3-Year Outcomes from the Amplatzer™ Amulet™ Left Atrial Appendage Occluder Randomized Controlled Trial (Amulet IDE)

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Disclosure Statement of Financial Interest

I, Dhanunjaya Lakkireddy, DO NOT have a financial interest/arrangement or affiliation with one or more organizations that could be perceived as a real or apparent conflict of interest in the context of the subject of this presentation.

The Amulet IDE trial was funded by Abbott

Faculty disclosure information can be found on the app

Disclosure Statement of Financial Interest

Within the past 12 months, I or my spouse/partner have had a financial interest/arrangement or affiliation with the organization(s) listed below.

Affiliation/Financial Relationship	Company
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	Abbott

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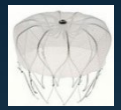
Amulet IDE Trial

1878 Randomized at 78 US Centers and 30 OUS Centers

934 Amulet™ Occluder

944 Watchman™ 2.5 Device



Primary Mechanism of Action Endpoint

Primary Safety Endpoint

Primary Effectiveness Endpoint

Key Follow-Up Outcomes

45 Day | 6M | 12M | 18M | 3Yr

Visit + TEE | Clinic Visit | Visit + TEE | Clinic Visit | Phone Visit

Medications:

Amulet Occluder	DAPT or OAC	DAPT	Aspirin throughout follow-up (both groups per protocol)
Watchman Device	Warfarin	DAPT	

CRF TCT

Primary Endpoints

- Results from the Amulet IDE trial were reported at the ESC congress on August 30, 2021
- Results Summary*:
  - All 3 primary endpoints were met: *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
  - At 45 days, the Amplatzer™ Amulet™ LAA occluder achieved *superior closure* (PDL ≤5mm) over the Watchman™ device

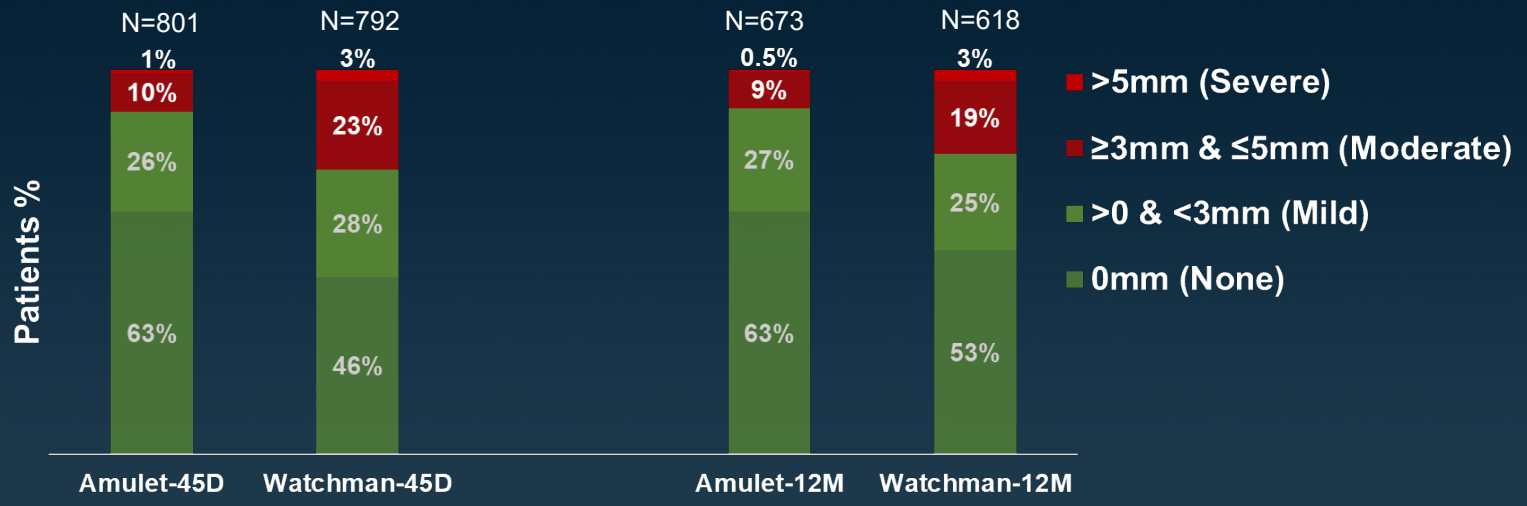
Endpoints	Amulet, n (%)	Watchman, n (%)
Closure (PDL ≤5mm) at 45 days[1]	792 (98.9%)	767 (96.8%)
Safety (procedure-related complications, major bleeding, all-cause death) at 12 months[2]	131 (14.5%)	130 (14.7%)
Effectiveness (ischemic stroke/systemic embolism) at 18 months[3]	25 (2.8%)	24 (2.8%)
Secondary endpoint (stroke, systemic embolism, cardiovascular death) at 18 months[4]	50 (5.6%)	67 (7.7%)

[1] Analyzed in patients who received a device as randomized
[2] Analyzed in per protocol population
[3] Analyzed in intent-to-treat population
[4] Analyzed in attempt as randomized population

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

Amulet™ Occluder had Higher Complete LAA Closure on Core Lab Analyzed TEEs

Amulet occluder patients had significantly higher complete LAA closure rate by TEE compared to Watchman™ device patients at both 45 days and 12 months



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

CRF TCT

Results presented at HRS 2022 (Ellis et al.)

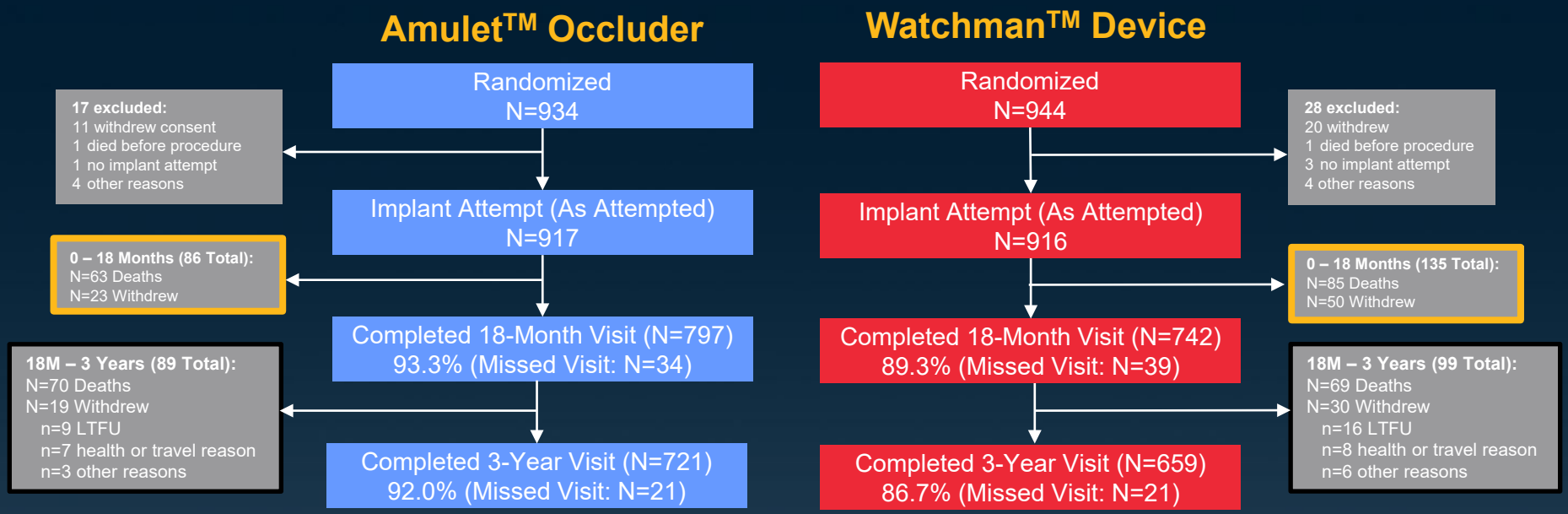
Objective

- To evaluate the device effect on 3-year outcomes in the Amulet IDE Trial

Methods

- Descriptive analyses of clinical outcomes are reported at 3 years based on the “as attempted” population to evaluate device effect:
  - Composite of stroke, systemic embolism, or cardiovascular death
  - All-cause death and cardiovascular death
  - Major bleeding
  - Composite of ischemic stroke or systemic embolism
- Kaplan-Meier method was used to summarize outcomes
- Annualized rates were calculated using recurrent events
- Patient-level details on outcomes >6 months
  - Medication regimen consistent between groups beyond 6 months (aspirin only recommended)

Patient Follow-Up Through 3 Years



Higher follow-up rate with Amulet occluder driven by increased deaths and withdrawals in the Watchman device group within 18 months

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

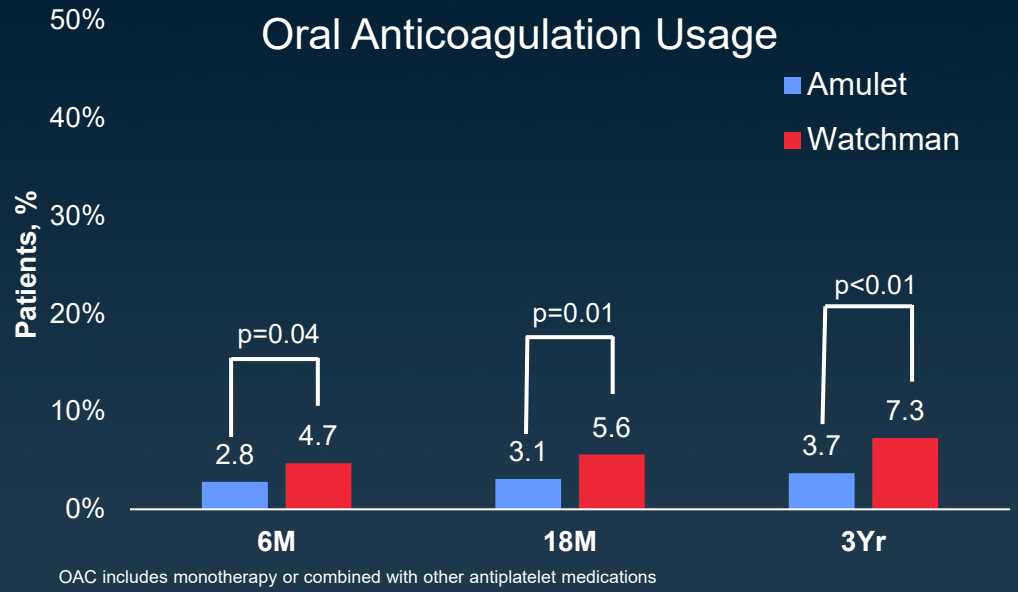
Baseline Characteristics are Well Matched Between Device Groups

Clinical Characteristics*	Amulet™ (N=917)	Watchman™ (N=916)
Age (yrs)	75.0 ± 7.6	75.2 ± 7.6
Male sex	58.6%	61.3%
AF Classification		
-Paroxysmal	56.7%	54.0%
-Persistent/Permanent	43.3%	46.0%
AF at procedure	39.7%	40.8%
CHA_2DS_2-VASc Score	4.5 ± 1.3	4.7 ± 1.4
HAS-BLED Score	3.2 ± 1.0	3.3 ± 1.0
Major or Minor Bleeding	72.2%	71.8%
Stroke/TIA/Thromboembolism	25.5%	28.9%

*Analyzed in as attempted population

Through 3 Years, OAC Usage was Lower with Amulet™ Occluder than Watchman™ Device

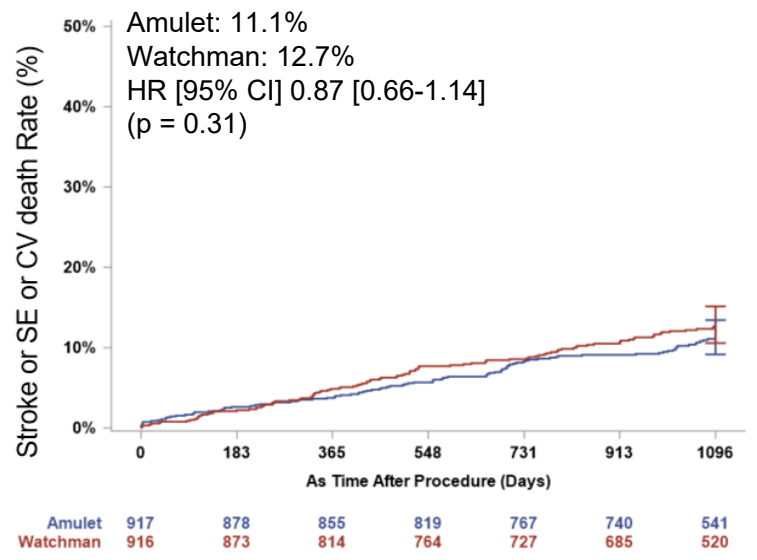
More patients were placed on OAC after identification of late DRT (>6 months) in Watchman device (n=23) than Amulet occluder (n=10)*



OAC includes monotherapy or combined with other antiplatelet medications

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

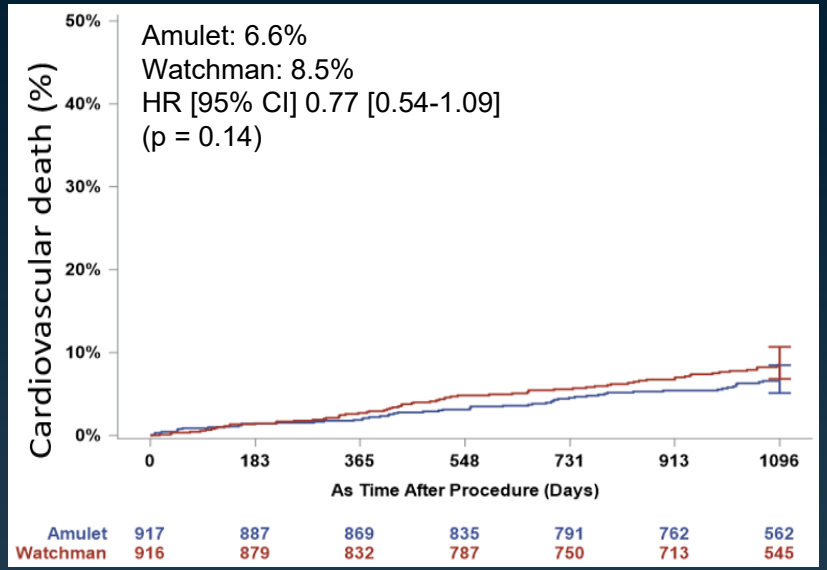
Composite Rates of Stroke/Systemic Embolism/CV Death at 3 Years are Comparable



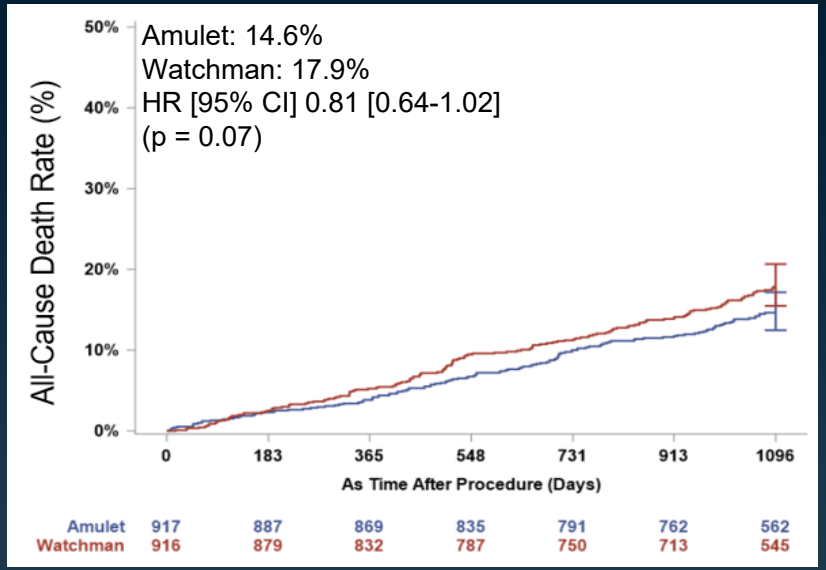
	Amulet™ (N=917)	Watchman™ (N=916)
Stroke/systemic embolism/CV death	11.1% (n=95)	12.7% (n=105)
All stroke	5.3% (n=44)	5.2% (n=42)
Systemic embolism	0.3% (n=3)	0.2% (n=2)
Cardiovascular death	6.6% (n=56)	8.5% (n=70)

Both Cardiovascular Death and All-Cause Death Trended Lower at 3 Years with Amulet™ Occluder than Watchman™ Device*

Cardiovascular Death



All-Cause Death



*Descriptive analysis of non-powered endpoints in a population with differential long-term follow-up at 3 years

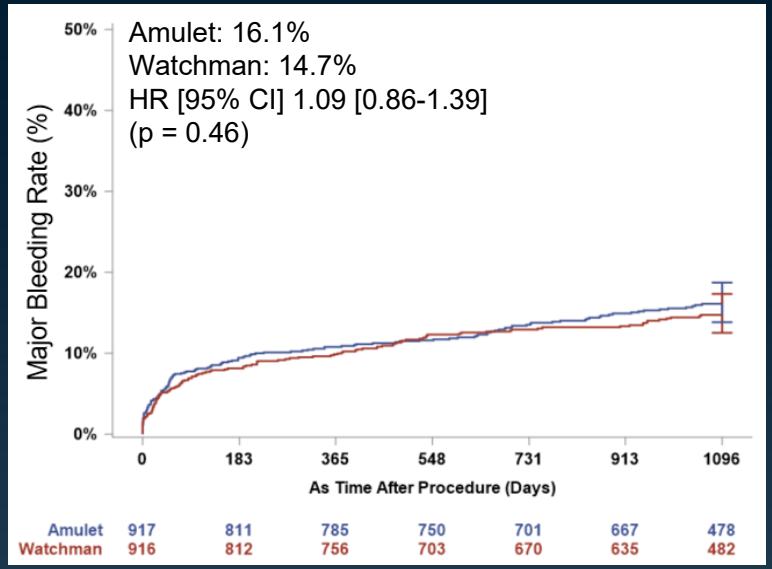
Device Factors More Often Observed in Watchman™ Device Patients with CV Death

Majority CV deaths in the Amulet™ occluder group were not preceded by a device factor, whereas device factors (DRT or PDL) frequently preceded CV deaths in the Watchman device group

CV Death Patient Details (6 Months – 3 Years)*	Amulet (n=43)	Watchman (n=58)
Patient factors		
CHA_2DS_2-Vasc score	5.0 ± 1.6	5.0 ± 1.4
HAS-BLED score	3.5 ± 0.9	3.4 ± 1.0
Device factors		
Device-related thrombus	1	4
Peridevice leak (≥3mm)	5	15
Pericardial effusion	0	0
OAC usage time of death	2	5

* ASA only recommended for both groups after 6 months

Major Bleeding Rates were Comparable at 3 Years



	Amulet™ (N=917)	Watchman™ (N=916)
Major bleeding	16.1% (n=141)	14.7% (n=127)
Non-procedure related	13.4% (n=116)	13.0% (n=110)
Annualized rate at 3 years	7.2%/year	6.9%/year
0 – 6 months annualized rate	22.2%/year	18.7%/year
6 months – 3 years annualized rate*	3.9%/year	4.2%/year

*ASA only recommended for both groups after 6 months

Major bleeding is defined as BARC Type 3 or greater (any transfusion with overt bleeding)

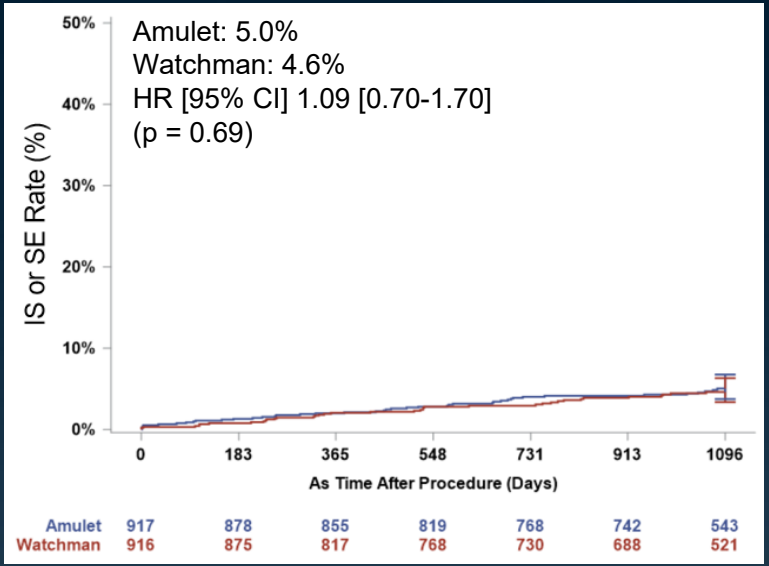
Major Bleeding Events During Aspirin Monotherapy were GI Related

Source of Bleeding (n of events) (6 Months – 3 Years)	Amulet™ (n=81)	Watchman™ (n=80)
Gastrointestinal	46	45
Trauma or fall	7	17
Hematoma*	8	4
Intracerebral or subdural hemorrhage	5	6
Pericardial effusion (PE)**	3	3
Hemothorax	4	1
Hematuria	2	2
Cancer	2	2
Epistaxis	3	0
Aortic aneurysm	1	0

*All hematoma events >6 months occurred from other elective procedures
(Amulet: 3 orthopedic, 2 lumbar laminectomy, 1 aneurysm, 1 craniotomy, 1 other;
Watchman: 1 orthopedic, 1 lumpectomy, 1 lumbar, 1 other)
**Amulet: 2 PEs undetermined cause, 1 PE from other elective procedure
Watchman: 2 PEs from secondary closure of PDL, 1 PE from other elective procedure

Major bleeding is defined as BARC Type 3 or greater (any transfusion with overt bleeding); ASA only recommended for both groups >6 months

Thromboembolic Event Rates were Comparable at 3 Years



	Amulet™ (N=917)	Watchman™ (N=916)
Ischemic stroke/systemic embolism	5.0% (n=42)	4.6% (n=37)
Ischemic stroke	4.7% (n=39)	4.5% (n=36)
Systemic embolism	0.3% (n=3)	0.2% (n=2)
Annualized ischemic stroke at 3 years	1.6%/year	1.6%/year
0 – 6 months annualized rate	2.2%/year	1.6%/year
6 months – 3 years annualized rate*	1.5%/year	1.6%/year

*ASA only recommended for both groups after 6 months

Device Factors More Often Observed in Stroke Patients with Watchman™ Device

Device factors (DRT or PDL) frequently preceded strokes in the Watchman device group; most patients were not on OAC at the time of stroke occurrence in both groups

Ischemic Stroke Patient Details (6 Months – 3 Years)*	Amulet™ (n=29)	Watchman™ (n=29)
Device factors**		
Device-related thrombus	1	2
Peridevice leak (≥3mm)	3	15
OAC usage at time of stroke	0	3

*ASA only recommended for both groups after 6 months
**Device factors had to occur prior to the stroke occurrence to be counted

The protocol required all patients with an ischemic stroke to undergo TEE/TOE within 7 days of neurological imaging confirming the event.

First Analysis of Amulet™ Occluder versus Watchman™ Device Long-Term Outcomes

DISCOVERED INSIGHTS FROM THE AMULET IDE TRIAL AT 3 YEARS

- Withdrawals occurred at a higher rate in the Watchman than Amulet device group
- Both cardiovascular and all-cause deaths trended higher in the Watchman than Amulet device group with no pericardial effusion related deaths in either group
- More patients were on OAC in the Watchman than Amulet device group
- Ischemic stroke and major bleeding rates were comparable between device groups
- Device factors (DRT or PDL) preceded strokes in more Watchman device patients than Amulet occluder patients

CONCLUSION

The dual-seal Amplatzer™ Amulet™ LAA occluder continued to demonstrate safety and effectiveness through 3 years