Rivaroxaban Monotherapy versus Combination Therapy in Patients with Atrial Fibrillation and Stable Coronary Artery Disease

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Declaration of interest

- Research contracts (Takeda)
- Others (Daiichi-Sankyo, Bristol-Meyers, Abbott)
Conflict of Interest Statement

Dr. Yasuda  receiving grant support from Takeda and Abbott, and lecture fees from Daiichi Sankyo and Bristol-Myers Squibb

Dr. Kaikita  receiving grant support from Bayer Yakuhin, Daiichi Sankyo, Novartis Pharma, SBI Pharma, and the Ministry of Education, Culture, Sports, Science and Technology of Japan

Dr. Akao  receiving lecture fees from Bristol-Myers Squibb and Nippon Boehringer Ingelheim, grant support and lecture fees from Bayer Yakuhin and Daiichi Sankyo, and grants from Japan Agency for Medical Research and Development, AMED

Dr. Ako  receiving lecture fees from Bayer Yakuhin and Sanofi, and grant support and lecture fees from Daiichi Sankyo;

Dr. Matoba  receiving fees for serving on a speakers bureau from Nippon Boehringer Ingelheim, Daiichi Sankyo, AstraZeneca, and Bayer Yakuhin, and grant support from Japan Cardiovascular Research Foundation;

Dr. Nakamura  receiving grant support and honoraria from Bayer Yakuhin, Daiichi Sankyo, Sanofi, and Nippon Boehringer Ingelheim, and honoraria from Bristol-Myers Squibb;

Dr. Miyauchi  receiving lecture fees from Amgen Astellas BioPharma, Astellas Pharma, MSD, Bayer Yakuhin, Sanofi, Takeda, Daiichi Sankyo, Nippon Boehringer Ingelheim, and Bristol-Myers Squibb;

Dr. Hagiwara  receiving grant support and lecture fees from Bayer Yakuhin and Nippon Boehringer Ingelheim, lecture fees from Bristol-Myers Squibb, and grant support from Daiichi Sankyo and Pfizer Japan;

Dr. Kimura  receiving lecture fees from Bristol-Myers Squibb and Nippon Boehringer Ingelheim, grant support, lecture fees, and advisory fees from Bayer Yakuhin, and grant support and lecture fees from Daiichi Sankyo and Sanofi, and grant support from Japan Cardiovascular Research Foundation;

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Dr. Ogawa  receiving fees for serving on a speakers bureau from TOWA Pharmaceutical and honoraria from Novartis Pharma.

No other potential conflict of interest relevant to this article was reported.
A Reduced Antithrombotic Regimen Recommended by Current Guidelines

The selection of the most effective antithrombotic treatment for patients with atrial fibrillation (AF) and coronary artery disease (CAD) is a clinical challenge.

A reduced antithrombotic regimen of patients with AF within the first 12 months after PCI was studied in PIONEER AF-PCI\(^2\), RE-DUAL PCI\(^3\), and AUGUSTUS\(^4\).

- Triple therapy (an oral anticoagulant plus aspirin and a P2Y\(_{12}\) inhibitor): for as short a duration as possible
- Combination therapy (an anticoagulant plus a P2Y\(_{12}\) inhibitor.): up to 12 mo. in selected patients

1) Valgimigli M, et al., Eur Heart J, 2018
After 1 year following PCI, Current Guidelines Recommend Oral Anticoagulant Monotherapy

- After 12 months of combination therapy, or in patients with AF and stable CAD not requiring intervention, current guidelines recommend monotherapy with an oral anticoagulant.

- However, this approach has yet to be supported by evidence from randomized, controlled trials.

- Furthermore, substantial numbers of patients in this situation continue to be treated with combination therapy, which indicates a gap between guidelines and clinical practice.  

1) Valgimigli M, et al., *Eur Heart J*, 2018  
In the AFIRE study, we aimed to investigate whether rivaroxaban monotherapy is noninferior to combination therapy (rivaroxaban plus an antiplatelet agent) in patients with AF and stable CAD more than 1 year after revascularization or in those with angiographically confirmed CAD not requiring revascularization.
Trial Organization

**Principal Investigator**  Satoshi Yasuda

**Steering Committee**  Hisao Ogawa (Deputy Principal Investigator), Kazuo Kimura, Nobuhisa Hagiwara, Atsushi Hirayama, Masato Nakamura, Katsumi Miyauchi

**Protocol Committee**  Junya Ako (Chair), Masaharu Akao, Koichi Kaikita, Tetsuya Matoba

**Clinical Events Committee**  Tetsuya Sumiyoshi, Yukihiro Koretsune, Takafumi Hiro, Yoichiro Hashimoto, Kazumi Kimura, Teruyuki Hirano

**Data Safety and Monitoring Committee**  Hiroyuki Daida (Chair), Yasushi Okada, Tsutomu Yamazaki

**Principal Statistician**  Kunihiko Matsui

**Funding**  Japan Cardiovascular Research Foundation
Atrial Fibrillation and Ischemic events with Rivaroxaban AFIRE in patients with stable coronary artery disease: AFIRE Study

A multicenter, prospective, randomized, open-label, parallel-group trial

2200 patients with AF (CHADS\textsubscript{2} $\geq$ 1) and stable CAD

**Key inclusion criteria**
- Underwent PCI or CABG more than 1 year earlier
- Angiographically confirmed CAD (with stenosis of ≥50%) not requiring revascularization

**Key exclusion criteria**
- A history of stent thrombosis
- Coexisting active tumor
- Poorly controlled hypertension

**Rivaroxaban Monotherapy**
- **Rivaroxaban** 10 or 15 mg/day
  *The level of rivaroxaban in blood samples obtained from Japanese patients who were taking rivaroxaban at the 15-mg dose was similar to the level in white patients who were taking the 20-mg dose.*

**Combination Therapy**
- **Rivaroxaban** 10 or 15 mg/day
- **Single antiplatelet**
  Aspirin 81 or 100 mg/day, Clopidogrel 50 or 75 mg/day, Prasugrel 2.5 or 3.75 mg/day

UMIN Clinical Trials Registry number, UMIN000016612.
ClinicalTrials.gov number, NCT02642419.

Primary End Points

Primary efficacy end point \(^1\):

- The composite of stroke, systemic embolism, myocardial infarction, unstable angina requiring revascularization, or death from any cause
- Assessed noninferiority of rivaroxaban monotherapy, as compared with combination therapy (noninferiority margin: 1.46 for the 95% CI, with a power of 80%)
- Performed in the modified ITT population

Primary safety end point \(^1\):

- A closed testing procedure was conducted after assessment of primary efficacy endpoint
- To determine superiority of rivaroxaban monotherapy, as compared with combination therapy
- Major bleeding, as defined according to the criteria of the ISTH* 
- Performed in the safety population

Sample size: Estimated that the enrollment of 2200 patients and the occurrence of at least 219 primary efficacy end points were required. \(^1\)

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Enrollment Period: From February 23, 2015 to September 30, 2017

Study Flow: Randomization and Follow-up

2236 underwent randomization

Monotherapy Group

1118 were assigned
1107 were included
1099 were included
1084 were included
1005 completed

Combination-therapy Group

1118 were assigned
1108 were included
1099 were included
1075 were included
968 completed

modified ITT population N=2215
Safety population n=2198
Per protocol population n=2159
Completed follow-up n=1973
### Characteristics of Patients at Baseline

#### Modified ITT Population

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Rivaroxaban Monotherapy (N=1107)</th>
<th>Combination Therapy (N=1108)</th>
<th>Rivaroxaban Monotherapy (N=1107)</th>
<th>Combination Therapy (N=1108)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age – (yr) mean ± SD</td>
<td>74.3±8.3</td>
<td>74.4±8.2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male sex – no. (%)</td>
<td>875 (79.0)</td>
<td>876 (79.1)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>BMI – (kg/m²) mean ± SD</td>
<td>24.5±3.7</td>
<td>24.5±3.7</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CrCl – (ml/min) mean ± SD</td>
<td>62.8±25.7</td>
<td>61.7±24.0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Current smoker – no. (%)</td>
<td>146 (13.2)</td>
<td>146 (13.2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes – no. (%)</td>
<td>461 (41.6)</td>
<td>466 (42.1)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Previous stroke – no. (%)</td>
<td>148 (13.4)</td>
<td>175 (15.8)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Previous MI – no. (%)</td>
<td>384 (34.7)</td>
<td>393 (35.5)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Previous PCI – no. (%)</td>
<td>781 (70.6)</td>
<td>783 (70.7)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Previous CABG – no. (%)</td>
<td>125 (11.3)</td>
<td>127 (11.5)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Type of stent – no. /total no. (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DES</td>
<td>500/723 (69.2)</td>
<td>477/721 (66.2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>BMS</td>
<td>171/723 (23.7)</td>
<td>171/721 (23.7)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>DES and BMS</td>
<td>19/723 (2.6)</td>
<td>36/721 (5.0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unknown</td>
<td>33/723 (4.6)</td>
<td>37/721 (5.1)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Type of AF – no. (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Paroxysmal</td>
<td>596 (53.8)</td>
<td>580 (52.3)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Persistent</td>
<td>164 (14.8)</td>
<td>175 (15.8)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Permanent</td>
<td>347 (31.3)</td>
<td>353 (31.9)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CHADS&lt;sub&gt;2&lt;/sub&gt; score - median</td>
<td>2</td>
<td>2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CHA&lt;sub&gt;2&lt;/sub&gt;DS&lt;sub&gt;2&lt;/sub&gt; -VASc score - median</td>
<td>4</td>
<td>4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HAS-BLED score - median</td>
<td>2</td>
<td>2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Received Aspirin - no. (%)</td>
<td>8 (0.7)</td>
<td>778 (70.2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Received P2Y&lt;sub&gt;12&lt;/sub&gt; inhibitor- no. (%)</td>
<td>4 (0.4)</td>
<td>297 (26.8)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Early Termination of the Trial

- The evaluation of the patients was planned to continue until September 2018.
- Because of a higher risk of death from any cause in the combination-therapy group, the independent data and safety monitoring committee recommended early termination of the trial in July 2018.
- The median treatment duration was 23.0 months (interquartile range, 15.8 to 31.0)
- The median follow-up period was 24.1 months (interquartile range, 17.3 to 31.5).
Primary Efficacy End Point
The composite of stroke, systemic embolism, myocardial infarction, unstable angina requiring revascularization, or death from any cause
Kaplan-Meier Estimates of First Occurrence of Primary Efficacy Events

Combination therapy
5.75% per patient-year

Monotherapy
4.14% per patient-year

HR, 0.72 (0.55 to 0.95)
P<0.001 (noninf.)

*In the assessment for superiority for the primary efficacy endpoint (that was not prespecified), the P value was 0.02.
Primary Safety End Point

Major bleeding, as defined according to the criteria of the ISTH
Kaplan-Meier Estimates of First Occurrence of Primary Safety Events

Combination therapy: 2.76% per patient-year

Monotherapy: 1.62% per patient-year

HR, 0.59 (0.39 to 0.89)

P=0.01 (sup.)
Secondary End Points

- The individual components of the primary efficacy end point
- All-cause mortality
- Net adverse clinical events
  (death from any cause, myocardial infarction, stroke, and major bleeding)
- Any bleeding events
- Selected subgroup analysis for efficacy and safety
# The Respective Incidence Rates of Secondary End Points

<table>
<thead>
<tr>
<th>End Point – no. (% per patient-year)</th>
<th>Rivaroxaban Monotherapy</th>
<th>Combination Therapy</th>
<th>HR (95% CI)*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>All-cause death #</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>26 ( 1.17)</td>
<td>43 ( 1.99)</td>
<td>0.59 (0.36 to 0.96)</td>
</tr>
<tr>
<td>Noncardiovascular</td>
<td>15 ( 0.68)</td>
<td>30 ( 1.39)</td>
<td>0.49 (0.27 to 0.92)</td>
</tr>
<tr>
<td><strong>CV events</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ischemic stroke #</td>
<td>21 ( 0.96)</td>
<td>28 ( 1.31)</td>
<td>0.73 (0.42 to 1.29)</td>
</tr>
<tr>
<td>Hemorrhagic stroke #</td>
<td>4 ( 0.18)</td>
<td>13 ( 0.60)</td>
<td>0.30 (0.10 to 0.92)</td>
</tr>
<tr>
<td>Myocardial infarction #</td>
<td>13 ( 0.59)</td>
<td>8 ( 0.37)</td>
<td>1.60 (0.67 to 3.87)</td>
</tr>
<tr>
<td>Unstable angina requiring revascularization</td>
<td>13 ( 0.59)</td>
<td>18 ( 0.84)</td>
<td>0.71 (0.35 to 1.44)</td>
</tr>
<tr>
<td>Systemic embolism</td>
<td>2 ( 0.09)</td>
<td>1 ( 0.05)</td>
<td>1.97 (0.18 to 21.73)</td>
</tr>
<tr>
<td><strong>Bleeding events</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Major bleeding #</td>
<td>35 ( 1.62)</td>
<td>58 ( 2.76)</td>
<td>0.59 (0.39 to 0.89)</td>
</tr>
<tr>
<td>Nonmajor bleeding</td>
<td>121 (5.89)</td>
<td>198 (10.31)</td>
<td>0.58 (0.46 to 0.72)</td>
</tr>
<tr>
<td>All bleeding</td>
<td>146 ( 7.22)</td>
<td>238 (12.72)</td>
<td>0.58 (0.47 to 0.71)</td>
</tr>
<tr>
<td><strong>Net adverse clinical events</strong></td>
<td>84 ( 3.90)</td>
<td>131 ( 6.28)</td>
<td>0.62 (0.47 to 0.82)</td>
</tr>
</tbody>
</table>

* The 95% CIs presented in this table have not been adjusted for multiplicity; therefore, # Components of net adverse clinical events.
## Primary Efficacy End Point, According to Subgroup

<table>
<thead>
<tr>
<th>Type of AF</th>
<th>nox / total no. (% per patient-year)</th>
<th>Hazard Ratio(95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>66 / 875 (3.9)</td>
<td>0.68 (0.50–0.93)</td>
</tr>
<tr>
<td>Female</td>
<td>23 / 232 (5.1)</td>
<td>0.90 (0.51–1.58)</td>
</tr>
<tr>
<td>&lt;75 years</td>
<td>33 / 525 (3.2)</td>
<td>0.89 (0.56–1.42)</td>
</tr>
<tr>
<td>≥75 years</td>
<td>56 / 582 (5.0)</td>
<td>0.64 (0.46–0.91)</td>
</tr>
<tr>
<td>Paroxysmal</td>
<td>37 / 596 (4.3)</td>
<td>0.74 (0.48–1.14)</td>
</tr>
<tr>
<td>Persistent</td>
<td>13 / 164 (4.3)</td>
<td>0.51 (0.26–1.00)</td>
</tr>
<tr>
<td>Permanent</td>
<td>39 / 347 (6.9)</td>
<td>0.85 (0.55–1.30)</td>
</tr>
<tr>
<td>Yes</td>
<td>45 / 461 (5.1)</td>
<td>0.68 (0.46–0.99)</td>
</tr>
<tr>
<td>No</td>
<td>44 / 646 (3.5)</td>
<td>0.77 (0.52–1.14)</td>
</tr>
<tr>
<td>&lt;30</td>
<td>11 / 54 (11.8)</td>
<td>0.87 (0.39–1.94)</td>
</tr>
<tr>
<td>30 to 50</td>
<td>39 / 300 (6.9)</td>
<td>0.83 (0.54–1.29)</td>
</tr>
<tr>
<td>≥50</td>
<td>36 / 699 (6.6)</td>
<td>0.57 (0.38–0.87)</td>
</tr>
<tr>
<td>10 mg od</td>
<td>52 / 497 (5.5)</td>
<td>0.73 (0.51–1.05)</td>
</tr>
<tr>
<td>15 mg od</td>
<td>35 / 599 (2.9)</td>
<td>0.70 (0.45–1.08)</td>
</tr>
</tbody>
</table>

### Hazard Ratio(95% CI)

- **Favors Monotherapy**
- **Favors Combination Therapy**

### Use of PPI
- Yes: 54 / 663 (4.2) 82 / 694 (6.3)
- No: 35 / 444 (4.0) 39 / 414 (4.8)

### Previous PCI or CABG
- Yes: 63 / 847 (3.8) 100 / 850 (6.2)
- No: 26 / 260 (5.1) 21 / 258 (4.3)

### Type of Stent
- DES: 38 / 500 (3.9) 48 / 477 (5.3)
- BMS: 13 / 171 (3.8) 25 / 171 (7.4)
- DES+BMS: 5 / 19 (15.0) 6 / 36 (10.0)

### CHADS<sub>2</sub>-VASc score
- 1: 9 / 230 (2.0) 13 / 241 (2.8)
- 2 to 6: 80 / 874 (4.7) 108 / 865 (6.6)

### CHA<sub>2</sub>DS<sub>2</sub>-VASc score
- 0 to 3: 22 / 429 (2.6) 31 / 436 (3.6)
- 4: 67 / 678 (5.2) 90 / 672 (7.2)

### HAS-BLED score
- 0 or 1: 16 / 224 (3.6) 17 / 193 (4.6)
- 2: 42 / 562 (3.8) 71 / 583 (6.2)
- 3 to 5: 28 / 283 (5.2) 32 / 290 (6.1)
<table>
<thead>
<tr>
<th>Subgroup</th>
<th>Rivaroxaban Monotherapy</th>
<th>Combination Therapy</th>
<th>Hazard Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>no. / total no. (% per patient-year)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>35 / 1099 (1.6)</td>
<td>58 / 1099 (2.8)</td>
<td>0.59 (0.39–0.89)</td>
</tr>
<tr>
<td>Male</td>
<td>23 / 867 (1.3)</td>
<td>51 / 870 (3.1)</td>
<td>0.44 (0.27–0.72)</td>
</tr>
<tr>
<td>Female</td>
<td>12 / 232 (2.6)</td>
<td>7 / 229 (1.6)</td>
<td>1.66 (0.66–4.23)</td>
</tr>
<tr>
<td>&lt;75 years</td>
<td>13 / 521 (1.3)</td>
<td>24 / 523 (2.3)</td>
<td>0.54 (0.27–1.05)</td>
</tr>
<tr>
<td>≥75 years</td>
<td>22 / 578 (2.0)</td>
<td>34 / 576 (3.2)</td>
<td>0.62 (0.36–1.06)</td>
</tr>
<tr>
<td>Paroxysmal</td>
<td>18 / 590 (1.6)</td>
<td>24 / 574 (2.2)</td>
<td>0.72 (0.39–1.32)</td>
</tr>
<tr>
<td>Persistent</td>
<td>7 / 163 (2.3)</td>
<td>11 / 174 (3.4)</td>
<td>0.65 (0.25–1.68)</td>
</tr>
<tr>
<td>Permanent</td>
<td>10 / 346 (1.4)</td>
<td>23 / 351 (3.4)</td>
<td>0.42 (0.20–0.88)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>Yes</td>
<td>13 / 458 (1.4)</td>
<td>29 / 462 (3.4)</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>22 / 641 (1.8)</td>
<td>29 / 637 (2.4)</td>
</tr>
<tr>
<td>&lt;30 CrCl (ml/min)</td>
<td>Yes</td>
<td>3 / 54 (3.2)</td>
<td>4 / 58 (4.0)</td>
</tr>
<tr>
<td>30 to 50</td>
<td>Yes</td>
<td>13 / 296 (2.3)</td>
<td>17 / 291 (3.2)</td>
</tr>
<tr>
<td>≥50</td>
<td>Yes</td>
<td>18 / 695 (3.2)</td>
<td>32 / 684 (2.4)</td>
</tr>
<tr>
<td>Rivaroxaban dose</td>
<td>10 mg od</td>
<td>17 / 497 (1.8)</td>
<td>26 / 513 (2.7)</td>
</tr>
<tr>
<td></td>
<td>15 mg od</td>
<td>18 / 599 (1.5)</td>
<td>32 / 585 (2.8)</td>
</tr>
</tbody>
</table>

**Hazard Ratio (95% CI):**

- **Rivaroxaban Monotherapy**
- **Combination Therapy**
- **0.1**
- **1**
- **10**

**Favors:**
- **Monotherapy**
- **Combination Therapy**

**Type of Stent:**
- **DES**
- **BMS**
- **DES+BMS**

**Diabetes mellitus:**
- **Yes**
- **No**

**CrCl (ml/min):**
- **<30**
- **30 to 50**
- **≥50**

**HAS-BLED score:**
- **0 or 1**
- **2**
- **3 to 5**

**CHADS2 score:**
- **1**
- **2 to 6**

**CHA2DS2-VASc score:**
- **0 to 3**
- **≥4**

**Previous PCI or CABG:**
- **Yes**
- **No**

**Use of PPI:**
- **Yes**
- **No**

**Diabetes mellitus:**
- **Yes**
- **No**

**CrCl (ml/min):**
- **<30**
- **30 to 50**
- **≥50**

**HAS-BLED score:**
- **0 or 1**
- **2**
- **3 to 5**

**CHADS2 score:**
- **1**
- **2 to 6**

**CHA2DS2-VASc score:**
- **0 to 3**
- **≥4**

**Previous PCI or CABG:**
- **Yes**
- **No**

**Use of PPI:**
- **Yes**
- **No**
Limitations

- The open-label trial design had the potential to introduce bias.
- There were relatively high rates of withdrawal of consent and loss of patients to follow-up.
- The trial population received the rivaroxaban dose approved in Japan (10 mg or 15 mg once daily, according to the patient’s creatinine clearance) rather than the globally approved once-daily dose of 20 mg.
- The choice of antiplatelet regimen, either aspirin or a P2Y_{12} inhibitor, is a factor that makes it uncertain whether the benefit of rivaroxaban monotherapy applies equally to the two combination regimens.
- The early termination of the trial may overestimate the efficacy data.
- The reductions in rate of ischemic events and death from any cause with rivaroxaban monotherapy were unanticipated and are difficult to explain.
Conclusion

The AFIRE study demonstrated that **rivaroxaban monotherapy** was **noninferior** to **combination therapy** with rivaroxaban plus an antiplatelet agent with respect to **CV events and death from any cause** and **superior** with respect to **major bleeding** in patients with AF and stable CAD.
AFIRE Investigators in JAPAN, 294 centers

Acknowledgments
Antithrombotic Therapy for Atrial Fibrillation with Stable Coronary Disease

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