WATCHMAN FLX™ Left Atrial Appendage Closure Device and Legacy WATCHMAN™ Clinical Data

Key Studies
Outcomes
Prospective Clinical Trials
Study Glossary

**WATCHMAN FLX™ LAAC Device**
- PINNACLE FLX
- PINNACLE FLX Prohibitive Anatomy
- IDE Trials
- SEAL FLX Study
- SWISS APERO Study
- SURPASS 45-Day Results
- SURPASS 1-Year Results
- Meta-Analysis
- ALSTER-FLX Registry
- Safety and Acute Procedural Outcomes of LAAO
- CHAMPION-AF Clinical Trial
- OPTION Clinical Trial
- DAPT FLX

**Legacy WATCHMAN™**
- PROTECT-AF and PREVAIL Clinical Trials
- NCDR-LAAO Registry™
- PROTECT-AF, PREVAIL, CAP2 Leak Analysis

**LAAC Therapy**
- LAA Occlusion Study (LAAOS III) Trial
- PRAGUE 17 4-Year Outcomes
Over **9,000 patients studied** and **20 years of experience** with WATCHMAN™ Left Atrial Appendage Closure Device
WATCHMAN™ Left Atrial Appendage Closure Device Clinical Timeline

7. ASAP TOO, N= Up to 888, Randomized US Indication Expansion, Worldwide study, unpublished to date.
10. OPTION, N=1600, Ongoing study in post-ablation patients, Randomized Efficacy and Bleeding Comparison: OAC vs WATCHMAN FLX Device, enrollment complete.
11. FLXibility Registry, N=300, Non-randomized, EU Post-Market Registry with WATCHMAN FLX Device, Presented at HRS 2021 by Dr. T. Betts.
12. ICE-LAA, N=100, Non-randomized, Assessing safety and efficacy of ICE.
13. CHAMPION-AF, N=3000, Randomized, WATCHMAN FLX vs. NOACs in a broader NVAF population, inclusive of lower risk patients, currently enrolling.
14. NCDR Late Breaking Clinical trial at HRS 2022 presented by Dr James Freeman.
WATCHMAN FLX™
Left Atrial Appendage Closure Device
WATCHMAN FLX™ Left Atrial Appendage Closure Device Design Differentiation

Built on WATCHMAN™ LAAC Device, the most studied and implanted LAAC device in the world, WATCHMAN FLX LAAC Device is designed to advance procedural performance and safety while expanding the treatable patient population.
WATCHMAN FLX™ Left Atrial Appendage Closure Device Design Differentiation

**WATCHMAN FLX™ LAAC Device**

- Treatment Range 14.0 – 31.5 mm Ostium Width
- Full Recapture and Redeployment
- Dual-Row Precision Anchors
- Closed End
- 18 Strut Frame
- Fully-Rounded WATCHMAN FLX Ball

**Legacy WATCHMAN™ LAAC Device**

- Treatment Range 16.8 – 30.5 mm Ostium Width
- Partial Recapture Only
- Single-Row Anchors
- Open End
- 10 Strut Frame
PINNACLE FLX, the WATCHMAN FLX™ Left Atrial Appendage Closure Device US IDE Trial, demonstrated unmatched 0.5% major adverse event rate, 100% Effective LAA Closure, and a low 1.7% Annualized Ischemic Stroke or Systemic Embolism rate at 24 months.¹,²

2 Doshi et al. JAHA, 2023.
PINNACLE FLX Study Overview
A US IDE to evaluate the safety and efficacy of the WATCHMAN FLX™ Left Atrial Appendage Closure Device

**Primary Safety Endpoint**
7-Day/Discharge Adverse Event

**Primary Efficacy Endpoint**
Effective Seal at 1 Year

**Secondary Efficacy Endpoint**
Ischemic Stroke or Systemic Embolism at 2 Years

*If no effective seal (defined as leak =<5mm) is observed at 45 days, patients continued on DOAC+ASA and had 6-month TEE; additional imaging performed as medically necessary after 1 year (ie, in case of an event).
WATCHMAN FLX™ Left Atrial Appendage Closure Device: The New Standard by Which Others Must be Judged

ADVANCED SAFETY

- Fully Rounded Ball for Safety: 0.5%* Major Adverse Event Rate¹
- Dual-Row Precision Anchors for Reliability: 0% Pericardial Effusions Requiring open cardiac surgery through 24 mos²
- 80% more LAA Contact Points for Improved Sealing: 0% Device Embolization 24 Months²
- DRT Through 24 Months: 1.8%

*Occurrence of one of the following events between the time of implant and within 7 days following 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.

¹ Kar, S., et al, Primary Outcome Evaluation of the Next Generation LAAC Device: Results from the PINNACLE FLX Trial, Circulation, 2021.
² Doshi et al. JAHA, 2023.
**Primary Safety Endpoint:**
Peri-procedural Adverse Events

- **Performance Goal**: 4.21%

- **EVENT RATE**:
  - 0.5% (P<0.0001)

Defined as major adverse events between implant and 7d/discharge. N=400.
*Based on the combined rate observed in PREVAIL and CAP2, plus a clinically acceptable delta.

**Primary Efficacy Endpoint:**
Effective LAA Closure at 12-Months

- **Performance Goal**: 97.0%

- **EVENT RATE**:
  - 100% (P<0.0001)

Defined as any per-device flow with jet size ≤5mm on TEE; all observed leaks were ≤3mm by core lab adjudication. N=344.
*Based on the combined rate observed in PREVAIL and CAP2, minus a clinically acceptable delta.

1 Kar, S., Circulation, 2021.
WATCHMAN FLX™ Left Atrial Appendage Closure Device Complete Closure Rates
WATCHMAN FLX LAAC Device has significantly improved complete closure rates over Legacy WATCHMAN™ Left Atrial Appendage Closure Device; any residual leak with WATCHMAN FLX LAAC Device was < 3 mm via TEE⁠¹

COMPLETE Closure Comparison

Note: Graph displays two separate clinical studies: PROTECT-AF AND PINNACLE FLX.
1 Kar, Circulation, 2021.
## PINNACLE FLX 24-Month Results Reinforce Long-Term Efficacy for WATCHMAN FLX™ Left Atrial Appendage Closure Device¹,²

### PROVEN LONG-TERM EFFICACY

<table>
<thead>
<tr>
<th>Condition</th>
<th>Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>80% Increase in Contact Points for Sealing</td>
<td>1.7%</td>
</tr>
<tr>
<td>Dual-Row Precision Anchors for Reliability</td>
<td>0%</td>
</tr>
<tr>
<td>80% more LAA Contact Points for Improved Sealing Based on Effective LAA Closure at 45 Days</td>
<td>0%</td>
</tr>
<tr>
<td>Ischemic Stroke/ Systemic Embolism (Per 100 patient yrs/annualized)²</td>
<td>0%</td>
</tr>
<tr>
<td>Pericardial Effusions Requiring open cardiac surgery through 24 mos²</td>
<td>0%</td>
</tr>
<tr>
<td>Device Embolization Through 24 Months²</td>
<td>100%†</td>
</tr>
<tr>
<td>LAA Effective Closure¹</td>
<td>96.2%</td>
</tr>
<tr>
<td>Patients Discontinued OAC at 45 Days¹</td>
<td></td>
</tr>
</tbody>
</table>

*† LAA effective closure at 12 months is defined as any peri-device flow with jet size <5mm per core laboratory-assessed TEE.
1 Kar, S., et al, Primary Outcome Evaluation of the Next Generation LAAC Device: Results from the PINNACLE FLX Trial, Circulation, 2021.
2 Doshi et al. JAHA, 2023.*
PINNACLE FLX 24-Month Data Demonstrates Proven Efficacy with a Low Annualized Stroke Rate\(^1\)

1 Doshi et al. JAHA, 2023.
This rate is consistent with expectations in this high stroke risk patient population.
Expected rate of 4.0% (derived from the combined PROTECT-AF, CAP, PREVAIL, and CAP-2 studies) plus a clinically relevant delta.
Ischemic Stroke Across WATCHMAN Trials

Long-term data continues to differentiate WATCHMAN FLX™ Left Atrial Appendage Closure Device and provides on-going clinical support for LAAC to reduce the risk of ischemic stroke in NVAF patients.

PINNACLE FLX
Prohibitive Anatomy

97% procedural success and zero leak in 91% of WATCHMAN FLX™ Left Atrial Appendage Closure Device patients with prior prohibitive anatomy for a Legacy WATCHMAN™ Left Atrial Appendage Closure Device.¹

View Full Study Results

**Study Design**

The purpose of this study was to evaluate the safety and efficacy of WATCHMAN FLX™ LAAC Device in patients with a failed Legacy WATCHMAN™ LAAC Device attempt or prohibitive LAA anatomy.

### STUDY COHORTS

- Patients with a prior failed Legacy WATCHMAN 2.5 attempt (N=11)
- Patients with prohibitive anatomy to attempt LAAC with Legacy WATCHMAN (N=88)
- These study cohorts represented 21.6% of all patients (99 of 458) in PINNACLE FLX

### CONTROL COHORT

- Patients (N=359) that did not meet the criteria for prior failed or prohibitive anatomy to receive a Legacy WATCHMAN Device
- (458 total patient – 99 in study cohorts = 359 in the control cohort)

The PINNACLE FLX study enrolled 58 roll-in patients and 400 primary study patients between May 2018 and November 2018. Outcomes in this analysis are through 1 year.

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Study Outcomes

The purpose of this study was to evaluate the safety and efficacy of WATCHMAN FLX™ LAAC Device in patients with a failed Legacy WATCHMAN™ LAAC Device attempt or prohibitive LAA anatomy.

There was zero leak in 91% of the prohibitive anatomy cohort.¹

**ZERO LEAK**

- Zero leak in 90.9% in the failed Legacy WATCHMAN cohort
- Zero leak in 91.3% in the prohibitive anatomy cohort
- Zero leak in 89.5% in the control cohort

**PROCEDURAL SUCCESS**

- 100% of patients (11/11) with a prior failed Legacy WATCHMAN were successfully implanted with WATCHMAN FLX LAAC Device
- 96.6% of patients (85/88) with prohibitive anatomy were successfully implanted with WATCHMAN FLX LAAC Device

IDE TRIALS

PINNACLE FLX (WATCHMAN FLX™ Left Atrial Appendage Closure Device) and Amulet IDE (Amplatzer™ Amulet™ LAA Occluder)

View Full PINNACLE FLX Results

View Full Amulet IDE Results
PINNACLE FLX and Amulet IDE Outcomes

PINNACLE FLX Clinical Trial\textsuperscript{1,2}

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>WATCHMAN FLX\textsuperscript{TM}</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients</td>
<td>400</td>
</tr>
<tr>
<td>Age</td>
<td>73.8 ± 8.6</td>
</tr>
<tr>
<td>CHA\textsubscript{2}DS\textsubscript{2}-VASc Score</td>
<td>4.2 ± 1.5</td>
</tr>
<tr>
<td>HAS-BLED Score</td>
<td>2.0 ± 1.0</td>
</tr>
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</table>

Amulet IDE\textsuperscript{3}

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Amulet\textsuperscript{TM}</th>
<th>Legacy WATCHMAN\textsuperscript{TM}</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients</td>
<td>934</td>
<td>944</td>
</tr>
<tr>
<td>Age</td>
<td>75.0 ± 7.6</td>
<td>75.1 ± 7.6</td>
</tr>
<tr>
<td>CHA\textsubscript{2}DS\textsubscript{2}-VASc Score</td>
<td>4.5 ± 1.3</td>
<td>4.7 ± 1.4</td>
</tr>
<tr>
<td>HAS-BLED Score</td>
<td>3.2 ± 1.0</td>
<td>3.3 ± 1.0</td>
</tr>
</tbody>
</table>

![Graph showing PINNACLE FLX and Amulet IDE outcomes](image-url)
PINNACLE FLX and Amulet IDE Outcomes

1 Kar S., MD, et. al, Primary Outcome Evaluation of a Next-Generation Left Atrial Appendage Closure Device Results From the PINNACLE FLX Trial, CIRCULATION, 2021.
2 Kar S., MD, 24-Month Outcomes of PINNACLE FLX Study with the WATCHMAN FLX™ Left Atrial Appendage Closure Device Presented as Late-Breaking Clinical Science, Presented at TVT July 21, 2021.
3 Primary Outcomes of the Amplatzer™ Amulet™ IDE Randomized Controlled Trial, Presented as an abstract at the European Society of Cardiology Congress, August 30, 2021.

*Procedure related complications is defined as the occurrence of one of the following events between the time of implant and within 7 days after the procedure or by hospital discharge, whichever was later: death, ischemic stroke, systemic embolism, or device or procedure-related events requiring open cardiac surgery or major endovascular intervention such as pseudoaneurysm repair, arteriovenous fistula repair, or another major endovascular repair.
†Procedure related complications is defined as adverse events which are adjudicated as procedure-related and require either an invasive surgical or percutaneous intervention.
±PINNACLE FLX data measured at 24 months; Amulet IDE data measured at 18 months.
SEAL FLX Study

WATCHMAN FLX™ Left Atrial Appendage Closure Device demonstrated statistical superiority for complete occlusion vs Amulet™ LAA Occluder.¹

View Full Study Results

¹ Korsholm K et al.; TCT 2021.
Study Design

First study to exclusively compare occlusion results of WATCHMAN FLX™ LAAC Device vs Amulet™ LAA Occluder using CT imaging.¹

- Single-center, retrospective study of LAAO implantation at Aarhus University Hospital (Denmark) between 2018-2020
  - 1st cohort: Amplatzer Amulet (N=150) 2018 – 2019
  - 2nd cohort: WATCHMAN FLX (N=150) 2019 – 2020
- Cardiac CT was performed 8 weeks after LAAO

Primary Outcome
Complete Occlusion* Based on Cardiac CT Imaging

*Complete LAA occlusion defined as no visible peri-device leak (PDL) and absence of contrast patency in the distal LAA (LAA/left atrium Hounsfield ratio <0.25).
1 Korsholm-K et al.; TCT 2021.
Study Outcomes

WATCHMAN FLX™ LAAC Device Demonstrated Statistically Superior Complete Occlusion* vs Amulet™ LAA Occluder (p=0.001).¹

**Complete Occlusion**

at 8 Weeks (per CT)

- **WATCHMAN FLX**: 72.60% (90/124) (p=0.001)
- **AMPLATZER AMULET**: 30.50% (39/128)

**More Leak Pathways with a Two-Component Device**

at 8 Weeks (per CT)

- Peri-Device Leak
  - **WATCHMAN FLX**: 16%
  - **AMPLATZER AMULET** (At Disc): 13%
  - **AMPLATZER AMULET** (At Lobe): 10%
  - **AMPLATZER AMULET** (At Disc and Lobe): 16%

**Leak Measurements were Statistically Larger with Amulet than WATCHMAN FLX (p=0.008)** at 8 Weeks (per CT)

- Leak Size (mm²)
  - **WATCHMAN FLX**: 32 (p=0.008)
  - **AMPLATZER AMULET (AT DISC)**: 90

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*Complete LAA occlusion defined as no visible peri-device leak (PDL) and absence of contrast patency in the distal LAA (LAA/Left Atrium Hounsfield Ratio <0.25).

¹ Korsholm K et al.; TCT 2021.
SWISS APERO Study

WATCHMAN FLX™ LAAC Device demonstrated statistical superiority for procedural complications over Amulet™ LAA Occluder.¹

View Full Study Results

SWISS APERO Study Design and Endpoints

Investigator-initiated, multicenter, randomized superiority trial to assess if Amulet™ LAA Occluder is superior to Legacy WATCHMAN™ LAAC Device/WATCHMAN FLX™ LAAC Device based on device crossover or complete LAA sealing.¹

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**Primary Endpoints**
- Composite of justified crossover to the non-randomized device
- LAA patency (via CT) at 45 days

**Secondary Endpoints**
- PDL at 45-day TEE
- DRT at 45-day TEE and CT
- Procedural complications
- Clinical outcomes at 45 days
  - composite of CV death, stroke or systemic embolism, all bleedings

221 patients were randomly assigned to either Amulet (N=111) or WATCHMAN (N=110) [Legacy WATCHMAN N=25, WATCHMAN FLX N=85]

Study Outcomes

Procedure Related Complications and Pericardial Effusions
Statistically significantly higher rate of procedural complications with Amulet™ LAA Occluder, despite European implanter experience with the device.¹

<table>
<thead>
<tr>
<th>Primary Safety Endpoint Components</th>
<th>Amulet (N=111)</th>
<th>WATCHMAN/FLX (N=110)</th>
<th>Amulet vs WATCHMAN Risk Ratio (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Major Procedure Related Complication No. (%)*</td>
<td>10 (9.0%)</td>
<td>3 (2.7%)</td>
<td>3.30 (0.93-11.68)</td>
<td>0.047</td>
</tr>
<tr>
<td>Death, No. (%)</td>
<td>2 (1.8%)</td>
<td>0 (0.0%)</td>
<td></td>
<td>0.497</td>
</tr>
<tr>
<td>Cerebrovascular Event, No. (%)</td>
<td>2 (1.8%)</td>
<td>0 (0.0%)</td>
<td></td>
<td>0.498</td>
</tr>
<tr>
<td>Systemic Embolism, No. (%)</td>
<td>0 (0.0%)</td>
<td>0 (0.0%)</td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>Major Bleeding (BARC 3-5), No. (%)</td>
<td>8 (7.2%)</td>
<td>2 (1.8%)</td>
<td>3.96 (0.86-18.25)</td>
<td>0.054</td>
</tr>
<tr>
<td>Clinically Relevant Pericardial Effusion, No. (%)</td>
<td>4 (3.6%)</td>
<td>0 (0.0%)</td>
<td></td>
<td>0.122</td>
</tr>
<tr>
<td>Device Embolization, No. (%)</td>
<td>1 (0.9%)</td>
<td>1 (0.9%)</td>
<td>3.99 (0.06-16.04)</td>
<td>0.995</td>
</tr>
<tr>
<td>Acute Kidney Injury, No. (%)</td>
<td>0 (0.0%)</td>
<td>0 (0.0%)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Composite of death, CVE, systemic embolism, major bleeding, cardiac tamponade, device embolization, or acute kidney injury occurring within 7 days or thereafter if deemed procedure-related. All cardiac tamponades observed within 45 days after LAAC occurred in the Amulet Group.¹ Presented as an abstract at TCT 2021, published Circulation, 2021.

Peri-Device Leak
WATCHMAN FLX™ LAAC Device showed lower PDL than Amulet. No statistically significant difference in LAA patency.¹

Peri-Device Leak

![Graph showing procedure-related complications and pericardial effusions](SH-1553805-AB)
Real-World Outcomes with WATCHMAN FLX™ LAAC Device: SURPASS Early Results (45-Days)$^1$

The SURPASS Early Results analysis of the NCDR-LAAO Registry reinforces the excellent safety profile WATCHMAN FLX LAAC Device in over 16,000 real-world NVAF Patients.

View Study Results

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$^1$ Late Breaking Clinical Trial, Presented at CRT 2022 by Dr. Samir Kapadia.
SURPASS Early Results Design

Objective
Assess safety and efficacy outcomes in patients in the NCDR-LAAO Registry who received a commercial WATCHMAN FLX™ LAAC Device.

Design
WATCHMAN FLX LAAC Device patients included in the NCDR-LAAO Registry from AUGUST 2020 through August 2022, will be followed through 2 years post-implant. No exclusion criteria.

THIS ANALYSIS
45-Day Outcomes, N=16,048
August 5, 2020 – March 31, 2021

Patient Characteristics and Medications

<table>
<thead>
<tr>
<th>CHA₂DS₂-VASc Score</th>
<th>4.8 ± 1.5</th>
</tr>
</thead>
<tbody>
<tr>
<td>HAS-BLED Score</td>
<td>2.4 ± 1.0</td>
</tr>
<tr>
<td>Clinically Relevant Bleeding Event, %</td>
<td>61.8</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Antiplatelet/Anticoagulant Medications</th>
<th>Discharge N=16,048</th>
</tr>
</thead>
<tbody>
<tr>
<td>Warfarin Alone, %</td>
<td>2.9</td>
</tr>
<tr>
<td>Warfarin + Aspirin, %</td>
<td>9.1</td>
</tr>
<tr>
<td>NOAC Alone, %</td>
<td>21.0</td>
</tr>
<tr>
<td>NOAC + Aspirin, %</td>
<td>49.1</td>
</tr>
<tr>
<td>DAPT, %</td>
<td>7.9</td>
</tr>
<tr>
<td>SAPT, %</td>
<td>2.5</td>
</tr>
<tr>
<td>No OAC or APT, %</td>
<td>0.5</td>
</tr>
</tbody>
</table>

SURPASS Endpoints

<table>
<thead>
<tr>
<th>Safety Endpoint</th>
<th>Composite of all-cause death, ischemic stroke, systemic embolism, or device/procedure-related events requiring open cardiac surgery or major endovascular intervention between device implantation and 7 days or hospital discharge (whichever is later)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Effectiveness Endpoint</td>
<td>Occurrence of ischemic stroke or systemic embolism at 24 months post-implant</td>
</tr>
<tr>
<td>Additional Endpoints</td>
<td>• All-Cause Death • Stroke • Device-Related Thrombus • Systemic Embolism • Major Bleeding • Effective Device Closure • Implant Success • Device Embolization</td>
</tr>
</tbody>
</table>

1 Late Breaking Clinical Trial at CRT 2022, Presented by Dr. Samir Kapadia.
The SURPASS Early Results Data Reinforces the Outstanding Safety, Simplicity, and Seal of the WATCHMAN FLX™ Left Atrial Appendage Closure Device.

**Safety**
- **Major Procedural Adverse Event Rate**
  - 0.37% (60/16,048)

**Simplicity**
- **Procedural Success**
  - 98% (16,048/16,446)

**Seal**
- **Complete LAA Closure at 45 Days**
  - 82%
- **LAA Closure <3mm at 45 Days**
  - 95%

*Key safety endpoint: occurrence of all-cause death, ischemic stroke, systemic embolism, or device or procedure-related events requiring open cardiac surgery or major endovascular intervention between device implantation and seven days or hospital discharge (whichever is later).*

SH-1553805-AB
Exceedingly Low Pericardial Effusion Rates Observed in WATCHMAN FLX™ Left Atrial Appendage Closure Device’s Earliest U.S. Experience

<table>
<thead>
<tr>
<th>Pericardial effusion requiring either surgical or percutaneous intervention</th>
<th>Discharge N=16,048</th>
<th>45-days N=14,107</th>
</tr>
</thead>
<tbody>
<tr>
<td>• PE requiring open cardiac surgery</td>
<td>0.01% (2/16,048)</td>
<td>0.03% (4/14,107)</td>
</tr>
<tr>
<td>• PE requiring percutaneous treatment</td>
<td>0.31% (50/16,048)</td>
<td>0.50% (70/14,107)</td>
</tr>
</tbody>
</table>
These Real-World Data Reinforce the Excellent Safety Profile WATCHMAN FLX™ Left Atrial Appendage Closure Device Demonstrated in the PINNACLE FLX Trial*

*Results from different clinical investigations are not directly comparable.

**Safety endpoint defined as Composite of all-cause death, ischemic stroke, systemic embolism, or device/procedure-related events requiring open cardiac surgery or major endovascular intervention between device implantation and 7 days or hospital discharge (whichever is later).

***45-day outcome.
REAL-WORLD OUTCOMES WITH WATCHMAN FLX™ LAAC DEVICE: SURPASS 1-YEAR RESULTS

The SURPASS 1-Year Outcomes analysis of the NCDR-LAAO Registry™ now includes the largest number of commercial WATCHMAN FLX Device patients to date. These data continue to support the best-in-class safety of the WATCHMAN FLX Device with a 0.49% major procedural adverse event rate within 7 days or hospital discharge (whichever is later) and 98% implant success in >66,000 real-world NVAF patients.¹

¹ Late Breaking Clinical Trial at CRT 2023, Presented by Samir Kapadia.
**SURPASS 1-Year Design**

**Study Design**
- The objective of this SURPASS analysis is to assess long term safety and efficacy outcomes at one year with WATCHMAN FLX™ in a routine, real-world setting.
- This analysis includes the largest commercial WATCHMAN FLX patient population to date, with 66,894 patients implanted between August 5, 2020 and March 31, 2022.

**Patient Characteristics**
- Age: 76.2 ± 7.9 Years
- CHA₂DS₂-VASc: 4.8 ± 1.5
- HAS-BLED – 2.4 ± 1.0
- Women: 41%
- Clinically Relevant Bleeding: 57.7%

**Safety Endpoint**
Composite of all-cause death, ischemic stroke, systemic embolism, or device/procedure-related events requiring open cardiac surgery or major endovascular intervention between device implantation and 7 days or hospital discharge (whichever is later).
The 0.49% major procedural adverse event rate within 7 days or hospital discharge demonstrated in the SURPASS 1-Year Outcomes analysis further supports the unmatched safety profile observed in separate controlled and real-world analyses.

Key Safety Endpoints
(Within 7 Days or Discharge)

- **0.49%**
  - **SURPASS 1-Year**
    - (N=66,894)
- **0.37%**
  - **SURPASS Early Results**
    - (N=16,048)
- **0.5%**
  - **PINNACLE FLX**
    - (N=400)
- **0.6%**
  - **Meta-Analysis**
    - (N=999)

1 Late Breaking Clinical Trial at CRT 2023, Presented by Samir Kapadia. 2 Kapadia, CRT 2022. 3 Kar, Circulation 2021. 4 Della Rocca et al. Heart Rhythm 2022.
SURPASS data reinforces the WATCHMAN FLX™ Device procedural success with 98% of patients implanted (N=66,894) across nearly all anatomies in a real-world setting, confirming the WATCHMAN FLX Device real world experience replicates clinical trial outcomes.

Procedural Success

<table>
<thead>
<tr>
<th>Study</th>
<th>Procedural Success</th>
</tr>
</thead>
<tbody>
<tr>
<td>SURPASS 1-Year (N=66,894)</td>
<td>98%</td>
</tr>
<tr>
<td>SURPASS Early Results (N=16,048)</td>
<td>98%</td>
</tr>
<tr>
<td>PINNACLE FLX (N=400)</td>
<td>99%</td>
</tr>
<tr>
<td>PINNACLE FLX Failed Legacy WATCHMAN (N=88)</td>
<td>97%</td>
</tr>
<tr>
<td>Danish Study (N=91)</td>
<td>99%</td>
</tr>
<tr>
<td>Alster Registry (N=164)</td>
<td>100%</td>
</tr>
<tr>
<td>FLXibility Registry (N=300)</td>
<td>99%</td>
</tr>
<tr>
<td>SWISS-APERO (N=110)</td>
<td>100%</td>
</tr>
<tr>
<td>WATCHMAN FLX vs. Legacy WATCHMAN (N=27,103)</td>
<td>98%</td>
</tr>
</tbody>
</table>

The 1-Year SURPASS Data confirms the excellent safety profile the WATCHMAN FLX™ Device demonstrated in the PINNACLE FLX trial, with the largest (N=66,894) WATCHMAN FLX Device patient population to date.

Comparison with PINNACLE FLX\textsuperscript{1}

45-Day Outcomes

*Results from different clinical investigations are not directly comparable.

\textsuperscript{1} Kar, Circulation 2021.
The WATCHMAN FLX™ Device delivers proven stroke reduction and positively sustained outcomes at 1 year in the largest and highest-risk patient population studied to date.

1-Year Stroke Rates

1.6% 1-Year All Stroke Rates
1.2% 1-Year Ischemic Stroke Rates

1-Year Outcomes Comparison with PINNACLE FLX

- Key Safety Endpoint: SURPASS 0.49%, PINNACLE FLX 0.5%
- All Stroke*: SURPASS 1.6%, PINNACLE FLX 2.6%
- Ischemic Stroke*: SURPASS 1.2%, PINNACLE FLX 2.6%
- Systemic Embolism*: SURPASS 0.1%, PINNACLE FLX 0.3%
- Pericardial Effusion*: SURPASS 0.7%, PINNACLE FLX 1.0%

*1-Year Outcomes (KM Rates). Results from different studies are not directly comparable. For illustration purposes only.
Procedural and Short-Term Follow-up Outcomes of Amplatzer Amulet™ LAA Occluder vs WATCHMAN FLX™ LAAC Device: A Meta-Analysis¹

The largest comparison of peri-procedural success and short-term outcomes of WATCHMAN FLX LAAC Device vs Amplatzer Amulet LAA Occluder reveals superior procedural safety, higher procedural success, and better LAA closure with WATCHMAN FLX LAAC Device.

View Full Study Results

Study Design

Meta-Analysis of 4186 Patients from 21 Studies
• 3187 Amulet implants
• 999 WATCHMAN™ FLX LAAC Implant Device

No Difference in Thromboembolic Risk Between Groups
• CHA₂DS₂-VASc: 4.3 ± 1.5 for Amulet LAA Occluder
• CHA₂DS₂-VASc: 4.2 ± 1.5 for WATCHMAN FLX LAAC Device

Safety endpoint was the occurrence of death, stroke, major bleeding, myocardial infarction, major vascular complications, device embolization, or pericardial effusion within 7 days post-procedure.

Data from a first imaging study performed within 3-month were used to assess the incidence of peri-device leaks >5mm and device-related thrombosis (DRT).
Key Results: Safety
WATCHMAN FLX™ Left Atrial Appendage Closure Device showed a significantly lower incidence of peri-procedural complications. (p<0.01)

Adverse Events within 7 days of Implant

- 0 device embolizations occurred with WATCHMAN FLX LAAC Device vs.15 with Amulet™ Occluder
- WATCHMAN FLX™ LAAC Device demonstrated lower DRT than Amulet Occluder (1% vs 1.6%)
- No difference was observed for death or stroke between groups
Key Results: Seal
WATCHMAN FLX™ Left Atrial Appendage Closure Device demonstrated fewer peri-device leaks >5mm than Amplatzer Amulet™ LAA Occluder (0.01% vs 0.34%, p=0.06).
The ALSTER-FLX Registry: 3-Month Outcomes Following Left Atrial Appendage Occlusion Employing a Next-Generation Device, a Matched-Pair-Analysis to EWOLUTION¹

WATCHMAN FLX™ LAAC Device showed significant improvement for safety, simplicity and seal vs Legacy WATCHMAN™ LAAC Device in this retrospective registry analysis comparing early experience with both devices.

View Full Study Results

¹ Paitazoglou C., MD, Heart Rhythm, Feb. 2022.
Comparison

Study Design

<table>
<thead>
<tr>
<th>WATCHMAN™ Device (EWOLUTION Registry) N=1025</th>
</tr>
</thead>
<tbody>
<tr>
<td>N=5 Withdraw Informed Consent Form</td>
</tr>
<tr>
<td>Patients with Successful Implantation N=1005/1020 (98.5%)</td>
</tr>
<tr>
<td>Patients with &gt; 3 Month FU Data N=943 (94%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>WATCHMAN FLX™ Device (ALSTER-FLX Registry) N=164</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients with Successful Implantation N=164 (100%)</td>
</tr>
<tr>
<td>Patients with &gt; 3 Month FU Data N=150 (92%)</td>
</tr>
</tbody>
</table>

Propensity Score Matching 1:1
Ewolution (N=1020) vs ALSTER FLX (N=164)

Patient Characteristics

Compared to the patients in the EWOLUTION Registry, the ALSTER-FLX Registry had statistically higher:

- Bleeding risk (EWOLUTION 2.3 ± 1.2 vs ALSTER FLX 3.2 ± 0.8, p <0.001)
- History of major bleeding (EWOLUTION 31% vs ALSTER FLX 77.4%, p <0.001)
- History of ischemic stroke (EWOLUTION 19% vs ALSTER FLX 34.1%, p <0.001)
All outcomes were improved with WATCHMAN FLX™ LAAC Device vs Legacy WATCHMAN™ LAAC Device despite a higher morbidity (higher risk) patient population in the WATCHMAN FLX LAAC Device group.

Safety
• 0% stroke and 0% device embolization in the ALSTER-Registry compared to EWOLUTION (stroke 0.5%, device embolization 0.4%)
• Lower DRT with ALSTER FLX patients (2.4%) as compared to EWOLUTION patients (3.7%)

Simplicity
• 100% Procedural Success vs in the ALSTER-Registry compared to 99% in EWOLUTION

Seal
• Statistically-significantly higher complete sealing rate in the ALSTER-Registry compared to EWOLUTION at three months (ALSTER FLX 90% vs EWOLUTION 79.4%, p=0.039 after matching)
High Procedural Success Across Multiple WATCHMAN FLX™ Left Atrial Appendage Closure Device Studies

1 Late Breaking Clinical Trial at CRT 2022, Presented by Dr. Samir Kapadia.  2 Kar, PINNACLE FLX; 12 Month Outcomes, CIRCULATION, 2021.  3 Ellis, Structural Heart, 2021.  4 Korsholm, WM FLX First Experience, JACC, 2020.  5 Bergmann, Alster-Registry, Presented ePCR 2021.  6 Betts, Poster Presentation HRS, 2021.  7 Galea, SWISS-APERO Trial, CIRCULATION, 2021.
Safety and Acute Procedural Outcomes of LAAO with the First-Generation WATCHMAN and Next-Generation WATCHMAN FLX™ Devices

In-Hospital Outcomes for the WATCHMAN FLX LAAC Device Compared with the Legacy WATCHMAN™ LAAC Device.

View Full Study Results
Key Results: Safety
The purpose of this study was to compare the safety and acute procedural success of the first-generation Legacy WATCHMAN™ device vs the next-generation WATCHMAN FLX™ device.\(^1\)

**Primary Endpoint:** In-hospital major adverse events (MAE) Composite of death, cardiac arrest, stroke, TIA, ICH, SE, major bleeding, major vascular complication, MI, pericardial effusion requiring intervention, and device embolization.

1 Late Breaking Clinical trial at HRS 2022 presented by Dr James Freeman.
Study Outcomes
The purpose of this study was to compare the safety and acute procedural success of the first-generation WATCHMAN 2.5 device vs the next-generation WATCHMAN FLX device.¹

In-Hospital Adverse Event Rates

- In a natural experiment era analysis, WATCHMAN FLX associated with a significant 43% fewer in-hospital adverse events
- WATCHMAN FLX associated with significantly lower rates of several components of MAEs
  - Death
  - Pericardial effusion requiring intervention
  - Cardiac arrest
  - Major bleeding
  - Device embolization

¹ Late Breaking Clinical trial at HRS 2022 presented by Dr James Freeman.
CHAMPION-AF
Clinical Trial

The CHAMPION-AF trial evaluates LAAC vs NOAC in the broadest NVAF patient population to establish WATCHMAN FLX™ Left Atrial Appendage Closure Device as a first-line option to reduce stroke risk.

View Trial Design and Rationale
The primary objective of the CHAMPION-AF Trial is to determine if left atrial appendage closure with the WATCHMAN FLX™ LAAC Device is a reasonable alternative compared with non-vitamin K oral anticoagulants (NOACs) in patients with non-valvular atrial fibrillation.
CHAMPION AF: Primary Endpoints and Patient Selection Criteria

**PRIMARY ENDPOINTS**

- WATCHMAN FLX™ LAAC Device is non-inferior for the occurrence of stroke (including ischemic and/or hemorrhagic), cardiovascular (CV) death (including unexplained death), and systemic embolism at 36 months.
- WATCHMAN FLX LAAC Device is superior for non-procedural bleeding (ISTH* major bleeding and clinically relevant non-major bleeding) at 36 months.
- WATCHMAN FLX LAAC Device is non-inferior for the occurrence of ischemic stroke and systemic embolism at 60 months.

**PATIENT SELECTION**

- Patient has documented non-valvular atrial fibrillation (i.e., atrial fibrillation in the absence of moderate or greater mitral stenosis or a mechanical heart valve).
- CHA₂DS₂-VASc score of ≥ 2 for men and ≥ 3 for women.
- Patient is deemed to be suitable for long-term NOAC.

*International Society of Thrombosis and Hemostasis, Bleeding Assessment Tool.*
OPTION Clinical Trial

The **OPTION Trial** evaluates LAAC with the **WATCHMAN FLX™ Left Atrial Appendage Closure Device** as a **reasonable alternative to OAC following catheter ablation** for patients with NVAF.

[View Trial Design and Rationale](#)
OPTION Trial¹

OBJECTIVE:
To determine if LAAC with the WATCHMAN FLX™ Left Atrial Appendage Closure Device is a reasonable alternative to oral anticoagulation following catheter ablation for patients with NVAF.

1600 randomized subjects at 130 sites world-wide (enrollment completed)
Randomized 1:1 (Device to OAC)
Follow-Up at 3, 12, 24, and 36 months

MEDICATION REGIMENS

**Device Group**
Market approved OAC and aspirin (75-100mg recommended) for 90 days followed by aspirin through at least 12-months post-implant (recommended for duration of the trial).

**Control (OAC) Group**
Market approved OAC used per IFU for atrial fibrillation stroke prevention for the duration of the trial.

PRIMARY ENDPOINTS

**Non-inferiority:** All cause death, stroke, SE through 36 months

**Superiority:** Major non-procedural bleeding through 36 months

¹Study protocol, manuscript in development for publication.
DAPT FLX
Comparative Effectiveness of Post-Procedure Medications Following Left Atrial Appendage Occlusion: A DAPT Analysis with the WATCHMAN FLX™ Device¹

Among over 7,000 patients, there were no differences in rates of death, stroke, major bleeding or DRT among those treated with DAPT vs. warfarin or DOAC plus aspirin at 45 days following LAAO with WATCHMAN FLX.

View Study Results
DAPT FLX Design

**Objective**
- To evaluate if dual antiplatelet therapy (DAPT) as an alternative post-implant drug regimen option is safe

**Design**
- National Cardiovascular Data LAAO Registry (NCDR) patients undergoing WATCHMAN FLX implant were included in unmatched and 1:1 propensity matched analyses comparing discharge on DAPT vs. Aspirin and OAC (Warfarin or DOAC)
- Inclusion criteria
  - Successful WATCHMAN FLX implant (defined as device margin residual leak ≤ 5 mm at time of implant)
  - CHA$_2$DS$_2$-VASc ≥2 in men or ≥3 in women
  - Prescribed either DAPT, DOAC + Aspirin or Warfarin + Aspirin at discharge
- Differences in the composite endpoint were evaluated between groups

**Primary Outcome**
Composite endpoint between discharge and 45 days:
- All cause death
- Stroke
- Major bleed
- Systemic embolism

| N = 17,369 | DAPT = 2,122 | DOAC + ASA = 13,113 | Warfarin + ASA = 2,134 |
DAPT FLX Design

Adjusted Baseline Characteristics
To adjust for differences in baseline characteristics, 1:1 propensity score matching between groups (DAPT vs warfarin + Aspirin; DAPT vs DOAC + Aspirin) was performed. Variables included age, gender, race/ethnicity, CHA2DS2-VASc and HAS BLED score components, atrial fibrillation pattern, diabetes, fall risk, history of bleeding, chronic lung disease, sleep apnea, cardiomyopathy, coronary artery disease, prior ablation, LVEF and post implant device margin residual leak.

<table>
<thead>
<tr>
<th></th>
<th>DAPT N = 2,122</th>
<th>DOAC + ASA N = 2,122</th>
<th>P-Value</th>
<th>DAPT N = 1,407</th>
<th>Warfarin + ASA N = 1,407</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>77.1 ± 7.5</td>
<td>76.9 ± 7.7</td>
<td>0.27</td>
<td>76.7 ± 7.6</td>
<td>76.7 ± 7.6</td>
<td>0.88</td>
</tr>
<tr>
<td>Female sex, %</td>
<td>42.0</td>
<td>41.1</td>
<td>0.53</td>
<td>39.9</td>
<td>38.8</td>
<td>0.49</td>
</tr>
<tr>
<td>CHA2DS2-VASC</td>
<td>5.06 ± 1.4</td>
<td>5.04 ± 1.5</td>
<td>0.75</td>
<td>5.0 ± 1.5</td>
<td>4.9 ± 1.4</td>
<td>0.21</td>
</tr>
<tr>
<td>Vascular disease, %</td>
<td>59.9</td>
<td>59.7</td>
<td>0.88</td>
<td>58.0</td>
<td>57.5</td>
<td>0.79</td>
</tr>
<tr>
<td>Coronary artery disease, %</td>
<td>51.9</td>
<td>51.1</td>
<td>0.60</td>
<td>50.2</td>
<td>49.5</td>
<td>0.71</td>
</tr>
<tr>
<td>Prior stroke, %</td>
<td>25.4</td>
<td>24.8</td>
<td>0.65</td>
<td>25.4</td>
<td>23.1</td>
<td>0.16</td>
</tr>
<tr>
<td>History of clinically relevant bleeding, %</td>
<td>81.5</td>
<td>80.9</td>
<td>0.61</td>
<td>72.3</td>
<td>71.5</td>
<td>0.64</td>
</tr>
</tbody>
</table>
No differences in death, stroke, bleeding or DRT between DAPT and DOAC + ASA or Warfarin + ASA at 45 days following LAAO with the WATCHMAN FLX™ Device.
THE ICE LAA STUDY

Intracardiac Echocardiography (ICE) can be used to successfully guide WATCHMAN FLX™ procedures, with excellent procedural success, a high rate of effective closure, and minimal periprocedural complications.¹

View Study Results

Objective and Design

- The objective of the ICE LAA Study was to investigate the efficacy and safety of ICE-guided LAAC with the WATCHMAN FLX™ device.
- Prospective, non-randomized, single-arm, multi-center.
- 100 patients enrolled at 7 centers in Europe.
- Independent adjudication of echocardiographic data by a core laboratory and clinical events by a clinical events committee.

Patient Characteristics

- Age: 76 ± 8 years
- CHA₂DS₂-VASc: 4.0 ± 1.5
- HAS-BLED: 2.5 ± 0.9
- Female: 33%

Primary Endpoint

The primary endpoint was effective closure defined as significant peri-device leak (>5 mm) based on the 45-day post-implant TEE and assessed by the echocardiographic core laboratory.
The ICE LAA results confirmed the safety of ICE-guided WATCHMAN FLX™ implant with excellent procedural success and low rates of short-term complications.

**Primary Endpoint**
The primary endpoint was met as the rate of leak >5 mm was 0.0% with an upper one-sided confidence interval of 4.8%, which is lower than the performance goal of 5.5% (p=0.01). (Performance goal was a post-hoc analysis).

**Peri-Device Leak**

![Graph showing peri-device leak](image)

- **Post-Procedure**: 98.5% No Leak, 1.5% >0 to 3mm, 2.7% >3 to 5mm
- **45-Days**: 74.7% No Leak, 22.7% >0 to 3mm, 2.7% >3 to 5mm

---

**Performance Goal 5.5%**
- Upper 1-Sided 95% Confidence Interval **4.8%**
- 0.0% Rate of Leak >5mm
The ICE LAA results confirmed the safety of ICE-guided WATCHMAN FLX™ implant with excellent procedural success and low rates of short-term complications.

**Key Procedural and 45 Day Outcomes**

**Procedural Outcomes**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>成功率</th>
</tr>
</thead>
<tbody>
<tr>
<td>Device Success*</td>
<td>100%</td>
</tr>
<tr>
<td>Technical Success**</td>
<td>100%</td>
</tr>
<tr>
<td>Procedural Success***</td>
<td>96%</td>
</tr>
<tr>
<td>Conversion to TEE During Implant</td>
<td>0.0%</td>
</tr>
</tbody>
</table>

**45-Day Outcomes**

<table>
<thead>
<tr>
<th>Event</th>
<th>Patients, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mortality</td>
<td>1.0</td>
</tr>
<tr>
<td>Stroke</td>
<td>0.0</td>
</tr>
<tr>
<td>Systemic Embolism</td>
<td>0.0</td>
</tr>
<tr>
<td>Major Bleeding</td>
<td>0.0</td>
</tr>
<tr>
<td>Pericardial Effusion</td>
<td>0.0</td>
</tr>
<tr>
<td>Device Embolism</td>
<td>0.0</td>
</tr>
<tr>
<td>DRT</td>
<td>0.0</td>
</tr>
</tbody>
</table>

OUTCOMES AT 45 DAYS IN ~40,000 PATIENTS FROM THE NCDR LAAO REGISTRY™

ICE-guided WATCHMAN FLX™ procedures achieved similar safety and efficacy as TEE-guided procedures both acutely and at 45-days post procedure.¹

¹Ferro EG et al. ACC, Mar. 2023.
Objective and Design
• The objective of this analysis from the SURPASS NCDR LAAO Registry™ was to assess ICE as an alternative intraprocedural imaging modality based on outcomes through 45 days in relation to TEE-guided procedures.
• Nationwide, multicenter, prospective, non-randomized post-market surveillance registry for LAAO devices.
• 39,759 procedures with the WATCHMAN FLX™ device from October 2020 to September 2021 were included in the analysis.

Key Safety Endpoints
• Composite Major Adverse Events at 45 Days
• All-Cause Mortality at 45 Days
• Pericardial Effusion at 45 Days

Key Efficacy Endpoints
• Successful LAAO Device Implant
• Complete Seal at 45 Days (PDL = 0 mm)
• Use of General Anesthesia

1 Ferro EG et al. ACC, Marr. 2023.
**SURPASS ICE vs. TEE: Study Design**

**Periprocedural and Patient Characteristics**
- Overall, 31,835 cases (80%) were performed with TEE guidance alone.
  - 2,272 cases (5.7%) were performed with ICE guidance alone.
  - 5,652 cases (12.7%) were performed with combined ICE and TEE.
- ICE cases had longer procedural times, however required less general anesthesia use.

### LAAO Imaging Use

<table>
<thead>
<tr>
<th>Variable</th>
<th>ICE (N=2,272)</th>
<th>TEE (N=31,835)</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years [Mean ± SD (N)]</td>
<td>75.8 ± 8.0</td>
<td>76.4 ± 7.9</td>
<td>0.0005</td>
</tr>
<tr>
<td>Female sex [% (N)]</td>
<td>907 (39.9%)</td>
<td>13,018 (40.9%)</td>
<td>0.36</td>
</tr>
<tr>
<td>CHA2DS2-VASc Score [Mean ±SD (N)]</td>
<td>4.8 ± 1.5</td>
<td>4.8 ±1.5</td>
<td>0.24</td>
</tr>
<tr>
<td>HAS-BLED Score [Mean ± SD (N)]</td>
<td>2.5 ± 1.0</td>
<td>2.4 ±1.0</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Procedure Time, minutes [Mean ±SD (N)]</td>
<td>81.9 ± 34.8</td>
<td>77.8 ± 65.6</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Contrast Volume, mL [Mean ±SD (N)]</td>
<td>43.5 ± 33.6</td>
<td>41.9 ± 36.2</td>
<td>0.03</td>
</tr>
<tr>
<td>Minimal Sedation (anxiolysis) [% (N)]</td>
<td>12 (0.53%)</td>
<td>29 (0.09%)</td>
<td></td>
</tr>
<tr>
<td>Moderate Conscious Sedation [% (N)]</td>
<td>869 (38.3%)</td>
<td>393 (1.2%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>General Anesthesia [% (N)]</td>
<td>1,387 (61.1%)</td>
<td>31,327 (98.7%)</td>
<td></td>
</tr>
<tr>
<td>LAA Orifice Max Width, mm [Mean ±SD]</td>
<td>21.8 ± 5.1</td>
<td>20.9 ± 4.2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>1 LAAO Device Used [% (N)]</td>
<td>2,046 (90.1%)</td>
<td>27,374 (86.0%)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

1 Ferro EG et al. ACC, Marr. 2023.
**Key Safety and Efficacy Outcomes**

- ICE- and TEE-guided WATCHMAN FLX™ procedures achieved similar safety and effectiveness, although, pericardial effusion rates were significantly higher in ICE-guided procedures, however, were found to decline with increasing operator experience.

### ICE vs. TEE Safety

<table>
<thead>
<tr>
<th>Outcome</th>
<th>ICE</th>
<th>TEE</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>45-Day Composite MAE</td>
<td>5.2%</td>
<td>4.4%</td>
<td>0.13</td>
</tr>
<tr>
<td>45-Day Mortality</td>
<td>1.0%</td>
<td>0.7%</td>
<td>0.27</td>
</tr>
<tr>
<td>45-Day Pericardial Effusion</td>
<td>1.0%</td>
<td>0.5%</td>
<td>0.02</td>
</tr>
</tbody>
</table>

### ICE vs. TEE Efficacy

<table>
<thead>
<tr>
<th>Outcome</th>
<th>ICE</th>
<th>TEE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Successful LAAO Device</td>
<td>97.5%</td>
<td>98.9%</td>
</tr>
<tr>
<td>Complete Seal at 45-Days</td>
<td>83.4%</td>
<td>82.2%</td>
</tr>
<tr>
<td>Reduced Use of General Anesthesia</td>
<td>61.2%</td>
<td>98.4%</td>
</tr>
</tbody>
</table>

1 Ferro EG et al. ACC, Marr. 2023.
Legacy WATCHMAN™
Left Atrial Appendage Closure Device
PROTECT-AF and PREVAIL Clinical Trials

These Legacy WATCHMAN™ LAAC Device pivotal IDE trials in the U.S. established the WATCHMAN LAAC Device as a safe and effective alternative to OAC in NVAF patients intolerant to long-term OAC use.¹

View Full Trial Results

### PROTECT-AF and PREVAIL Clinical Trials¹ (U.S. Legacy WATCHMAN™ Left Atrial Appendage Closure Device IDE trials)

<table>
<thead>
<tr>
<th>PROTECT-AF</th>
<th>PREVAIL</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Enrollment</strong></td>
<td></td>
</tr>
<tr>
<td>2005-2008</td>
<td>2010-2012</td>
</tr>
<tr>
<td><strong>Purpose</strong></td>
<td></td>
</tr>
<tr>
<td>Demonstrate safety and effectiveness of the WATCHMAN implant compared to long-term warfarin</td>
<td>Demonstrate safety and effectiveness of the WATCHMAN implant compared to long-term warfarin</td>
</tr>
<tr>
<td><strong>Study Design</strong></td>
<td></td>
</tr>
<tr>
<td>2:1 Randomized, non-inferiority</td>
<td>2:1 Randomized, non-inferiority</td>
</tr>
<tr>
<td><strong>Primary Endpoints</strong></td>
<td></td>
</tr>
<tr>
<td>• Effectiveness: Stroke, systemic embolism and cardiovascular/unexplained death</td>
<td>• Effectiveness: Stroke, systemic embolism and cardiovascular/unexplained death</td>
</tr>
<tr>
<td>• Safety: Life-threatening events, which include device embolization requiring retrieval and bleeding events</td>
<td>• Effectiveness: Ischemic stroke or systemic embolism, occurring after 7 days post-randomization or WATCHMAN implant procedure</td>
</tr>
<tr>
<td></td>
<td>• Safety: Death, ischemic stroke, systemic embolism and procedure/device-related complications within 7 days of implantation procedure</td>
</tr>
</tbody>
</table>

Legacy WATCHMAN™ Left Atrial Appendage Closure Device – PROTECT-AF and PREVAIL Clinical Trials (5-Year Meta-analysis)¹

### Efficacy

<table>
<thead>
<tr>
<th>Event</th>
<th>HR</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>All stroke or SE</td>
<td>0.96</td>
<td>0.87</td>
</tr>
<tr>
<td>Ischemic stroke or SE</td>
<td>1.71</td>
<td>0.08</td>
</tr>
<tr>
<td>Hemorrhagic stroke</td>
<td>0.20</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Ischemic stroke or SE &gt;7 days</td>
<td>1.40</td>
<td>0.28</td>
</tr>
<tr>
<td>Disabling/Fatal Stroke (MRS change of ≥2)</td>
<td>0.45</td>
<td>0.03</td>
</tr>
<tr>
<td>Non-Disabling Stroke</td>
<td>1.37</td>
<td>0.35</td>
</tr>
<tr>
<td>CV/unexplained death</td>
<td>0.59</td>
<td>0.03</td>
</tr>
<tr>
<td>All-cause death</td>
<td>0.73</td>
<td>0.04</td>
</tr>
<tr>
<td>Major bleed, all</td>
<td>0.91</td>
<td>0.60</td>
</tr>
<tr>
<td>Major bleeding, non procedure-related</td>
<td>0.48</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

**55%**
Relative Risk Reduction in Disabling Strokes, Compared to Warfarin

**72%**
Relative Risk Reduction in Bleeding*, Compared to Warfarin

**27%**
Relative Risk Reduction in All-Cause Mortality, Compared to Warfarin

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NCDR-LAAO Registry™

Real-world registry data for the Legacy WATCHMAN™ Left Atrial Appendage Closure Device shows a low procedural adverse event rate and ischemic stroke rates comparable to prior Legacy WATCHMAN studies.¹,²

View Full Early Results

View Full Long-Term Results

¹ Virtual presentation at ACC 2020 by Dr. James Freeman. Late Breaking Clinical Trial, March 29, 2020.
² Virtual Presentation at ACC 2021 by Dr. Matthew Price.
Baseline clinical characteristics of Legacy WATCHMAN™ LAAC Device patients enrolled in the NCDR-LAAO Registry within the first 3 years\(^1\)

<table>
<thead>
<tr>
<th>NCDR LAAO Registry (N=36,681)</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean</td>
<td>76.0±8.1</td>
<td></td>
</tr>
<tr>
<td>Female Sex (%)</td>
<td>15,086 (41.1)</td>
<td></td>
</tr>
<tr>
<td>CHA(_2)DS(_2) VASc Score</td>
<td>4.8±1.5</td>
<td></td>
</tr>
<tr>
<td>HAS-BLED Score</td>
<td>3.0±1.1</td>
<td></td>
</tr>
</tbody>
</table>

- NCDR-LAAO Registry provides commercial device FDA surveillance for LAAO devices with active follow up of adverse events and clinical outcomes.
- All U.S. LAAO implants must be included in this Registry and is mandated for CMS reimbursement.
- The NCDR-LAAO Registry was developed through a collaboration with:
  - American College of Cardiology (ACC)
  - Society for Coronary Angiography and Intervention (SCAI)
  - Food and Drug Administration (FDA)
  - Centers for Medicare and Medicaid Services (CMS)
  - Boston Scientific

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\(^1\) Virtual presentation at ACC 2020 by Dr. James Freeman. Late Breaking Clinical Trial, March 29, 2020.
Review of the First 3 Years of Registry Data¹
This three-year registry analysis of >38,000 Legacy WATCHMAN™ LAAC Device in a high-risk patient population showed low acute adverse events and high procedural success.

### Adverse Event Rate

- **4.8%** PROTECT AF¹
- **4.1%** CAP¹
- **4.2%** PREVAIL¹
- **3.8%** CAP2¹
- **2.8%** EWOLUTION²
- **2.2%** NCDR-LAA³

### Procedural Success
- **98%**

### Closed with Leak <5mm
- **99.2%**

---

1-Year Clinical Outcomes

>36,000 real-world Legacy WATCHMAN™ patient’s studies at 1-year show an ischemic stroke rate comparable to prior WATCHMAN studies and better than what would be expected in untreated patients with the same stroke risk.

Rate of 1-Year Ischemic Stroke in NCDR-LAAO Registry Compared with Imputed Placebo

Ischemic Stroke

WATCHMAN Ischemic Stroke rate represented a >70% reduction compared to the expected ischemic stroke rate* in this patient population.

The 1-year Kaplan-Meier estimate of the ischemic stroke rate was 1.53%.

This low rate represented a >70% reduction compared to the expected ischemic stroke rate in this patient population.

*The imputed placebo method used to determine the expected event rate was derived from baseline thromboembolic risk and has been used in multiple prior publications.

1 Virtual Presentation at ACC 2021 by Dr. Matthew Price.
PROTECT-AF, PREVAIL, CAP2 Leak Analysis

This analysis showed **Legacy WATCHMAN™ LAAC Device** patients with and without leak continued to demonstrate a meaningful stroke reduction through 5 years.¹

View Full Study Results

¹ Presented at AHA, 2021, Vivek Reddy, M.D.
Study Design
Retrospective, post-hoc analysis of the Legacy WATCHMANTM Left Atrial Appendage Closure Device using the PROTECT-AF, PREVAIL studies and CAP2 registry data.¹

Assessment of peri-device leak (PDL) impact at 45 days and 12 months on long-term ischemic stroke or systemic embolism outcomes.

Peri-device leak from pooled patient data was categorized at 45 days and 1-year based on:

- Severity of leak (0mm vs >0-3mm vs >3-5mm vs >5mm)
- No leak vs any leak (>0mm to 5mm)

¹ Presented at AHA, 2021, Vivek Reddy, M.D.
CAP-1 was not included because leak assessment was not consistently captured.
>5mm leaks were excluded from this analysis as larger leaks are established as associated with adverse outcomes.
Study Outcome

There was meaningful stroke reduction at 5 years in patients with and without leak, with a combined annualized risk of 1.6% per year versus an expected ~6% risk for untreated patients.*³

Expected vs Observed Ischemic Stroke Rate for Leak

- There was no association between leak at 45 days and long-term outcomes (similar-to findings from the previous published PROTECT-AF study)
- Peri-device leak at 1-year was associated with an increased risk of ischemic stroke or systemic embolism with the Legacy WATCHMAN™ Left Atrial Appendage Closure Device

*Expected annualized rate of ischemic stroke for a patient population with identical baseline CHADSVASC score.
3 Presented at AHA, 2021, Vivek Reddy, M.D.
LAAC Therapy
LAA Occlusion Study (LAAOS III) Trial

The **LAAOS III trial** confirms that surgical **LAA occlusion reduced the risk of ischemic stroke and systemic embolism** in patients with atrial fibrillation.¹

View Full Trial Results

¹ Presented by Dr. Richard Whitlock at ACC Virtual 2021, Published – Whitlock R NEJM, 2021.
Afib patients undergoing cardiac surgery

Randomized 1:1

No LAA occlusion
N=2,391

Surgical LAA exclusion
N=2,379

Both arms received OAC with 75% of patients continuing OAC use at 3 years

Primary endpoint: Ischemic stroke or systemic embolism
## Study Primary Outcome at 3.8 years

The LAAOS III trial confirms that LAA occlusion had a statistically-significant reduction in the risk of ischemic stroke or systemic embolism vs no LAA occlusion in patients with atrial fibrillation.

<table>
<thead>
<tr>
<th>Event</th>
<th>LAAO (%)</th>
<th>No LAAO (%)</th>
<th>Risk Reduction</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Ischemic Stroke or Systemic Embolism</strong></td>
<td>4.8</td>
<td>7.0</td>
<td>33%</td>
<td>0.001</td>
</tr>
<tr>
<td>Ischemic Stroke</td>
<td>4.6</td>
<td>6.9</td>
<td>34%</td>
<td></td>
</tr>
<tr>
<td>Systemic Embolism</td>
<td>0.3</td>
<td>0.3</td>
<td>14%</td>
<td></td>
</tr>
</tbody>
</table>

**Landmark Analysis**

<table>
<thead>
<tr>
<th>Event</th>
<th>LAAO (%)</th>
<th>No LAAO (%)</th>
<th>Risk Reduction</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ischemic Stroke or Systemic Embolism within 30 Days after Surgery</td>
<td>2.2</td>
<td>2.7</td>
<td>18%</td>
<td></td>
</tr>
<tr>
<td>Ischemic Stroke or Systemic Embolism beyond 30 Days after Surgery</td>
<td>2.7</td>
<td>4.6</td>
<td>42%</td>
<td></td>
</tr>
</tbody>
</table>

1 Presented by Dr. Richard Whitlock at ACC Virtual 2021, Published – Whitlock R NEJM, 2021.
PRAGUE 17
4-Year Outcomes

Confirms the clinical benefit of LAAC in high-risk NVAF patients over NOAC therapy.¹

View Full Study Results

¹Presented TCT 2021, Published – Pavel Osmancik, MD, et al, JACC 2022, 4-Year Outcomes After LAAC Versus NOAC for Atrial Fibrillation.
**Design:**
Investigator-initiated, multi-center (10 centers/Czech Republic), prospective, randomized non-inferiority study.

**Objective:**
Evaluate if LAAC (Amplatzer Amulet™ LAA Occluder/Legacy WATCHMAN™ Left Atrial Appendage Closure Implant Device) in a high-risk NVAF patient population [mean CHA₂DS₂-VASc score 4.7] is non-inferior to NOAC for:

- Stroke or transient ischemic attack (TIA)
- Systemic Embolism
- Clinically significant bleeding*
- Cardiovascular death, or
- Significant peri-procedural or device-related complication

*Clinically significant bleeding = ISTH major or non-major clinically significant bleeding.

1 Presented TCT 2021, Published – Pavel Osmancik, MD, et al, JACC 2022, 4-Year Outcomes After LAAC Versus NOAC for Atrial Fibrillation.
Study Outcome at 48 Months
Confirms the clinical benefit of LAAC in high-risk NVAF patients over NOAC therapy.¹

Primary Endpoint
Stoke, TIA, SE, CV Death, Bleeding or Complications

- 4-year primary outcomes show non-inferiority for LAAC vs NOAC in a very high risk NVAF patients, Mean CHA₂DS₂-VASc score 4.7
- Non-procedural bleeding was significantly reduced with LAAC

```
sHR = 0.81 (95% CI, 0.56-1.18)
Gray’s test: P = 0.27
P Value for noninferiority = 0.006
```

¹ Present TCT 2021, Published – Pavel Osmancik, MD, et al, JACC 2022, 4-Year Outcomes After LAAC Versus NOAC for Atrial Fibrillation.
CAUTION: Federal law (USA) restricts this device to sale by or on the order of a physician. Rx only. Prior to use, please see the complete "Instructions for Use" for more information on Indications, Contraindications, Warnings, Precautions, Adverse Events, and Operator’s Instructions.

INTENDED USE/INDICATIONS FOR USE
The WATCHMAN FLX™ 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 CHA2DS2-VASc scores and are recommended for anticoagulation therapy;
• Are deemed by their physicians to be suitable for anticoagulation therapy;
• 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 FLX 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 Closure Device (see Table 62 of the eIFU).
• The patient has a known hypersensitivity to any portion of the device material or the individual components (see Device Description section of the eIFU) such that the use of the WATCHMAN FLX Device is contraindicated.
• Any of the customary contraindications for other percutaneous catheterization procedure (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 P2Y12 inhibitor.

WARNINGS
Implantation of the WATCHMAN FLX Device should only be performed by interventional cardiologists and/or electrophysiologists who are proficient in percutaneous procedures, transseptal procedures, the imaging modality utilized and who have completed the WATCHMAN FLX Physician Training program.
• 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 transesophageal or intracardiac echocardiographic imaging guidance in multiple views to avoid improper Closure Device sizing. For TEE recommended in multiple angles [e.g., 0°, 45°, 90°, 135°]; For ICE imaging, visualization of the LAA is recommended with the following anatomical structures: aortic valve (short-axis), mitral valve (long-axis), and pulmonary artery (short-axis), to assess the minimum and maximum diameter of the LAA ostium.

Brief Summary
WATCHMAN FLX™ Left Atrial Appendage Closure Device with Delivery System and WATCHMAN™ Access System

CAUTION: Federal law (USA) restricts this device to sale by or on the order of a physician. Rx only. Prior to use, please see the complete "Instructions for Use" for more information on Indications, Contraindications, Warnings, Precautions, Adverse Events, and Operator’s Instructions.

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PATIENT SELECTION FOR TREATMENT

In considering the use of the WATCHMAN FLX 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.

- The presence of indication(s) for long-term anticoagulation therapy, 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 FLX Device has not been established in patients for whom long-term anticoagulation is determined to be contraindicated. Factors that need to be considered for the WATCHMAN FLX 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, transseptal 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 FLX Device implant pharmacologic regimen (see Post-Procedure Information section) especially for patients at high risk for bleeding.

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 medication, 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, Hemoptyis, 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, Myocardial infarction, Nausea, Oral bleeding, Pericardial effusion/tamponade, Pleural effusion, Prolonged bleeding from a laceration, Pseudoaneurysm, Pulmonary edema, Radiation injury, 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.

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