL VCD** group over MC with a mean time to ambulation of 2.64 ± 5.43 hours compared with 6.24 ± 13.34 hours in the MC group, with the -3.60 hour difference 95% CI: [-6.56, -0.64] *P*=0.0066.

Tables 5 and 6 show the primary and secondary effectiveness results for the 6F ECLIPSE Trial and for the 7F **EXOSEAL VCD** group versus 6F MC group comparison.

Table 5 Primary Effectiveness Results – All Patients (ITT) Treated

	6F ECLIPSE Trial			Pooled 7F VCD Data Compared to 6F MC Data	
Primary Effective Endpoints	**6F VCD**	**6F MC**	**P-value[a]**	**Pooled 7F VCD**	**P-value[b]**
ITT Patients	**N=267**	**N=134**		**N=88**	
Time to Hemostasis (min)					
Mean ± STD (N)	4.38±11.59(267)	20.05±22.54(131)	<0.0001	3.25 ±4.25 (88)	<0.0001
Median, Range (Min, Max)	2.0 (2.0, 175.0)	15.0 (3.0, 220.0)		2.0 (2.0, 35.0)	
Time to Ambulation (hr)					
Mean ± STD (N)	2.54±5.02(264)	6.24±13.34(129)	0.0028	2.64 ±5.43 (88)	0.0066
Median, Range (Min, Max)	1.2 (0.9, 69.1)	4.3 (1.3, 152.2)		1.1 (0.01, 24.3)	
Diagnostic ITT Patients	**N=134**	**N=66**		**N=43**	
Time to Hemostasis (min)					
Mean ± STD (N)	3.34±4.86(134)	14.80±5.85(65)	<0.0001	2.86 ±2.77 (43)	<0.0001
Median, Range (Min, Max)	2.0 (2.0, 34.0)	15.0 (3.0, 30.0)		2.0 (2.0, 15.0)	
Time to Ambulation (hr)					
Mean ± STD (N)	1.59±1.22(133)	6.63±18.40(66)	0.0295	2.15 ±4.90 (43)	0.0637
Median, Range (Min, Max)	1.1 (0.9, 8.4)	4.1 (1.3, 152.2)		1.1, (0.01, 24.2)	
Interventional ITT Patients	**N=133**	**N=68**		**N=45**	
Time to Hemostasis (min)					
Mean ± STD (N)	5.43±15.64(133)	25.23±30.45(66)	<0.0001	3.62 ±5.31 (45)	<0.0001
Median, Range (Min, Max)	2.0 (2.0, 175.0)	20.0 (10.0, 220.0)		2.0 (2.0, 35.0)	
Time to Ambulation (hr)					
Mean ± STD (N)	3.51±6.90(131)	5.83±3.52(63)	0.0022	3.11 ±5.90 (45)	0.0074
Median, Range (Min, Max)	2.0 (0.9, 69.1)	4.8 (2.8, 21.8)		1.1, (1.0, 24.3)	

Numbers are Mean ± STD (Sample Size). Numbers of patients for the summary of continuous measures are based on number of non-missing values.

(a) P-values were calculated using unpaired t-test of inequality in mean differences of the continuous outcomes between 6F VCD and 6F MC group
(b) P-values were calculated using unpaired t-test of inequality in mean differences of the continuous outcomes between pooled 7F VCD and 6F MC group

Table 6 Secondary Effectiveness Results – All Patients (ITT) Treated

Secondary Effective Endpoints	6F ECLIPSE Trial			Pooled 7F VCD Data Compared to 6F MC Data	
	6F VCD	6F MC	P-value[a]	Pooled 7F VCD	P-value[b]
ITT Patients	**N=267**	**N=134**		**N=88**	
Time to Eligibility for Hospital Discharge (hr)					
Mean ± STD (N)	12.57±13.91 (257)	16.26±27.49 (128)	0.1540	12.54±23.85 (75)	0.3301
Median, Range (Min, Max)	5.0 (0.6, 116.1)	14.1 (0.0, 283.7)		6.9 (1.1, 190.7)	
Time to Actual Hospital Discharge (hr)					
Mean ± STD (N)	16.77±19.79 (264)	19.35±29.23 (133)	0.3612	33.22±45.90 (73)	0.0214
Median, Range (Min, Max)	17.9 (1.1, 196.1)	18.4 (3.0, 285.4)		22.6 (1.5, 288.7)	
Time for Device Deployment (min)					
Mean ± STD (N)	1.01±2.12 (260)	-	-	0.62 ±0.25 (88)	-
Median, Range (Min, Max)	0.7 (0.0, 23.3)			0.6 (0.2, 1.4)	
Procedure Success	245/267 (91.8%)	122/134 (91.0%)	0.8500	83 /88 (94.3%)	0.4462
Device Success	238/267 (89.1%)	-	-	82 /88 (93.2%)	-
Diagnostic ITT Patients	**N=134**	**N=66**		**N=43**	
Time to Eligibility for Hospital Discharge (hr)					
Mean ± STD (N)	4.94±7.41(131)	11.88±35.40(64)	0.1257	7.00 ±6.98 (37)	0.2894
Median, Range (Min, Max)	2.1 (0.6, 47.0)	4.4 (0.4, 283.7)		6.3 (1.1, 28.4)	
Time to Actual Hospital Discharge (hr)					
Mean ± STD (N)	8.72±20.15(132)	14.78±38.79(65)	0.2402	17.49±25.33 (35)	0.6749
Median, Range (Min, Max)	3.0 (1.1, 196.1)	5.2 (3.0, 285.4)		8.9 (1.5, 142.8)	
Time for Device Deployment (min)					
Mean ± STD (N)	1.19±2.87(131)	-	-	0.62 ±0.23 (43)	-
Median, Range (Min, Max)	0.7 (0.0, 23.3)			0.6 (0.2, 1.4)	
Procedure Success	126/134 (94.0%)	65/66 (98.5%)	0.2763	41 /43 (95.3%)	0.5606
Device Success	125/134 (93.3%)	-	-	41 /43 (95.3%)	-
Interventional ITT Patients	**N=133**	**N=68**		**N=45**	
Time to Eligibility for Hospital Discharge (hr)					
Mean ± STD (N)	20.49±14.67(126)	20.64±15.22(64)	0.9460	17.94±32.09 (38)	0.6273
Median, Range (Min, Max)	21.3 (1.0,116.1)	19.0 (0.0, 119.0)		7.2 (1.3, 190.7)	
Time to Actual Hospital Discharge (hr)					
Mean ± STD (N)	24.83±15.80(132)	23.71±14.35(68)	0.6270	47.71±55.32 (38)	0.0122
Median, Range (Min, Max)	23.2 (1.5, 119.3)	20.9 (4.6, 119.0)		24.3 (13.1, 288.7)	
Time for Device Deployment (min)					
Mean ± STD (N)	0.82±0.83(129)	-	-	0.61 ±0.26 (45)	-
Median, Range (Min, Max)	0.7 (0.0, 7.0)			0.6 (0.3, 1.3)	
Procedure Success	119/133(89.5%)	57/68(83.8%)	0.2651	42 /45 (93.3%)	0.1565
Device Success	113/133(85.0%)	-	-	41 /45 (91.1%)	-

Numbers are Mean ± STD (Sample Size). Numbers of patients for the summary of continuous measures are based on number of non-missing values.

(a) P-values were calculated using unpaired t-test of inequality in mean differences of the continuous outcomes between 6F VCD and 6F MC group
(b) P-values were calculated using unpaired t-test of inequality in mean differences of the continuous outcomes between pooled 7F VCD and 6F MC group

Table 7 shows the cumulative times to hemostasis, ambulation, eligibility for hospital discharge, and hospital discharge for the total patients in the 6F ECLIPSE Trial.

Table 7 Effectiveness Results by Post-Procedure Time Interval for ITT Patients

Variable	6F ECLIPSE Trial		Pooled 7F VCD Data
	VCD (n=267 patients)	MC (n=134 patients)	Pooled 7F VCD (n=88 patients)
Time to Hemostasis (min)			
Mean ± STD (n)	4.38±11.59 (267)	20.05±22.54 (131)	3.25±4.25 (88)
Median	2.00	15.00	2.00
Range (Min, Max)	2.00, 175.0	3.00, 220.0	2.00, 35.00
Distribution	Cumulative n (%)	Cumulative n (%)	Cumulative n (%)
≤ 2 min	69.7% (186/267)	0.0% (0/131)	71.6% (63/88)
≤ 5 min	89.5% (239/267)	2.3% (3/131)	93.2% (82/88)
≤ 10 min	92.9% (248/267)	25.2% (33/131)	95.5% (84/88)
≤ 20 min	97.0% (259/267)	80.2% (105/131)	98.9% (87/88)
≤ 30 min	99.3% (265/267)	96.2% (126/131)	98.9% (87/88)
Time to Ambulation (hour)			
Mean ± STD (n)	2.54± 5.02 (264)	6.24±13.34(129)	2.64±5.43 (88)
Median	1.21	4.30	1.07
Range (Min, Max)	0.88, 69.09	1.33, 152.2	0.01, 24.32
Distribution	Cumulative n (%)	Cumulative n (%)	Cumulative n (%)
≤ 1 hour	3.8% (10/264)	0.0% (0/129)	11.4% (10/88)
≤ 2 hours	68.2% (180/264)	0.8% (1/129)	89.8% (79/88)
≤ 5 hours	91.3% (241/264)	66.7% (86/129)	92.0% (81/88)
≤ 7 hours	95.1% (251/264)	93.0% (120/129)	92.0% (81/88)
≤ 10 hours	97.3% (257/264)	94.6% (122/129)	93.2% (82/88)
≤ 15 hours	98.1% (259/264)	96.9% (125/129)	93.2% (82/88)
Time to Eligible Discharge (Hour)			
Mean ± STD (n)	12.57±13.91 (257)	16.26±27.49 (128)	12.54±23.85 (75)
Median	5.03	14.08	6.94
Range (Min, Max)	0.56, 116.1	0.00, 283.7	1.08, 190.73
Distribution	Cumulative n (%)	Cumulative n (%)	Cumulative n (%)
≤ 2 hour	22.2% (57/257)	2.3% (3/128)	16.0% (12/75)
≤ 4 hours	46.7% (120/257)	18.0% (23/128)	30.7% (23/75)
≤ 8 hours	54.5% (140/257)	45.3% (58/128)	72.0% (54/75)
≤ 12 hours	54.9% (141/257)	46.9% (60/128)	72.0% (54/75)
≤ 24 hours	86.4% (222/257)	93.8% (120/128)	93.3% (70/75)
≤ 48 hours	98.8% (254/257)	98.4% (126/128)	97.3% (73/75)
Time to Actual Discharge (Hour)			
Mean ± STD (n)	16.77±19.79 (264)	19.35±29.23 (133)	33.22±45.90 (73)
Median	17.93	18.36	22.63
Range (Min, Max)	1.11, 196.1	2.98, 285.4	1.47, 288.70
Distribution	Cumulative n (%)	Cumulative n (%)	Cumulative n (%)
≤ 2 hour	10.2% (27/264)	0.0% (0/133)	2.7% (2/73)
≤ 4 hours	34.5% (91/264)	9.0% (12/133)	12.3% (9/73)
≤ 8 hours	45.8% (121/264)	39.9% (53/133)	19.2% (14/73)
≤ 12 hours	47.0% (124/264)	40.6% (54/133)	28.8% (21/73)
≤ 24 hours	75.4% (199/264)	85.0% (113/133)	60.3% (44/73)
≤ 48 hours	97.0% (256/264)	97.7% (130/133)	82.2% (60/73)

Denominators for percentage calculations are based on number of non-missing responses. Numbers of patients for the summary of continuous measures are based on number of non-missing values.

The primary and secondary effectiveness results for the interventional patients in the 6F ECLIPSE Trial who received GP IIb/IIIa inhibitor therapy are shown in Table 8.

Table 8 Effectiveness Results – Interventional ITT Patients who have Received GP IIb/IIIa inhibitor in 6F ECLIPSE Trial

Effectiveness Measures	VCD (n=37 patients)	MC (n=14 patients)	Difference [[95% CI][a]	P-value[b]
Primary Effectiveness Endpoints				
Time to Hemostasis (min)				
Mean ± STD (N)	4.95±5.63(37)	47.14±61.86(14)	-42.20[-62.52,-21.88]	0.0242
Median, Range (Min, Max)	2.0 (2.0, 30.0)	17.5 (10.0, 220.0)		
Time to Ambulation (hr)				
Mean ± STD (N)	4.25±4.35(36)	8.63±6.02(14)	-4.39[-7.46,-1.31]	0.0061
Median, Range (Min, Max)	2.2 (1.2, 22.3)	6.1 (3.6, 21.8)		
Secondary Effectiveness Endpoints				
Time to Eligibility for Hospital Discharge (hr)				
Mean ± STD (N)	22.79±12.93(35)	24.81±14.81(14)	-2.02[-10.59,6.55]	0.6377
Median, Range (Min, Max)	22.2 (2.1, 72.5)	20.5 (0.0, 47.0)		
Time to Actual Hospital Discharge (hr)				
Mean ± STD (N)	28.31±15.58(36)	28.47±12.12(14)	-0.16[-9.48,9.16]	0.9730
Median, Range (Min, Max)	24.1 (17.3, 96.4)	23.5 (14.9, 47.5)		
Time for Device Deployment (min)				
Mean ± STD (N)	0.81±0.61(37)	-	-	-
Median, Range (Min, Max)	0.7 (0.1, 2.9)			
Procedure Success	31/37 (83.78%)	8/14 (57.14%)	26.64% [0.49, 52.64]	0.0664
Device Success	28/37 (75.68%)	0/14 (0.00%)	75.68% [48.97, 86.64]	<0.0001

Numbers are Mean ± STD (Sample Size). Numbers of patients for the summary of continuous measures are based on number of non-missing values.

(a) Two-sided 95% Confidence Intervals (CI) were calculated using Newcombe-Wilson Hybrid Score method for binary outcomes. Two sided 95% confidence intervals for continuous outcomes are based on least-squares estimation from analysis of variance.

(b) P-values were calculated using unpaired t-test of inequality in mean differences of the continuous outcomes between 6F VCD and 6F MC group. Fisher Exact tests are used for comparison of binary outcomes between 6F VCD and 6F MC group.

Sex/Gender Subgroup Analysis

To evaluate for possible sex-based differences in outcome of treatment with the **EXOSEAL VCD**, sex/gender-specific analyses were performed on safety and effectiveness endpoints. The results suggest that the general conclusions of the overall study regarding both safety and effectiveness can be generalized for males and females.

In the **EXOSEAL** 6F ECLIPSE trial ITT population, of the 267 subjects randomized to **EXOSEAL VCD**, 182 subjects were male (68.2%) and 85 subjects were female (31.8%). The proportions in the manual compression control group were similar (61.9% male, 38.1% female). In the **EXOSEAL** pooled 7F ITT population, of the 88 subjects randomized to **EXOSEAL VCD**, 63 subjects were male (71.6%) and 25 subjects were female (28.4%). In comparison, recently published rates of diagnostic and interventional catheterization procedures in the U.S. range from 59.7% to 68.8% for men and 31.2% to 40.3% for women.[1,2] Tavris et.al. have also shown that the percentage of women decreases as the size of the catheter introducer sheath increases.[3]

The **EXOSEAL** 6F Eclipse trial and Mexican and German 7F trials were not powered to study safety or effectiveness of the **EXOSEAL VCD** versus Manual compression in sex-specific subgroups. The **EXOSEAL** 6F Eclipse trial and Mexican and German 7F trials primary and secondary endpoint data were assessed for differences between male and female subgroups, as well as for any interaction between treatment group and gender (Table 15). The results of these post hoc analyses are presented below in Tables 9-12.

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[1] Lloyd-Jones, D. MD, et. al, On behalf of the American Heart Association Statistics Committee and Stroke Statistics Subcommittee. Heart Disease and Stroke Statistics_2010 Update: A Report From the American Heart Association. Circulation. 2010;121:e46-e215.

[2] Wayne Rosamond, W., et al, and for the American Heart Association Statistics Committee and Stroke Statistics Subcommittee. Heart Disease and Stroke Statistics 2008 Update. A Report From the American Heart Association Statistics Committee and Stroke Statistics Subcommittee. Circulation. 2008;117:e1-e122.

[3] Tavris DR, et. al., Risk of local adverse events by gender following cardiac catheterization. Pharmacoepidemiol Drug Saf 2007; 16: 125–131.

Table 9. Principal Effectiveness and Safety Results – Diagnostic Male Patients (ITT) Treated

Primary Effective Endpoints	6F ECLIPSE Trial			Pooled 7F VCD Data Compared to 6F MC Data	
	VCD (n=83 patients)	MC (n=35 patients)	P-Values[(a)]	Pooled 7F VCD (n=28 patients)	P-values[(b)]
Time to Hemostasis (min)					
Mean ± STD (N)	3.48±5.09(83)	15.12±6.24(34)	<0.0001	2.79 ±2.47 (28)	<0.0001
Median, Range (Min, Max)	2.00(2.00,34.00)	15.00(3.00,25.00)		2.00(2.00,15.00)	
Time to Ambulation (hr)					
Mean ± STD (N)	1.59±1.26(82)	8.18±25.09(35)	0.1299	1.94 ±4.36 (28)	0.1576
Median, Range (Min, Max)	1.12(0.94,8.35)	3.97(1.33,152.24)		1.08(0.98,24.18)	

Description of Event (Event Based)	6F ECLIPSE Trial					Pooled 7F VCD Data Compared to 6F MC Data			
	VCD (n=83 patients)	MC (n=35 patients)	Difference VCD-MC[1]	Upper Bound[2]	P-Values[3]	Pooled 7F VCD (n=28 patients)	Difference VCD-MC[4]	Upper Bound[5]	P-values[6]
Major Adverse Events (Combined Event Rate) at 30-days	0/83(0.00%)	0/35(0.00%)	0.00%	3.68%	0.0404	0/28(0.00%)	0.00%	10.15%	0.3189
Vascular Repair	0/83(0.00%)	0/35(0.00%)	0.00%	3.68%	0.0404	0/28(0.00%)	0.00%	10.15%	0.3189
Access site-related bleeding requiring transfusion	0/83(0.00%)	0/35(0.00%)	0.00%	3.68%	0.0404	0/28(0.00%)	0.00%	10.15%	0.3189
Access site-related infection requiring treatment	0/83(0.00%)	0/35(0.00%)	0.00%	3.68%	0.0404	0/28(0.00%)	0.00%	10.15%	0.3189
Any new documented ipsilateral lower extremity ischemia	0/83(0.00%)	0/35(0.00%)	0.00%	3.68%	0.0404	0/28(0.00%)	0.00%	10.15%	0.3189
Surgery for access site-related nerve injury	0/83(0.00%)	0/35(0.00%)	0.00%	3.68%	0.0404	0/28(0.00%)	0.00%	10.15%	0.3189
Permanent(>30 days) access site-related nerve injury	0/83(0.00%)	0/35(0.00%)	0.00%	3.68%	0.0404	0/28(0.00%)	0.00%	10.15%	0.3189
Secondary Adverse Events (Combined Event Rate) at 30-days	3/83(3.61%)	0/35(0.00%)	3.61%	9.08%	-	1/28(3.57%)	3.57%	15.85%	
Rebleeding Following Initial Hemostasis	1/83(1.20%)	0/35(0.00%)	1.20%	5.59%	-	0/28(0.00%)	0.00%	10.15%	-
Pseudoaneurysm not Requiring Treatment	0/83(0.00%)	0/35(0.00%)	0.00%	3.68%	-	0/28(0.00%)	0.00%	10.15%	-
Treated Pseudoaneurysm	0/83(0.00%)	0/35(0.00%)	0.00%	3.68%	-	0/28(0.00%)	0.00%	10.15%	-
Documented Arteriovenous Fistula	0/83(0.00%)	0/35(0.00%)	0.00%	3.68%	-	0/28(0.00%)	0.00%	10.15%	-
·ccess Site Hematoma >= 6cm	1/83(1.20%)	0/35(0.00%)	1.20%	5.59%	-	1/28(3.57%)	3.57%	15.85%	-
Access Site-Related Bleeding Requiring > 30 min for Hemostasis	1/83(1.20%)	0/35(0.00%)	1.20%	5.59%	-	0/28(0.00%)	0.00%	10.15%	-
Post-Hospital Discharge Access Site-Related Bleeding	0/83(0.00%)	0/35(0.00%)	0.00%	3.68%	-	0/28(0.00%)	0.00%	10.15%	-
Ipsilateral Lower Extremity Arterial Emboli	0/83(0.00%)	0/35(0.00%)	0.00%	3.68%	-	0/28(0.00%)	0.00%	10.15%	-
Transient Loss of Ipsilateral Lower Extremity Pulse	0/83(0.00%)	0/35(0.00%)	0.00%	3.68%	-	0/28(0.00%)	0.00%	10.15%	-
Ipsilateral Deep Vein Thrombosis	0/83(0.00%)	0/35(0.00%)	0.00%	3.68%	-	0/28(0.00%)	0.00%	10.15%	-
Access Site-Related Vessel Laceration	0/83(0.00%)	0/35(0.00%)	0.00%	3.68%	-	0/28(0.00%)	0.00%	10.15%	-
Transient Access Site-Related Nerve Injury	0/83(0.00%)	0/35(0.00%)	0.00%	3.68%	-	0/28(0.00%)	0.00%	10.15%	-
Access Site Wound Dehiscence	0/83(0.00%)	0/35(0.00%)	0.00%	3.68%	-	0/28(0.00%)	0.00%	10.15%	-
Treated, Localized Access Site Infection	0/83(0.00%)	0/35(0.00%)	0.00%	3.68%	-	0/28(0.00%)	0.00%	10.15%	-
Retroperitoneal Bleeding	0/83(0.00%)	0/35(0.00%)	0.00%	3.68%	-	0/28(0.00%)	0.00%	10.15%	-
Ipsilateral Peripheral Artery Total Occlusion	0/83(0.00%)	0/35(0.00%)	0.00%	3.68%	-	0/28(0.00%)	0.00%	10.15%	-
Ecchymosis >= 6cm	0/83(0.00%)	0/35(0.00%)	0.00%	3.68%	-	0/28(0.00%)	0.00%	10.15%	-
Intraluminal Plug Delivery Not Requiring Surgical Intervention	0/83(0.00%)	0/35(0.00%)	0.00%	3.68%	-	0/28(0.00%)	0.00%	10.15%	-
Decrease in Pedal Pulse	0/83(0.00%)	0/35(0.00%)	0.00%	3.68%	-	0/28(0.00%)	0.00%	10.15%	-
Death	0/83(0.00%)	0/35(0.00%)	0.00%	3.68%	-	0/28(0.00%)	0.00%	10.15%	-

Numbers are % (counts/sample size) or Mean ± STD (Sample Size). Numbers of patients for the summary of continuous measures are based on number of non-missing values.

[(a)] P-values were calculated using unpaired t-test of inequality in mean differences of the continuous outcomes between 6F VCD and 6F MC group

[(b)] P-values were calculated using unpaired t-test of inequality in mean differences of the continuous outcomes between pooled 7F VCD and 6F MC group

[1] Proportion differences between 6F VCD group and 6F MC group ($P_{VCD} - P_{MC}$)

[2] One-sided upper bound of 95% Confidence Intervals (CI) of the difference of two binomial proportions: between 6F VCD group and 6F MC group ($P_{VCD} - P_{MC}$). The calculation was performed using unconditional exact method

[3] P-values were calculated using unconditional exact test of non-inferiority using difference of two binomial proportions (6F VCD group vs. 6F MC group) with the pre-specified margin of 4.0%. The calculation was performed using StatXact.

[4] Proportion differences between pooled 7F VCD group and 6F MC group ($P_{VCD} - P_{MC}$)

[5] One-sided upper bound of 95% Confidence Intervals (CI) of the difference of two binomial proportions: between pooled 7F VCD group and 6F MC group ($P_{VCD} - P_{MC}$). The calculation was performed using unconditional exact method

[6] P-values were calculated using unconditional exact test of non-inferiority using difference of two binomial proportions (7F VCD group vs. 6F MC group) with the pre-specified margin of 4.0%. The calculation was performed using StatXact.

Table 10. Principal Effectiveness and Safety Results – Diagnostic Female Patients (ITT) Treated

Primary Effective Endpoints	6F ECLIPSE Trial			Pooled 7F VCD Data Compared to 6F MC Data	
	VCD (n=51 patients)	MC (n=31 patients)	P-Values[a]	Pooled 7F VCD (n=15 patients)	P-values[b]
Time to Hemostasis (min)					
Mean ± STD (N)	3.10±4.50(51)	14.45±5.48(31)	<0.0001	3.00 ±3.34 (15)	<0.0001
Median, Range (Min, Max)	2.00(2.00,25.00)	15.00(5.00,30.00)		2.00(2.00,15.00)	
Time to Ambulation (hr)					
Mean ± STD (N)	1.58±1.19(51)	4.88±3.72(31)	<0.0001	2.52 ±5.93 (15)	0.1733
Median, Range (Min, Max)	1.10(0.99,6.94)	4.16(2.28,24.29)		1.05(0.01,23.94)	

Description of Event (Event Based)	6F ECLIPSE Trial					Pooled 7F VCD Data Compared to 6F MC Data			
	VCD (n=51 patients)	MC (n=31 patients)	Difference VCD-MC[1]	Upper Bound[2]	P-Values[3]	Pooled 7F VCD (n=15 patients)	Difference VCD-MC[4]	Upper Bound[5]	P-values[6]
Major Adverse Events (Combined Event Rate) at 30-days	0/51 (0.00%)	0/31 (0.00%)	0.00%	5.70%	0.1247	0/15 (0.00%)	0.00%	18.10%	0.5421
Vascular Repair	0/51 (0.00%)	0/31 (0.00%)	0.00%	5.70%	0.1247	0/15 (0.00%)	0.00%	18.10%	0.5421
Access site-related bleeding requiring transfusion	0/51 (0.00%)	0/31 (0.00%)	0.00%	5.70%	0.1247	0/15 (0.00%)	0.00%	18.10%	0.5421
Access site-related infection requiring treatment	0/51 (0.00%)	0/31 (0.00%)	0.00%	5.70%	0.1247	0/15 (0.00%)	0.00%	18.10%	0.5421
Any new documented ipsilateral lower extremity ischemia	0/51 (0.00%)	0/31 (0.00%)	0.00%	5.70%	0.1247	0/15 (0.00%)	0.00%	18.10%	0.5421
Surgery for access site-related nerve injury	0/51 (0.00%)	0/31 (0.00%)	0.00%	5.70%	0.1247	0/15 (0.00%)	0.00%	18.10%	0.5421
Permanent(>30 days) access site-related nerve injury	0/51 (0.00%)	0/31 (0.00%)	0.00%	5.70%	0.1247	0/15 (0.00%)	0.00%	18.10%	0.5421
Secondary Adverse Events (Combined Event Rate) at 30-days	1/51(1.96%)	1/31(3.23%)	-1.27%	6.03%	-	0/15 (0.00%)	-3.23 %	12.64%	-
Rebleeding Following Initial Hemostasis	1/51(1.96%)	1/31(3.23%)	-1.27%	6.03%	-	0/15 (0.00%)	-3.23 %	12.64%	-
Pseudoaneurysm not Requiring Treatment	0/51(0.00%)	0/31(0.00%)	0.00%	5.70%	-	0/15 (0.00%)	0.00%	18.10%	-
Treated Pseudoaneurysm	0/51(0.00%)	0/31(0.00%)	0.00%	5.70%	-	0/15 (0.00%)	0.00%	18.10%	-
Documented Arteriovenous Fistula	0/51(0.00%)	0/31(0.00%)	0.00%	5.70%	-	0/15 (0.00%)	0.00%	18.10%	-
ccess Site Hematoma >= 6cm	0/51(0.00%)	0/31(0.00%)	0.00%	5.70%	-	0/15 (0.00%)	0.00%	18.10%	-
Access Site-Related Bleeding Requiring > 30 min for Hemostasis	0/51(0.00%)	0/31(0.00%)	0.00%	5.70%	-	0/15 (0.00%)	0.00%	18.10%	-
Post-Hospital Discharge Access Site-Related Bleeding	0/51(0.00%)	0/31(0.00%)	0.00%	5.70%	-	0/15 (0.00%)	0.00%	18.10%	-
Ipsilateral Lower Extremity Arterial Emboli	0/51(0.00%)	0/31(0.00%)	0.00%	5.70%	-	0/15 (0.00%)	0.00%	18.10%	-
Transient Loss of Ipsilateral Lower Extremity Pulse	0/51(0.00%)	0/31(0.00%)	0.00%	5.70%	-	0/15 (0.00%)	0.00%	18.10%	-
Ipsilateral Deep Vein Thrombosis	0/51(0.00%)	0/31(0.00%)	0.00%	5.70%	-	0/15 (0.00%)	0.00%	18.10%	-
Access Site-Related Vessel Laceration	0/51(0.00%)	0/31(0.00%)	0.00%	5.70%	-	0/15 (0.00%)	0.00%	18.10%	-
Transient Access Site-Related Nerve Injury	0/51(0.00%)	0/31(0.00%)	0.00%	5.70%	-	0/15 (0.00%)	0.00%	18.10%	-
Access Site Wound Dehiscence	0/51(0.00%)	0/31(0.00%)	0.00%	5.70%	-	0/15 (0.00%)	0.00%	18.10%	-
Treated, Localized Access Site Infection	0/51(0.00%)	0/31(0.00%)	0.00%	5.70%	-	0/15 (0.00%)	0.00%	18.10%	-
Retroperitoneal Bleeding	0/51(0.00%)	0/31(0.00%)	0.00%	5.70%	-	0/15 (0.00%)	0.00%	18.10%	-
Ipsilateral Peripheral Artery Total Occlusion	0/51(0.00%)	0/31(0.00%)	0.00%	5.70%	-	0/15 (0.00%)	0.00%	18.10%	-
Ecchymosis >= 6cm	0/51(0.00%)	0/31(0.00%)	0.00%	5.70%	-	0/15 (0.00%)	0.00%	18.10%	-
Intraluminal Plug Delivery Not Requiring Surgical Intervention	0/51(0.00%)	0/31(0.00%)	0.00%	5.70%	-	0/15 (0.00%)	0.00%	18.10%	-
Decrease in Pedal Pulse	0/51(0.00%)	0/31(0.00%)	0.00%	5.70%	-	0/15 (0.00%)	0.00%	18.10%	-
Death	0/51(0.00%)	0/31(0.00%)	0.00%	5.70%	-	0/15 (0.00%)	0.00%	18.10%	-

Numbers are % (counts/sample size) or Mean ± STD (Sample Size). Numbers of patients for the summary of continuous measures are based on number of non-missing values.

[a] P-values were calculated using unpaired t-test of inequality in mean differences of the continuous outcomes between 6F VCD and 6F MC group

[b] P-values were calculated using unpaired t-test of inequality in mean differences of the continuous outcomes between pooled 7F VCD and 6F MC group

[1] Proportion differences between 6F VCD group and 6F MC group ($P_{VCD} - P_{MC}$)

[2] One-sided upper bound of 95% Confidence Intervals (CI) of the difference of two binomial proportions: between 6F VCD group and 6F MC group ($P_{VCD} - P_{MC}$). The calculation was performed using unconditional exact method

[3] P-values were calculated using unconditional exact test of non-inferiority using difference of two binomial proportions (6F VCD group vs. 6F MC group) with the pre-specified margin of 4.0%. The calculation was performed using StatXact.

[4] Proportion differences between pooled 7F VCD group and 6F MC group ($P_{VCD} - P_{MC}$)

[5] One-sided upper bound of 95% Confidence Intervals (CI) of the difference of two binomial proportions: between pooled 7F VCD group and 6F MC group ($P_{VCD} - P_{MC}$). The calculation was performed using unconditional exact method

[6] P-values were calculated using unconditional exact test of non-inferiority using difference of two binomial proportions (7F VCD group vs. 6F MC group) with the pre-specified margin of 4.0%. The calculation was performed using StatXact.

Table 11. Principal Effectiveness and Safety Results – Interventional Male Patients (ITT) Treated

Primary Effective Endpoints	6F ECLIPSE Trial			Pooled 7F VCD Data Compared to 6F MC Data	
	VCD (n=99 patients)	MC (n=48 patients)	P-Values[(a)]	Pooled 7F VCD (n=35 patients)	P-values[(b)]
Time to Hemostasis (min)					
Mean ± STD (N)	5.55±17.73(99)	28.17±35.64(47)	0.0001	3.89 ±5.90 (35)	<0.0001
Median, Range (Min, Max)	2.00(2.00,175.00)	20.00(10.00,220.00)		2.00(2.00,35.00)	
Time to Ambulation (hr)					
Mean ± STD (N)	3.13±3.90(97)	6.04±3.84(46)	<0.0001	3.66 ±6.60 (35)	0.0633
Median, Range (Min, Max)	1.95(0.88,22.30)	4.98(3.00,21.83)		1.08(0.98,24.32)	

Description of Event (Event Based)	6F ECLIPSE Trial					Pooled 7F VCD Data Compared to 6F MC Data			
	VCD (n=99 patients)	MC (n=48 patients)	Difference VCD-MC[1]	Upper Bound[2]	P-Values[3]	Pooled 7F VCD (n=35 patients)	Difference VCD-MC[4]	Upper Bound[5]	P-values[6]
Major Adverse Events (Combined Event Rate) at 30-days	0/99 (0.00%)	0/48 (0.00%)	0.00%	3.29%	0.0307	0/35 (0.00%)	0.00%	8.20%	0.2396
Vascular Repair	0/99 (0.00%)	0/48 (0.00%)	0.00%	3.29%	0.0307	0/35 (0.00%)	0.00%	8.20%	0.2396
Access site-related bleeding requiring transfusion	0/99 (0.00%)	0/48 (0.00%)	0.00%	3.29%	0.0307	0/35 (0.00%)	0.00%	8.20%	0.2396
Access site-related infection requiring treatment	0/99 (0.00%)	0/48 (0.00%)	0.00%	3.29%	0.0307	0/35 (0.00%)	0.00%	8.20%	0.2396
Any new documented ipsilateral lower extremity ischemia	0/99 (0.00%)	0/48 (0.00%)	0.00%	3.29%	0.0307	0/35 (0.00%)	0.00%	8.20%	0.2396
Surgery for access site-related nerve injury	0/99 (0.00%)	0/48 (0.00%)	0.00%	3.29%	0.0307	0/35 (0.00%)	0.00%	8.20%	0.2396
Permanent(>30 days) access site-related nerve injury	0/99 (0.00%)	0/48 (0.00%)	0.00%	3.29%	0.0307	0/35 (0.00%)	0.00%	8.20%	0.2396
Secondary Adverse Events (Combined Event Rate) at 30-days	17/99(17.17%)	3/48(6.25%)	10.92%	19.53%	-	1/35(2.86%)	-3.39%	6.24%	-
Rebleeding Following Initial Hemostasis	9/99(9.09%)	0/48(0.00%)	9.09%	15.33%	-	0/35(0.00%)	0.00%	8.20%	-
Pseudoaneurysm not Requiring Treatment	0/99(0.00%)	0/48(0.00%)	0.00%	3.29%	-	0/35(0.00%)	0.00%	8.20%	-
Treated Pseudoaneurysm	0/99(0.00%)	0/48(0.00%)	0.00%	3.29%	-	0/35(0.00%)	0.00%	8.20%	-
Documented Arteriovenous Fistula	0/99(0.00%)	0/48(0.00%)	0.00%	3.29%	-	0/35(0.00%)	0.00%	8.20%	-
Access Site Hematoma >= 6cm	5/99(5.05%)	1/48(2.08%)	2.97%	8.54%	-	1/35(2.86%)	0.77%	10.02%	-
Access Site-Related Bleeding Requiring > 30 min for Hemostasis	0/99(0.00%)	1/48(2.08%)	-2.08%	1.11%	-	0/35(0.00%)	-2.08%	5.51%	-
Post-Hospital Discharge Access Site-Related Bleeding	0/99(0.00%)	0/48(0.00%)	0.00%	3.29%	-	0/35(0.00%)	0.00%	8.20%	-
Ipsilateral Lower Extremity Arterial Emboli	0/99(0.00%)	0/48(0.00%)	0.00%	3.29%	-	0/35(0.00%)	0.00%	8.20%	-
Transient Loss of Ipsilateral Lower Extremity Pulse	0/99(0.00%)	0/48(0.00%)	0.00%	3.29%	-	0/35(0.00%)	0.00%	8.20%	-
Ipsilateral Deep Vein Thrombosis	0/99(0.00%)	0/48(0.00%)	0.00%	3.29%	-	0/35(0.00%)	0.00%	8.20%	-
Access Site-Related Vessel Laceration	0/99(0.00%)	0/48(0.00%)	0.00%	3.29%	-	0/35(0.00%)	0.00%	8.20%	-
Transient Access Site-Related Nerve Injury	1/99(1.01%)	0/48(0.00%)	1.01%	4.76%	-	0/35(0.00%)	0.00%	8.20%	-
Access Site Wound Dehiscence	0/99(0.00%)	0/48(0.00%)	0.00%	3.29%	-	0/35(0.00%)	0.00%	8.20%	-
Treated, Localized Access Site Infection	0/99(0.00%)	0/48(0.00%)	0.00%	3.29%	-	0/35(0.00%)	0.00%	8.20%	-
Retroperitoneal Bleeding	2/99(2.02%)	0/48(0.00%)	2.02%	6.22%	-	0/35(0.00%)	0.00%	8.20%	-
Ipsilateral Peripheral Artery Total Occlusion	0/99(0.00%)	0/48(0.00%)	0.00%	3.29%	-	0/35(0.00%)	0.00%	8.20%	-
Ecchymosis >= 6cm	0/99(0.00%)	1/48(2.08%)	-2.08%	1.11%	-	0/35(0.00%)	-2.08%	5.51%	-
Intraluminal Plug Delivery Not Requiring Surgical Intervention	0/99(0.00%)	0/48(0.00%)	0.00%	3.29%	-	0/35(0.00%)	0.00%	8.20%	-
Decrease in Pedal Pulse	0/99(0.00%)	0/48(0.00%)	0.00%	3.29%	-	0/35(0.00%)	0.00%	8.20%	-
Death	0/99(0.00%)	0/48(0.00%)	0.00%	3.29%	-	0/35(0.00%)	0.00%	8.20%	-

Numbers are % (counts/sample size) or Mean ± STD (Sample Size). Numbers of patients for the summary of continuous measures are based on number of non-missing values.

[(a)] P-values were calculated using unpaired t-test of inequality in mean differences of the continuous outcomes between 6F VCD and 6F MC group

[(b)] P-values were calculated using unpaired t-test of inequality in mean differences of the continuous outcomes between pooled 7F VCD and 6F MC group

[1] Proportion differences between 6F VCD group and 6F MC group ($P_{VCD} - P_{MC}$)

[2] One-sided upper bound of 95% Confidence Intervals (CI),of the difference of two binomial proportions: between 6F VCD group and 6F MC group ($P_{VCD} - P_{MC}$). The calculation was performed using unconditional exact method

[3] P-values were calculated using unconditional exact test of non-inferiority using difference of two binomial proportions (6F VCD group vs. 6F MC group) with the pre-specified margin of 4.0%. The calculation was performed using StatXact.

[4] Proportion differences between pooled 7F VCD group and 6F MC group ($P_{VCD} - P_{MC}$)

[5] One-sided upper bound of 95% Confidence Intervals (CI) of the difference of two binomial proportions: between pooled 7F VCD group and 6F MC group ($P_{VCD} - P_{MC}$). The calculation was performed using unconditional exact method

[6] P-values were calculated using unconditional exact test of non-inferiority using difference of two binomial proportions (7F VCD group vs. 6F MC group) with the pre-specified margin of 4.0%. The calculation was performed using StatXact.

Table 12. Principal Effectiveness and Safety Results – Interventional Female Patients (ITT) Treated

Primary Effective Endpoints	6F ECLIPSE Trial			Pooled 7F VCD Data Compared to 6F MC Data	
	VCD (n=34 patients)	MC (n=20 patients)	P-Values[(a)]	Pooled 7F VCD (n=10 patients)	P-values[(b)]
Time to Hemostasis (min)					
Mean ± STD (N)	5.09±6.73(34)	17.95±4.78(19)	<0.0001	2.70 ±2.21 (10)	<0.0001
Median, Range (Min, Max)	2.00(2.00,30.00)	15.00(10.00,30.00)		2.00(2.00,9.00)	
Time to Ambulation (hr)					
Mean ± STD (N)	4.60±11.90(34)	5.27±2.49(17)	0.7570	1.17 ±0.30 (10)	<0.0001
Median, Range (Min, Max)	1.85(1.02,69.09)	4.33(2.79,13.25)		1.11(0.96,2.00)	

Description of Event (Event Based)	6F ECLIPSE Trial					Pooled 7F VCD Data Compared to 6F MC Data			
	VCD (n=34 patients)	MC (n=20 patients)	Difference VCD-MC[1]	Upper Bound[2]	P-Values[3]	Pooled 7F VCD (n=10 patients)	Difference VCD-MC[4]	Upper Bound[5]	P-values[6]
Major Adverse Events (Combined Event Rate) at 30-days	0/34 (0.00%)	0/20 (0.00%)	0.00%	8.43%	0.2496	0/10 (0.00%)	0.00%	25.89%	0.6648
Vascular Repair	0/34 (0.00%)	0/20 (0.00%)	0.00%	8.43%	0.2496	0/10 (0.00%)	0.00%	25.89%	0.6648
Access site-related bleeding requiring transfusion	0/34 (0.00%)	0/20 (0.00%)	0.00%	8.43%	0.2496	0/10 (0.00%)	0.00%	25.89%	0.6648
Access site-related infection requiring treatment	0/34 (0.00%)	0/20 (0.00%)	0.00%	8.43%	0.2496	0/10 (0.00%)	0.00%	25.89%	0.6648
Any new documented ipsilateral lower extremity ischemia	0/34 (0.00%)	0/20 (0.00%)	0.00%	8.43%	0.2496	0/10 (0.00%)	0.00%	25.89%	0.6648
Surgery for access site-related nerve injury	0/34 (0.00%)	0/20 (0.00%)	0.00%	8.43%	0.2496	0/10 (0.00%)	0.00%	25.89%	0.6648
Permanent(>30 days) access site-related nerve injury	0/34 (0.00%)	0/20 (0.00%)	0.00%	8.43%	0.2496	0/10 (0.00%)	0.00%	25.89%	0.6648
Secondary Adverse Events (Combined Event Rate) at 30-days	3/34(8.82%)	2/20(10.00%)	-1.18%	13.94%	-	1/10(10.00%)	0.00%	28.73%	-
Rebleeding Following Initial Hemostasis	3/34(8.82%)	2/20(10.00%)	-1.18%	13.94%	-	0/10(0.00%)	-10.00%	14.32%	-
Pseudoaneurysm not Requiring Treatment	0/34(0.00%)	0/20(0.00%)	0.00%	8.43%	-	0/10(0.00%)	0.00%	25.89%	-
Treated Pseudoaneurysm	0/34(0.00%)	0/20(0.00%)	0.00%	8.43%	-	0/10(0.00%)	0.00%	25.89%	-
Documented Arteriovenous Fistula	0/34(0.00%)	0/20(0.00%)	0.00%	8.43%	-	0/10(0.00%)	0.00%	25.89%	-
ccess Site Hematoma >= 6cm	0/34(0.00%)	0/20(0.00%)	0.00%	8.43%	-	1/10(10.00%)	10.00%	39.42%	-
Access Site-Related Bleeding Requiring > 30 min for Hemostasis	0/34(0.00%)	0/20(0.00%)	0.00%	8.43%	-	0/10(0.00%)	0.00%	25.89%	-
Post-Hospital Discharge Access Site-Related Bleeding	0/34(0.00%)	0/20(0.00%)	0.00%	8.43%	-	0/10(0.00%)	0.00%	25.89%	-
Ipsilateral Lower Extremity Arterial Emboli	0/34(0.00%)	0/20(0.00%)	0.00%	8.43%	-	0/10(0.00%)	0.00%	25.89%	-
Transient Loss of Ipsilateral Lower Extremity Pulse	0/34(0.00%)	0/20(0.00%)	0.00%	8.43%	-	0/10(0.00%)	0.00%	25.89%	-
Ipsilateral Deep Vein Thrombosis	0/34(0.00%)	0/20(0.00%)	0.00%	8.43%	-	0/10(0.00%)	0.00%	25.89%	-
Access Site-Related Vessel Laceration	0/34(0.00%)	0/20(0.00%)	0.00%	8.43%	-	0/10(0.00%)	0.00%	25.89%	-
Transient Access Site-Related Nerve Injury	0/34(0.00%)	0/20(0.00%)	0.00%	8.43%	-	0/10(0.00%)	0.00%	25.89%	-
Access Site Wound Dehiscence	0/34(0.00%)	0/20(0.00%)	0.00%	8.43%	-	0/10(0.00%)	0.00%	25.89%	-
Treated, Localized Access Site Infection	0/34(0.00%)	0/20(0.00%)	0.00%	8.43%	-	0/10(0.00%)	0.00%	25.89%	-
Retroperitoneal Bleeding	0/34(0.00%)	0/20(0.00%)	0.00%	8.43%	-	0/10(0.00%)	0.00%	25.89%	-
Ipsilateral Peripheral Artery Total Occlusion	0/34(0.00%)	0/20(0.00%)	0.00%	8.43%	-	0/10(0.00%)	0.00%	25.89%	-
Ecchymosis >= 6cm	0/34(0.00%)	0/20(0.00%)	0.00%	8.43%	-	0/10(0.00%)	0.00%	25.89%	-
Intraluminal Plug Delivery Not Requiring Surgical Intervention	0/34(0.00%)	0/20(0.00%)	0.00%	8.43%	-	0/10(0.00%)	0.00%	25.89%	-
Decrease in Pedal Pulse	0/34(0.00%)	0/20(0.00%)	0.00%	8.43%	-	0/10(0.00%)	0.00%	25.89%	-
Death	0/34(0.00%)	0/20(0.00%)	0.00%	8.43%	-	0/10(0.00%)	0.00%	25.89%	-

Numbers are % (counts/sample size) or Mean ± STD (Sample Size). Numbers of patients for the summary of continuous measures are based on number of non-missing values.

[(a)] P-values were calculated using unpaired t-test of inequality in mean differences of the continuous outcomes between 6F VCD and 6F MC group

[(b)] P-values were calculated using unpaired t-test of inequality in mean differences of the continuous outcomes between pooled 7F VCD and 6F MC group

[1] Proportion differences between 6F VCD group and 6F MC group ($P_{VCD} - P_{MC}$)

[2] One-sided upper bound of 95% Confidence Intervals (CI) of the difference of two binomial proportions: between 6F VCD group and 6F MC group ($P_{VCD} - P_{MC}$). The calculation was performed using unconditional exact method

[3] P-values were calculated using unconditional exact test of non-inferiority using difference of two binomial proportions (6F VCD group vs. 6F MC group) with the pre-specified margin of 4.0%. The calculation was performed using StatXact.

[4] Proportion differences between pooled 7F VCD group and 6F MC group ($P_{VCD} - P_{MC}$)

[5] One-sided upper bound of 95% Confidence Intervals (CI) of the difference of two binomial proportions: between pooled 7F VCD group and 6F MC group ($P_{VCD} - P_{MC}$). The calculation was performed using unconditional exact method

[6] P-values were calculated using unconditional exact test of non-inferiority using difference of two binomial proportions (7F VCD group vs. 6F MC group) with the pre-specified margin of 4.0%. The calculation was performed using StatXact.

The treatment effect of **EXOSEAL VCD** and manual compression differed slightly in Time to Ambulation between men and women. Time to Ambulation for interventional patients getting the 6F **EXOSEAL VCD** showed statistically significant differences for males, but did not exhibit statistically significant differences in females. Similarly, Time to Ambulation for diagnostic patients getting the 6F **EXOSEAL VCD** showed statistically significant differences for females, but did not exhibit statistically significant differences in males.

Time to Ambulation for interventional patients getting the 7F **EXOSEAL VCD** showed statistically significant differences for females, but did not exhibit statistically significant differences in males.

These analyses are limited by small sample sizes and the results appear to be driven largely by single patient data results which appear to be outliers. In addition, when comparing the treatment effect of **EXOSEAL VCD** to manual compression for all females to the results of all males, the results show that females and males had observed Time to Hemostasis and Time to Ambulation that showed statistically significant differences (see Tables 13 and 14 below).

Table 13. Principal Effectiveness and Safety Results - All Male Patients (ITT) Treated

Primary Effective Endpoints	6F ECLIPSE Trial			Pooled 7F VCD Data Compared to 6F MC Data	
	VCD (n=182 patients)	MC (n=83 patients)	P-Values[a]	Pooled 7F VCD (n=63 patients)	P-values[b]
Time to Hemostasis (min)					
Mean ± STD (N)	4.60±13.53(182)	22.69±28.08(81)	<0.0001	3.40 ±4.70 (63)	<0.0001
Median, Range (Min, Max)	2.00(2.00,175.00)	20.00(3.00,220.00)		2.00(2.00,35.00)	
Time to Ambulation (hr)					
Mean ± STD (N)	2.42±3.09(179)	6.96±16.64(81)	0.0170	2.90 ±5.74 (63)	0.0433
Median, Range (Min, Max)	1.25(0.88,22.30)	4.41(1.33,152.24)		1.08(0.98,24.32)	

Description of Event (Event Based)	6F ECLIPSE Trial					Pooled 7F VCD Data Compared to 6F MC Data			
	VCD (n=182 patients)	MC (n=83 patients)	Difference VCD-MC[1]	Upper Bound[2]	P-Values[3]	Pooled 7F VCD (n=63 patients)	Difference VCD-MC[4]	Upper Bound[5]	P-values[6]
Major Adverse Events (Combined Event Rate) at 30-days	0/182(0.00%)	0/83(0.00%)	0.00%	1.76%	0.0038	0/63(0.00%)	0.00%	4.64%	0.0764
Vascular Repair	0/182(0.00%)	0/83(0.00%)	0.00%	1.76%	0.0038	0/63(0.00%)	0.00%	4.64%	0.0764
Access site-related bleeding requiring transfusion	0/182(0.00%)	0/83(0.00%)	0.00%	1.76%	0.0038	0/63(0.00%)	0.00%	4.64%	0.0764
Access site-related infection requiring treatment	0/182(0.00%)	0/83(0.00%)	0.00%	1.76%	0.0038	0/63(0.00%)	0.00%	4.64%	0.0764
Any new documented ipsilateral lower extremity ischemia	0/182(0.00%)	0/83(0.00%)	0.00%	1.76%	0.0038	0/63(0.00%)	0.00%	4.64%	0.0764
Surgery for access site-related nerve injury	0/182(0.00%)	0/83(0.00%)	0.00%	1.76%	0.0038	0/63(0.00%)	0.00%	4.64%	0.0764
Permanent(>30 days) access site-related nerve injury	0/182(0.00%)	0/83(0.00%)	0.00%	1.76%	0.0038	0/63(0.00%)	0.00%	4.64%	0.0764
Secondary Adverse Events (Combined Event Rate) at 30-days	20/182(10.99%)	3/83(3.61%)	7.37%	12.53%	-	2/63(3.17%)	-0.44%	5.95%	-
Rebleeding Following Initial Hemostasis	10/182(5.49%)	0/83(0.00%)	5.49%	9.14%	-	0/63(0.00%)	0.00%	4.64%	-
Pseudoaneurysm not Requiring Treatment	0/182(0.00%)	0/83(0.00%)	0.00%	1.76%	-	0/63(0.00%)	0.00%	4.64%	-
Treated Pseudoaneurysm	0/182(0.00%)	0/83(0.00%)	0.00%	1.76%	-	0/63(0.00%)	0.00%	4.64%	-
Documented Arteriovenous Fistula	0/182(0.00%)	0/83(0.00%)	0.00%	1.76%	-	0/63(0.00%)	0.00%	4.64%	-
Access Site Hematoma >= 6cm	6/182(3.30%)	1/83(1.20%)	2.09%	5.38%	-	2/63(3.17%)	1.97%	8.12%	-
Access Site-Related Bleeding Requiring > 30 min for Hemostasis	1/182(0.55%)	1/83(1.20%)	-0.66%	1.72%	-	0/63(0.00%)	-1.20%	3.08%	-
Post-Hospital Discharge Access Site-Related Bleeding	0/182(0.00%)	0/83(0.00%)	0.00%	1.76%	-	0/63(0.00%)	0.00%	4.64%	-
Ipsilateral Lower Extremity Arterial Emboli	0/182(0.00%)	0/83(0.00%)	0.00%	1.76%	-	0/63(0.00%)	0.00%	4.64%	-
Transient Loss of Ipsilateral Lower Extremity Pulse	0/182(0.00%)	0/83(0.00%)	0.00%	1.76%	-	0/63(0.00%)	0.00%	4.64%	-
Ipsilateral Deep Vein Thrombosis	0/182(0.00%)	0/83(0.00%)	0.00%	1.76%	-	0/63(0.00%)	0.00%	4.64%	-
Access Site-Related Vessel Laceration	0/182(0.00%)	0/83(0.00%)	0.00%	1.76%	-	0/63(0.00%)	0.00%	4.64%	-
Transient Access Site-Related Nerve Injury	1/182(0.55%)	0/83(0.00%)	0.55%	2.59%	-	0/63(0.00%)	0.00%	4.64%	-
Access Site Wound Dehiscence	0/182(0.00%)	0/83(0.00%)	0.00%	1.76%	-	0/63(0.00%)	0.00%	4.64%	-
Treated, Localized Access Site Infection	0/182(0.00%)	0/83(0.00%)	0.00%	1.76%	-	0/63(0.00%)	0.00%	4.64%	-
Retroperitoneal Bleeding	2/182(1.10%)	0/83(0.00%)	1.10%	3.43%	-	0/63(0.00%)	0.00%	4.64%	-
Ipsilateral Peripheral Artery Total Occlusion	0/182(0.00%)	0/83(0.00%)	0.00%	1.76%	-	0/63(0.00%)	0.00%	4.64%	-
Ecchymosis >= 6cm	0/182(0.00%)	1/83(1.20%)	-1.20%	0.58%	-	0/63(0.00%)	-1.20%	3.08%	-
Intraluminal Plug Delivery Not Requiring Surgical Intervention	0/182(0.00%)	0/83(0.00%)	0.00%	1.76%	-	0/63(0.00%)	0.00%	4.64%	-
Decrease in Pedal Pulse	0/182(0.00%)	0/83(0.00%)	0.00%	1.76%	-	0/63(0.00%)	0.00%	4.64%	-
Death	0/182(0.00%)	0/83(0.00%)	0.00%	1.76%	-	0/63(0.00%)	0.00%	4.64%	-

Numbers are % (counts/sample size) or Mean ± STD (Sample Size). Numbers of patients for the summary of continuous measures are based on number of non-missing values.

[a] P-values were calculated using unpaired t-test of inequality in mean differences of the continuous outcomes between 6F VCD and 6F MC group

[b] P-values were calculated using unpaired t-test of inequality in mean differences of the continuous outcomes between pooled 7F VCD and 6F MC group

[1] Proportion differences between 6F VCD group and 6F MC group ($P_{VCD} - P_{MC}$)

[2] One-sided upper bound of 95% Confidence Intervals (CI) of the difference of two binomial proportions: between 6F VCD group and 6F MC group ($P_{VCD} - P_{MC}$). The calculation was performed using unconditional exact method

[3] P-values were calculated using unconditional exact test of non-inferiority using difference of two binomial proportions (6F VCD group vs. 6F MC group) with the pre-specified margin of 4.0%. The calculation was performed using StatXact.

[4] Proportion differences between pooled 7F VCD group and 6F MC group ($P_{VCD} - P_{MC}$)

[5] One-sided upper bound of 95% Confidence Intervals (CI) of the difference of two binomial proportions: between pooled 7F VCD group and 6F MC group ($P_{VCD} - P_{MC}$). The calculation was performed using unconditional exact method

[6] P-values were calculated using unconditional exact test of non-inferiority using difference of two binomial proportions (7F VCD group vs. 6F MC group) with the pre-specified margin of 4.0%. The calculation was performed using StatXact.

Table 14. Principal Effectiveness and Safety Results - All Female Patients (ITT) Treated

Primary Effective Endpoints	6F ECLIPSE Trial			Pooled 7F VCD Data Compared to 6F MC Data	
	VCD (n=85 patients)	MC (n=51 patients)	P-Values[a]	Pooled 7F VCD (n=25 patients)	P-values[b]
Time to Hemostasis (min)					
Mean ± STD (N)	3.89±5.55(85)	15.78±5.45(50)	<0.0001	2.88 ±2.89 (25)	<0.0001
Median, Range (Min, Max)	2.00(2.00,30.00)	15.00(5.00,30.00)		2.00(2.00,15.00)	
Time to Ambulation (hr)					
Mean ± STD (N)	2.79±7.66(85)	5.02±3.31(48)	0.0216	1.98 ±4.58 (25)	0.0018
Median, Range (Min, Max)	1.17(0.99,69.09)	4.17(2.28,24.29)		1.05(0.01,23.94)	

Description of Event (Event Based)	6F ECLIPSE Trial					Pooled 7F VCD Data Compared to 6F MC Data			
	VCD (n=85 patients)	MC (n=51 patients)	Difference VCD-MC[1]	Upper Bound[2]	P-Values[3]	Pooled 7F VCD (n=25 patients)	Difference VCD-MC[4]	Upper Bound[5]	P-values[6]
Major Adverse Events (Combined Event Rate) at 30-days	0/85 (0.00%)	0/51 (0.00%)	0.00%	3.46%	0.0318	0/25 (0.00%)	0.00%	11.29%	0.3604
Vascular Repair	0/85 (0.00%)	0/51 (0.00%)	0.00%	3.46%	0.0318	0/25 (0.00%)	0.00%	11.29%	0.3604
Access site-related bleeding requiring transfusion	0/85 (0.00%)	0/51 (0.00%)	0.00%	3.46%	0.0318	0/25 (0.00%)	0.00%	11.29%	0.3604
Access site-related infection requiring treatment	0/85 (0.00%)	0/51 (0.00%)	0.00%	3.46%	0.0318	0/25 (0.00%)	0.00%	11.29%	0.3604
Any new documented ipsilateral lower extremity ischemia	0/85 (0.00%)	0/51 (0.00%)	0.00%	3.46%	0.0318	0/25 (0.00%)	0.00%	11.29%	0.3604
Surgery for access site-related nerve injury	0/85 (0.00%)	0/51 (0.00%)	0.00%	3.46%	0.0318	0/25 (0.00%)	0.00%	11.29%	0.3604
Permanent(>30 days) access site-related nerve injury	0/85 (0.00%)	0/51 (0.00%)	0.00%	3.46%	0.0318	0/25 (0.00%)	0.00%	11.29%	0.3604
Secondary Adverse Events (Combined Event Rate) at 30-days	4/85(4.71%)	3/51(5.88%)	-1.18%	5.97%	-	1/25(4.00%)	-1.88%	11.29%	-
Rebleeding Following Initial Hemostasis	4/85(4.71%)	3/51(5.88%)	-1.18%	5.97%	-	0/25(0.00%)	-5.88%	4.22%	-
Pseudoaneurysm not Requiring Treatment	0/85(0.00%)	0/51(0.00%)	0.00%	3.46%	-	0/25(0.00%)	0.00%	11.29%	-
Treated Pseudoaneurysm	0/85(0.00%)	0/51(0.00%)	0.00%	3.46%	-	0/25(0.00%)	0.00%	11.29%	-
ocumented Arteriovenous Fistula	0/85(0.00%)	0/51(0.00%)	0.00%	3.46%	-	0/25(0.00%)	0.00%	11.29%	-
Access Site Hematoma >= 6cm	0/85(0.00%)	0/51(0.00%)	0.00%	3.46%	-	1/25(4.00%)	4.00%	17.61%	-
Access Site-Related Bleeding Requiring > 30 min for Hemostasis	0/85(0.00%)	0/51(0.00%)	0.00%	3.46%	-	0/25(0.00%)	0.00%	11.29%	-
Post-Hospital Discharge Access Site-Related Bleeding	0/85(0.00%)	0/51(0.00%)	0.00%	3.46%	-	0/25(0.00%)	0.00%	11.29%	-
Ipsilateral Lower Extremity Arterial Emboli	0/85(0.00%)	0/51(0.00%)	0.00%	3.46%	-	0/25(0.00%)	0.00%	11.29%	-
Transient Loss of Ipsilateral Lower Extremity Pulse	0/85(0.00%)	0/51(0.00%)	0.00%	3.46%	-	0/25(0.00%)	0.00%	11.29%	-
Ipsilateral Deep Vein Thrombosis	0/85(0.00%)	0/51(0.00%)	0.00%	3.46%	-	0/25(0.00%)	0.00%	11.29%	-
Access Site-Related Vessel Laceration	0/85(0.00%)	0/51(0.00%)	0.00%	3.46%	-	0/25(0.00%)	0.00%	11.29%	-
Transient Access Site-Related Nerve Injury	0/85(0.00%)	0/51(0.00%)	0.00%	3.46%	-	0/25(0.00%)	0.00%	11.29%	-
Access Site Wound Dehiscence	0/85(0.00%)	0/51(0.00%)	0.00%	3.46%	-	0/25(0.00%)	0.00%	11.29%	-
Treated, Localized Access Site Infection	0/85(0.00%)	0/51(0.00%)	0.00%	3.46%	-	0/25(0.00%)	0.00%	11.29%	-
Retroperitoneal Bleeding	0/85(0.00%)	0/51(0.00%)	0.00%	3.46%	-	0/25(0.00%)	0.00%	11.29%	-
Ipsilateral Peripheral Artery Total Occlusion	0/85(0.00%)	0/51(0.00%)	0.00%	3.46%	-	0/25(0.00%)	0.00%	11.29%	-
Ecchymosis >= 6cm	0/85(0.00%)	0/51(0.00%)	0.00%	3.46%	-	0/25(0.00%)	0.00%	11.29%	-
Intraluminal Plug Delivery Not Requiring Surgical Intervention	0/85(0.00%)	0/51(0.00%)	0.00%	3.46%	-	0/25(0.00%)	0.00%	11.29%	-
Decrease in Pedal Pulse	0/85(0.00%)	0/51(0.00%)	0.00%	3.46%	-	0/25(0.00%)	0.00%	11.29%	-
Death	0/85(0.00%)	0/51(0.00%)	0.00%	3.46%	-	0/25(0.00%)	0.00%	11.29%	-

Numbers are % (counts/sample size) or Mean ± STD (Sample Size). Numbers of patients for the summary of continuous measures are based on number of non-missing values.

[a] P-values were calculated using unpaired t-test of inequality in mean differences of the continuous outcomes between 6F VCD and 6F MC group

[b] P-values were calculated using unpaired t-test of inequality in mean differences of the continuous outcomes between pooled 7F VCD and 6F MC group

[1] Proportion differences between 6F VCD group and 6F MC group ($P_{VCD} - P_{MC}$)

[2] One-sided upper bound of 95% Confidence Intervals (CI) of the difference of two binomial proportions: between 6F VCD group and 6F MC group ($P_{VCD} - P_{MC}$). The calculation was performed using unconditional exact method

[3] P-values were calculated using unconditional exact test of non-inferiority using difference of two binomial proportions (6F VCD group vs. 6F MC group) with the pre-specified margin of 4.0%. The calculation was performed using StatXact.

[4] Proportion differences between pooled 7F VCD group and 6F MC group ($P_{VCD} - P_{MC}$)

[5] One-sided upper bound of 95% Confidence Intervals (CI) of the difference of two binomial proportions: between pooled 7F VCD group and 6F MC group ($P_{VCD} - P_{MC}$). The calculation was performed using unconditional exact method

[6] P-values were calculated using unconditional exact test of non-inferiority using difference of two binomial proportions (7F VCD group vs. 6F MC group) with the pre-specified margin of 4.0%. The calculation was performed using StatXact.

Differences in the p-values exhibited between males and females in comparing the safety results are not clinically significant since no major adverse events were observed in either trial for the **EXOSEAL VCD**.

No significant treatment-by-gender interaction effect was observed in the **EXOSEAL** 6F Eclipse ITT population and pooled 7F ITT populations for the primary effectiveness endpoints of Time to Hemostasis and Time to Ambulation, in the Diagnostic ITT patient group and the Interventional ITT patient group.

Table 15. Primary Effectiveness Results: Treatment by Gender Interaction - All Patients (ITT) Treated

Primary Effective Endpoints	6F ECLIPSE Trial				Pooled 7F VCD Data Compared to 6F MC Data		
	6F VCD	6F MC	P-Values[a]	P-Values[b]	Pooled 7F VCD	P-Values[c]	P-values[d]
ITT Patients	N=267	N=134			N=88		
Time to Hemostasis (min)							
Mean ± STD (N)	4.38±11.59 (267)	20.05±22.54 (131)	<.0001	0.0817	3.25 ±4.25 (88)	<.0001	0.2209
Median, Range (Min, Max)	2.0 (2.0, 175.0)	15.0 (3.0, 220.0)			2.0 (2.0, 35.0)		
Time to Ambulation (hr)							
Mean ± STD (N)	2.54±5.02 (264)	6.24±13.34 (129)	0.0006	0.2376	2.64 ±5.43 (88)	0.0299	0.7523
Median, Range (Min, Max)	1.2 (0.9, 69.1)	4.3 (1.3, 152.2)			1.1 (0.01, 24.3)		
Diagnostic ITT Patients	N=134	N=66			N=43		
Time to Hemostasis (min)							
Mean ± STD (N)	3.34±4.86 (134)	14.80±5.85 (65)	<.0001	0.8598	2.86 ±2.77 (43)	<.0001	0.6588
Median, Range (Min, Max)	2.0 (2.0, 34.0)	15.0 (3.0, 30.0)			2.0 (2.0, 15.0)		
Time to Ambulation (hr)							
Mean ± STD (N)	1.59±1.22 (133)	6.63±18.40 (66)	0.0025	0.3119	2.15 ±4.90 (43)	0.1521	0.5171
Median, Range (Min, Max)	1.1 (0.9, 8.4)	4.1 (1.3, 152.2)			1.1, (0.01, 24.2)		
Interventional ITT Patients	N=133	N=68			N=45		
Time to Hemostasis (min)							
Mean ± STD (N)	5.43±15.64 (133)	25.23±30.45 (66)	<.0001	0.1814	3.62 ±5.31 (45)	0.0003	0.3986
Median, Range (Min, Max)	2.0 (2.0, 175.0)	20.0 (10.0, 220.0)			2.0 (2.0, 35.0)		
Time to Ambulation (hr)							
Mean ± STD (N)	3.51±6.90 (131)	5.83±3.52(63)	0.0888	0.2833	3.11 ±5.90 (45)	0.0029	0.4200
Median, Range (Min, Max)	2.0 (0.9, 69.1)	4.8 (2.8, 21.8)			1.1, (1.0, 24.3)		

Numbers are Mean ± STD (Sample Size). Numbers of patients for the summary of continuous measures are based on number of non-missing values.

(c) P-values for the difference between 6F VCD vs. 6F MC were based on two way Analysis of Variance with treatment (6F VCD vs. 6F MC), gender, and treatment by gender interaction as covariates.

(d) P-values for treatment by gender interaction were based on two way Analysis of Variance with treatment (6F VCD vs. 6F MC), gender, and treatment by gender interaction as covariates.

(e) P-values for the difference between 7F VCD vs. 6F MC were based on two way Analysis of Variance with treatment (7F VCD vs. 6F MC), gender, and treatment by gender interaction as covariates.

(f) P-values for treatment by gender interaction were based on two way Analysis of Variance with treatment (7F VCD vs. 6F MC), gender, and treatment by gender interaction as covariates.

Treatment-by-gender interaction could not be calculated for primary safety endpoint since there were zero (0) Major Adverse Events in either study.

Considering the small sample size and the lack of observed interaction effect for the primary effectiveness endpoint, there does not appear to be a clinically significant treatment-by-gender interaction in the **EXOSEAL** 6F Eclipse trial and Mexican and German 7F trials. This suggests that the overall conclusions of this trial regarding both safety and effectiveness of the **EXOSEAL VCD** can be generalized for males and females.

X. Evaluation of 5F EXOSEAL Vascular Closure Device (VCD)

The use of the **EXOSEAL VCD** with a standard 5F sheath introducer was evaluated with an engineering analysis that compared the design of the 5F **EXOSEAL VCD** to the design of the 6F **EXOSEAL VCD** which was evaluated clinically. This engineering analysis demonstrates that the design of the 5F **EXOSEAL VCD** is equivalent to the design of the 6F **EXOSEAL VCD.**

XI. Evaluation of EXOSEAL VCD Compatibility with 12 cm Sheath Introducer

The **EXOSEAL VCD** was used with an 11 cm vascular sheath introducer length in the 6F ECLIPSE Trial and the 7F German and Mexican studies. However, the **EXOSEAL VCD** was designed to be used with a 12 cm sheath introducer length. The maximum compatible length was increased to make a wider range of sheath introducers available for use with the **EXOSEAL VCD**.

Testing of the **EXOSEAL VCD** with the 12 cm length sheath introducer included both bench testing (sheath introducer compatibility and Design Verification testing) as well as simulated use testing in an animal model. Based on this testing it was determined that the **EXOSEAL VCD** is equally compatible with a 12 cm sheath introducer length as with an 11 cm sheath introducer length.

XII. Conclusions

The results of the 6F ECLIPSE Trial and the 7F German and Mexican studies demonstrate that patients who have undergone cardiac or peripheral diagnostic or interventional procedures utilizing a 6F or 7F vascular sheath introducer and who have received the **EXOSEAL VCD** have statistically and clinically significant decreased times to hemostasis and ambulation while maintaining the safety profile when compared to that for patients treated with manual compression. The engineering analysis comparing the 5F **EXOSEAL VCD** design to the 6F **EXOSEAL VCD** demonstrates that the 5F **EXOSEAL VCD** design is equivalent to the 6F **EXOSEAL VCD** design. The data generated and reported in these clinical and engineering evaluations demonstrate the increased patient benefits without increased patient risk for closure of femoral artery access sites with the **EXOSEAL VCD**.

XIII. Examination and Selection of Products

1. Select the size **EXOSEAL VCD** corresponding to the vascular sheath introducer French size in use.
2. After carefully inspecting the packaging for damage to the sterile barrier, remove the device from the package.
3. **WARNING:** FOR SINGLE USE ONLY. Do not resterilize or reuse. Reuse, reprocessing, or resterilization may compromise the structural integrity of the device and/or lead to device failure, which in turn, may result in patient injury, illness, or death. Use aseptic technique when handling the product.
4. Exercise care when using additional surgical instruments such as forceps or needle holders during device handling, to reduce the possibility of accidental device breakage.

XIV. Sheath Introducers Compatible with EXOSEAL Vascular Closure Device (VCD)

Appropriate training is required prior to use. Read the instructions packaged with the vascular sheath introducer carefully. USE ONLY WITH A STANDARD SHEATH INTRODUCER with up to a 12 cm working length. Cordis test results have shown that the sheath introducers in **Table 16** are compatible with the **EXOSEAL VCD** and those listed in **Table 17** are incompatible. Cordis has not tested the **EXOSEAL VCD** with other sheath introducers and use with sheath introducers not listed in Table 16 may result in malfunctioning of the **EXOSEAL VCD**.

Table 16

MANUFACTURER	DESCRIPTION
Cordis®	AVANTI® + Sheath Introducer 11 cm AVANTI® + Sheath Introducer MS 11 cm
Medtronic	InPut® Introducer Sheaths 11 cm
Merit Medical™	Prelude® Sheath Introducers 11 cm
St. Jude Medical™	Maximum™ Hemostasis Introducers 12 cm ULTIMUM™ Introducers 12cm
Terumo®	PINNACLE® Introducer Sheaths 10 cm

Table 16. List of compatible sheath introducers when used with corresponding French size-specific VCD. The third-party trademarks used herein are trademarks of their respective owners.
Note: Testing conducted on sheath introducers available as of March 2009.

Table 17

MANUFACTURER	DESCRIPTION
Boston Scientific	SUPER Sheath™
Cook®	CHECK FLO® PERFORMER®

Table 17. List of incompatible sheath introducers. The third-party trademarks used herein are trademarks of their respective owners.
Note: Testing conducted on sheath introducers available as of March 2009.

The safety and effectiveness of the **EXOSEAL VCD** used with a reinforced sheath introducer that may have a larger outer diameter than that of a standard sheath introducer has not been assessed.

XV. Closure Procedure

Note: The following instructions provide technical direction but do not obviate the necessity of formal training in the use of the **EXOSEAL Vascular Closure Device.** The techniques and procedures described below are not intended as a substitute for operator

experience and judgment in treating any specific patients. The specific technique used to place the **EXOSEAL VCD** may be slightly altered to provide the physician with flexibility during the closure procedure.

1. After completion of the catheterization, remove all catheters, instrumentation, wires, and other devices from the vascular sheath introducer. Using fluoroscopy, verify the femoral artery's suitability for arteriotomy closure with the **EXOSEAL VCD**, including the insertion angle (30 – 45°) of the vascular sheath introducer.
2. Select the corresponding French size VCD based on the existing sheath introducer French size. Remove the **EXOSEAL VCD** from the sterile packaging using aseptic technique. Hold the **EXOSEAL VCD** in the right hand and position the left hand on the patient at the insertion site holding the vascular sheath introducer hub. Using the left hand's thumb and index finger insert the distal end of the Delivery Shaft into the vascular sheath introducer hub using the right hand to support and guiding the **EXOSEAL VCD**.
   Caution: The **EXOSEAL VCD** is designed for use with a standard corresponding French size vascular sheath introducer with up to 12 cm working length. The indwelling sheath introducer must allow the Bleed-Back Port to extend beyond the distal tip of the sheath introducer. The French size of the **EXOSEAL VCD** must correspond to the French size of the sheath introducer in use. Do not use the **EXOSEAL VCD** in a sheath with a working length greater than 12 cm.
3. Orient the **EXOSEAL VCD** such that the Indicator Window on the Handle Assembly is facing upwards. Advance the Delivery Shaft into the proximal end of the vascular sheath introducer to the Marker Band, keeping the **EXOSEAL VCD** oriented upwards and advancing at the angle of the tissue tract (30 – 45°).
   Caution: If resistance is felt during Delivery Shaft insertion, do not apply excess force; instead, retract the Delivery Shaft slightly, rotate the vascular sheath introducer 180°, and try to readvance the Delivery Shaft. If resistance is still present, discontinue the use of the **EXOSEAL VCD**.
4. Without advancing the **EXOSEAL VCD**, use the left hand to retract the vascular sheath introducer proximally towards the Handle Assembly.
5. While still holding the **EXOSEAL VCD** stationary, use the left hand to continue retracting the vascular sheath introducer proximally. Once the hub of the sheath introducer engages with the Indicator Wire Cowling, retract them together using one fluid motion until they lock into position against the Handle Assembly and an audible "click" signifies proper connection. The Indicator Wire will automatically deploy at this point.
   Caution: Do not reinsert the **EXOSEAL VCD** into the vascular sheath introducer if it is removed prior to locking into position.
   Caution: If for any reason it is desired to abort the procedure once the **EXOSEAL VCD** has been introduced into the bloodstream, remove the **EXOSEAL VCD** and the vascular sheath introducer as a unit. Do not attempt to withdraw the **EXOSEAL VCD** from the sheath introducer, as Plug dislodgement may occur.
6. Observe pulsatile flow from the Bleed-Back Indicator. Using the left hand, slowly retract the **EXOSEAL VCD** and vascular sheath introducer at the angle of the tissue tract (30 – 45°) until pulsatile flow has significantly slowed or stopped from the Bleed-Back Indicator.

Caution: Pulsatile flow is necessary for proper **EXOSEAL VCD** positioning. If pulsatile flow is not observed from the Bleed-Back Indicator, discontinue the procedure.

7. While holding the **EXOSEAL VCD** in the right hand, making sure the thumb is not placed on the Plug Deployment Button, continue retracting the **EXOSEAL VCD** and vascular sheath introducer very slowly (controlling retraction with the left hand) until the graphic pattern in the Indicator Window changes to a solid black color, at which point the Plug is correctly positioned for deployment.
   Caution: The **EXOSEAL VCD** sheath adapter should remain together with the vascular sheath introducer hub during retraction and for the remaining procedural steps. If separation is observed, remove the **EXOSEAL VCD** and the sheath introducer as a unit. Do not attempt to reconnect the **EXOSEAL VCD** with the sheath introducer hub. Withdraw the **EXOSEAL VCD** and sheath introducer simultaneously, as Plug dislodgement may occur.
   Caution: If the graphic pattern in the Indicator Window does not change to a solid black color after approximately 1 cm of retraction from the point at which pulsatile flow significantly slowed or stopped, discontinue the use of the **EXOSEAL VCD**.
   Caution: Further retraction of the **EXOSEAL VCD** and the vascular sheath introducer will cause a set of red and white bars to appear in the Indicator Window, as a warning that no further retraction should occur prior to Plug deployment. If further retraction occurs, discontinue the use of the **EXOSEAL VCD**.
8. Use the left hand to anchor the vascular sheath introducer and the **EXOSEAL VCD** in a stationary position. Press the Deployment Button to deploy the Plug, ensuring that the Deployment Button is fully depressed and flush against the Handle Assembly. The Indicator Wire will automatically withdraw and the Plug will be deployed.
   Caution: Care should be taken to ensure that no further pullback of the **EXOSEAL VCD** and vascular sheath introducer occurs prior to, or during, deployment of the Plug.
9. Approximately 1 – 2 seconds after depressing the Deployment Button retract the **EXOSEAL VCD** and vascular sheath introducer as a unit until the system is fully removed from the patient and apply light, non-occlusive pressure to the wound site.
   Note: A small amount of non-pulsatile blood flow may appear from the Bleed-Back Indicator until the **EXOSEAL VCD** and vascular sheath introducer are removed from the tissue tract.
10. Wipe the entry site and evaluate for hemostasis.
11. If hemostasis has not occurred, continue applying light manual pressure to achieve hemostasis.

XVI. Post-Procedure Patient Management

1. Observe that the puncture site is dry when light, non-occlusive pressure is released.
2. Apply an appropriate sterile dressing to the puncture site.
3. Assess the insertion site, as per hospital protocol.
4. Ensure that the site remains clean and dry.

Reabsorption

The Plug exhibits partial to advanced absorption at 30 days, with complete absorption between 60 and 90 days post-implant.

Pre-Discharge Patient Information

1. Patients should be informed that a reabsorbable Plug has been used to close the access site.
2. Patients should be told to expect soreness or tenderness during the first week, as well as light drainage. Bruising may last up to two weeks.
3. Physicians should be alerted to the following:
   - Excessive bleeding
   - Swelling of the groin or leg
   - Pain in the groin or leg
   - Any sign of infection (redness, swelling, drainage, warmth, fever, chills, or non-healing of wound)
4. Patients should be provided with an "Instructions & Care Information" card to be carried for at least 60 days following implantation of the **EXOSEAL VCD.** This card should be presented to the healthcare practitioner upon re-hospitalization within the 60-day time frame.
5. Activity limits and specific wound care instructions should be provided by the physician. Normal activity, including driving, can usually be resumed within two days. It is recommended that no lifting of objects greater than 10 lbs in weight is done for one week or until the wound has healed.

XVII. How Supplied

The **EXOSEAL VCD** is provided sterile and non-pyrogenic. The product is sterilized with electron beam radiation.

XVIII. Storage and Disposal

The **EXOSEAL VCD** should be stored in a cool, dark, and dry location.

Dispose of the contaminated device and/or packaging materials using standard hospital procedures and universally accepted practices for bio-hazardous wastes.

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