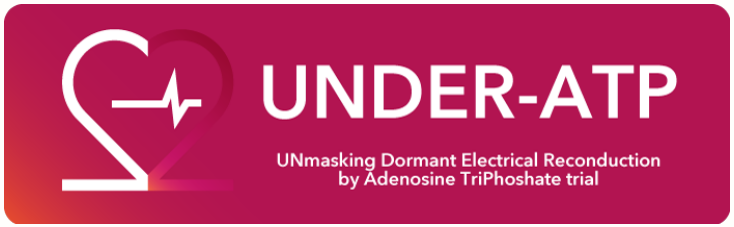
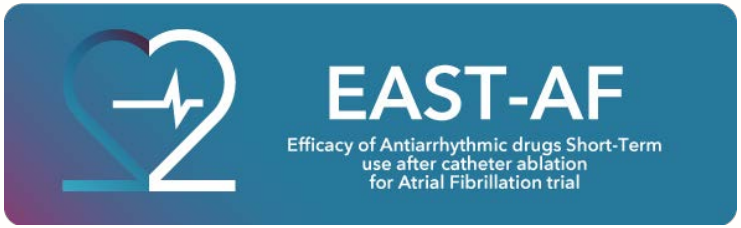
# KPAF trial

- The Kansai Plus Atrial Fibrillation (KPAF) trial is a 2x2 factorial randomized controlled trial, composed of the UNDER-ATP and EAST-AF trials.

KPAF

Kansai Plus Atrial Fibrillation



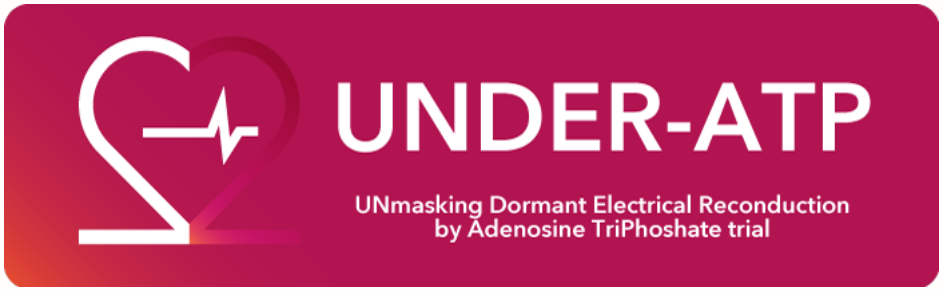



# DECLARATION OF INTEREST

- I have nothing to declare

Efficacy of adenosine triphosphate guided ablation for atrial fibrillation:

# UNmasking Dormant Electrical Reconduction by Adenosine TriPhosphate

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Kansai region, Japan.

# Background

- Adenosine (triphosphate) has been reported to provoke dormant electrical conduction between the left atrium and Pulmonary Veins (PV) after an initially successful PV isolation (PVI).

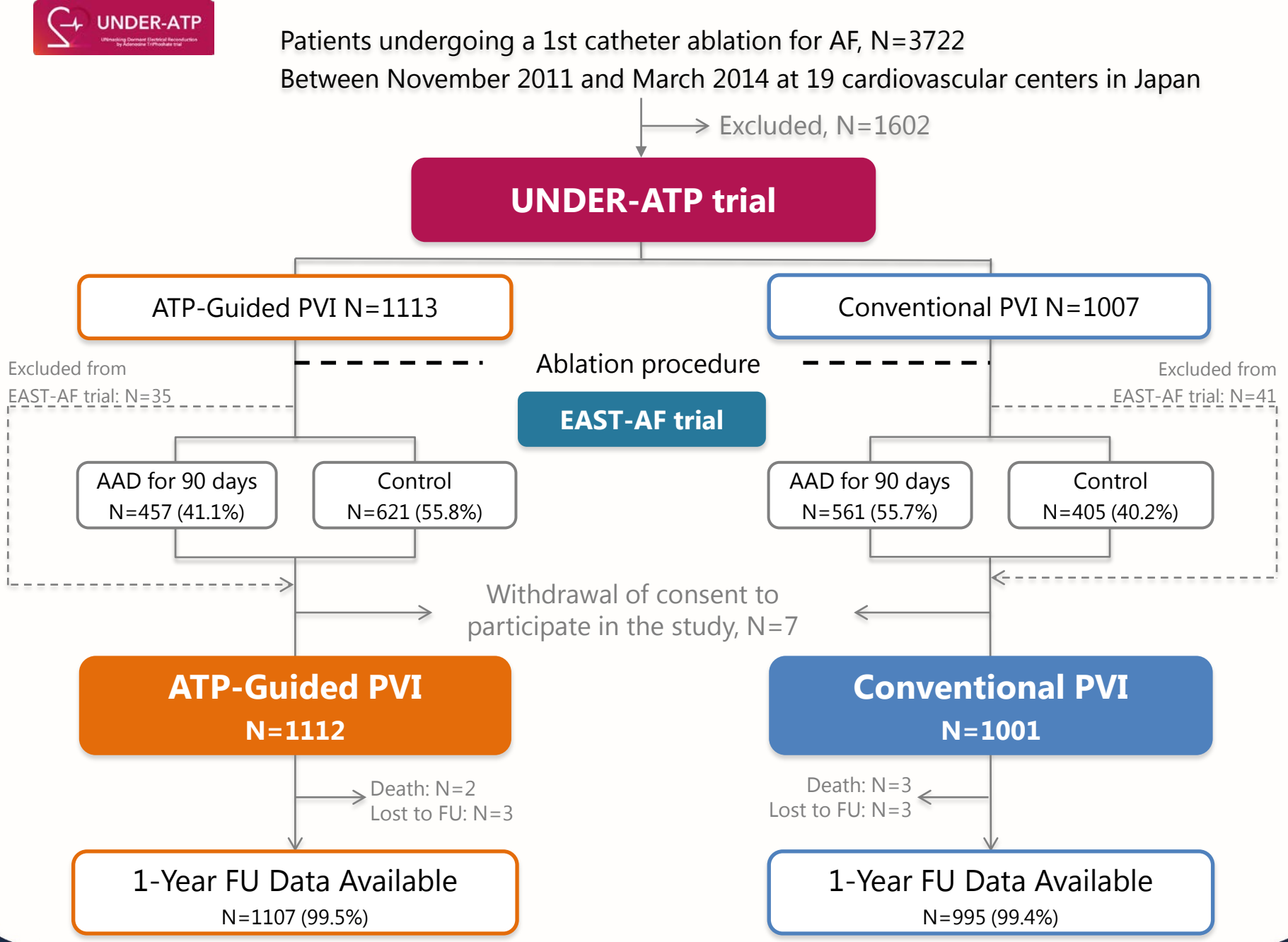
- Adenosine triphosphate (ATP) guided PVI has been shown to improve the outcomes of AF ablation.

Hachiya H, et al. J Cardiovasc Electrophysiol. 2007;18(4):392.
Matsuo S, et al. J Cardiovasc Electrophysiol. 2007;18(7):704.
Kumagai K, et al. J Cardiovasc Electrophysiol. 2010;21(5):494.
Macle L, et al. Lancet 2015;386,9994:672.

UNDER-ATP

# Aim

- The aim of this large-scale (>2,000) randomized controlled trial was to evaluate the efficacy of ATP-guided PVI as compared with conventional PVI in patients undergoing AF ablation.


UNDER-ATP
Patients undergoing a 1st catheter ablation for AF, N=3722
Between November 2011 and March 2014 at 19 cardiovascular centers in Japan
Excluded, N=1602
UNDER-ATP trial
ATP-Guided PVI N=1113
Conventional PVI N=1007
Excluded from EAST-AF trial: N=35
Ablation procedure
EAST-AF trial
Excluded from EAST-AF trial: N=41
AAD for 90 days N=457 (41.1%)
Control N=621 (55.8%)
AAD for 90 days N=561 (55.7%)
Control N=405 (40.2%)
Withdrawal of consent to participate in the study, N=7
ATP-Guided PVI N=1112
Conventional PVI N=1001
Death: N=2
Lost to FU: N=3
Death: N=3
Lost to FU: N=3
1-Year FU Data Available N=1107 (99.5%)
1-Year FU Data Available N=995 (99.4%)

UNDER-ATP

# Eligibility

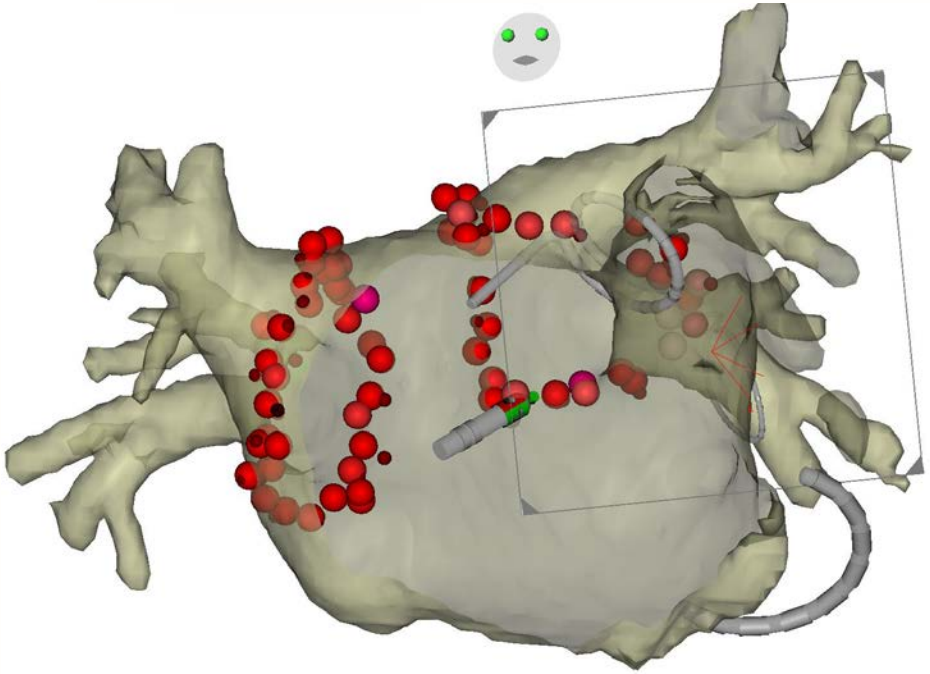
## Inclusion criteria

- Planned De Novo ablation for paroxysmal, persistent or long-lasting AF

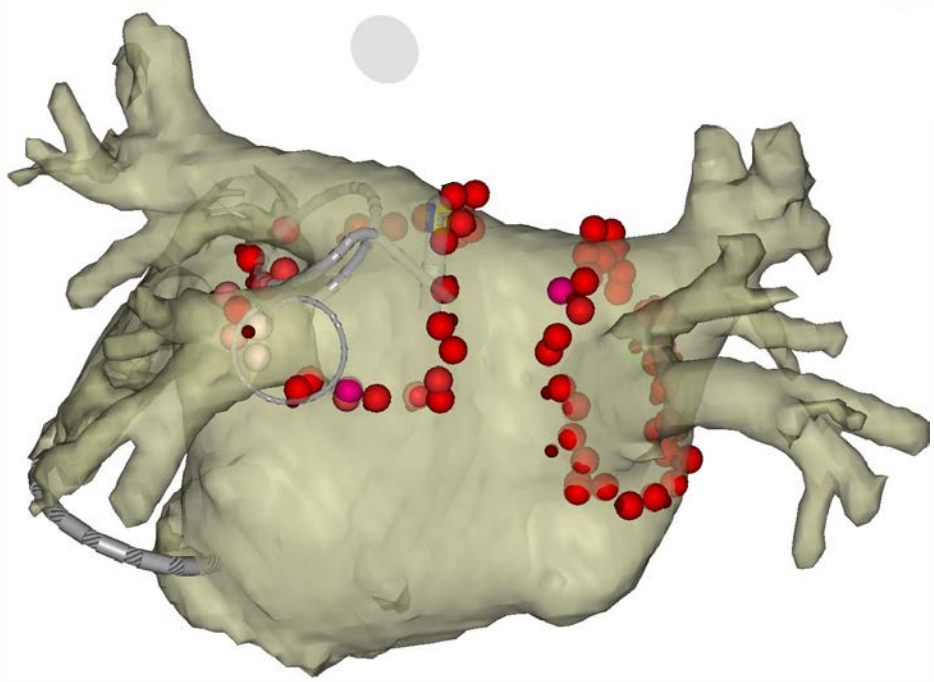
## Exclusion criteria

- Age < 20 or >80
- Contraindications to or intolerance to ATP or AADs
  - ✓ Severe bronchial asthma
  - ✓ Severe vasospastic angina
  - ✓ Substantial bradycardia
- Severe heart failure (LVEF < 40% or NYHA VI)
- Severe LA enlargement (LAD > 55mm)
- Very long-lasting AF ≥ 5 years

# Style of the PVI

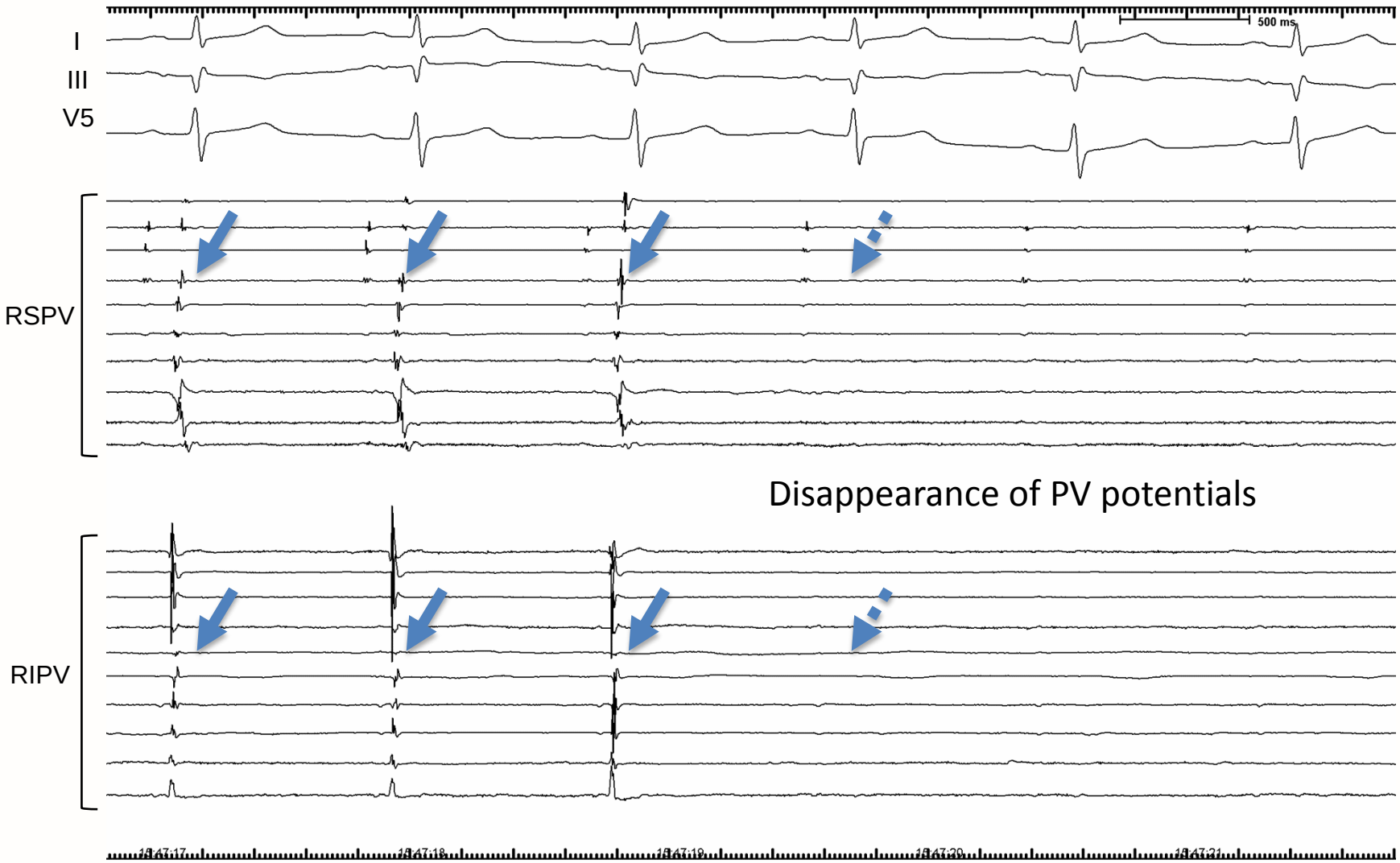


**Endoscopic AP view**
of the reconstructed LA



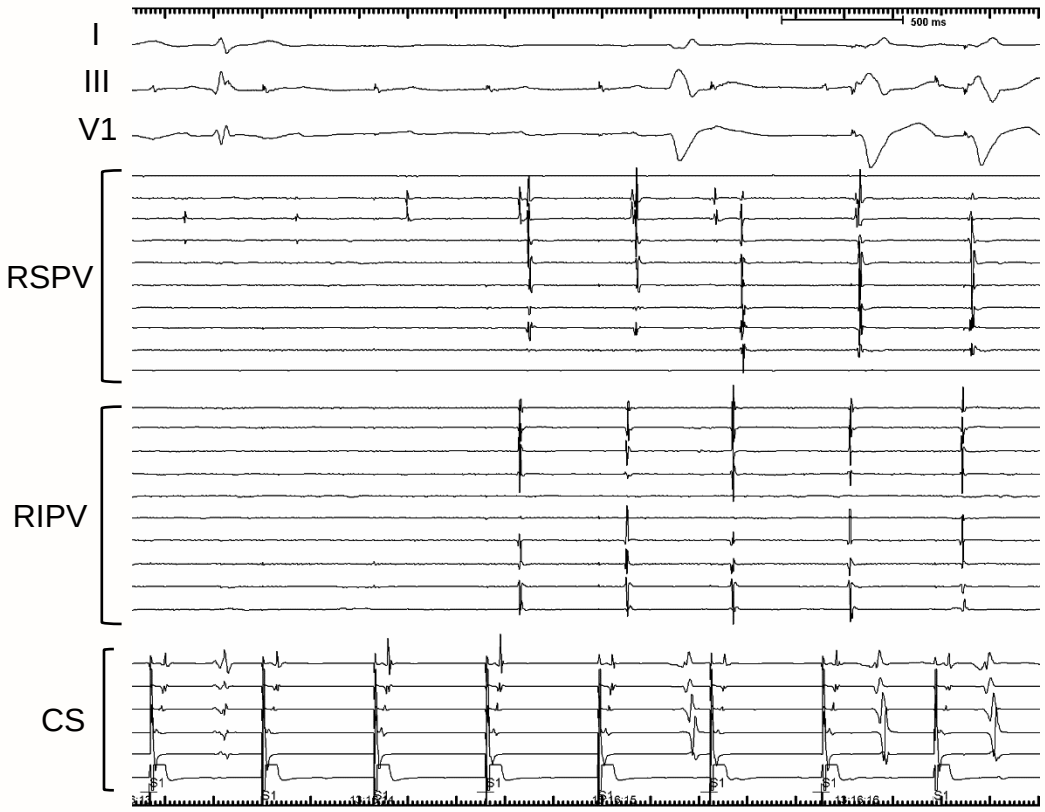
**PA view**
of the reconstructed LA

# End point of the PVI



# ATP test

Recurrence of PV conduction followed AV block by ATP infusion




- In ATP-guided PVI, 0.4 mg/kg-body-weight of ATP was rapidly administered.
- When dormant conduction was provoked, additional ablations were performed until the disappearance of any dormant conductions.

UNDER-ATP

# Endpoint

## Primary endpoint

Recurrent atrial tachyarrhythmias* at 1-year with a blanking period of 90 days post ablation.

**Recurrent atrial tachyarrhythmias was defined as documented AF/AFL/AT lasting for >30 seconds or requiring repeat ablation, hospital admission or usage of Vaughan Williams class I or III AADs.*

UNDER-ATP

# Clinical Follow-up

- Periodical visits: @ 3-, 6-, and 12-month
  (ECG, blood samples etc.)
- 2-week ambulatory electrogram recording:
  @ hospital-discharge, 6-month and 12-month
- 24-hour Holter monitoring : @ 6- and 12-month
- Additional symptom driven ECG-monitoring

# Baseline Characteristics

| | All Patients (N=2113) | ATP-guided PVI (N=1112) | Conventional PVI (N=1001) | P value |
|---|---|---|---|---|
| Age (years) | 63.3±10.0 | 58.6 ± 8.6 | 68.5 ± 8.8 | <0.001 |
| Male | 1589 (74.7) | 856 (77.0) | 723 (72.7) | 0.01 |
| History of AF (m) | 25.9 [9.0-62.9] | 23.3 [8.8-60.8] | 26.4 [9.4-67.5] | 0.37 |
| Type of AF | | | | 0.34 |
| Paroxysmal | 1420 (67.2) | 737 (66.3) | 683 (68.2) | |
| Persistent | 479 (22.7) | 245 (22.0) | 234 (23.4) | |
| Long-lasting | 214 (10.1) | 130 (11.7) | 84 (8.4) | |
| $CHADS_2$ score | | | | <0.001 |
| 0, 1 | 1557 (73.7) | 910 (81.8) | 647 (64.6) | |
| 2 | 356 (16.8) | 141 (12.7) | 215 (21.5) | |
| ≧3 | 200 (9.5) | 61 (5.5) | 139 (13.9) | |
| LVEF (%) | 64.3±7.6 | 64.2±7.9 | 64.6±7.3 | 0.22 |
| LA dimension (mm) | 39.0±6.2 | 38.9±6.3 | 39.2±6.2 | 0.26 |

UNDER-ATP

# Procedural Characteristics

| | ATP-guided PVI (N=1112) | Conventional PVI (N=1001) | P value |
|---|---|---|---|
| 3-dimensional mapping system (%) | 1112 (100) | 1000 (99.9) | 0.47 |
| Double circular catheters | 820 (73.7) | 773 (77.4) | 0.05 |
| Deflectable sheath | 606 (54.5) | 575 (57.4) | 0.17 |
| Irrigation catheter (%) | 1102 (99.1) | 984 (98.3) | 0.10 |
| Strategy | | | |
| Extensive encircling PVI (%) | 1110 (99.8) | 996 (99.5) | 0.20 |
| CFAE ablation (%) | 131 (11.8) | 107 (10.7) | 0.43 |
| Left atrial roof line (%) | 197 (17.7) | 212 (21.2) | 0.04 |
| Mitral isthmus line (%) | 74 (6.7) | 78 (7.8) | 0.31 |
| GP ablation (%) | 59 (5.3) | 59 (5.9) | 0.56 |
| Tricuspid valve isthmus ablation (%) | 803 (77.0) | 745 (74.4) | 0.25 |
| SVC isolation (%) | 155 (13.9) | 140 (14.0) | 0.98 |

UNDER-ATP

# PVI and ATP test

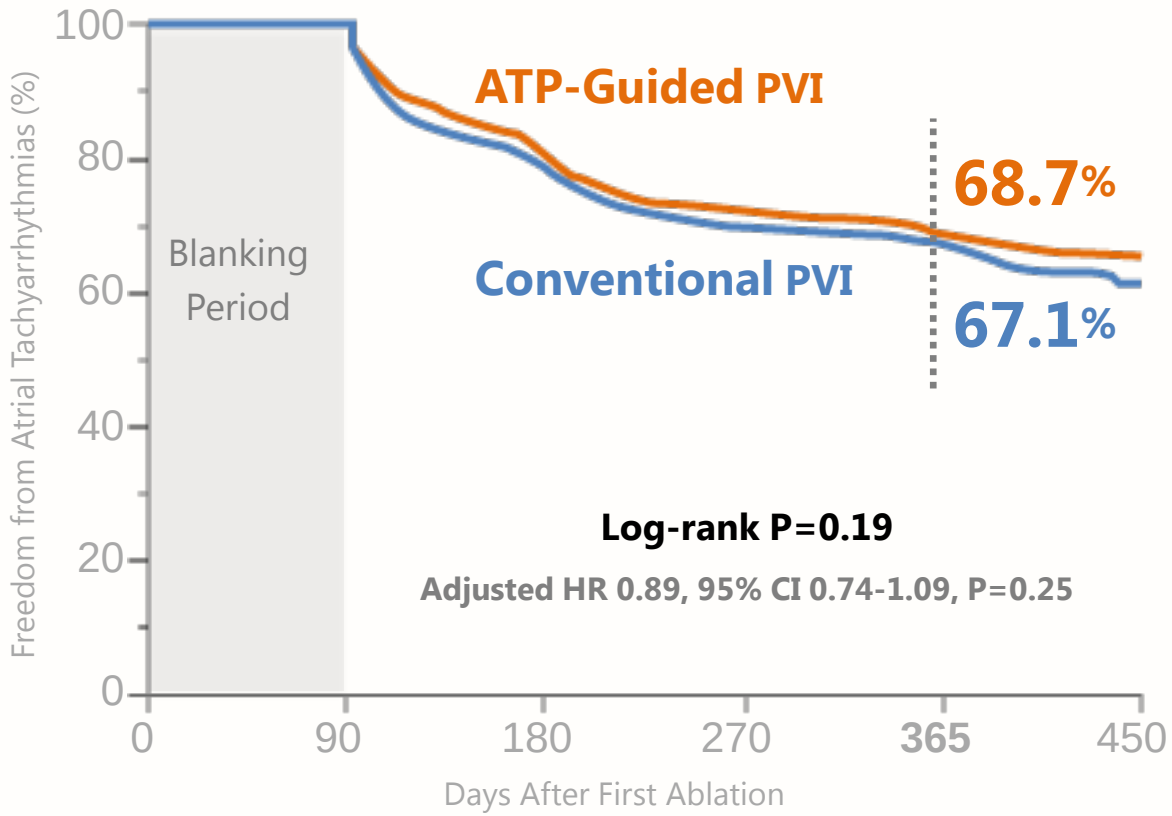
| | ATP-guided PVI (N=1112) | Conventional PVI (N=1001) | P value |
|---|---|---|---|
| Spontaneous PV reconnection (%) | 474 (42.6) | 419 (41.9) | 0.72 |
| Time from initial PVI to PV reconnection, minutes [IQR] | 43 [30-60] | 43 [30-60] | 0.94 |
| Time from initial PVI to ATP test, minutes [IQR] | 57 [33-87] | • | • |
| Dormant PV conduction by ATP (%) | 307 (27.6) | • | • |
| Left sided PV (%) | 194 (17.4) | | |
| Right sided PV (%) | 172 (15.5) | | |
| Number of additional applications for dormant conduction [IQR] | 5 [3-9] | • | • |
| Elimination of all dormant conduction (%) | 302 (98.4) | • | • |
| Total duration of energy applications for PVI, minutes [IQR] | 37.1 [28.7-45.6] | 35.1 [27.3-44.3] | 0.005 |
| Time from initial success to final check in PVI, minutes [IQR] | 67 [42-96] | 61 [38-91] | <0.001 |

UNDER-ATP

# Procedure and Safety Outcomes

| | ATP-guided PVI (N=1112) | Conventional PVI (N=1001) | P value |
|---|---|---|---|
| Total number of energy applications | 106±61 | 101±40 | 0.02 |
| Total duration of energy applications, minutes [IQR] | 47.1 [35.3-59.6] | 45.5 [34.7-58.8] | 0.11 |
| Total procedure time, minutes [IQR] | 195 [163-230] | 192 [160-230] | 0.22 |
| Total fluoroscopy time, minutes [IQR] | 58.4 [35.5-86.8] | 58.0 [34.1-88.2] | 0.99 |
| Total radiation dose, mGy [IQR] | 399 [141-756] | 370 [164-721] | 0.92 |
| Complications | | | |
| Cardiac tamponade requiring drainage (%) | 10 (0.9) | 12 (1.2) | 0.50 |
| Stroke (%) | 0 (0) | 1 (0.1) | 0.47 |
| Asthma attack (%) | 0 (0) | 0 (0) | - |
| Ischemic cardiac events (%) | 1 (0.1) | 4 (0.4) | 0.20 |

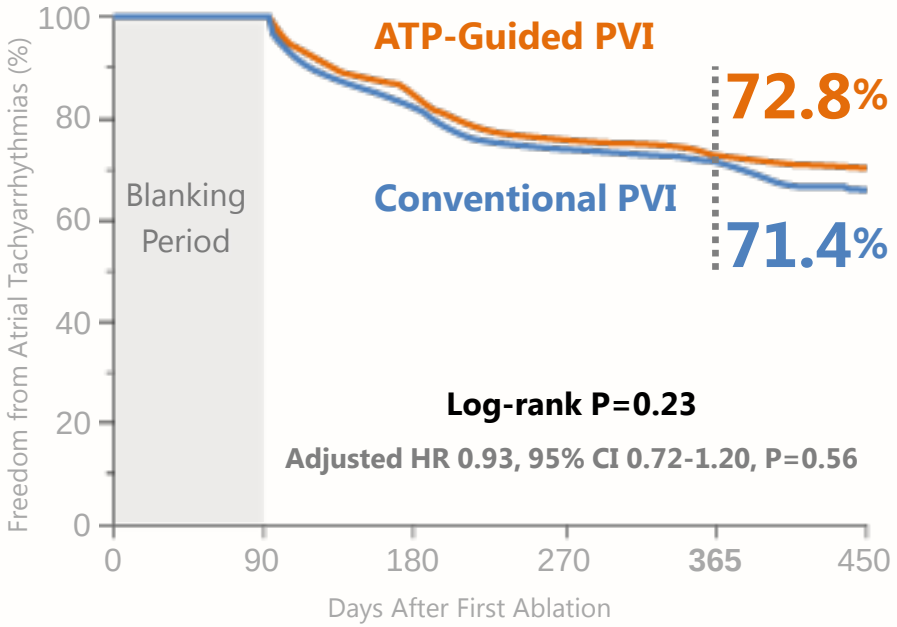
# Event-free Survival from the Primary Endpoint




| Interval | 0d | 90d | 180d | 270d | 365d | 450d |
|---|---|---|---|---|---|---|
| ATP-Guided PVI; N at risk | 1112 | 1111 | 896 | 800 | 625 | 190 |
| Conventional PVI; N at risk | 1001 | 999 | 787 | 701 | 533 | 155 |

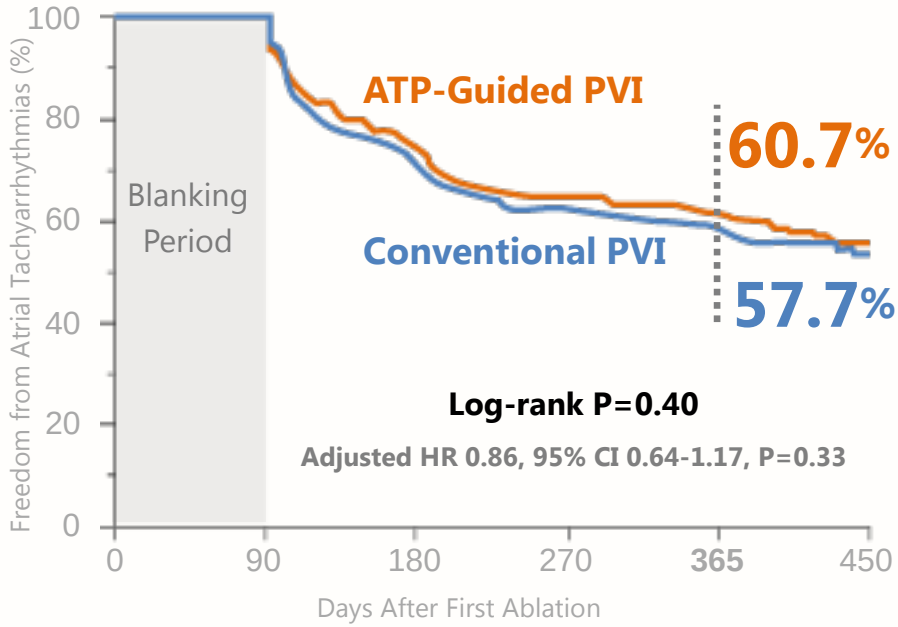
UNDER-ATP

## Paroxysmal AF




| Interval | 0d | 180d | 365d |
|---|---|---|---|
| ATP-Guided PVI; N at risk | 737 | 616 | 434 |
| AAD group; N at risk | 683 | 562 | 386 |

## Persistent / Long-Lasting AF

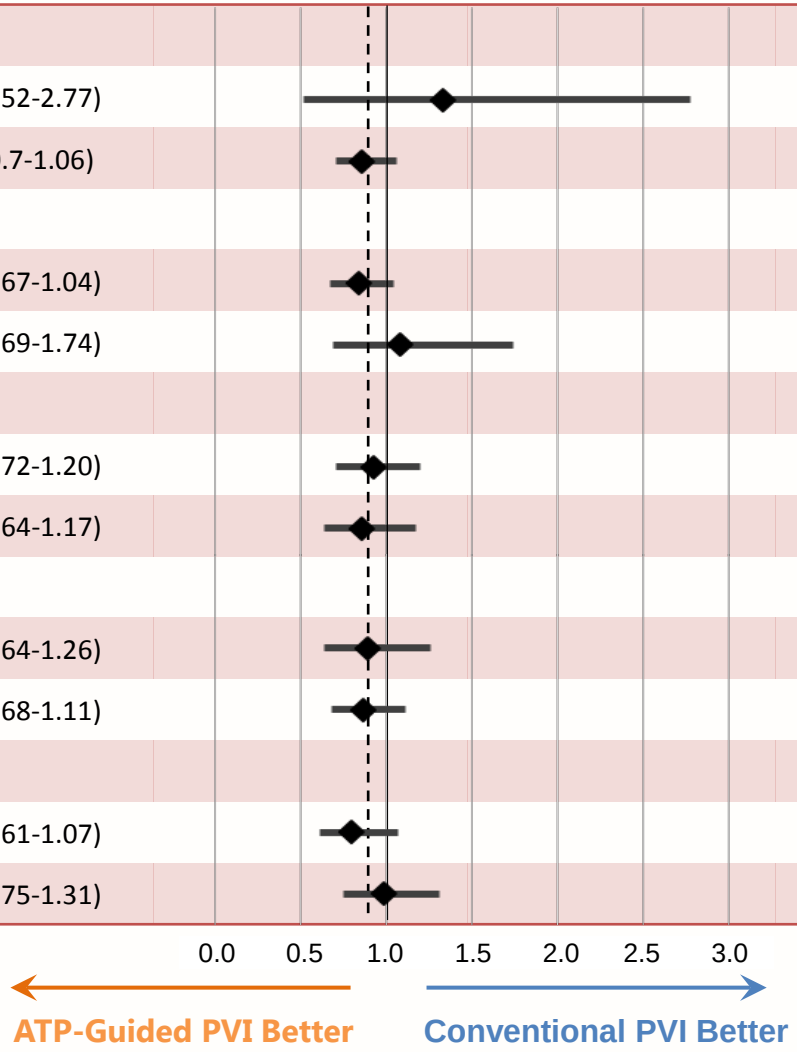



| Interval | 0d | 180d | 365d |
|---|---|---|---|
| ATP-Guided PVI; N at risk | 375 | 281 | 191 |
| AAD group; N at risk | 318 | 225 | 147 |

UNDER-ATP

# Primary Endpoint in the Prespecified Patient Subgroups

| | No. of Patients | Adjusted HR (95% CI) | P for Interaction |
|---|---|---|---|
| Age | | | 0.33 |
| ≥ 70 years | 631 | 1.33 (0.52-2.77) | |
| < 70 years | 1482 | 0.86 (0.7-1.06) | |
| Gender | | | 0.08 |
| Male | 1579 | 0.84 (0.67-1.04) | |
| Female | 534 | 1.08 (0.69-1.74) | |
| Type of Atrial Fibrillation | | | 0.90 |
| Paroxysmal | 1420 | 0.93 (0.72-1.20) | |
| Persistent / Long Lasting | 693 | 0.86 (0.64-1.17) | |
| 90-day use of AAD | | | 0.97 |
| AAD | 1016 | 0.89 (0.64-1.26) | |
| No AADs | 1022 | 0.87 (0.68-1.11) | |
| Left Atrial Dimension | | | 0.78 |
| ≥ 40 mm | 952 | 0.80 (0.61-1.07) | |
| < 40 mm | 1146 | 0.99 (0.75-1.31) | |



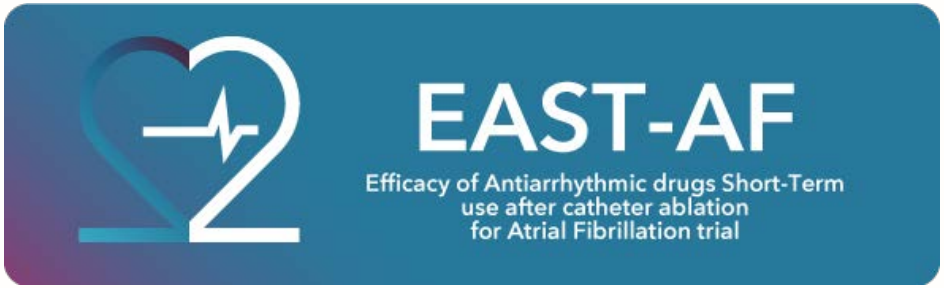
# Limitations

- Randomization programming error regarding age, requiring adjustment by the Cox proportional hazard model
- No continuous ECG-monitoring

# Conclusions

- We found no significant reduction in the incidence of recurrent atrial tachyarrhythmias after catheter ablation of AF with the ATP-guided PVI as compared to the conventional PVI.

# Efficacy of Antiarrhythmic Drugs Short-Term Use After Catheter Ablation for Atrial Fibrillation trial

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Tenri Hospital, Sakurabashi Watanabe Hospital, Kobe City Medical Center General Hospital, Shiga University of Medical Science, Shiroyama Hospital, Ogaki Municipal Hospital, Nara Prefecture Western Medical Center, Hyogo College of Medicine, Kyoto University Graduate School of Medicine
Kansai region, Japan.

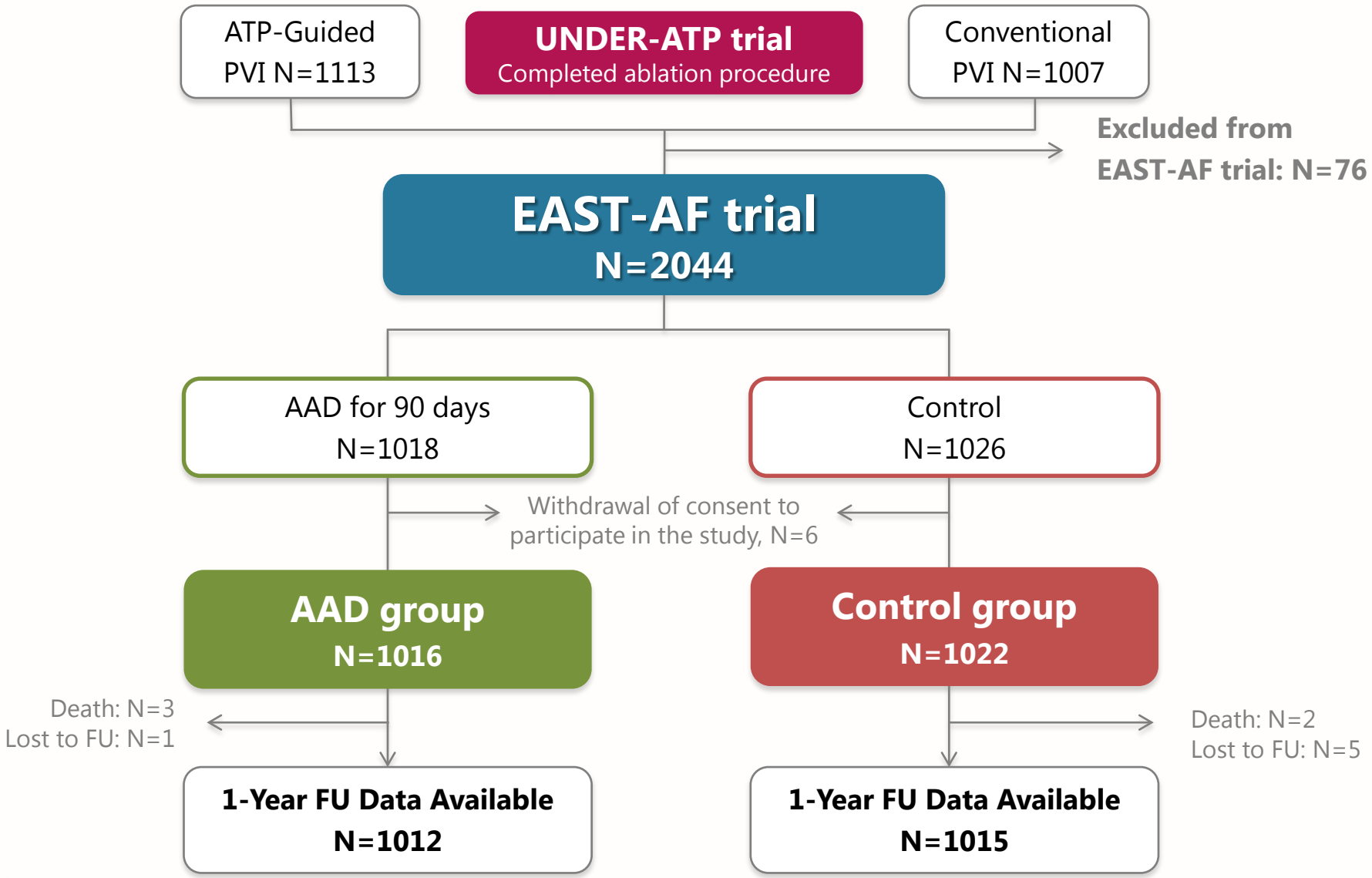
# Background

- Transient atrial tachyarrhythmias occur frequently in the first few months following atrial fibrillation (AF) ablation.
- A sizable portion of early recurrence is related to the irritability from the ablation procedure.
- This phenomenon is a strong predictor of later recurrence of atrial arrhythmias.

# Hypothesis

- 90 days use of antiarrhythmic drug (AAD) following AF ablation could reduce the incidence of early arrhythmia recurrence and thereby promote reverse remodeling of left atrium, leading to improved long-term clinical outcomes.

# Patient flowchart



# Endpoints

## Primary endpoint

- Recurrent atrial tachyarrhythmias* at 1-year with a blanking period of 90 days post ablation.

## Secondary endpoints

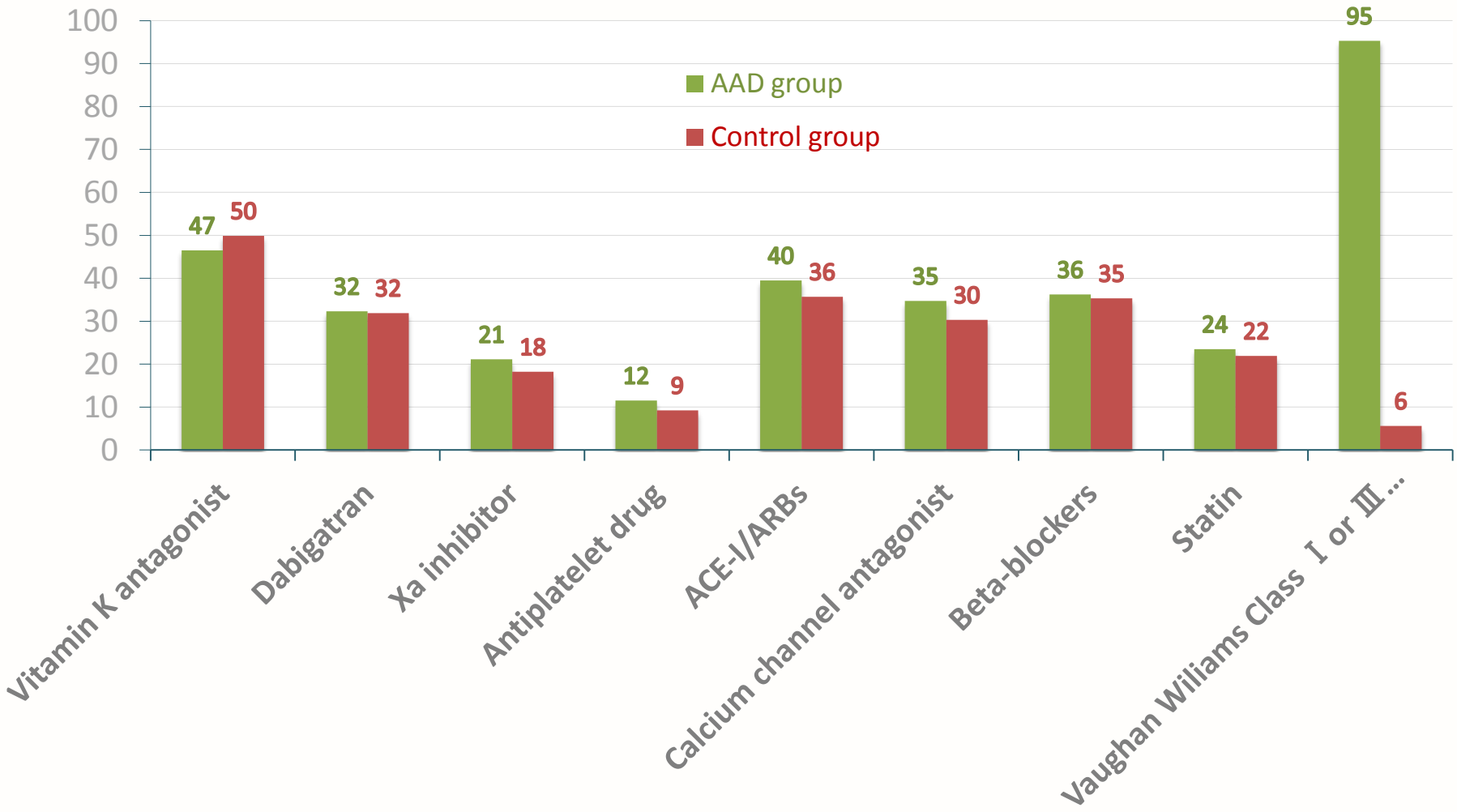
- Recurrent atrial tachyarrhythmias* within the blanking period of 90 days
- Adverse events/safety

*Recurrent atrial tachyarrhythmias was defined as documented AF/AFL/AT lasting for >30 seconds or requiring repeat ablation, hospital admission or usage of Vaughan Williams class I or III AADs.*

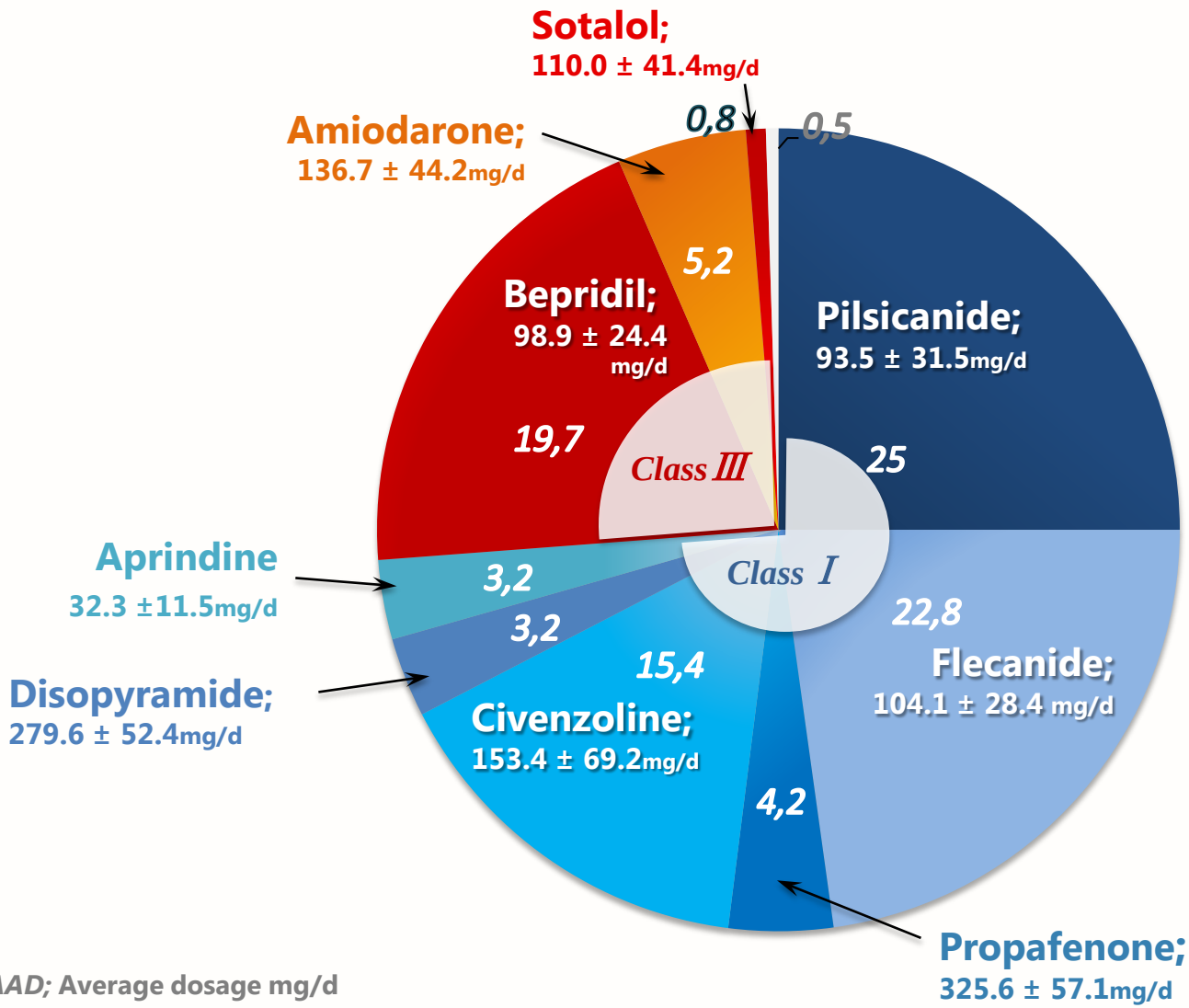
# Baseline Characteristics

| | AAD group (N=1016) | Control group (N=1022) | P value |
|---|---|---|---|
| Age (years) | 65.9 ± 9.6 | 60.7 ± 9.6 | <0.001 |
| Male | 741 (72.9) | 789 (77.2) | 0.03 |
| History of AF (m) | 24.7 [8.8-62.8] | 26.1 [9.3-62.9] | 0.41 |
| Body Weight (kg) | 64.7 ± 11.5 | 67.4 ± 12.7 | <0.001 |
| Type of AF | | | 0.48 |
| Paroxysmal | 692 (68.1) | 684 (66.9) | |
| Persistent | 232 (22.8) | 229 (22.4) | |
| Long-lasting | 92 (9.1) | 109 (10.7) | |
| $CHADS_2$ score | | | <0.001 |
| 0, 1 | 711 (81.8) | 793 (77.6) | |
| 2 | 192 (18.9) | 153 (15.0) | |
| e3 | 113 (11.1) | 76 (7.4) | |
| LVEF (%) | 64.5 ± 7.8 | 64.2 ± 7.8 | 0.42 |
| LA dimension (mm) | 38.9 ± 6.2 | 39.0 ± 6.2 | 0.77 |

# Rate of medication use at discharge



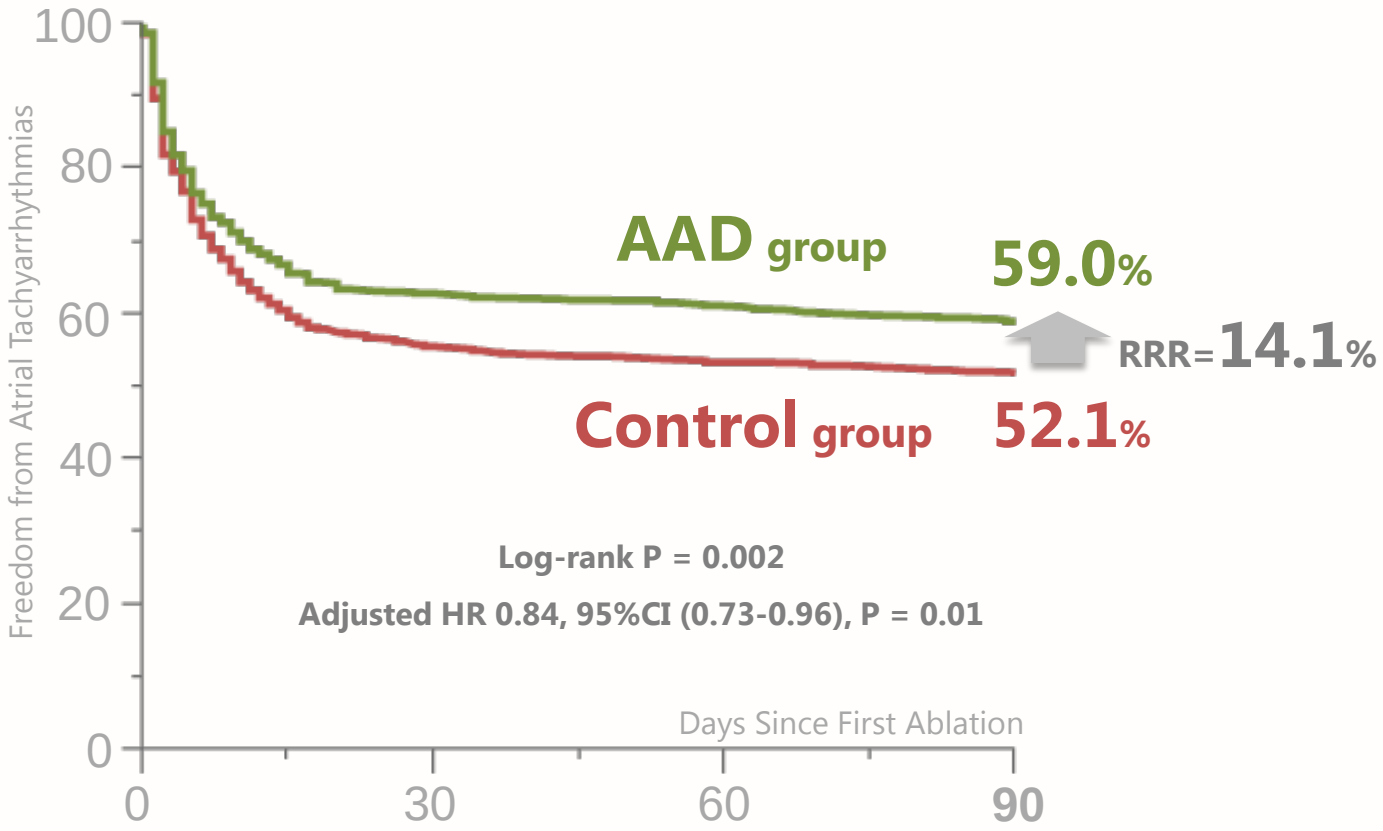
# Antiarrhythmic drugs used in the AAD group




*AAD;* Average dosage mg/d

# Secondary endpoint

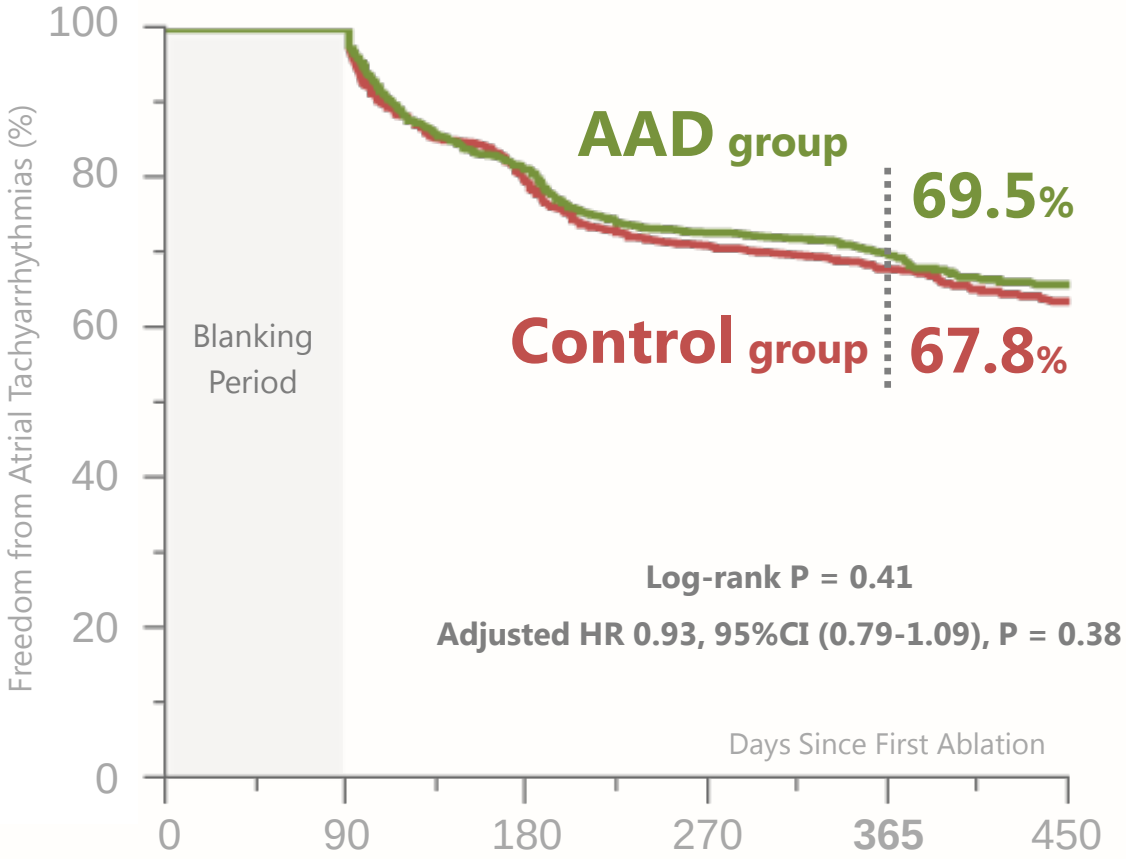
## Freedom from AF/AT during the blanking period




| Interval | 0d | 30d | 60d | 90d |
|---|---|---|---|---|
| AAD group; N at risk | 1016 | 640 | 623 | 600 |
| Control group; N at risk | 1022 | 569 | 549 | 532 |

# Primary endpoint

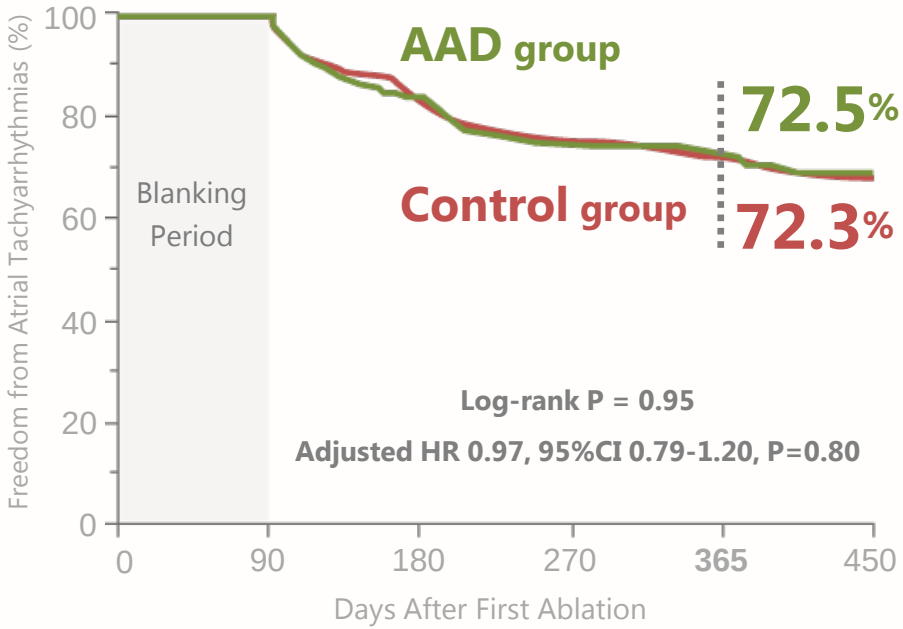
## Freedom from AF/AT at 12-months of follow-up




| Interval | 0d | 90d | 180d | 270d | 365d | 450d |
|---|---|---|---|---|---|---|
| AAD group; N at risk | 1016 | 1016 | 828 | 737 | 570 | 163 |
| Control group; N at risk | 1022 | 1021 | 810 | 723 | 557 | 165 |

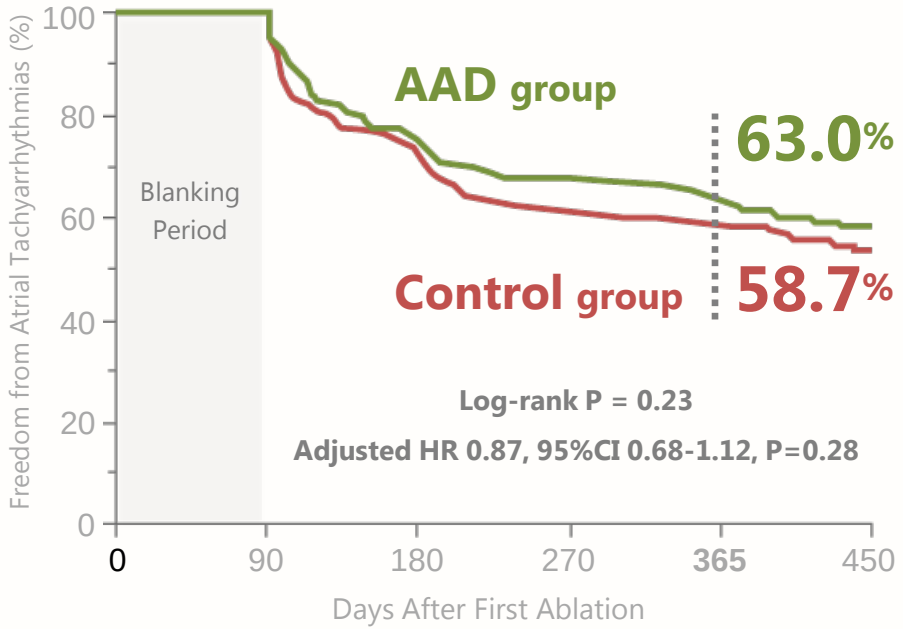
EAST-AF

## Paroxysmal AF




| Interval | 0d | 180d | 365d |
|---|---|---|---|
| AAD group; N at risk | 692 | 582 | 402 |
| Control group; N at risk | 684 | 565 | 395 |

## Persistent / Long-Lasting AF




| Interval | 0d | 180d | 365d |
|---|---|---|---|
| AAD group; N at risk | 324 | 246 | 168 |
| Control group; N at risk | 338 | 245 | 162 |

# Adverse events

| | AAD group (N=1016) | Control group (N=1022) |
|---|---|---|
| Death (%) | 3 (0.3) | 2 (0.2) |
| Cardiovascular death (%) | 0 (0) | 1 (0.1) |
| Ischemic Stroke / TIA (%) | 3 (0.3) | 1 (0.1) |
| Systemic embolism (%) | 0 (0) | 1 (0.1) |
| Intracranial hemorrhage (%) | 4 (0.4) | 2 (0.2) |
| Myocardial infarction (%) | 1 (0.1) | 1 (0.1) |
| Hospitalization for heart failure (%) | 4 (0.4) | 4 (0.4) |
| Cardioversion | 113 (11.1) | 117 (11.5) |
| ≤ 90 Days | 85 (8.4) | 104 (10.2) |
| > 90 Days | 28 (2.7) | 13 (1.3) |
| Side effect of AAD (%) | 41 (4.1) | - |
| Bradycardia | 13 (1.3) | - |
| Ventricular tachyarrhythmias (%) | 0 (0) | - |
| Others | 28 (3.0) | - |

# Limitations

- Randomization programming error regarding age, requiring adjustment by the Cox proportional hazard model
- No continuous ECG-monitoring
- Differences in the recommended AADs and their dosages between the present study and the Western AF guidelines

# Conclusions

- Short-term AAD treatment for 90 days following AF ablation significantly reduced the AT/AF recurrence during the treatment period of 90 days.

- However, it did not lead to improved clinical outcomes at the 1-year follow-up.

# Acknowledgments and Funding


## Acknowledgments

**Division of Cardiology, Tenri Hospital/ Cardiovascular center, Sakurabashi Watanabe Hospital/ Division of Cardiology, Kobe City Medical Center General Hospital/ Department of Cardiovascular Medicine, Heart Rhythm Center, Shiga University of Medical Science/ Cardiovascular center, Shiroyama Hospital/ Department of Cardiology, Ogaki Municipal Hospital/ Department of Cardiology, Hiroshima City Hiroshima Citizens Hospital/ Cardiovascular Center, Kansai Rosai Hospital/ Department of Cardiovascular Medicine, Nara Prefecture Western Medical Center/ First Department of Internal Medicine, Nara Medical University/ Division of Cardiology, Osaka General Medical Center/ Department of Cardiovascular Medicine, Kyoto Prefectural University of Medicine/ Department of Cardiology, Japanese Red Cross Society Wakayama Medical Center/ Department of Cardiology, Himeji Cardiovascular Center/ Department of Cardiovascular Medicine, Okamura Memorial Hospital/ Division of Cardiology, Osaka Rosai Hospital/ Division of Arrhythmia and Electrophysiology, Department of Cardiovascular Medicine, National Cerebral and Cardiovascular Center/ Cardiovascular Center, Tazuke Medical Research Institute Kitano Hospital/ Department of Cardiovascular Medicine, Kyoto University Graduate School of Medicine/ Department of Cardiovascular Medicine, Graduate School of Medicine, Nippon Medical School/ Division of General Medicine, Department of Internal Medicine, Hyogo College of Medicine**


KPAF
Kansai Plus Atrial Fibrillation

UNDER-ATP

EAST-AF


## Funding

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