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WATCHMAN®

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Left Atrial Appendage Closure Device with Delivery System

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℞ ONLY

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

WARNING

Contents supplied STERILE using an ethylene oxide (EO) process. Do not use if sterile barrier is damaged. If damage is found, call your Boston Scientific representative. For single use only. Do not reuse, reprocess or resterilize. Reuse, reprocessing or resterilization may compromise the structural integrity of the device and/or lead to device failure which, in turn, may result in patient injury, illness or death. Reuse, reprocessing or resterilization may also create a risk of contamination of the device and/or cause patient infection or cross-infection, including, but not limited to, the transmission of infectious disease(s) from one patient to another. Contamination of the device may lead to injury, illness or death of the patient. After use, dispose of product and packaging in accordance with hospital, administrative and/or local government policy.

DEVICE DESCRIPTION

The WATCHMAN Left Atrial Appendage Closure (LAAC) Technology is intended for percutaneous, transcatheter closure of the left atrial appendage and consists of the WATCHMAN Access System (Access Sheath and Dilator) and WATCHMAN Delivery System (Delivery Catheter and WATCHMAN Device). The Access System and Delivery System permit device placement in the left atrial appendage (LAA) via femoral venous access and inter-atrial septum crossing into the left atrium. The WATCHMAN Device is a self-expanding nitinol (nickel titanium alloy) structure with a polyethylene terephthalate (PET) porous membrane on the proximal face. The device is constrained within the Delivery System until deployment in the LAA. The device is available in 5 sizes from 21 mm to 33 mm. Appropriate device sizing is determined by LAA measurements using echocardiographic imaging guidance (TEE recommended).

The WATCHMAN Device is designed to be permanently implanted at or slightly distal to the ostium (opening) of the LAA to trap potential emboli before they exit the LAA. The placement procedure can be done under local or general anesthesia in a hospital cardiac catheterization or electrophysiology laboratory setting.

User Information

Intended users of the WATCHMAN Device are interventional cardiologists and/or electrophysiologists who are trained in percutaneous and transseptal procedures and who have completed the WATCHMAN Physician Training program. The WATCHMAN Physician Training program is a one-time training program; no re-training is required. Implantation of the WATCHMAN Device should only be performed by these Intended Users.

Contents

Quantity	Description
(1)	WATCHMAN Left Atrial Appendage Closure Device with Delivery System

INTENDED USE / INDICATIONS FOR USE

The WATCHMAN Device is indicated to reduce the risk of thromboembolism from the left atrial appendage in patients with non-valvular atrial fibrillation who:

- Are at increased risk for stroke and systemic embolism based on $CHADS_2$ or CHA_2DS_2-VASc[1] scores and are recommended for anticoagulation therapy;

- Are deemed by their physicians to be suitable for anticoagulation therapy; and
- Have an appropriate rationale to seek a non-pharmacologic alternative to anticoagulation therapy, taking into account the safety and effectiveness of the device compared to anticoagulation therapy.

CONTRAINDICATIONS

Do not use the WATCHMAN® Device if:

- Intracardiac thrombus is present.
- An atrial septal defect repair or closure device or a patent foramen ovale repair or closure device is present.
- The LAA anatomy will not accommodate a device. See **Table 45.**
- The patient has a known hypersensitivity to any portion of the device material or the individual components (see Device Description section) such that the use of the WATCHMAN Device is contraindicated.
- Any of the customary contraindications for other percutaneous catheterization procedures (e.g., patient size too small to accommodate TEE probe or required catheters) or conditions (e.g., active infection, bleeding disorder) are present.
- There are contraindications to the use of anticoagulation therapy, aspirin, or $P2Y_{12}$ inhibitor.

WARNINGS

Implantation of the WATCHMAN Device should only be performed by interventional cardiologists and/ or electrophysiologists who are trained in percutaneous and transseptal procedures and who have completed the WATCHMAN Physician Training program.

- For single use only. Do not reuse, reprocess, or resterilize. Reuse, reprocessing, or resterilization may compromise the structural integrity of the Closure Device and/or lead to Closure Device failure which, in turn, may result in patient injury, illness, or death. Reuse, reprocessing, or resterilization may also create a risk of contamination of the Closure Device and/or cause patient infection or cross-infection, including, but not limited to, the transmission of infectious disease(s) from one patient to another. Contamination of the Closure Device may lead to injury, illness, or death of the patient.
- This device has not been studied in pregnant or breastfeeding women. Careful consideration should be given to use of the Closure Device in pregnant and/ or breastfeeding women due to the risk of significant exposure to x-rays and the use of anticoagulation medication.
- Device selection should be based on accurate LAA measurements obtained using echocardiographic imaging guidance in multiple views (TEE recommended in multiple angles [e.g., 0°, 45°, 90°, 135°]) to avoid improper Closure Device sizing.
- Do not release (i.e., unscrew) the WATCHMAN Device from the core wire unless all release criteria (see step 14) are satisfied to avoid suboptimal results.
- Potential for Closure Device embolization exists with cardioversion <30 days following Closure Device implantation; verify Closure Device position after cardioversion during this period.
- If thrombus is observed on the device, anticoagulation therapy is recommended until resolution of thrombus is demonstrated by TEE.
- Appropriate post-procedure drug therapy should be followed. See Post-Procedure Information section for further detail.

PRECAUTIONS

- The safety and effectiveness (and benefit-risk profile) of the WATCHMAN Device has not been established in patients for whom long-term anticoagulation is determined to be contraindicated.
- The LAA is a thin-walled structure. Use caution when accessing the LAA and deploying the Closure Device.
- Use caution when introducing a WATCHMAN Access System to prevent damage to cardiac structures.
- Use caution when introducing the Delivery System to prevent damage to cardiac structures.
- To prevent damage to the Delivery Catheter or Closure Device, do not allow the WATCHMAN Device to protrude beyond the distal tip of the Delivery Catheter when inserting the Delivery System into the Access Sheath.
- If using a power injector, the maximum pressure **should not** exceed 100 psi.
- Use caution when manipulating the Delivery System. Excessive counterclockwise rotation of the deployment knob or Delivery System hub independent from the rest of the Delivery System can cause premature implant detachment.

PATIENT SELECTION FOR TREATMENT

In considering the use of the WATCHMAN Device, the rationale for seeking an alternative to long-term anticoagulation therapy and the safety and effectiveness of the device compared to anticoagulation should be taken into account. See "Patient Counseling Information," "Summary of Primary Clinical Studies," and "Clinical Studies," sections for additional information.

Non-valvular atrial fibrillation is associated with an increased risk of cardioembolic stroke. However, there are many sources of thromboembolism in patients with non-valvular atrial fibrillation. The WATCHMAN Device is designed to reduce the risk of thromboembolism originating from the LAA. Although thromboembolism from the LAA is a common source of stroke in this setting, it is not the sole source. Therefore, the WATCHMAN Device would not be expected to reduce the risk of ischemic stroke unrelated to cardioembolism from the LAA, and other potential risk factors for stroke should be considered (e.g., cerebrovascular disease, hypercoagulable states).

Approved oral anticoagulants effectively reduce the risk of cardioembolic stroke and are the most commonly used treatments in at-risk patients with non-valvular atrial fibrillation. Following a careful assessment of the safety and effectiveness of the available approved oral anticoagulants, the WATCHMAN Device is an option that may be considered in selected patients to reduce the risk of cardioembolism from the LAA.

Selection among available treatment options must first take into account whether anticoagulation is indicated to reduce the risk of stroke based on $CHADS_2$ or CHA_2DS_2-VASc scores. Next, in a patient who is deemed by their physicians to be suitable for anticoagulation therapy, physicians and patients should consider the rationale for implantation of the WATCHMAN Device as an alternative to long-term anticoagulation therapy. Specific factors may include one or more of the following:

- A history of major bleeding while taking therapeutic anticoagulation therapy.
- The patient's prior experience with oral anticoagulation (if applicable).
- A medical condition, occupation, or lifestyle placing the patient at high risk of major bleeding secondary to trauma. Some studies of patients with a history of falls, or at risk for falls and head trauma, have shown that the benefits of anticoagulation therapy to reduce the risk of stroke outweigh the risk of major, life-threatening bleeding. An individualized benefit and risk assessment should be made in such patients[2,3,4]
- The presence of indication(s) for long-term anticoagulation therapy use, other than non-valvular atrial fibrillation (e.g. mechanical heart valve, hypercoagulable states, recurrent deep venous thrombosis).

Details regarding the indications, contraindications, warnings and precautions for oral anticoagulants approved for patients with non-valvular atrial fibrillation are provided in their respective Instructions for Use. Of note:

- The safety and effectiveness (and benefit-risk profile) of the WATCHMAN Device has not been established in patients for whom long-term anticoagulation is determined to be contraindicated.

Specific factors that need to be considered for the WATCHMAN Device and implantation procedure include the following:

- Overall medical status, including conditions which might preclude the safety of a percutaneous, transcatheter procedure.
- Suitability for percutaneous, trans-septal procedures, including considerations of:
  - Cardiac anatomy relating to the LAA size and shape.
  - Vascular access anatomy (e.g., femoral vein size, thrombus, or tortuosity.)
  - Ability of the patient to tolerate general or local anesthesia.
  - Ability of the patient to undergo required imaging.

Ability to comply with the recommended post-WATCHMAN Device implant pharmacologic regimen (see Post-Procedure Information section) especially for patients at high risk for bleeding.

PATIENT COUNSELING INFORMATION

Physicians should review the following information when counseling patients about the WATCHMAN Device and implant procedure:

- The safety and effectiveness of systemic anticoagulation and localized percutaneous LAA closure with the WATCHMAN Device.
- There are non-LAA sources of cardiac emboli and other etiologies of stroke that may result in ischemic stroke independent of LAA closure that should be considered.
- The procedural risks associated with WATCHMAN Device implantation. **Table 4** and **Table 40** details the major clinical events related to the device or procedure as observed in the WATCHMAN clinical trial program.
- The need for adherence to a defined pharmacologic regimen of anticoagulation therapy and antiplatelet therapy following WATCHMAN Device implantation.
- Clinical conditions may arise that require continuation or resumption of anticoagulation therapy following WATCHMAN Device implantation.
- The risk of the device implantation procedure plus post-procedure related bleeding weighed against the risk of bleeding on long-term anticoagulation therapy.

Additional counseling information can be found in the Patient Guide and in the clinical studies section of these Directions for Use.

MAGNETIC RESONANCE IMAGING

Non-clinical testing demonstrated that the WATCHMAN Device is MR Conditional. A patient with the device can be scanned safely, immediately after placement of this implant, under the following conditions:

- Static magnetic fields of 3.0 Tesla or 1.5 Tesla
- Spatial gradient field of 2500 Gauss/cm or less
- The maximum whole body averaged specific absorption rate (SAR) shall be limited to 2.0 W/kg (normal operating mode only) for 15 minutes of scanning
- Normal operating mode of the MRI scanner

The WATCHMAN Device should not migrate in this MRI environment. This device has not been evaluated to determine if it is MR Conditional beyond these parameters.

3.0 Tesla Temperature Information

In non-clinical testing, the WATCHMAN Device produced a temperature rise of <1.1 °C at a maximum MR system-reported SAR of 2.0 W/kg as measured by calorimetry for 15 minutes of continuous MR scanning in a 3.0 Tesla MR system (Excite, Software G3.0-052B, GE Healthcare, Milwaukee, WI).

These calculations do not take into consideration the cooling effects of blood flow.

1.5 Tesla Temperature Information

Non-clinical testing of RF-induced heating in the WATCHMAN Device was performed at 64 MHz in a 1.5 Tesla whole body coil MR scanner (Intera, Software Release 10.6.2.4, 2006-03-10, Philips Medical Systems, Andover, MA) and produced a temperature rise of <1.5 °C at an MR extrapolated SAR of 2.0 W/kg for 15 minutes of continuous MR scanning.

These calculations do not take into consideration the cooling effects of blood flow.

Image Artifact Information

In non-clinical testing, the image artifact caused by the device extends less than 3 mm from the WATCHMAN Device when imaged with a spin echo pulse sequence and a 3-Tesla MRI system. The image artifact caused by the device extends less than 5 mm from the WATCHMAN Device when imaged with a gradient echo pulse sequence and a 3-Tesla MRI system. MR image quality may be compromised if the area of interest is relatively close to the WATCHMAN Device. Optimization of MR imaging parameters is recommended.

SUMMARY OF PRIMARY CLINICAL STUDIES

Treatment with the WATCHMAN Left Atrial Appendage Closure (LAAC) Device, a permanent implant intended to reduce the risk of thromboembolism from the LAA, was evaluated in subjects with non-valvular atrial fibrillation who are suitable for warfarin therapy. The pivotal WATCHMAN LAAC Therapy for Embolic PROTECTion in Patients with Atrial Fibrillation (PROTECT AF) study was followed by three additional studies in this population: a continued access (CAP) registry to the PROTECT AF study; and a second randomized study, the Prospective Randomized Evaluation of the WATCHMAN LAAC Device in Patients With Atrial Fibrillation Versus Long Term Warfarin Therapy (PREVAIL) study; and a continued access (CAP2) registry to the PREVAIL study. Upon WATCHMAN LAAC Device approval, the New Enrollment PoST-approval Surveillance Analysis Plan (NESTed SAP) prospectively enrolled patients that received a commercial device.

The Protection Against Embolism for Non-valvular AF Patients: Investigational Device Evaluation of the WATCHMAN FLX LAA Closure Technology (PINNACLE FLX) trial was a non-randomized study enrolling patients to receive the next generation WATCHMAN FLX Device. PINNACLE FLX evaluated subjects with non-valvular atrial fibrillation who were suitable for oral anticoagulation therapy and had a rationale to seek non-pharmacologic alternative. Table 1 shows a summary of study designs, number of study subjects enrolled, and planned follow-up for each study. Transesophageal echocardiography (TEE) and fluoroscopy were used in the WATCHMAN pivotal clinical trials for selection of device size.

[1] January CT, Wann LS, Alpert JS, et al., 2014 AHA/ACC/HRS Guideline for the Management of Patients With Atrial Fibrillation, A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the Heart Rhythm Society, Circulation, 2014; 130: e199-e267.

[2] American Geriatrics Society/British Geriatrics Society Clinical Practice Guideline for Prevention of Falls in Older Persons. J Am Geriat Soc. 2010 (http://www. americangeriatrics.org/files/documents/health_care_pros/JAGS.Falls.Guidelines.pdf)

[3] Seller MB, Newby LK. Atrial Fibrillation, Anticoagulation, Fall Risk, and Outcomes in Elderly Patients. Am Heart J. 2011; 161:241-246.

[4] Donzé J, Clair C, Hug B, Rodondi N, Waeber G, Cornuz J, Aujesky D. Risk of Falls and Major Bleeds in Patients on Oral Anticoagulation Therapy. Am J Med. 2012 Aug;125(8):773-8.

Table 1. Summary of WATCHMAN® Clinical Studies

Patient Population	Subjects with non-valvular atrial fibrillation who were deemed by their physicians to be suitable for oral anticoagulation* (OAC) therapy to reduce the risk of ischemic stroke and systemic embolism					
Study	**PROTECT AF**	**CAP**	**PREVAIL**	**CAP2**	**NESTed SAP**	**PINNACLE FLX**
Purpose	Demonstrate safety and effectiveness of the WATCHMAN Device compared to long-term warfarin	Continued access registry	Demonstrate safety and effectiveness of the WATCHMAN Device compared to long-term warfarin	Continued access registry	Post approval surveillance analysis plan	Demonstrate safety and effectiveness of the WATCHMAN FLX™ Device
Device	WATCHMAN	WATCHMAN	WATCHMAN	WATCHMAN	WATCHMAN	WATCHMAN FLX
Study Design	2:1 Randomized, non-inferiority	Non-randomized	2:1 Randomized, non-inferiority	Non-randomized	Non-randomized	Non-randomized
Primary Endpoints	1. Effectiveness: Stroke, cardiovascular death, and systemic embolism 2. Safety: Life-threatening events which include device embolization requiring retrieval and bleeding events		1. Effectiveness: Stroke, systemic embolism, and cardiovascular/unexplained death 2. Effectiveness: Ischemic stroke or systemic embolism occurring after seven days post-randomization or WATCHMAN implant procedure 3. Safety: Death, ischemic stroke, systemic embolism and procedure/device-related complications** within seven-days of the implantation procedure		1. Effectiveness: Stroke, systemic embolism, and all-cause death 2. Effectiveness: Ischemic stroke or systemic embolism 3. Safety: Death, ischemic stroke, systemic embolism and procedure/device-related complications** within seven-days of the implantation procedure	1. Effectiveness: The rate of effective LAA closure defined as any peri-device leak ≤ 5mm demonstrated by TEE at 12 months. 2. Safety: Death, ischemic stroke, systemic embolism and procedure/device-related complications** within seven-days of the implantation procedure

Number of Patients Enrolled	800 subjects
	• 93 roll-in WATCHMAN
	• 707 randomized
	  • 463 WATCHMAN
	  • 244 Control
		566 WATCHMAN subjects	461 subjects
			• 54 roll-in WATCHMAN
			• 407 randomized
			  • 269 WATCHMAN
			  • 138 Control
				576 WATCHMAN subjects	Primary Cohort: 1000 subjects
					Secondary Cohort: 1000 subjects
						458 Subjects
						• 58 roll-in
						• 400 WATCHMAN FLX

Status of Subject Follow-Up	Study Complete 2717 patient-years	Study Complete 2293 patient-years	Study Complete 1626 patient-years	Study Complete 2329 patient-years	Study Ongoing 839 patient-years	Study Ongoing 426 patient-years
Post Implant Drug Regiment	45-days warfarin + aspirin then DAPT (Dual Antiplatelet Therapy) until 6-months	45-days warfarin + aspirin then DAPT until 6-months	45-days warfarin + aspirin then DAPT until 6-months	45-days warfarin + aspirin then DAPT until 6-months	45-days warfarin + aspirin then DAPT until 6-months	45-days NOAC (non-vitamin K antagonist oral anticoagulant) + aspirin then DAPT until 6-months
Scheduled Follow-Up Duration	5 years					2 years

* PROTECT AF, CAP, PREVAIL, CAP2, and NESTed-SAP studies used warfarin, and PINNACLE FLX used non-vitamin K antagonist OAC.
** Events requiring open cardiac surgery or major endovascular intervention such as pseudoaneurysm repair, AV fistula repair, or other major endovascular repair complications within seven-days of the implantation procedure.

PROTECT AF Study

The PROTECT AF study was a multicenter, prospective randomized controlled study comparing the WATCHMAN Device to long-term warfarin therapy. The purpose of the study was to demonstrate that the WATCHMAN Device is safe and effective in subjects with non-valvular atrial fibrillation who were deemed by their physicians to be suitable for warfarin therapy. A 2:1 randomization allocation ratio was used with stratification by center such that for every one subject randomized to the Control arm (long-term warfarin therapy); two subjects were randomized to the Device arm to receive the WATCHMAN Device.

The primary effectiveness composite endpoint was the rate of the composite of stroke (including ischemic and hemorrhagic), systemic embolism, and cardiovascular death (cardiovascular and unexplained). The primary safety endpoint was the rate of life-threatening events as determined by the Clinical Events Committee (CEC), which included device embolization requiring retrieval, bleeding events such as pericardial effusion requiring drainage, cranial bleeding events due to any source, gastrointestinal bleeds requiring transfusion, and any bleeding related to the device or procedure that necessitated a surgical procedure. The primary statistical objective was to determine if the device group is non-inferior to the Control group with respect to the event rate for the composite primary effectiveness endpoint.

A total of 800 subjects were enrolled in the study at 59 centers. The 800 subjects included 463 subjects randomized to the WATCHMAN Device group, 244 subjects randomized to the Control group, and 93 roll-in WATCHMAN Device subjects.

PREVAIL Study

The PREVAIL study was a multicenter, prospective randomized controlled study to evaluate the safety and effectiveness of the WATCHMAN Device compared to long-term warfarin therapy. PREVAIL was a second pivotal, randomized study of the WATCHMAN Device, and the analyses of the primary endpoints included historical data from the PROTECT AF study.

There were three primary endpoints (two effectiveness and one safety) as follows: 1) the composite of ischemic stroke, hemorrhagic stroke, systemic embolism, and cardiovascular or unexplained death; 2) the composite ischemic stroke and systemic embolism, excluding events occurring in the first 7 days following randomization; and 3) the occurrence of all-cause mortality, ischemic stroke, systemic embolism, or device or procedure-related events requiring open cardiac surgery or major endovascular intervention between the time of randomization and 7 days of the procedure or by hospital discharge, whichever is later. A total of 461 subjects at 41 U.S. investigational sites were enrolled from November 2010 through June 2012. The 461 subjects included 269 subjects randomized to the WATCHMAN Device group, 138 subjects randomized to the Control group, and 54 roll-in WATCHMAN Device subjects.

CAP Registry

The CAP registry was a multi-center prospective non-randomized study allowing continued access to the WATCHMAN Device during regulatory review of the pre-market application for the WATCHMAN Device. Entry criteria were the same as the PROTECT AF study. A total of 26 centers (24 U.S., 2 European) actively participated by enrolling at least one subject in the study. A total of 566 subjects were enrolled from August 2008 through June 2010.

The primary effectiveness and safety endpoints were similar to the PROTECT AF.

CAP2 Registry

The CAP2 registry was a multi-center prospective non-randomized study allowing continued access to the WATCHMAN Device during regulatory review of the pre-market application for the WATCHMAN Device. Entry criteria were the same as the PREVAIL study. A total of 576 subjects at 47 U.S. investigational sites were enrolled from September 2012 through March 2014.

The primary effectiveness and safety endpoints were similar to the PREVAIL study.

NESTed Surveillance Analysis Plan

The NESTed registry assesses long-term safety and effectiveness outcomes associated with the use and implantation of the WATCHMAN Left Atrial Appendage (LAA) Closure Technology in a routine clinical setting.

The WATCHMAN New Enrollment PoST Approval Surveillance Analysis Plan (NESTed SAP) is a multi-center, prospective, non-randomized registry utilizing data captured in the Left Atrial Appendage Occlusion Registry (LAAO Registry) within the American College of Cardiology Foundation's (ACCF) National Cardiovascular Data Registry (NCDR). Two cohorts of 1,000 patients (primary and secondary) will be included in the analysis. The Primary Cohort will consist of subjects who are eligible for a WATCHMAN Device according to current U.S. indications with a calculated CHADS2 score of ≥2 or a CHA2DS2-VASc score of ≥3 and exclude any patients who are contraindicated for a WATCHMAN Device according to this document or patients with concomitant cardiac or non-cardiac procedures (including, but not limited to: cardiac ablation, trans-catheter valve implantation, coronary intervention, etc.). Once the primary cohort was complete, the next consecutive 1,000 patients implanted were included in the secondary cohort.

PINNACLE FLX Study

PINNACLE FLX is a prospective, non-randomized, multi-center investigation to establish the safety and effectiveness of the WATCHMAN FLX LAA Closure Device for subjects with non-valvular atrial fibrillation who are eligible for long-term non-vitamin K antagonist oral anticoagulation (NOAC) therapy to reduce the risk of stroke but who have a rationale to seek a non-pharmacologic alternative. For PINNACLE FLX, NOACs were used as the post-implant drug regimen. Due to the similarities in the WATCHMAN Closure Device with Delivery System and WATCHMAN FLX Closure Device with Delivery System designs, the results of the PINNACLE FLX study are applicable to the WATCHMAN Closure Device with Delivery System and support use of NOACs with the WATCHMAN Closure Device with Delivery System.

This study had two primary endpoints: 1) The rate of effective LAA closure defined as any peri-device leak ≤ 5mm demonstrated by TEE at 12 months; and 2) the occurrence of all-cause mortality, ischemic stroke, systemic embolism, or device or procedure related events requiring open cardiac surgery or major endovascular intervention between the time of implant and 7 days following the procedure or by hospital discharge, whichever was later.

Table 2. Summary of Baseline Demographics

	PROTECT AF			PREVAIL			CAP N=566	CAP2 N=576	NESTed SAP N=1000	PINNACLE FLX N=400
Characteristic	**WATCHMAN® N=463**	**Control N=244**	**P-value**	**WATCHMAN N=269**	**Control N=138**	**P-value**				
Study Device	WATCHMAN	N/A	N/A	WATCHMAN	N/A	N/A	WATCHMAN	WATCHMAN	WATCHMAN	WATCHMAN FLX™
Age, years	71.7 ± 8.8 (463) (46.0, 95.0)	72.7 ± 9.2 (244) (41.0, 95.0)	0.179	74.0 ± 7.4 (269) (50.0, 94.0)	74.9 ± 7.2 (138) (53.0, 90.0)	0.260	74.0 ± 8.3 (566) (44.0, 94.0)	75.3 ± 8.0 (576) (33.0, 94.0)	76.5 ± 8.1 (37.0, 100.0)	73.8 ± 8.6 (400) (44.0, 98.0)
Sex										
Female	137/463 (29.6%)	29.9% (73/244)	0.928	32.3% (87/269)	25.4% (35/138)	0.146	34.5% (195/566)	39.4% (227/576)	38.1% (381/1000)	35.5% (142/400)
Male	326/463 (70.4%)	70.1% (171/244)		67.7% (182/269)	74.6% (103/138)		65.5% (371/566)	60.6% (349/576)	61.9% (619/1000)	64.5% (258/400)
Race/Ethnicity										
American Indian or Alaskan	N/A	N/A	0.779	N/A	N/A	0.603	N/A	0.3% (2/576)	0.4% (4/1000)	0.3% (1/382)
Asian	0.9% (4/463)	0.4% (1/244)		0.4% (1/269)	0.7% (1/138)		1.6% (9/566)	0.7% (4/576)	1.3% (13/1000)	0.5% (2/382)
Black/African American	1.3% (6/463)	2.0% (5/244)		2.2% (6/269)	0.7% (1/138)		1.9% (11/566)	1.2% (7/576)	4.0% (40/1000)	4.7% (18/382)
Caucasian	91.8% (425/463)	91.0% (222/244)		94.1% (253/269)	94.9% (131/138)		91.9% (520/566)	94.1% (542/576)	93.9% (939/1000)	93.7% (358/382)
Hispanic/Latino	5.4% (25/463)	6.1% (15/244)		2.2% (6/269)	3.6% (5/138)		3.5% (20/566)	2.1% (12/576)	4.0% (40/1000)	2.6% (10/382)
Hawaiian/ Pacific Islander	1/463 (0.2%)	0.4% (1/244)		0.4% (1/269)	0.0% (0/138)		0.2% (1/566)	0.0% (0/576)	N/A	0.0% (0/382)
Other	2/463 (0.4%)	0.0% (0/244)		0.7% (2/269)	0.0% (0/138)		0.9% (5/566)	0.7% (4/576)	0.7% (7/1000)	0.0% (0/382)
Paroxysmal AF	43.2% (200/463)	40.6% (99/244)	0.762	48.7% (131/269)	51.4% (71/138)	0.571	42.8% (242/566)	53.6% (309/576)	44.8% (448/1000)	51.8% (207/400)
Persistent AF	97/463 (21.0%)	20.5% (50/244)		31.6% (85/269)	28.3% (39/138)		30.2% (171/566)	25.7% (148/576)	36.0% (360/1000)	36.5% (146/400)
Permanent AF	160/463 (34.6%)	38.1% (93/244)		31.6% (42/269)	15.9% (22/138)		24.0% (136/566)	14.4% (83/576)	18.7% (187/1000)	10.5% (42/400)
Paced AF	N/A	N/A		2.6% (7/269)	3.6% (5/138)		0% (0/566)	6.3% (36/576)	N/A	1.3% (5/400)
Unknown	1.3% (6/463)	0.8% (2/244)		1.5% (4/269)	0.7% (1/138)		3.0% (17/566)	0% (0/576)	0.2% (2/1000)	N/A

Table 3. Summary of Baseline Characteristics

PROTECT AF				PREVAIL			CAP N=566	CAP2 N=576	NESTed SAP N=1000	PINNACLE FLX N=400
Characteristic	**WATCHMAN N=463**	**Control N=244**	**P-value**	**WATCHMAN N=269**	**Control N=138**	**P-value**				
Study Device	WATCHMAN	N/A	N/A	WATCHMAN	N/A	N/A	WATCHMAN	WATCHMAN	WATCHMAN	WATCHMAN FLX
$CHADS_2$ Score (Continuous)	2.2 ± 1.2 (463) (1.0, 6.0)	2.3 ± 1.2 (244) (1.0, 6.0)	0.072	2.6 ± 1.0 (269) (1.0, 6.0)	2.6 ± 1.0 (138) (1.0, 5.0)	0.838	2.5 ± 1.2 (566) (1.0, 6.0)	2.7 ± 1.1 (576) (1.0, 6.0)	3.2 ± 1.2 (1000) (0.0, 6.0)	2.3 ± 1.2(400) (0, 6.0)
CHA_2DS_2-VASc Score (Continuous)	3.2 ± 1.4 (460)	3.5 ± 1.5 (239)	0.022	4.0 ± 1.1 (269) (2.0, 8.0)	4.1 ± 1.2 (138) (2.0, 7.0)	0.399	3.9 ± 1.5 (564) (1.0, 9.0)	4.5 ±1.3 (576) (2.0, 9.0)	5.0 ± 1.4 (1000) (2.0, 9.0)	4.2 ± 1.5 (400) (2.0,9.0)
CHF	26.8% (124/463)	27.0% (66/244)	0.9392	23.4% (63/269)	23.2% (32/138)	0.958	19.1% (108/566)	27.1% (156/576)	N/A	31.8% (127/400)
Hypertension	89.6% (415/463)	90.2% (220/244)	0.8243	88.5% (238/269)	97.1% (134/138)	0.003	89.0% (503/565)	92.5% (533/576)	N/A	85.8% (343/400)
Age 65-74	N/A	N/A	N/A	N/A	N/A	N/A	37.5% (212/566)	N/A	N/A	35.8% (143/400)
Age >=75	41.0% (190/463)	47.1% (115/244)	0.1198	52.0% (140/269)	56.5% (78/138)	0.391	51.8% (293/566)	59.5% (344/576)	N/A	50.5% (202/400)
Diabetes	24.4% (113/463)	29.5% (72/244)	0.1423	33.8% (91/269)	29.7% (41/138)	0.401	24.9% (141/566)	33.7% (194/576)	N/A	30.5% (122/400)
Previous stroke, TIA, or TE	17.7% (82/463)	20.1% (49/244)	0.4404	27.5% (74/269)	28.3% (39/138)	0.873	30.4% (172/566)	29.0% (167/576)	N/A	22.3% (89/400)
Vascular disease	N/A	N/A	N/A	N/A	N/A	N/A	45.1% (255/566)	45.8% (265/576)	N/A	55.0% (220/400)
HAS-BLED Score (Continuous)	N/A	N/A	N/A	N/A	N/A	N/A	N/A	2.00 ± 0.94 (576) (0.00, 5.00)	2.7±1.1 (1000) (0.0, 6.0)	2.0±1.0 (400) (0.0, 5.0)

Observed adverse events related to the WATCHMAN® Device or implantation procedure (as evaluated by the Clinical Events Committee) in patients from the PROTECT AF, CAP, PREVAIL, CAP2, and PINNACLE FLX studies are shown in **Table 4.**

Table 4. PROTECT AF, CAP, PREVAIL, CAP2 and PINNACLE FLX Major Clinical Events Related to the WATCHMAN Device or Implant Procedure

Event	PROTECT AF n (%) N=463	CAP n (%) N=566	PREVAIL n (%) N=269	CAP2 n (%) N=576
Pericardial effusion with cardiac tamponade	13 (2.8)	7 (1.2)	4 (1.5)	8 (1.4)
Pseudoaneurysm	3 (0.6)	5 (0.9)	0 (0.0)	3 (0.5)
Device embolization	3 (0.6)	1 (0.2)	2 (0.7)	0 (0.0)
Ischemic stroke related to device or implant procedure*	7 (1.5)	2 (0.4)	4 (1.5)	12 (2.0)
• Ischemic stroke related to device thrombus	2 (0.4)	2 (0.4)	3 (1.1)	4 (0.7)
• Ischemic stroke related to air embolism	3 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
• Ischemic stroke related to procedure/device (excluding air embolism and device thrombus)	2 (0.4)	0 (0.0)	1 (0.4)	8 (1.4)
Systemic embolism*	0 (0.0)	0 (0.0)	1 (0.4)	2 (0.3)
Pericardial effusion - no intervention required	4 (0.9)	5 (0.9)	0 (0.0)	3 (0.5)
Cardiac perforation (surgical repair)	7 (1.5)	1 (0.2)	1 (0.4)	3 (0.5)
Bruising or hematoma	4 (0.9)	1 (0.2)	2 (0.7)	2 (0.3)
Major bleed requiring transfusion	1 (0.2)	5 (0.9)	3 (1.1)	3 (0.5)
Groin bleeding	4 (0.9)	0 (0.0)	0 (0.0)	0 (0.0)
Respiratory failure	0 (0.0)	4 (0.7)	2 (0.7)	4 (0.7)
Infection	2 (0.4)	0 (0.0)	3 (1.1)	1 (0.2)
Arrhythmias	2 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)
Transient ischemic attack (TIA)	1 (0.2)	2 (0.4)	0 (0.0)	0 (0.0)
AV fistula	1 (0.2)	0 (0.0)	1 (0.4)	0 (0.0)
Chest pain	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)
Atrial septal defect	0 (0.0)	2 (0.4)	0 (0.0)	0 (0.0)
Ventricular tachycardia	0 (0.0)	2 (0.4)	0 (0.0)	0 (0.0)
Device migration	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)

*The overall rates of ischemic stroke and systemic embolism, including those independent of the WATCHMAN Device implant procedure, are shown in **Table 6, Table 14, Table 22**, and **Table 27**.
** Please note, due to differences in methodologies for event adjudication and for assessment of device/procedure relatedness among the studies, the results of PINNACLE FLX (Table 40) are not directly comparable to the results of the studies in **Table 4.**

ADVERSE EVENTS

Potential adverse events (in alphabetical order) which may be associated with the use of a left atrial appendage closure device or implantation procedure include but are not limited to:

- Air embolism
- Airway trauma
- Allergic reaction to the contrast media, anesthetic, WATCHMAN Implant material, or medications
- Altered mental status
- Anemia requiring transfusion
- Anesthesia risks
- Angina
- Anoxic encephalopathy
- Arrhythmias
- Atrial septal defect
- Bruising, hematoma, or seroma near the catheter insertion site
- Cardiac perforation
- Chest pain/discomfort
- Confusion post procedure
- Congestive heart failure
- Contrast related nephropathy
- Cranial bleed
- Death
- Decreased hemoglobin
- Deep vein thrombosis
- Device embolism
- Device fracture
- Device thrombosis
- Edema
- Embolism
- Excessive bleeding
- Fever
- Fistula
- Groin pain
- Groin puncture bleed
- Hematuria
- Hemoptysis
- Hypotension
- Hypoxia
- Improper wound healing
- Inability to reposition, recapture, or retrieve the device
- Infection/pneumonia
- Interatrial septum thrombus
- Intratracheal bleeding
- Major bleeding requiring transfusion
- Misplacement of the device/improper seal of the appendage/movement of device from appendage wall
- Myocardial erosion
- Nausea
- Oral bleeding
- Pericardial effusion/tamponade
- Pleural effusion
- Prolonged bleeding from a laceration
- Pseudoaneurysm
- Pulmonary edema
- Renal failure
- Respiratory insufficiency/failure
- Stroke - Hemorrhagic
- Stroke - Ischemic
- Surgical removal of the device
- TEE complications (e.g., throat pain, bleeding, esophageal trauma)
- Thrombocytopenia
- Thrombosis
- Transient ischemic attack (TIA)
- Valvular or vascular damage
- Vasovagal reactions

There may be other potential adverse events that are unforeseen at this time.

CLINICAL STUDIES

PROTECT AF Study

Primary Objective: To demonstrate that the WATCHMAN Device is safe and effective in subjects with non-valvular atrial fibrillation who are deemed by their physicians to be suitable for warfarin therapy to prevent thromboembolism from the LAA.

Design: The PROTECT AF study was a multi-center prospective randomized controlled trial comparing the WATCHMAN Device to long-term warfarin therapy. A 2:1 randomization allocation ratio (two Device subjects to one Control subject) was used with stratification by center.

Main entry criteria included, but were not limited to, at least 18 years of age, non-valvular atrial fibrillation, a CHADS2 score of 1 or greater, and eligibility for long-term warfarin therapy. Following randomization, subjects were assessed at 45 days, at 6-, 9-, and 12-month visits, and semi-annually thereafter through 5 years. A non-randomized roll-in phase was added to permit physicians to become experienced with the WATCHMAN Device implant procedure. Subjects randomized to receive the WATCHMAN Device underwent TEE at 45 days, 6-, and 12-month visits after successful implantation. Subjects randomized to the Control group were to remain on warfarin with INR monitored every other week through 6 months and monthly thereafter.

The primary effectiveness endpoint was the rate of the composite of stroke (including ischemic and hemorrhagic), systemic embolism, cardiovascular death (cardiovascular and unexplained). The primary safety endpoint was rate of life-threatening events, which included events such as device embolization requiring retrieval, bleeding events such as pericardial effusion requiring drainage, cranial bleeding events due to any source, gastrointestinal bleeds requiring transfusion and any bleeding related to the device or procedure that necessitates an operation.

The effectiveness event rate was defined as the number of events per 100 pt-yrs of follow-up. A Bayesian Poisson-Gamma model stratified by $CHADS_2$ score was used for evaluation of the statistical objective. The first sequential interim analysis was performed after collection of 600 pt-yrs of follow-up, which included 300 subjects with one year of follow-up and 100 subjects with two years of follow-up. Subsequent analyses were allowed after each additional 150 pt-yrs up to a maximum of 1500 pt-yrs of follow-up. The criterion for establishing non-inferiority at an interim analysis required that the posterior probability that the primary effectiveness event rate for the WATCHMAN group being less than 2 times the event rate for the Control group be at least 0.975 (or equivalently, the upper bound of the equitailed 2-sided 95% credible interval for the rate ratio be less than 2).

Enrollment: The study enrolled 800 subjects with 707 randomized and the remaining 93 participating in the WATCHMAN roll-in group. Of the 707 randomized subjects, 463 were assigned to the WATCHMAN group and 244 assigned to the warfarin control group as shown in **Table 5.**

Table 5. PROTECT AF Enrollment Summary

Group	N
WATCHMAN Device Group	
Randomized	463
Implant Attempted	449
Device Implanted	408
Control Group	
Randomized	244
Warfarin Administered	241
Warfarin Never Administered	3
Roll-in Group	
Enrolled	93
Implant Attempted	93
Device Implanted	77

The PROTECT AF study is complete with 5 years and 2717 patient years of follow-up.

Demographics and Baseline Clinical Features: For subjects randomized to the WATCHMAN group, the mean CHADS2 score was 2.2 ± 1.2, the mean CHA2DS2-VASc score was 3.2 ± 1.4, the mean age was 72 years, 70% were male, and 92% were Caucasian. For subjects randomized to the Control group, the mean CHADS2 score was 2.3 ± 1.2, the mean CHA2DS2-VASc score was 3.5 ± 1.6, the mean age was 73 years, 70% were male, and 91% were Caucasian. The two treatment groups had no statistically significant differences in baseline demographic and clinical characteristics as shown in **Tables 2 and 3**.

Results: WATCHMAN Device implant success (defined as successful release of the device) was achieved in 408/449 (90.9%) subjects who underwent the implant procedure.

Effectiveness: Results of the final 5 year follow-up representing 2717 patient years for the primary effectiveness endpoint of the composite of stroke, systemic embolism, and death (cardiovascular or unexplained) are displayed in **Table 6**. The primary effectiveness event rate was 2.2 events per 100 patient years for the Device group and 3.7 events per 100 patient years for the Control group, resulting in a relative risk or rate ratio of 0.61. The criterion for non-inferiority and superiority of the WATCHMAN Device vs. the Control group were met and were driven by the rates of hemorrhagic stroke and cardiovascular or unexplained death in favor of the Device group. The ischemic stroke rate numerically favored the control group.

Table 6. PROTECT AF Primary Effectiveness Results (Intent-to-Treat) and % of subjects who experienced 1 or more events (2717 patient years)

Randomization Allocation (2 Device: 1 Control)

	WATCHMAN®		Control		
	Event Rate (per 100 Pt-yrs)	Event Rate/ Subject	Event Rate (per 100 Pt-yrs)	Event Rate/ Subject	Rate Ratio (95% CrI)*
Primary effectiveness	2.2 (40/1788)	8.6% (40/463)	3.7 (34/929)	13.9% (34/244)	0.61 (0.42, 1.07)
Ischemic stroke	1.3 (24/1782)	5.2% (24/463)	1.1 (10/933)	4.1% (10/244)	
Hemorrhagic stroke	0.2 (3/1838)	0.6% (3/463)	1.1 (10/946)	4.1% (10/244)	
Systemic embolism	0.2 (3/1837)	0.6% (3/463)	0.0 (0/949)	0.0% (0/244)	
Death (CV/unexplained)	1.0 (19/1843)	4.1% (19/463)	2.3 (22/949)	9.0% (22/244)	
Ischemic stroke and systemic embolism	1.5 (26/1781)	5.6% (26/463)	1.1 (10/933)	4.1% (10/244)	
Stroke (all)	1.5 (26/1782)	5.6% (26/463)	2.2 (20/929)	8.2% (20/244)	

*Posterior probability >0.999 for non-inferiority and 0.954 for superiority
The Rate Ratio is based on the event rates per 100 pt-yrs
CrI = credible interval
Rate = event rate per 100 patient years (calculated as 100*N events/Total patient-years)
Rel.risk = relative risk or rate ratio, calculated as Device rate over Control rate.

The primary effectiveness endpoint for PROTECT AF is shown as time to event in a Kaplan-Meier curve in **Figure 1.**

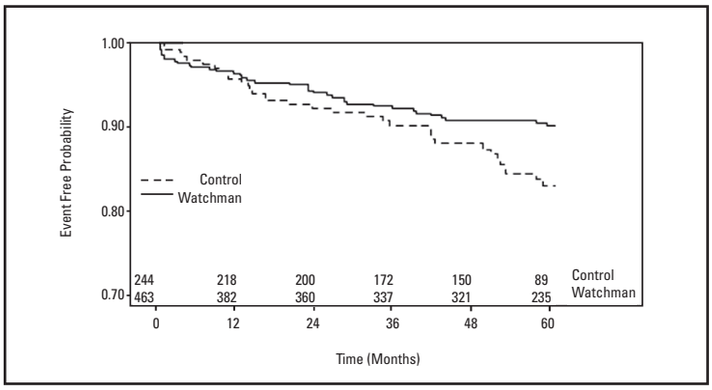

Figure 1. PROTECT AF Primary Effectiveness (2717 patient-years)

Safety: The primary safety rate was 3.5 events per 100 patient years for the Device group and 3.2 events per 100 patient years for the Control group resulting in a relative risk ratio of 1.08. These results are summarized in **Table 7**.

Table 7. PROTECT AF Primary Safety Results (Intent-to-Treat) (2717 patient-years)

Randomization Allocation (2 Device: 1 Control)

WATCHMAN Rate (N events/total pt-yrs)	Control Rate (N events/total pt-yrs)	Relative Risk (95% CrI)
3.5 (60/1729.6)	3.2 (29/904.9)	1.08 (0.72, 1.77)

*Rate = event rate per 100 patient years (calculated as 100*N events/Total patient-years)*

Rel. risk = relative risk or rate ratio, calculated as Device rate over Control rate.

CrI = credible interval

PROTECT AF Major Bleeding Analysis

The rates of major bleeding complications, defined as bleeding events adjudicated as serious adverse events, are shown in **Table 8**. There were more bleeding events in the WATCHMAN group immediately post-procedure through day 45 with a lower rate of bleeding thereafter. The overall major bleeding rates were similar between the WATCHMAN group and the Control group.

Table 8. PROTECT AF Major Bleeding

	WATCHMAN		Control	
Major Bleeding	N Events/ Subjects (%)	Rate per 100 Pt-yrs (N Events/Total Pt-yrs)	N Events/ Subjects (%)	Rate per 100 Pt-yrs (N Events/Total Pt-yrs)
Procedure-related	28/463 (6.0%)	NA	NA	NA
Non-procedure related	24/463 (5.2%)	1.3 (24/1803.7)	29/244 (11.9%)	3.2 (29/904.9)
0-45 days	5/463 (1.1%)	9.2 (5/54.6)	2/244 (0.8%)	6.7 (2/29.7)
46 days – 6 months	4/431 (0.9%)	2.6 (4/153.6)	4/239 (1.7%)	4.6 (4/87.8)
>6 months	15/397 (3.8%)	0.9 (15/1595.5)	23/228 (10.1%)	2.9(23/787.5)
Total major bleeding	50/463 (10.8%)	2.9 (50/1743.4)	29/244 (11.9%)	3.2 (29/904.9)

Serious Adverse Events: A summary of all serious adverse events for the WATCHMAN and Control groups is presented in **Table 9**. Serious adverse events related to the WATCHMAN Device or implant procedure are shown in **Table 4**.

Table 9. PROTECT AF Serious Adverse Events

Event	WATCHMAN N=463			Control N=244		
	Number of Events	Number of Subjects	Percent of Subjects	Number of Events	Number of Subjects	Percent of Subjects
Adjudicated as Non-Event	1	1	0.2%	0	0	0
Anemia Requiring Transfusion	2	2	0.4%	1	1	0.4%
Arrhythmias	2	2	0.4%	0	0	0
AV Fistula	1	1	0.2%	0	0	0
Bleeding from Varicose Veins	1	1	0.2%	0	0	0
Bruising - Hematoma	5	5	1.1%	0	0	0
Cardiac Perforation	7	7	1.5%	0	0	0
Cranial Bleed	4	4	0.9%	1	1	0.4%
Death	59	59	12.7%	44	44	18.0%
Device Embolization	4	3	0.6%	0	0	0
Device Thrombus	2	2	0.4%	0	0	0
Epistaxis	4	4	0.9%	0	0	0
Gastrointestinal Bleeding	32	26	5.6%	27	22	9.0%
Hematuria	4	4	0.9%	0	0	0
Infection	2	2	0.4%	0	0	0
Major Bleed Requiring Transfusion	2	2	0.4%	1	1	0.4%
Oral Bleeding	0	0	0	1	1	0.4%
Other Study Related	18	17	3.7%	2	2	0.8%
Pericardial Effusion with Cardiac Tamponade	13	13	2.8%	0	0	0
Pericardial Effusion-Serious	4	4	0.9%	0	0	0
Pleural Effusion	1	1	0.2%	0	0	0
Pseudoaneurysm	3	3	0.6%	0	0	0
Pulmonary Edema	1	1	0.2%	0	0	0
Rectal Bleeding	1	1	0.2%	1	1	0.4%
Stroke - Hemorrhagic	3	3	0.6%	10	10	4.1%
Stroke - Ischemic	26	24	5.2%	11	10	4.1%
Systemic Embolization	3	3	0.6%	0	0	0
Thrombosis	1	1	0.2%	0	0	0
Transient Ischemic Attack	5	5	1.1%	0	0	0

PROTECT AF Device Thrombus Rates

The device thrombus-related stroke rate was 0.1 events per 100 patient-years as shown in **Table 10**.

Table 10. PROTECT AF Device-related Thrombus

	N=408
Thrombus Subjects	16 (3.9%)
Thrombus Events	17
Experienced Ischemic Stroke	2
Experienced Serious Adverse Event	3
Device Thrombus-Related Stroke Rate (per 100 pt-yrs)	0.1

Discontinuation of warfarin among WATCHMAN® subjects: Among subjects successfully implanted with the WATCHMAN Device, 87% discontinued warfarin therapy by 45 days, and 93% discontinued warfarin therapy by 12 months.

PREVAIL Study

Primary Objective: To evaluate the safety and effectiveness of the WATCHMAN Device in subjects with atrial fibrillation who are deemed by their physicians to be suitable for long term warfarin therapy.

Design: The PREVAIL study was a multicenter, prospective, randomized controlled study comparing the WATCHMAN Device to long-term warfarin therapy. A 2:1 randomization allocation ratio (two Device subjects to one Control subject) was used with stratification by center. Subjects were eligible to participate in PREVAIL if they were at least 18 years of age, had non-valvular atrial fibrillation and were eligible for long-term warfarin therapy with a $CHADS_2$ score of at least 2. Subjects with a $CHADS_2$ score of 1 were also permitted to enroll if they had any of the following characteristics (consistent with the recommendations presented in the ACC/AHA/ESC 2006 Guidelines for the Management of Patients with Atrial Fibrillation):

- The subject was female age 75 or older.
- The subject had a baseline LVEF ≥30% and <35%.
- The subject was age 65-74 and had diabetes or coronary artery disease.
- The subject was age 65 or greater and had documented congestive heart failure.

A roll-in phase permitted physicians to gain experience with the WATCHMAN implant procedure. Subjects randomized to receive the WATCHMAN Device underwent TEE at 45 days, 6-, and 12-months after successful device implantation. Subjects randomized to the Control group were to remain on warfarin with INR monitoring every other week through 6 months and monthly thereafter. All randomized subjects underwent follow-up at 45 days, 6-, 9-, and 12-months, semiannually through 3 years and annually thereafter through 5 years.

This study had three primary endpoints:

- First primary endpoint: The 18-month rates of the composite of stroke (including hemorrhagic or ischemic), systemic embolism, and cardiovascular or unexplained death. The non-inferiority success criterion for the WATCHMAN group vs. the control group was a rate ratio of less than 1.75 with posterior probability of at least 97.5% (or equivalently that the upper bound of the equitailed 2-sided 95% credible interval for the 18-month rate ratio would be less than 1.75).
- Second primary endpoint: The 18-month rates of ischemic stroke or systemic embolism excluding the first 7 days post-randomization. The non-inferiority success criterion for the WATCHMAN group vs. the control group was either: (1) a rate ratio of less than 2.0, or (2) a rate difference of less than 0.0275, each with a posterior probability of at least 97.5% (or equivalently that (1) the upper bound of the equitailed 2-sided 95% credible interval for the 18-month rate ratio would be less than 2.0 or (2) the upper bound of the equitailed 2-sided 95% credible interval for the 18-month rate difference would be less than 0.0275).
- Third primary endpoint: The percentage of WATCHMAN subjects that experienced one of the following events between the time of randomization and within 7 days of the procedure or by hospital discharge, whichever was later: all-cause death, ischemic stroke, systemic embolism, or device or procedure-related events requiring open cardiac surgery or major endovascular intervention such as pseudoaneurysm repair, AV fistula repair, or other major endovascular repair. The following events were not included in the assessment of this endpoint: percutaneous catheter drainage of pericardial effusions, snaring of an embolized device, thrombin injection to treat a femoral pseudoaneurysm, and non-surgical treatments of access site complications. The third primary endpoint event rate was compared to a performance goal of 2.67%.

A Bayesian approach based on a piecewise exponential model was used to evaluate the first and second primary endpoints based on time to first event. In addition, this approach included prior PROTECT AF historical data at 1,500 patient-years of follow-up from subjects with the same $CHADS_2$ enrollment criteria as the PREVAIL subjects with a discounting weight of 50%. For the third primary endpoint, a Bayesian approach based on a beta-binomial model was used to incorporate historical data from the PROTECT AF study and CAP registry through a prior distribution (without discounting) from subjects with the same $CHADS_2$ score enrollment criteria as the PREVAIL subjects.

Enrollment: The study enrolled 461 subjects with 407 randomized and the remaining 54 participating in the WATCHMAN roll-in group. Of the 407 randomized subjects, 269 were assigned to the WATCHMAN group and 138 assigned to the warfarin control group as shown in **Table 11**.

Table 11. PREVAIL Enrollment Summary

Group	N
WATCHMAN Group	
Randomized	269
Implant Attempt*	265
Implanted	252
No Implant Attempt	4
Control Group	
Randomized	138
Roll-in Group	
Enrolled	54
Implant Attempt*	54
Implanted	51
No Implant Attempt	0

*Implant attempt is defined as venous access.

Subject Demographics and Baseline Clinical Features: For subjects randomized to the WATCHMAN group, the mean $CHADS_2$ score was 2.6 ± 1.0, the mean CHA_2DS_2-VASc score was 3.8 ± 1.2, the mean age was 74 years, 68% were male, and 94% were Caucasian. For subjects randomized to the Control group, the mean $CHADS_2$ score was 2.6 ± 1.0, the mean CHA_2DS_2-VASc score was 3.9 ± 1.2, the mean age was 75 years, 75% were male, and 95% were Caucasian. The two treatment groups had no statistically significant differences in baseline demographic and clinical characteristics as shown in **Tables 2** and **3**.

Results: WATCHMAN Device implant success (defined as successful release of the device) was achieved in 252/265 (95%) subjects who underwent the implant procedure.

The term "PREVAIL Only" refers to data from subjects enrolled in the PREVAIL study without the prior PROTECT AF study information used in the Bayesian analysis.

The pre-specified analyses were based on the data available at 6 months following the completion of enrollment. When this was achieved in the January 2013 dataset, the PREVAIL Only subject mean follow-up post-randomization was 11.8 ± 5.8 months, and 113 of 407 (28%) randomized subjects reached or passed the window for their 18-month follow-up visit. Final follow-up was completed in October of 2017, with the PREVAIL Only subject mean follow-up was 49.4 months, and 272 of 407 randomized subjects completed the 5 year follow-up visit (**Table 12**).

Table 12. Total Patient-Years for PREVAIL-Only Subjects and Prior Data Borrowed from PROTECT AF With 50% Discount

Dataset	PREVAIL-Only data in pt-yrs			PROTECT AF Prior Information in pt-yrs		
	WATCHMAN	Control	Total	WATCHMAN	Control	Total
Pre-specified: January 2013	256.2	140.0	396.2	395.3	223.5	618.8
Final: October 2017 (final)	1119.5	556.42	1675.9	395.3	223.5	618.8

First Primary Endpoint: Results of the Bayesian analysis for the first primary endpoint of all stroke (ischemic and hemorrhagic), systemic embolism, and death (cardiovascular or unexplained) are shown in **Table 13**. The 18-month rate is the model-based probability of an event occurring within 18 months.

Table 13. PREVAIL First Primary Endpoint Results (Intent-to-Treat)

Bayesian Approach	WATCHMAN 18-Month Rate	Control 18-Month Rate	18-Month Rate Ratio (95% CrI)	Posterior Probability of NI	Rate Ratio NI Criterion 95% CrI Upper Bound <1.75 (Post Probability ≥97.5%)
Pre-specified: Prior PROTECT AF information (618.8 pt-yrs) + PREVAIL-Only January 2013 Dataset (396.2 pt-yrs)	0.064	0.063	1.07 (0.57, 1.89)	95.69%	No
Final: Prior PROTECT AF PREVAIL-Only October 2017 Dataset (1626 pt-yrs)	0.066	0.051	1.33 (0.78, 2.13)	88.39%	No

CrI = credible interval, NI = non-inferiority

In the January 2013 pre-specified Bayesian analysis, the 18-month event rate was 0.064 for the WATCHMAN group and 0.063 for the control group. The Bayesian estimate for the 18-month rate ratio was 1.07 with a 95% credible interval of 0.57 to 1.89. Since the upper bound of 1.89 was not lower than the non-inferiority margin of 1.75 defined in the statistical analysis plan, the non-inferiority criterion was not met (the posterior probability of non-inferiority was 95.69%). At final follow-up, the Bayesian rate for the 18-month rate ratio was 1.33 with a 95% credible interval of 0.78 to 2.13. Since the upper bound of 2.13 was not lower than the 1.75 non-inferiority margin, the non-inferiority criterion was still not met (posterior probability of non-inferiority was 88.39%).

The primary effectiveness endpoint analysis from the final PREVAIL-Only subjects is shown as time to event in a Kaplan-Meier curve in **Figure 2.**

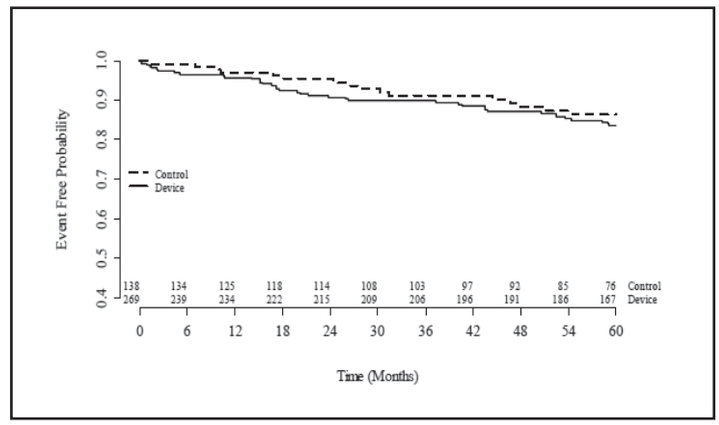

Figure 2. PREVAIL-Only Subjects – First Primary Endpoint Event

Table 14 shows the individual event rates of the composite endpoint for PREVAIL-Only subjects. The ischemic stroke rate (1.7 vs. 0.7 per 100 pt-years) favored the Control group, while the hemorrhagic stroke rate (0.2 vs. 0.5 per 100 pt-years) favored WATCHMAN®, and death (cardiovascular or unexplained) rate (1.9 vs. 2.0 per 100 pt-years) was equivalent.

Table 14. PREVAIL Effectiveness Results and % of subjects who experienced 1 or more events – Final Dataset (PREVAIL-Only Subjects)

Randomization Allocation (2 Device: 1 Control)

	WATCHMAN		Control	
Component of First Primary Endpoint	**Event Rate (per 100 Pt-yrs)**	**N Events / Subjects (%)**	**Event Rate (per 100 Pt-yrs)**	**N Events / Subjects (%)**
Stroke - Ischemic	1.7 (18/1075)	18/269 (6.7%)	0.7 (4/547)	4/138
Stroke - Hemorrhagic	0.2 (2/1119)	2/269 (0.7%)	0.54 (3/554)	3/138
Systemic Embolism	0.1 (1/1116)	1/269 (7.8%)	0 (0/557)	0/138
Death (Cardiovascular or Unexplained)	1.9 (21/1119.5)	21/269 (7.8%)	1.9 (11/557)	11/138
Ischemic Stroke and Systemic Embolism	1.8 (19/1070.5)	19/269 (7.0%)	1.3 (7/543.2)	4/138
All stroke	1.9 (20/1073.9)	20/269 (7.4%)	0.7 (4/546.1)	7/138

Second Primary Endpoint: Results of the Bayesian analysis for the second primary endpoint are shown in **Table 15**. The 18-month rate is the model-based probability of an event occurring within 18 months.

Table 15. PREVAIL Second Primary Endpoint Results (Intent-to-Treat)

Bayesian Approach	WATCHMAN 18-Month Rate	Control 18-Month Rate	18-Month Rate Ratio (95% CrI) (Posterior Prob)	18-Month Rate Difference (95% CrI) (Posterior Prob)	Rate Ratio Non-Inferiority Criterion or Rate Difference Non-Inferiority Criterion 95% CrI Upper Bound <0.0275
Pre-specified: Prior PROTECT AF information (618.8 pt-yrs) + PREVAIL-Only January 2013 Dataset (396.2 pt-yrs)	0.0253	0.0200	1.6 (0.5, 4.2) 77.2%	0.0053 (-0.0190, 0.0273) 97.6%	Yes
Final: Prior PROTECT AF information (618.8 pt-yrs) + PREVAIL-Only October 2017 Dataset (1626 pt-yrs)	0.0255	0.0135	2.2 (0.8, 4.9) 52.1%	0.0120 (-0.0036, 0.02748) 97.5%	Yes

CrI = credible interval

In the January 2013 pre-specified Bayesian analysis, the 18-month rate was 0.0253 for the WATCHMAN group and 0.0200 for the control group. The non-inferiority criterion was met for the rate difference of 0.0053 with an upper bound of 0.0273, which was less than the allowable 95% credible interval upper bound of 0.0275. The non-inferiority criterion was not met for the rate ratio of 1.6 with an upper bound of 4.2, which exceeded the allowable 95% credible interval upper bound of 2.0.

In the final Bayesian analysis, the 18-month rate was 0.0255 for the WATCHMAN group and 0.0135 for the control group. The non-inferiority criterion was met for the rate difference (0.0120 with an upper bound of 0.02748, which was less than the allowable 95% credible interval upper bound of 0.0275), with a posterior probability for non-inferiority of 97.5%. The non-inferiority criterion was not met for the rate ratio of 2.2 with an upper bound of 4.9, which exceeded the allowable 95% credible interval upper bound of 2.0 (posterior probability for non-inferiority of 52.1%).

The second effectiveness endpoint for the PREVAIL-Only subjects (final dataset) is shown as time to event analysis in a Kaplan Meier curve in **Figure 3**.

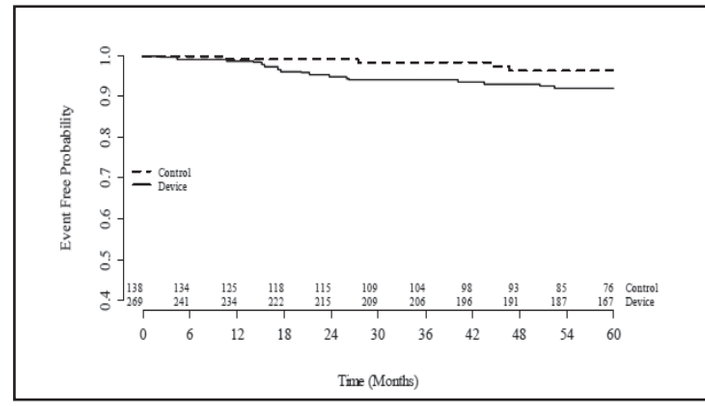

Figure 3. PREVAIL-Only Subjects – Second Primary Endpoint Event

Third Primary Endpoint: Of 269 PREVAIL-Only WATCHMAN subjects, 6 experienced a third primary endpoint event between the time of randomization and within 7 days of the procedure or by hospital discharge, corresponding to an event rate of 2.2% (**Table 16**).

Table 16. PREVAIL Third Primary Endpoint Results (Intent-to-Treat)

WATCHMAN Group		
N Subjects	**% (n/N)**	**95% CrI**
269	2.2% (6/269)	2.652%

CrI is one-sided, N = number, CrI = credible interval

Based on the Bayesian analysis incorporating prior information from PROTECT AF and CAP via a beta-binomial model, the one-sided 95% credible interval upper bound was 2.652%, which met the performance goal of 2.67%. The third primary endpoint events occurring in 6 PREVAIL-Only subjects are shown in **Table 17**.

Table 17. Third Primary Endpoint Events by Type of Initial Event (Intent-to-Treat)

PREVAIL-Only WATCHMAN Group N=269		
Type	**N Events**	**% of Subjects**
Device Embolization	2	0.7%
AV Fistula	1	0.4%
Cardiac Perforation	1	0.4%
Pericardial Effusion with Cardiac Tamponade	1	0.4%
Major Bleed Requiring Transfusion	1	0.4%

PREVAIL-Only Major Bleeding Analysis: The rates of major bleeding complications, defined as events adjudicated as serious adverse events, are shown in **Table 18**. There were more bleeding events in the WATCHMAN group immediately post-procedure through 45 days, an equivalent rate of bleeding through 6 months, and a lower rate 6 months post-procedure. The overall major bleeding rates were lower in the WATCHMAN group versus the Control Group.

Table 18. PREVAIL-Only Major Bleeding

	WATCHMAN		Control	
Major Bleeding	**N Events/ Subjects (%)**	**Rate per 100 Pt-yrs (N Events/ Total Pt-yrs)**	**N Events/ Subjects (%)**	**Rate per 100 Pt-yrs (N Events/ Total Pt-yrs)**
Procedure-related	12/269 (4.5%)	N/A	N/A	N/A
Non-procedure related	24/269 (8.9%)	2.3 (24/1051.4)	22/138 (15.9%)	4.3 (22/506.1)
0-45 days	7/269 (2.6%)	21.9 (7/32.0)	0/138 (0.0%)	0.0 (0/169)
46 days – 6 months	6/269 (2.4%)	0.6 (6/1019.4)	3/138 (2.2%)	0.6 (3/489.2)
>6 months	11/269 (4.8%)	1.2 (11/930.9)	19/138 (14.5%)	4.3 (19/438.8)
Total major bleeding	35/269 (13.0%)	3.5 (35/1012.6)	21/138 (15.2%)	4.1 (21/509.6)

Serious Adverse Events: A summary of all serious adverse events for the WATCHMAN and Control groups is presented in **Table 19**. Serious adverse events related to the WATCHMAN Device or implant procedure are shown in **Table 4**.

Table 19. PREVAIL-Only Serious Adverse Events

	WATCHMAN® N=269				Control N=138			
Event Type	**Events**	**% of Events**	**Subjects with Events**	**% of Subjects**	**Events**	**% of Events**	**Subjects with Events**	**% of Subjects**
AV Fistula	1	0.7	1	0.4	0	0	0	0
Anemia Requiring Transfusion	4	2.8	4	1.5	0	0	0	0
Bleeding, Other	0	0	0	0	2	3.1	2	1.4
Cardiac Perforation	1	0.7	1	0.4	0	0	0	0
Cranial Bleed	1	0.7	1	0.4	0	0	0	0
Death	42	29.6	42	15.6	29	44.6	29	21.0
Device Embolization	2	1.4	2	0.7	0	0	0	0
Device Thrombus	1	0.7	1	0.4	0	0	0	0
Endocarditis	1	0.7	1	0.4	0	0	0	0
Epistaxis	2	1.4	1	0.4	2	3.1	2	1.4
Gastrointestinal Bleeding	20	14.1	19	7.1	12	18.5	12	8.7
Hematoma	2	1.4	2	0.7	1	15	1	0.7
Hematuria	1	0.7	1	0.4	2	3.1	2	1.4
Infection	3	2.1	3	1.1	0	0	0	0
Major Bleed Requiring Transfusion	8	5.6	8	3.0	4	6.2	4	2.9
Other Study Related	7	4.9	6	2.2	1	1.5	1	0.7
Pericardial Effusion with Cardiac Tamponade	4	2.8	4	1.5	0	0	0	0
Pseudoaneurysm	1	0.7	1	0.4	0	0	0	0
Rectal Bleeding	2	1.4	2	0.7	1	1.5	1	0.7
Respiratory Failure	4	2.8	4	1.5	0	0	0	0
Respiratory Insufficiency	1	0.7	1	0.4	0	0	0	0
Stroke - Hemorrhagic	2	1.4	2	0.7	3	4.6	3	2.2
Stroke - Ischemic	20	14.1	18	6.7	6	9.2	4	2.9
Subdural Hematoma	2	1.4	2	0.7	0	0	0	0
Systemic Embolism	1	0.7	1	0.4	0	0	0	0
Transient Ischemic Attack (TIA)	9	6.3	8	3.0	2	3.1	2	1.4

PREVAIL-Only Device Thrombus Rates

The device thrombus-related stroke rate was 0.3 events per 100 patient-years as shown in **Table 20.**

Table 20. PREVAIL-Only Device-related Thrombus

	N=252
Thrombus Subjects	16 (6.4%)
Thrombus Events	17
Experienced Ischemic Stroke	3
Experienced Serious Adverse Event	5
Device Thrombus-related Stroke Rate (per 100 pt-yrs)	0.3

Discontinuation of warfarin among WATCHMAN subjects: Among subjects successfully implanted with the WATCHMAN Device and followed for at least 12 months, 92% discontinued warfarin therapy by 45 days, and 99% discontinued warfarin therapy by 12 months.

CAP Registry

Primary Objective: To collect additional safety and effectiveness data on the WATCHMAN Device in subjects with non-valvular atrial fibrillation who are deemed by their physicians to be suitable for warfarin therapy.

Design: The CAP registry was a multi-center prospective non-randomized study allowing continued access to the WATCHMAN Device during regulatory review of the pre-market application for the WATCHMAN Device. Up to 30 investigative centers with prior WATCHMAN Device experience in the PROTECT AF study were allowed to participate. Study participants were required to be at least 18 years of age with non-valvular atrial fibrillation, have a $CHADS_2$ score of 1 or greater, and be eligible for long-term warfarin therapy. Following baseline evaluation and device implantation, subjects were seen at 45 days, at 6-, 9-, and 12-month visits, and semi-annually thereafter through 5 years.

The endpoints of the CAP registry were identical to those in the PROTECT AF study, but there were no pre-defined statistical hypotheses. The primary effectiveness endpoint was the rate of the composite of stroke (including ischemic and hemorrhagic), systemic embolism, and cardiovascular death (cardiovascular or unexplained). The primary safety endpoint was the rate of life-threatening events as determined by the CEC, which included device embolization requiring retrieval, bleeding events such as pericardial effusion requiring drainage, cranial bleeding events due to any source, gastrointestinal bleeding requiring transfusion, and any bleeding related to the device or procedure that necessitated a surgical procedure.

Enrollment: A total of 26 centers (24 U.S., 2 European) participated by enrolling at least one subject. A total of 566 subjects were enrolled. The average $CHADS_2$ score was 2.5 ± 1.2, the mean CHA_2DS_2-VASc score was 3.9 ± 1.5, the mean age was 74 years, and 66% of subjects were male as shown in **Tables 2** and **3**.

The CAP Registry is complete. Follow-up of the 566 subjects was 2293 patient-years.

Results: The WATCHMAN Device was successfully implanted in 534/566 (94%) subjects. For the primary effectiveness endpoint, a rate of 3.1 events/100 patient-years was observed, with cardiovascular or unexplained death and ischemic stroke being the two most common events over a mean follow-up duration of 50.1 months as shown in **Tables 21** and **22**. The primary safety rate was 3.1 events per 100-patient years.

Table 21. CAP Primary Effectiveness Endpoint (2293 Patient Years)

Event Type	Rate Per 100 Pt-yrs (N Events/Pt-yrs)	95% CI
Primary Effectiveness	3.1 (70/2292.5)	2.4, 3.9
Primary Safety	3.1 (66/2160.9)	2.4, 3.9

Table 22. CAP Effectiveness Results and % of subjects who experienced 1 or more events

	Event Rate (per 100 Pt-yrs)	N Events/ Subjects (%)
Stroke - Ischemic	1.30 (30/2300.1)	5.3% (30/566)
Stroke - Hemorrhagic	0.17 (4/2359.1)	0.7% (4/566)
Systemic Embolism	0.04 (1/2359.8)	0.2% (1/566)
Death (Cardiovascular or Unexplained)	1.69 (40/2363.2)	6.2% (35/566)

CAP Major Bleeding Analysis: The rates of major bleeding complications, defined as events adjudicated as serious adverse events, are shown in **Table 23**.

Table 23. CAP Major Bleeding

WATCHMAN		
Major Bleeding	**N Events/ Subjects (%)**	**Rate per 100 Pt-yrs (N Events/ Pt-yrs)**
Procedure-related	18/566 (3.2%)	N/A
Non-procedure related	68/566 (12.0%)	3.1 (68/2179.2)
0-45 days	14/566 (2.5%)	20.4 (14/68.6)
46 days – 6 months	14/566 (2.5%)	0.7 (14/2110.6)
>6 months	40/566 (8.0%)	2.1 (40/1918.8)
Total major bleeding	81/566 (14.3%)	3.8 (81/2125.0)

Serious Adverse Events:

A summary of all serious adverse events for the WATCHMAN is presented in **Table 24**. Serious adverse events related to the WATCHMAN Device or implant procedure are provided in **Table 4**.

Table 24. CAP Registry Serious Adverse Events

Event	Number of Events	Number of Subjects	% of Subjects N=566
Death	101	101	17.8%
Stroke - Ischemic	34	30	5.3%
Stroke - Hemorrhagic	5	4	0.7%
Systemic Embolization	1	1	0.2%
Gastrointestinal Bleeding	73	46	8.1%
Other Study Related	22	20	3.5%
Transient Ischemic Attack (TIA)	14	12	2.1%
Major Bleed Requiring Transfusion	9	8	1.4%
Pericardial Effusion with Cardiac Tamponade	7	7	1.2%
Anemia Requiring Transfusion	5	4	0.7%
Pericardial Effusion	5	5	0.9%
Pseudoaneurysm	5	5	0.9%
Prolonged Bleeding from a Laceration	3	3	0.5%
Cranial Bleed	1	1	0.2%
Epistaxis	2	2	0.4%
Hematuria	2	2	0.4%
Ventricular Tachyarrhythmia	2	2	0.4%
Arrhythmias	1	1	0.2%
Bruising - Hematoma	1	1	0.2%
Cardiac Perforation	1	1	0.2%
Chest Pain/ Discomfort	1	1	0.2%
Device Embolization	1	1	0.2%
Device Thrombus	1	1	0.2%
Rectal Bleeding	1	1	0.2%

CAP Device Thrombus Rates: The device thrombus-related stroke rate was 0.1 events per 100 patient-years as shown in **Table 25**.

Table 25. CAP Device-related Thrombus

	N=534
Thrombus Subjects	14 (2.6%)
Thrombus Events	21
Experienced Ischemic Stroke	2
Experienced Serious Adverse Event	10
Device Thrombus-related Stroke Rate (per 100 pt-yrs)	0.1

Discontinuation of warfarin among WATCHMAN® subjects: Among subjects successfully implanted with the WATCHMAN Device and followed for at least 12 months, 96% discontinued warfarin therapy by 45 days, and 96% discontinued warfarin therapy by 12 months.

CAP2 Registry

Primary Objective: To collect additional safety and effectiveness data on the WATCHMAN Device in subjects with non-valvular atrial fibrillation who are deemed by their physicians to be suitable for warfarin therapy.

Design: The CAP2 Registry is a multi-center prospective non-randomized study allowing continued access to the WATCHMAN Device during regulatory review of the pre-market application for the WATCHMAN Device. Up to 60 investigative centers with prior WATCHMAN experience in the PREVAIL study were allowed to participate. Study participants were required to be at least 18 years of age with non-valvular atrial fibrillation, be eligible for long-term warfarin therapy, and have a $CHADS_2$ score of at least 2. Subjects with a $CHADS_2$ score of 1 were also permitted to enroll if they had any of the following characteristics (consistent with the recommendations presented in the ACC/AHA/ESC 2006 Guidelines for the Management of Patients with Atrial Fibrillation):

- The subject was female age 75 or older.
- The subject had a baseline LVEF ≥30% and <35%.
- The subject was age 65-74 and had diabetes or coronary artery disease.
- The subject was age 65 or greater and had documented congestive heart failure.

Following baseline evaluation and device implantation, subjects were seen at 45 days, 6- and 12-month visits, and semi-annually through 3 years and annually thereafter through 5 years.

The endpoints of the CAP2 registry were similar to those used in the PREVAIL study, but there were no pre-defined statistical hypotheses. There were three primary endpoints (two effectiveness and one safety) as follows: 1) the rate of the composite of stroke (including hemorrhagic and ischemic), systemic embolism, and cardiovascular or unexplained death; 2) the rate of the composite of ischemic stroke and systemic embolism, excluding events occurring in the first 7 days following device implantation; and 3) the occurrence of all-cause mortality, ischemic stroke, systemic embolism, or device or procedure related events requiring open cardiac surgery or major endovascular intervention between the time of randomization and 7 days of the procedure or by hospital discharge, whichever was later.

Demographics: A total of 47 U.S. investigational sites actively participated by enrolling at least one subject in the study. A total of 576 subjects were enrolled. The average $CHADS_2$ score was 2.7 ± 1.1, the mean CHA_2DS_2-VASc score was 4.5 ± 1.3, the mean age was 75 years, and 61% of subjects were male as shown in **Table 2**.

Values presented are mean ± standard deviation, n (minimum, maximum) or number of subjects/total number of subjects (%) as appropriate.

The CAP Registry is complete. Follow-up of the 576 subjects was 2329 patient-years.

Table 26. CAP2 First Primary Endpoint (2227 Patient Years)

Rate Per 100 Pt-yrs (N Events/Pt-yrs)	95% CI for Rate
4.8 (107/2220.5)	(4.0, 5.8)

Table 27. CAP2 Effectiveness Results and % of subjects who experienced 1 or more events

	Event Rate (per 100 Pt-yrs)	Event Rate/ Subject
Stroke - Ischemic	2.2 (49/2230.0)	8.5% (49/576)
Stroke - Hemorrhagic	0.1 (2/2322.2)	0.3% (2/576)
Systemic Embolism	0.1 (2/2324.3)	0.3% (2/576)
Death (Cardiovascular or Unexplained)	2.9 (68/2329.6)	12.0% (69/576)

Second Primary Endpoint: A rate of 2.2 events/100 patient-years was observed, with ischemic stroke being the most common event over a mean follow-up duration of 50.3 months as shown in **Tables 28** and **29**.

Table 28. CAP2 Second Primary Endpoint (2329 Patient Years)

Rate Per 100 Pt-yrs (N Events/Pt-yrs)	95% CI for Rate
2.2 (49/2227.0)	(1.7, 2.9)

Table 29. CAP2 Events Contributing to Second Primary Endpoint

Endpoint Event Type	N Events	% of Subjects N=576
Stroke - Ischemic	53	8.1%
Systemic Embolism	2	0.3%

Third Primary Endpoint: Eight subjects experienced a third primary endpoint event between time of enrollment and within 7 days of procedure or by hospital discharge corresponding to an event rate of 1.4% as shown in **Tables 30** and **31**.

Table 30. CAP2 Third Primary Endpoint

N Subjects	% (n/N)	95% CI
576	1.4% (8/576)	(0.6%, 2.7%)

Table 31. CAP2 Events Contributing to Third Primary Endpoint

Type	N Events	% of Subjects N=576
Cardiac Perforation	3	0.5%
Death	1	0.2%
Major Bleeding Requiring Transfusion	1	0.2%
Myocardial Infarction	1	0.2%
Stroke (Ischemic)	1	0.2%
Valvular Damage	1	0.2%

Serious Adverse Events: A summary of all adjudicated serious adverse events for the WATCHMAN is presented in **Table 32**. Serious adverse events related to the WATCHMAN Device or implant procedure are provided in **Table 4**.

Table 32. CAP2 Registry Serious Adverse Events

Type	N Events	% (N Pats with Event/ 576) N=576
Anemia Requiring Transfusion	11	1.4% (8/576)
Pericardial Effusion with Cardiac Tamponade	8	1.4% (8/576)
Subdural Hematoma	8	1.4% (8/576)
Hematoma	7	1.0% (6/576)
Death - Non-Cardiovascular	76	13.2% (76/576)
Death - Cardiovascular/Unexplained	68	11.8% (68/576)
Cranial Bleed	6	1.0% (6/576)
Stroke (Ischemic)	51	7.8% (45/576)
Rectal Bleeding	5	0.9% (5/576)
Cardiac Perforation	3	0.5% (3/576)
Myocardial Infarction	3	0.5% (3/576)
Ventricular Fibrillation	3	0.5% (3/576)
Pseudoaneurysm	3	0.5% (3/576)
Major Bleed Requiring Transfusion	32	4.3% (25/576)
Device Thrombus (thrombus on the atrial facing side of the device)	25	3.6% (21/576)
Other (Non-Study Related)	31	5.4% (31/576)
Gastrointestinal Bleeding	25	3.8% (22/576)
Oral Bleeding	2	0.3% (2/576)
Bleeding, Other	2	0.3% (2/576)
Respiratory Insufficiency	2	0.3% (2/576)
Stroke (Hemorrhagic)	2	0.3% (2/576)
Systemic Embolism	2	0.3% (2/576)
Infection	3	0.5% (3/576)
Respiratory Failure	20	3.5% (20/576)
Other (Study Related)	14	2.4% (14/576)
Pericardial Effusion	13	2.3% (13/576)
Epistaxis	12	1.6% (9/576)
Hematuria	10	1.6% (9/576)
Transient Ischemic Attack (TIA)	12	2.1% (12/576)
Bleeding from Varicose Veins	1	0.2% (1/576)
Hemothorax	1	0.2% (1/576)
Valvular Damage	1	0.2% (1/576)
Arrhythmias	1	0.2% (1/576)

CAP2 Device Thrombus Rates:

The device thrombus-related stroke rate was 0.2 events per 100 patient-years as shown in **Table 33**.

Table 33. CAP2 Device-related Thrombus

	N=545
Thrombus Subjects	21 (3.9%)
Thrombus Events	25
Experienced Ischemic Stroke	4
Experienced Serious Adverse Event	6
Device Thrombus-related Stroke Rate (per 100 pt-yrs)	0.2

Discontinuation of warfarin among WATCHMAN subjects: The CAP2 Registry is ongoing and data collection is ongoing. Among subjects successfully implanted with the WATCHMAN Device and followed for at least 12 months, 93% discontinued warfarin therapy by 45 days, and 97% discontinued warfarin therapy by 12 months.

NESTed Surveillance Analysis Plan (SAP)

Primary Objective: To assess long-term safety and effectiveness outcomes associated with the use and implantation of the WATCHMAN Left Atrial Appendage (LAA) Closure Technology in a routine clinical setting.

Design: The WATCHMAN New Enrollment PoST Approval Surveillance Analysis Plan (NESTed SAP) is a multi-center, prospective, non-randomized registry utilizing data captured in the Left Atrial Appendage

Occlusion Registry (LAAO Registry) within the American College of Cardiology Foundation's (ACCF) National Cardiovascular Data Registry (NCDR). Two cohorts of 1,000 patients (primary and secondary) will be included in the analysis. The Primary Cohort will consist of subjects who are eligible for a WATCHMAN® Device according to current U.S. indications with a calculated $CHADS2_2$score of ≥2 or a CHA_2DS_2-VASc score of ≥3 and exclude any patients who are contraindicated for a WATCHMAN Device according to this document or patients with concomitant cardiac or non-cardiac procedures (including, but not limited to: cardiac ablation, trans-catheter valve implantation, coronary intervention, etc.). Once the primary cohort is complete, the next consecutive 1,000 patients implanted will be included in the secondary cohort.

The pre-specified primary efficacy endpoints will only be applied to the primary cohort and are as follows: 1) the rate of stroke (including ischemic and/or hemorrhagic), all-cause death and systemic embolism at 24 months, 2) the rate of ischemic stroke or systemic embolism at 24 months as adjudicated by the Clinical Events Adjudication Team. The formal analysis of these endpoints will take place after all patients have completed the 24-month follow-up.

The Primary Safety event rate is calculated as the percent of all implanted or attempted patients who experience a Primary Safety event, defined as occurrence of one of the following events between the time of first implant procedure and within 7 days of the procedure or by hospital discharge, whichever is later: all-cause death, ischemic stroke, systemic embolism, or device or procedure-related events requiring open cardiac surgery or major endovascular intervention such as pseudoaneurysm repair, AV fistula repair, or other major endovascular repair. Percutaneous catheter drainage of pericardial effusions, snaring of an embolized device, thrombin injection to treat femoral pseudoaneurysm and nonsurgical treatments of access site complications are excluded from this endpoint. Events related to subsequent WATCHMAN implant procedures are also excluded from this endpoint.

Demographics: A total of 1,000 subjects were enrolled in the primary cohort. The mean $CHADS_2$ score was 3.2 ± 1.2, the mean CHA_2DS_2-VASc score was 5.0 ± 1.4, the mean HAS-BLED score was 2.7 ± 1.1, the mean age was 76.5 years, and 62% of subjects were male as shown in **Tables 2** and **3**.

The NESTed SAP is ongoing. Current follow-up of the primary cohort is a median of 12 months and 838.9 patient-years.

Results: The WATCHMAN Device was successfully implanted in 947/993 (95%) subjects. The first and second primary endpoint will be evaluated after all patients complete 2 years of follow-up.

Third Primary Endpoint: Fifteen subjects experienced a third primary endpoint event between time of enrollment and within 7 days of procedure or by hospital discharge corresponding to an event rate of 1.5% as shown in **Tables 34** and **35**.

Table 34. NESTed Third Primary Endpoint

N Subjects	% (n/N)	95% CI
1000	1.5% (15/1000)	2.3%

CrI is one-sided, N = number, CrI = credible interval

The one-sided 95% confidence interval upper bound was 2.3%, which met the performance goal of 3.36% (p=0.0002). The 17 third primary endpoint events that occurred in 15 NESTed Subjects are shown in **Table 35**.

Table 35. Third Primary Endpoint Events by Type of Initial Event (Intent-to-Treat)

NESTed Primary Cohort N=1000		
Type	**N Events**	**% of Subjects**
Pericardial Effusion (requirement open cardiac surgery)	1	0.1%
Death*	4	0.4%
Ischemic stroke	2	0.2%
Surgery (unspecified)	5	0.5%
Systemic Thromboembolism (other than stroke)	2	0.2%
Retroperitoneal Bleeding	3	0.3%

*The 4 deaths were adjudicated as follows: 2 pulmonary, 1 stroke, and 1 sudden cardiac death.

PINNACLE FLX Study

Primary Objective: The primary objective of this study is to establish the safety and effectiveness of the WATCHMAN FLX™ Left Atrial Appendage Closure (LAAC) Device for subjects with non-valvular atrial fibrillation who are eligible for non-vitamin K antagonist oral anticoagulation (NOAC) therapy to reduce the risk of stroke.

Design: PINNACLE FLX is a prospective, non-randomized, multi-center investigation to establish the safety and effectiveness of the WATCHMAN FLX LAA Closure Device for subjects with non-valvular atrial fibrillation who are eligible for NOAC anticoagulation therapy to reduce the risk of stroke but have a rationale to seek a non-pharmacologic alternative.

Main study entry criteria included, but were not limited to, at least 18 years of age with non-valvular atrial fibrillation, be eligible for short-term OAC therapy, and have a CHA_2DS_2-VASc score of at least 2 for males and 3 for females. Following baseline evaluation and device implantation, subjects are seen at 45 days, at 6-, 12-, 18-, and 24-month visits. Implanted subjects underwent TEE at 45 days and 12-month visits. Investigators include physicians with WATCHMAN implant experience. Sites were limited to two implanting investigators per institution. All sites were required to enroll two roll-in subjects prior to enrollment in the main cohort of subjects.

The study had two primary endpoints:

1) Effectiveness: the rate of effective LAA closure defined as any peri-device leak ≤ 5mm demonstrated by TEE at 12 months; and
2) Safety: the occurrence of all-cause mortality, ischemic stroke, systemic embolism, or device or procedure related events requiring open cardiac surgery or major endovascular intervention between the time of implant and 7 days following the procedure or by hospital discharge, whichever was later.

Due to the similarities in the WATCHMAN Closure Device with Delivery System and WATCHMAN FLX Closure Device with Delivery System designs, the results of the PINNACLE FLX study are applicable to the WATCHMAN Closure Device with Delivery System and support use of NOACs with the WATCHMAN Closure Device with Delivery System.

Enrollment: The study enrolled 508 subjects at 29 investigational centers in the United States between May 7, 2018 and November 9, 2018. Of these, 29 subjects failed the screening, and 21 subjects met the clinical eligibility criteria but did not undergo an implant. Of the remaining 458 subjects, there were 400 main cohort subjects and 58 roll-in subjects.

The PINNACLE FLX study is ongoing. Average follow-up of the 400 main cohort patients was 12.8 months at the time of the primary analysis. The secondary endpoint (the occurrence of ischemic stroke or systemic embolism at 24 months from the time of implant) will be evaluated after all patients complete 2 years of follow-up.

The PINNACLE FLX follow-up attendance is presented in **Table 36**.

Table 36. Visit Compliance Main Cohort

Visit	All Enrolled Subjects(N=400)
45-day	100.0% (400/400)
6-month	96.1% (370/385)
12-month	95.4% (355/372)
18-month	91.5% (86/94)
24-month	N/A
Values presented are % (# visits observed / # visits expected).	

Demographics and Baseline Clinical Features: The mean age of the main cohort was 73.8 ± 8.6 years, 35.5% were female, and 93.7% were Caucasian. The mean CHA_2DS_2-VASc score was 4.2 ± 1.5, and the mean HAS-BLED score was 2.0 ± 1.0.

Results: The WATCHMAN FLX Device was successfully implanted in 395/400 (98.8%) subjects who underwent the implant procedure.

Effectiveness: The primary efficacy endpoint is the rate of effective LAA closure defined as any peri-device leak ≤ 5mm demonstrated by TEE at 12 months. The primary efficacy endpoint was met with a rate of 100% (lower one-sided 95% CI = 99.1%), which was above the performance goal of 97%. These results are summarized in **Table 37**. At 45-day follow-up, 100% of subjects (389/389) exhibited adequate LAA closure. **Table 38** reports the rate of effective LAA closure (peri-device leak ≤ 5mm demonstrated by TEE) at implant, 45-day and 12-month.

Table 37: Primary Effectiveness Endpoint

Event	Event Rate (n/N)	Lower 1-sided 95% Confidence Interval	P Value
Primary effectiveness endpoint	100.0% (342/342)	99.1%	<0.0001

Table 38: LAA Closure (per Core Laboratory assessment)

Peri-device Leak	Implant	45 Days	12 Months
Jet size 0 ≤ 5mm	100.0% (376/376) [99.0%, 100.0%]	100.0% (389/389) [99.1%, 100.0%]	100.0% (344/344) [98.9%, 100.0%]
Jet size >0 and ≤ 5mm	7.4% (28/376) [5.0%, 10.6%]	17.2% (67/389) [13.6%, 21.4%]	10.5% (36/344) [7.4%, 14.2%]
Complete seal (i.e., Jet Size = 0 mm)	92.6% (348/376) [100%]	82.8% (322/389) [100%]	89.5% (308/344) [100%]
Jet size > 5mm	0.0% (0/376) [0.0%, 1.0%]	0.0% (0/389) [0.0%, 0.9%]	0.0% (0/344) [0.0%, 1.1%]
TEE deemed not evaluable for leak by Core Laboratory*	2.3% (9/385) [1.1%, 4.4%]	0.8% (3/392) [0.2%, 2.2%]	0.9% (3/347) [0.2%, 2.5%]

Data are % (n/N) [min, max]

*Site evaluation of TEEs assessed peri-device flow as < 5mm in all cases.

Safety: The primary safety endpoint was met with a rate of 0.5% (upper one-sided 95% CI=1.6%), which was below the performance goal of 4.21% (This is equivalent to Third Primary Endpoint from PREVAIL and CAP2). These results are summarized in **Table 39**. Two ischemic stroke events occurred within 7 days of the implant procedure.

Table 39: Primary Safety Endpoint

Event	Event Rate (n/N)	Upper 1-sided 95% Confidence Interval	P Value
Primary safety endpoint	0.5% (2/400)	1.6%	< 0.0001

Major Clinical Events: The CEC adjudicated all major clinical events, including: all-cause stroke and TIA, systemic embolism, all-cause death, major bleeding events (BARC 3 or 5), device embolization, device thrombus, and pericardial effusion resulting in an invasive intervention. A summary of CEC adjudicated Major Clinical Events reported through the time of data cutoff is presented in **Table 40**.

Table 40: PINNACLE FLX Major Clinical Events*

Event	Number of Events	Number of Subjects with an Event
All-cause death	27	27
Cardiovascular/ Unknown Death	16	16
All stroke	12	12
Ischemic stroke	11	11
Hemorrhagic stroke	1	1
Transient Ischemic Attack (TIA)	1	1
Systemic Embolism	1	1
Device Embolization	0	0
Device Thrombus	7	7
Pericardial Effusion (PE) resulting in invasive intervention	5	5
PE requiring open cardiac surgery	0	0
PE requiring pericardiocentesis or pericardial puncture	4	4
Major Bleeding (BARC 3 or 5)	36	32
BARC 3 bleeding	34	30
BARC 5 bleeding	2	2

* Please note, due to differences in methodologies for event adjudication and for assessment of device/procedure relatedness among the studies, the results of PINNACLE FLX (**Table 40**) are not directly comparable to the results of the studies in **Table 4**.

Table 41: Oral Anticoagulant (OAC) Use (Post-Implant through 45 Days)

OAC	Percent of Total % (n/N)
Apixaban	76.7% (303/395)
Rivaroxaban	20.3% (80/395)
Dabigatran	2.0% (8/395)
Warfarin/VKA[a]	0.5% (2/395)
Edoxaban	0.3% (1/395)
Nonea	0.3% (1/395)

[a]Documented as a protocol deviation

PINNACLE FLX Major Bleeding Analysis: The rates of major bleeding events, defined as CEC adjudicated BARC 3 or 5 as bleeding, are shown in **Table 42**.

Table 42: PINNACLE FLX Major Bleeding

	WATCHMAN FLX™	
Major Bleeding	N Events/ Subjects (%)	Rate Per 100 Pt-yrs (N Events/ Total Pt-yrs)
Procedure-related	1% (3/400)	0.07 (3/426.7)
Non-procedure related	7% (29/400)	6.8 (29/426.7)
0-45 days	2% (9/400)	2.1 (9/426.7)
46 days – 6 months	4% (16/400)	3.7 (16/426.7)
>6 months	1% (4/400)	0.9 (4/426.7)
Total major bleeding	8% (32/400)	7.5 (32/426.7)

Device or Procedure-Related Serious Adverse Events: A summary of device or procedure-related serious adverse events is presented in **Table 43.**

Table 43. Device or Procedure-Related Serious Adverse Events

	All Device or Procedure Related Events	
Type	**Events**	**% Subjects with Events**
Anemia requiring transfusion	1	0.3% (1/400)
Arrhythmias	2	0.3% (1/400)
Atrial Fibrillation (AF)	1	0.3% (1/400)
Death*	1	0.3% (1/400)
Device thrombus atrial facing – Post procedure	7	1.8% (7/400)
Fluid Overload	1	0.3% (1/400)
Gastrointestinal	1	0.3% (1/400)
Gastrointestinal bleeding	1	0.3% (1/400)
Peri-device leak[a]	10	2.5% (10/400)
Pericardial effusion	3	0.8% (3/400)
Prolonged bleeding from a laceration	1	0.3% (1/400)
Pulmonary	2	0.5% (2/400)
Respiratory insufficiency	1	0.3% (1/400)
Stroke (ischemic)	7	1.5% (6/400)
Systemic embolism	1	0.3% (1/400)
TEE/TTE related event	1	0.3% (1/400)
Thrombocytopenia	1	0.3% (1/400)
Total	**42**	**8.5% (34/400)**

Abbreviations: TEE, transesophageal echocardiography; TTE, transthoracic echocardiography

Device and procedure relationship were primarily based on site assessment; this evaluation could be changed based on CEC assessment. Individual n's may not add to total N if subject experienced multiple events.

[a]Core Laboratory evaluation of TEEs assessed peri-device leak as ≤ 5 mm in all cases.

*Cause of death (133 days following procedure): ischemic stroke. Autopsy revealed premortem thrombus on the surface of the left atrial appendage closure device.

PINNACLE FLX Device Thrombus Rates

The device-related thrombus stroke rate was 0.2 events per 100 patient-years as shown in **Table 44.**

Table 44 to PINNACLE FLX Device-related Thrombus

	N=400
Thrombus Subjects	7 (1.8%)
Thrombus Events	7
Experienced Ischemic Stroke	1
Experienced Serious Adverse Event	2
Device Thrombus-related Stroke Rate (per 100 pt-yrs)	0.2

Discontinuation of NOAC among WATCHMAN FLX subjects: The PINNACLE FLX trial and data collection are ongoing. Among subjects successfully implanted with the WATCHMAN FLX Device and followed for at least 12 months, 96.2% discontinued NOAC therapy by 45 days.

HOW SUPPLIED

- The WATCHMAN® Left Atrial Appendage Closure Device is pre-loaded in the Delivery System.
- The WATCHMAN products are supplied STERILE using an ethylene oxide (EO) process.
- Do not use if package is opened or damaged.
- Do not use if labeling is incomplete or illegible.
- WATCHMAN Access Systems are packaged separately.
- This device meets pyrogen limit specifications.

Note: Contents of inner package are STERILE.

Handling and Storage

Store in a cool, dry, dark place.

OPERATIONAL INSTRUCTIONS

Pre-Procedural Instructions

Baseline imaging should be performed to verify that a patient's anatomy is appropriate for a WATCHMAN Device to be implanted.

1. Perform the following in multiple views:

- Measure the LAA length and width at the ostium.
- Assess LAA size/shape, number of lobes and location of lobes relative to the ostium.
- Confirm the absence of thrombus.

Note: TEE imaging recommendations: Measure the LAA ostium at approximately these angles as anatomy permits:
- at 0° measure from coronary artery marker to a point approximately 2 cm from tip of the "limbus."
- at 45° measure from top of the mitral valve annulus to a point approximately 2 cm from tip of the "limbus."
- at 90° measure from top of the mitral valve annulus to a point approximately 2 cm from tip of the "limbus."
- at 135° measure from top of the mitral valve annulus to a point approximately 2 cm from tip of the "limbus."

2. Determine the maximum diameter

Note: Successful Closure Device sizing is dependent on multiple imaging views.

3 Use **Table 45** as a guide for device selection. Measured maximum LAA ostium width must be ≥17 mm or ≤31 mm to accommodate available device sizes

Note: Patient hydration can affect the size of the LAA.

Note: The maximum LAA ostium width and depth measurements determine Closure Device size selection.

PROCEDURAL INSTRUCTIONS

Equipment Needed for Implantation Procedure

- Venous Introducer (optional)
- Standard transseptal access system
- 0.035 inch guidewire (exchange length extra support)
- 5F or 6F angiographic pigtail catheter
- Any WATCHMAN Access System (Access Sheath and Dilator)

Implantation Procedure

Note: Aspirin should be started one day prior to scheduled procedure and continued daily.

Note: Use of fluoroscopy and echocardiographic imaging should be used when implanting the device (TEE is recommended as an aid in placing the WATCHMAN Device).

Note: Patients should be fully heparinized throughout the procedure with a recommended minimum activated clotting time (ACT) of 200-300 seconds recorded after transseptal puncture.

1. Use standard practice to puncture vessel and insert 0.035 in guidewire and vessel dilator. Use a standard transseptal access system to cross inter-atrial septum.
2. Exchange crossing sheath with exchange length extra support 0.035 in guidewire. Position guidewire in left upper pulmonary vein (LUPV) or loop in left atrium.
3. Prepare a WATCHMAN Access System

Note: Inspect sterile package and WATCHMAN Access System prior to use. If sterile barrier, labeling, packaging, or device have been compromised in any way, DO NOT USE.

A. Remove Access Sheath and Dilator from package under sterile conditions.
B. Inspect prior to use to ensure no damage.
C. Flush Access Sheath and Dilator with sterile saline prior to use.
D. Insert Dilator into hemostasis valve of Access Sheath until the two snap together.

Note: Do not tighten the hemostasis valve while the Dilator is inserted in the Access System. The Dilator by itself will occlude the lumen of the Access Sheath, creating hemostasis. Tightening the valve onto the Dilator may damage the valve threads, which can lead to subsequent difficulty in closing the valve and an incomplete seal once the Dilator is removed.

4. Advance a WATCHMAN Access System over guidewire into left atrium (LA). As the Access Sheath nears the center of LA, unsnap the Access Sheath from the Dilator, hold Dilator and advance Access Sheath into initial position in LA or ostium of LUPV.

Precaution: Use caution when introducing a WATCHMAN Access System to prevent damage to cardiac structures.

5. Remove Dilator and guidewire, leaving Access Sheath in LA or LUPV. Allow back bleed to minimize potential for introducing air before tightening valve. Flush the Access Sheath with saline.

If continued back bleed is observed from the valve after the Dilator is removed despite attempting to close it, loosen the valve cap (counter-clockwise rotation) until the cap spins freely. Then re-attempt closure of the valve while exerting gentle forward pressure on the valve cap during closure (clockwise rotation) to ensure proper engagement of the valve thread. While these steps are being undertaken, manual occlusion of the valve opening using a gloved finger is recommended to minimize blood loss.

Note: These steps may be repeated, if necessary. However, if this does not mitigate the blood leak, the user should remove and replace the WATCHMAN Access Sheath before proceeding with the procedure.

6. Confirm LAA size and select appropriate WATCHMAN Device. Transesophageal echocardiography (TEE) and fluoroscopy were used in most WATCHMAN clinical trials for selection of device size and implant guidance. There is limited evidence to support the use of ICE and fluoroscopy to guide LAAC implantation.

A. Perform the following in multiple views:

- Measure the LAA length and width at the ostium.
- Assess LAA size/shape, number of lobes and location of lobes relative to the ostium.
- Confirm the absence of thrombus.

Note: If using TEE, measure the LAA ostium at approximately these angles as anatomy permits:

- at 0° measure from coronary artery marker to a point approximately 2 cm from tip of the "limbus."
- at 45° measure from top of the mitral valve annulus to a point approximately 2 cm from tip of the "limbus."
- at 90° measure from top of the mitral valve annulus to a point approximately 2 cm from tip of the "limbus."
- at 135° measure from top of the mitral valve annulus to a point approximately 2 cm from tip of the "limbus."

B. Choose a device based on **maximum** LAA ostium width recorded. The LAA depth must be at least as long as the LAA ostium width. Use **Table 45** as a guide.

Note: LAA anatomy should accommodate a single WATCHMAN® Device as described in **Table 45**.

Table 45: WATCHMAN Device Selection

Max LAA Ostium (mm)	Device Size (mm)
17 – 19	21
20 – 22	24
23 – 25	27
26 – 28	30
29 – 31	33

Note: These values are based on TEE. Other imaging modalities may vary.

Note: Record multiple views on cine with contrast prior to advancing Access Sheath into LAA. Use fluoroscopic and/or echocardiographic guidance while advancing pigtail catheter and while advancing the Access Sheath. Stop if resistance is felt.

C. Carefully advance pigtail catheter through Access Sheath into distal portion of the LAA under fluoroscopic and/or echocardiographic guidance. Carefully advance Access Sheath over pigtail catheter until Access Sheath radiopaque (RO) marker band corresponding to device size **(see Figure 4)** is at or just distal to LAA ostium. Slowly remove pigtail catheter.

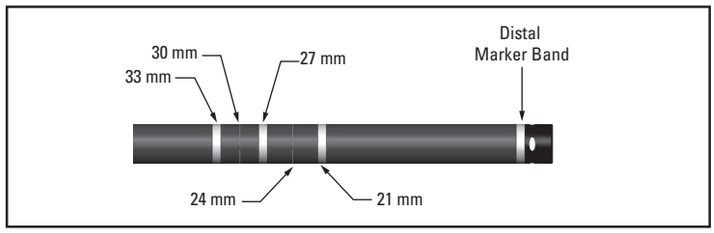

Figure 4 . WATCHMAN Device Size Relative to Access Sheath Marker Bands

7. Prepare WATCHMAN Delivery System

A. Remove Delivery System under sterile conditions.

B. Inspect prior to use to ensure no damage to handle, catheter connections and device (through Delivery System).

Note: If sterile barrier, labeling, packaging, or device have been compromised in any way, or Delivery System appears damaged DO NOT USE.

C. Confirm that the distal tip of the device is aligned with the RO marker band on Delivery System.

D. Flush Delivery System with saline removing all air and maintaining fluid throughout system. Open and flush hemostasis valve.

Precaution: Use caution when manipulating the Delivery System. Excessive counterclockwise rotation of the deployment knob or Delivery System hub independent from the rest of the Delivery System can cause premature implant detachment.

Note: To avoid introducing air, apply pressurized saline bag to the side port of the Access Sheath, or submerge Access Sheath hub in saline. Saline may be dripped from Delivery System during introduction into Access Sheath by injecting through flush port.

8. Loosen hemostasis valve of Access Sheath allowing bleed back before inserting Delivery System. Note: Hemostasis valve should spin freely (fully open).

Note: Tightening the valve onto the WATCHMAN Delivery System may damage the valve threads, which can lead to subsequent difficulty in closing the valve and an incomplete seal, once the WATCHMAN Delivery System is removed.

9. To avoid introduction of air, slowly advance Delivery System into Access Sheath under fluoro guidance.

Precaution: Use caution when introducing Delivery System to prevent damage to cardiac structures.

10. Under fluoroscopic guidance, align the most distal marker band on the Delivery System with most distal marker band on Access Sheath. Once marker bands are aligned, stabilize Delivery System, retract Access Sheath and snap together as Access Sheath/ Delivery System assembly.

11. Using fluoroscopic and/or echocardiographic guidance confirm position of Delivery System tip before deploying the device.

Note: To inject contrast, a syringe or manifold must be attached to flush port of Delivery System.

Precaution: If using a power injector, the maximum pressure **should not** exceed 100 psi.

12. If repositioning is required, unsnap the Delivery System from the Access Sheath and slowly remove Delivery System from Access Sheath. If necessary, reinsert pigtail catheter to reposition Access Sheath. Reinsert Delivery System as described in Steps 9 and 10.

13. Deploy WATCHMAN Device by loosening valve on Delivery System and holding deployment knob stationary while retracting the Access Sheath/Delivery System assembly to completely deploy device. Leave core wire attached.

14. Closure Device release criteria: **P**osition, **A**nchor, **S**ize, and **S**eal (PASS™ Criteria)

A. **Position:** Plane of maximum diameter of the Closure Device should be at, or just distal to, the LAA ostium, where possible (see Figure 5), while meeting all other PASS criteria.

Note: Closure Device position in relation to the LAA ostium may vary based on individual patient anatomy and the imaging view.

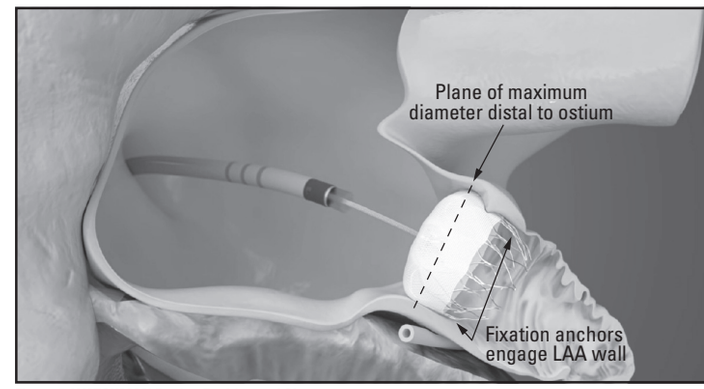

Figure 5. WATCHMAN Device Position and Size

B. **Anchor:** Gently pull back then release deployment knob to visualize movement of device and LAA together.

C. **Size (compression):** Measure plane of maximum diameter of device (See **Figure 5**). Use Table 46 as a guide.

D. **Seal:** Ensure all lobes are distal to device and sealed, i.e., no leak >5 mm.

Table 46. WATCHMAN Device Diameter

Original Diameter (mm)	Deployed Diameter (80-92% of original) (mm)
21	16.8-19.3
24	19.2-22.1
27	21.6-24.8
30	24.0-27.6
33	26.4-30.4

15. Partial device recapture, if necessary.

Note: Partially recapture and redeploy WATCHMAN Device if too distal to LAA ostium.

A. Advance the tip of the Access/Delivery System assembly up to device (do not unsnap). Fix deployment knob position with right hand and gently advance Access/Delivery System assembly over shoulders of device. Position right thumb against Delivery System hub for stability. Resistance will be felt as device shoulders collapse. Continue to advance assembly up to but not past fixation anchors. When resistance is felt a second time (anchor contact), stop, tighten hemostasis valve.

Note: If device is retrieved past fixation anchors, recapture fully and replace Delivery System with a new system. Refer to Step 16. The WATCHMAN Device and Delivery System are for single use only. Do not reuse or resterilize.

B. Reposition Access Delivery/System assembly proximally and re-deploy by holding deployment knob and retracting Access Sheath until device is completely deployed. Leave core wire attached.

Warning: Do not release the WATCHMAN Device from the core wire if the device does not meet release criteria (Step 14).

16. Full device recapture.

Note: The WATCHMAN Device should be fully recaptured into the delivery system, removed and discarded if the device is deployed too proximal or does not meet the release criteria test. The WATCHMAN Device and Delivery System are for single use only. Do not reuse or resterilize the fully recaptured device.

A Advance tip of Access/Delivery System assembly up to face of device (do not unsnap).

B Fix deployment knob with right hand and gently advance Access/Delivery System assembly over shoulders of device. Position right thumb against Delivery System for stability. Resistance will be felt as device shoulders collapse. Continue to advance assembly until device is completely collapsed and fully recaptured (past anchors).

C. Withdraw the device until distal anchors are proximal to the RO marker band, then tighten hemostasis valve.

D. Unsnap Delivery System from Access Sheath while maintaining position. Slowly remove the entire Delivery System.

E. Insert pigtail catheter to reposition Access Sheath in LAA, if necessary.

F. Repeat Steps 7-14 with new Delivery System.

17. WATCHMAN Device release criteria: Confirm proper Position, Anchor, Size, and Seal (PASS criteria), and then advance assembly to face of device. Rotate deployment knob counter clockwise 3-5 full turns. Confirm core wire is disconnected.

18. Remove Access Sheath and Delivery System based on parameters for hemostasis.

19. Use standard of care for post-procedure bleeding at access site.

POST-PROCEDURE INFORMATION

1. Post-procedure oral anticoagulation (OAC) therapy is required in ALL patients receiving a WATCHMAN® Device (see **Figure 6**). Patients should remain on 81 mg-100 mg of aspirin. OAC therapy should be added post-implant. At 45 days (± 15 days) post-implant, perform WATCHMAN Device assessment with TEE. Cessation of OAC therapy is at physician discretion provided that any leak demonstrated is <= 5 mm. If adequate seal is not demonstrated, subsequent OAC therapy cessation decisions are contingent on demonstrating leak is <= 5 mm. At the time the patient ceases OAC therapy, the patient should continue aspirin and begin a P2Y12 inhibitor daily. This regimen should continue until 6 months have elapsed after implantation. Patients should then remain on aspirin indefinitely. If a patient remains on OAC therapy and aspirin 81 mg-100 mg for at least 6 months after implantation and then ceases OAC therapy, the patient should not require a P2Y12 inhibitor but should continue aspirin daily.
2. At 45 days and at 12 months, perform imaging to assess the WATCHMAN Device with TEE.
   - Confirm absence of intra-cardiac thrombus.
   - Perform color Doppler assessment to include the device/ LAA border at the following approximate TEE angles (0°, 45°, 90° and 135°). Measure any residual leak around the device into the LAA. If there is evidence of leak > 5 mm, continuing or restarting anticoagulation therapy is recommended.
   - If thrombus is observed on the device, use of anticoagulation is recommended until resolution of thrombus is demonstrated by TEE.
3. Prescribe appropriate endocarditis prophylaxis for 6 months following Closure Device implantation. The decision to continue endocarditis prophylaxis beyond 6 months is at physician discretion.

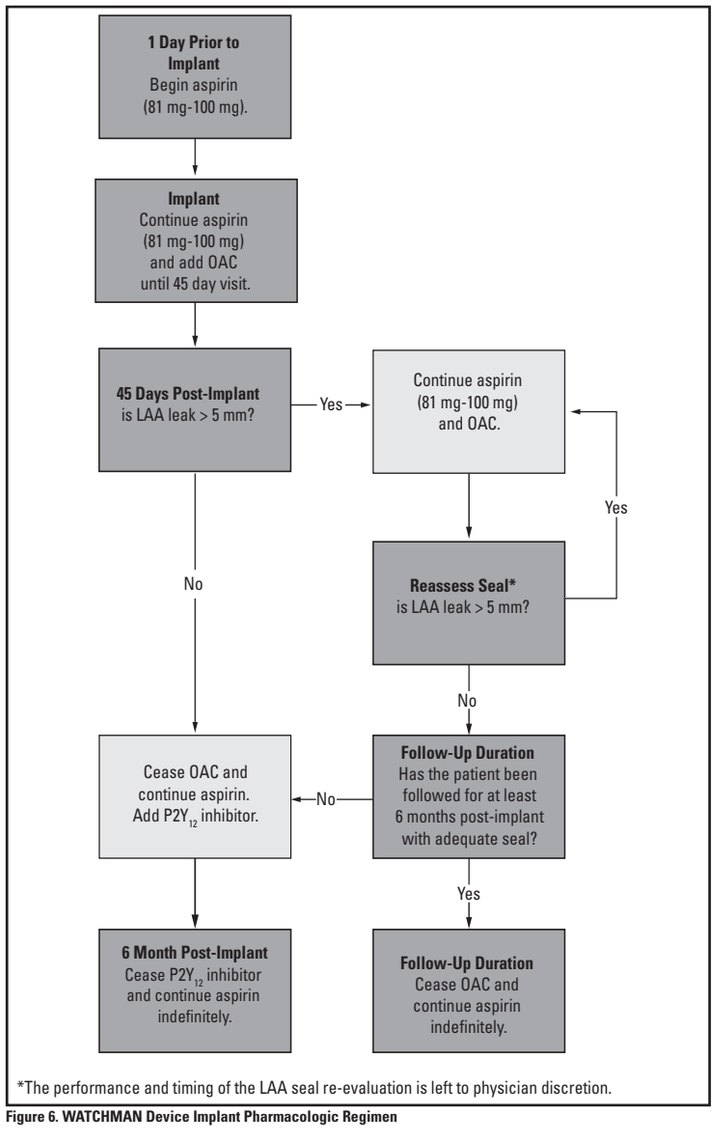

Figure 6. WATCHMAN Device Implant Pharmacologic Regimen

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EC REP **EU Authorized Representative**

Boston Scientific Limited
Ballybrit Business Park
Galway
IRELAND

AUS **Australian Sponsor Address**

Boston Scientific (Australia) Pty Ltd
PO Box 332
BOTANY
NSW 1455
Australia
Free Phone 1800 676 133
Free Fax 1800 836 666

ARG **Argentina Local Contact**

Para obtener información de contacto de Boston Scientific Argentina SA, por favor, acceda al link www.bostonscientific.com/arg

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Boston Scientific Corporation
300 Boston Scientific Way
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