WATCHMAN® Left Atrial Appendage Closure System

A Proven Device Alternative To Warfarin™
Facts about Atrial Fibrillation (AF)

AF is the most common cardiac arrhythmia

1. Affects 1% - 2% of general population
   - Projected to increase steadily with aging demographics

2. Patients with AF have a 5-fold higher risk of stroke

3. Origin of stroke
   3.1 Over 87% of strokes are thromboembolic
   3.2 Greater than 90% of thrombus accumulation originates in the Left Atrial Appendage (LAA)

4. AF-related strokes are more debilitating due to size of clots

5. Stroke is the number one cause of long-term disability and the third leading cause of death in patients with AF

Heart Disease and Stroke Statistical Update: 2009 Update Circulation 1-27-09
AHA Statistical Update: Heart Disease and Stroke Statistics-2008 Update; NHLBI and ARIC Circulation 1-29-08
Hylek EM, et.al. NEJM. 2003; 349: 1019-1026
Johnson. Eur J Cardiothoracic Surg 2000;17
Atrial Fibrillation is a Disease that Affects Over Seven Million Worldwide . . .

Atrial Fibrillation Patient Population in millions

<table>
<thead>
<tr>
<th>Year</th>
<th>International</th>
<th>US</th>
</tr>
</thead>
<tbody>
<tr>
<td>2009</td>
<td>3.3</td>
<td>3.6</td>
</tr>
<tr>
<td>2010</td>
<td>3.5</td>
<td>3.8</td>
</tr>
<tr>
<td>2011</td>
<td>3.6</td>
<td>4.0</td>
</tr>
<tr>
<td>2012</td>
<td>3.8</td>
<td>4.2</td>
</tr>
<tr>
<td>2013</td>
<td>4.0</td>
<td>4.4</td>
</tr>
</tbody>
</table>

Source: American Heart Association and Frost & Sullivan; projections based on management estimates of 5% annual growth rate
Current AF Treatment Options

- Ablation
- Pacing
- Drugs for Rate Control
- Embolic Management
  - Drugs (Warfarin)
  - Interventions
    - Surgical Ligation
    - LAA Clips
    - Endovascular LAA
Challenges in Treating AF

Warfarin is not always well-tolerated

- Narrow therapeutic range (INR between 2.0 – 3.0)
- Effectiveness is impacted by interactions with some foods and medications
- Requires frequent monitoring and dose adjustments

Major Complications

- Major bleeding with warfarin use is estimated to occur at a frequency as high as 16%²
- Warfarin associated bleeding experience a rate of mortality hospitalization, life threatening disability or intervention as high as 90%²
Thrombus in LAA
The WATCHMAN device reduces the risk of stroke by closing off the left atrial appendage, which is known to be the main source of blood clots in patients with atrial fibrillation.
WATCHMAN® LAA Closure Procedure
WATCHMAN LAAC - WATCHMAN Device

Nitinol Frame
- Radially expands to maintain position in LAA
- Available sizes:
  - 21, 24, 27, 30, 33 mm (diameter)
- 10 Active fixation anchors around device perimeter designed to engage LAA tissue for stability and retention
- Contour shape accommodates most LAA anatomies

160 Micron Membrane
- Polyethylene terephthalate (PET) cap
- Designed to block emboli from exiting the LAA
- Intended to promote healing process
WATCHMAN LAAC - Access Sheath

Preformed curve shapes guide position in LAA

Designated for Safety and Ease of Use

Transseptal Access System
- Double or Single Curve styles
- 14F O.D. (4.7 mm), 12F I.D. (4 mm)
- 75 cm working length
WATCHMAN LAAC – Delivery System

Designed for Safety and Ease of Use

- **Deployment Knob**
- **Core Wire**
- **Hemostasis Valve**
- **Preloaded Device**
  - Saves time
- **Distal Marker Band**
  - Guides placement
- **Preassembled 12Fr (4 mm) Delivery System**
  - Compatible with all device sizes
Sheath Navigation / Manipulation
Marker Bands – Designed for Precise Positioning

- Radiopaque marker bands guide initial sheath placement/depth in the LAA
- Align appropriate marker band with the LAA ostium according to device size selected

<table>
<thead>
<tr>
<th>Access Sheath Marker Band</th>
<th>Loaded Device Length</th>
</tr>
</thead>
<tbody>
<tr>
<td>21mm</td>
<td>20.2mm</td>
</tr>
<tr>
<td>24mm</td>
<td>22.9mm</td>
</tr>
<tr>
<td>27mm</td>
<td>26.5mm</td>
</tr>
<tr>
<td>30mm</td>
<td>29.4mm</td>
</tr>
<tr>
<td>33mm</td>
<td>31.5mm</td>
</tr>
</tbody>
</table>
## Assessment of LAA

**Confirm the absence of LA / LAA thrombus**

<table>
<thead>
<tr>
<th>Measure LAA ostium in at least 4 TEE views</th>
<th>At 0 deg (from left coronary artery to a point 2 cm from tip of the LUPV limbus)</th>
</tr>
</thead>
<tbody>
<tr>
<td>At 45, 90, 135 deg (from the top of the MV annulus to a point 2 cm from tip of the LUPV limbus)</td>
<td>Measure the approximate LAA useable length from the ostium line to the apex of the LAA</td>
</tr>
</tbody>
</table>
Obtain multiple views with

1. Angiography – RAO 30 Cranial / Caudal
2. TEE – 0-180 degree sweep
Device Deployment Process

1. Unsheathe device with slow stable motion for optimal control (at least 3-5 seconds)

2. Observe distal end of device to ensure NO forward advancement occurs

3. NO forward pushing (or repositioning relative to ostium) during unsheathing process
Device Recapture Process

1. Advance sheath to device BEFORE recapture starts
2. Recapture device by retracting device into sheath and pushing sheath over device
3. Recapture device with slow and stable motion
4. Avoid inadvertent pulling, pushing implant during recapture process
5. Options include partial or complete recapture
Device Release Criteria

All criteria must be met prior to device release (PASS)

**Position** – device is distal to or at the ostium of the LAA

**Anchor** – fixation anchors engaged / device is stable

**Size** – device is compressed 8-20% of original size

**Seal** – device spans ostium, all lobes of LAA are covered

– If necessary, device can be recaptured (partial or full)
Device Release Criteria – Position
Device Release Criteria – Anchor

Pass or Fail Test

1. To test stability, gently retract deployment knob and let go, observe device returns to original position

2. If the device moves to where position is no longer acceptable or the compression is no longer sufficient, the device should be recaptured

3. Test stability more than once if device stability is questionable
Device Release Criteria – Size

### Compression

<table>
<thead>
<tr>
<th>Device Size (uncompressed diameter)</th>
<th>Maximum (20%) Compression Measured Diameter*</th>
<th>Minimum (8%) Compression Measured Diameter*</th>
</tr>
</thead>
<tbody>
<tr>
<td>21</td>
<td>16.8 mm</td>
<td>19.3 mm</td>
</tr>
<tr>
<td>24</td>
<td>19.2 mm</td>
<td>22.1 mm</td>
</tr>
<tr>
<td>27</td>
<td>21.6 mm</td>
<td>24.8 mm</td>
</tr>
<tr>
<td>30</td>
<td>24.0 mm</td>
<td>27.6 mm</td>
</tr>
<tr>
<td>33</td>
<td>26.4 mm</td>
<td>30.4 mm</td>
</tr>
</tbody>
</table>

*Measure in-situ device diameter at approximate TEE angles of 0, 45, 90 and 135 degrees to accurately assess device compression.

Maximum diameter at “shoulders”

“threaded insert” must be visible when measuring on echo to ensure device was measured at widest cross-section in all angles.
Device Release Criteria – Seal

- No residual flow noted around device

- If all 4 device release criteria are met (PASS), device can be released

- Counter clockwise on proximal handle 3-5 turns
WATCHMAN® LAA Closure Device

45 Day Follow-UP
Healing Process

Canine Model – 30 day

Canine Model – 45 day

Human Pathology - 9 months post-implant (non-device related)
Clinical Trial Update
## WM Clinical Studies

<table>
<thead>
<tr>
<th>STUDY</th>
<th>PATIENTS</th>
<th>SITES</th>
<th>COMMENTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pilot</td>
<td>66</td>
<td>8</td>
<td>• 318 patient years of follow-up&lt;br&gt;• 30 patients with 5+ years of follow-up&lt;br&gt;• Enrollment complete, continue to follow patients on annual basis</td>
</tr>
<tr>
<td>PROTECT AF</td>
<td>800</td>
<td>59</td>
<td>• 1,500 patient years of follow-up&lt;br&gt;• 27 months average follow-up per patient&lt;br&gt;• Enrollment complete, continue to follow patients for 5 years</td>
</tr>
<tr>
<td>Continued Access Registry (CAP)</td>
<td>566</td>
<td>26</td>
<td>• Significantly improved safety results&lt;br&gt;• Enrollment complete, continue to follow patients for 5 years</td>
</tr>
<tr>
<td>ASAP</td>
<td>150</td>
<td>4</td>
<td>• Treat patients contra-indicated for warfarin&lt;br&gt;• Enrollment complete, continue to follow patients for 2 years</td>
</tr>
<tr>
<td>EVOLVE</td>
<td>69</td>
<td>3</td>
<td>• Evaluate next generation WATCHMAN&lt;br&gt;• Enrollment complete, continue to follow patients for 1 year</td>
</tr>
<tr>
<td>PREVAIL</td>
<td>369</td>
<td>≤50</td>
<td>• Same endpoints as PROTECT AF&lt;br&gt;• Revised inclusion/exclusion criteria&lt;br&gt;• Initial enrollment November 2010&lt;br&gt;• Enrollment up to 400 randomized, anticipated enrollment completion June 2012</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>2,020</strong></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Three Trials of the WATCHMAN® Device Have Reached Their Primary Endpoints; a Fourth is Ongoing

<table>
<thead>
<tr>
<th>PROTECT AF(^1,2)</th>
<th>CAP(^2)</th>
<th>ASAP(^3)</th>
<th>PREVAIL</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Control</strong></td>
<td>Patients able to take warfarin</td>
<td>Warfarin contraindicated patients</td>
<td>Patients able to take warfarin</td>
</tr>
<tr>
<td><strong>Primary Endpoint</strong></td>
<td>All stroke, systemic embolism and cardiovascular death</td>
<td>All stroke, systemic embolism and cardiovascular death</td>
<td>N/A</td>
</tr>
<tr>
<td>Mean age /CHADS</td>
<td>72 /2.2</td>
<td>74 /2.4</td>
<td>72.5/2.8</td>
</tr>
<tr>
<td>Total Enrolled Subjects</td>
<td>707 randomized(^1), 93 pts rolled in(^2)</td>
<td>460</td>
<td>150</td>
</tr>
<tr>
<td>Total Patients Implanted</td>
<td>542(^2)</td>
<td>437</td>
<td>142</td>
</tr>
<tr>
<td>Implantation Success</td>
<td>89.5(^2)%</td>
<td>95%</td>
<td>94.7%</td>
</tr>
<tr>
<td>Warfarin discontinuation at 45 days</td>
<td>86.6%</td>
<td>94.9%</td>
<td>No warfarin used</td>
</tr>
<tr>
<td><strong>Stroke</strong></td>
<td>Rate ratio 0.71 (0.35–1.64) [Hemorrhagic Stroke: 0.09 (0.00–0.45(^*)]</td>
<td>Reduction in procedure related stroke vs PROTECT AF ((P=0.04))</td>
<td>1.7% ischemic stroke rate (per 100 patient yrs); 77% reduction in expected event rate</td>
</tr>
<tr>
<td><strong>Bleeding</strong></td>
<td>HR 1.69 (1.01–3.19)</td>
<td>Reduction in pericardial effusions vs PROTECT AF ((P=0.02))</td>
<td></td>
</tr>
</tbody>
</table>
**Study Objective:** Evaluate the efficacy and safety of the WATCHMAN LAA Closure Device as compared to long-term warfarin therapy in patients with non-valvular atrial fibrillation and CHADS$_2$ score $\geq 1$

**Study Design:** Prospective, randomized (2 Device: 1 Control), non-inferiority study of the Watchman device compared to long-term warfarin therapy

**Primary Endpoint:** Non-inferiority of the WATCHMAN device to warfarin therapy for the composite of ischemic stroke, hemorrhagic stroke, systemic embolism and cardiovascular/unexplained death

**Additional Endpoints:** Life-threatening events including device embolization requiring retrieval, pericardial effusion requiring intervention, cranial and GI bleeding, and bleeding requiring transfusion $\geq 2$ units PRBCs

**Patient Population:**
- WATCHMAN: n=463
- Control: n=244
- Roll-in: n=93

**Number of Sites:** 59 (55 U.S., 4 EU)
### Therapy Timeline

**Day 0**

**Pre-implant interval**
- Patient gets WATCHMAN
- Patient takes Warfarin

**Day 2-14**
- Patient discontinues Warfarin / takes Clopidogrel
- Patient discontinues Clopidogrel

**Day 45**
- Randomize

**Day 180**
- Post-implant interval

**Control**
- Control patient takes Warfarin

**Ongoing**

- Therapy Timeline
PROTECT AF – Primary Efficacy Endpoint – 1065 pt yrs

38% Reduction

Incidence Rate (%)

Primary Efficacy
- WATCHMAN Group: 3.0%
- Warfarin Group: 4.9%

All stroke
- WATCHMAN Group: 2.3%
- Warfarin Group: 3.2%

Cardiovascular/Unexplained Death
- WATCHMAN Group: 0.7%
- Warfarin Group: 2.7%

Systemic Embolism
- WATCHMAN Group: 0.3%
- Warfarin Group: 0.0%

P_{NI} = >99.9%
P_{NI} = 99.3%
P_{NI} = >99.9%
P_{NI} = >99.9%

P_{NI} = Posterior non inferiority Probabilities

38% lower
29% lower

David R Holmes, Lancet Vol 374 August 15, 2009
PROTECT AF – Primary Efficacy Endpoint

Primary Efficacy Endpoint (Stroke, Cardiovascular Death, Systemic Embolism)

Days Since Randomization
0  365  730  1095

Probability
0.00  0.05  0.10  0.15  0.20

Control
Device
244  174  67  17
463  332  132  34

David R Holmes, Lancet Vol 374 August 15, 2009
PROTECT AF – Primary Safety Endpoint

- Primary Safety Endpoint
- Days Since Randomization: 0, 365, 730, 1095
- Probability: 0.00, 0.05, 0.10, 0.15, 0.20
- Control
  - 244
  - 463
- Device
  - 171
  - 317
  - 65
  - 126
  - 16
  - 30

Peri-procedural events

On going bleeding events
PROTECT AF – All Stroke

Ongoing stroke risk in the Warfarin group

Peri-procedural stroke

Days Since Randomization

0 365 730 1095

Probability

Control
Device

244 174 67 17
463 332 132 34
PROTECT AF – All Cause Mortality

Days Since Randomization
0 365 730 1095
Probability
0.00
0.05
0.10
0.15
0.20
Control
Device

244
463
176
337
68
136
17
35

David R Holmes, Lancet Vol 374 August 15, 2009
Continued Access PROTECT AF (CAP Registry)
**Continued Access PROTECT AF (CAP Registry)**

<table>
<thead>
<tr>
<th>Study Objective:</th>
<th>Allow continued access to the WATCHMAN LAA Closure Device to a subset of PROTECT AF centers for patients with non-valvular atrial fibrillation and CHADS&lt;sub&gt;2&lt;/sub&gt; score ≥ 1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study Design:</td>
<td>Prospective, non-randomized study of the WATCHMAN device</td>
</tr>
<tr>
<td>Primary Endpoint:</td>
<td>Efficacy composite endpoint of ischemic stroke, hemorrhagic stroke, systemic embolism and cardiovascular/unexplained death</td>
</tr>
<tr>
<td>Additional Endpoints:</td>
<td>Life-threatening events including device embolization requiring retrieval, pericardial effusion requiring intervention, cranial and GI bleeding, and bleeding requiring transfusion ≥ 2 units PRBCs</td>
</tr>
<tr>
<td>Patient Population:</td>
<td>WATCHMAN n=566</td>
</tr>
<tr>
<td>Number of Sites:</td>
<td>26 (24 U.S., 2 EU)</td>
</tr>
</tbody>
</table>
Performance Metrics – Learning Curve Effect
PROTECT-AF vs. CAP

With experience procedure time decreased by 30%

- Procedure Time
  - PROTECT AF Early: 67 minutes
  - PROTECT AF Late: 58 minutes
  - CAP: 50 minutes

- Implant Success
  - PROTECT AF Early: 88%
  - PROTECT AF Late: 91%
  - CAP: 95%

- 45 Day Discontinuation Rate Among Implanted
  - PROTECT AF Early: 83%
  - PROTECT AF Late: 91%
  - CAP: 95%

With increased operator experience
- The average procedure time reduced from 67 minutes to 50 minutes
- Implant success improved from 88% to 95%
- Discontinuation of Warfarin improved from 83% to 95% of patients

Warfarin cessation increased to 95%
With increased operator experience, the procedure related adverse events and serious pericardial effusions were reduced significantly. Peri-procedural strokes were eliminated.
ASA Plavix Feasibility Study with WATCHMAN LAA Closure Technology (ASAP)
# ASAP (Aspirin and Plavix) Study

<table>
<thead>
<tr>
<th>Study Objective:</th>
<th>Characterize the performance of the WATCHMAN LAA Closure Device in patients with non-valvular atrial fibrillation and CHADS$_2$ score $\geq$ 1 for which long-term warfarin therapy is contraindicated</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study Design:</td>
<td>Prospective, non-randomized feasibility study of the WATCHMAN device utilizing aspirin and plavix post procedure</td>
</tr>
<tr>
<td>Primary Endpoint:</td>
<td>Efficacy composite endpoint of ischemic stroke, hemorrhagic stroke, systemic embolism and cardiovascular/unexplained death</td>
</tr>
<tr>
<td>Additional Endpoints:</td>
<td>Device and procedure related serious adverse events</td>
</tr>
<tr>
<td>Patient Population:</td>
<td>Up to 150 WATCHMAN $n=126$ as of July 2011</td>
</tr>
<tr>
<td>Number of Sites:</td>
<td>4 EU sites</td>
</tr>
</tbody>
</table>
Aspirin and Plavix® registry (ASAP)

The ASAP registry is a non-randomized feasibility study designed to evaluate if the WATCHMAN® Device is a safe and effective treatment for people unable to take warfarin.

- AF patients who are contraindicated or intolerant of warfarin have few options for thromboembolic prophylaxis.

- Patients may be treated with aspirin and/or clopidogrel; this treatment paradigm has a higher stroke risk than warfarin.

The WATCHMAN® Device is not approved for patients contraindicated to OACs.
ASAP (Aspirin Plavix) Study

- Patients history of hemorrhagic & bleeding tendencies or a warfarin hypersensitivity
- 150 patients, 4 European centers
- Average CHADS$_2$ = 2.8
- Post procedure anti-platelet regimen
  - Clopidogrel through 6 months
  - Aspirin indefinitely
- Patients followed to 2 years
  - Follow up @ 3, 6, 12, 18 & 24 months
  - TEE at 3 and 12 months
  - Average follow-up was 14.4 months

Rate of success with implantation in warfarin contraindicated patients

94.7% successfully implanted

Ave Procedure Time = 51.5 mins

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1 Braut A et al, LAA closure with the WATCHMAN Device in patients with contraindications to warfarin: preliminary results from the ASA Plavix registry (ASAP), ESC Congress 2011, Paris 27-31 August 2011

The WATCHMAN Device is not approved for patients contraindicated to OACs
## ASAP Registry
### Patient Risk Factors

<table>
<thead>
<tr>
<th>Baseline Characteristic</th>
<th>Count/Total (Percentage)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Congestive Heart Failure</td>
<td>43/150 (28.7%)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>142/150 (94.7%)</td>
</tr>
<tr>
<td>Age 75 or older</td>
<td>64/150 (42.7%)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>48/150 (32.0%)</td>
</tr>
<tr>
<td>Prior TIA / Stroke</td>
<td>61/150 (40.7%)</td>
</tr>
</tbody>
</table>
## ASAP Registry

### Event Rates

<table>
<thead>
<tr>
<th>Event Rate</th>
<th>Events/Pt-Yrs (Rate / 100 Pt-Yrs)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death</td>
<td>9/180.0 (5.0)</td>
</tr>
<tr>
<td>Stroke</td>
<td>4/176.0 (2.3)</td>
</tr>
<tr>
<td>Ischemic Stroke</td>
<td>3/176.9 (1.7)</td>
</tr>
<tr>
<td>Hemorrhagic Stroke</td>
<td>1/179.1 (0.6)</td>
</tr>
<tr>
<td>Device Thrombus</td>
<td>6/173.8 (3.5)</td>
</tr>
</tbody>
</table>
ASAP Registry Results

Expected and Observed Stroke Rates (per 100 patient-years)

- Observed rate of ischemic stroke represents a 77% reduction from the expected event rate.

2. ACTIVE trial AHJ 2006 151(6): 1187-93
3. Vivek Reddy, HRS Late Breaking Trial, 2012
ASAP Registry Conclusions

• The average ASAP baseline CHADS$_2$ of 2.8 equates to a predicted ischemic stroke rate of 7.1-7.4% per year

• 3 strokes were observed over a follow-up of 176.9 patient years (1.7 events per 100 patient years)

• The observed rate of 1.7 per 100 patient years in ASAP compares favorably to PROTECT-AF with 2.2 events per 100 patient years despite the difference in CHADS$_2$ score distribution

• Left Atrial Appendage Closure with the WATCHMAN device produced a significant reduction in the expected ischemic stroke rate for patients contra-indicated to Warfarin
AGA AMPLATZER® Cardiac Plug
German Cardiac Society Meeting; April 2011
Abstract Re: Thrombus on ACP Device

31/32 ACP devices successfully implanted

Thrombus detected in 3 patients at pre-discharge TEE

Thrombus detected in additional 3 patients at 3 month follow-up (Total 6)

19.3% Thrombus Rate

In three out of six patients, thrombus resolved in 1 week after I.V. Heparin

In the remainder three patients with thrombus, OAT had to be restarted

Despite OAT, one patient still had persistent thrombus remnants on the surface

Conclusion:
“Thrombus formation on the new ACP device is a serious complication that should lead to caution. A change of the anticoagulation regime post implantation and a close TEE monitoring has to be discussed. Our data does not support the hypothesis of a too deep implantation into the LAA as a risk factor for thrombus formation.”

1Klinik für Kardiologie, Westdeutsches Herzzentrum, Universitätsklinikum Essen, Essen
US AGA Cardiac Plug Study (Atritech Estimates)

2010
- 1st Enrollment

2011
- 30th Enrollment

2012
- Pivotal Study Start
- Data Submitted

2013
- First Efficacy Analysis
- 2H Expected approval of WATCHMAN

2014
- 2H Expected approval of ACP

2015

FDA protocol mandates that patients must take warfarin for 45 days post implantation
WATCHMAN vs. ACP
# WATCHMAN®

The proven device alternative to Warfarin™ for Atrial Fibrillation patients
Designed for ease of use – preloaded, repositionable and retrievable, precise and stable implantation

<table>
<thead>
<tr>
<th></th>
<th>WATCHMAN®</th>
<th>ACP Plug</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>CE Mark</td>
<td>2005</td>
<td>2008</td>
<td>WATCHMAN has longer term follow-up</td>
</tr>
<tr>
<td>Device design</td>
<td>Designed specifically to close the LAA with a complete enclosure within the LAA</td>
<td>Part of the device is in the LAA, part remains outside</td>
<td>WATCHMAN is specifically designed for Left Atrial Appendage closure</td>
</tr>
<tr>
<td>Device materials</td>
<td>Nitinol frame, with fixation anchors for stability, PET fiber cap (160 microns), which allows blood to flow, but traps the thrombus</td>
<td>Nitinol mesh, and polyester patch (waist, lobe and disc)</td>
<td>WATCHMAN PET filter is designed for filtration of potential clots that may form inside the LAA</td>
</tr>
<tr>
<td>Pre-loaded</td>
<td>✔️</td>
<td>Needs assembly in the lab</td>
<td>All WATCHMAN devices come preloaded inside the delivery sheath. The ACP device requires the clinician to load the device into the delivery system at the time of the procedure</td>
</tr>
<tr>
<td>One access sheath for the entire procedure</td>
<td>✔️</td>
<td>Multiple device and access sheath exchanges are needed</td>
<td>All WATCHMAN sizes can be delivered through a single sheath size. With the ACP device the implanter must choose the device size and match it to the sheath. If the implanter needs to change the size during the procedure he must change the sheath size.</td>
</tr>
<tr>
<td>Retrievable and Repositionable</td>
<td>✔️</td>
<td>✔️</td>
<td>Both devices can be partially or fully recaptured. However, after a partial recapture of the WATCHMAN device the same device can be re deployed. The ACP device must be replaced after any recapture event. After recapturing the ACP device the sheath must also be replaced</td>
</tr>
<tr>
<td>Number of device sizes required to carry by the hospital labs</td>
<td>5 (21-33, 3 mm increment)</td>
<td>8 (8,16-28)</td>
<td>Fewer device size, fewer delivery systems and access sheaths, means easier maintenance of inventory for the hospital</td>
</tr>
<tr>
<td>Procedure time</td>
<td>56¹ minutes</td>
<td>90² minutes</td>
<td>WATCHMAN design features such as - preloaded, single size of access sheath that accommodates all the device sizes results in time savings for physicians.</td>
</tr>
</tbody>
</table>

¹ Safety of percutaneous left atrial appendage closure, Reddy, Circulation 2011
² Left Atrial Appendage Closure with Amplatzer Cardiac Plug for Stroke Prevention in Atrial Fibrillation: Initial Asia-Pacific ExperienceAPAC registry, Lam, CCI 2011
Clinical Evidence
**WATCHMAN® is the proven device alternative to Warfarin™ for Atrial Fibrillation patients**

<table>
<thead>
<tr>
<th></th>
<th>WATCHMAN®</th>
<th>ACP Plug</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre clinical data</td>
<td>Extensive preclinical data published</td>
<td>No preclinical data shown</td>
<td>Published data shows that watchman has a predictable healing profile in canine animal models. Recently published data also shows excellent healing in a human patient at 9 months. No preclinical data has been shown for the ACP device.</td>
</tr>
<tr>
<td>Number of prospective randomized trials evaluating the safety and efficacy</td>
<td>2</td>
<td>0</td>
<td>Prospective randomized trials are considered the highest level of evidence of safety and effectiveness of a medical device, WATCHMAN has been evaluated in randomized trials.</td>
</tr>
<tr>
<td>Number of prospective registries evaluating the safety and efficacy</td>
<td>3</td>
<td>0</td>
<td>Prospective registries supplement the randomized trials by providing real world data for the WATCHMAN.</td>
</tr>
<tr>
<td>Number of patients studied in prospective studies</td>
<td>~1800</td>
<td>0</td>
<td>Large number of prospectively studied patients provide confidence in the outcomes of the WATCHMAN device.</td>
</tr>
<tr>
<td>Number of patients in years of follow-up</td>
<td>&gt; 2700</td>
<td>Unknown, has not been evaluated in randomized trials</td>
<td>Longer term follow-up with the WATCHMAN device provides evidence of durability of the product.</td>
</tr>
<tr>
<td>Proven reduction in combined Stroke, Mortality and Systemic Embolism compared to warfarin</td>
<td>38%³</td>
<td>Unknown, has not been evaluated in randomized trials</td>
<td>WATCHMAN provides important data to help make clinical risk/benefit decisions for physicians.</td>
</tr>
<tr>
<td>Proven reduction in stroke compared to warfarin</td>
<td>29%³ in all stroke, 90%³ in hemorrhagic stroke</td>
<td>Unknown, has not been evaluated in randomized trials</td>
<td>WATCHMAN demonstrates impressive reduction in stroke risk.</td>
</tr>
<tr>
<td>Success in stopping Warfarin</td>
<td>95%¹ at 45 days</td>
<td>Unknown</td>
<td>WATCHMAN demonstrates that Warfarin therapy can be stopped successfully in 95% of the patients.</td>
</tr>
<tr>
<td>Number of safety warnings on the product issued by regulatory agencies/company itself</td>
<td>0</td>
<td>3</td>
<td>WATCHMAN is being implanted responsibly with patient safety in mind and with well designed physician training and implant support programs.</td>
</tr>
</tbody>
</table>

There are no safety warnings for the WATCHMAN device.
Published Data On Safety

31/32 ACP devices successfully implanted
- 3 patients had thrombus detected pre discharge TEE
- 3 other patients had thrombus detected at 3 month TEE
- 19.3% thrombus rate
- 3 patients had thrombus resolved within one week (heparin)
- 3 patients had OAT restarted
- 1 patient still has thrombus remnants on the ACP device

Authors conclusion: “Thrombus formation on the new ACP device is a serious complication that should lead to caution. A change of the anticoagulation regime post implantation and a close TEE monitoring has to be discussed. Our data does not support the hypothesis of a too deep implantation into the LAA as a risk factor for thrombus formation.”
Dabigatran Etexilate
# PROTECT AF vs. RE – LY

<table>
<thead>
<tr>
<th></th>
<th>PROTECT AF</th>
<th>RE – LY</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Study Purpose</strong></td>
<td>Medical Device (WATCHMAN) to Drug (Warfarin) comparison</td>
<td>Drug (Dabigatran) to Drug (Warfarin) comparison</td>
</tr>
<tr>
<td><strong>Study design and Number of patients studied</strong></td>
<td>Prospective RCT, 800 patients</td>
<td>Prospective RCT, 18,000 patients</td>
</tr>
<tr>
<td><strong>Efficiency endpoint definition</strong></td>
<td>All stroke, systemic embolization and CV death</td>
<td>All stroke, systemic embolization</td>
</tr>
<tr>
<td><strong>CHADS(_2) Score</strong></td>
<td>2.2</td>
<td>2.1</td>
</tr>
<tr>
<td><strong>Time in therapeutic range for Warfarin patients</strong></td>
<td>66%</td>
<td>64%</td>
</tr>
<tr>
<td><strong>Results</strong></td>
<td>Relative risk WATCHMAN vs. warfarin – 0.71</td>
<td>Dabigatran (110 mg) vs. warfarin – 0.91</td>
</tr>
<tr>
<td><strong>Relative risk</strong></td>
<td></td>
<td>Relative risk Dabigatran (150 mg) vs. warfarin – 0.66</td>
</tr>
</tbody>
</table>

**David R Holmes, Lancet Vol 374 August 15, 2009**

**Stuart Connolly, NEJM 2009;361**
# PROTECT AF vs. RE – LY
Drug vs. Device Consideration

<table>
<thead>
<tr>
<th>Drug</th>
<th>Device</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systematic Solution</td>
<td>Local Solution</td>
</tr>
<tr>
<td>Long Term Risk (continual bleeding events)</td>
<td>Short Term Risk (complications during implant)</td>
</tr>
<tr>
<td>20% discontinue drug</td>
<td>After successful implant &amp; follow-up, 87% can discontinue Warfarin</td>
</tr>
<tr>
<td>Dabigatran- Twice daily dose compliance is needed, has a half life period of 17 hours requiring 2 daily doses to maintain benefit</td>
<td>No on-going activity needed to maintain benefit of WATCHMAN</td>
</tr>
<tr>
<td>Dabigatran effect not reversible if bleeding develops</td>
<td>Risk is of bleeding due to device is primarily in the procedure or peri-procedure</td>
</tr>
</tbody>
</table>