ATRIAL FIBRILLATION
NETWORK

EAST - AFNET 4

Hauptergebnis

AFNET e.V.

east

early treatment of
atrial fibrillation for
stroke prevention trial

EHRA
European Heart
Rhythm Association
European Society of Cardiology

Early rhythm control therapy in patients with atrial fibrillation: Primary results of the EAST – AFNET 4 trial

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EAST – AFNET 4 Patient characteristics

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		Early Rhythm Control (n=1395)	Usual Care (n=1394)
Age [years]		70.2 ± 8.4	70.4 ± 8.2
Female sex		645 (46.2%)	648 (46.5%)
Weight [kg]		85.0 ± 18.4	85.0 ± 18.2
CHA_2DS_2-VASc Score [N=2784, Mean ± SD]		3.4 ± 1.3	3.3 ± 1.3
Stable heart failure (NYHA stage II-III or LVEF < 50%)		396 (28.4%)	402 (28.8%)
Atrial Fibrillation Characteristics			
Type of AF	First episode	528/1391 (38.0%)	520/1394 (37.3%)
	Paroxysmal	501/1391 (36.0%)	493/1394 (35.4%)
	Persistent	362/1391 (26.0%)	381/1394 (27.3%)
Sinus rhythm at baseline		762/1389 (54.9%)	743/1393 (53.3%)
Time since AF diagnosis (days, Median [IQR])		36.0 [6.0; 114.0]	36.0 [6.0; 112.0]
Without AF-related symptoms (EHRA score I)		395/1305 (30.3%)	406/1328 (30.6%)
Medication at Discharge			
Oral anticoagulation (NOAC or VKA)		1267/1389 (91.2%)	1250/1393 (89.7%)
Digoxin or Digitoxin		46/1389 (3.3%)	85/1393 (6.1%)
Beta blockers		1058/1389 (76.2%)	1191/1393 (85.5%)
ACE inhibitors, angiotensin II receptor blocker, or neprilysin/valsartan		953/1389 (68.6%)	979/1393 (70.3%)
Statins		628/1389 (45.2%)	568/1393 (40.8%)
Platelet inhibitors		229/1389 (16.5%)	226/1393 (16.2%)

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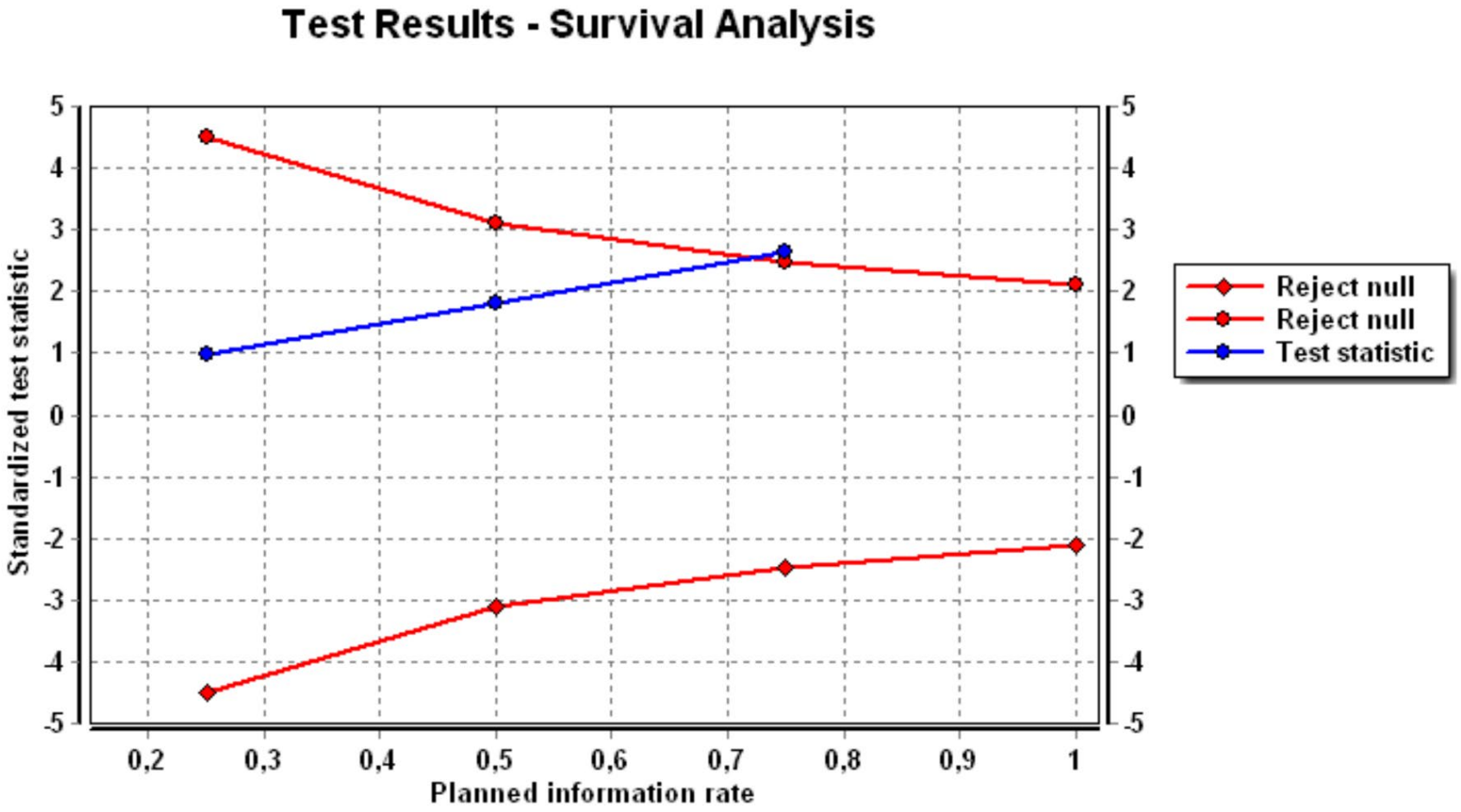
EAST – AFNET 4 Termination at 3rd interim analysis



Median follow-up 5.1 [3.8-6.4] years / patient
Final analysis includes the overrun of events until 6 March 2020

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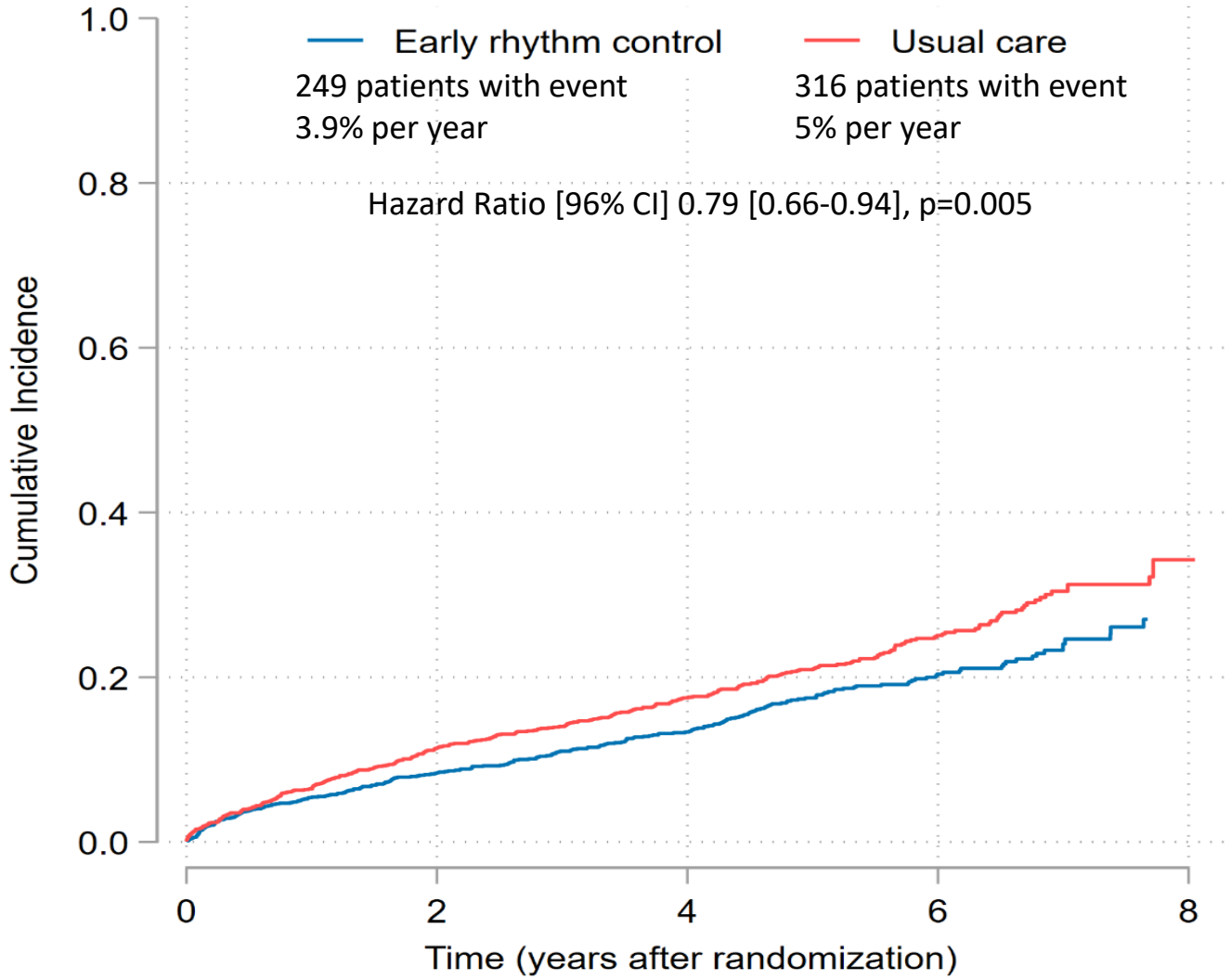
EAST – AFNET 4 Analysis of first primary outcome



Patients at risk

Early rhythm control	1395	1193	913	404	26
Usual care	1394	1169	888	405	34

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EAST – AFNET 4 Components of the first primary outcome

	Patients with event in Early Rhythm Control (n=1395)	Patients with event in Usual Care (n=1394)	Uncorrected Hazard Ratio [95% CI]
Cardiovascular death	67 / 6915 (1.0)	94 / 6988 (1.3)	0.72 [0.52-0.98]
Stroke	40 / 6813 (0.6)	62 / 6856 (0.9)	0.65 [0.44-0.97]
Hospitalization with worsening of heart failure	139 / 6620 (2.1)	169 / 6558 (2.6)	0.81 [0.65-1.02]
Hospitalization with acute coronary syndrome	53 / 6762 (0.8)	65 / 6816 (1.0)	0.83 [0.58-1.19]

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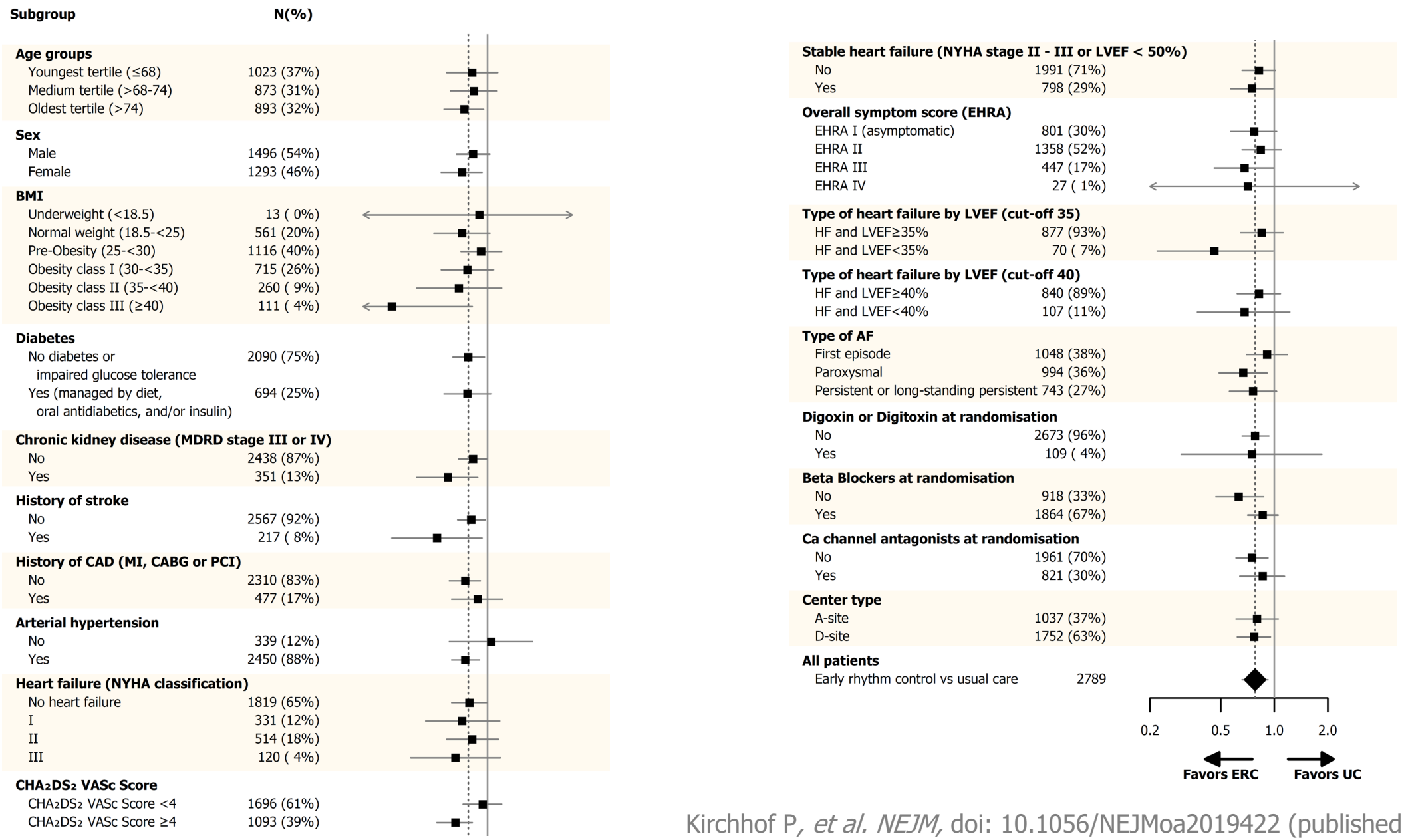
EAST – AFNET 4 First primary outcome by subgroups



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EAST – AFNET 4 Second primary outcome, key secondary outcomes

	Early Rhythm Control (n=1395)	Usual Care (n=1394)	Treatment Effect
Second primary outcome	**Mean ± SD**		**IRR [99% CI]**
Nights spent in hospital per year	5.8 ± 21.9	5.1 ± 15.5	1.08 [0.92-1.28]
	Patients with feature/total (%)		**Odds ratio [95% CI]**
Sinus rhythm	921/1122 (82.1)	687/1135 (60.5)	3.13 [2.55 - 3.84]
Asymptomatic (EHRA I)	861/1159 (74.3)	850/1171 (72.6)	1.14 [0.93 - 1.40]
Key secondary outcomes at 2 years	**Mean ± SD**		**Adjusted mean difference [95% CI]**
Change in LVEF	1.5% ± 9.8%	0.8% ± 9.8%	0.23% [-0.46% - 0.91%]
Change in EQ-5D (VAS state of health)	-1.0 ± 21.4	-2.7 ± 22.3	1.07 [-0.68 - 2.82]
Change in SF-12 Mental Score	0.7 ± 10.6	1.6 ± 10.1	-1.20 [-2.04 - -0.37]
Change in SF-12 Physical Score	0.3 ± 8.5	0.1 ± 8.2	0.33 [-0.39 - 1.06]
Change in MoCA score	0.1 ± 3.3	0.1 ± 3.2	-0.14 [-0.39 - 0.12]

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EAST – AFNET 4 Safety outcomes

	Early Rhythm Control (n=1395)	Usual Care (n=1394)
Occurrence of a primary safety outcome	231 (16.6%)	223 (16.0%)
Occurrence of stroke	40 (2.9%)	62 (4.4%)
Occurrence of death	138 (9.9%)	164 (11.8%)
Occurrence of a serious adverse event of special interest related to rhythm control therapy (detailed listing of events given in lines below)	68 (4.9%)	19 (1.4%)
Serious adverse events related to antiarrhythmic drug therapy		
Non-fatal cardiac arrest	1 (0.1%)	1 (0.1%)
Drug toxicity of AF-related drug therapy	10 (0.7%)	3 (0.2%)
Drug-induced bradycardia	14 (1.0%)	5 (0.4%)
AV block	2 (0.1%)	0 (0.0%)
Torsade de Pointes tachycardia	1 (0.1%)	0 (0.0%)
Serious adverse events related to AF ablation		
Pericardial tamponade	3 (0.2%)	0 (0.0%)
Bleeding related to AF ablation, major	6 (0.4%)	0 (0.0%)
Bleeding related to AF ablation, non-major	1 (0.1%)	2 (0.1%)
Other serious adverse events of special interest related to rhythm control therapy		
Blood pressure related (hypotension, hypertension; except syncope)	1 (0.1%)	0 (0.0%)
Hospitalization for AF	11 (0.8%)	3 (0.2%)
Other cardiovascular event	5 (0.4%)	1 (0.1%)
Other event	1 (0.1%)	3 (0.2%)
Syncope	4 (0.3%)	1 (0.1%)
Hospitalization for worsening of heart failure with decompensated heart failure	3 (0.2%)	0 (0.0%)
Implantation of a pacemaker, defibrillator, cardiac resynchronization device, or other device	8 (0.6%)	4 (0.3%)

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EAST – AFNET 4 Conclusions

Early initiation of rhythm control therapy reduced cardiovascular outcomes in patients with early AF and cardiovascular conditions without affecting nights spent in hospital.

As expected, the early rhythm control strategy was associated with more adverse events related to rhythm control therapy, but the overall safety of both treatment strategies was comparable.

These results have the potential to inform the future use of rhythm control therapy, further improving the care of patients with early AF.

You can read more about the results of the EAST – AFNET 4 trial at https://www.nejm.org/doi/full/10.1056/NEJMoa2019422

EAST – AFNET 4 Acknowledgements

We thank all participating patients,

the local study teams,

the staff at AFNET and CRI,

all committee members,

and the financial supporters of the trial.