

#AHA24

FIVE-YEAR RESULTS FROM THE AMPLATZER AMULET LEFT ATRIAL APPENDAGE OCCLUDER RANDOMIZED CONTROLLED TRIAL (AMULET IDE)

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All content provided by Dhanunjaya Lakkireddy, MD unless otherwise noted.



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DISCLOSURES

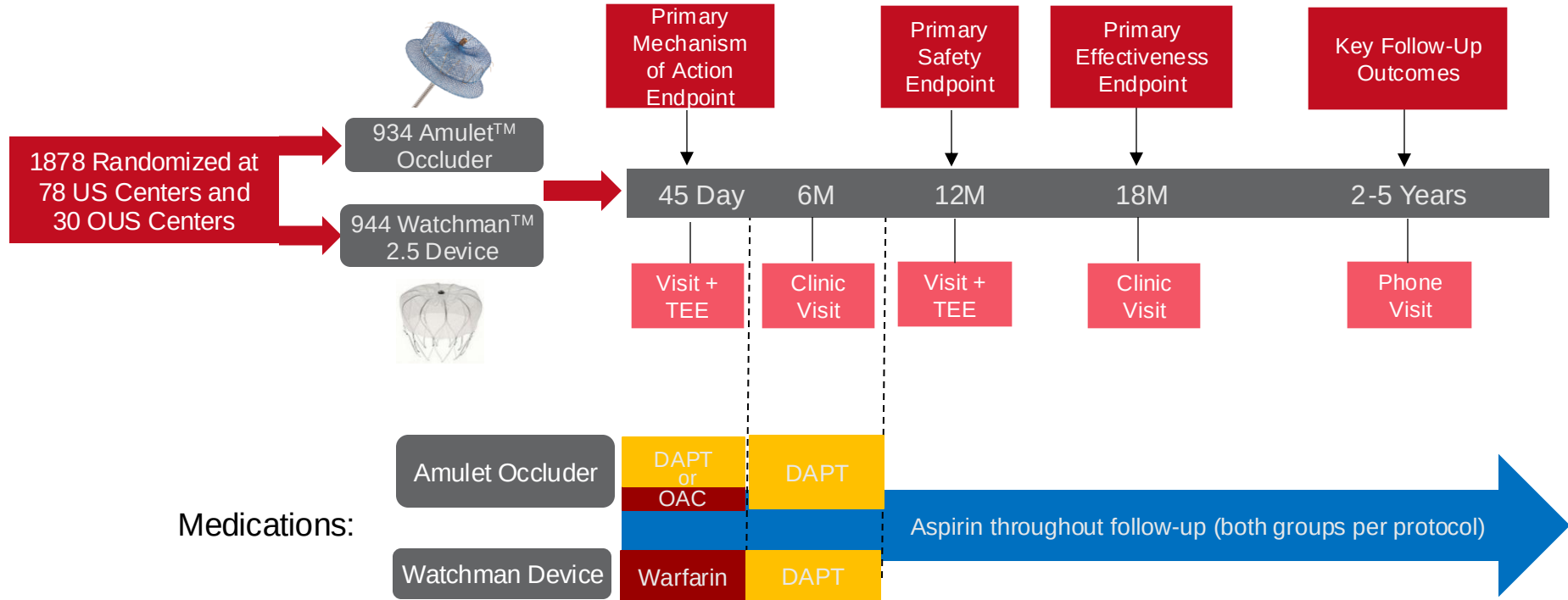
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Affiliation/Financial Relationship

- Grant/Research Support: Abbott, Atricure, Alta Thera, Medtronic, Biosense Webster, Biotronik, Boston Scientific
- Speaker honorarium: Abbott, Medtronic, Biotronik, Boston Scientific
- Principal investigator of the Amulet IDE trial

The Amulet IDE trial was funded by Abbott

AMULET IDE TRIAL OVERVIEW



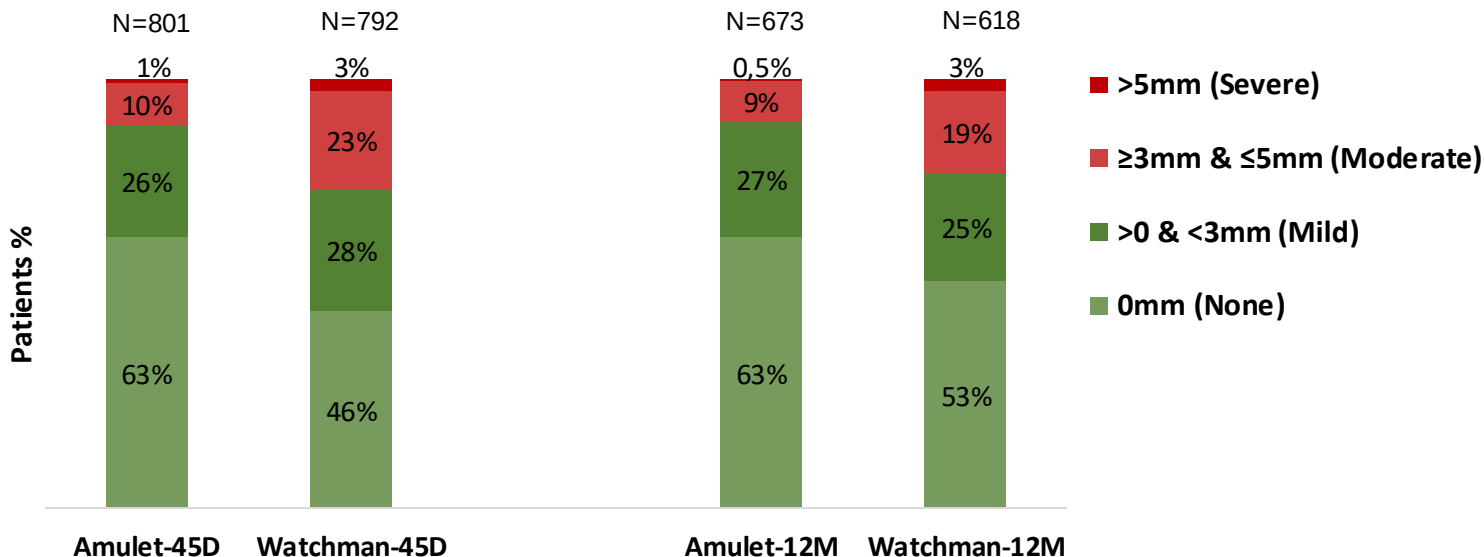
PRIMARY ENDPOINTS

- Results from the Amulet IDE trial were reported at the 2021 ESC congress
- Results Summary¹:**
 - Non-inferiority of all 3 primary endpoints:
 - Closure** (PDL ≤5mm) at 45 days
 - Safety** at 12 months
 - Effectiveness** at 18 months
 - Non-inferiority of secondary composite endpoint (stroke, SE, CV death) at 18 months was met
 - Superiority of closure** at 45 days with Amulet over Watchman

Endpoints	Amulet, n (%)	Watchman, n (%)
Closure (PDL ≤5mm) at 45 days	792 (98.9%)	767 (96.8%)
Safety (procedure-related complications, major bleeding, all-cause death) at 12 months	131 (14.5%)	130 (14.7%)
Effectiveness (ischemic stroke/systemic embolism) at 18 months	25 (2.8%)	24 (2.8%)
Secondary endpoint (stroke, systemic embolism, cardiovascular death) at 18 months	50 (5.6%)	67 (7.7%)

1) Lakkireddy et al. Circulation 2021;144:1543-1552.

AMULET OCCLUDER HAD SIGNIFICANTLY HIGHER LAA CLOSURE AT 45 DAYS AND 12 MONTHS



$p < 0.01$ for None, $\geq$ Mild, $\geq$ Moderate, and Severe categories at 45 days and 12 months

Results presented at HRS 2022 (Ellis et al.)

OBJECTIVE

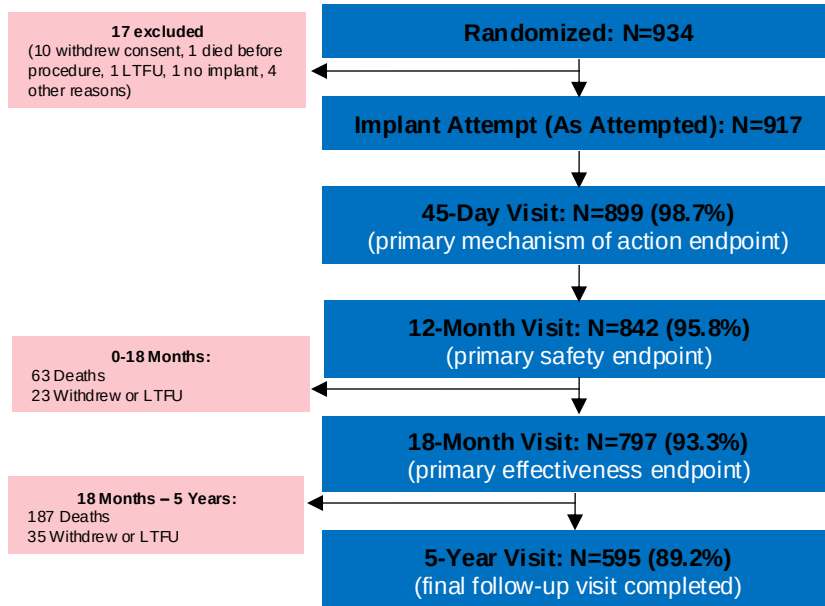
To assess 5-year outcomes of Amulet and Watchman LAA occluders in a randomized trial

METHODS

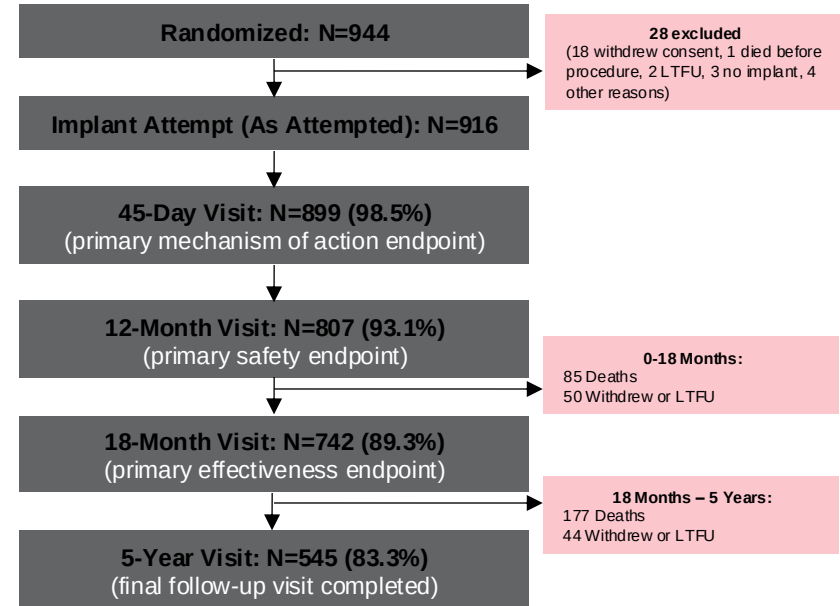
- The following clinical outcomes are reported at 5 years:
 - Composite of stroke, systemic embolism, or cardiovascular death
 - Composite of ischemic stroke or systemic embolism
 - Major bleeding
 - Cardiovascular death
 - All-cause death
- Kaplan-Meier method was used to summarize time to event data
- Annualized rates for recurrent events were calculated using recurrent events methods

PATIENT FOLLOW-UP THROUGH 5 YEARS

Amulet



Watchman



Higher follow-up rate with Amulet occluder driven by Watchman device group having more deaths and withdrawals within 18 months

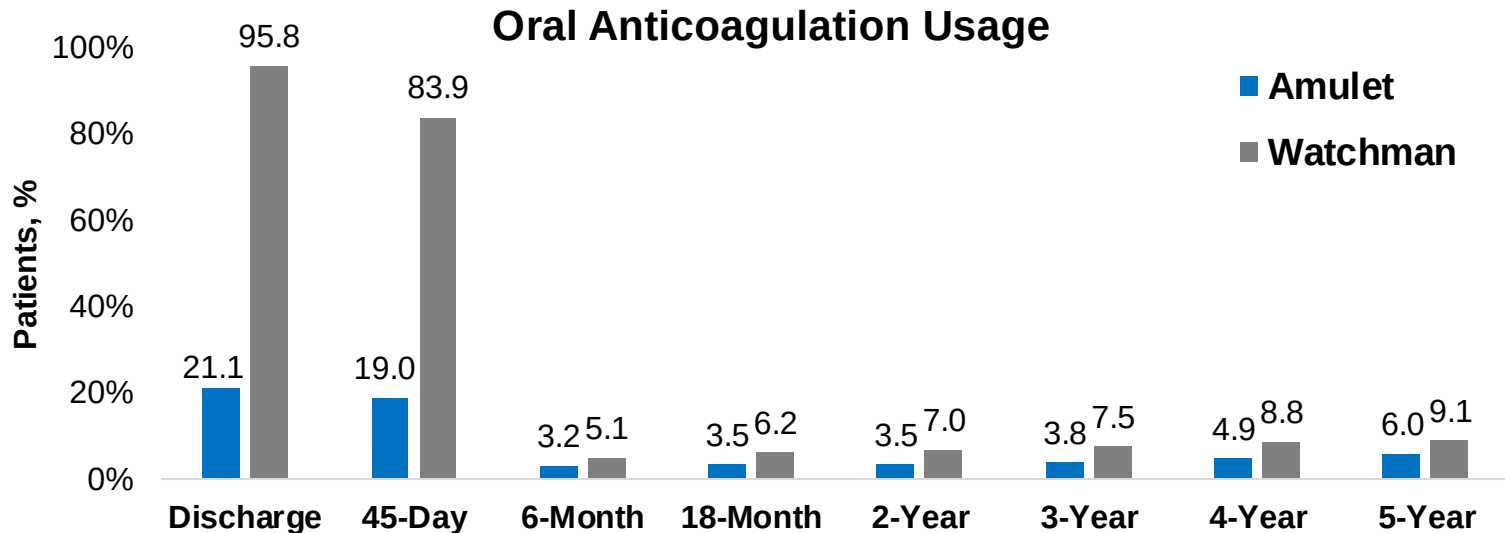
*Actual Follow-up Rate % - Visit Complete / (Visit Complete + Missed or Overdue Visits + Withdrawal (cumulative) + Lost to Follow-up (cumulative)).

BASELINE CHARACTERISTICS WERE WELL MATCHED BETWEEN DEVICE GROUPS

Clinical Characteristics	Amulet (N=917)	Watchman (N=916)
Age (yrs)	75.0 ± 7.6	75.2 ± 7.6
Male Sex	58.6%	61.4%
AF Classification		
Paroxysmal	56.7%	54.1%
Persistent/Permanent	43.3%	45.9%
AF at Procedure	39.7%	40.8%
Stroke/TIA/Thromboembolism	25.5%	28.9%
CHA ₂ DS ₂ -VASc Score	4.5 ± 1.3	4.7 ± 1.4
Major or Minor Bleeding	72.2%	71.8%
HAS-BLED Score	3.2 ± 1.0	3.3 ± 1.0

p>0.05 for all baseline characteristics

THROUGH 5 YEARS, OAC USAGE WAS SIGNIFICANTLY LOWER WITH AMULET COMPARED TO WATCHMAN

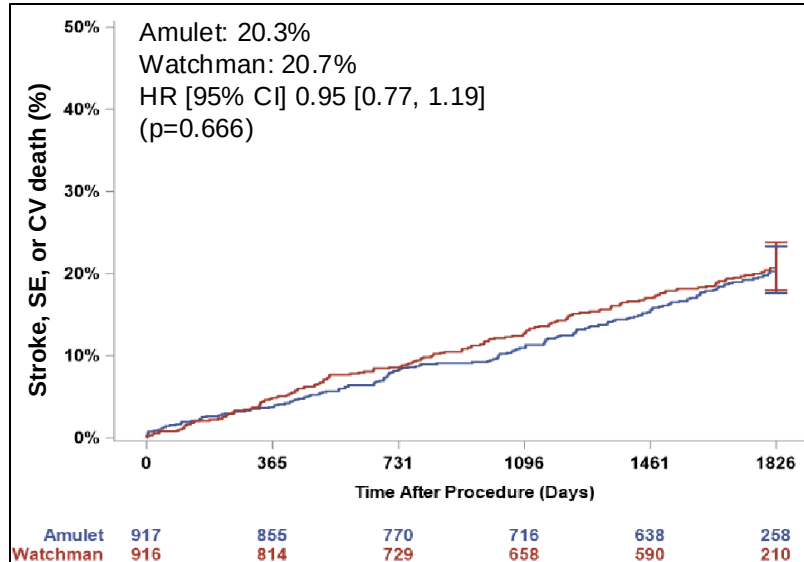


$p < 0.05$ between device groups for all time points

- More PDLs and late DRTs identified on the Watchman device attributed to patients resuming OAC after 45 days*
- 94% of Amulet occluder patients were free of OAC at 5 Years

*Results presented at HRS 2022 (Ellis et al.) and ACC 2022 (Schmidt et al.)

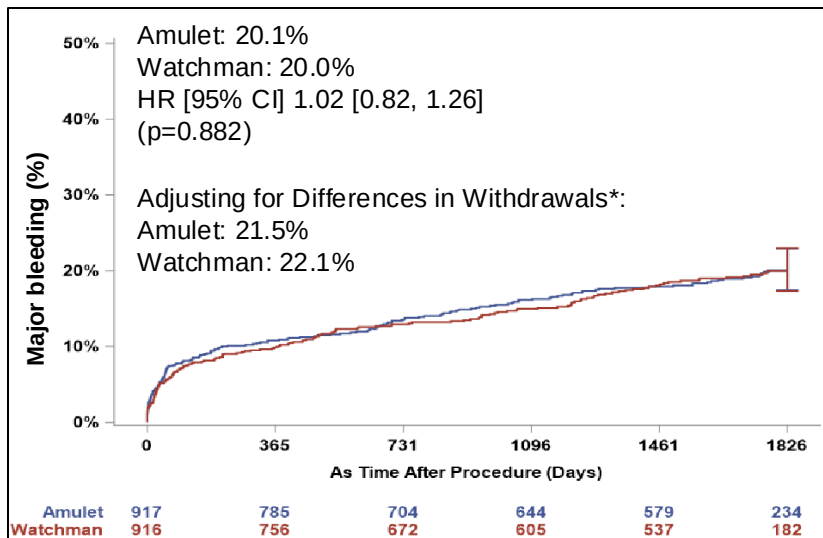
COMPOSITE RATES OF STROKE/SYSTEMIC EMBOLISM/CV DEATH AT 5 YEARS ARE COMPARABLE



	Amulet (N=917)	Watchman (N=916)
Stroke/systemic embolism/CV death	20.3% (n=163)	20.7% (n=161)
All stroke	8.1% (n=63)	7.8% (n=59)
Systemic embolism	0.3% (n=3)	0.4% (n=3)
Cardiovascular/unexplained death	14.3% (n=112)	15.4% (n=117)

Kaplan-Meier event rates

MAJOR BLEEDING RATES WERE COMPARABLE AT 5 YEARS



	Amulet (N=917)	Watchman (N=916)
Major bleeding*	20.1% (n=169)	20.0% (n=162)
Non-procedure related	17.4% (n=144)	18.2% (n=145)
Annualized rate at 5 years	6.0%/year	5.9%/year
0-6 months annualized rate	22.2%/year	18.7%/year
6 months – 5 years annualized rate*	3.8%/year	4.0%/year

*BARC type 3 or higher, including any transfusion with overt bleeding plus a hemoglobin drop of ≥ 3 g/dL

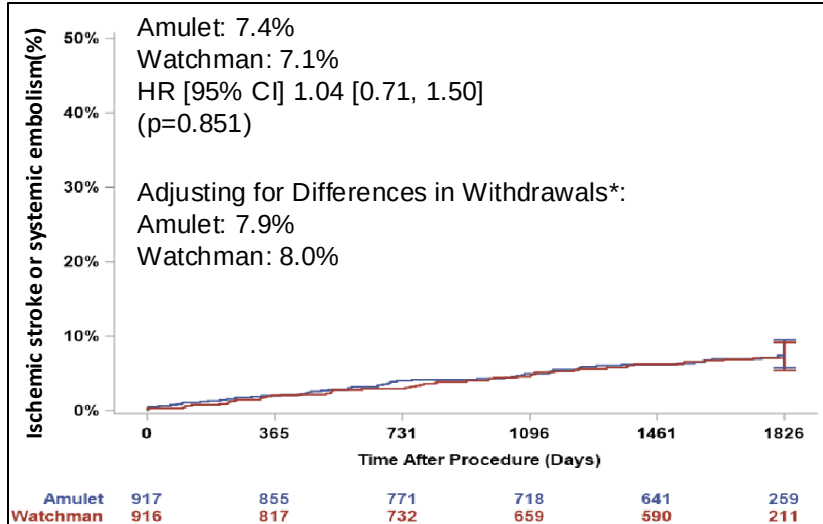
**aspirin only recommended for both groups after 6 months

- Excluding early follow-up post procedure, bleeding rates are low and comparable through 5 years
- >85% of major bleeding events adjudicated as not related to the procedure, highlighting the trial's high-bleeding risk population

Kaplan-Meier event rates

*Multiple imputation based on age, gender, CHA₂DS₂-VASc score, and HAS-BLED score (excluding withdrawal due to death)

THROMBOEMBOLIC EVENT RATES WERE COMPARABLE AT 5 YEARS



Kaplan-Meier event rates

*Multiple imputation based on age, gender, CHA₂DS₂-VASc score, and HAS-BLED score (excluding withdrawal due to death)

	Amulet (N=917)	Watchman (N=916)
Ischemic stroke/systemic embolism	7.4% (n=58)	7.1% (n=53)
Ischemic stroke	7.1% (n=55)	6.8% (n=51)
Systemic embolism	0.3% (n=3)	0.4% (n=3)
Annualized ischemic stroke rate at 5 years	1.6%/year	1.6%/year
Predicted annualized ischemic stroke rate	7.2%/year	7.6%/year
% reduction in the risk of stroke*	78%	79%

*Annualized ischemic stroke rates (events/patient-years) were compared to the anticipated rate by baseline CHA₂DS₂-VASc score for NVAf patients not treated with OAC through 5 years (ref. Friberg et al. *Eur Heart J.* 2012;33:1500-10).

LAO therapy demonstrated a low rate of annualized ischemic stroke through 5 years (1.6%/year)

DEVICE FACTORS MORE OFTEN OBSERVED PRIOR TO STROKE AND CV DEATHS WITH WATCHMAN DEVICE

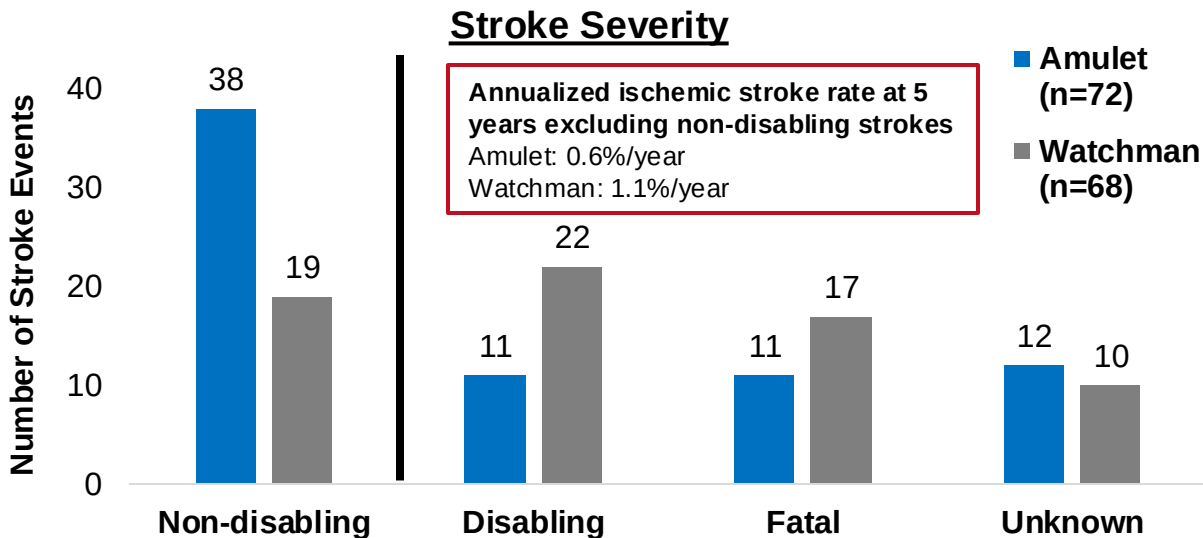
Strokes	Amulet (N=63)	Watchman (N=59)
Patient factors		
Age	75.6 ± 7.6	75.1 ± 8.9
CHA ₂ DS ₂ -VASc score	4.9 ± 1.3	4.7 ± 1.4
HAS-BLED score	3.5 ± 1.1	3.3 ± 1.0
Device factors		
Device-related thrombus	3	6
Peri-device leak (≥3mm)	4	18

Cardiovascular Deaths	Amulet (N=112)	Watchman (N=117)
Patient factors		
Age	76.9 ± 6.7	77.1 ± 8.2
CHA ₂ DS ₂ -VASc score	5.1 ± 1.4	4.9 ± 1.4
HAS-BLED score	3.5 ± 1.1	3.3 ± 1.0
Device factors		
Device-related thrombus	7	8
Peri-device leak (≥3mm)	17	31
Pulmonary artery laceration from device	0	0
Pericardial effusion leading to death	0	1

- **Watchman had nearly twice as many device factors (DRT or PDL) preceding strokes and CV deaths (63 vs. 31)**
- **No pulmonary artery injuries or pericardial effusions that led to death with Amulet**

Values are number of patients with stroke or cardiovascular deaths and experienced a device factor prior to the event through 5 years. Numbers are not mutually exclusive.

SIGNIFICANTLY MORE SEVERE STROKES WITH THE WATCHMAN DEVICE



Fatal: adjudicated cause of death was related to the stroke

Disabling: mRS score was ≥ 2 at the 90-day stroke assessment and increased ≥ 1 point compared to the pre-stroke baseline

Non-disabling: mRS score was < 2 at the 90-day stroke assessment or ≥ 2 without an increase of at least 1 point compared to the pre-stroke baseline

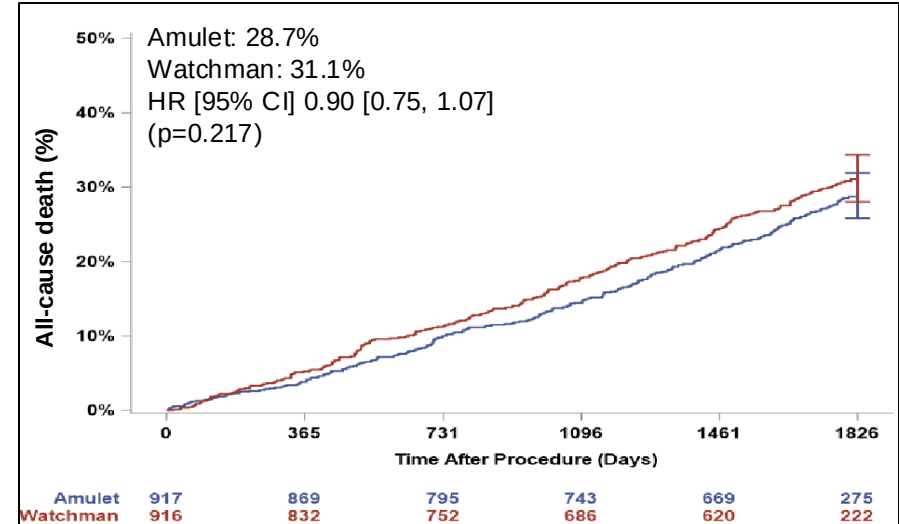
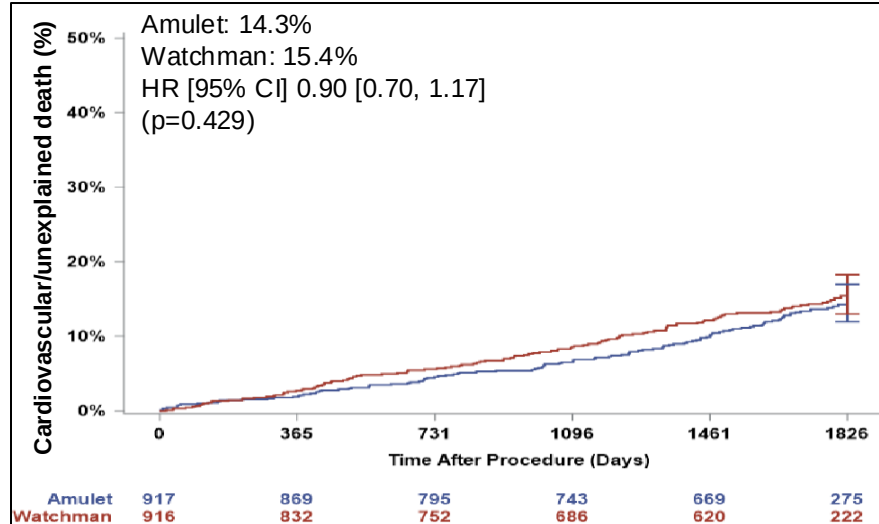
Unknown: unable to classify stroke (i.e. missing mRS assessment)

Severe strokes (fatal or disabling): 39 Watchman vs. 22 Amulet; $p=0.030$

Device factor (DRT or PDL) prior to fatal or disabling stroke: 19 Watchman vs. 4 Amulet

- Watchman had significantly more severe strokes than Amulet (39 Watchman vs. 22 Amulet; $p=0.030$)
- Device factors (DRT or PDL) preceded severe strokes more often with Watchman than Amulet (19 Watchman vs. 4 Amulet)

CARDIOVASCULAR/UNEXPLAINED DEATH AND ALL-CAUSE DEATH WERE COMPARABLE AT 5 YEARS



Kaplan-Meier event rates

LIMITATIONS & FUTURE IMPLICATIONS

- Less follow-up with the Watchman group compared to the Amulet group
- Newer generation Watchman device iterations now available
 - Watchman 2.5 was the only FDA approved device at the time of enrollment
- Differences in required antithrombotic regimens between the two devices may influence clinical events
- More data will be presented on the use of Amulet from the real-world

KEY TAKEAWAYS FROM THE LARGEST LAAO RANDOMIZED CONTROLLED TRIAL THROUGH 5 YEARS

Amulet LAAO compared to Watchman LAAC device demonstrated:

- Significantly **higher LAA closure** with Amulet LAAO at 45 Days and 12 months
- Significantly **higher freedom from OAC** with Amulet LAAO
- Comparable thromboembolic, major bleeding, and mortality event rates through 5 years
- Device-related factors (DRT and PDL) preceded strokes and CV deaths **less often with Amulet**
- **No PE-attributed deaths with Amulet** LAAO compared to one with Watchman LAAC
- **Low annualized ischemic stroke rate** in both device groups at 5 years (1.6%/year)
- Most strokes with Amulet LAAO were **non-disabling** (0.6%/year annualized severe ischemic stroke rate vs. 1.1%/year with Watchman LAAC)

CONCLUSION

The Amulet IDE trial demonstrated that the Amulet LAA occluder with **dual-seal technology** provides **superior closure** vs. the single-lobe Watchman device, with **fewer PDL and DRT**, **less severe strokes**, and significantly **higher freedom from OACs**.

THANK YOU

Results now available in JACC



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Rx Only

Important Safety Information

AMPLATZER™ AMULET™ LEFT ATRIAL APPENDAGE OCCLUDER

Indication for Use

The Amplatzer™ Amulet™ Left Atrial Appendage Occluder is a percutaneous transcatheter device intended to reduce the risk of thrombus embolization from the left atrial appendage (LAA) in patients who have nonvalvular atrial fibrillation and who are at increased risk for stroke and systemic embolism based on CHADS2 or CHA2DS2-VASc scores, are suitable for short term anticoagulation therapy, and have appropriate rationale to seek a non-pharmacologic alternative to oral anticoagulation, taking into consideration the safety and effectiveness of the device.

Contraindications

The Amplatzer™ Amulet™ Left Atrial Appendage (LAA) Occluder is contraindicated for patients:

- With the presence of intracardiac thrombus.
- With active endocarditis or other infections producing bacteremia.
- Where placement of the device would interfere with any intracardiac or intravascular structures.

Potential Adverse Events

Potential adverse events associated with the device or implant procedure include, but are not limited to, the following: Air embolism; Airway trauma; Allergic reaction; Anemia; Anesthesia reaction (nausea, vasovagal reaction, confusion/altered mental status or other); Arrhythmia; Atrial septal defect; Bleeding; Cardiac arrest; Cardiac tamponade; Chest pain/discomfort; Congestive heart failure; Death; Device embolization; Device erosion; Device malfunction; Device malposition; Device migration; Device-related thrombus; Fever; Hematuria; Hypertension/hypotension; Infection; Multi-organ failure; Myocardial infarction; Perforation; Pericardial effusion; Pleural effusion; Renal failure/dysfunction; Respiratory failure; Seizure; Significant residual flow; Stroke; Thrombocytopenia; Thromboembolism: peripheral and pulmonary; Thrombus formation; Transient ischemic attack; Valvular regurgitation/insufficiency; Vascular access site injury (hematoma, pseudoaneurysm, arteriovenous fistula, groin pain or other); Vessel trauma/injury.

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