Supplementary Online Content

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This supplementary material has been provided by the authors to give readers additional information about their work.

eAppendix. Acknowledgments

Site Principal Investigators: E. Hummers, F. Merali, S. Henein, C. Nichol, W. Domanko, P. Frydrych, R. Blachowitz, D. Zizzo, A. Kushner, M. Kopp, A. Bell, R. Ward, R. Allison, D. Mutasingwa, M. Scherer, B. Kerley, P. Smith, J. Charles, K. Deichert, K. Ng, N. Ivers, H. Vlaar, R. Birtwhistle, M. Robertson, D. Moores, S. Fikry, M. Wong, S. Aggarwal, T. Remillard, W. Keske, M.A. Lang, T. Koch, H-D Reimann, M. Luckerath, C Schneider, D. Jacob, M. Eckert, A. Boettiger, K. Meier-Ahrens, M. Bahr, H. Windmann, A. Hafer, K. Michels, H.M. Beulshausen, J-H Wernicke, R. Beverungen, G. Hartleb, M. Harder

Statistical Assistance: P. Rao-Melacini

Study Coordination (PHRI, Canada): H. Beresh, A. Thornton, A. Djuric, A. Grinvalds, R. Napoleoni, M. Bishop

Study Coordination (Germany): K. Schmalstieg-Bahr, D. von Grünhagen, J. Suerbaum, S. Werhahn, B. Linn, H. Mahler, D. Lühmann, A. Rakebrandt

eMethods. Methods – Additional Details

Sample Size Calculation

Our sample size was based on estimated rates of AF detection from previous studies and an assumption that detection of a 4% absolute difference between groups in the primary outcome would be clinically meaningful. Given the efficacy of anticoagulation, even small increases in AF detection and anticoagulant treatment rates are considered important given the potential implications for stroke prevention at a population level.

Calculations were done in nQuery Advisor, using the Fisher's exact test of equal proportions. We had hypothesized that the 6-month rate of AF detection would be 5% (screening group) vs. 1% (control group). To detect this difference with 90% statistical power at a two-sided alpha of 5% required 390 per group. This sample size would be able to detect at least a 3.5% between-group difference in the secondary outcome of anticoagulant treatment at 6 months (4.5% vs. 1%) with 83% power. To compensate for attrition, we increased the total sample size by 5%, yielding 822 participants.

Home BP Monitor

The WatchBP device was programmed in the device's 'Usual Mode' setting, in which AF is indicated if ≥2 of 3 consecutive measurements are positive for AF. For the analysis, we separately considered 2 different definitions of a positive screen for AF: (1) if the BP monitor detected AF (≥2 of 3 consecutive measurements) at least once in any given day, and (2) if the device detected AF (≥2 of 3 consecutive measurements) on both the morning and evening screens in any given day. These definitions approximate what was specified in the study protocol. We were unable to determine how many patients had 3 out of 3 consecutive positive screens, as originally intended, because of how the BP monitors were programmed for the trial, and we do

not have data on any additional measurements that patients may have recorded beyond a morning and evening screen.

The sensitivity of the BP monitor for AF detection in our cohort overall was 35.0% (95% CI, 15.4%-59.2%). Sensitivity was influenced by the AF duration: sensitivity was 26.7% (95% CI, 7.8-55.1) for detection of AF episodes ≤12 hours, and sensitivity increased to 60.0% (95% CI, 14.7-94.7) for detection of AF episodes >12 hours and to 66.7% (9.4-99.2) for detection of AF >24 hours.

The specificity of the BP monitor was 81.0% (95% CI, 76.7%-84.8%). The specificity increased to 93.4% (95% CI, 90.4-95.7%) if a patient's morning and evening screens were both positive for AF in a given day.

The BP monitor had a positive predictive value of 2.7%-7.4% and negative predictive value of 99.2%-99.7% for detecting AF >12 hours or >24 hours, based on a single positive screen or 2 positive screens (morning and evening) in a given day.

The BP monitor missed AF in 1 of the 3 patients who had AF >24 hours, 2 of 5 patients who had an AF episode duration of >12 hours, 11 of 15 patients who had AF ≤12 hours, and 15 of 17 patients who had AF ≤24 hours.

eResults. Results – Additional Details

Sensitivity Analysis for the Primary Outcome

In a sensitivity analysis, we analyzed the primary outcome using a slightly modified definition of AF: detection new AF (atrial fibrillation or atrial flutter) within 6 months post-randomization, with AF defined as at least one episode of continuous AF lasting >5 minutes (or AF documented on two separate12-lead ECGs performed >5 minutes apart). Using this definition, AF was detected in 20/434 (4.6%) in the screening group vs. 0 in in the control group (absolute difference, 4.6%; 95% CI, 2.6% to 6.6%; $p<0.001$).

Details of Stroke Outcome Events

Patient 1. This patient was hospitalized for an acute embolic anterior cerebral artery branch occlusion 74 days after randomization, which was adjudicated as an embolic stroke of undetermined source. A post-stroke Holter monitor was negative for AF. Echocardiography revealed severe left atrial enlargement and mild left ventricular wall motion abnormalities. Vascular imaging showed no extracranial or intracranial artery stenosis. The study ECG monitor (before the stroke event) was negative for AF and showed rare supraventricular ectopy (<1%).

Patient 2. This patient was hospitalized with an acute subcortical infarct 64 days after randomization compatible with a small-vessel disease etiology. Vascular imaging showed no intracranial or extracranial artery stenosis. Echocardiography was significant for a bioprosthetic aortic valve and severe left atrial enlargement. No AF was diagnosed in hospital. Both study ECG monitors (one before the stroke event, one afterwards) were negative for AF and showed rare supraventricular ectopy (<1%).

Patient 3. This patient was hospitalized with a clinical diagnosis of a probable TIA 30 days post-randomization and had ECG-documented rapid AF during that hospitalization requiring treatment. Anticoagulant therapy was initiated. Echocardiography showed moderate to severe mitral regurgitation. This patient's study ECG monitor (before the TIA event) was negative for AF and showed rare supraventricular ectopy (<1%).

eTable 1. Eligibility Criteria

Inclusion Criteria

1. Age ≥75 years without known atrial fibrillation or atrial flutter.
2. The participant is clinically in sinus rhythm (both heart auscultation and 30-second pulse palpation have been performed by the enrolling physician and neither detects an irregular rhythm suggestive of atrial fibrillation).
3. History of hypertension requiring antihypertensive medication.
4. Written informed consent.

Exclusion Criteria

1. Any previously documented atrial fibrillation or atrial flutter ≥30 seconds.
2. Implanted pacemaker, cardiac defibrillator, cardiac loop recorder, or deep brain stimulator.
3. Likely to be poorly compliant or unreliable using home screening devices or with study follow-up requirements because of cognitive or other issues, or life expectancy <6 months due to concomitant disease.
4. Has a condition which in the opinion of the enrolling physician would not permit chronic treatment with oral anticoagulant therapy.
5. Patient already taking long-term oral anticoagulant therapy.
6. Known allergic reaction/intolerance to skin adhesives.

eTable 2. Incidence of Other Prespecified Device-Detected Arrhythmias in the Screening Group (n=434)

Non-AF Arrhythmias Detected by Zio Patch	n (%)
3rd degree AV block or Mobitz type 2 second degree AV block	13 (3.0%)
Pauses ≥5 seconds	4 (0.9%)
Heart rate <40 beats/minute for ≥30 seconds	17 (3.9%)
Heart rate >160 beats/minute for ≥30 seconds	3 (0.7%).
Ventricular tachycardia >100 beats/minute for ≥30 seconds, or polymorphic ventricular tachycardia or ventricular fibrillation of any duration	none

eTable 3. Performance of Home BP Monitor for AF Detection

		Documentation of AF by cECG (Zio XT Patch)	
AF Screening Results by Home BP Monitor		AF Present	AF Absent
	Screen Positive	7	72
	Screen Negative	13	307
	Total	20	379

	Value	**95% CI**
Sensitivity	35.0%	15.4% - 59.2%
Specificity	81.0%	76.7% - 84.8%
Positive predictive value	8.9%	4.9% - 15.5%
Negative predictive value	95.9%	94.5% - 97.0%

