ATRIAL FIBRILLATION
NETWORK

EAST - AFNET 4

STUDIENDESIGN

Background and rationale

Even on optimal current management, patients with AF suffer stroke, acute coronary syndrome, heart failure, and cardiovascular death at a rate of approximately 5% of patients per year.

Previous trials have failed to demonstrate superiority of rhythm control using antiarrhythmic drugs over rate control in patients with established AF.

Antiarrhythmic drugs and AF ablation are safe in patients with AF and concomitant cardiovascular conditions.

An earlier initiation of rhythm control therapy and the combination of antiarrhythmic drugs and AF ablation should maintain sinus rhythm more effectively than the current, delayed approach to rhythm control.

Ruff CT, et al. *Lancet* 383:955-62 (2014)
Marijon E, et al. *Circulation* 128:2192-201 (2013)
Roy D et al. *N Engl J Med* 358:2667-77.(2008)
Carlsson J, et al. *J Am Coll Cardiol* 41:1690-6 (2003)
Van Gelder I, et al. *N Engl J Med* 347:1834-40 (2002)
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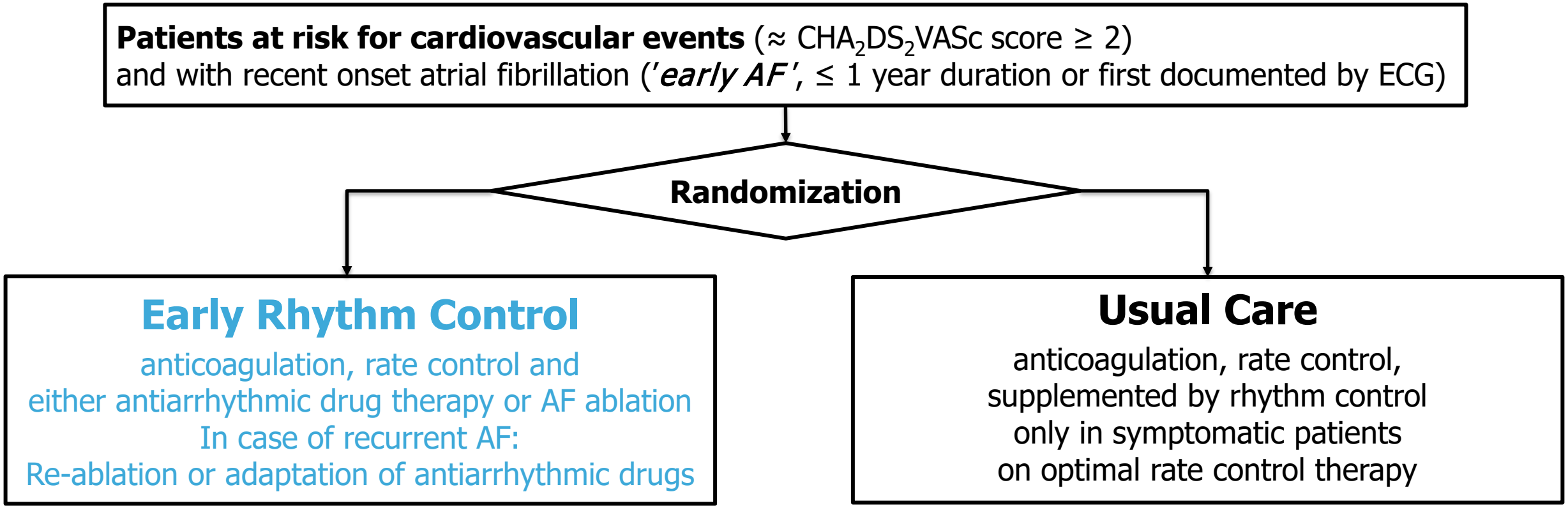
Packer DL et al. *JAMA*. 321: 1261-1274 (2019)
Willems S, et al *Eur Heart J* 40:3793-9c (2019)
Nattel S et al. *Eur Heart J* 35:1448-56.(2014)
Van Gelder IC et al. *Europace* 13:1517-25.(2011)
Hohnloser SH et al. *N Engl J Med* 360: 668-678 (2009)
Kirchhof P et al. *Eur Heart* J 30:2969-77c.(2009)

EAST – AFNET 4 Hypothesis and setting

Does early rhythm control therapy improve outcomes compared to usual care in patients with early, recently diagnosed atrial fibrillation at risk of stroke?

EAST- AFNET 4 is a multi-centre, investigator-initiated trial. Sponsor is AFNET, supported by AFNET, BMBF, DHS, DZHK, EHRA, Sanofi, St Jude Medical/Abbott.

EAST – AFNET 4 Design



therapy of concomitant cardiovascular diseases (both randomized groups)
in-person follow-up at 1 and 2 years
all patients were followed up until the end of the study

www.easttrial.org

Kirchhof P, et al. *Am H J* 166:442-448 (2013)

EAST – AFNET 4 sample size & power

PROBE design (Prospective, Randomised, Open, Blinded outcomE assessment)

Two primary outcomes

1. Composite of cardiovascular death, stroke, worsening of heart failure or acute coronary syndrome
2. Nights spent in hospital per year

20% reduction in the first primary outcome was deemed clinically relevant.

Power 80% to detect a 20% improvement in the first primary outcome, requiring 685 events.

4% alpha was spent on the first primary outcome, 1% on the second primary outcome.

An Event Review Committee blind to randomized group centrally adjudicated all events.

Sample size was estimated as 2810 patients, adjusted to 2745 patients following a planned blind analysis of event rates 42 months after enrollment of first patient.

Three interim analyses were planned and conducted by DSMB after accrual of 171 events (25%), 342 events (50%), and 514 events (75%), with corresponding alpha spending.

Kirchhof P, *et al. Am H J* 166:442-448 (2013)

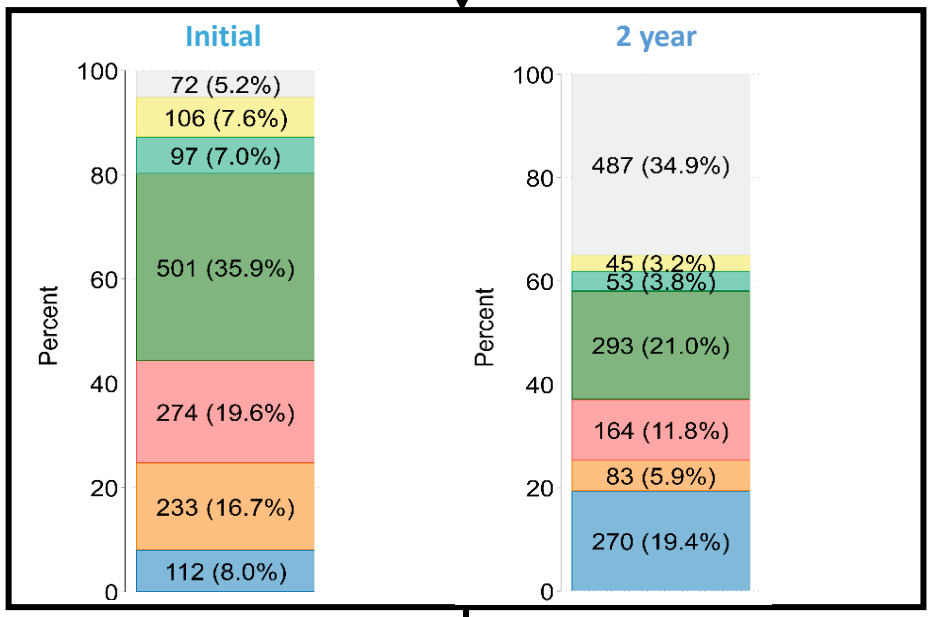
EAST – AFNET 4 CONSORT diagram

2789 patients randomized by 135 sites in 11 countries

Randomization

Early Rhythm Control (n=1,395)

Included in primary analysis n=1,395



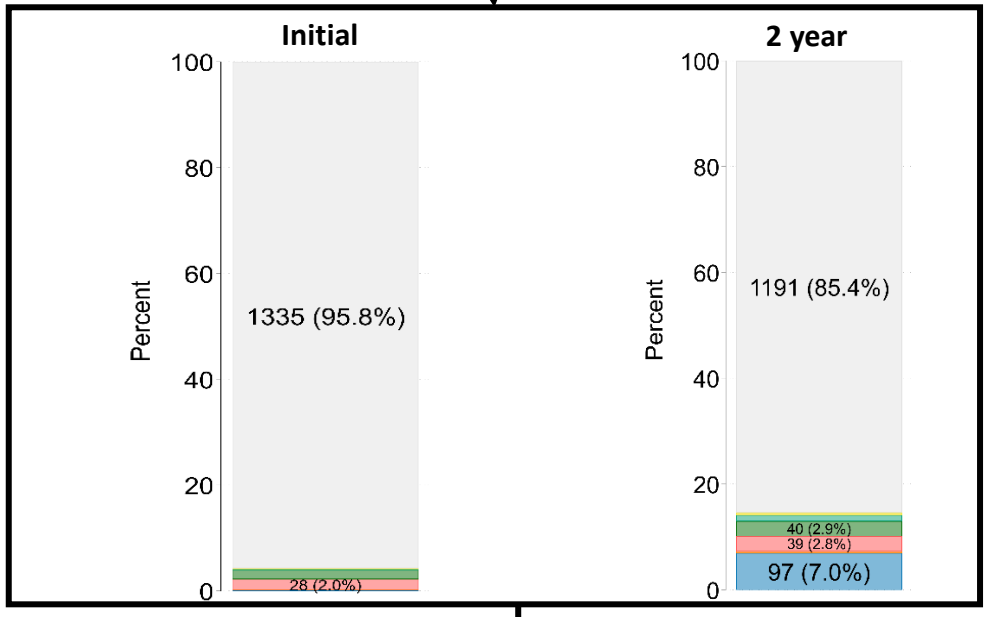
Total FU-years lost: 681/7596 (9.0%)

524 (6.9%) FU-years lost because 123 withdrew
157 (2.1%) FU-years lost because 102 were lost to FU

None
Other antiarrhythmic drug
Propafenone
Flecainide
Amiodarone
Dronedarone
AF ablation

Usual Care (n=1,394)

Included in primary analysis n=1,394



Total FU-years lost: 491/7479 (6.6%)

339 (4.5%) FU-years lost because 83 withdrew
152 (2.0%) FU-years lost because 106 were lost to FU