Safety and Efficacy of Uninterrupted Anticoagulation with Dabigatran Etexilate versus Warfarin in Patients Undergoing Catheter Ablation of Atrial Fibrillation:

The RE-CIRCUIT™ Study

Frederick A Masoudi, MD, MSPH, FACC

Professor of Medicine, University of Colorado

Chief Science Officer, ACC NCDR

ACC Latin America Conference

June 23 2017

Disclosures

No commercial relationships

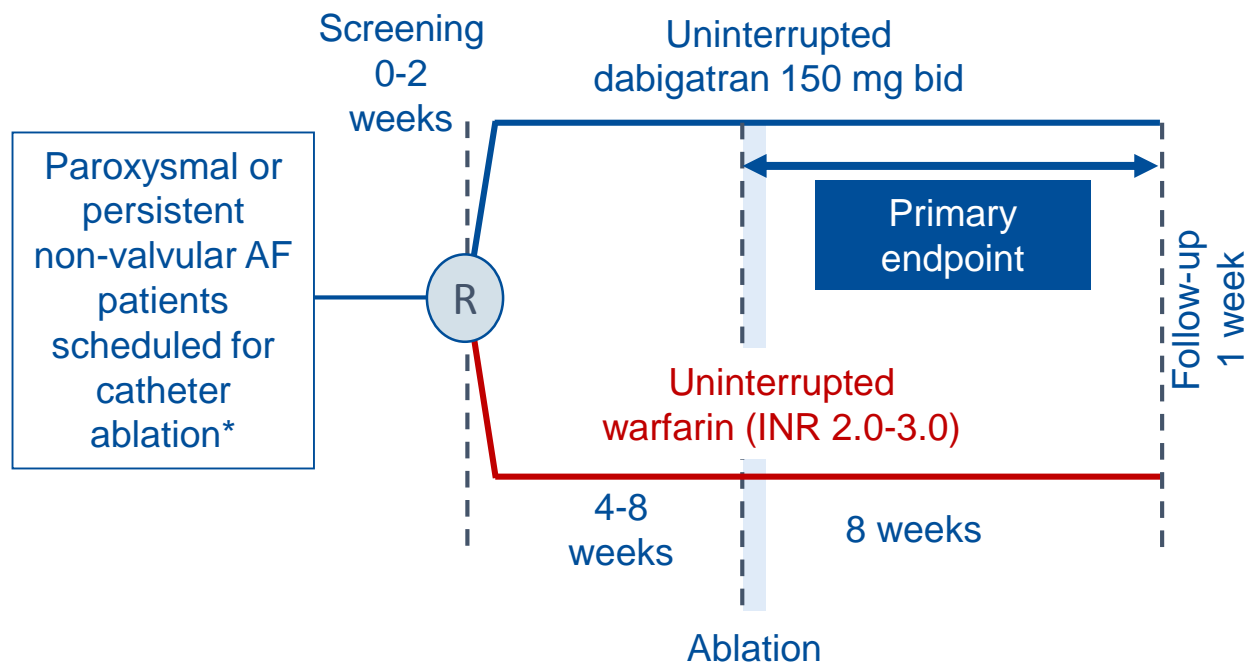**Slides thanks to Hugh Calkins, MD (RE-CIRCUIT PI)**

Background

- Thromboembolic and bleeding events, including cardiac tamponade, are some of the most feared complications of AF ablation

- Uninterrupted anticoagulation with a vitamin K antagonist (VKA) helps to minimize the risk of these complications, and is now a well established strategy

- This approach is cumbersome as many AF patients are anticoagulated with a non-VKA oral anticoagulant (NOAC) prior to AF ablation. Therefore the VKA strategy requires transition to VKA prior to ablation

- Dabigatran etexilate has established efficacy and safety for stroke prevention in AF

- Data on the outcomes of AF ablation on uninterrupted NOAC therapy are limited

OBJECTIVE & DESIGN

- To investigate the safety and efficacy of uninterrupted dabigatran vs.warfarin for peri-procedural anticoagulation in patients undergoing catheter ablation of AF

- Prospective randomized open-label multicenter clinical trial of 704 patients in104 sites in 11 countries between April 2015 and July 2016

Screening
0-2
weeks

Uninterrupted
dabigatran 150 mg bid

Paroxysmal or persistent non-valvular AF patients scheduled for catheter ablation*

R

Primary endpoint

Follow-up
1 week

Uninterrupted
warfarin (INR 2.0-3.0)

4-8
weeks

8 weeks

Ablation

- **Primary endpoint:** adjudicated major bleeding events from venous access up to 8 weeks post-ablation[†]

- **Secondary endpoints** adjudicated thromboembolic events from venous access to 8 weeks post-ablation[†]

*And eligible for dabigatran 150 mg bid according to local prescribing information.

[†]Primary end point assessed from the start of the ablation procedure and up to 8 weeks post-ablation.
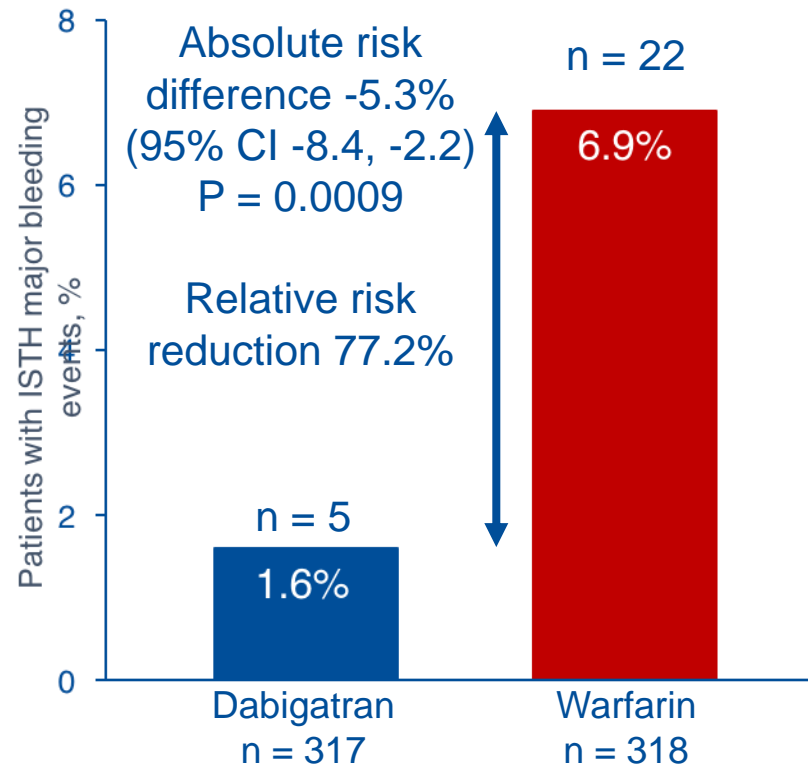
BASELINE CHARACTERISTICS

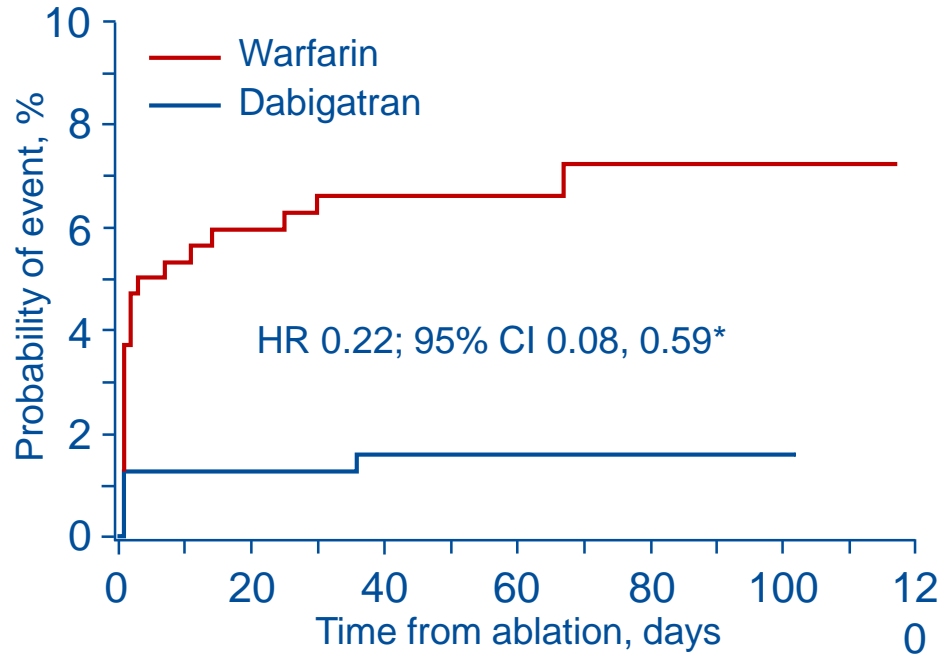| Characteristics	Dabigatran 150 mg bid (n = 317)	Warfarin (n = 318)
Mean age (standard deviation), years	59.1 (10.4)	59.3 (10.3)
Atrial fibrillation, n (%)		
Paroxysmal	213 (67.2)	219 (68.9)
Persistent	86 (27.1)	81 (25.5)
Longstanding persistent	18 (5.7)	18 (5.7)
CHA_2DS_2-VASc score, mean	2.0	2.2
Medical history, n (%)		
Congestive heart failure	31 (9.8)	34 (10.7)
Hypertension	166 (52.4)	177 (55.7)
Diabetes mellitus	30 (9.5)	34 (10.7)
Previous stroke	10 (3.2)	9 (2.8)
Coronary artery disease	32 (10.1)	48 (15.1)
Previous myocardial infarction	10 (3.2)	15 (4.7)
Prior major bleeding or predisposition	3 (0.9)	4 (1.3)
TTR during study, mean %*	–	66.4

TTR, time in therapeutic range of INR 2.0-3.0. *Based on treated set, n = 330.

RESULTS

- Significantly fewer major bleeding events with uninterrupted dabigatran compared with warfarin

Bar chart titled "Patients with ISTH major bleeding events, %" (y-axis 0 to 8).

- Dabigatran (n = 317): 1.6%, n = 5
- Warfarin (n = 318): 6.9%, n = 22

Absolute risk difference -5.3% (95% CI -8.4, -2.2) P = 0.0009

Relative risk reduction 77.2%

TIMING OF BLEEDING EVENTS

*Cox proportional hazard model and Wald confidence limits.

SECONDARY ENDPOINTS

Low Rate of Thromboembolic Events

- Stroke: no events

- Systemic embolism: no events

- Transient ischemic attack: dabigatran 0 vs warfarin 1

Minor Bleeding Events Similar

- Dabigatran 59 (18.6%) vs warfarin 54 (17.0%)

Summary

- AF ablation on uninterrupted dabigatran results in lower rate of major bleeding compared with uninterrupted warfarin

- Absolute bleeding risk reduction with dabigatran was 5.3% (RR=77% lower)

- No thromboembolic events in either group and one TIA in a patient on warfarin

- Minor bleeding events similar

- No deaths

Conclusion

- AF ablation on uninterrupted dabigatran is a better anticoagulation strategy compared with uninterrupted warfarin

- The reversal agent idarucizumab, while not needed in this trial, also a consideration in adopting uninterrupted dabigatran as the preferred anticoagulation strategy around AF ablation

Uninterrupted Dabigatran versus Warfarin for Ablation in Atrial Fibrillation

Hugh Calkins, M.D., Stephan Willems, M.D., Edward P. Gerstenfeld, M.D.,
Atul Verma, M.D., Richard Schilling, M.D., Stefan H. Hohnloser, M.D.,
Ken Okumura, M.D., Ph.D., Harvey Serota, M.D., Matias Nordaby, M.D.,
Kelly Guiver, M.Sc., Branislav Biss, M.D., Marc A. Brouwer, M.D., Ph.D.,
and Massimo Grimaldi, M.D., Ph.D., for the RE-CIRCUIT Investigators*