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# Left Atrial Appendage Closure


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# Disclosures

| | |
|---|---|
| Scientific Advisory Board: | Medtronic |
| | Boston Scientific |
| | Abbott Vascular |
| Consultant: | SentreHeart |
| | Foldax |

# Atrial Fibrillation

- Most common sustained arrhythmia disorder[1]
- Affects over 5 million Americans[1]
- Expected to affect up to 16 million Americans by 2050[1]
- Causes 460,000 hospitalizations and contributes to 80,000 deaths annually[1]
- Responsible for 10-15% of ischemic strokes and 50% of cardioembolic strokes[2]

[1]Lip GY. J Thromb Haemost
[2] Hart RG., et. *JACC* 2000; 35:183

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# 2014 AHA/ACC/HRS Guidelines for Management of Patients with Atrial Fibrillation

| Recommendations | COR | LOE | References |
|---|---|---|---|
| Antithrombotic therapy based on shared decision making, discussion of risks of stroke and bleeding, and patient's preferences | I | C | N/A |
| Selection of antithrombotic therapy based on risk of thromboembolism | I | B | (167-170) |
| With prior stroke, TIA, or $CHA_2DS_2$-VASc score ≥2, oral anticoagulants recommended. Options include: | | | |
| Warfarin | I | A | |
| Dabigatran, rivaroxaban, or apixaban | I | B | |
| With warfarin, determine INR at least weekly during initiation of therapy and monthly when stable | I | A | (180-182) |
| Direct thrombin or factor Xa inhibitor recommended if unable to maintain therapeutic INR | I | C | N/A |
| Reevaluate the need for anticoagulation at periodic intervals | I | C | N/A |

January, CT, et al. JACC 2014: 64(21) e1-e76

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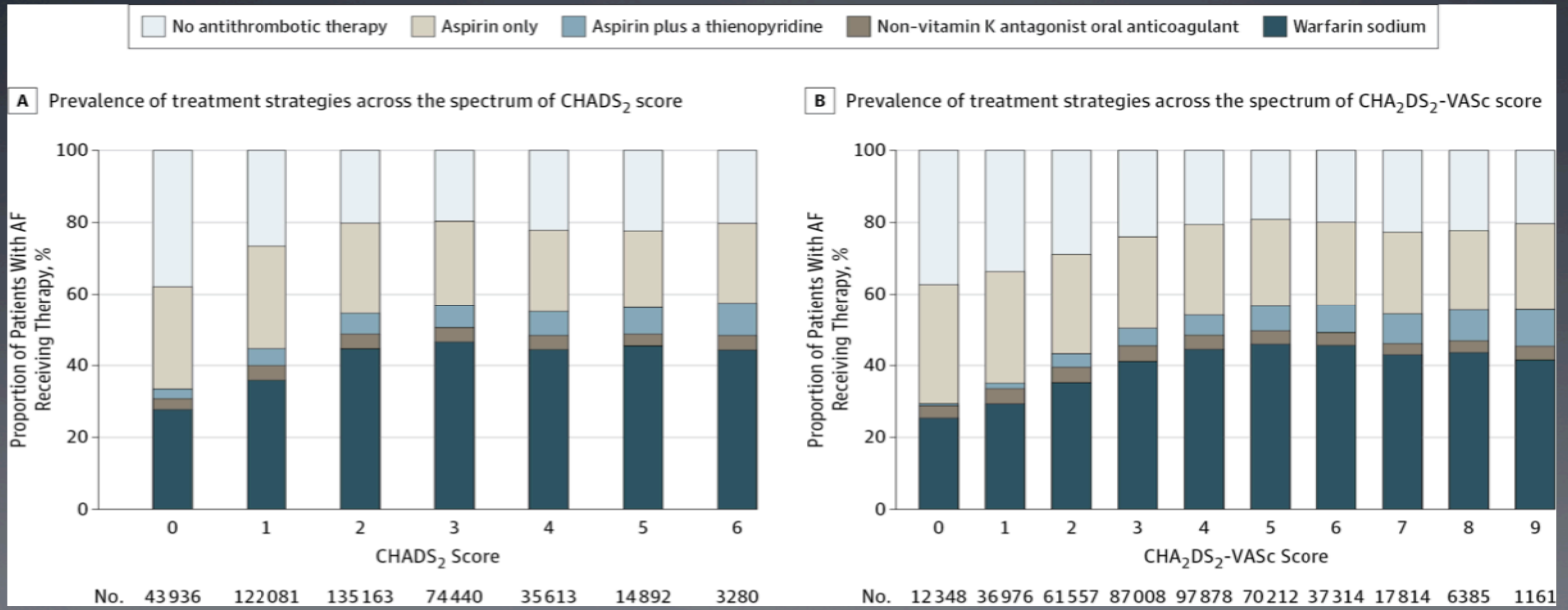
# Less Than Half of Eligible Patients with Atrial Fibrillation are Anticoagulated




Hsu, et al. JAMA, April 2016.

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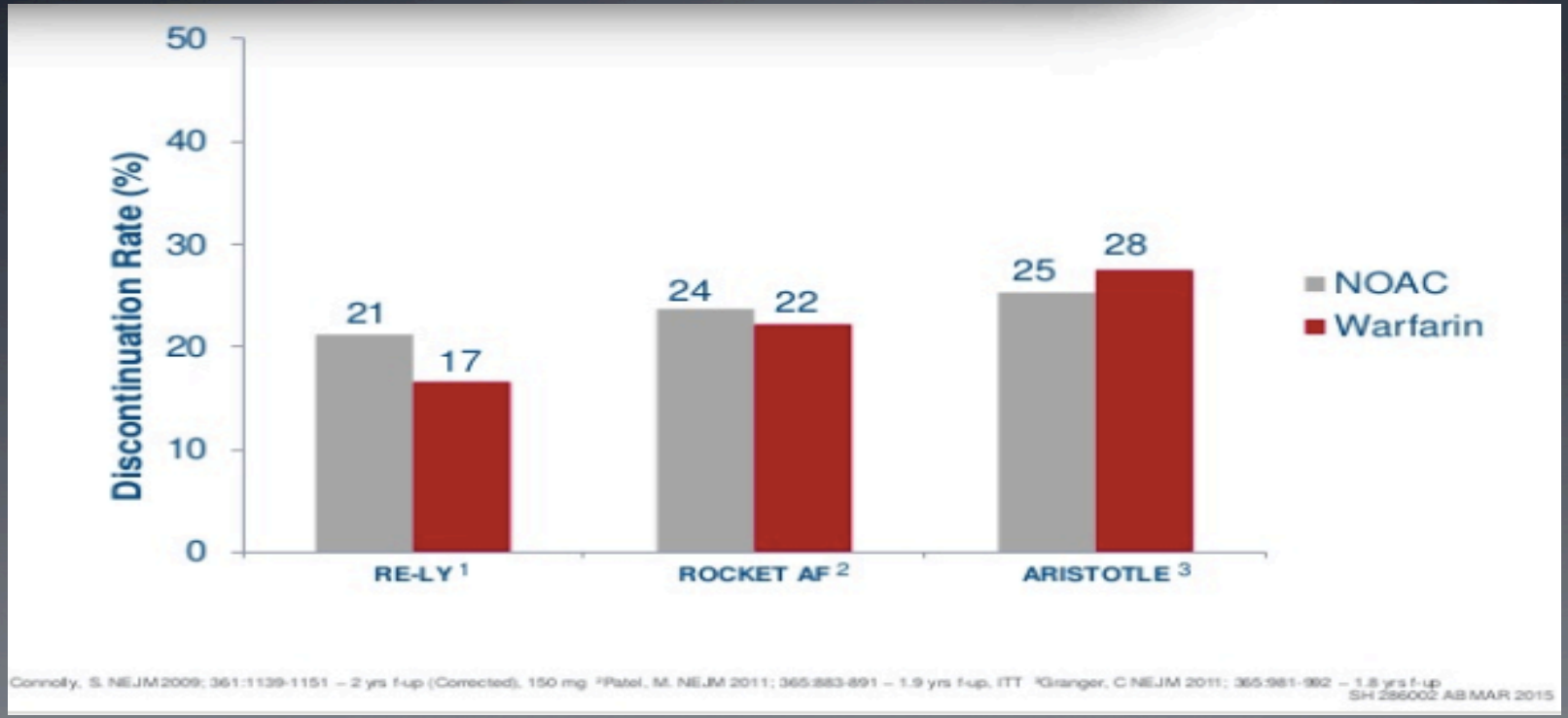
# NOAC Discontinuation in Clinical Trials




Connolly, S. NEJM 2009; 361:1139-1151 – 2 yrs f-up (Corrected), 150 mg ²Patel, M. NEJM 2011; 365:883-891 – 1.9 yrs f-up, ITT ³Granger, C NEJM 2011; 365:981-992 – 1.8 yrs f-up

SH 286002 AB MAR 2015

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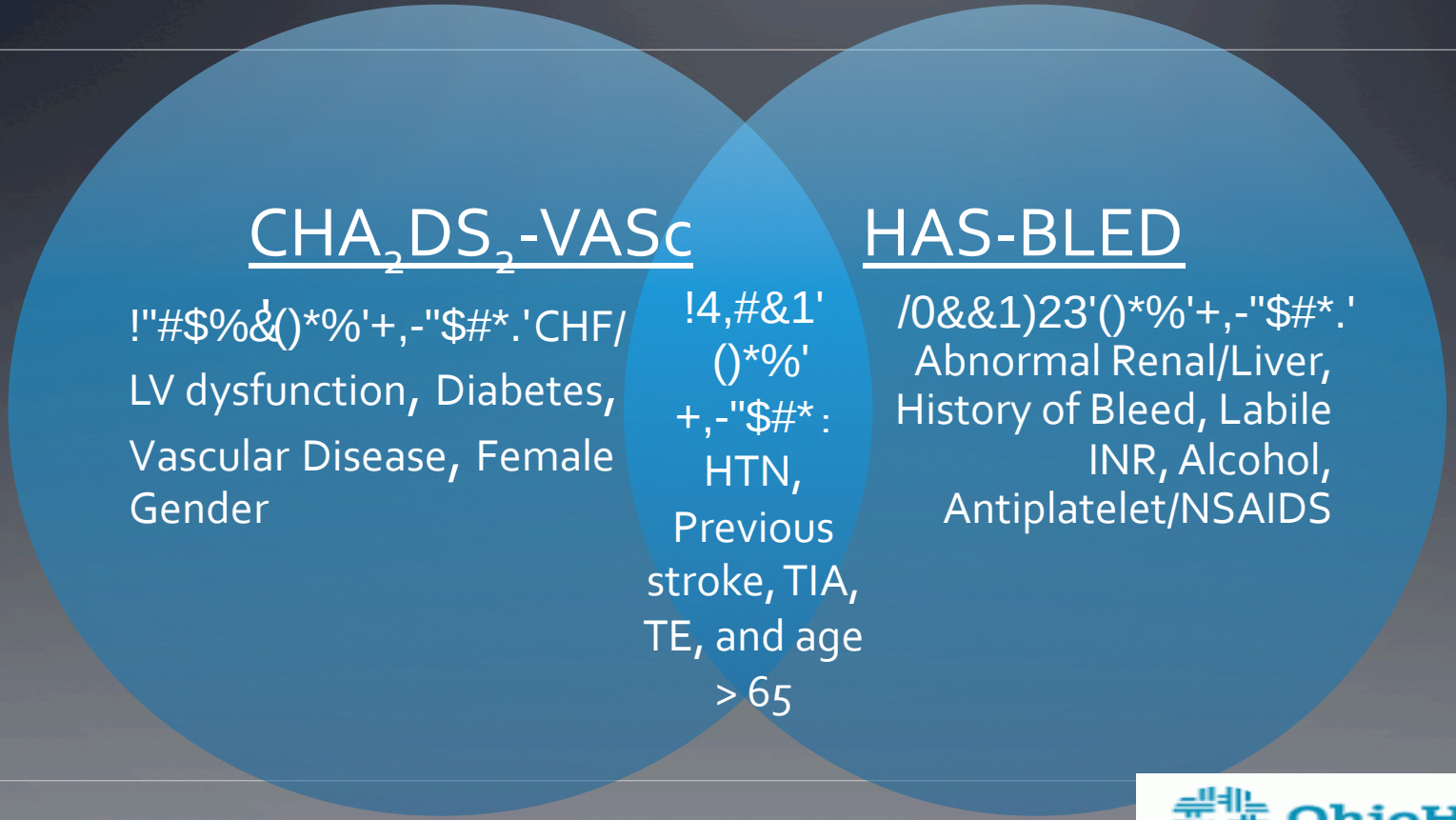
# Common reasons for not prescribing or discontinuing anticoagulation

- Advanced Age
- Frailty
- Falls Risk
- Labile INRs
- Patient Preference
- Previous Bleeding or Risk Factors for Bleeding

# Risk Assessment

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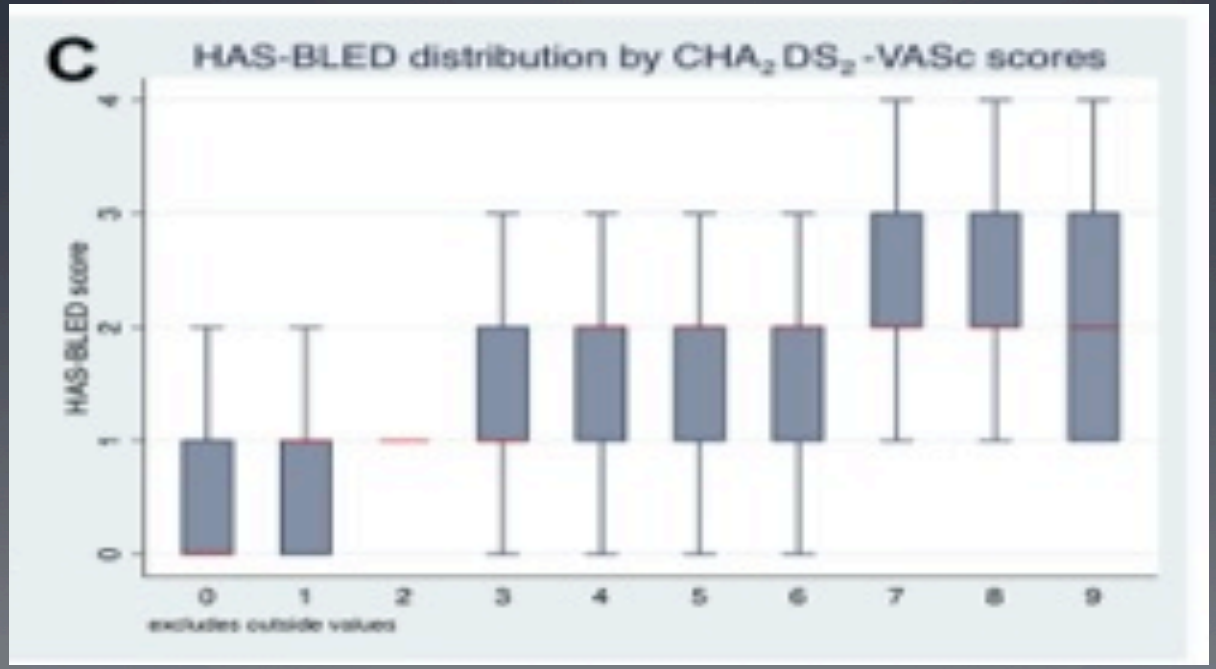
# Bleeding Risk Increases with Stroke Risk




Marcucci, M, et al. Am J Med. 2014 Oct;127(10): 979-986.e2

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# Stroke Pathology in Non-Valvular Atrial Fibrillation

- Insufficient LAA contraction leads to stagnant blood flow
- Most likely culprit: embolization of LAA clot
- 90% of thrombus found in LAA
- Risk factors identifiable on TEE include
  - Enlarged LAA
  - Spontaneous echo contrast
  - Reduced LAA flow velocities

Blackshear, Ann Thoracic Surg 61, 1996
Johnson, Eur J Cardiothoracic Surg 17, 2000
Eagan: Echocardiograpgy 17, 2000

# FDA Approval and Labeling

FDA Approval in March 2015 with an indication to reduce the risk of thromboembolism from the left atrial appendage in patients

1.) with non valvular atrial fibrillation

2.) who are recommended anticoagulation based on their CHADS2 or CHADS VASC score to decrease stroke risk

3.) are deemed suitable for warfarin

4.) who have an appropriate rationale to seek a non pharmacologic alternative to warfarin

# CMS National Coverage Decision

- $CHA_2DS_2$-VASc of ≥ 3 or CHADS2 ≥ 2.
- Formal shared decision making (SDM) interaction utilizing an independent, non-interventional physician whose opinion must be written in the medical record.
- Suitability for short-term warfarin, but deemed unable to take long-term anticoagulation, after the conclusion of SDM, as LAAC is only covered as second line to oral anticoagulation
- Procedure must be performed in a hospital with an established structural heart disease or electrophysiology program.
- Procedure must be performed by an interventional cardiologist, electrophysiologist or cardiovascular surgeon, who must have received formal training by the manufacturer, have performed ≥ 25 transeptal procedures, and continue to perform ≥ 25 transeptal procedures, including 12 of which are LAA occlusion, over a two year period.
- Patient is enrolled, and physicians and hospital participate in a prospective, national, audited registry for at least four years from the time of implantation.

# Suggested Contraindications to *Long Term* Warfarin Use

- History of intracranial bleeding, or other spontaneous or non ICH bleeding such as GI or retroperitoneal bleeding
- Documented poor compliance with AC or labile INRs
- Intolerance of warfarin or new oral anticoagulants
- High risk of recurrent falls
- Cognitive impairment
- Severe renal failure
- Occupation related high bleeding risk
- Need for prolonged dual antiplatelet therapy
- Increased bleeding risk not reflected by the HAS-BLED score (e.g. thrombocytopenia, cancer, or risk of tumor associated bleeding in case of systemic anticoagulation)
- Other situations for which anticoagulation is inappropriate.

# The Data

# PROTECT AF

## Superiority of Watchman over Warfarin

- RCT: Can the WATCHMAN device ***replace*** Warfarin?

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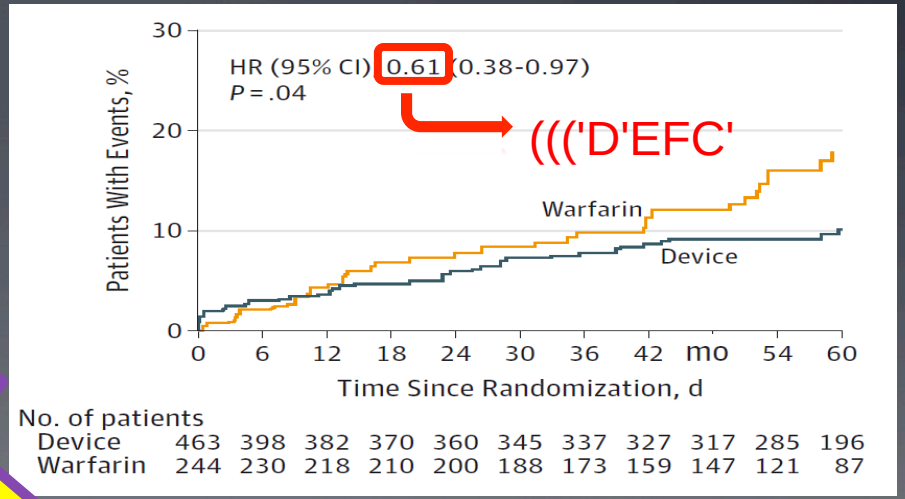
**Non-Valvular AF**
**$HADS_2 \geq 1$**

**Anticoagulation Regimen**

- Implant to 6 weeks
  - Warfarin
  - Aspirin
- 6 weeks to 6 months
  - Clopidogrel
  - Aspirin
- After 6 months
  - Aspirin

**Follow-Up**

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V.Reddy, H.Sievert, J.Halperin et al, *JAMA*, 312:1988 (2014)

# PROTECT AF: Watchman *vs* Warfarin

## Mortality Benefit with Watchman

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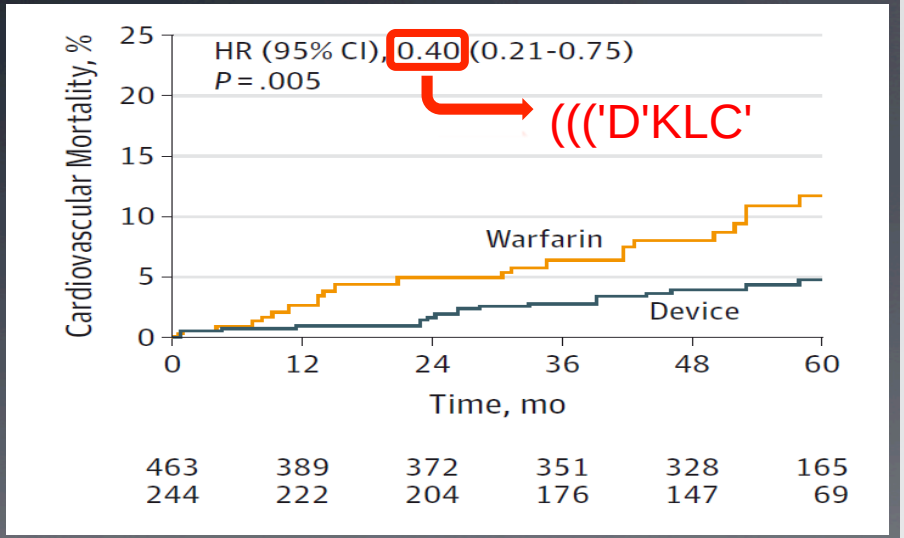


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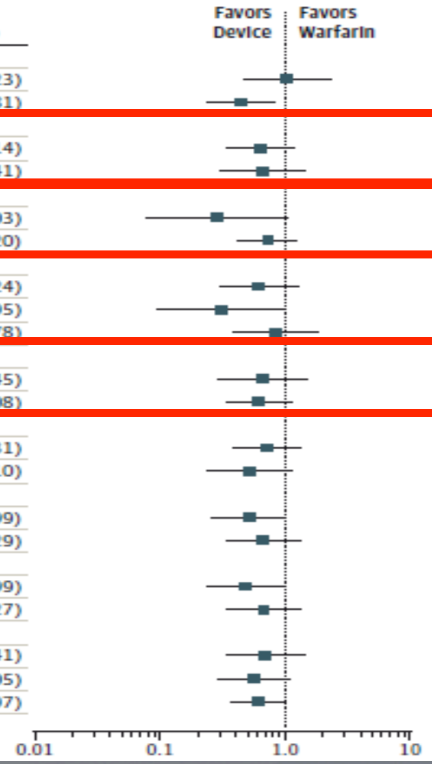
V.Reddy, H.Sievert, J.Halperin et al, *JAMA*, 312:1988 (2014)

# PROTECT AF: Watchman *vs* Warfarin

## Benefit by Sub-Groups

| Source | Device Group No. of Events | Device Group No. of Patients | Warfarin Group No. of Events | Warfarin Group No. of Patients | HR (95% CI) |
|---|---|---|---|---|---|
| Sex | | | | | |
| Female | 18 | 137 | 10 | 73 | 1.03 (0.48-2.23) |
| Male | 21 | 326 | 24 | 171 | 0.45 (0.25-0.81) |
| Age | | | | | |
| ≥ 75 y | 22 | 190 | 22 | 115 | 0.63 (0.35-1.14) |
| < 75 y | 17 | 273 | 12 | 129 | 0.67 (0.32-1.41) |
| $CHADS_2$ score | | | | | |
| 1 | NA | NA | NA | NA | 0.29 (0.08-1.03) |
| >1 | NA | NA | NA | NA | 0.73 (0.44-1.20) |
| AF pattern | | | | | |
| Paroxysmal | 18 | 200 | 14 | 99 | 0.62 (0.31-1.24) |
| Persistent | 5 | 97 | 8 | 50 | 0.31 (0.10-0.95) |
| Permanent | 16 | 160 | 12 | 93 | 0.84 (0.40-1.78) |
| History of TIA or stroke | | | | | |
| Yes | 13 | 82 | 12 | 49 | 0.66 (0.30-1.45) |
| No | 26 | 381 | 22 | 195 | 0.61 (0.35-1.08) |
| Prior years taking warfarin | | | | | |
| <1 | 25 | 226 | 19 | 125 | 0.72 (0.40-1.31) |
| ≥1 | 14 | 230 | 14 | 116 | 0.52 (0.25-1.10) |
| LAA ostium | | | | | |
| ≥ Median (21 mm) | 18 | 249 | 18 | 128 | 0.52 (0.27-0.99) |
| < Median | 20 | 208 | 16 | 111 | 0.67 (0.35-1.29) |
| LAA length | | | | | |
| ≥ Median (30 mm) | 16 | 235 | 16 | 124 | 0.49 (0.25-0.99) |
| < Median | 22 | 222 | 18 | 115 | 0.68 (0.36-1.27) |
| LV ejection fraction | | | | | |
| ≥ Median (60%) | 19 | 236 | 14 | 123 | 0.70 (0.35-1.41) |
| < Median | 20 | 224 | 19 | 116 | 0.56 (0.30-1.05) |
| All patients | | | | | 0.61 (0.38-0.97) |




V.Reddy, H.Sievert, J.Halperin et al, *JAMA*, 312:1988 (2014)

# PROTECT-AF & PREVAIL
## Combined Analysis

**TABLE 1** PROTECT AF and CAP: Largest Data Sets to Evaluate Totality of Data

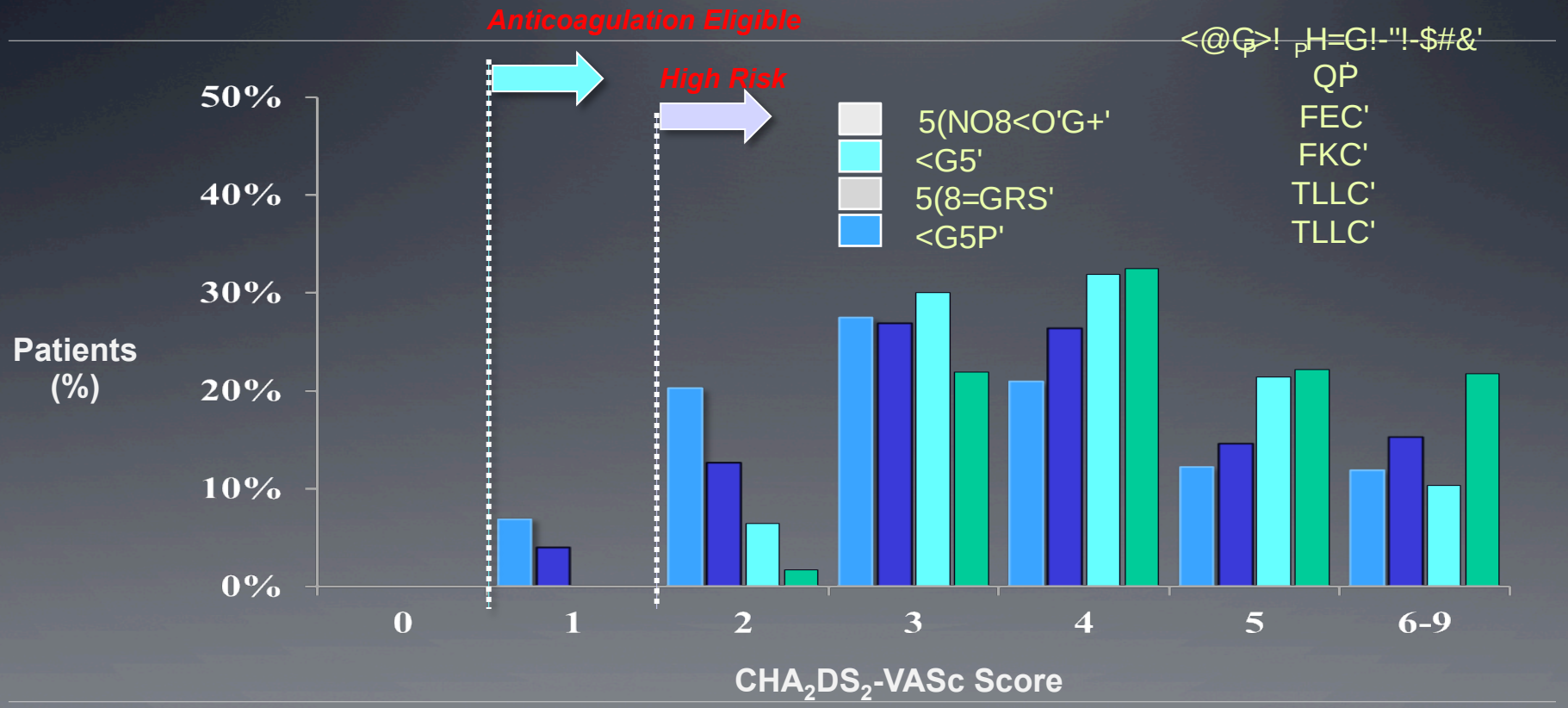
| | PROTECT AF | PREVAIL | CAP | CAP2 | Total |
|---|---|---|---|---|---|
| Enrollment | 2005–2008 | 2010–2012 | 2008–2010 | 2012–2014 | |
| Enrolled | 800 | 461 | 566 | 579 | 2,406 |
| Randomized | 707 | 407 | — | — | 1,114 |
| Watchman:warfarin (2:1) | 463:244 | 269:138 | 566 | 579 | 1,877:382 |
| Mean follow-up, yrs | 4.0 | 2.2 | 3.7 | 0.58 | N/A |
| Patient-years | 2,717 | 860 | 2,022 | 332 | 5,931 |

CAP = Continued Access to PROTECT AF registry; CAP2 = Continued Access to PREVAIL registry; N/A = not applicable; PREVAIL = Prospective Randomized Evaluation of the Watchman LAA Closure Device In Patients With Atrial Fibrillation Versus Long Term Warfarin Therapy; PROTECT AF = Watchman Left Atrial Appendage System for Embolic Protection in Patients with Atrial Fibrillation.

D.Holmes / V.Reddy *JACC* 65:2614 (2015)

# Clinical Trial Patient Characteristics

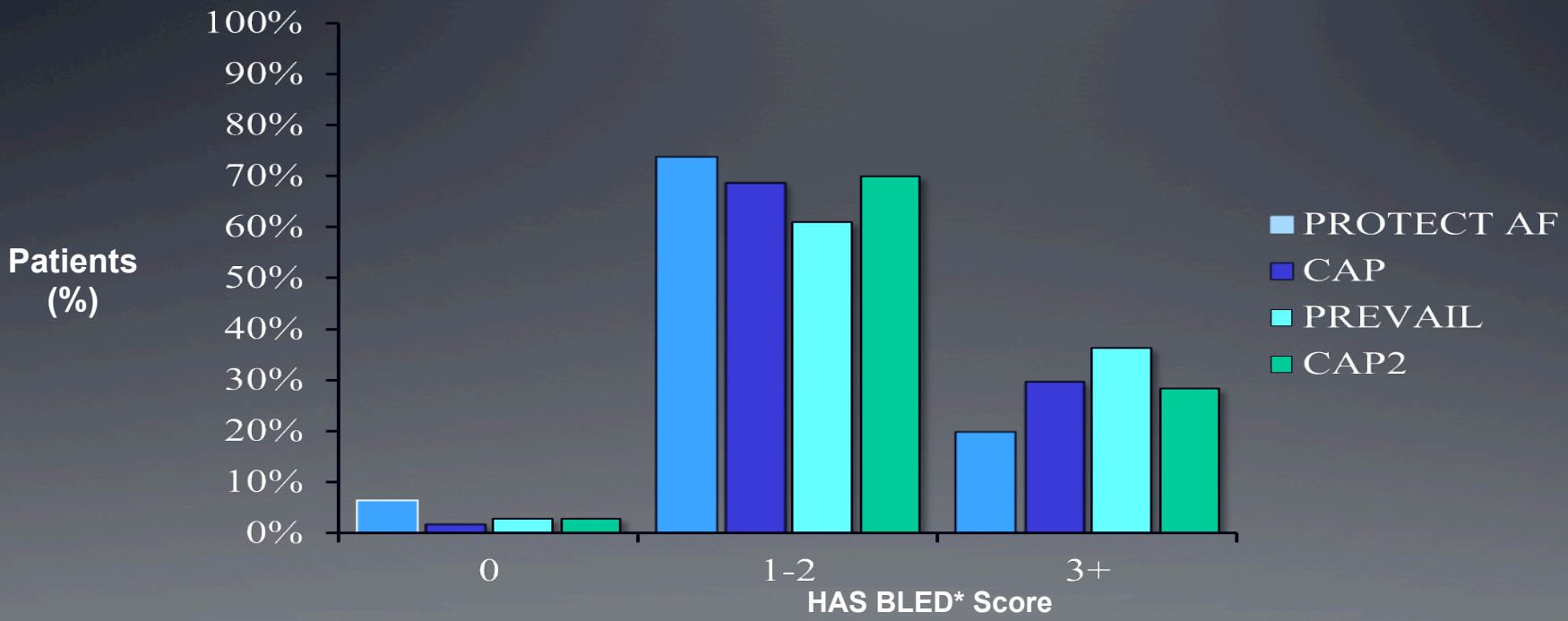
## Most at a High Stroke Risk




D.Holmes / V.Reddy *J Am Coll Cardiol* 65:2614 (2015)

# Clinical Trial Patient Characteristics

## Most at Moderate to High Bleeding Risk




* Estimated HAS BLED score. Labile INR and liver function were not collected and given a score of zero

D.Holmes / V.Reddy *J Am Coll Cardiol* 65:2614 (2015)

# Stroke Severity in PROTECT AF/PREVAIL

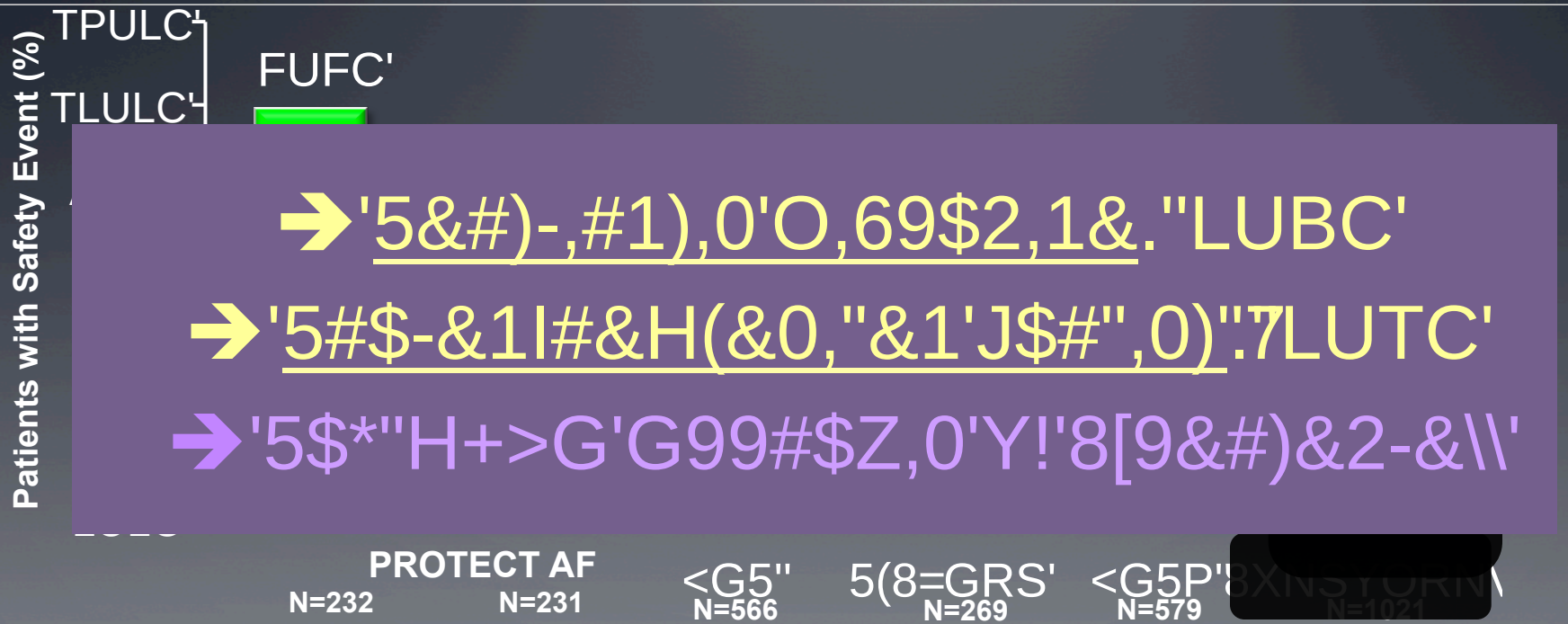
## Non-Disabling *vs* Disabling/Fatal


- Disabling stroke defined as MRS change of 2 or more or death
- Similar results if defined as absolute MRS > 2

V.Reddy et al, *FDA Panel Presentation*, October 2014.

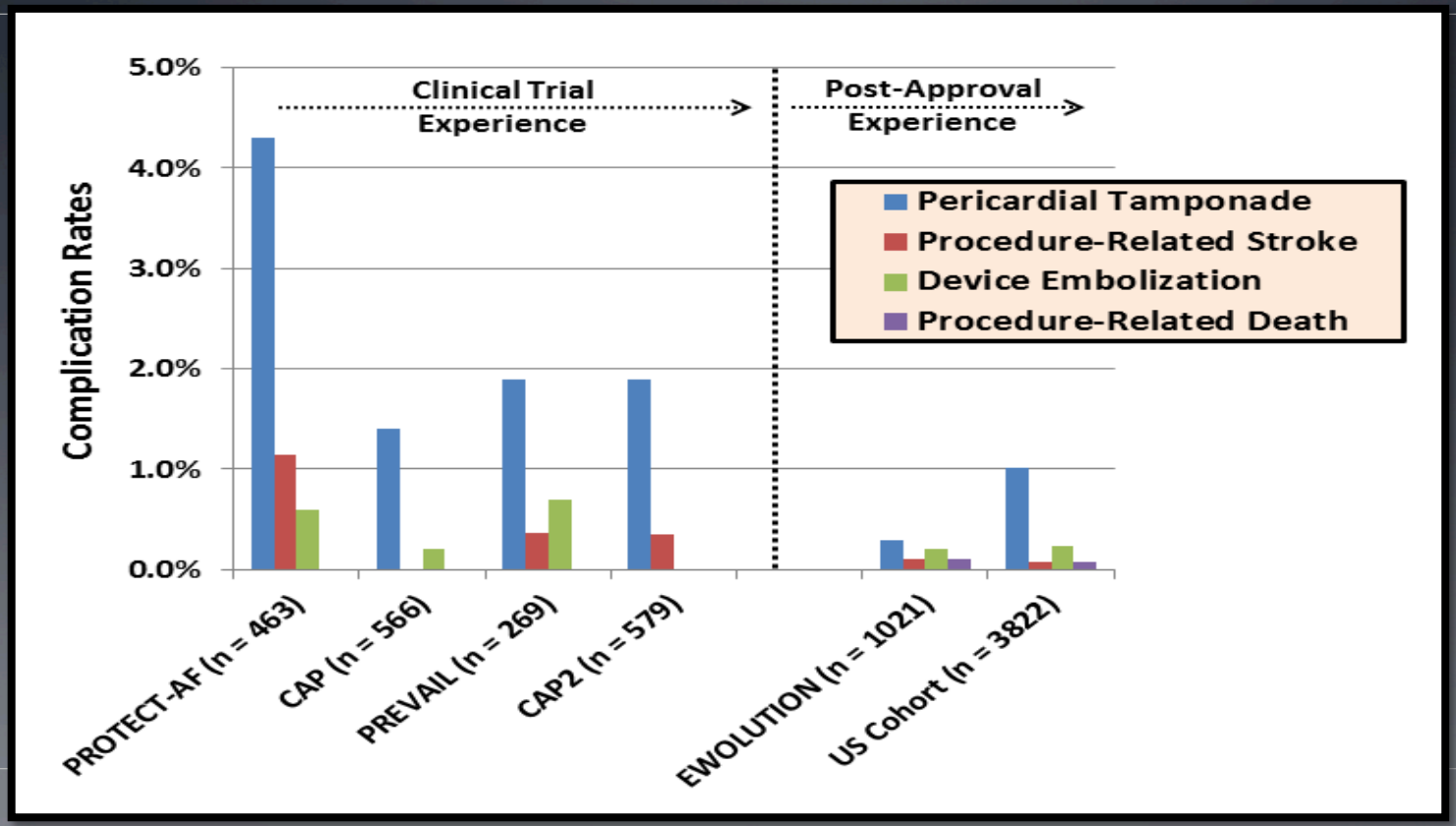
# Safety Events Across Trials

## FDA Trials *vs* "Real World" (EWOLUTION)

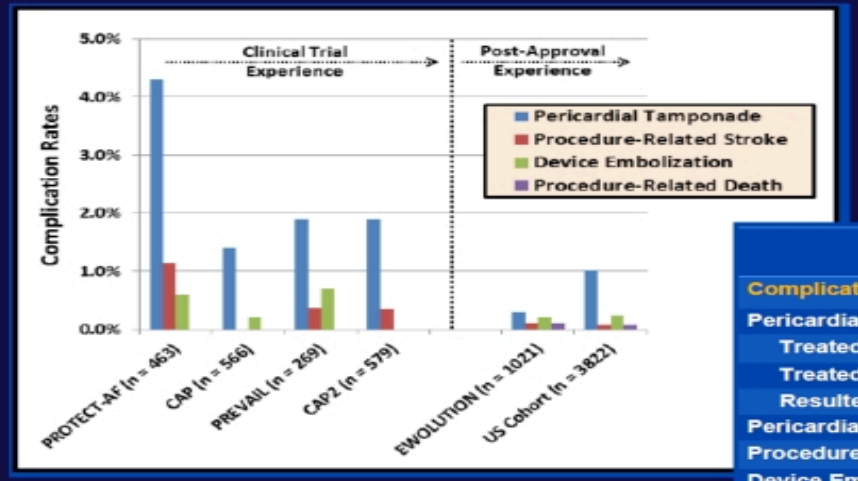



L.Boersma et al, *Eur Heart J* 37:2465-74 (2016)

# Comparison of Procedural Complications Across Watchman Studies



# Post Approval Experience




| | Post-FDA Approval Experience |
|---|---|
| **Complications** | |
| Pericardial Tamponade | 39 (1.02%) |
| Treated with Pericardiocentesis | 24 (0.63%) |
| Treated Surgically | 12 (0.31%) |
| Resulted in Death | 3 (0.078%) |
| Pericardial Effusion – No Intervention | 11 (0.29%) |
| Procedure-Related Stroke | 3 (0.078%) |
| Device Embolization | 9 (0.24%) |
| Removed Percutaneously | 3 |
| Removed Surgically | 6 |
| **Death** | |
| Procedure-Related Mortality | 3 (0.078%) |
| Additional Mortality within 7 days | 1 (0.026%) |

Reddy et al. J Am Coll Cardiol. 2017;69:253-261

# Outcomes in the Post-FDA Approval Watchman Experience N=3822

| | Post-FDA Approval Experience |
|---|---|
| **Complications** | |
| Pericardial Tamponade | 39 (1.02%) |
| Treated with Pericardiocentesis | 24 (0.63%) |
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| **Death** | |
| Procedure-Related Mortality | 3 (0.078%) |
| Additional Mortality within 7 days | 1 (0.026%) |

# Comparison of Procedural Complications Across Watchman Studies

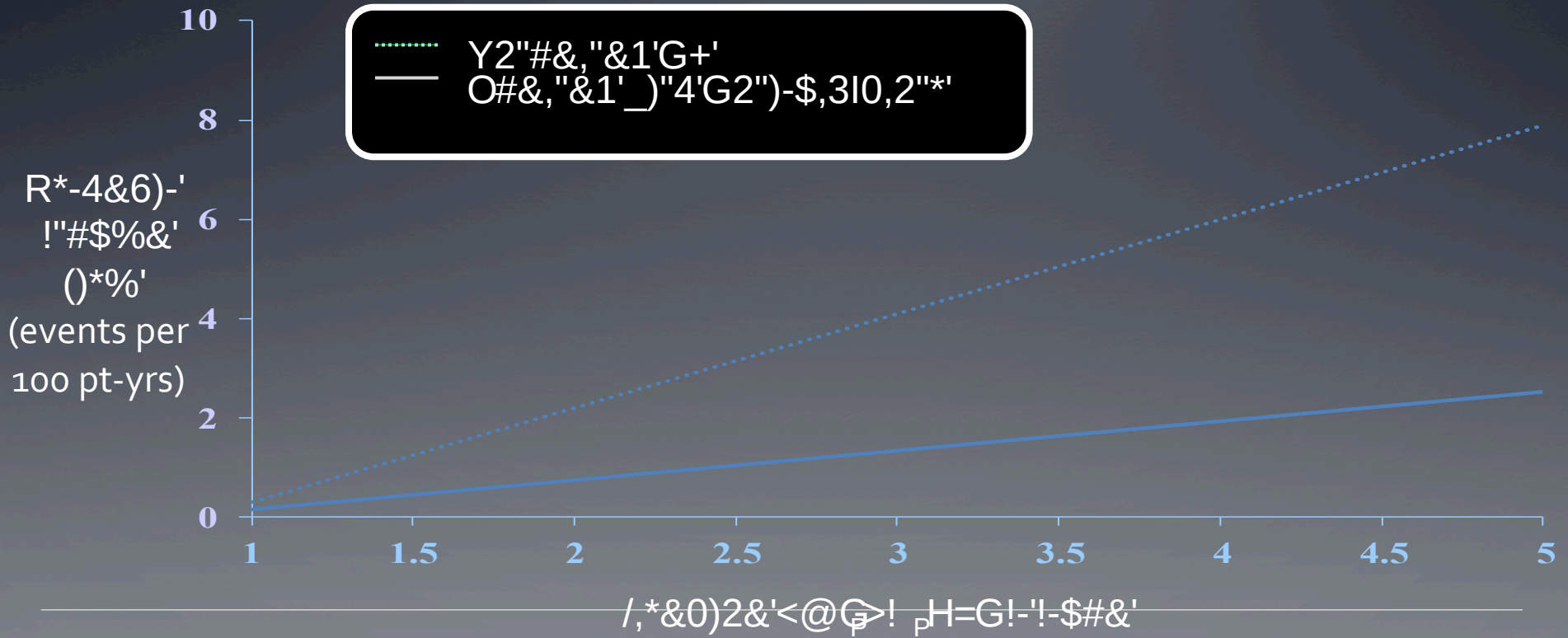
| | 5(NO8<OHG+' | 5(8=GRS' | <G5' | <G5P' | 8XNSYORNV' | 5$*"H+>G' G99#$Z,0' | G33#&3,"&'>,",' |
|---|---|---|---|---|---|---|---|
| 5&#)-,#1),0'O,69$2,1&' | PL']MUEC^' | B']TUFC^' | A']TUMC^' | TT']TUFC^' | E']LUPFC^' | EF']TULPC^' | AK']TUPAC^' |
| "O#&,"&1'_)"4' "9&#)-,#1)$-&2"&*)*' | TE']PUAC^' | M']TUBC^' | `']TUPC^' | 2;,' | P']LUPLC^' | PM']LUKEC^' | |
| "O#&,"&1'*I#3)-,007' | `']TUBC^' | T']LUMC^' | T']LUPC^' | 2;,' | T']LUTLC^' | TP']LUETC^' | |
| "(&*I0"&1')2'1&,"4' | L' | L' | L' | L' | L' | E']LU`AC^' | |
| 5&#)-,#1),0'&aI*)$2'b'2$')2"&#Z&2")$2' | M']LUFC^' | L' | B']LUFC^' | E']LUBC^' | M']LUEFC^' | TT']LUPFC^' | P`']LUMLC^' |
| 5#$-&1I#&H#&0,"&1'*"#$%&' | B']TUTBC^' | T']LUE`C^' | L' | P']LUEBC^' | T']LUTLC^' | E']LUL`AC^' | TP']LUTAC^' |
| >&Z)-&'&6W$0)c,")$2' | E']LUKC^' | P']LU`C^' | T']LUPC^' | L' | P']LUPLC^' | F']LUPMC^' | T`']LUPBC^' |
| "(&6$Z&1" "9&#-I",2&$I*07' | T' | L' | L' | L' | T' | E' | |
| "(&6$Z&1'*I#3)-,007' | P' | P' | T' | L' | T' | K' | |
| >&,"4' | | | | | | | |
| "5#$-&1I#&H#&0,"&1' "6$#",0)"7' | L' | L' | L' | L' | T']LUTC^' | E']LUL`AC^' | M']LULKC^' |
| "G11)")$2,0'6$#",0)"7' "_)"4)2'`1,7*' | L' | L' | L' | T']LUT`C^' | E']LUPFC^' | T']LULPKC^' | B']LUL`C^' |

# Device Embolization Details

| Device Size | Method of Removal |
|---|---|
| 21 mm | Percutaneous Snare |
| 21 mm | Percutaneous Snare |
| 33 mm | Surgical |
| 33 mm | Surgical |
| 30 mm | Surgical |
| 24 mm | Percutaneous Snare |
| 27 mm | Surgical |
| 27 mm | Surgical |
| 27 mm | Surgical |

# Ischemic Stroke by $CHA_2DS_2$-VASc Score

*Current Treatment*




*Friberg. Eur Heart J (2012); NICE UK (2014). WATCHMAN FDA Panel Sponsor Presentation. Oct 2014*

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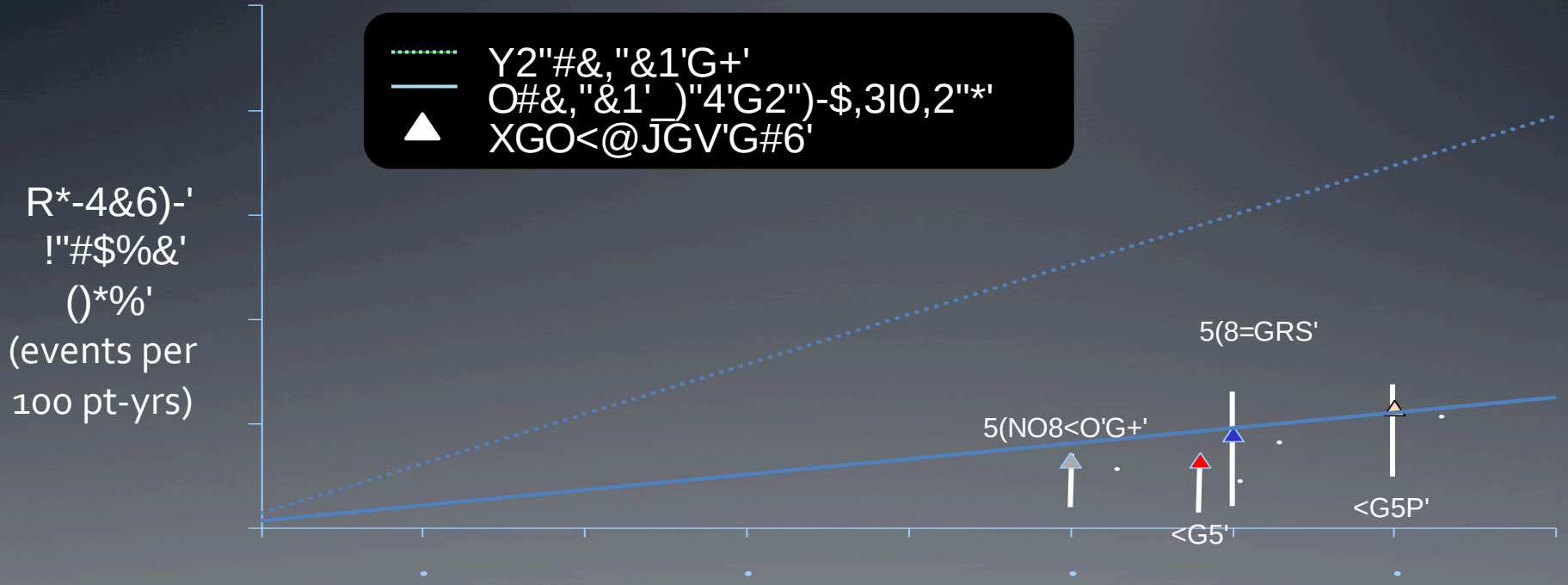
## *PROTECT AF 5 Yrs / PREVAIL 3 Yrs*

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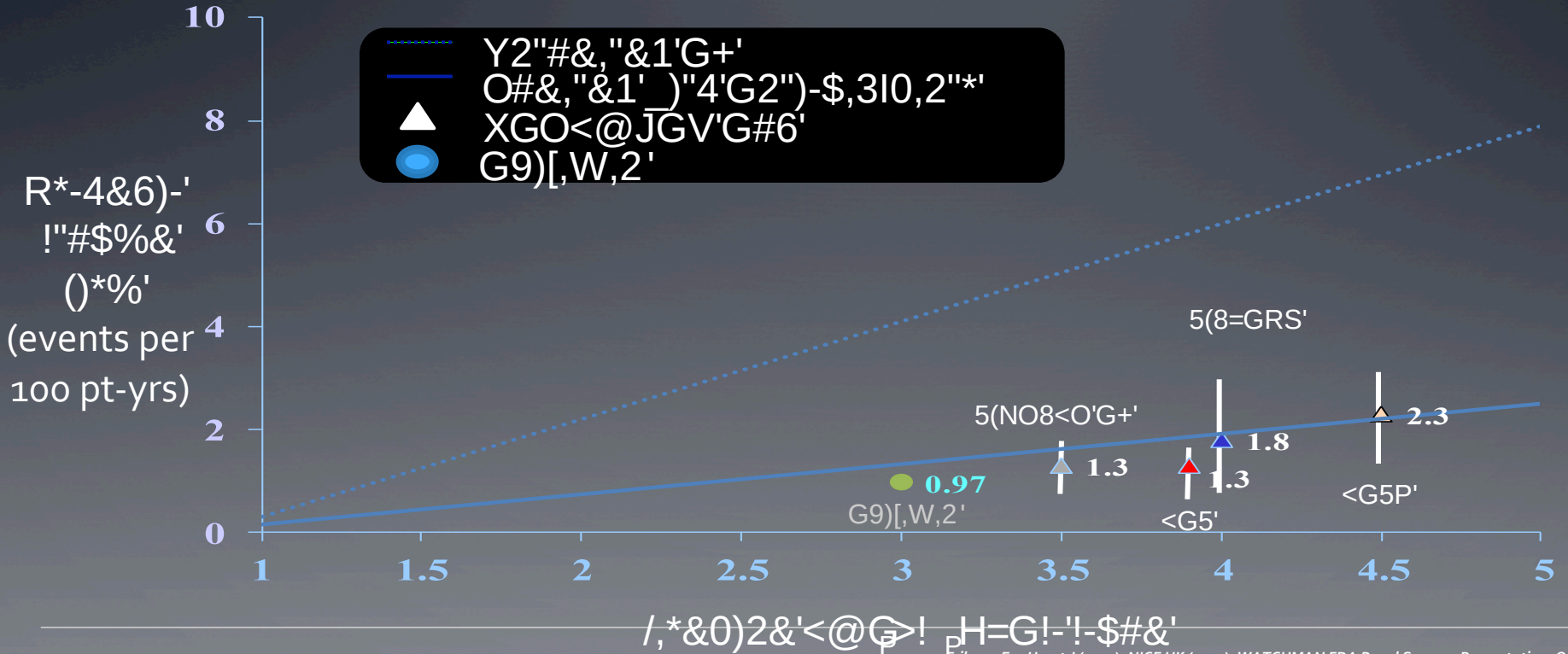
*Friberg. Eur Heart J (2012); NICE UK (2014). WATCHMAN FDA Panel Sponsor Presentation. Oct 2014*

# R*-4&6)-'!"#$%&'W7'<@>G pH=G!-'!-$#&'

***Rates in Perspective'***

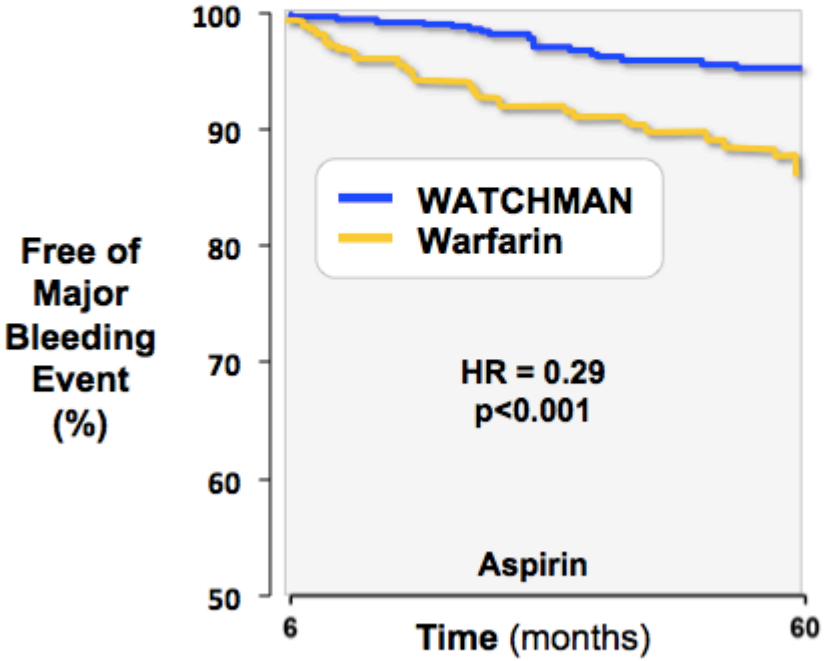



*Friberg. Eur Heart J (2012); NICE UK (2014). WATCHMAN FDA Panel Sponsor Presentation. Oct 2014; Lopes, R, et al. Lancet 2012; 380: 1749–58.; Granger, C et al. N Engl J Med 2011;365:981-92.*

# PROTECT-AF & PREVAIL Combined Analysis

## Reduction in Major Bleeding (>6-mo)

- **Late Major Bleeding was Reduced by 71%**

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MOUNT SINAI SCHOOL OF MEDICINE

MJ.Price, VY.Reddy, M.Valderrabano et al, *JACC CV Intv* 8:1925-32 (2015)

# PROTECT-AF & PREVAIL Combined Analysis

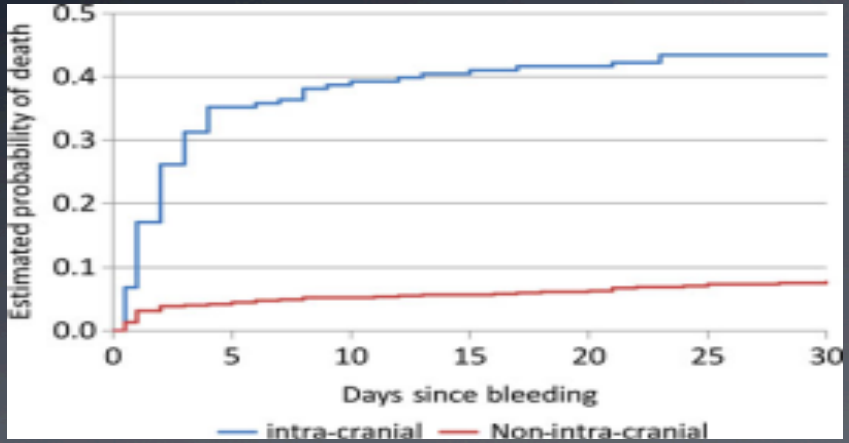
## *Late* (>6-mo) Bleeding by Subgroups

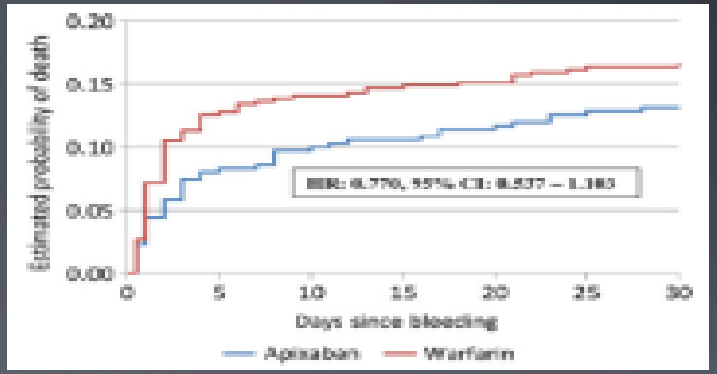
**TABLE 5** Major Bleeds Beyond 6 Months Post-Randomization According to Subgroup

| | LAA Closure | Warfarin | Hazard Ratio (95% Confidence Interval) | p Value | p Interaction |
|---|---|---|---|---|---|
| Age ≤75 yrs | 1.4 (6/436) | 7.8 (17/217) | 0.17 (0.147–0.196) | <0.001 | 0.005 |
| Age >75 yrs | 4.4 (13/296) | 10.9 (18/165) | 0.43 (0.264–0.701) | 0.001 | |
| $CHA_2DS_2$-VASc ≤4 | 1.8 (10/551) | 8.5 (22/258) | 0.21 (0.138–0.321) | <0.001 | 0.28 |
| $CHA_2DS_2$-VASc >4 | 5.1 (9/178) | 10.7 (13/121) | 0.47 (0.161–1.378) | 0.17 | |
| Modified HAS-BLED <3 | 1.4 (8/561) | 7.9 (23/291) | 0.17 (0.173–0.174) | <0.001 | 0.001 |
| Modified HAS-BLED ≥3 | 6.4 (11/171) | 13.2 (12/91) | 0.55 (0.282–1.070) | 0.078 | |
| No history of TIA/stroke | 2.3 (13/570) | 8.9 (26/292) | 0.26 (0.216–0.305) | <0.001 | 0.67 |
| History of TIA/stroke | 3.7 (6/162) | 10.0 (9/90) | 0.35 (0.102–1.225) | 0.10 | |
| Female | 1.8 (4/224) | 12.0 (13/108) | 0.17 (0.074–0.369) | <0.001 | 0.02 |
| Male | 3.0 (15/508) | 8.0 (22/274) | 0.35 (0.320–0.393) | <0.001 | |

MJ.Price, VY.Reddy, M.Valderrabano et al, *JACC CV Intv* (In press – 2015)

# Impact of Bleeding on 30-Day Mortality
## *ARISTOTLE* Sub-Analysis




***Odds Ratio of 30-day Mortality After ISTH Major Bleeding:***

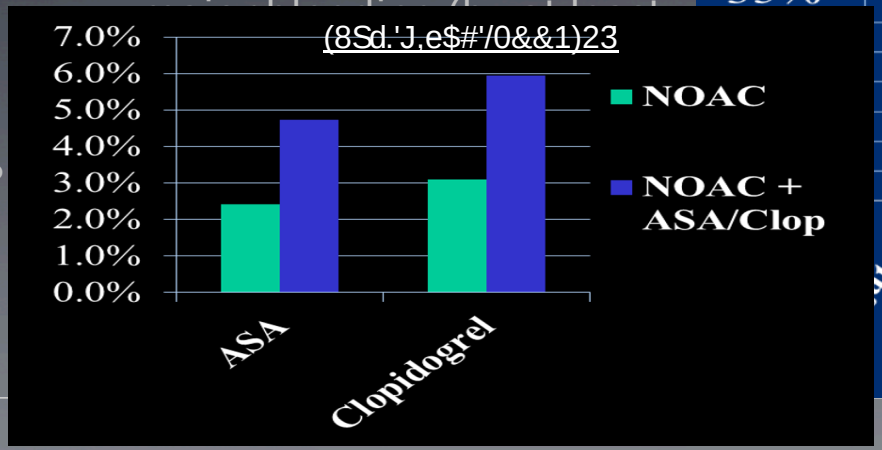
***Intracranial Bleeding:*** ***121.5***

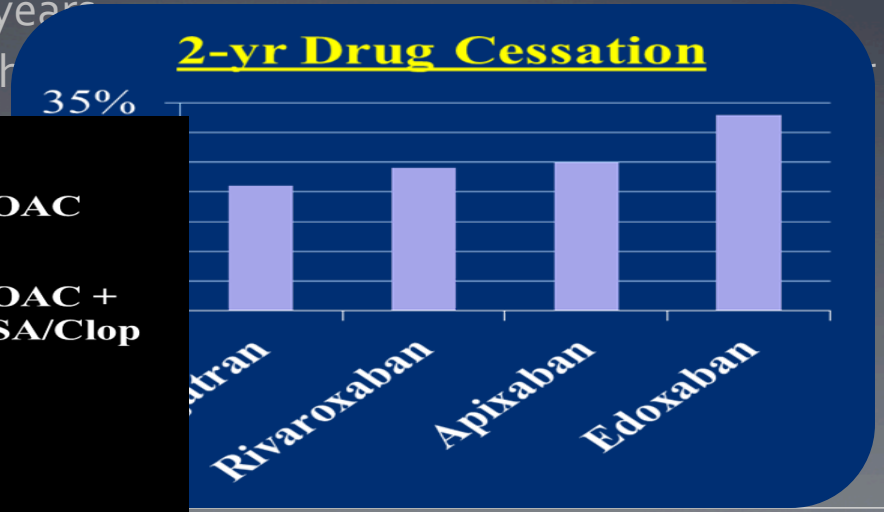
***Non-Intracranial Bleeding:*** ***11.6'***

C.Held, CM.Hylek, JH.Alexander et al, *Eur Heart J* 36:1264-1272 (2016)

# Ok, LAAC is as good as (or better than) Warfarin
## But we now have NOACs…

- NOACs are excellent medications → Preferred Rx
- But NOACs are not a panacea:
  - Even in the NOAC clinical trials between 25%-33% of patients stopped taking the medication by 2 yea
  - Concomitant treatment with

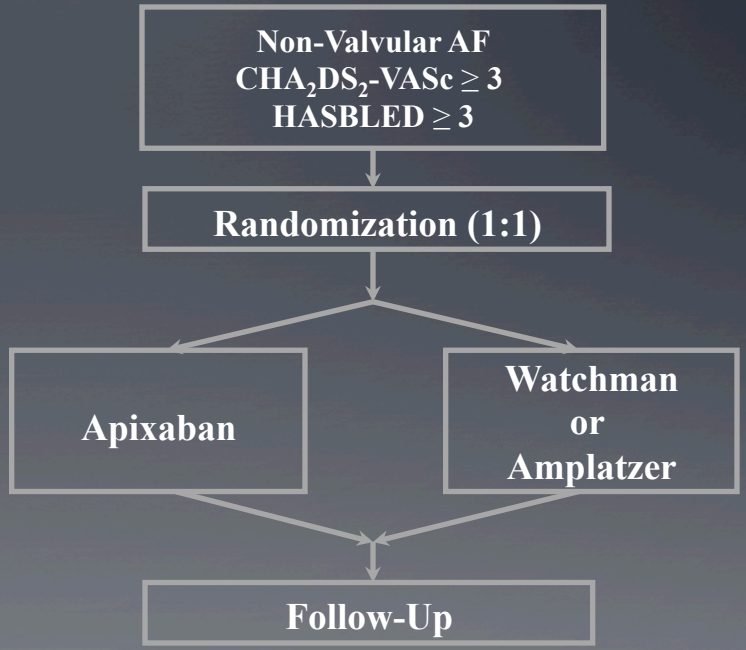


# Comparing LAAC with NOACs

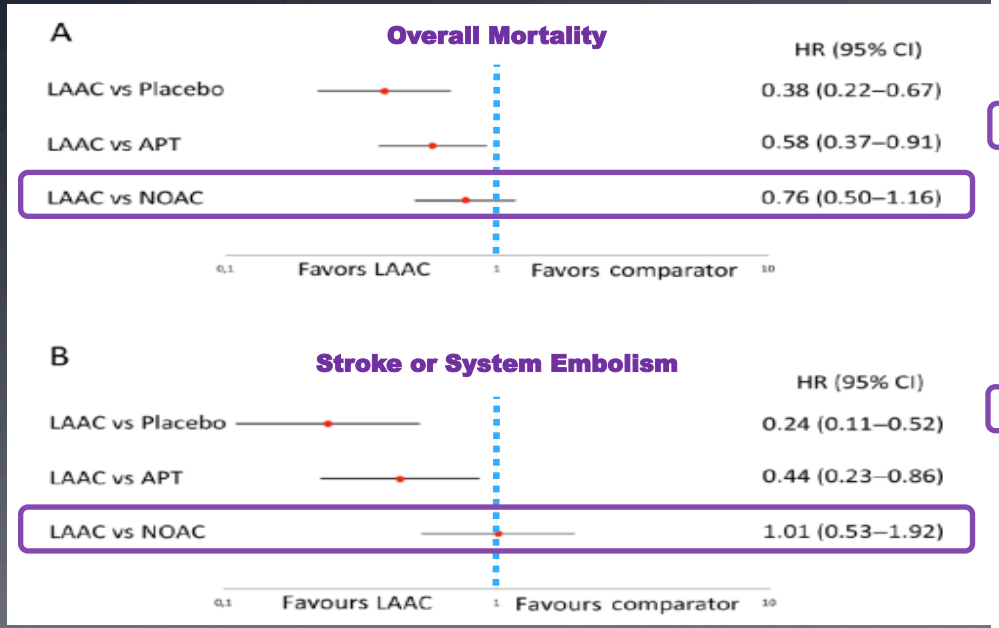
## *PRAGUE-17*: Watchman/Amplatzer *vs* Apixaban

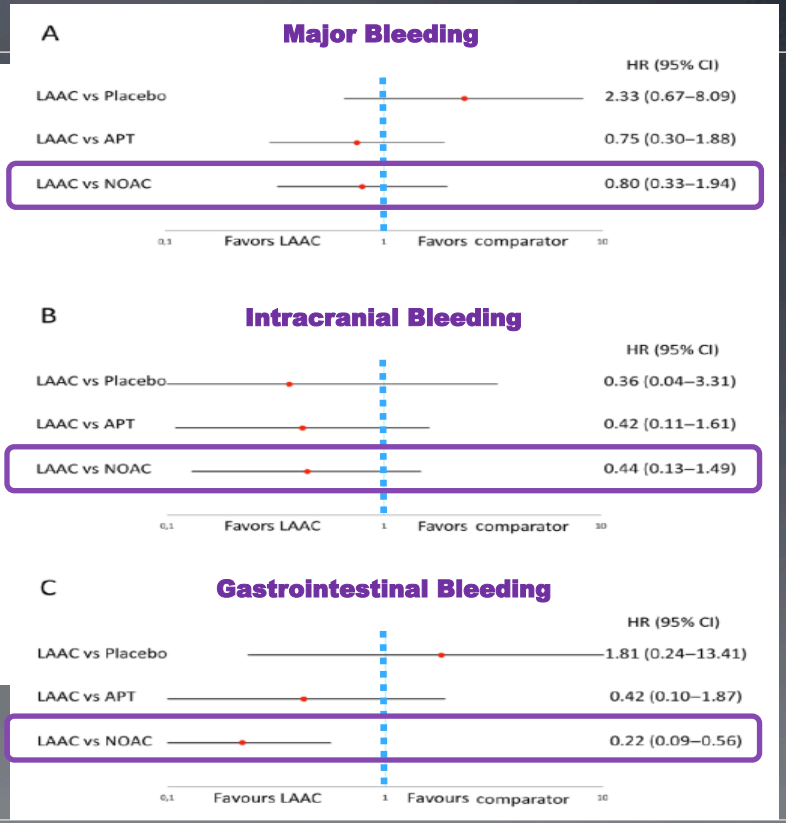
- Multicenter (n=7) RCT
- PI: Pavel Osmancik, Charles University
- Primary Funding: Ministry of Health, Czech Republic
- Inclusion Criteria
  - <@G>! H=G!-'Q'E& HASBLED ≥ 3, or
  - Major Bleeding on warfarin, or
  - Embolic event on warfarin
- Randomization, 1:1
  - LAAC: Watchman or ACP-Amulet
  - NOAC: Apixaban
- Total sample size = MLL'9,")&2"*'
- Composite Primary Endpoint:
  - Stroke, Systemic Embolism, CV Death, Procedural Complications, Major Bleeding, N"4&#'!)32)f-,2"' /0&&1)23"'



# Comparing LAAC & NOACs

## Network Meta-Analysis

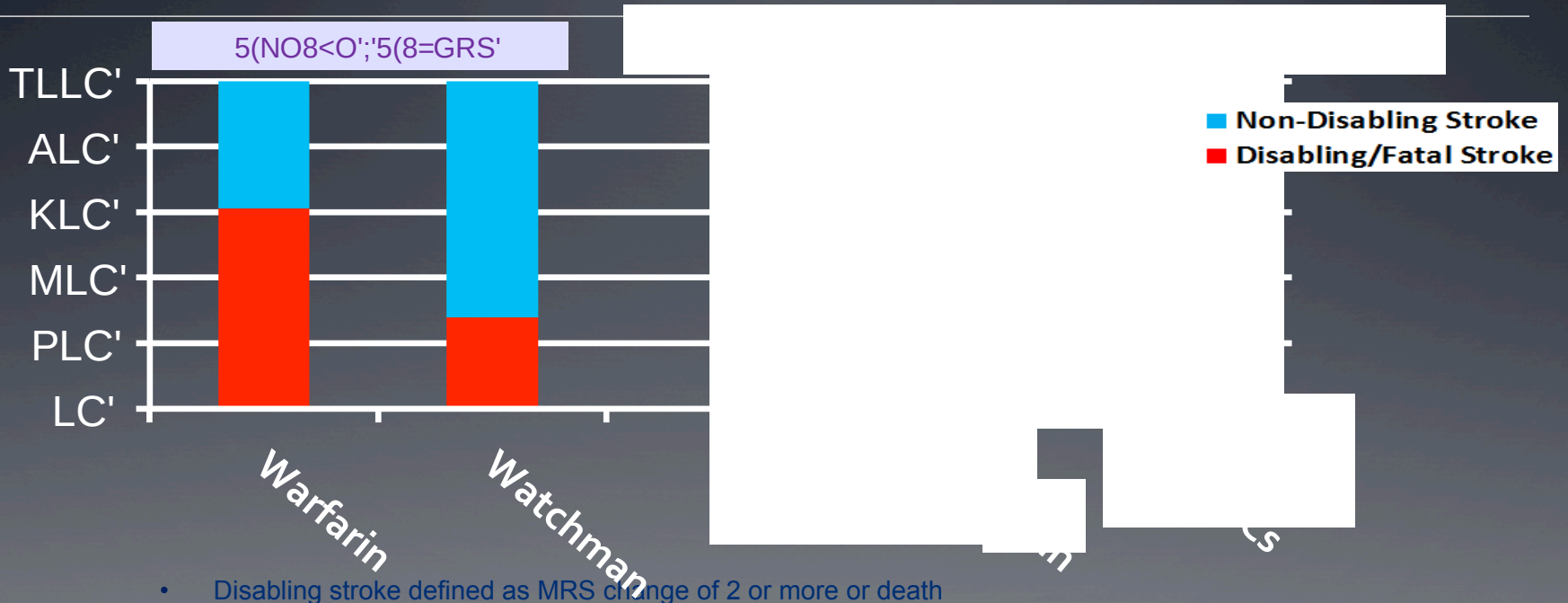



S.Sahay, L.Nombela-Franco, J.Rodes-Cabau et al, *Heart* doi:10.1136/heartjnl-2016-309782 **(2016)**

# Stroke Severity in LAAC *vs* NOAC Trials

## Non-Disabling *vs* Disabling/Fatal



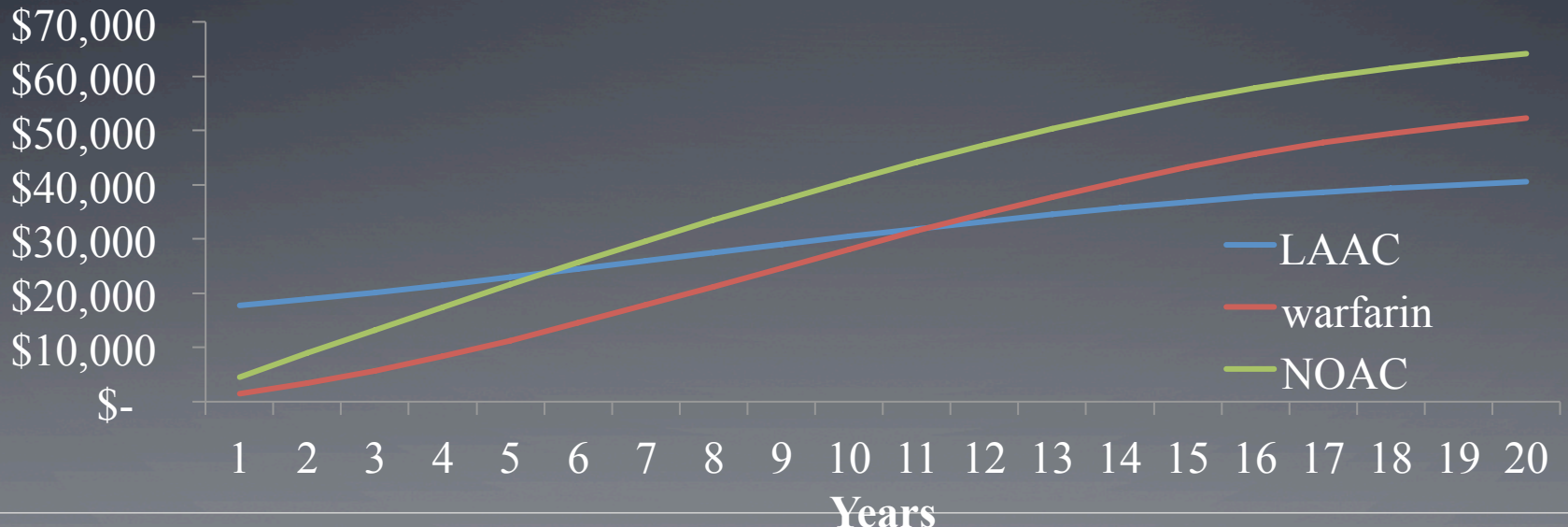

- Disabling stroke defined as MRS change of 2 or more or death
- Similar results if defined as absolute MRS > 2

V.Reddy et al, *Manuscript in Preparation*

# Economic Analysis: Cost Effectiveness

## Watchman$_{\text{PROTECT AF + PREVAIL}}$ *vs* NOACs *vs* Warfarin

- Patient level Markov micro-simulation decision analytic model
- Watchman Inputs: Combined *PROTECT AF* (5 yrs) + *PREVAIL* (3 yrs)
- NOAC meta-analysis of all 4 NOACs (Ruff et al, *Lancet* 383:955, 2014)
- Incorporated costs based on the level of disability resulting from strokes

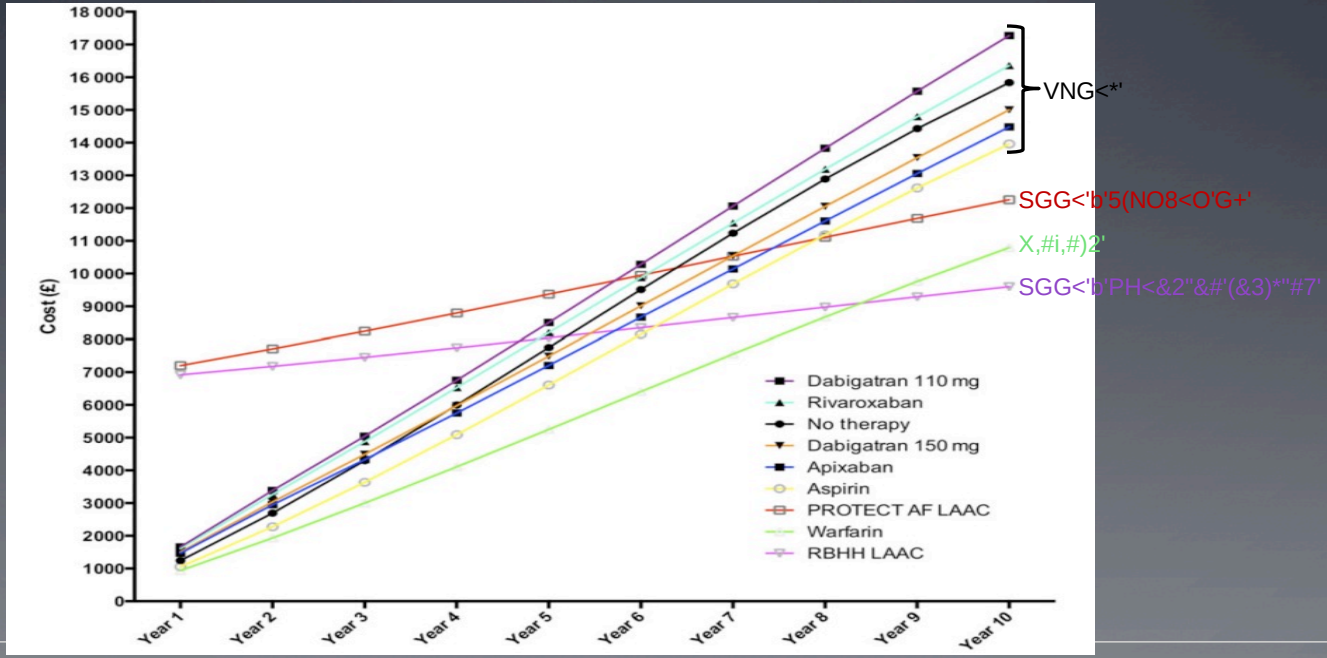



VY.Reddy, RL.Akehurst, SO.Armstrong et al, *TCT Abstract* (2016)

# Cost Analysis

## Watchman *vs* OACs: Clinical Trial *vs* Real-World

- Economic costs from the U.K. perspective
- Watchman Cohorts: i) PROTECT AF, ii) 2-Center Registry (n=110 pts)
- OACs: A network meta-analysis (Dogliotti et al, *Heart* 100:396, 2014)

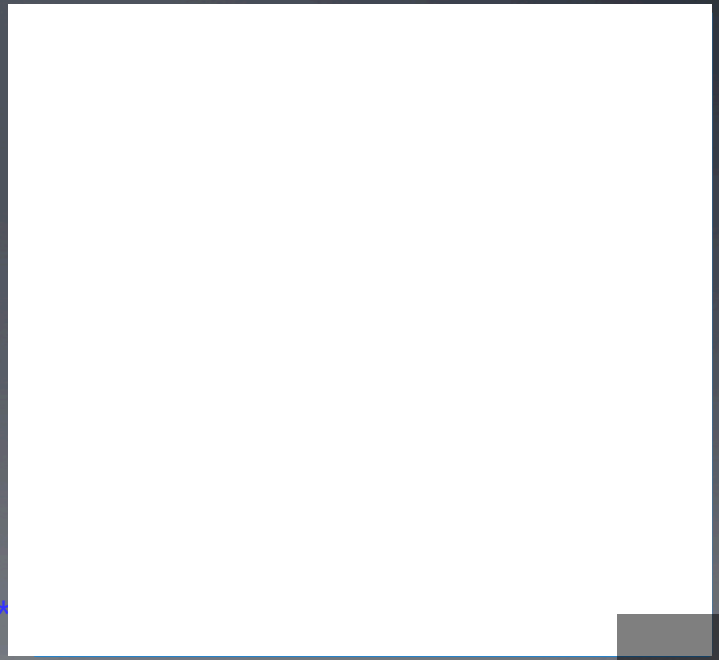



S.Panikker, J.Lord, JWE.Jarman et al, *Eur Heart J* doi:10.1093/eurheartj/ehw048 **(2016)**

# Left Atrial Appendage Closure

## Why not use it in everybody???

- Number of patients in FDA trials
- Who were the patients enrolled in the LAAC trials?
  - Inclusion Criteria:
    - Paroxysmal / Persistent / Permanent AF
    - CHADS ≥ 1
    - Eligible for long-term Warfarin therapy
  - Exclusion Criteria
    - Mechanical valve
    - Symptomatic Carotid disease
    - LVEF < 30%



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# After a Major Bleeding Episode

## Should OAC be restarted???

STUDY PROTOCOL Open Access

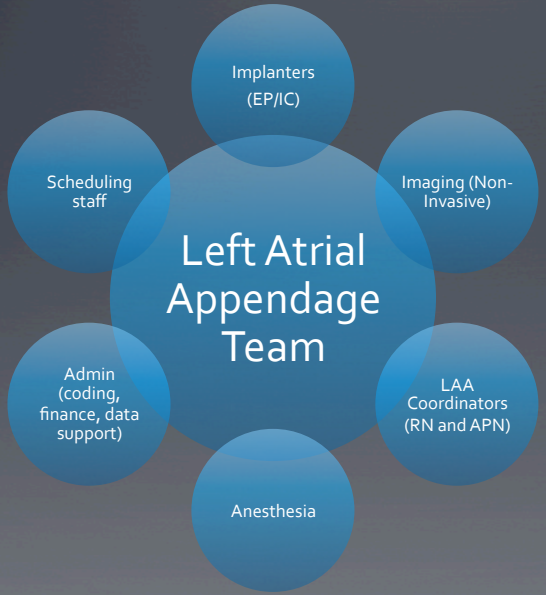
CrossMark

### Apixaban versus Antiplatelet drugs or no antithrombotic drugs after anticoagulation-associated intraCerebral HaEmorrhage in patients with Atrial Fibrillation (APACHE-AF): study protocol for a randomised controlled trial

Koen M. van Nieuwenhuizen[1*], H. Bart van der Worp[1], Ale Algra[1,2], L. Jaap Kappelle[1], Gabriel J. E. Rinkel[1], Isabelle C. van Gelder[3], Roger E. G. Schutgens[4], and Catharina J. M. Klijn[1,5] on behalf of the APACHE-AF investigators

# How Are Patients Evaluated for LAAC

# OhioHealth Heart and Vascular Institute LAAO Program: ***Team Based Care***

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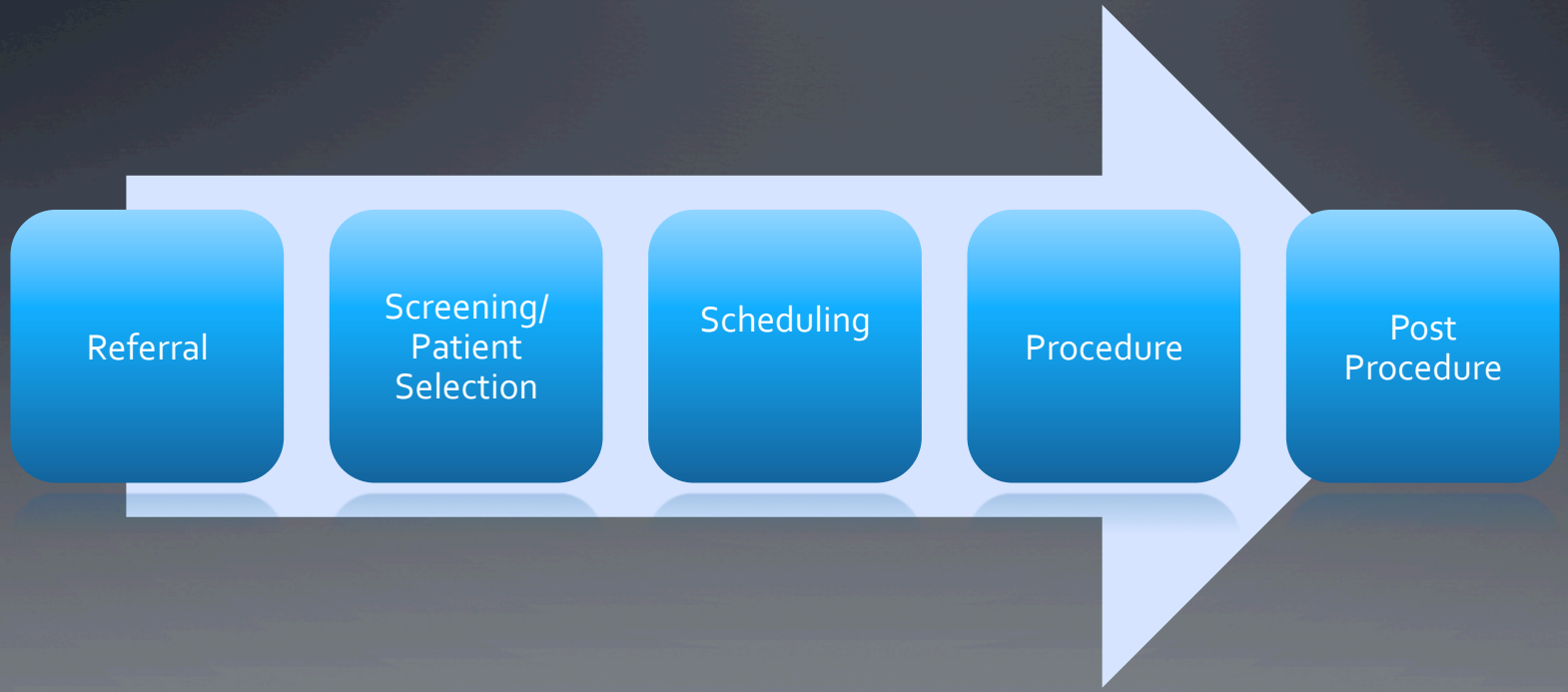
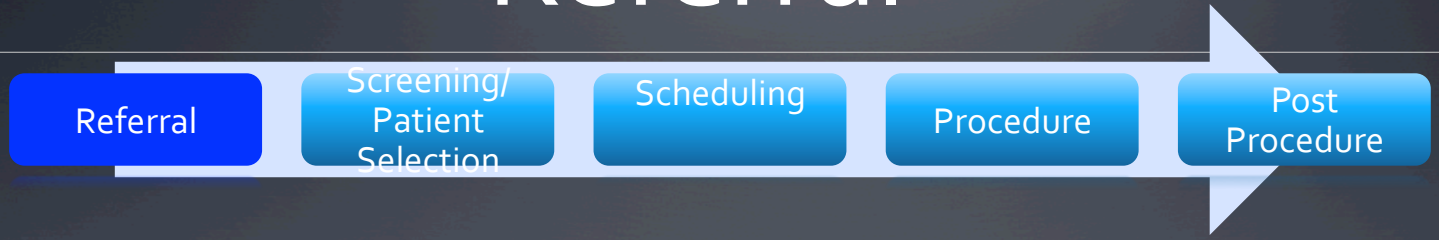
# OhioHealth Heart and Vascular Institute LAAO Program



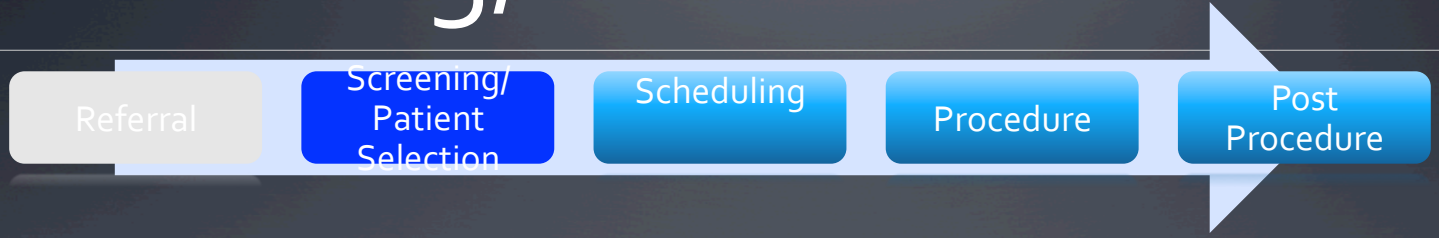

OhioHealth

# Referral




Referral base: cardiology, neurology, internal medicine, hematology, gastrointestinal, nephrology, ophthalmology

# Screening/Patient Selection




- Pre-visit Chart Review- obtain outside records
- Eligibility: Review NCD requirements
- Specialist consultation/collaboration (GI/Neuro/Hematology)
- Shared Decision Making
- AC Clinic referral

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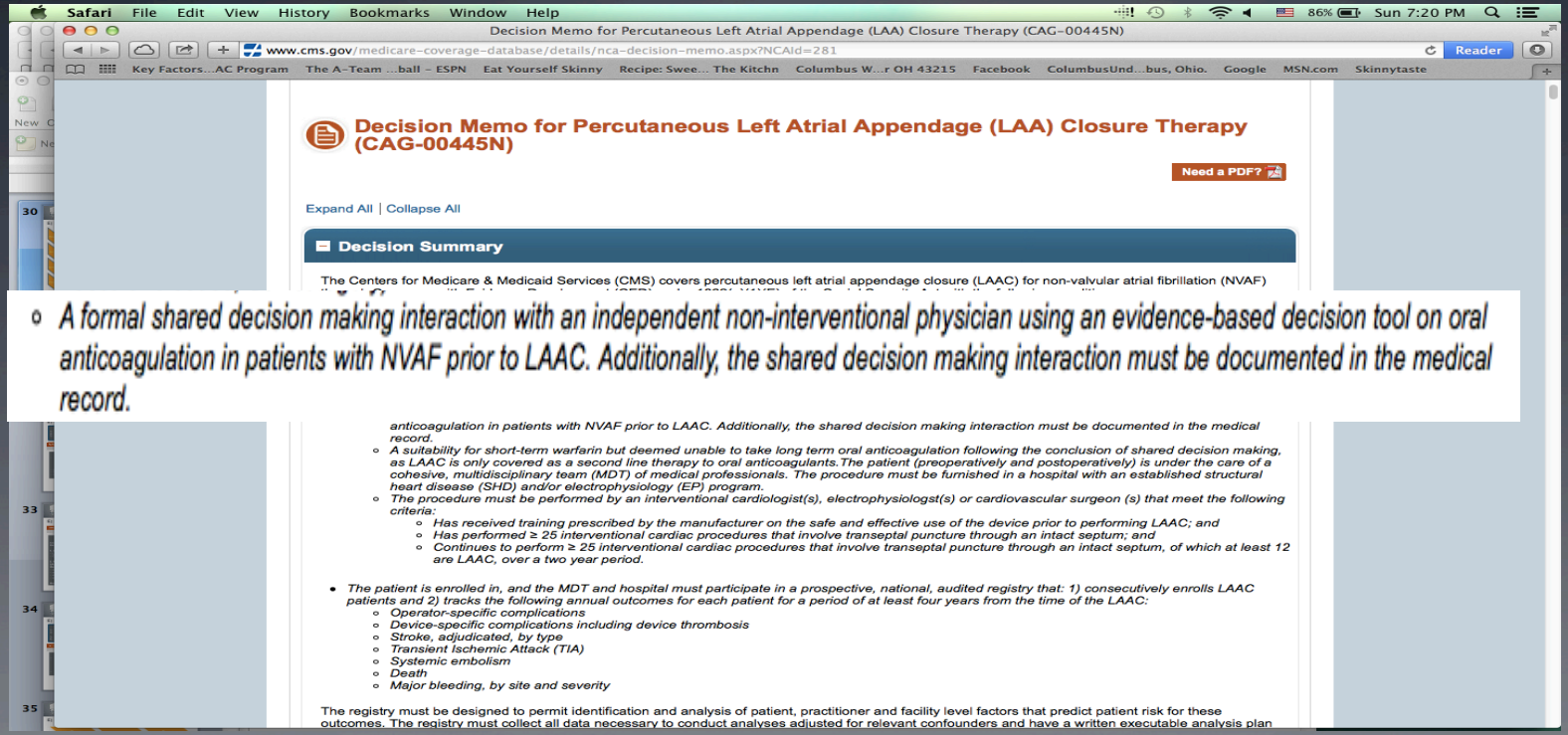
# Shared Decision Making




- *A formal shared decision making interaction with an independent non-interventional physician using an evidence-based decision tool on oral anticoagulation in patients with NVAF prior to LAAC. Additionally, the shared decision making interaction must be documented in the medical record.*

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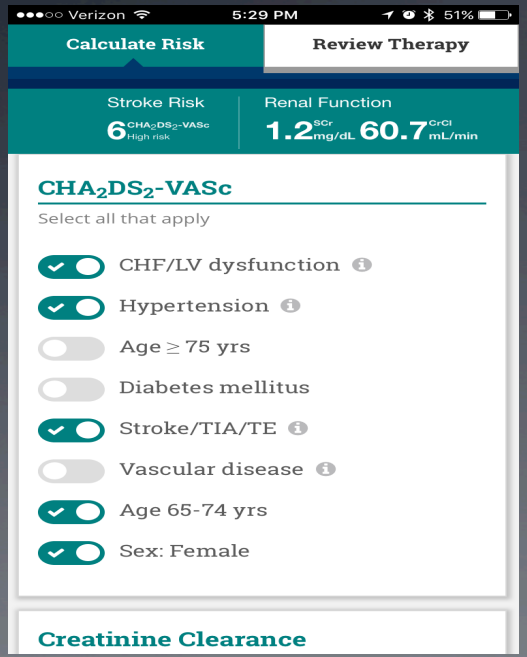
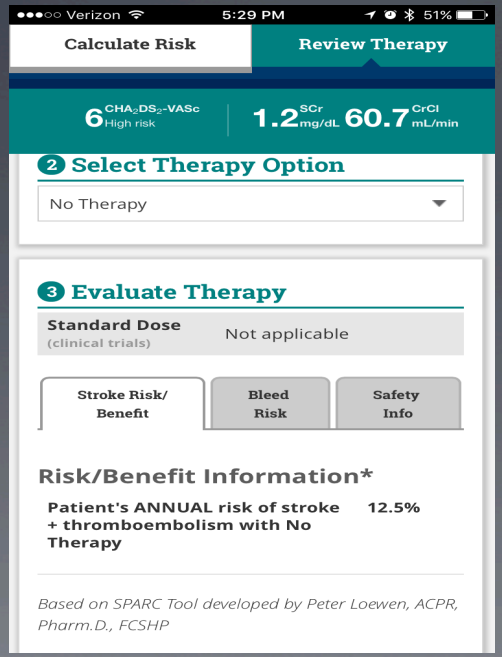
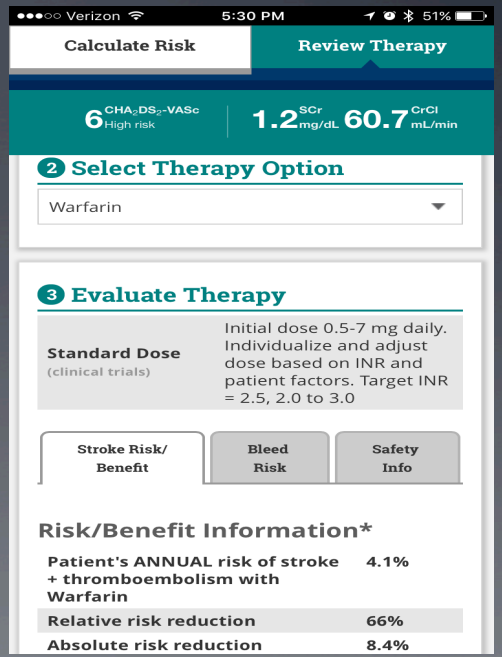
# Shared Decision Making

"The process by which the optimal decision may be reached for a patient at a fateful health crossroads is called shared decision making and involves, at minimum, a clinician and the patient, although other members of the health care team or friends and family members may be invited to participate. In shared decision making, both parties share information: the clinician offers options and describes their risks and benefits, and the patient expresses his or her preferences and values. Each participant is thus armed with a better understanding of the relevant factors and shares responsibility in the decision about how to proceed." Barry and Edgman-Levitan (2012)

# Shared Decision Making



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# Shared Decision Tools

ACP American College of Physicians

https://www.acponline.org/patients_families/products/brochures/afib_booklet.pdf

NICE National Institute for Health and Care Excellence

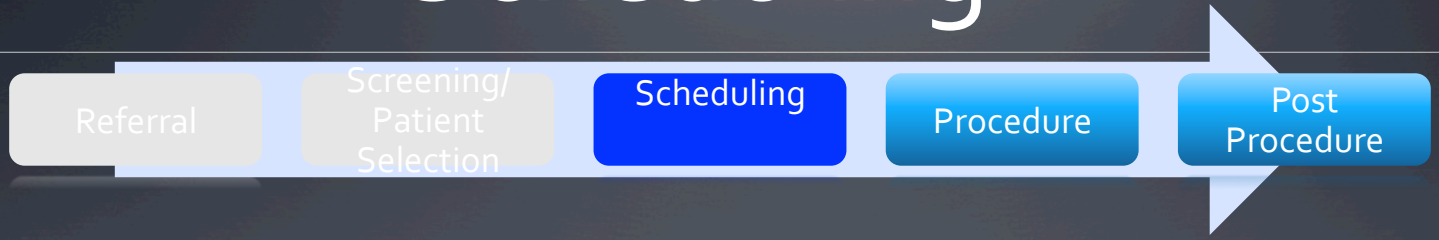
Patient decision aid

https://www.nice.org.uk/guidance/cg180/resources/patient-decision-aid-243734797

CardioSmart American College of Cardiology

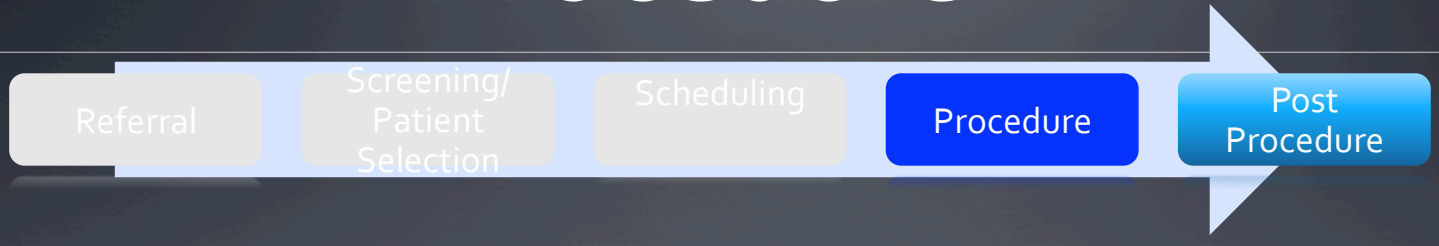
http://www.acc.org/tools-and-practice-support/quality-programs/anticoagulation-initiative/anticoagulation-shared-decision-making-tool

# Scheduling



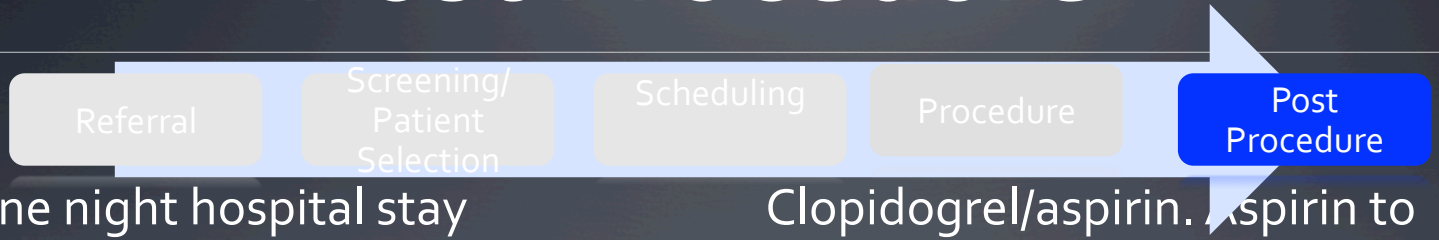

- Start or continue anticoagulation 3 weeks prior to scheduled implant
- Start working on prior authorization for commercial insurance payers. NCD established uniform coverage for Medicare. For Commercial can leverage NCD. May need peer-peer review or letter
- Obtain CCTA or TEE prior to implant to assess LAA anatomy and evaluate for thrombus

# Procedure




- CT/TEE images sent to company representative, physician review prior to procedure
- Coordinated schedules of EP/IC implanters, Non-Invasive Cardiologist for intra-procedural TEE, Anesthesiologist, Company Representative, Hybrid Lab
- INR in acceptable range, NOAC appropriately held
- Type and Cross

# Post Procedure




- One night hospital stay
- Limited echo prior to discharge
- Start warfarin and aspirin 81 mg
- 30-45 day follow up with APN
- 45 day TEE. If no or minimal (<5mm) peridevice leak then transition to 6 months

Clopidogrel/aspirin. Aspirin to continue indefinitely. If inadequate closure, continue warfarin and repeat TEE at 6 months

- Antibiotic endocarditis prophylaxis for 6 months
- 4 years data collection as specified by NCDR Registry

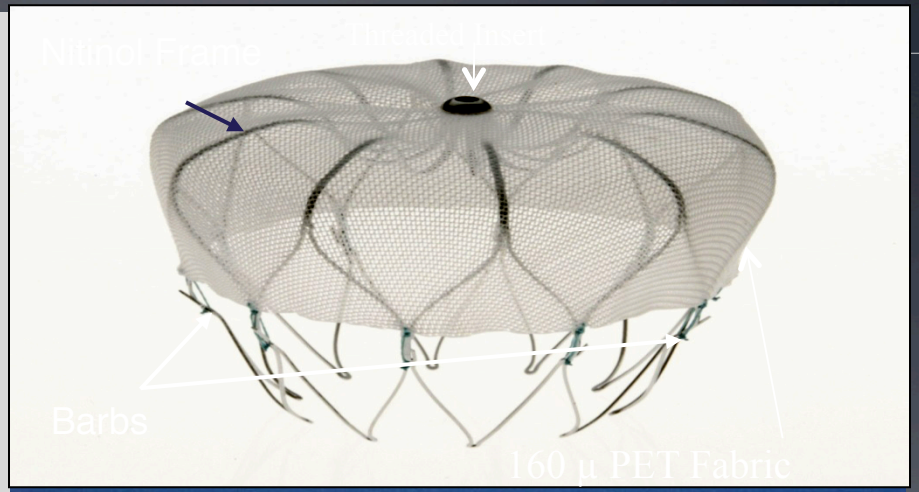
- How To Perform Watchman

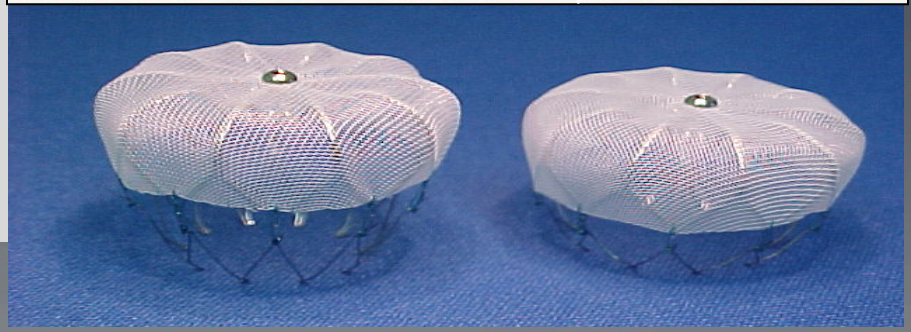
# Procedural Steps

- Transseptal Puncture
  - TEE
  - Transseptal access system
- Measurement of LAA
- Engagement of LAA
  - Pigtail catheter
  - Guide selection
- Positioning of the Device
- Release of Device

# Watchman™ LAA occlusion Device

- Nitinol Frame
- PET Fabric Cap( 160 micron filter)
- Fixation anchors
- Threaded Insert
- Various Sizes (21,24,27,30,33mm)



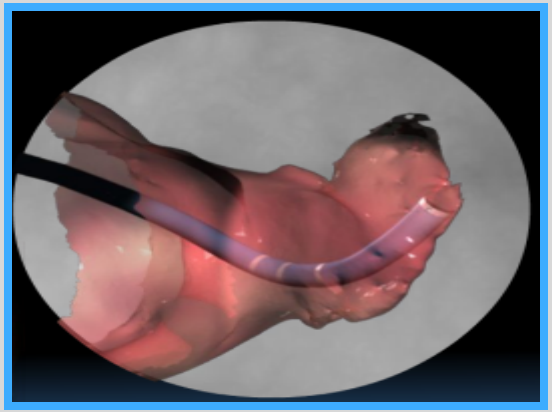



# Watchman™ LAA occlusion system
## *Access Sheath*

Preformed curve shapes guide position in LAA

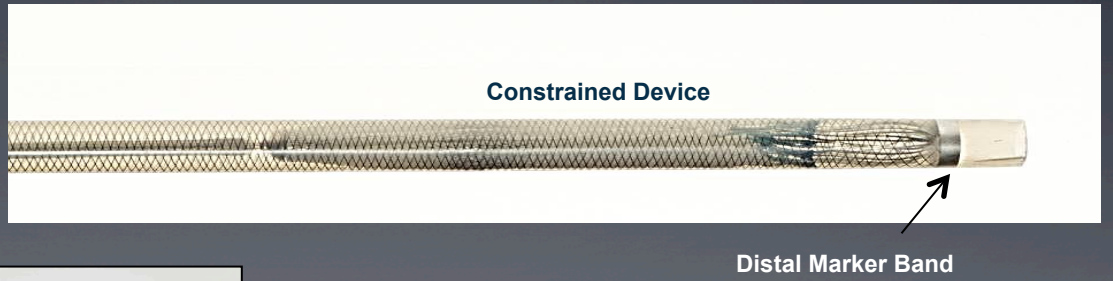

Trans-septal Access System

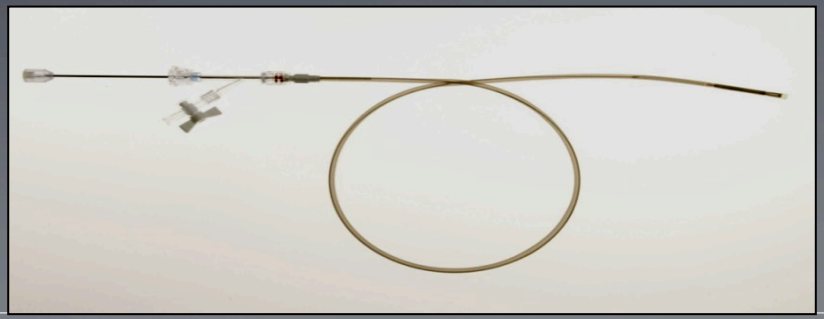
- Double, Single or Anterior Curve styles
- 14F outer diameter (4.7mm) 12F inner diameter (4 mm)
- 75 cm working length



# Watchman™ LAA occlusion system

## *Delivery system*

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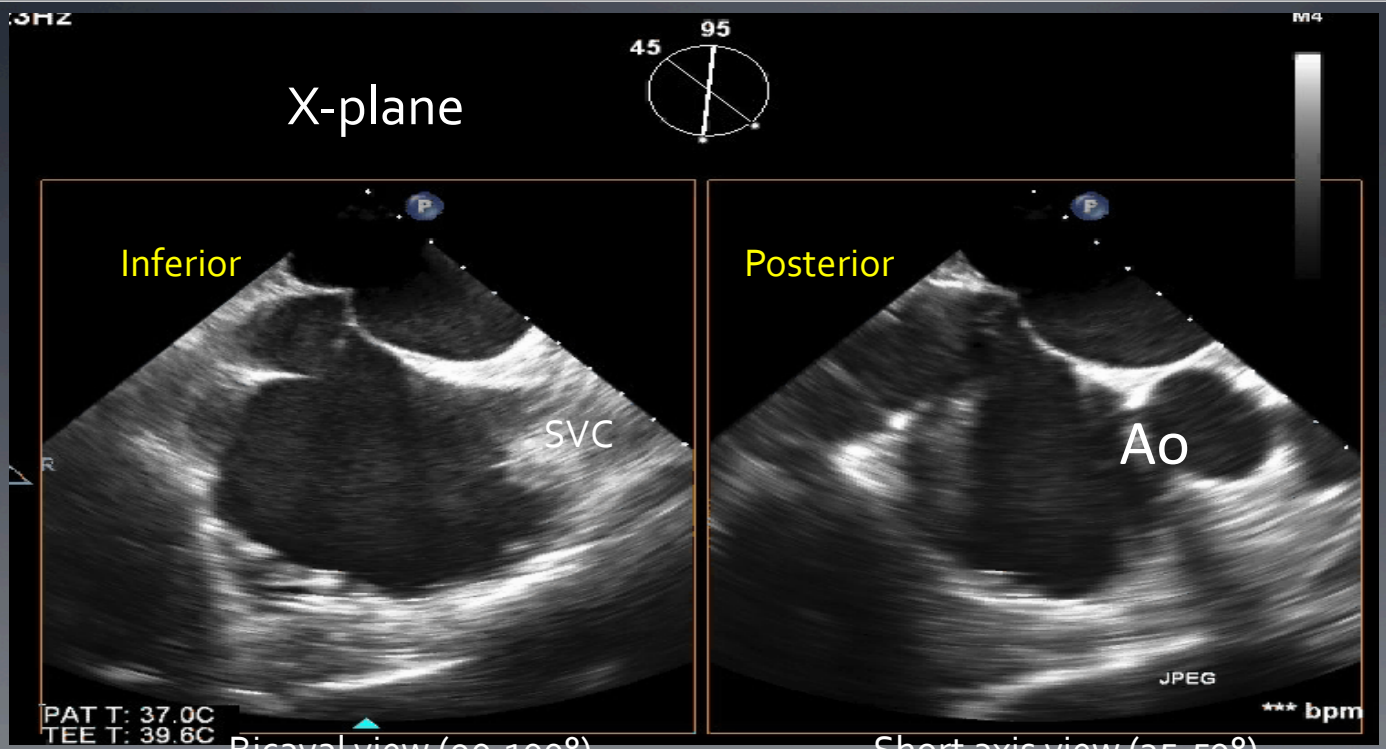
# Procedural Steps

- Transseptal Puncture
  - TEE
  - Transseptal access system
- Measurement of LAA
- Engagement of LAA
  - Pigtail catheter
  - Guide selection
- Positioning of the Device
- Release of Device

# Use of Fluoro & TEE for Transseptal puncture

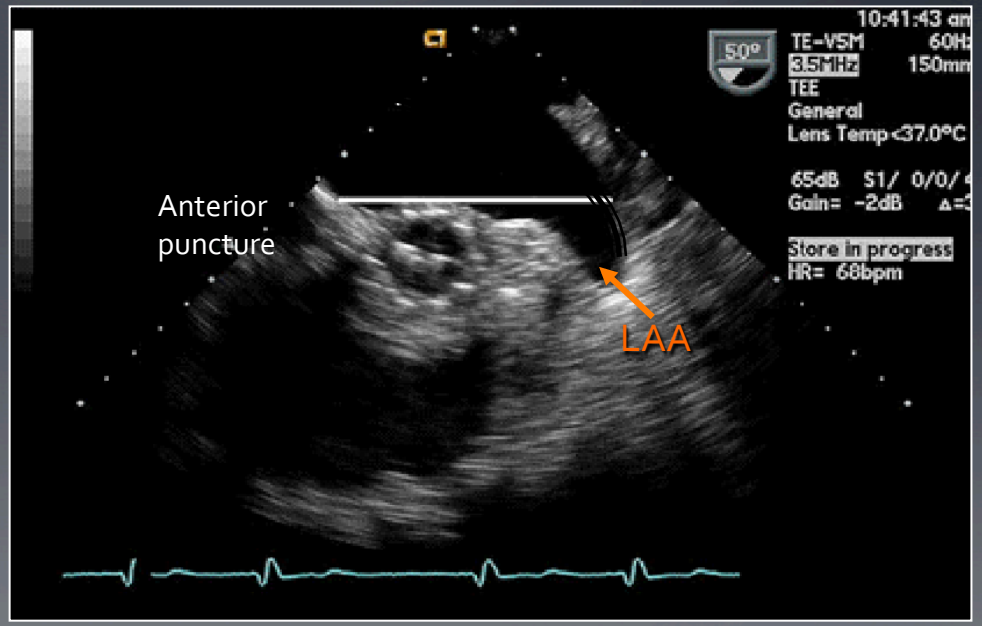



Bicaval view (90-100°)

Short axis view (35-50°)

# *Advantages of TEE guided Transseptal puncture*

- Accurate localization
- Avoid Puncture of the posterior wall or roof of LA
- Early detection of pericardial effusion
- Usually do not use PFO (too superior)



# Procedural Steps

- Transseptal Puncture
  - TEE
  - Transseptal access system
- Measurement of LAA
- Engagement of LAA
  - Pigtail catheter
  - Guide selection
- Positioning of the Device
- Release of Device

# Working View Correlation

| Echo View | Fluoroscopic views |
|---|---|
| 0 degrees | AP cranial |
| 45 degrees | RAO 30 cranial 20 |
| 90 degrees | RAO 30 |
| 135 degrees | RAO 30 caudal 20 |

- Maximal LAA diameter measured usually in 0 and 135°
- RAO caudal is usually maximal LAA angiographic diameter (working view)

| Access Sheath Marker Band | Loaded Device Length* |
|---|---|
| 21mm | 20.2mm |
| 24mm | 22.9mm |
| 27mm | 26.5mm |
| 30mm | 29.4mm |
| 33mm | 31.5mm |

| Maximum LAA Ostium (mm) | Device Size (mm) (uncompressed diameter) |
|---|---|
| 17-19 | 21 |
| 20-22 | 24 |
| 23-25 | 27 |
| 26-28 | 30 |
| 29-31 | 33 |

| Device Size (uncompressed diameter) | Maximum (20%) Compression Measured Diameter* | Minimum (8%) Compression Measured Diameter* |
|---|---|---|
| 21 | 16.8 mm | 19.3 mm |
| 24 | 19.2 mm | 22.1 mm |
| 27 | 21.6 mm | 24.8 mm |
| 30 | 24.0 mm | 27.6 mm |
| 33 | 26.4 mm | 30.4 mm |

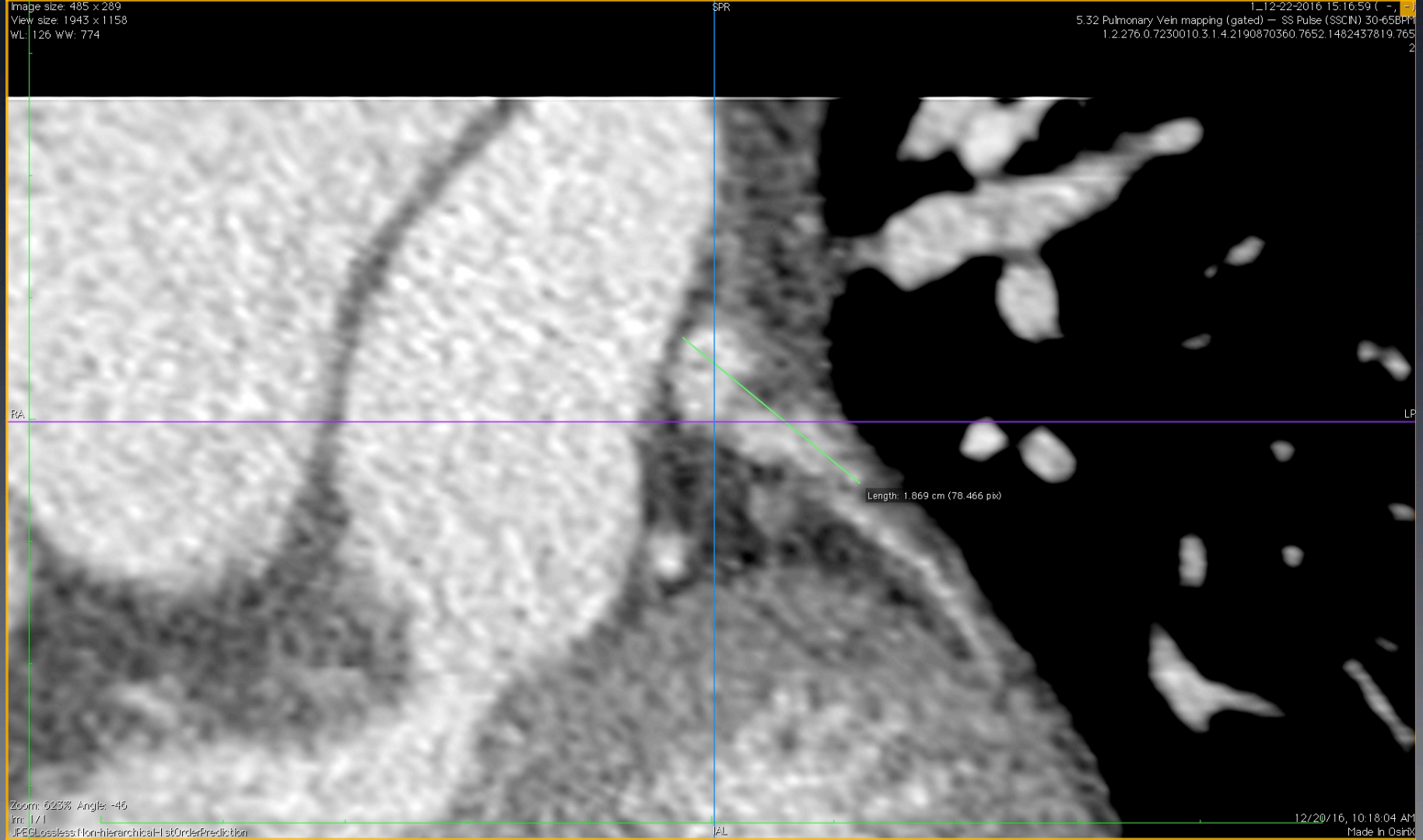


Image size: 485 x 289
View size: 1943 x 1158
WL: 126 WW: 774
SPR
1_12-22-2016 15:16:59 ( - ,
5.32 Pulmonary Vein mapping (gated) — SS Pulse (SSCIN) 30-65BPM
1.2.276.0.7230010.3.1.4.2190870360.7652.1482437819.765
2
RA
LP
Length: 1.869 cm (78.466 pix)
Zoom: 623% Angle: -46
Im: 1 / 1
JPEGLossless:Non-hierarchical-1stOrderPrediction
IAL
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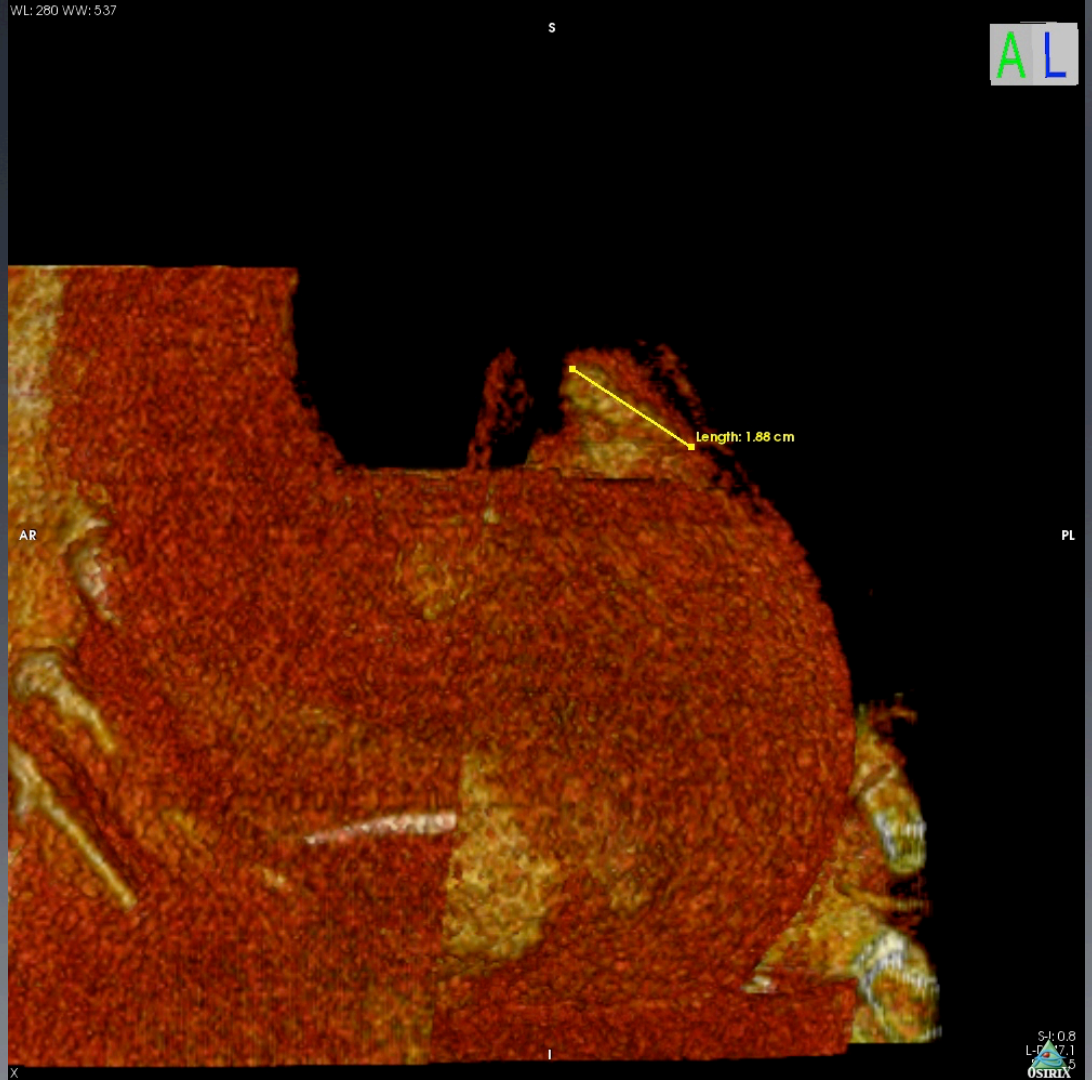
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Length: 1.88 cm
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PL
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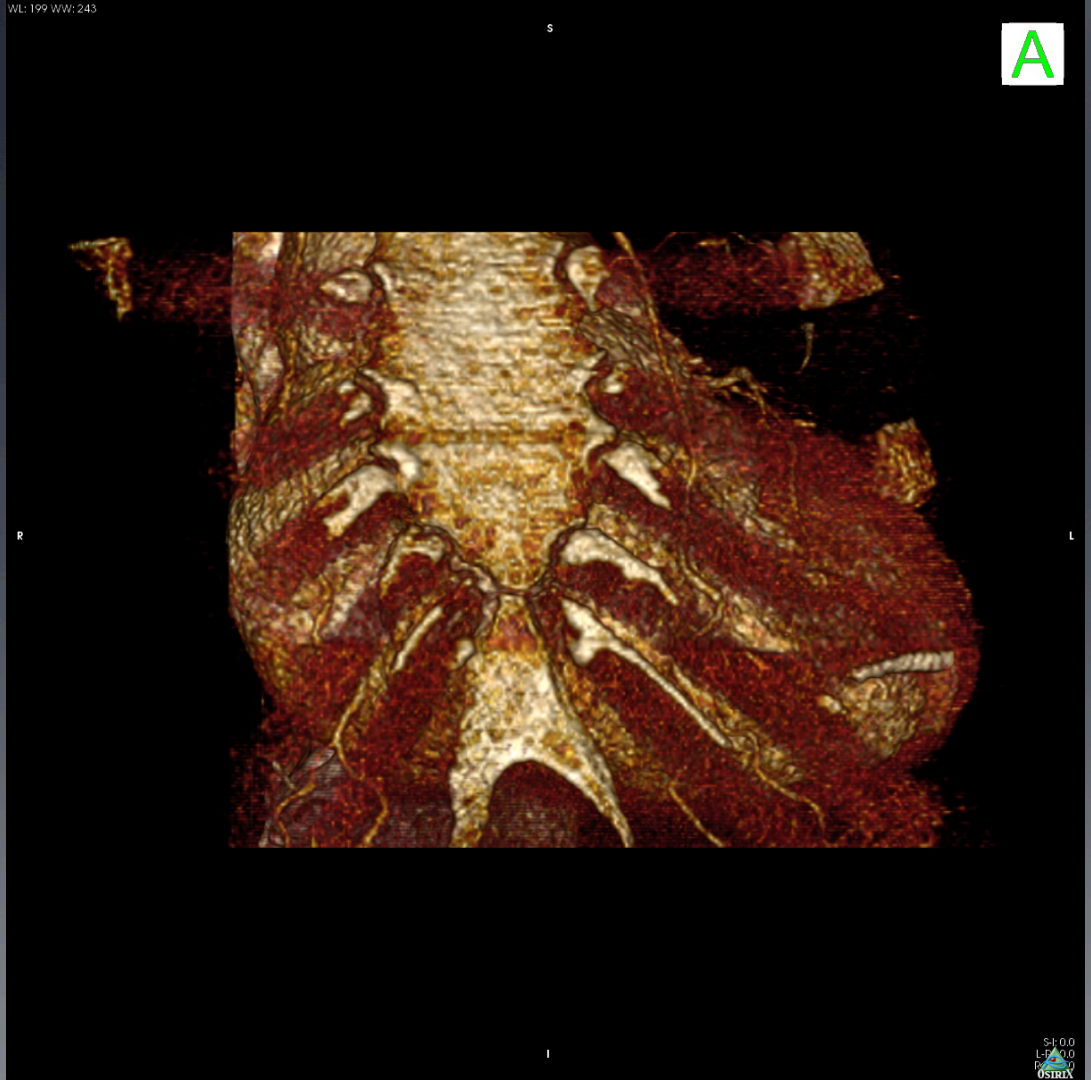
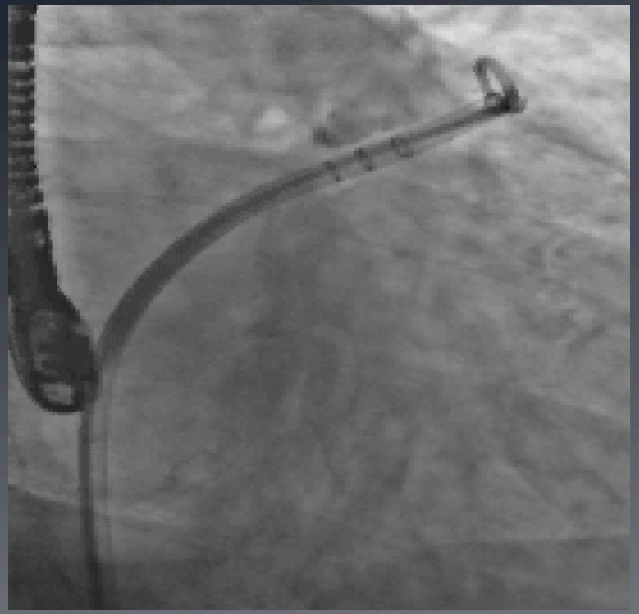
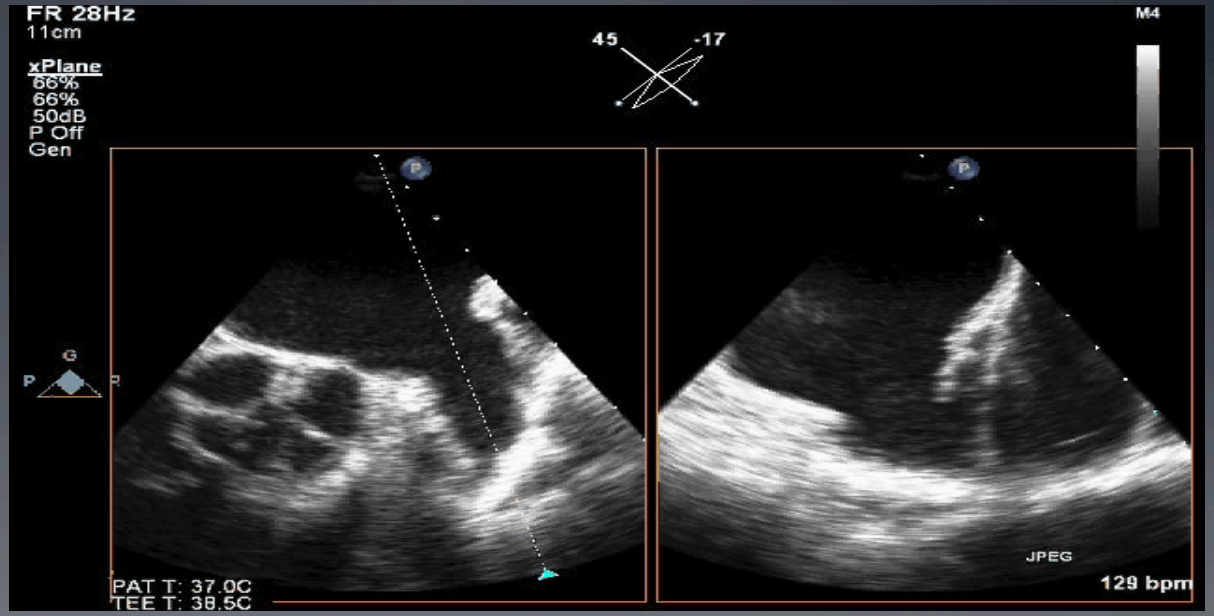
X
S: 0.8
OSIRIX


WL: 199 WW: 243
S
A
R
L
I

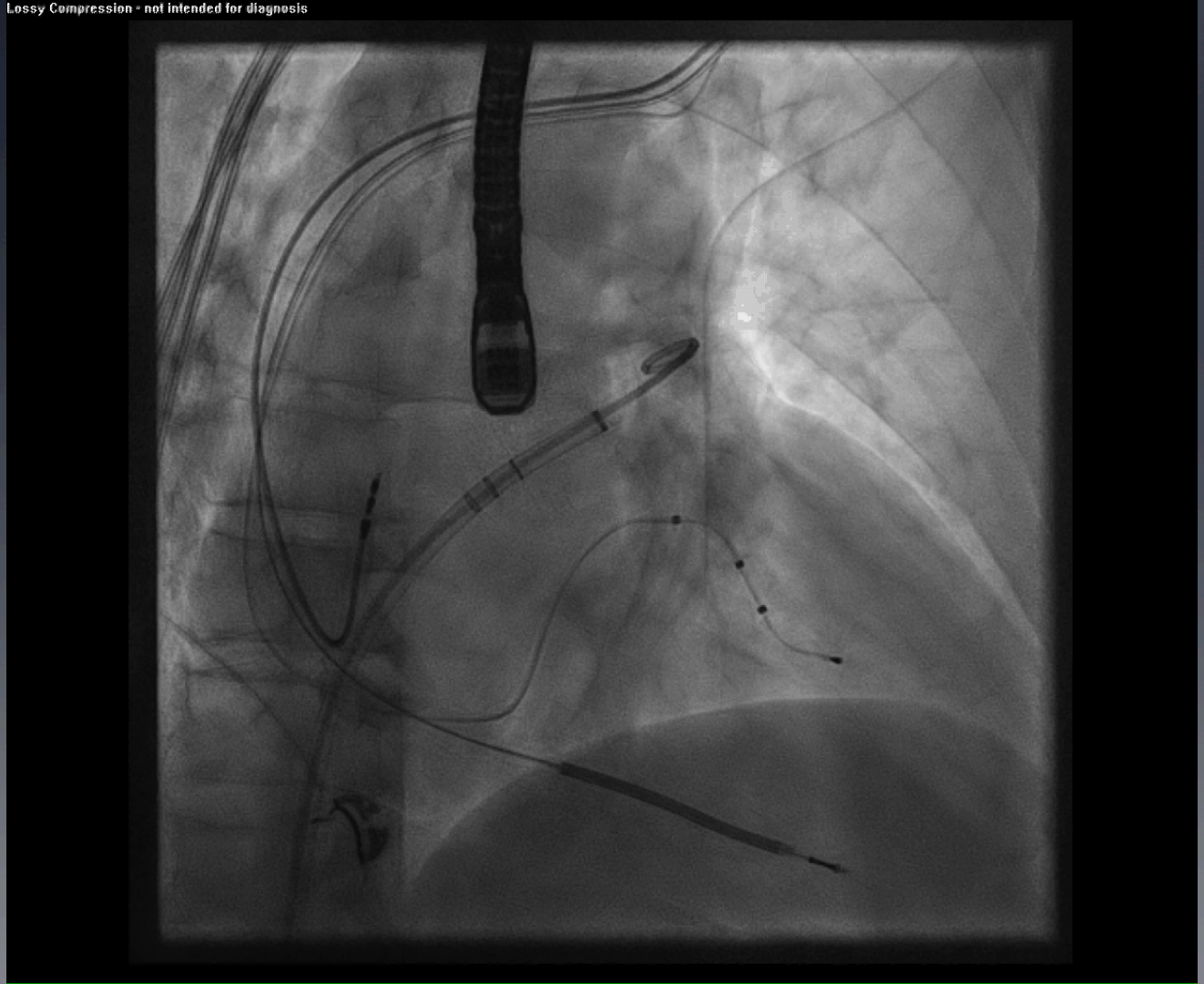
# The best working views






*"RAO Caudal"*

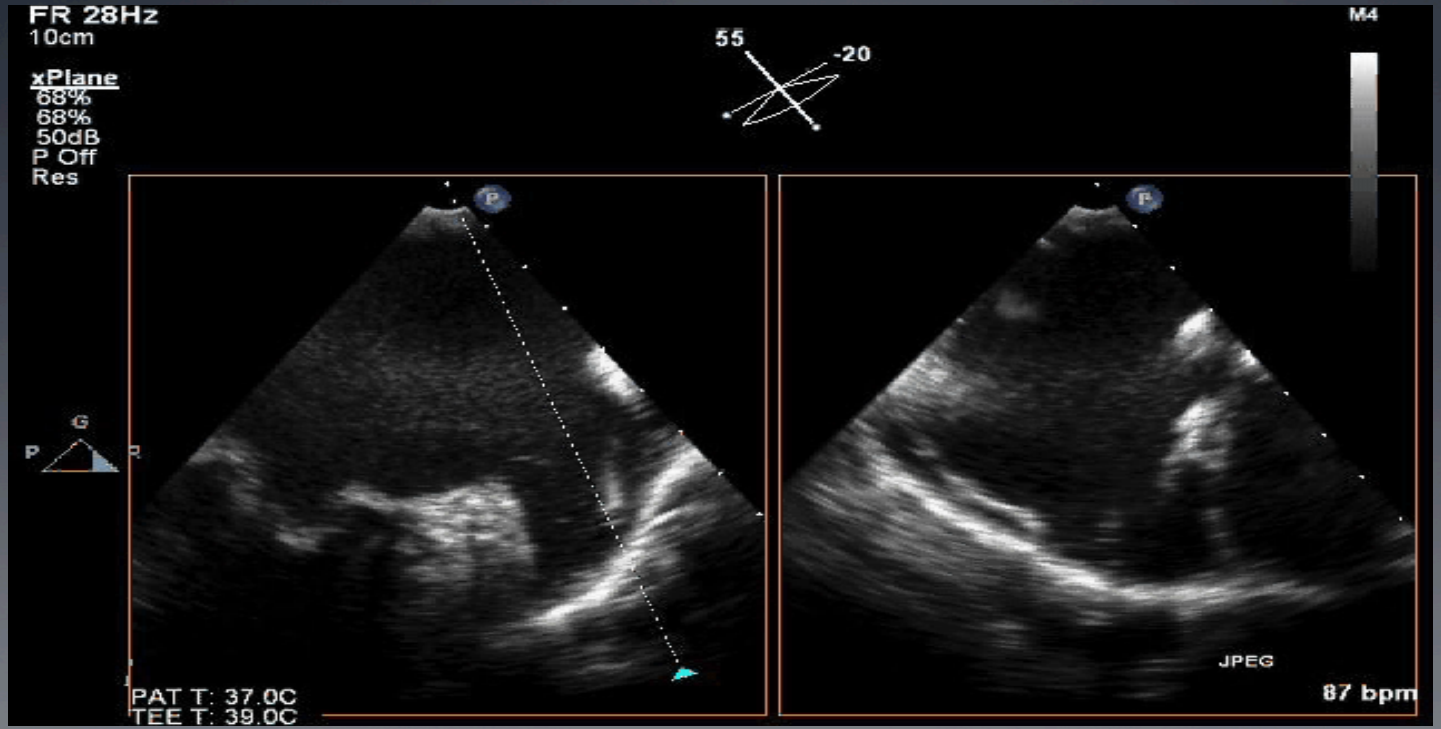
*"X plane 45 & 135 degrees"*



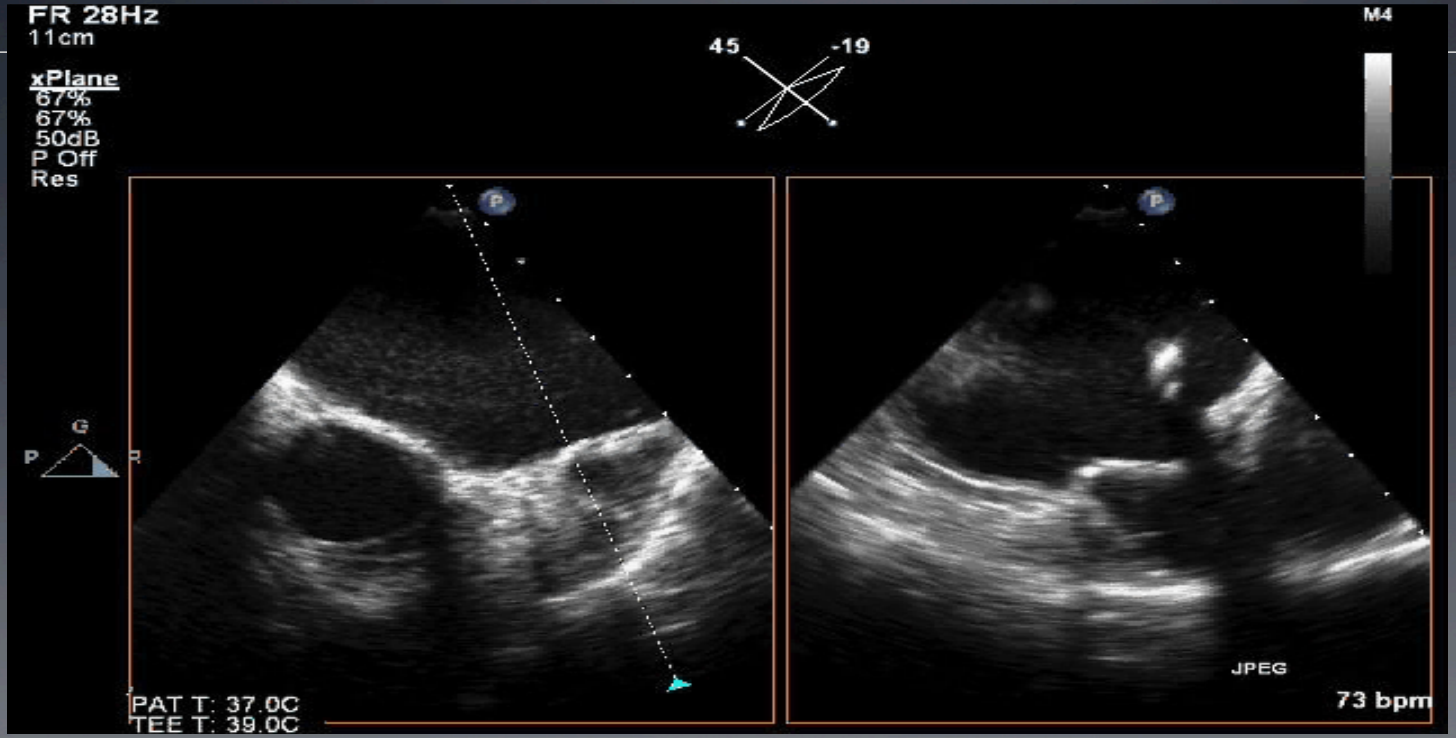
# Procedural Steps

- Transseptal Puncture
  - TEE
  - Transseptal access system
- Measurement of LAA
- Engagement of LAA
  - Pigtail catheter
  - Guide selection
- Positioning of the Device
- Release of Device

# Best device placement:
## Sheath alignment biased towards anterior aspect of LAA



# Deployment of LAA occluder

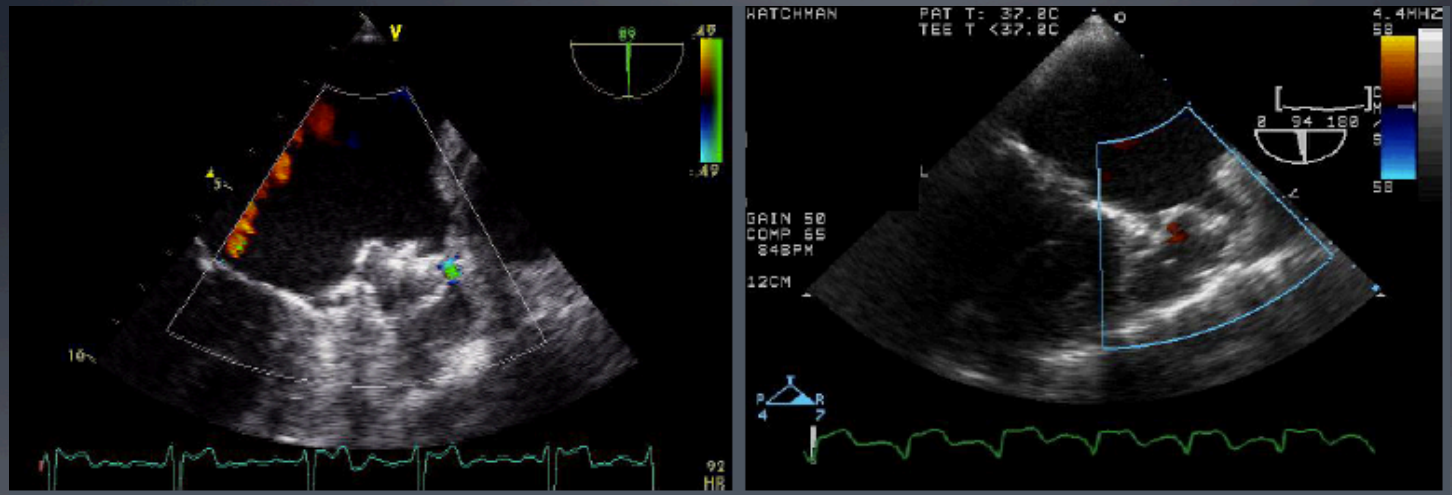



*45°* *135°*

***All criteria must be met prior to device release***

- ✓ **Position** – device is distal to or at the ostium of the LAA
- ✓ **Anchor** – (stability) fixation anchors engaged / device is stable using tug test
- ✓ **Size** – device is compressed at least 8-20% of original size
- ✓ **Seal** - device spans ostium so no color flow Doppler is seen, all lobes of LAA are covered

***If necessary, device can be recaptured (partial or full)***




- Jet must be < 5mm for acceptable release criteria
- If device not yet released, improve position or sealing through partial recapture and reposition or full recapture and replacement

# ASAP TOO

Purpose: US indication expansion for patients deemed contraindicated to oral anticoagulation

- 888 subjects, 100 sites, Global and multi center
- Randomized 2:1 WATCHMAN +DAPT vs Single antiplatelet or no therapy
- Primary Effectiveness endpoint: Ischemic stroke/systemic embolism
- 5 year follow up
- Status: Enrolling

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|---|---|---|
| Discharge through 3 month visit | Yes, suggested dose: 75-100 mg | Yes, suggested dose 75 mg |
| 3 month visit through 12 month visit | Yes, suggested dose: 75-100 mg | No, unless other indication |
| Following the 12 month visit | No, unless other indication | No, unless other indication |

# amaze

Left Atrial Appendage Ligation with the LARIAT® Suture Delivery System as Adjunctive Therapy to Pulmonary Vein Isolation for Persistent or Longstanding Persistent Atrial Fibrillation

# Rationale for amaze Trial

- LAA ligation produces electrical isolation of the LAA, decreases AF burden and recurrence of AF, thus creating a "closed-chested MAZE" procedure

- Demonstrate LARIAT + PVI will lead to reduced incidence of recurrent AF compared to PVI alone, with a high safety profile

# amaze Trial Protocol

| | |
|---|---|
| Principal Purpose | Evaluate the additional efficacy of LARIAT to decrease the 12-month rate of AF, and to confirm an acceptable safety profile |
| Patient Population | Patients (18-80 y.o.) with documented persistent or longstanding persistent AF (< 3 yrs continuous AF) planned for catheter ablation |
| Design | Prospective, multicenter, RCT (2:1)<br>Bayesean Adaptive Design; 400 – 600 subjects total; ~50 sites<br>2 randomized stages: Stage 1 ≤ 175 subjects; interim safety and performance analysis of first 100 |
| Investigational Tx | LARIAT LAA ligation followed by PVI catheter ablation (4 weeks) |
| Control Tx | PVI catheter ablation without LAA ligation |

# amaze Primary Endpoints

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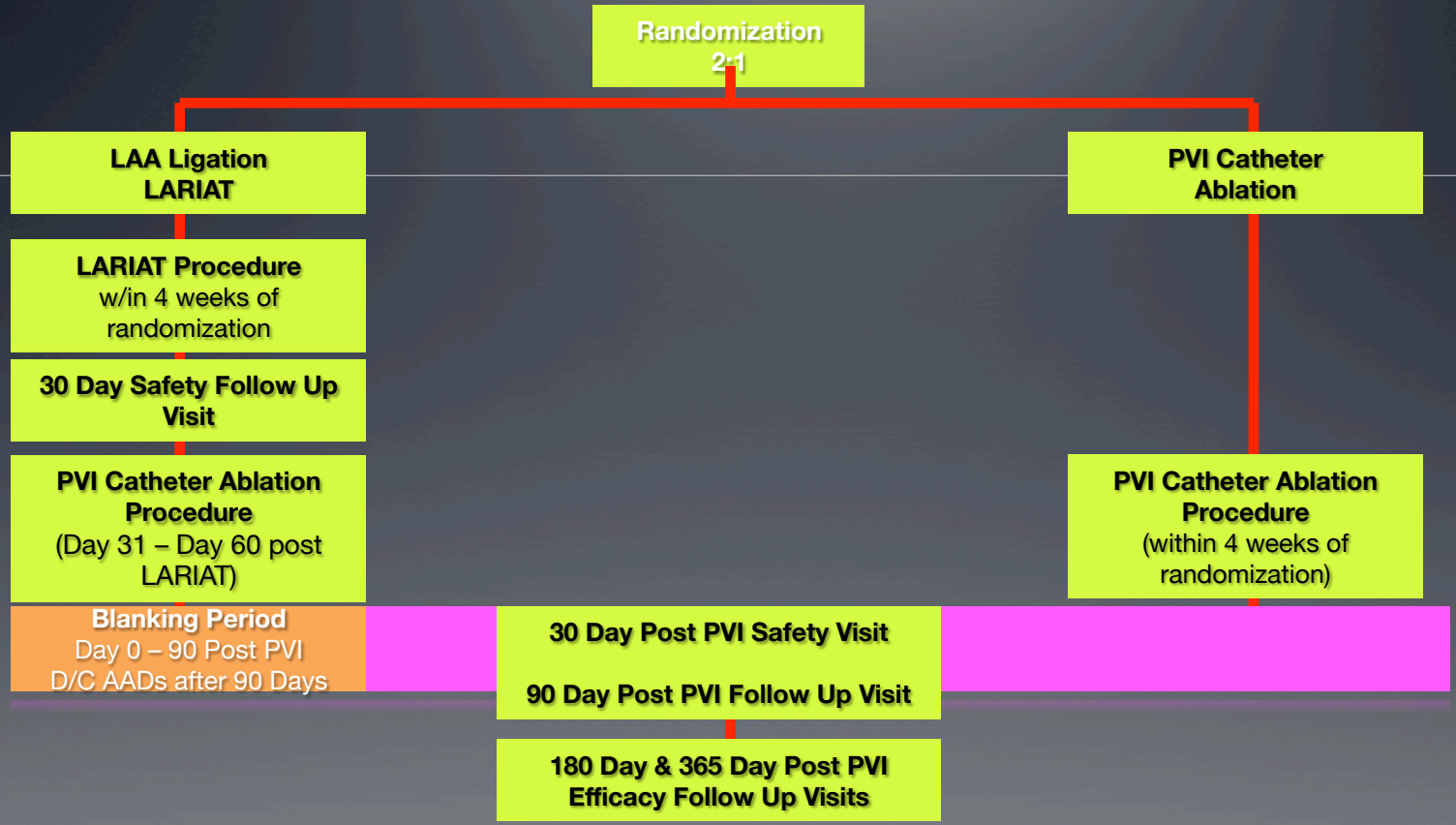
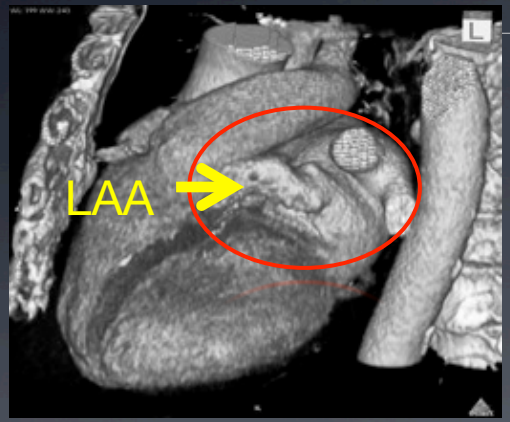
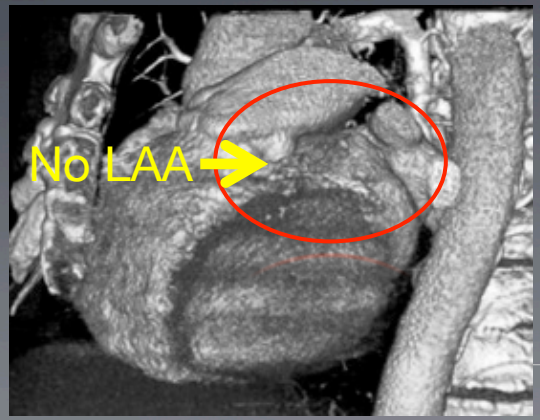
|---|---|
| Primary Effectiveness Endpoint | Freedom from episodes of AF > 30 seconds and no requirement for new Class I or III AAD therapy at 12 months post PVI, measured by 24-hr holter or symptomatic event monitoring. |
| Primary Safety Endpoint | The incidence of significant LARIAT device or procedure-related SAEs occurring within 30 days after the LAA ligation procedure (Performance Goal). |

# Treatment Scheme & Patient Flow



# amaze Summary




Clinically relevant solution to adjunctive treatment of persistent and longstanding persistent AF.

Multiple studies demonstrate the clinical benefits of mechanical & electrical isolation of the LAA with LARIAT in over 4,000 procedures.

Opportunity to improve poor outcomes of existing standard of care (ablation only)

# Thank You