



Risk Factor Driven Upstream Therapy in Early Atrial Fibrillation

The Routine versus Aggressive upstream rhythm Control for prevention of Early persistent atrial fibrillation in heart failure study

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Background



- Maintenance of sinus rhythm improves AF-related symptoms
- However, maintenance of sinus rhythm is cumbersome due to atrial remodelling, caused by risk factors and diseases underlying AF, and AF itself
- Recognition of the consequences of atrial remodelling has led to the notion that early intervening may prevent AF progression
- Risk factor driven upstream therapy refers to interventions that aim to modify the atrial substrate, and has a favourable effect on risk factors and diseases underlying AF



Hypothesis and trial design



- **Hypothesis:**

Risk factor driven upstream therapy is superior to conventional therapy for maintenance of sinus rhythm in patients with early persistent AF and HF

- **RACE 3 trial design:**

- Prospective, randomized, open label, superiority trial
- Investigator-initiated
- Multicenter: 14 sites in The Netherlands and 3 in United Kingdom
- Enrolment between 2009 and 2015
- 1 year follow-up

Flowchart

Patients with early persistent AF and HF

Causal treatment of AF and HF

Risk factor driven upstream

Conventional

ECV after 3 weeks

Guideline-recommended rhythm and rate control

7-day Holter at 1-year

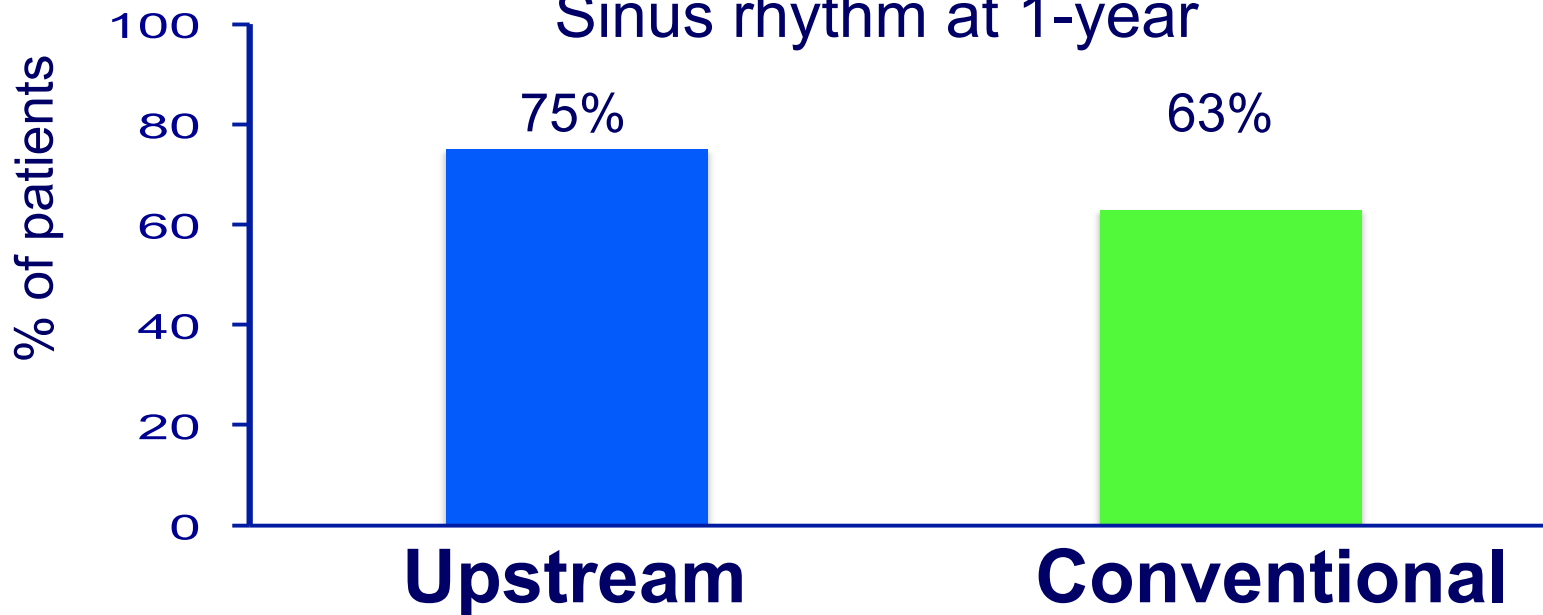
Upstream therapy consists of:

- 1) Mineralocorticoid receptor antagonist
- 2) Statin
- 3) ACE-inhibitors and/or angiotensin-receptor blockers
- 4) Cardiac rehabilitation:
 - physical activity
 - dietary restrictions



Primary endpoint

Sinus rhythm at 1-year



Odds ratio

1.765

Lower 95% confidence limit

1.115

Superiority hypothesis was proven (p=0.021)



Conclusion and implication



- The RACE 3 study shows that risk factor driven upstream therapy, including treatment of risk factors and change of lifestyle, is effective and feasible to improve maintenance of sinus rhythm in patients with early persistent AF and HF
- The effect of upstream therapy on reduction of risk factors and cardiovascular diseases, instead of atrial remodeling, was favourable



RACE 3 study organisation



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