SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

Device Generic Name: Vascular Closure Device

Device Trade Name: EXOSEAL™ Vascular Closure Device

Applicant: Cordis Corporation
430 Route 22 East
Bridgewater, NJ 08807-0908

Date of Panel Recommendation: None

Premarket Approval Application (PMA) Number: P100013

Date of FDA Notice of Approval: May 19, 2011

Expedited: Not applicable

II. INDICATIONS FOR USE

The **EXOSEAL Vascular Closure Device (VCD)** 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 VCD** 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.

III. CONTRAINDICATIONS

None

IV. WARNINGS AND PRECAUTIONS

The Warnings and Precautions can be found in the Cordis **EXOSEAL VCD** Instructions for Use.

V. DEVICE DESCRIPTION

A. Materials and Configuration

The **EXOSEAL 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. (NOTE: The French size of the **EXOSEAL VCD** must correspond to the French size of the vascular sheath introducer in use: 5F, 6F or 7F).

B. Principles of Operation for the EXOSEAL VCD System:

The Delivery shaft is inserted into the existing sheath introducer and locked into position. A Bleed-Back Indicator provides visual feedback to the user that the device is correctly positioned within the vessel. A nitinol indicator wire connected to an indicator window provides feedback to the user as to the position of the Polyglycolic Acid (PGA) Plug relative to the vessel wall. When the Plug is in the correct position the Plug Deployment Button is depressed to sequentially retract the indicator wire and delivery shaft, deploying the plug extravascularly to the arteriotomy site. Light compression is applied to promote hemostasis. The PGA Plug is fully resorbed into the body within 60-90 days of implantation.

VI. ALTERNATIVE PRACTICES AND PROCEDURES

Alternative practices and procedures for attaining hemostasis at the femoral artery puncture site post-catheterization include mechanical compression, manual compression, percutaneous delivery of sutures at the femoral access site, collagen-based hemostasis devices and staples. Pressure dressings and sandbags are routinely used in combination with compression methods to control oozing.

VII. MARKETING HISTORY

The **EXOSEAL VCD** has been approved for sale in the following countries. The **EXOSEAL VCD** has not been withdrawn from marketing for any reason related to its safety or effectiveness.

- Armenia
- Australia
- Azerbaijan
- Bangladesh
- Bahrain
- Bosnia and Herzegovina
- Chile
- Colombia
- Dominican Republic
- El Salvador
- European Union
- Ghana
- Guatemala
- Honduras
- Iran
- Israel
- Jamaica
- Jordan
- Kenya
- Kuwait
- Lebanon
- Libya
- Macedonia
- Madagascar
- Malaysia
- Mauritius
- Mongolia
- Mozambique
- New Zealand
- Nicaragua
- Nigeria
- Oman
- Pakistan
- Palestine
- Panama
- Paraguay
- Qatar
- Saudi Arabia
- Serbia and Montenegro
- Singapore
- South Africa
- Sudan
- Syria
- Tanzania
- Trinidad and Tobago
- Turkey
- Turkmenistan
- United Arab Emirates
- Yemen

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

Below is a list of the potential adverse effects (e.g., complications) associated with the use of the device.

- Vascular injury requiring repair
- Access site-related bleeding requiring transfusion
- Access site-related infection
- New lower extremity ischemia
- Access site-related nerve injury requiring surgical repair
- Retroperitoneal Bleed
- Permanent access site-related nerve injury
- Death
- Rebleeding following initial hemostasis requiring intervention
- Pseudoaneurysm
- Arteriovenous fistula
- Access site hematoma
- Prolonged access site-related bleeding
- Lower extremity arterial emboli
- Transient loss of lower extremity pulse
- Deep vein thrombosis
- Access site-related vessel laceration
- Transient access site-related nerve injury
- Access site wound dehiscence
- Ecchymosis
- Vasovagal response
- Peripheral artery total occlusion

For the specific adverse events that occurred in the clinical studies, please see Section X below.

IX. SUMMARY OF PRECLINICAL STUDIES

A. Laboratory Studies

Engineering & Shelf Life

Testing of the functionality of the device as well as its packaging has confirmed the device is protected during customary shipping, storage and handling throughout shelf-life. The data submitted support the claimed 1-year shelf-life.

Functional Testing is summarized in Table 1.

Table 1. EXOSEAL VCD Functional Testing

Table 1 Functional Testing Summary				
Test	Acceptance Criteria	Results (t =0 / t = 1 year)		
		5F	6F	7F
Delivery System with Plug Testing				
Marker Band Visibility Test	Visible on the Delivery Shaft	Pass / Pass	Pass / Pass	Pass /Pass
Sheath Insertion Test	< 2.5 lb_f	Not Required	Pass / Pass	Pass /Pass
Introducer Hub Engagement Test	≤ 15 lb_f	Not Required	Pass / Pass	Not Required
Introducer Hub Disengagement Test	≥ 1.55 lb_f.	Not Required	Pass / Pass	Not Required
Deployed Plug Length	≤ 9 mm	Pass / Pass	Pass / Pass	Pass /Pass
Plug Placement Test	Plug shall be placed 0-2 mm proximal to the intima wall	Pass / Pass	Pass / Pass	Pass /Pass
Plunger Shaft to Plunger Disk Bond Test	≥ 1 lb_f	Pass / Pass	Pass / Pass	Not Required
Indicator Wire Lumen to PI Collar Pull Test	≥ 1.8 lbf	Not Required	Pass / Pass	Not Required
Plug Deployment Force Test	< 2.7 lb_f	Pass / Pass	Pass / Pass	Pass /Pass
Indicator Wire to Indicator Wire End Pull Test	≥ 0.50 lb_f	Not Required	Pass / Pass	Not Required
Delivery Shaft to PI Collar Assembly Pull Test	≥ 3.0 lb_f	Pass / Pass	Pass / Pass	Pass /Pass
Indicator to Indicator Tube Bond Test	≥ 0.50 lb_f	Not Required	Pass / Pass	Not Required
Lens to Left Case Pull Test	≥ 2 lb_f.	Pass / Pass	Pass / Pass	Pass /Pass
Handle Integrity Test	Handle must remain intact	Pass / Pass	Pass / Pass	Pass /Pass
Indicator Wire Lumen Protrusion Test	≤ 0.030"	Pass / Pass	Pass / Pass	Pass /Pass
Marker Band Location Test	≤ 5.06"	Pass / Pass	Pass / Pass	Pass / Pass
Delivery Shaft Over / Under Travel Test	-0.020" ≤ Travel ≤ 0.040"	Pass / Pass	Pass / Pass	Pass /Pass
Deployment Profile Force Test	≤ 18.0 lb_f.	Pass / Pass	Pass / Pass	Pass /Pass
Trigger Lockout Force Test	> 18.0 lb_f	Not Required	Pass / Pass	Not Required
Feedback System Testing				
Indicator Wire Deployment Test	Full deployment of indicator wire.	Pass / Pass	Pass / Pass	Pass / Pass
Bleed Back Reduction Test	Bleed-back signal visibly reduced	Pass / Pass	Pass / Pass	Pass /Pass
Indicator Wire Spring Force Test	≥ 0.016 lb_f to ≤ 0.070 lb_f	Not Required	Pass / Pass	Not Required
Particulates and Chemical Compatibility				
Particulate Count	• ≤ 3000 particles ≥ 10μm • ≤ 300 particles ≥ 25μm	Pass / Pass	Pass/Pass	Pass / Pass

Table 1 Functional Testing Summary				
Test	Acceptance Criteria	Results (t =0 / t = 1 year)		
		5F	6F	7F
	• ≤ 1 particle between 250µm and 650µm • no particles > 650µm.			
Chemical Compatibility Test	No degradation after exposure to following solutions: • Saline Solution (0.9%) • Contrast Medium • 50 / 50 Contrast - Saline Solution	Pass/NA	Pass/NA	Pass/NA
Packaging Testing				
Primary Package Seal Strength Test	≥ 3.5 lb_f/in.	Not Required	Pass / Pass	Not Required
Primary Package Pressurized Integrity Test	No evidence of pinholes or leaks	Not Required	Pass / Pass	Not Required
Visual Packaging Integrity Test	Visual integrity of packaging	Not Required	Pass / Pass	Not Required
Hang Hook Test	Visual/Hang Hook Adherence	Not Required	Pass / Pass	Not Required
Picture IFU Securing Feature Test	Visual placement	Not Required	Pass / Pass	Not Required
Shipper Label Adhesion / Label Integrity Test	Visual adhesion/label integrity	Not Required	Pass / Pass	Not Required
Inner Pouch and Outer Carton Label Adhesion / Label Legibility Test	Visual adhesion/label integrity	Not Required	Pass / Pass	Not Required
Device and Desiccant Holding Feature Test	Visual securement	Not Required	Pass / Pass	Not Required
Desiccant Clearance Test	>1cm	Not Required	Pass / Pass	Not Required
Barcode "Peelability" Test	Barcode label peelable	Not Required	Pass / Pass	Not Required
Placement and Legibility of Ambulate sticker and Multilingual Patient Card Test	Visual location/legibility	Not Required	Pass / Pass	Not Required
Legibility of Instructions for Use (IFU) Test	IFU is Legible	Not Required	Pass / Pass	Not Required
Legibility of Picture IFU	Label is Legible	Not Required	Pass / Pass	Not Required

Sterilization

The **EXOSEAL VCD** is sterilized using Electron Beam irradiation sterilization (E-Beam). The packaging system has been demonstrated to be an appropriate sterile barrier for the device and remains intact throughout shelf-life. The sterilization process has been validated to deliver a minimum Sterility Assurance Level (SAL) of 10^{-6} for the device and its packaging.

Biocompatibility

Biocompatibility testing of the **EXOSEAL VCD** was conducted in accordance with the ISO-10993 "Biological Evaluation of Medical Devices Part I: Evaluation and Testing", to ensure that the device was biocompatible for its intended use. The components of the device were evaluated based upon patient contact (i.e., the plug- long term contact and delivery device identified patient contact elements-transient contact). As seen in Table 2 below, samples passed all testing and results concluded that the **EXOSEAL VCD** is non-toxic, non-sensitizing, non-irritant, non-mutagenic, non-pyrogenic and non-hemolytic.

A complete list of biocompatibility tests completed for the **EXOSEAL VCD** is included in the following table.

Table 2. EXOSEAL VCD Biocompatibility Summary

Table 2 EXOSEAL VCD Biocompatibility Summary		
Biocompatibility Test	**Standard Method**	**Result / Specification**
Cytotoxicity	ISO 10993-5	Pass / Non-toxic
Maximization Sensitization	ISO 10993-10	Pass / Non-Sensitizing
Intracutaneous Irritation Reactivity	ISO 10993-10	Pass / Non-irritating
Acute Systemic Toxicity	ISO 10993-11	Pass / No evidence of systemic toxicity
Bacterial Mutagenicity – Ames	ISO 10993-3	Pass / Non-mutagenic
In-Vitro Chromosome Aberration	ISO 10993-3	Pass / Non-clastogenic
In Vitro Mouse Lymphome	ISO 10993-3	Pass / Non-mutagenic
Hemolysis	ISO 10993-4	Pass / Non-hemolytic
Material Mediated Pyrogenicity	ISO 10993-11	Pass / Non-pyrogenic
Partial Thomboplastin Time	ISO 10993-4	Pass / Non-Activator of the intrinsic coagulation pathway.
Platelet and Leukocyte Count	ISO 10993-4	Pass / No significant difference in the platelet and leukocyte counts.
Physicochemical Test	USP <661> & EP section 3.2.6	Pass / Met the acceptance criteria for the USP & EP.
Complement Activation (C3a & SC5b-9Assay)	ISO 10993-4	Pass / Non-activating
In vivo Thrombogenicity	ISO 10993-4	Pass / Non-thrombogenic

*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**.

*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.

B. Animal Studies

A series of acute and chronic animal studies were performed to characterize the safety and effectiveness of the **EXOSEAL VCD.** The porcine model has previously been identified as an appropriate cardiovascular surrogate for the human subject, as such it was the primary model (rat and rabbit models were also used). Studies were conducted to evaluate the functionality of the delivery device as well as the vascular and physiologic responses to the PGA plug. The data demonstrate:

- The PGA plug is well tolerated and is fully resorbed by the body within 90 days.
- Compatibility with the Introducer Sheaths identified in the Instructions For Use.

X. SUMMARY OF PIVOTAL CLINICAL STUDY

The applicant performed a clinical study *to establish a reasonable assurance of safety and effectiveness of arterial closure with the* **EXOSEAL VCD** intended for closure of the femoral artery following arterial access in the US under IDE G050160. Data from this clinical study were the basis for the PMA approval decision. A summary of the clinical study is presented below.

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 $\geq$ 5 mm. The primary protocol exclusions were: acute ST-elevation myocardial infarction $\leq$ 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 $\leq$ 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 $\leq$ 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 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 $\pm$ 11.13 years, and in the MC group the mean age was 61.4 $\pm$ 10.47 years. BMI in the 6F **EXOSEAL VCD** group averaged 28.9 $\pm$ 4.99 kg/m^2 and in the MC group averaged 29.5 $\pm$ 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 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 $\pm$ 7 days following the catheterization procedure. The secondary safety endpoint was the combined rate of secondary complications within 30 $\pm$ 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.

Key Inclusion Criteria for Clinical Studies

1. Patient is between 18 and 85 years of age, inclusive;
2. Patient/guardian provides written informed consent;
3. Patient is scheduled for a coronary or peripheral diagnostic or interventional procedure;
4. Patient is able to undergo emergent vascular surgery if a complication related to the VCD necessitates such surgery;
5. Patient has a 6F arterial puncture located in the common femoral artery;
6. Target vessel has a lumen diameter $\geq$ 5 mm; and
7. Patient is willing and able to complete follow-up.

Key Exclusion Criteria for Clinical Studies

1. Acute ST-elevation myocardial infarction $\leq$ 48 hours prior to the cardiac or peripheral catheterization procedure;
2. Uncontrolled hypertension at time of closure (BP $\geq$ 180/110 mmHg);
3. 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;
4. Prior femoral vascular surgery or vascular graft in region of access site;
5. Pre-existing systemic or cutaneous infection;
6. Pre-existing severe non-cardiac systemic disease or pre-existing terminal illness;
7. Patient has known allergy to any materials used in the VCD;
8. Patient is known or suspected to be pregnant, or is lactating;
9. Thrombolytic therapy (e.g. streptokinase, urokinase, t-PA) $\leq$ 24 hours prior to the cardiac or peripheral catheterization procedure;
10. Angiomax (bivalirudin) or other thrombin-specific anticoagulants or low molecular weight heparin $\leq$ 24 hours prior to the cardiac or peripheral catheterization procedure;
11. BMI > 40 kg/m^2;
12. Symptomatic leg ischemia in the target vessel limb including severe claudication (< 100 feet) or weak/absent pulse;
13. Planned arterial access at the same access site $\leq$ 30 days following the femoral artery closure procedure;
14. Patient is known to require an extended hospitalization (e.g. patient is undergoing CABG surgery);
15. Arterial puncture in the femoral artery of both legs;
16. Prior target artery closure with any closure device, or closure with manual compression $\leq$ 30 days prior to the cardiac or peripheral catheterization procedure;
17. Prior or recent use of an intra-aortic balloon pump through the arterial access site;

18. Patient is ineligible for in-lab catheterization lab introducer sheath removal;
19. Evidence of a preexisting hematoma, arteriovenous fistula, or pseudoaneurysm at the access site prior to start of femoral artery closure procedure;
20. The targeted femoral artery is tortuous or requires an introducer sheath length > 11 cm;
21. Fluoroscopically visible calcium, atherosclerotic disease, or stent ≤ 1 cm of the puncture site that would interfere with the placement of the VCD's plug;
22. Targeted femoral artery diameter stenosis ≥ 50%;
23. Difficulty in obtaining vascular access resulting in multiple arterial punctures and/or posterior arterial puncture;
24. Antegrade puncture;
25. Heparinized patient with elevated pre-closure ACT level:
    Vascular Closure Device: > 250 seconds with GP IIb/IIIa inhibitor
    > 300 seconds no GP IIb/IIIa inhibitor
    Manual Compression: > 180 seconds;
26. Cardiogenic shock (hemodynamic instability requiring intravenous medications or mechanical support) experienced during or immediately post-catheterization;
27. Concurrent participation in another investigational device or drug trial;
28. Patient is unable to ambulate at baseline;
29. Patient has already participated in this trial;
30. Patient is unavailable for follow-up; and
31. Any angiographic or clinical evidence that the investigator feels would place the patient at increased risk with the use of the VCD.

The exclusion criteria for the 7F German and Mexican studies were identical to that for the 6F ECLIPSE Trial except for the following 2 exclusion criteria in the 7F studies, which varied from the corresponding exclusion criteria for the 6F ECLIPSE Trial:

- Heparinized patients with elevated pre-closure ACT level:
  > 250 seconds with GP IIb/IIIa inhibitor
  > 300 seconds no GP IIb/IIIa inhibitor;
- Symptomatic leg ischemia in the target vessel limb including severe claudication (< 50 meter) or weak/absent pulse.

The 7F German and Mexican studies also included two additional exclusion criteria not listed in the 6F ECLIPSE Trial:

32. Patient has known allergy to contrast medium; and
33. Required simultaneous ipsilateral or contralateral venous puncture.

Safety Results from ECLIPSE Trial and German and Mexican Studies

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 3-5 show the major and secondary complications data for the 6F ECLIPSE Trial and for the 7F VCD group versus 6F MC group comparison.

Table 3 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 4 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 5 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 GP IIb/IIIa inhibitor therapy before and/or during the catheterization procedure. Table 6 shows the major and secondary complication data for the interventional patients receiving GP IIb/IIIa inhibitor therapy in the 6F ECLIPSE Trial.

Table 6 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 transfustion	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.

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 7 and 8 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 7 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 8 Secondary Effectiveness Results – All Patients (ITT) Treated

	6F ECLIPSE Trial			Pooled 7F VCD Data Compared to 6F MC Data	
Secondary Effectiveness Endpoints	**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 9 shows the cumulative times to hemostasis, ambulation, eligibility for hospital discharge, and actual hospital discharge for the total patients in the 6F ECLIPSE Trial.

Table 9 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 10.

Table 10 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-Specific 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 receiving therapy from a VCD 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 17). The results of these post hoc analyses are presented below in Tables 11-14.

Table 11. 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
ccess 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%	-
Access 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 12. 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
ccess 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%	-
Access 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 13. 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
ıy 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 14. 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
...ly 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%	-
Access 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. 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 15 and 16 below).

Table 15. 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%	-
reated 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 16. 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 17. 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.

XI. PANEL MEETING RECOMMENDATION AND FDA'S POST-PANEL ACTION

In accordance with the provisions of section 515(c)(2) of the act as amended by the Safe Medical Devices Act of 1990, this PMA was not referred to the Circulatory System Devices Panel, an FDA advisory committee, for review and recommendation because the information in the PMA substantially duplicates information previously reviewed by this panel.

XII. CONCLUSIONS DRAWN FROM PRECLINICAL AND CLINICAL STUDIES

A. Safety Conclusions

The adverse effects of the device are based on data collected in clinical studies conducted to support PMA approval as described above. 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 minor complications within 30 ± 7 days following the catheterization procedure. The data showed that in the total (diagnostic and interventional), diagnostic, and interventional randomized ITT populations, patients treated with the EXOSEAL VCD had incidences of major and minor complications at 30 days post-procedure which are not clinically significantly different from the incidences of major and minor complications at 30 days post-procedure for patients treated with manual compression.

B. Effectiveness Conclusions

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 actual hospital discharge, time for device deployment, procedure success, and device success. The clinical data show that the total patients treated with the EXOSEAL VCD had a lower mean time to hemostasis and a lower mean time to ambulation than the corresponding times for those patients treated with manual compression, and that the differences in these times are statistically and clinically significant. The data also show that the total patients treated with the EXOSEAL VCD device had a mean time to eligibility for hospital discharge time to actual hospital discharge, time for device deployment that is not statistically or clinically significantly different from the corresponding time for those patients treated with manual compression

C. Overall Conclusions

The data provided in PMA Application P100013 support the safety and effectiveness of the EXOSEAL vascular closure device when used in patients who have undergone diagnostic or interventional endovascular procedures utilizing a 5, 6, or 7 French procedural sheath. The data support the claims of improved time-to-hemostasis and time-to-ambulation in diagnostic and interventional patients.

XIII. CDRH DECISION

CDRH issued an approval order on May 19, 2011.

The applicant's manufacturing facility was inspected and found to be in compliance with the device Quality System (QS) regulation (21 CFR 820).

XIV. APPROVAL SPECIFICATIONS

Directions for use: See device labeling.

Hazards to Health from Use of the Device: See Indications, Contraindications, Warnings, Precautions, and Adverse Events in the device labeling.

Post-approval Requirements and Restrictions: See approval order.

XV. REFERENCES

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, Gallauresi B, Rich SE, Bell C. Risk of local adverse events by gender following cardiac catheterization. Pharmacoepidemiol Drug Saf 2007; 16: 125–131.