WATCHMAN™: A CLINICALLY PROVEN AND SAFE THERAPY FOR YOUR NVAF PATIENTS

1. WATCHMAN reduces the risk of stroke in NVAF patients as effectively as warfarin
2. WATCHMAN *also* reduces the long-term risk of bleeding associated with warfarin
3. WATCHMAN is a one-time, minimally invasive treatment option
4. WATCHMAN LAAC is the only device with proven safety, efficacy and patient benefits from RCTs and prospective registries
5. WATCHMAN has been implanted in more than 40,000 patients worldwide and is the only device of this kind approved by the FDA

Asses the risks of stroke and bleeding in your NVAF patients with the **Stroke-Bleed Risks Calculator app** available on the Apple App-Store or Android Google Play.

SH-453911-AB DEC2017

FIND AN IMPLANTING CENTRE NEAR YOU AT:

www.watchman.lat

Refer your patient to one of the medical centres across EU that is certified to implant WATCHMAN.

Contact: contacto@watchman.com

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THINK OUTSIDE THE PILLBOX

WATCHMAN™

LEFT ATRIAL APPENDAGE CLOSURE DEVICE

A proven one-time procedure that reduces the risk of stroke in your non-valvular atrial fibrillation (NVAF) patients and the risk of bleeding that comes with a lifetime of oral anticoagulant use.

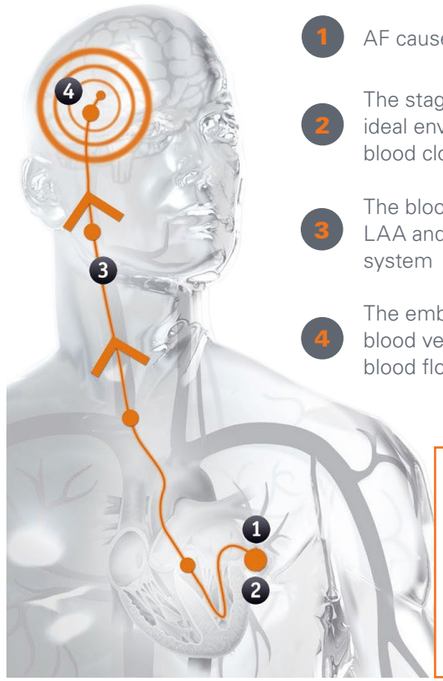
PATIENTS WITH ATRIAL FIBRILLATION ARE AT AN INCREASED RISK OF STROKE

Atrial Fibrillation (AF) increases the risk of stroke by 5 times.[1]

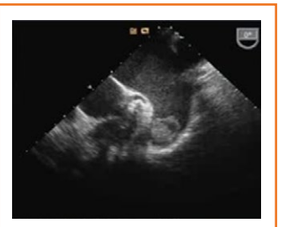
Strokes in patients with AF are:

- #1 Cause of long-term disability
- #3 Leading cause of death

In non-valvular atrial fibrillation patients (NVAF), 90% of left atrium blood clots originate in the left atrial appendage (LAA).[2]



1. AF causes blood to stagnate in the LAA
2. The stagnant blood becomes an ideal environment for a thrombus or blood clot to form
3. The blood clot dislodges from the LAA and travels through the arterial system
4. The embolism lodges itself in the blood vessels of the brain, restricting blood flow and causing a stroke



TREATMENT OPTIONS

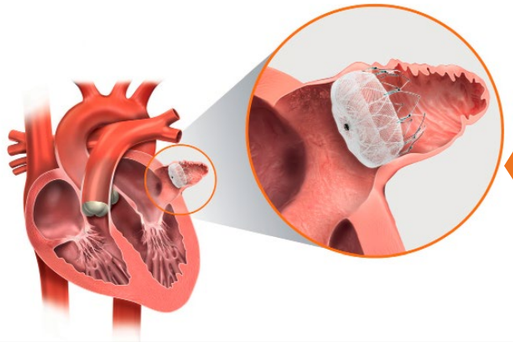
Oral anticoagulation (OAC) with vitamin K antagonists (VKA) or non-VKA oral anticoagulants (NOAC) are good treatment options for some patients.

However

- discontinuation of the OAC therapy rates remain high (at 2 years, 50% of patients on VKA and 30% on NOAC treatment[3])
- bleeding risks are not eliminated
- other AF patients have contraindications to OAC, or a history of bleeding on OAC, or may suffer a systemic thromboembolisation event despite adequate OAC

REDUCING THE RISK OF STROKE WITH WATCHMAN™ LEFT ATRIAL APPENDAGE CLOSURE (LAAC) DEVICE

The WATCHMAN LAAC procedure is a local, minimally invasive therapy that reduces the risk of stroke and the risk of bleeding that comes with the use of OACs in non-valvular atrial fibrillation patients (NVAF).



The WATCHMAN device is designed to close off the LAA, preventing the migration of blood clots.

The WATCHMAN device is a self-expanding nitinol frame covered by a permeable fabric (PET) to facilitate endothelialisation.

It is available in 5 different sizes to adapt to individual LAA anatomy (from 21 to 33 mm diameter).

WHICH OF YOUR NVAF PATIENTS ARE RIGHT FOR WATCHMAN?

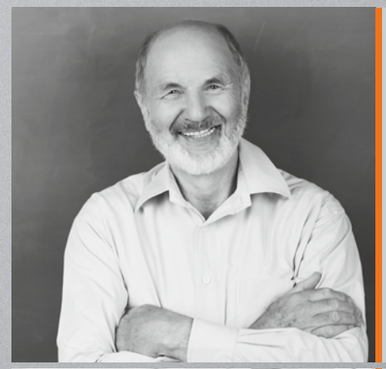
The WATCHMAN device may be an appropriate option for your NVAF patients who:

1. Are at an increased risk of stroke (CHA_2DS_2-VASc≥2)*
2. Are contraindicated or intolerant to oral anticoagulants
3. Have a history of bleeding while taking oral anticoagulants
4. Have suffered a prior stroke or transient ischemic attack (TIA)

- Patients who are NOT ELIGIBLE for OAC therapy can now BENEFIT from a therapy to protect them from stroke
- Patients who are ELIGIBLE for OAC therapy can REDUCE the risk of bleeding that comes with life-long usage of OAC

*__C__=congestive heart failure; __H__=hypertension; __A_2__=age≥75 years; __D__=diabetes mellitus; __S_2__=prior stroke or transient ischemic attack or thromboembolism; __V__=vascular disease; __A__=age 65–74 years; __Sc__=sex category

PATIENT PROFILES



NIKOLAS, 77 contraindicated to OAC

Occupation: Retired teacher

Medical conditions: NVAF; Hypertension; Previous stroke

CHA_2DS_2-VASc score: 5 - **HAS-BLED score:** 4

Nikolas has a history of bleeding, especially gastrointestinal, which makes him contraindicated to oral anticoagulants.

What approach do you take with your NVAF patients who cannot take OAC?

GWEN, 65 previous bleeding events

Occupation: Home healthcare assistant

Medical conditions: NVAF; Hypertension; Previous TIA

CHA_2DS_2-VASc score: 5 - **HAS-BLED score:** 3

Gwen is currently taking 100 mg of aspirin daily. She experienced gastrointestinal bleeding on warfarin and on apixaban. She has been taking only ASA since her last GI bleed.

What approach do you take with your NVAF patients who experienced bleeding?

ABIGAIL, 72 high risk for bleeding

Occupation: Retired flight attendant

Medical conditions: NVAF; Hypertension; Diabetes

CHA_2DS_2-VASc score: 4 - **HAS-BLED score:** 3

Abigail has severe kidney dysfunction, which precludes her from being able to use several kinds of oral anticoagulants. Her physician also believes she is at high risk for bleeding as a result of her kidney failure.

What approach do you take with your NVAF patients who are at a high risk of bleeding?

Case description for educational purposes; not real patient cases.

HOW THE WATCHMAN™ IMPLANT WORKS

WATCHMAN LAAC is a one-time, minimally invasive procedure that closes off the LAA, preventing the migration of blood clots.

The procedure is performed under general anaesthesia or conscious sedation in a catheterisation laboratory using a standard transseptal technique.

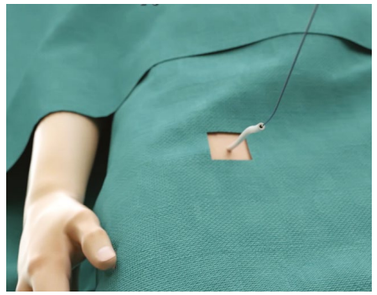
The procedure usually lasts about an hour and patients typically stay in hospital for a day.

In the EWOLUTION prospective registry, WATCHMAN was successfully implanted in ***98.5%*** *of patients*[*4]

The Implant Procedure

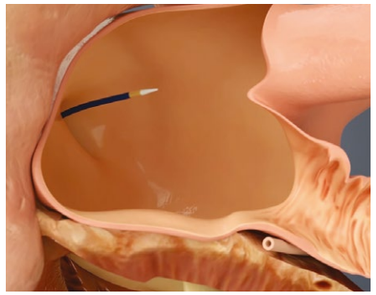
1

Using a standard percutaneous technique, a guidewire and vessel dilator are inserted into the femoral vein.

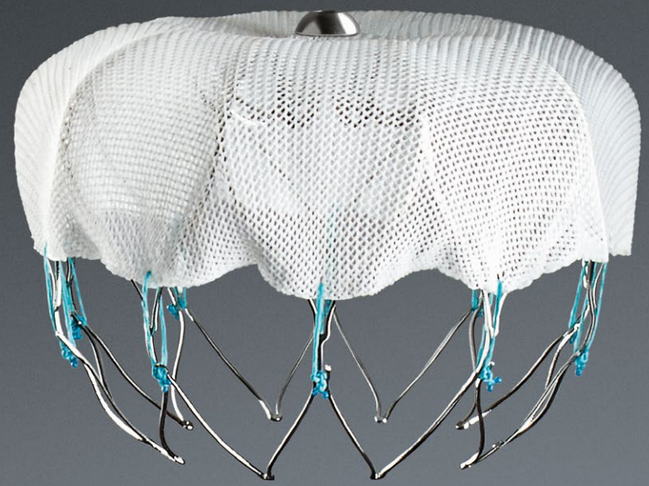


2

The implant procedure is performed with fluoroscopy and transesophageal echocardiography (TEE). The interatrial septum is crossed using a standard transseptal access system.

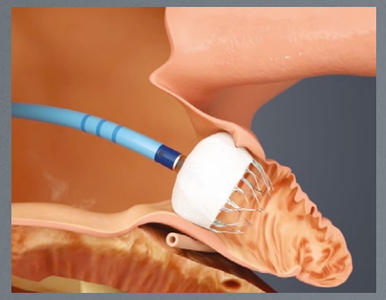


*The most common reason for the deployment failures was unfavourable anatomy or mismatch between the size of the device and the LAA.



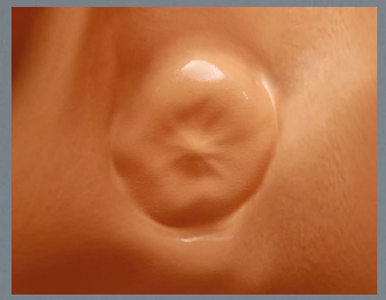
3

WATCHMAN is then deployed and released in the LAA.



4

Heart tissue grows over the WATCHMAN implant and the LAA is permanently sealed.



Post Procedure

Following the procedure, physicians may prescribe an individual post-implant medication considering patient preference, stroke and bleeding risk.

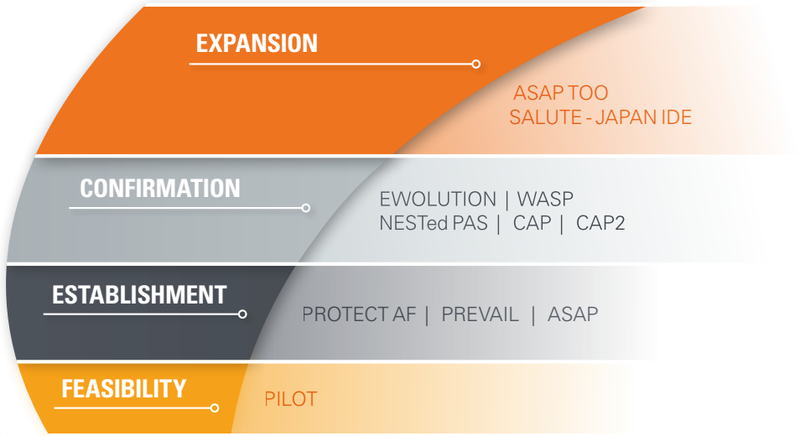
Treatment options may include a dual antiplatelet therapy (DAPT) or an oral anticoagulation therapy with warfarin or NOAC (non-Vitamin-K oral anticoagulation) along with aspirin for at least three months.

If the patient receives OAC, switching to DAPT after 45 days could be considered. Aspirin is recommended for at least 12 months post-implant.

WATCHMAN: A CLINICALLY PROVEN THERAPY

The WATCHMAN clinical evidence consists of over 5,800 patients studied in 2 randomised trials (with 5 years of follow-up of PROTECT AF and PREVAIL) and multiple prospective registries.

The WATCHMAN implant reduces the risk of stroke as effectively as warfarin and the long-term risk of bleeding associated with warfarin use.[5,6]



MORE THAN
5,800 PATIENTS AND
10,000 PATIENT YEARS
OF FOLLOW-UP

Long term data from PROTECT AF and PREVAIL demonstrated that WATCHMAN offered comparable stroke risk reduction as well as statistically significant reductions in disabling and fatal stroke* (55%), non-procedure related major bleeding (52%), and mortality (41% CV death) vs. warfarin after 5 years of follow-up.[11]

5-Year Patient-Level Meta-Analysis of PROTECT AF and PREVAIL

Endpoint	Reduction	Hazard Ratio (95 % CI)	P-Value	Statistical Significance
Primary Efficacy	**18%**	0.82 (0.58 – 1.17)	0.27	Non-inferior
All Cause Stroke	**4%**	0.96 (0.60 – 1.54)	0.87	No statistical difference
Disabling / Fatal Stroke*	**55 %**	0.45 (0.21 – 0.94)	0.03	Statistically significant
Ischemic Stroke	**N/A**	1.71 (0.94 – 3.11)	0.08	No statistical difference
Hemorrhagic Stroke	**80%**	0.20 (0.07 – 0.56)	0.0022	Statistically significant
Non-procedure related major bleeding	**52%**	0.48 (0.32 – 0.71)	0.0003	Statistically significant
Mortality				
All-Cause	**27%**	0.73 (0.54 – 0.98)	0.04	Statistically significant
CV/Unexplained	**41%**	0.59 (0.37 – 0.94)	0.03	Statistically significant

WATCHMAN Group N=732
WARFARIN Group N=382

In a real-world clinical setting, studied in the prospective E*W*OLUTION registry, WATCHMAN at 1 year of follow-up[12] confirmed to be safe and effective in a high risk population showing: 84% reduction in ischemic strokes (annual stroke rate was 1.1%) as compared to no therapy[13] and 48% reduction in major bleeding events (annual major bleeding rate was 2.6%) compared to warfarin.[14]

*Two strokes in PREVAIL are excluded because the baseline MRS score was unavailable.

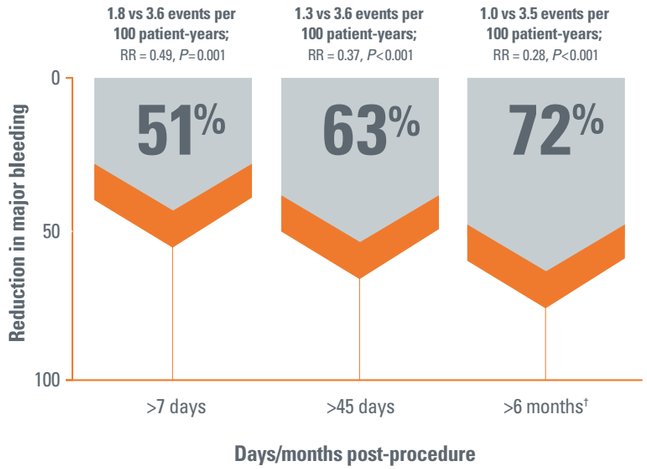
The patient-level meta-analysis of the PROTECT AF and PREVAIL trials found that the longer a patient has a WATCHMAN implant, the greater the reduction in bleeding events.[5]

At 6 months post-procedure, WATCHMAN reduced major bleeding events vs warfarin by 72% (1.0 vs 3.5; *P*<0.001).[5]

* Major bleeding defined as adverse event that was assigned one of several bleeding codes and was adjudicated by an independent Clinical Events Committee as significant (life-threatening or resulting in hospitalisation , prolongation of hospitalisation, substantial disability, or death).

WATCHMAN REDUCED BLEEDING EVENTS VS WARFARIN*

The longer a patient has a WATCHMAN implant, the greater the reduction in bleeding events[5]



STUDY DESIGN

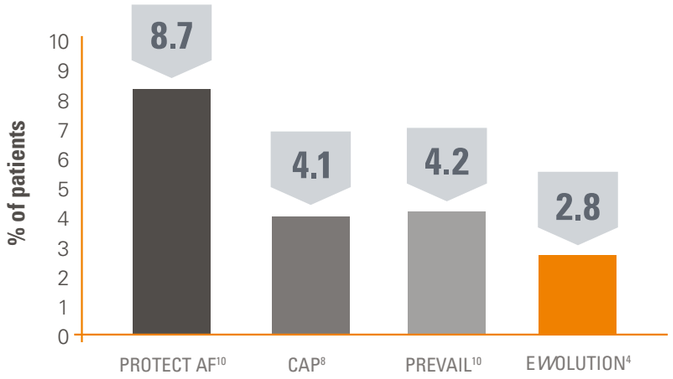
The patient-level meta-analysis of the PROTECT AF and PREVAIL trials also compared the relative risk of major bleeding with WATCHMAN and long-term warfarin therapy. In both trials, patients who were randomly assigned to WATCHMAN continued to take warfarin and aspirin 45 days after the procedure. Transesophageal echocardiography was then performed to confirm adequate left atrial appendage (LAA) sealing (peridevice leak <5 mm in diameter). If the LAA was adequately sealed, patients discontinued warfarin and were treated with aspirin and clopidogrel for 6 months after the procedure, followed by ongoing aspirin therapy. If LAA sealing was inadequate, patients remained on warfarin and aspirin and did not receive clopidogrel. Post-hoc analyses were performed at 3 intervals (7 days, 45 days, and 6 months post-procedure) to assess the procedural complications and relative risk to events like major bleeding.[5]

†PROTECT AF followed patients for five years.

WATCHMAN DEMONSTRATED FAVORABLE SAFETY OUTCOMES IN CLINICAL STUDIES

WATCHMAN maintains favorable safety outcomes from clinical studies to real-world experience.

Serious adverse procedure or device related events (SAE)* at 7 days



*EW*OLUTION (Registry on WATCHMAN Outcomes in Real-Life Utilisation) is the largest prospective real-life registry with over 1,000 patients studied and more than 70% of patients contraindicated to OAC.[4]

* SAE: Serious Adverse Event - Composite of vascular complications includes cardiac perforation, pericardial effusion with tamponade, ischemic stroke, device embolisation, and other vascular complications

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