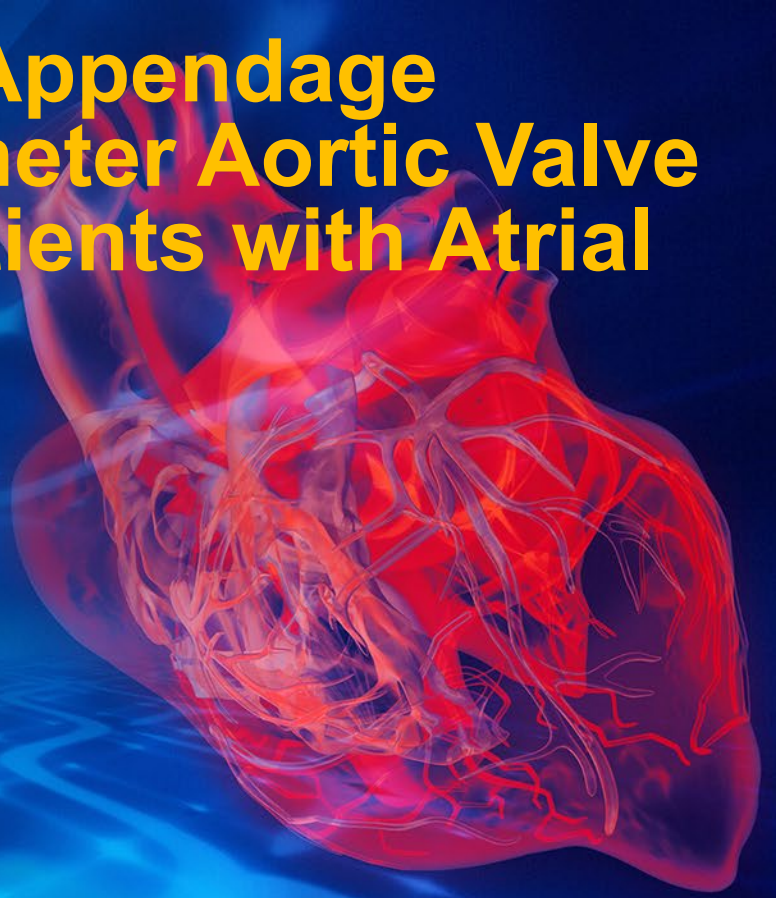
Concomitant Left Atrial Appendage Occlusion and Transcatheter Aortic Valve Replacement Among Patients with Atrial Fibrillation

WATCH-TAVR Trial



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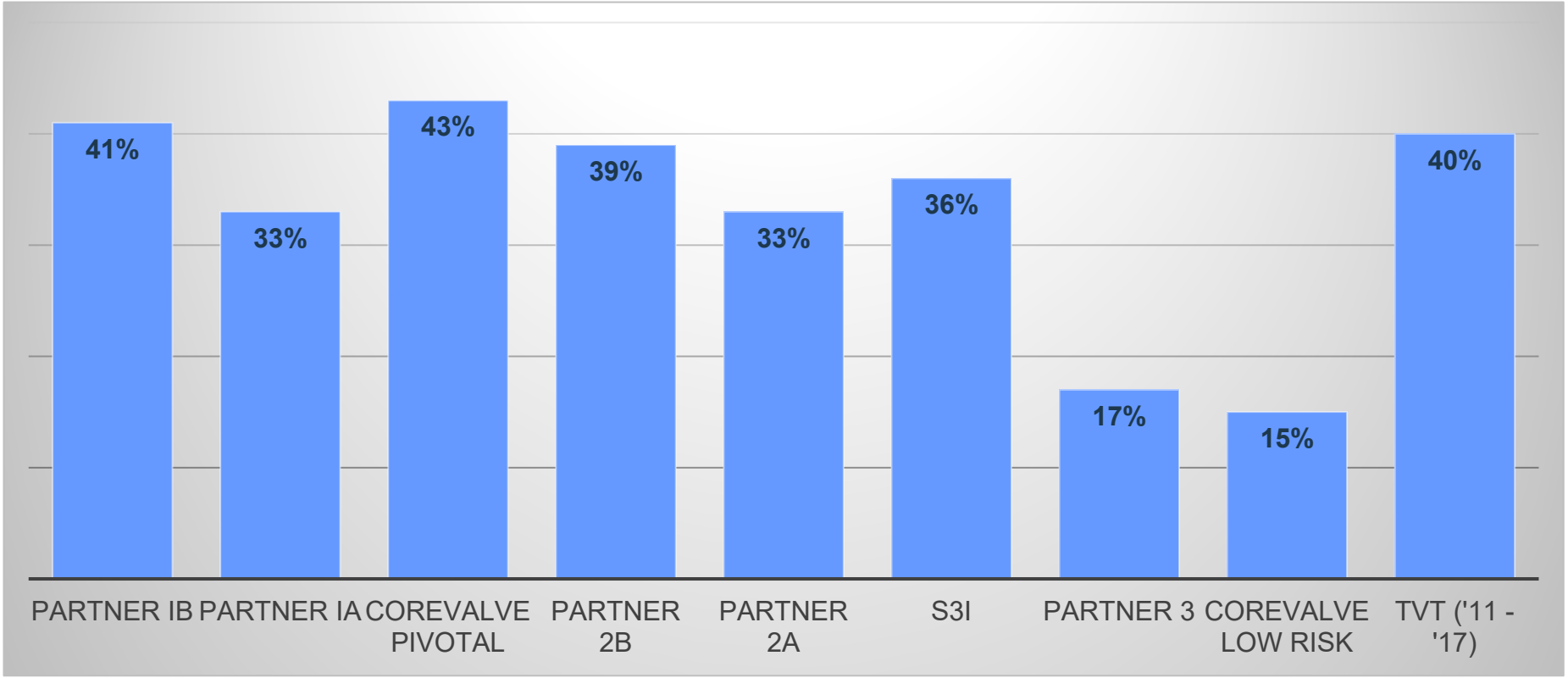
Disclosure Statement of Financial Interest

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	Boston Scientific
Stock Shareholder/Equity	Navigate

Faculty disclosure information can be found on the app

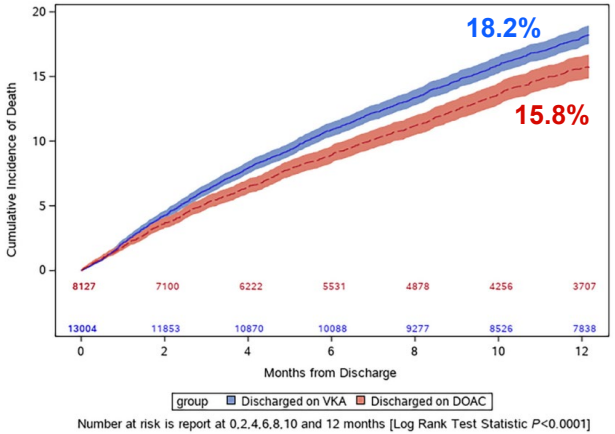
Atrial Fibrillation in Patients Undergoing TAVR



Mortality, Stroke and Bleeding After TAVR in AF Patients

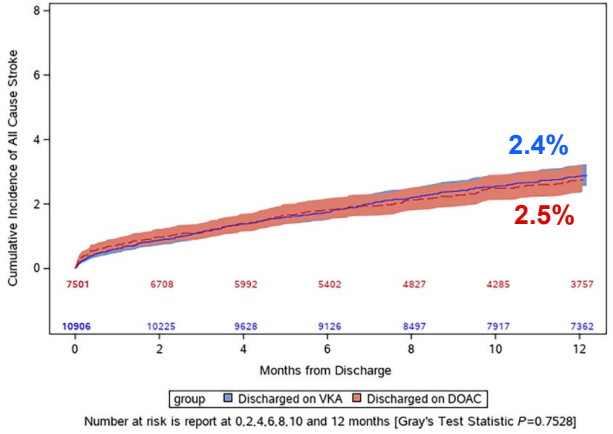
TVT Registry

MORTALITY



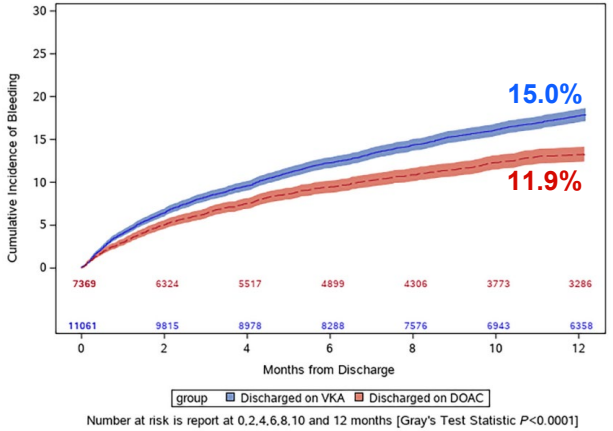
Number at risk is report at 0,2,4,6,8,10 and 12 months [Log Rank Test Statistic $P<0.0001$]

STROKE



Number at risk is report at 0,2,4,6,8,10 and 12 months [Gray's Test Statistic $P=0.7528$]

BLEEDING



Number at risk is report at 0,2,4,6,8,10 and 12 months [Gray's Test Statistic $P<0.0001$]

WARFARIN **DOAC**

Tanawuttiwat et al, JAHA, 2022, Jan 4;11(1):e023561

WATCH TAVR STUDY

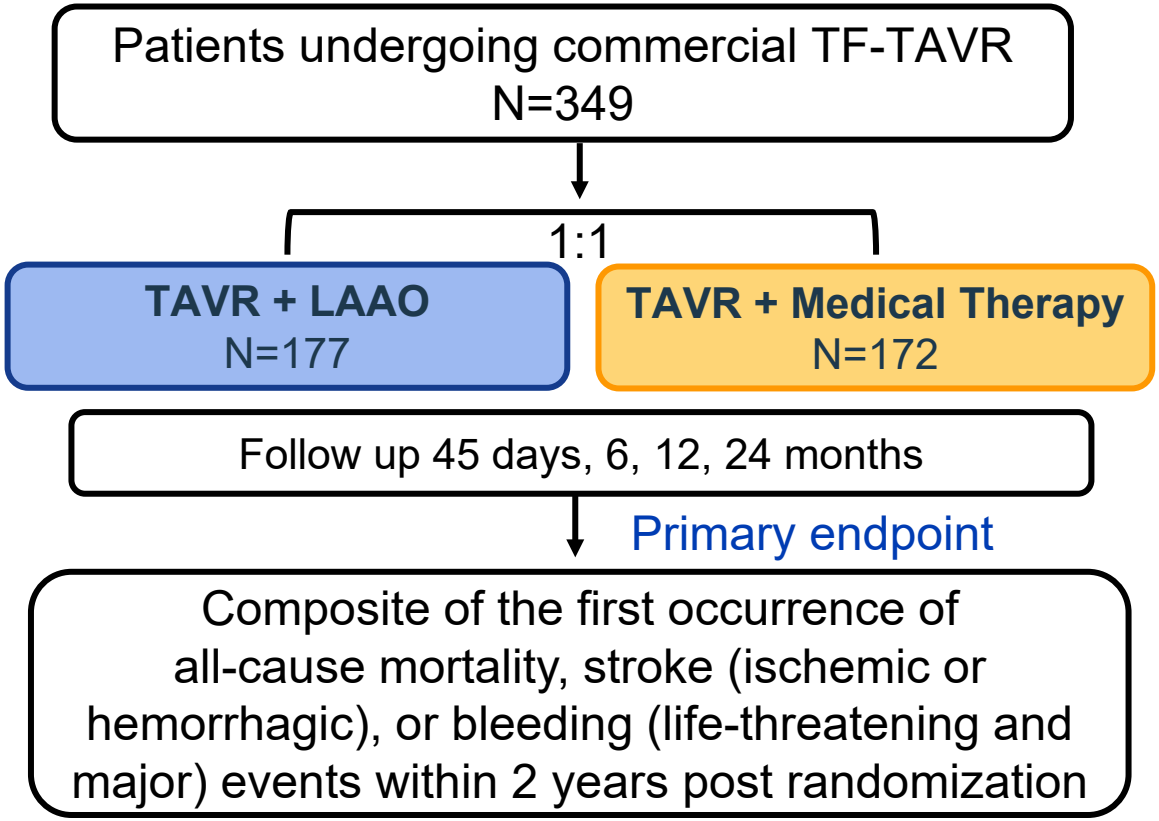
OBJECTIVE

To evaluate feasibility, safety and effectiveness of concomitant TAVR + LAAO with WATCHMAN (2.5) in AF patients with severe AS compared to contemporary medical therapy

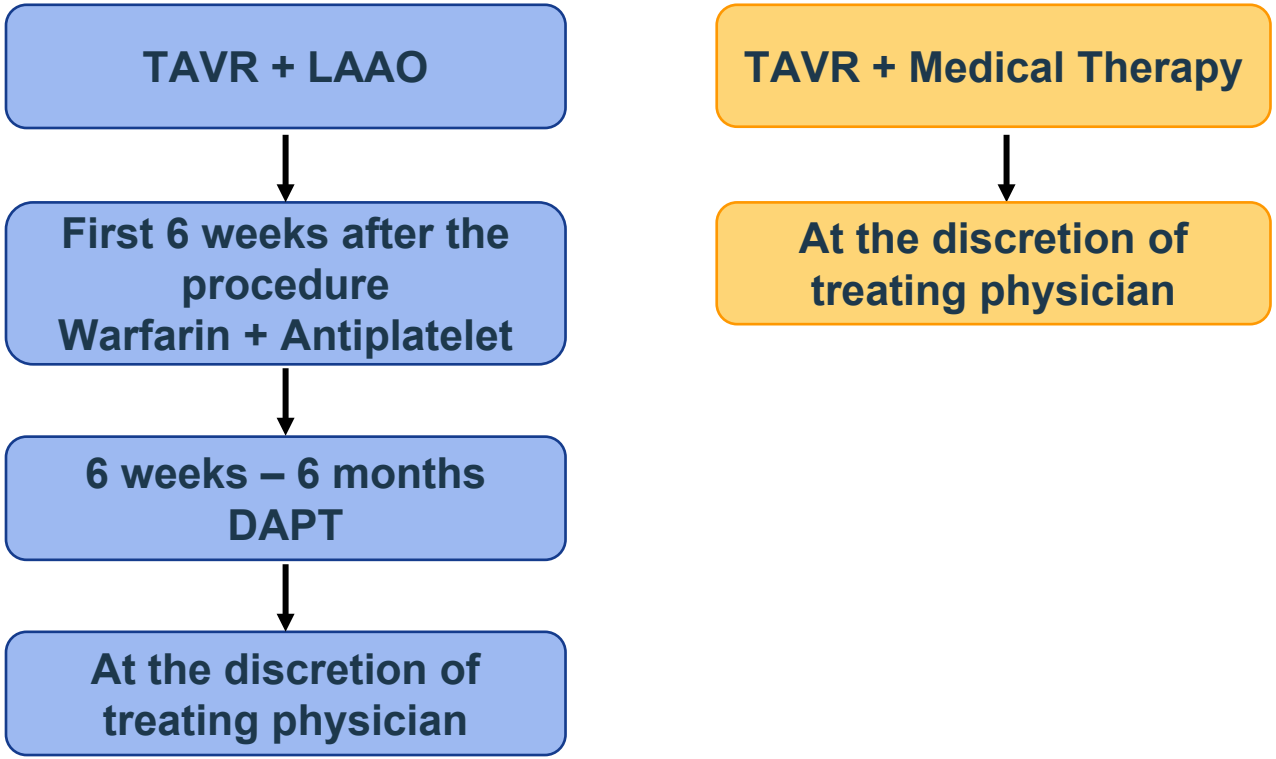
DESIGN

Investigator initiated, prospective, multicenter, randomized controlled trial at 34 centers in North America

WATCH TAVR Study Design



Medical Therapy



Study Endpoints

- Primary endpoint
  - Composite outcome of all-cause mortality, stroke (ischemic or hemorrhagic), or bleeding (life-threatening and major) events within 2 years post randomization (VARC 2 Definition)

- Secondary endpoints
  - Cardiovascular Mortality
  - Ischemic and hemorrhagic stroke
  - Arterial and venous thromboembolism
  - Rehospitalization due to WATCHMAN device or procedure

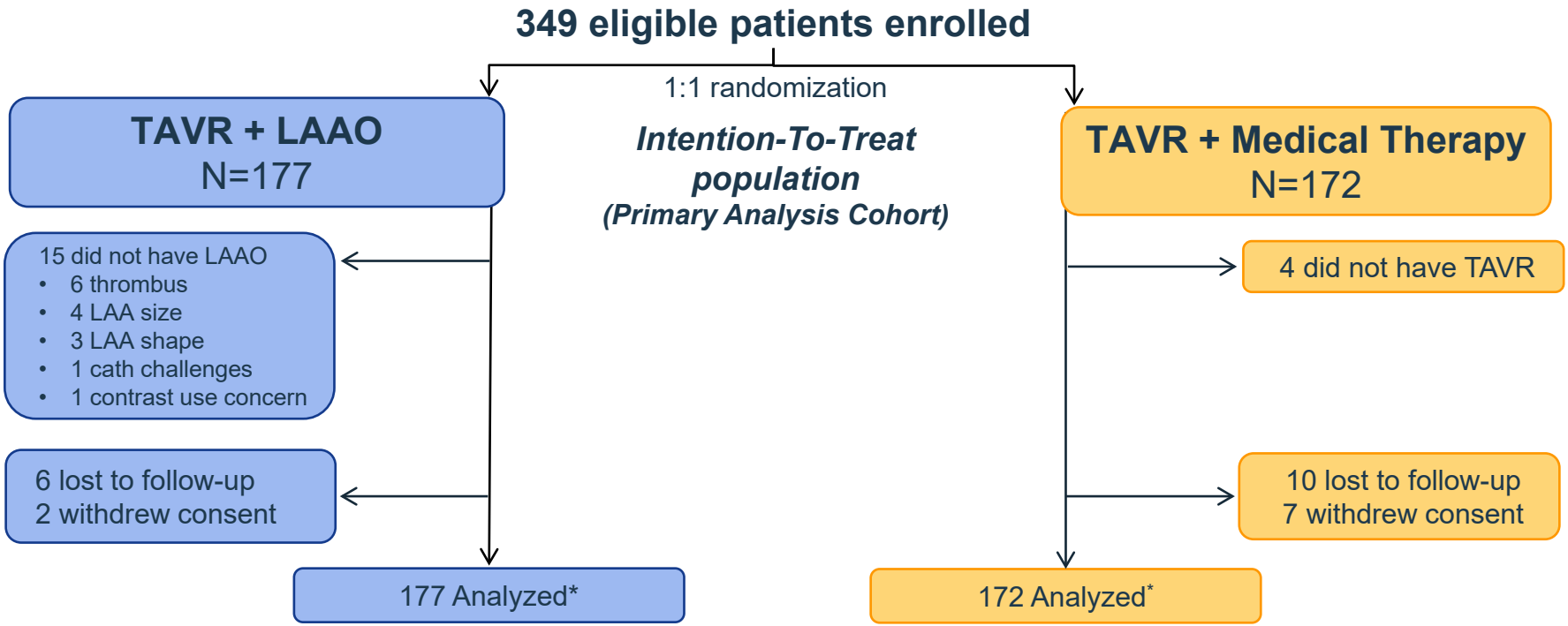
Statistical Analysis

- The primary endpoint and all additional endpoints up to 2 years were analyzed on an intent-to-treat (ITT) basis.

- Cox proportional-hazards regression model was used to estimate the hazard ratio and its two-sided 95% confidence interval for the primary composite endpoint.

- Non-inferiority was demonstrated if the 1-sided 97·5% upper confidence limit for the hazard ratio is less than 1·5.

Study Flow



* Patients that were lost to follow-up or withdrew consent are included in the analysis until end of participation

Baseline Demographics (1)

	TAVR + LAAO (N=177)	TAVR + Medical Therapy (N=172)
Age - Years	80.8 ± 7.8	81.5 ± 6.4
Female sex – no. (%)	69 (39.0)	66 (38.4)
Race – Caucasian (%)	173 (97.7)	167 (97.1)
Congestive heart failure	140 (79.1)	145 (84.3)
Hypertension	163 (92.1)	158 (91.9)
Diabetes	76 (42.9)	68 (39.5)
Previous TIA/Ischemic Stroke	23 (13.1)	23 (13.5)
LV dysfunction (EF<55%)	40 (22.6)	45 (26.2)
Renal dysfunction	48 (27.1)	55 (32.0)

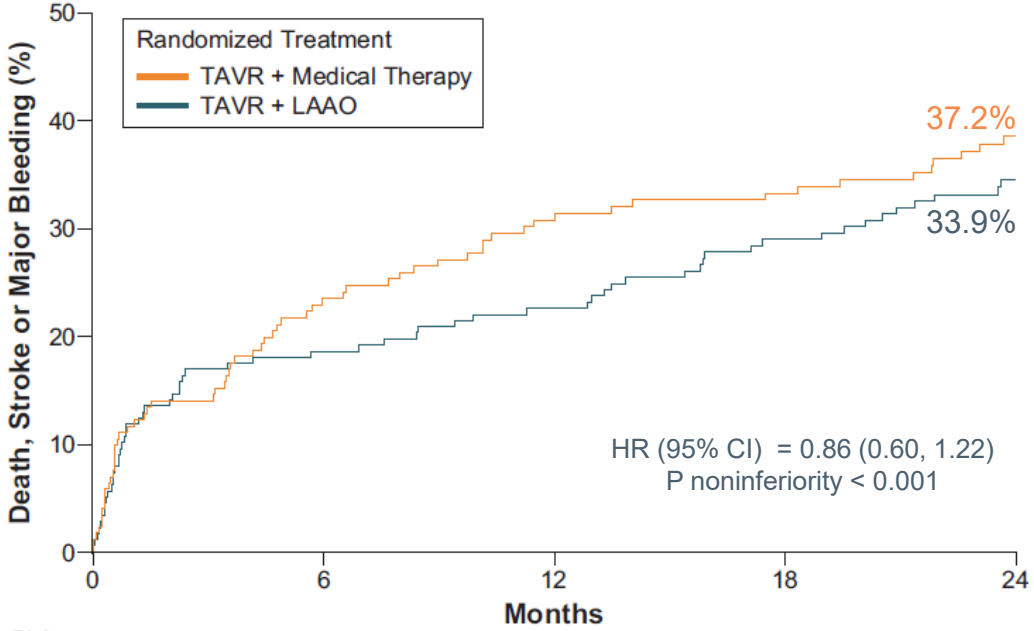
Baseline Demographics (2)

	TAVR + LAAO (N=177)	TAVR + Medical Therapy (N=172)
CHA2DS2-VASC Score	4.8 ± 1.2	4.9 ± 1.2
HAS-BLED Score	3.0 ± 1.1	3.0 + 1.2
Classification of AF		
Paroxysmal	84 (47.5)	83 (48.3)
Persistent	31 (17.5)	40 (23.3)
Permanent	41 (23.2)	33 (19.2)
Unknown	21 (11.9)	16 (9.3)
Anticoagulation	154 (87)	49 (83.7)
Warfarin	97 (54.8)	43 (25.0)
DOAC	57 (32.2)	101 (58.7)
Antiplatelet therapy	129 (72.8)	120 (69.7)

Procedural Details

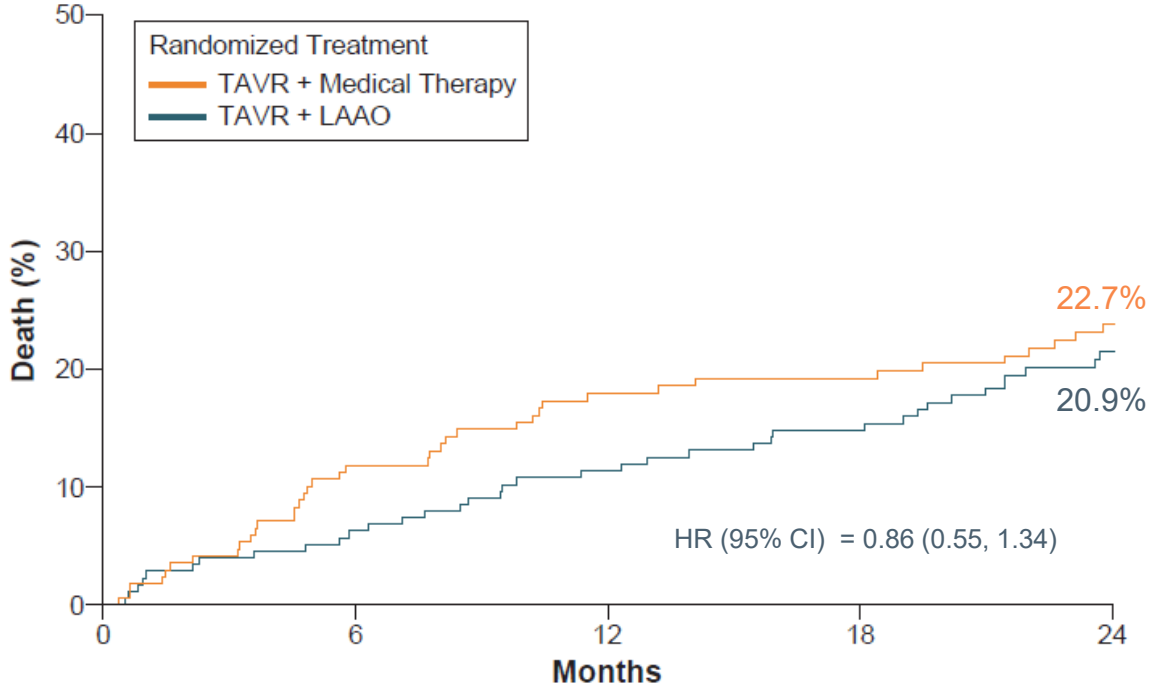
	TAVR + LAAO (N=177)	TAVR + Medical Therapy (N=172)
General anesthesia – no. (%)	149 (84.2)	63 (36.6)
Duration of TAVR procedure (minutes)	52.5 ± 37.6	60.3 ± 37.8
Duration of WATCHMAN procedure (minutes)	43.6 ± 26.8	
Contrast volume (ml)	125.7 ± 70.0	81.9 ± 41.5
Length of stay	3.5 ± 2.7	4.0 ± 5.0
Discharge to home – no. (%)	158 (89.3)	151 (87.8)
Acute Kidney Injury	5 (2.8%)	6 (3.4%)
Pericardial Effusion (moderate or large)	4 (2.4)	1 (0.5)
Emergent cardiac surgery	0	1 (0.6%)
In-hospital mortality – no. (%)	1 (0.6)	1 (0.6)

Primary Outcome
Death, Stroke, Major Bleeding



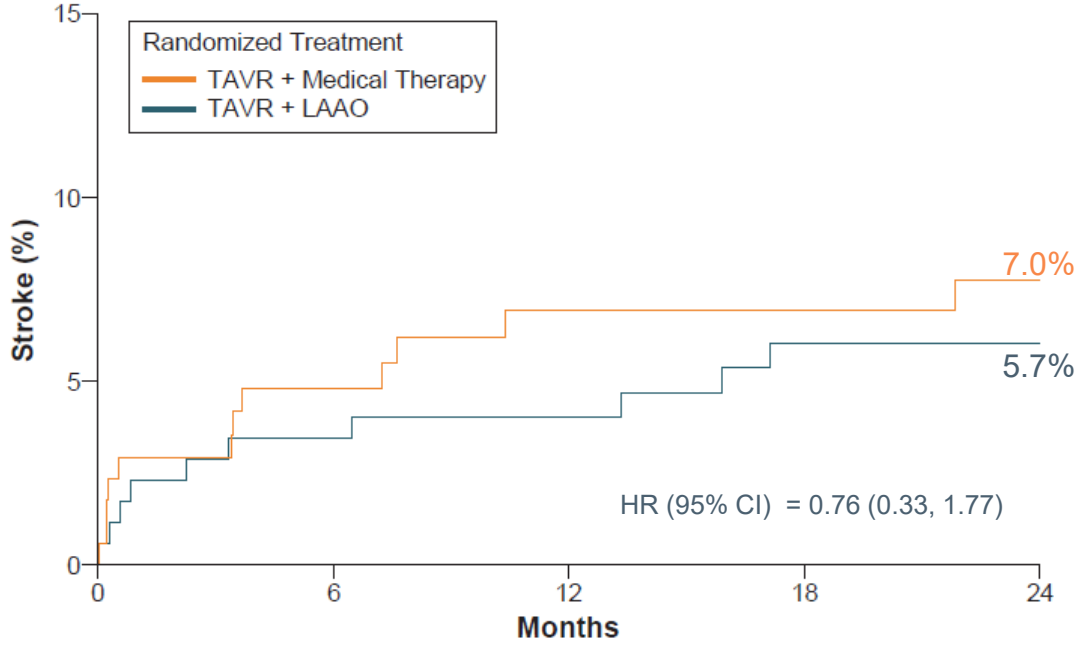
Number at Risk					
TAVR + Medical Therapy	172	128	112	106	75
TAVR + LAAO	177	144	134	121	75

All Cause Mortality



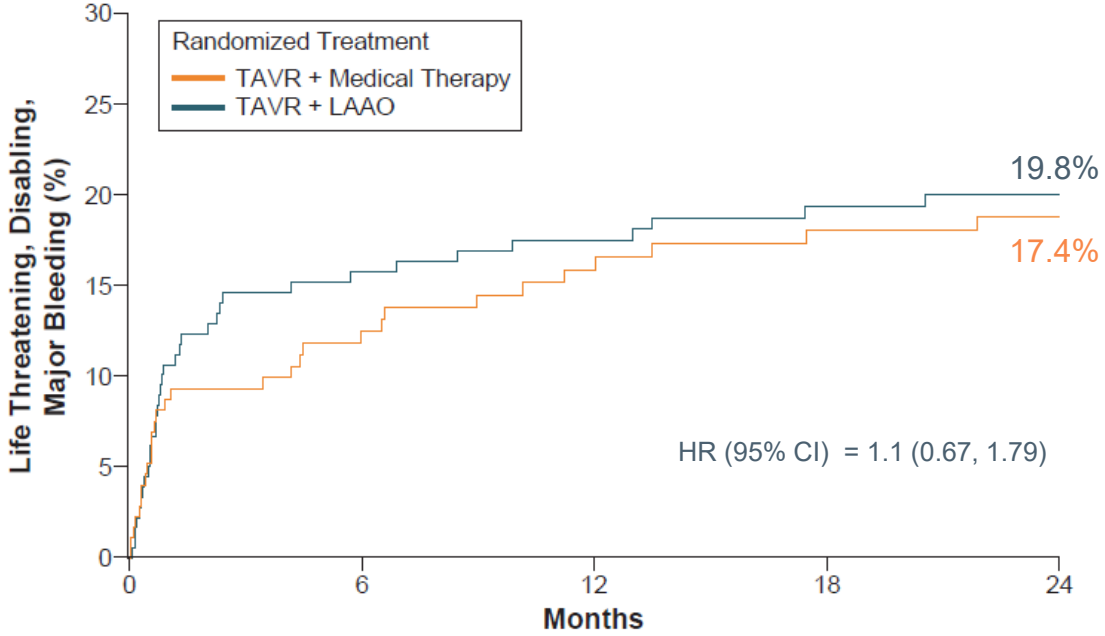
Number at Risk					
TAVR + Medical Therapy	172	148	133	129	91
TAVR + LAAO	177	166	154	146	94

All Strokes



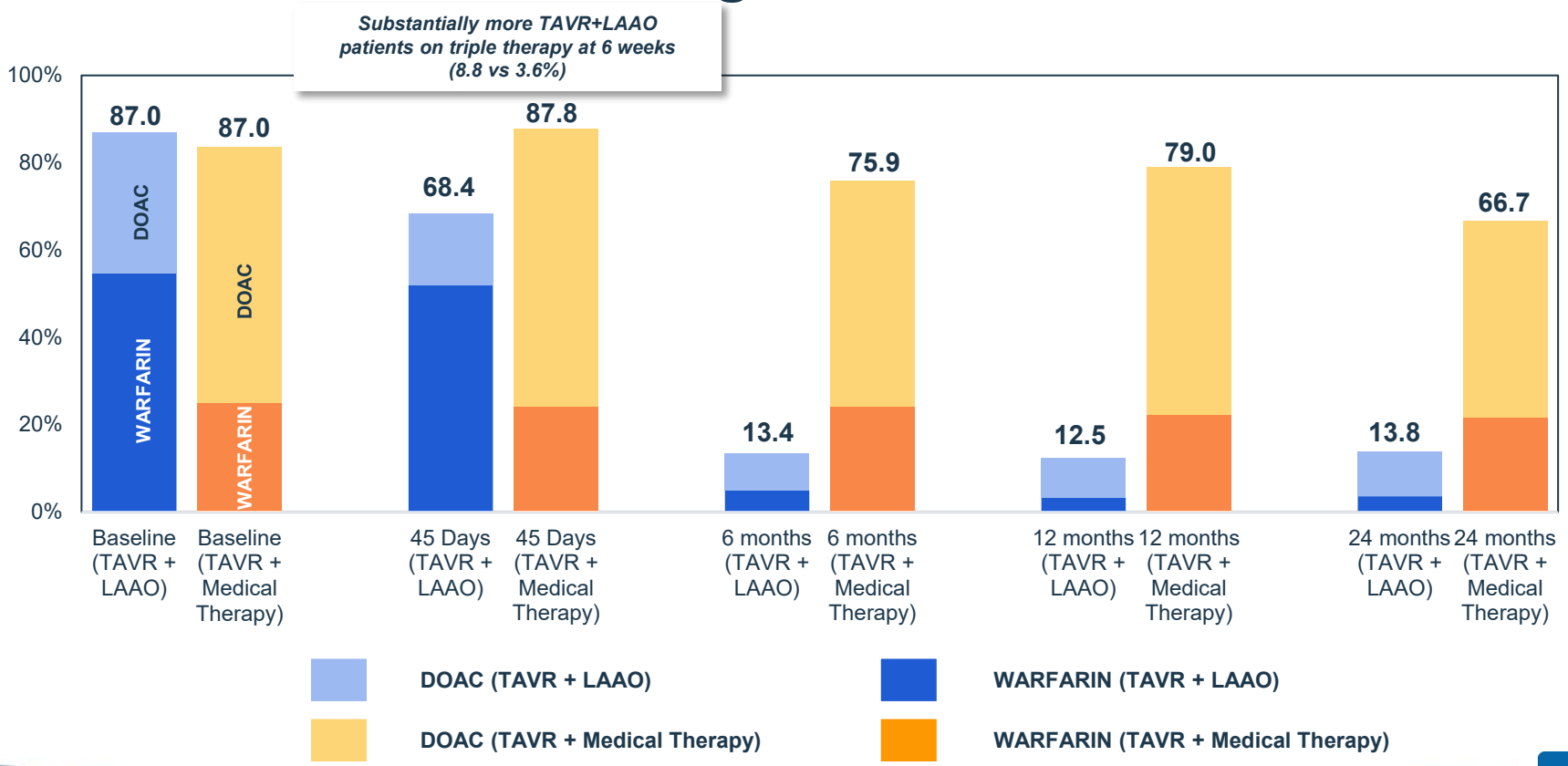
Number at Risk					
TAVR + Medical Therapy	172	141	125	121	84
TAVR + LAAO	177	163	150	139	89

Major Bleeding

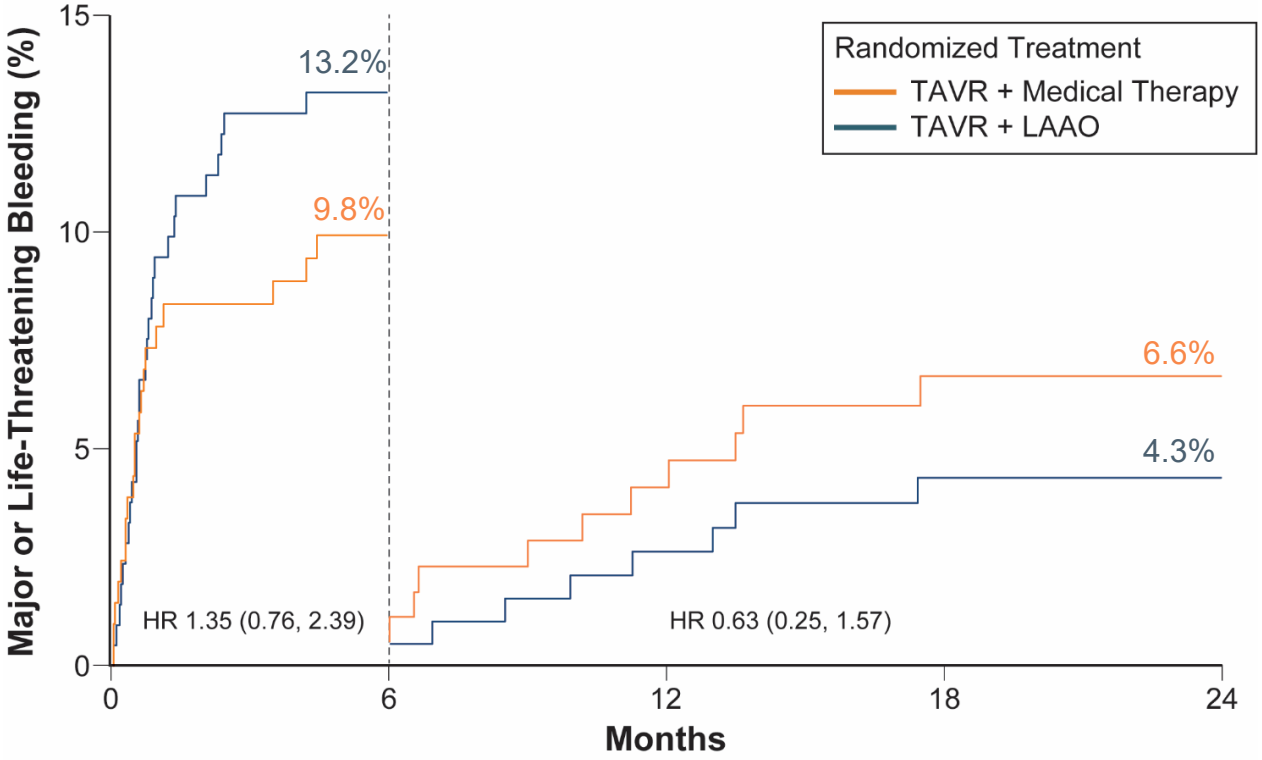


Number at Risk					
TAVR + Medical Therapy	172	133	117	111	80
TAVR + LAAO	177	146	136	126	78

Anticoagulation Use



Bleeding – Landmark Analysis

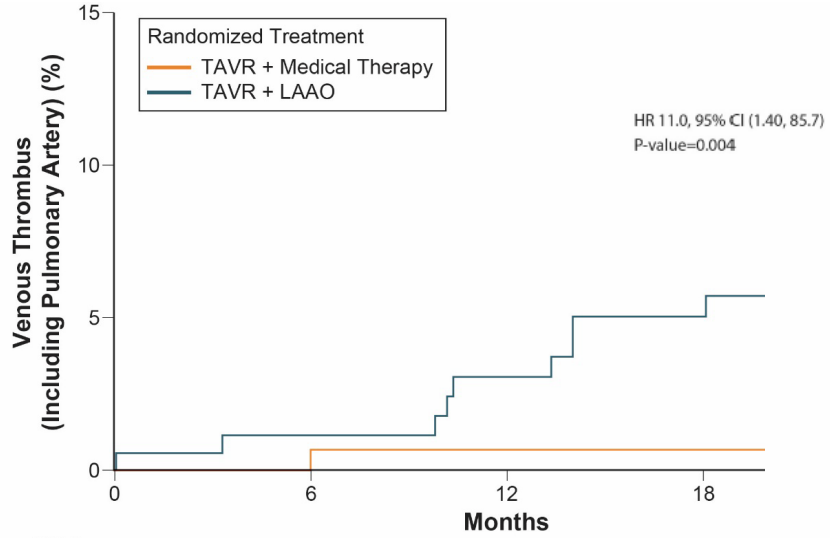


Secondary Endpoints

	TAVR + LAAO (N=177) n(%)	TAVR + Medical Therapy (N=172) n (%)	TAVR + LAAO vs TAVR + Medical Therapy Hazard Ratio (95% CI)
All-cause mortality	37 (20.9)	39 (22.7)	0.86 (0.55, 1.34)
Stroke	10 (5.7)	12 (7.0)	0.76 (0.33, 1.77)
Major/life-threatening bleeding	35 (19.8)	30 (17.4)	1.10 (0.67, 1.79)
Cardiovascular death	20 (11.3)	22 (12.8)	0.82 (0.45, 1.51)
Ischemic stroke	10 (5.7)	11 (6.4)	0.83 (0.35, 1.96)
Hemorrhagic stroke	0 (0.0)	1 (0.6)	..
Arterial or venous thrombosis or embolism	16 (9.0)	3 (1.7)	5.03 (1.47,17.26)
Rehospitalization	18 (10.2)	22 (12.8)	0.76 (0.41, 1.42)

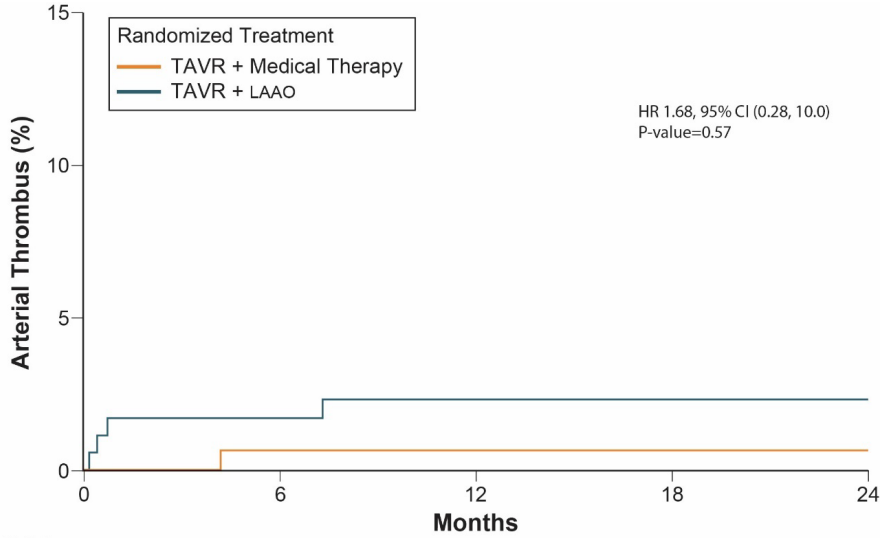
Thrombosis

Venous



Number at Risk				
TAVR + Medical Therapy	172	148	132	128
TAVR + LAAO	177	164	150	140

Arterial



Number at Risk					
TAVR + Medical Therapy	172	147	132	128	91
TAVR + LAAO	177	164	152	144	93

Limitations

- The study was designed as a noninferiority trial for the combined primary endpoint and was not powered to detect differences in individual components of this endpoint.
- The study was limited to the Watchman 2.5 device and its prescribed adjunctive pharmacology. How the current study data can be extrapolated to current generation devices and current adjunctive pharmacology regimens remains to be proven.
- The study does not account for differences between therapies beyond 2 years.
- Subgroup analysis to identify specific patient populations that may benefit form a concomitant strategy is not feasible due to sample size limitation.

Conclusions

- LAAO with the WATCHMAN 2.5 device at time of TAVR is non-inferior to contemporary medical therapy for the primary composite endpoint of all-cause mortality, stroke, and major bleeding at 2 years in patients with AF and severe symptomatic AS.
- Cardiovascular mortality, stroke, and rehospitalization due to WATCHMAN device or procedure were similar between groups. Arterial and venous thromboembolism was more frequent in patients undergoing TAVR + LAAO compared to TAVR + medical therapy.
- In-hospital mortality was low (0.6%) in both groups with similar length of stay and AKI. Pericardial effusion occurred in 2.4% of combined procedures compared to 0.5% in TAVR alone.
- Almost one third of the patients randomized to TAVR + medical therapy were not taking anticoagulants at 2 year follow up.

Implications

- Concomitant WATCHMAN LAAO and TAVR provides a noninferior treatment option to TAVR with medical therapy in severe AS patients with AF.
- Concomitant WATCHMAN LAAO and TAVR can be safely performed with low in-hospital mortality. The increased complexity of the combined procedure should be considered when concomitant LAAO is viewed as an alternative to medical therapy for patients with AF undergoing TAVR.
- The current generation WATCHMAN FLX device is safer and requires less aggressive adjunctive pharmacology which may further mitigate bleeding risks after the combined procedures compared to the WATCHMAN 2.5, the LAAO device used in the WATCH TAVR study.

Top-Enrolling Sites (>10 patients per site)

Clinical Center	Site PI	Pts Enrolled
Intermountain Medical Center	Whisenant, Brian	50
The Heart Hospital Baylor Plano	Potluri, Srini	38
Cleveland Clinic	Krishnaswamy, Amar	36
University of Buffalo	Iyer, Vijay	30
Santa Barbara Cottage Hospital	Aragon, Joseph	23
Banner University Medical Center-Phoenix	Gideon, Philip	22
Medical Center of the Rockies	Strote, Justin	19
Lexington Medical Heart and Vascular Center	Leonardi, Robert	18
CHI Health Research Center	Agarwal, Himanshu	14
Aspirus Research Institute	Larrain, German	14
OhioHealth Research Institute	Sanchez, Carlos	14

Circulation

Back-up

Prespecified Subgroups

	TAVR + LAAO (N=177) n(%)	TAVR + Medical Therapy (N=172) n (%)	TAVR + LAAO vs TAVR + Medical Therapy Hazard Ratio (95% CI)
Gender			
Males (n=214)	36/108 (33·3)	40/106 (37·7)	0·85 (0·54, 1·33)
Females (n=135)	24/69 (34·8)	24/66 (36·4)	0·87 (0·50, 1·54)
Age			
<75 yrs (n=65)	11/38 (29·0)	6/27 (22·2)	1·32 (0·49, 3·56)
≥75 yrs (n=284)	49/139 (35·3)	58/145 (40·0)	0·82 (0·56, 1·19)
History of diabetes			
Yes (n=144)	29/76 (38·2)	27/68 (39·7)	0·89 (0·53, 1·51)
No (n=204)	31/100 (31·0)	37/104 (35·6)	0·83 (0·51, 1·33)
History of stroke			
Yes (n=41)	6/21 (28·6)	11/20 (55·0)	0·46 (0·17, 1·25)
No (n=308)	54/156 (34·6)	53/152 (34·9)	0·94 (0·65, 1·38)
Type of atrial fibrillation			
Paroxysmal (n=167)	26/84 (31·0)	28/83 (33·7)	0·87 (0·51, 1·48)
Persistent, Permanent, or Other (n=182)	34/93 (36·6)	36/89 (40·5)	0·85 (0·53, 1·36)

As Treated Population