ReACT

Randomized evaluation of routine follow-up coronary Angiography after percutaneous Coronary intervention Trial (ReACT)

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On behalf of the ReACT Investigators

Disclosure Statement of Financial Interest

Within the past 12 months, I or my spouse/partner have had a financial interest/arrangement or affiliation with the organization(s) listed below.

Affiliation/Financial Relationship	Company
• Grant/Research Support	• The Research Institute for Production Development (Kyoto, Japan)
• Consulting Fees/Honoraria	• Company Names
• Major Stock Shareholder/Equity	• Company Names
• Royalty Income	• Company Names
• Ownership/Founder	• Company Names
• Intellectual Property Rights	• Company Names
• Other Financial Benefit	• Company Names

Background

- ***Previous clinical trials reported that routine FUCAG after PCI did not improve clinical outcome, but increased the rate of coronary revascularization due to "Oculostenotic reflex".***

Trial Name	Design	Sample size	FU interval	Primary endpoint	Repeat Revascularization
BMS era					
Benestent II (JACC 1999)	**RCT**	N=827	1Y	**MACE: AF>CF** (N=50>27, P<0.01)	**AF>CF** HR:2.05 (1.24-3.37), P=0.003
BAAS (JACC 2001)	**RCT**	N=1058	3Y	**MACE: AF>CF** (23.2% vs 16.7%, P=0.01)	**AF>CF** HR 1.7 (1.3-2.3), P<0.001
DES era					
Taxus IV (JACC 2006)	**Non-RCT**	PES=556 BMS=566	1Y	**TVR: AF>CF** (13.7% vs 9.9%, P=0.06)	**AF>CF** TVR: adjusted HR 1.46, P=0.04
SPIRIT III (AJC 2012)	**Non-RCT**	EES=669 PES=333	3Y	**MACE: AF=CF** (12.0% vs 10.6%, P=0.64)	**AF=CF** TLR: 10.3% vs 7.5%, P=0.14

Background

The Recommendations for FUCAG in the Guidelines

- **The 2011 ACCF/AHA/SCAI Guidelines for PCI have already disregarded routine FUCAG even after PCI for left main CAD.**

The 2005 PCI guideline recommended routine angiographic follow-up 2 to 6 months after stenting for unprotected left main CAD. However, because angiography has limited ability to predict stent thrombosis and the results of SYNTAX suggest good intermediate-term results for PCI in subjects with left main CAD, this recommendation was removed in the 2009 STEMI/PCI focused update.

- **The 2014 ESC/EACTS Guidelines on myocardial revascularization regarded routine FUCAG after high-risk PCI as Class IIb.**

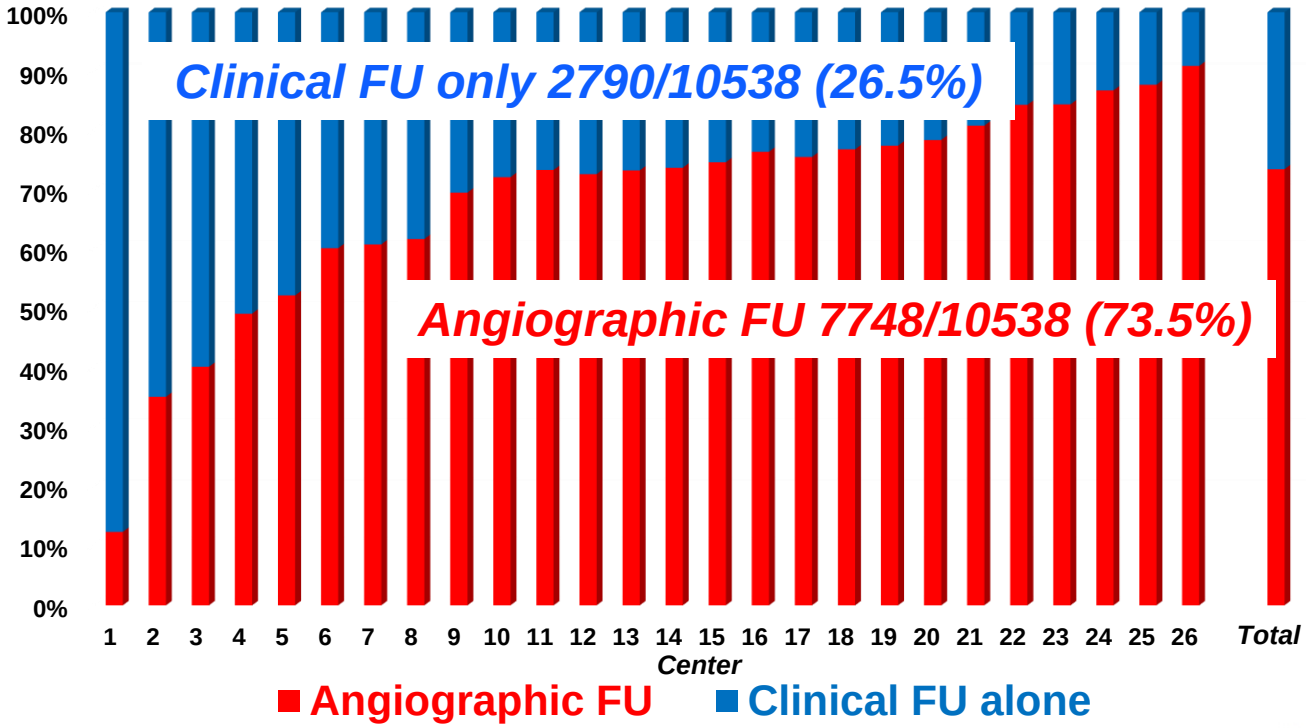
Recommendations	Class[a]	Level[b]	Ref[c]
Asymptomatic patients			
After high-risk PCI (e.g. unprotected LM stenosis) late (3–12 months) control angiography may be considered, irrespective of symptoms.	IIb	C	

Levine GN et al. Circulation 2011;124:e574-651
Windecker S et al. Eur Heart J 2014;35:2541-619

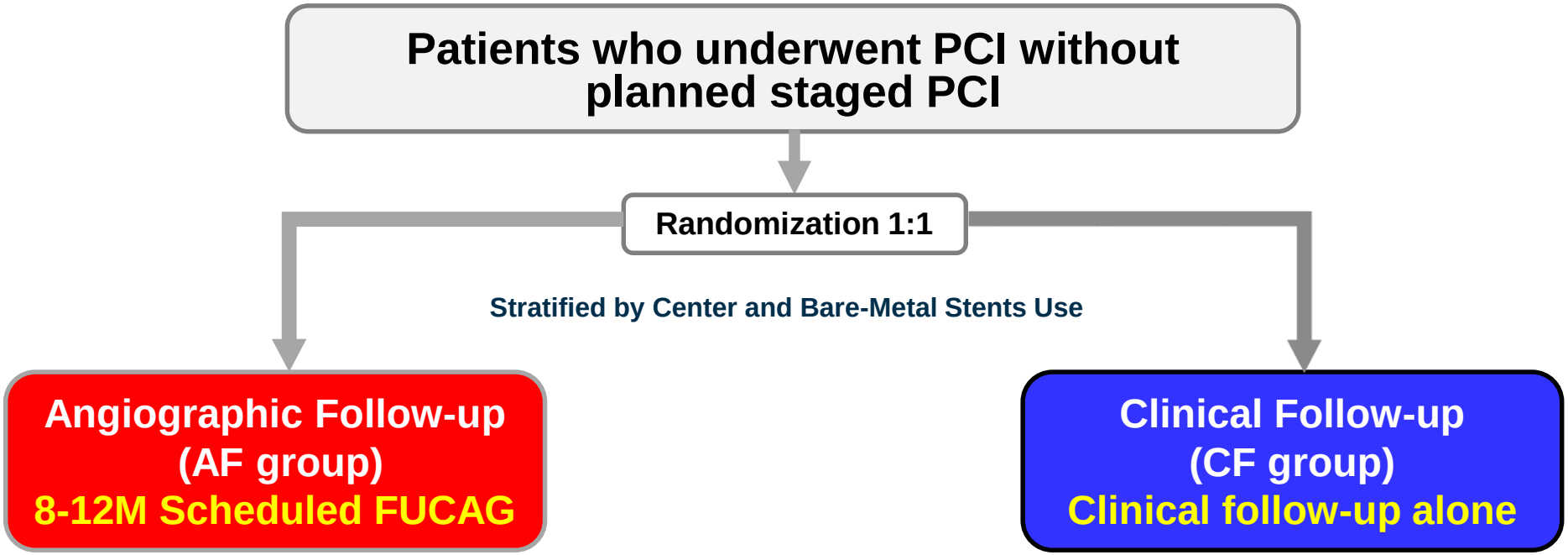
Background

- *Previous studies evaluating routine angiographic follow-up in the DES era were conducted in the context of pivotal RCTs of DES.*
- *In Japan, routine FUCAG is still performed for many PCI patients as a usual care.*

Prevalence of Routine Angiographic Follow-up in Japan from CREDO-Kyoto Registry Cohort-2 (2005-2007)



Study Design



- ***Primary Endpoint: A composite of death/MI/stroke/ACS/HF***
- ***Secondary Endpoints: Any coronary revascularization***

  Target lesion revascularization, etc

Study Organization

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- **Steering Committee**

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- **Clinical Event Committee**

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- **Date Safety Monitoring Board**

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- Nishi-Kobe Medical Center: Shintaro Matsuda, Hiroshi Eizawa
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- Osaka Red Cross Hospital: Masaru Tanaka, Tsukasa Inada
- Tsukuba Medical Center Hospital: Yuichi Noguchi
- Tenri Hospital: Yoshihisa Nakagawa, Makoto Motooka
- Tokai University: Yuji Ikari
- Kitaharima Medical Center: Kojiro Awano
- Hirakata Kohsai Hospital: Yoshisumi Haruna, Shoji Kitaguchi
- Nagoya Daini Red Cross Hospital: Haruo Hirayama, Mamoru Nanasato

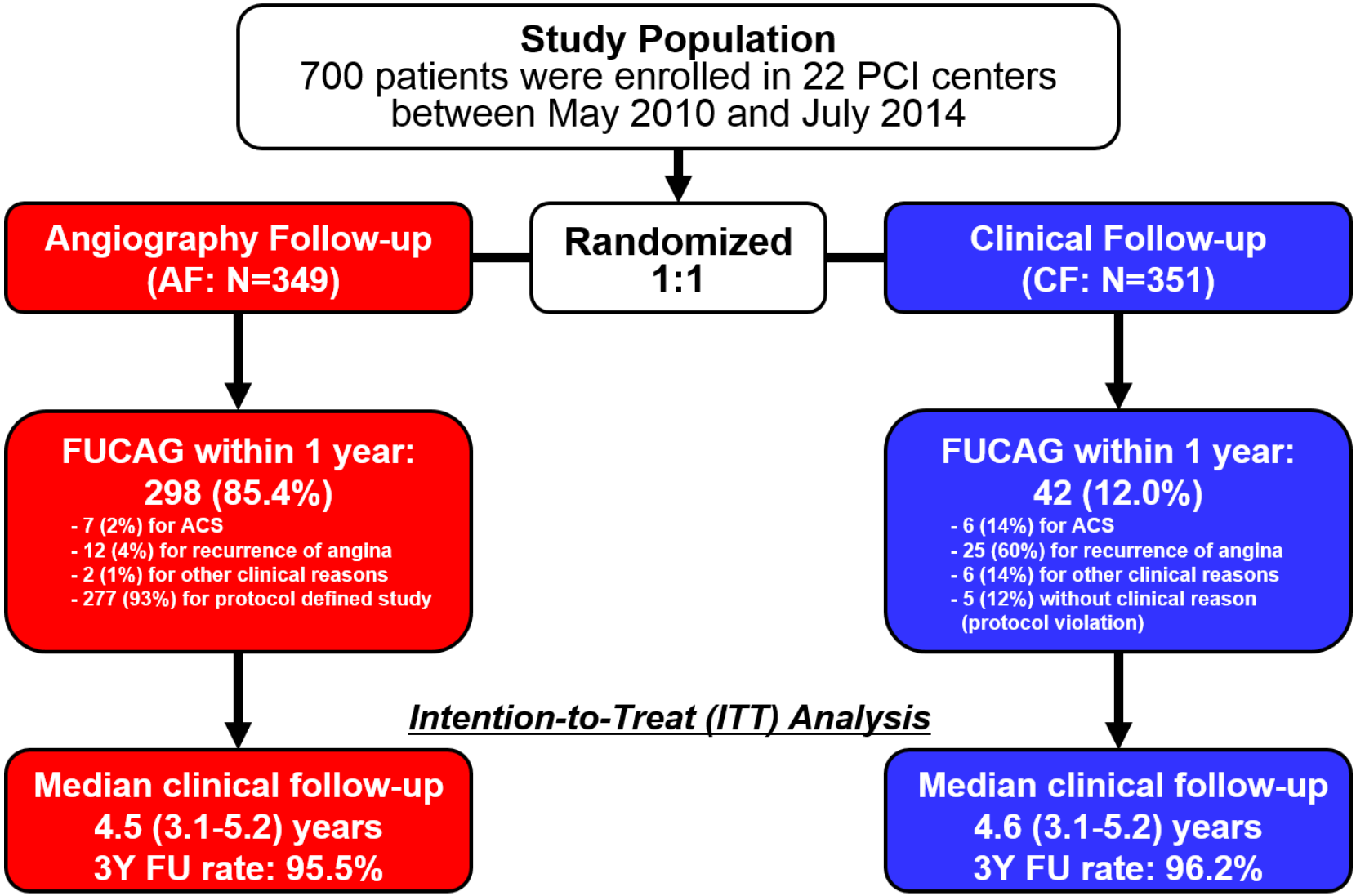
Power Calculation and Amendment of Protocol

- ***Original Sample Size Calculation***
  - **Estimated event rate at 3 year: 25% in CF group**
  - **Sample size: N=3300**
  - **15% relative reduction of the primary endpoint in AF group**
  - **α= 0.05 (2-tailed), 1-β= 0.80**

- ***Amendment of Protocol (June, 2014)***

  Due to the enrollment rate slower than expected with longer follow-up interval, the target sample size was amended to 700 patients with minimum of 1.5 year follow-up (estimated median FU: 5 years).

ReACT Patient Flow Chart



Patient Characteristics

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	AF group (N=349)	CF group (N=351)
Age – years	68.9±10.0	68.2±9.1
Male sex	260 (75%)	291 (83%)
Body mass index	24.3±3.4	24.2±3.2
Hypertension	252 (72%)	275 (78%)
Diabetes mellitus	141 (40%)	166 (47%)
Dyslipidemia	267 (77%)	277 (79%)
Hemodialysis	13 (3.7%)	12 (3.4%)
Prior myocardial infarction	56 (16%)	62 (18%)
Prior PCI	106 (30%)	122 (35%)
Prior Stroke	25 (7.2%)	36 (10%)
Past history of heart failure	18 (5.2%)	23 (6.6%)
Atrial fibrillation	19 (5.4%)	28 (8.0%)

Patient Characteristics

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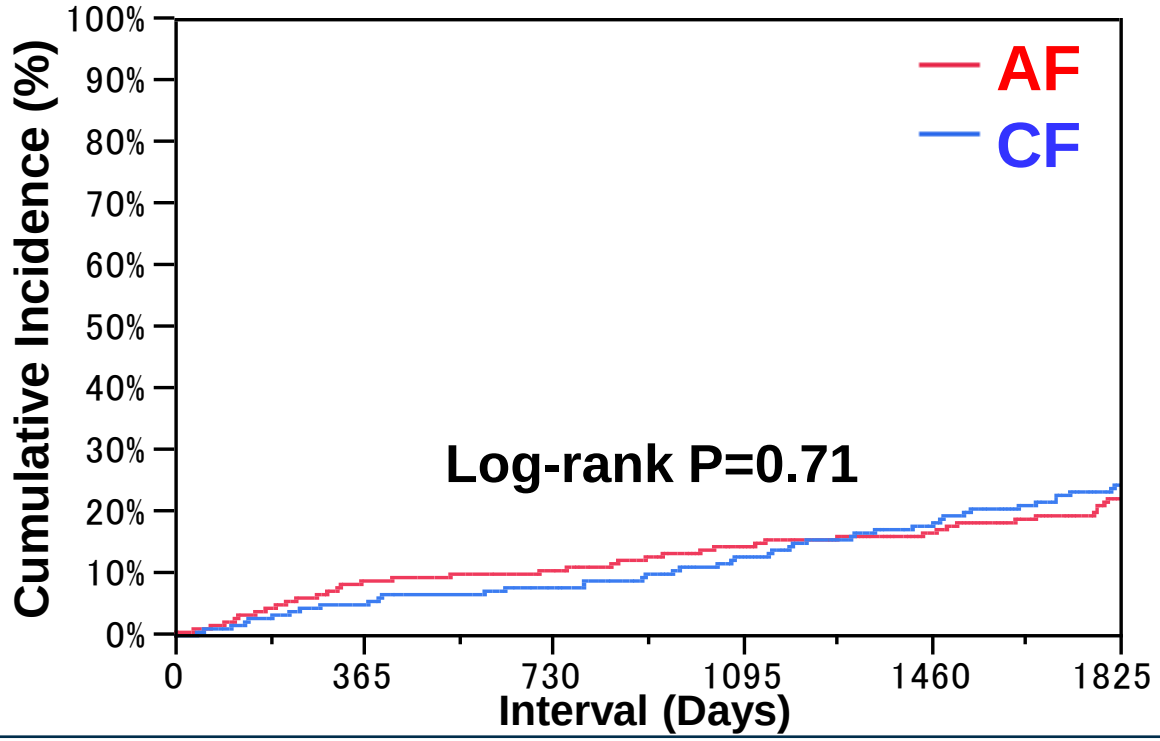
	AF group (N=349)	CF group (N=351)
Clinical characteristics		
Stable CAD	222 (64%)	221 (63%)
Unstable angina	57 (16%)	62 (18%)
Acute myocardial infarction	70 (20%)	68 (19%)
Peripheral artery disease	43 (12%)	41 (12%)
Multivessel disease	144 (41%)	150 (43%)
Target-vessel location		
LMCA	15 (4.3%)	12 (3.4%)
LAD	193 (55%)	195 (56%)
LCx	96 (28%)	85 (24%)
RCA	122 (35%)	123 (35%)
Bypass graft	3 (0.9%)	3 (0.9%)

Lesion and Procedural Characteristics

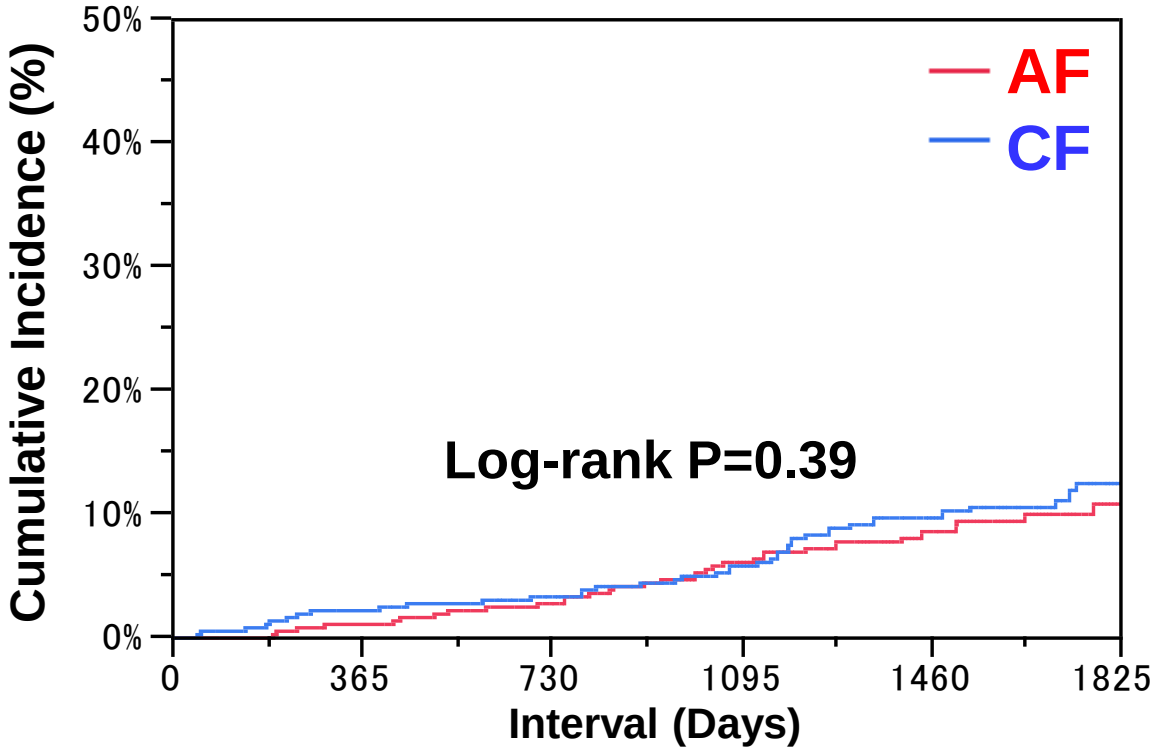
	AF group (N=349)	CF group (N=351)
Target of STEMI culprit lesion	57 (16%)	53 (15%)
Target of bifurcation lesion	119 (34%)	107 (30%)
Target of chronic total occlusion	23 (6.7%)	16 (4.6%)
Target of restenosis lesion	29 (8.3%)	28 (8.0%)
No. of treated lesions per patient	1.30±0.62	1.27±0.54
No. of stents used (per patient)	1.54±0.97	1.44±0.82
Total stent length - mm (per patient)	32.9±24.5	31.1±21.1
Drug-eluting stents use	298 (86%)	298 (87%)

Primary Endpoint: Death/MI/Stroke/ACS/HF



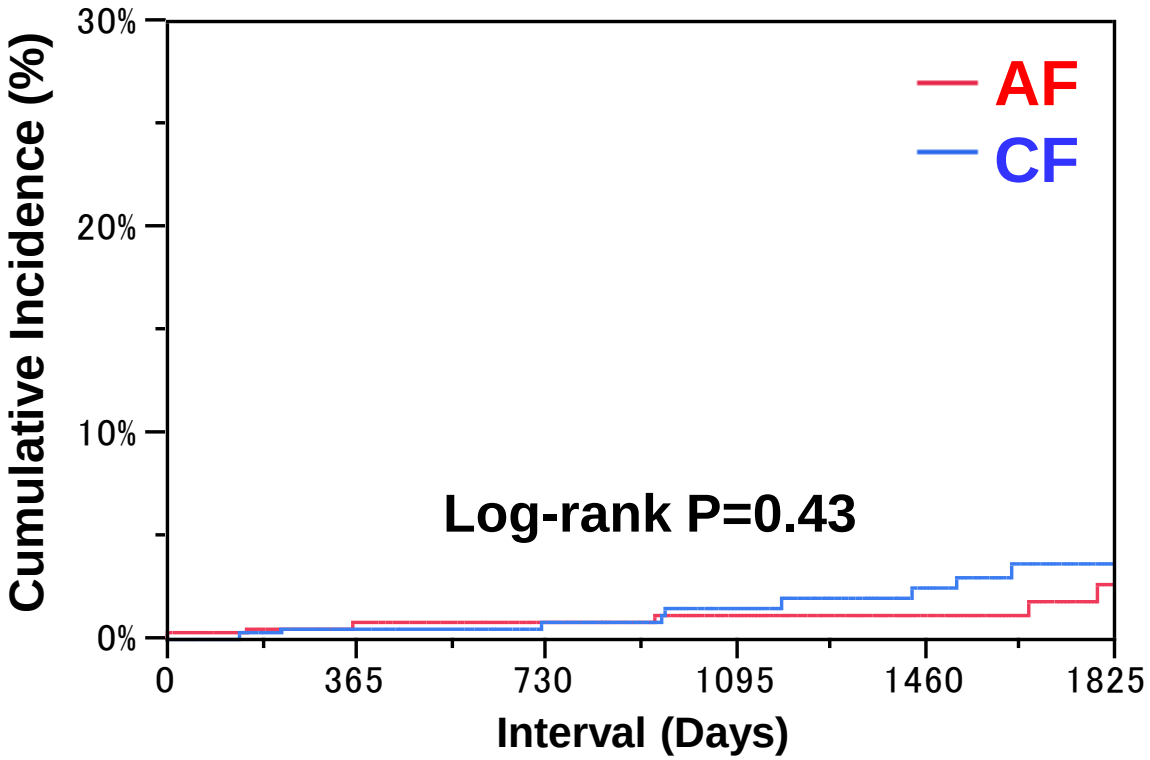
Interval	0 day	30 days	1 year	2 years	3 years	4 years	5 years
AF group							
N of patients with event		2	31	36	49	54	64
N of patients at risk	349	347	313	296	243	182	96
Cumulative incidence		0.6%	8.9%	10.4%	14.6%	16.9%	22.4%
CF group							
N of patients with event		0	18	28	42	56	67
N of patients at risk	351	351	331	303	247	175	90
Cumulative incidence		0%	5.1%	8.0%	12.6%	18.4%	24.7%

All-cause Death



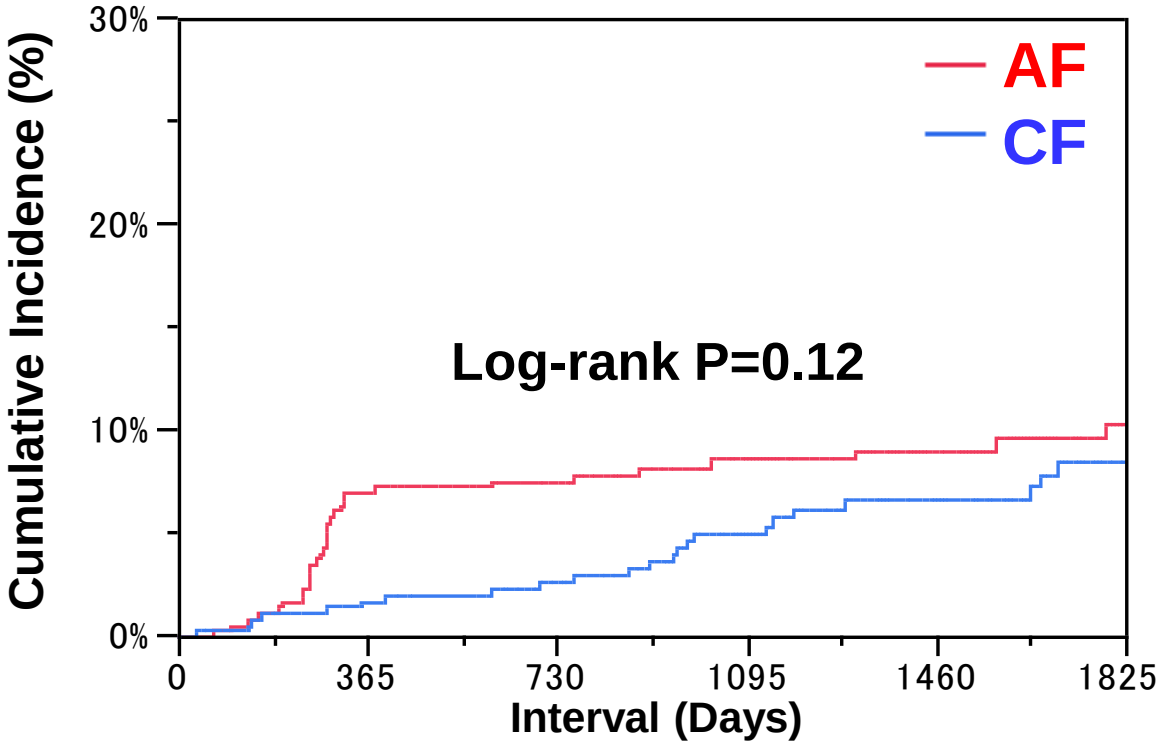
Interval	0 day	30 days	1 year	2 years	3 years	4 years	5 years
AF group							
N of patients with event		0	4	10	20	26	30
N of patients at risk	349	349	340	321	266	198	110
Cumulative incidence		0%	1.2%	2.9%	6.2%	8.6%	10.8%
CF group							
N of patients with event		0	8	12	19	29	34
N of patients at risk	351	351	341	319	267	197	108
Cumulative incidence		0%	2.3%	3.5%	5.7%	9.7%	12.5%

Myocardial Infarction



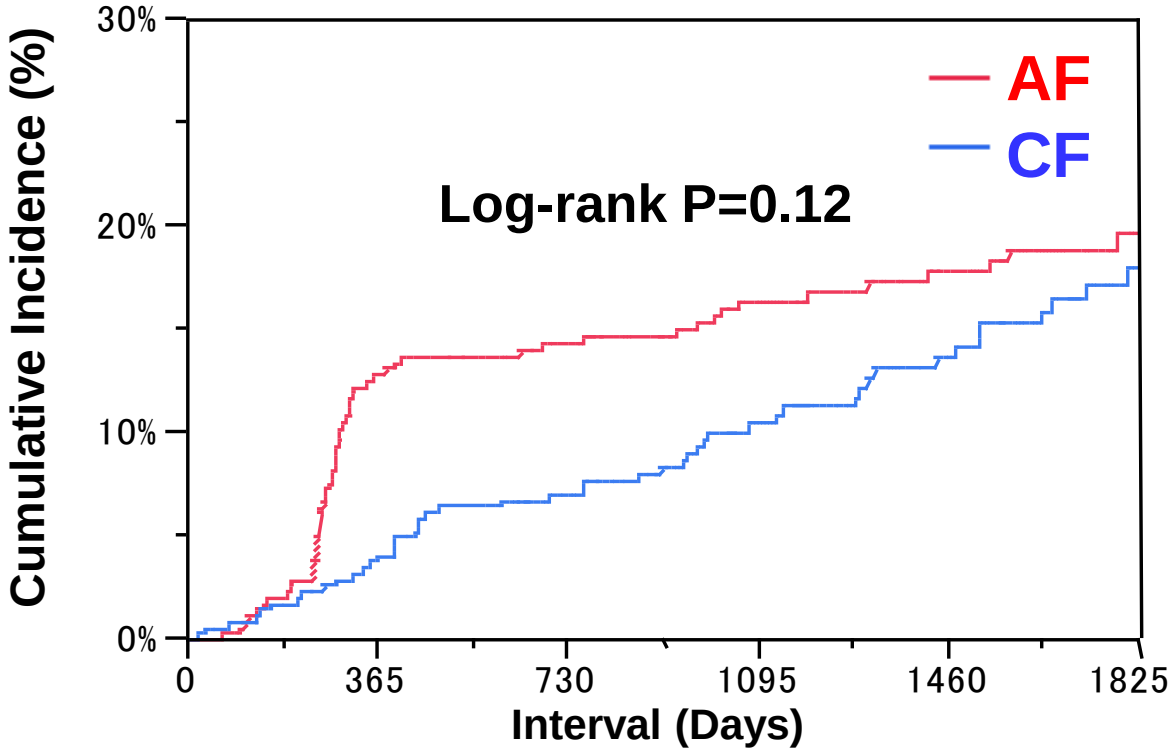
Interval	0 day	30 days	1 year	2 years	3 years	4 years	5 years
AF group							
N of patients with event		1	3	3	4	4	6
N of patients at risk	349	347	338	318	264	197	108
Cumulative incidence		0.3%	0.9%	0.9%	1.2%	1.2%	2.7%
CF group							
N of patients with event		0	2	3	5	7	9
N of patients at risk	351	351	339	315	263	192	102
Cumulative incidence		0%	0.6%	0.9%	1.6%	2.5%	3.6%

Target Lesion Revascularization



Interval	0 day	30 days	1 year	2 years	3 years	4 years	5 years
AF group							
N of patients with event		0	24	26	29	30	32
N of patients at risk	349	348	317	297	245	180	101
Cumulative incidence		0%	7.0%	7.6%	8.6%	9.0%	10.4%
CF group							
N of patients with event		0	6	9	16	20	23
N of patients at risk	351	351	335	310	254	181	98
Cumulative incidence		0%	2.0%	2.9%	5.0%	6.7%	8.5%

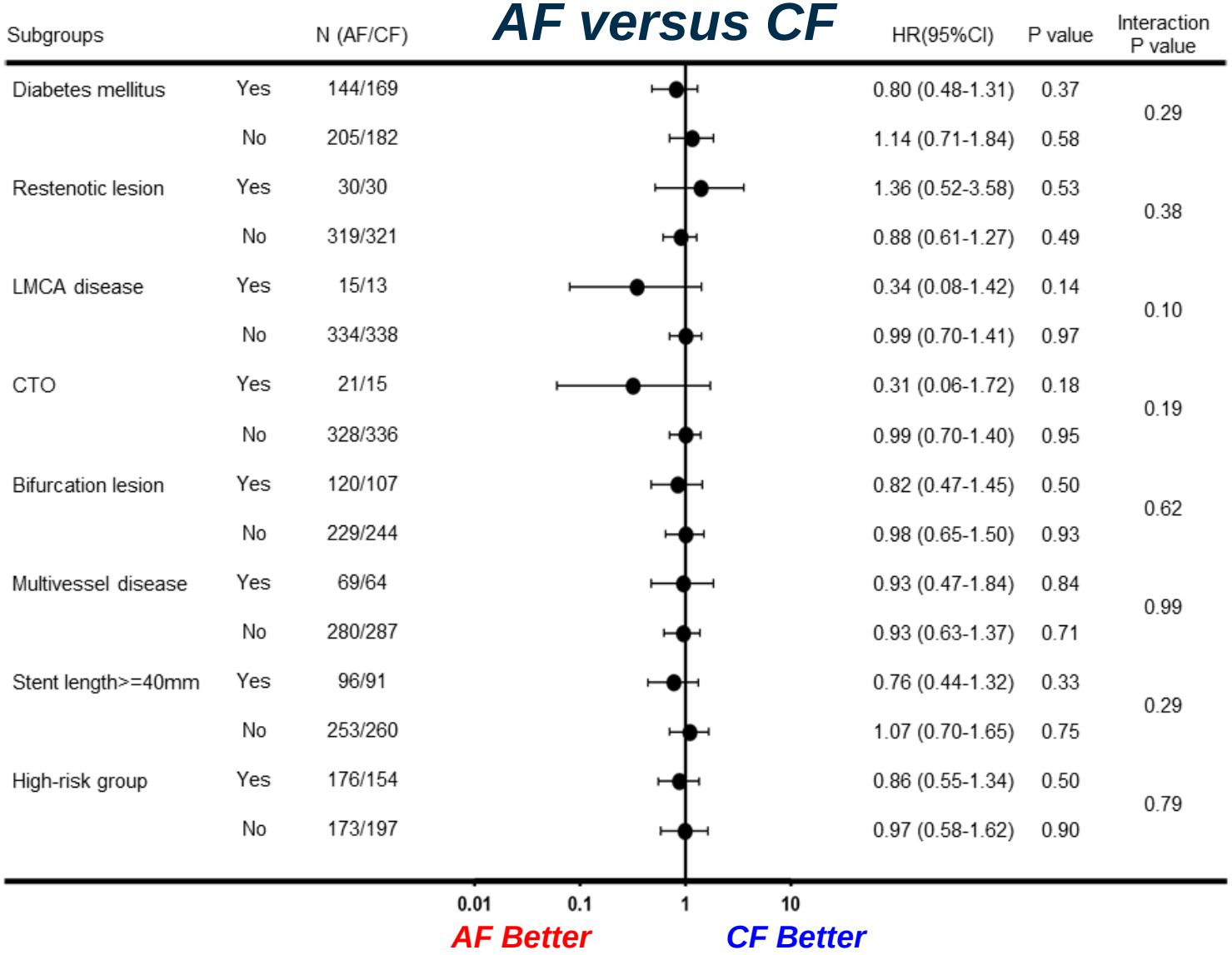
Any Coronary Revascularization



Interval	0 day	30 days	1 year	2 years	3 years	4 years	5 years
AF group							
N of patients with event		0	44	49	55	58	61
N of patients at risk	349	348	297	275	221	164	93
Cumulative incidence		0%	12.8%	14.3%	16.4%	17.8%	19.6%
CF group							
N of patients with event		1	13	24	34	41	48
N of patients at risk	351	350	328	295	239	165	89
Cumulative incidence		0.3%	3.8%	7.0%	10.5%	13.7%	18.1%

Subgroup Analysis for the Primary Endpoint

AF versus CF



High-risk group with at least 1 risk feature such as LMCA disease, bifurcation lesion, multivessel disease, and total stent length>= 40mm

Limitations

- **Underpowered to detect modest differences in the primary endpoint due to the reduced final sample size and the actual event rate lower than anticipated.**

- **Unable to address the role of routine angiographic follow-up in the high-risk subgroups such as left main or multi-vessel CAD.**

Conclusions

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- **No clinical benefits were observed for routine FUCAG after PCI and early revascularization rates were increased within this approach in the current trial. Thus, routine FUCAG cannot be recommended as a clinical strategy.**

- **However, the present study was underpowered to detect modest benefits (or harm) of routine FUCAG, and larger-scale trials (especially in high-risk patients) are warranted to definitively address this issue.**