Atrial Fibrilation Medical Therapy

Treating for symptoms

+ Rhythm control strategy
+ Rate control strategy

Rhythm control strategy

+ Sotalol
+ Flecainide (Propafenone)
+ Amiodarone (Dronedarone)

Sotalol and Amiodarone

- 2000
  - Canadian trial of atrial fibrillation – open label
- 2005
  - SAFE-T trial – double-blind

What sort of patients are we talking about?

Canadian Trial

+ PAROXSYMAL and PERSISTENT in the last 6 months
+ Required to have ECG documented AF lasting > 10 minutes but < 6 months
+ Their definition of persistent – "if in the opinion of the investigator more than 50% of episodes required intravenous drug therapy or electrical cardioversion"

SAFE-T Trial

+ PERSISTENT AF
+ ECG documented AF ≥ 72 hours, still had AF at randomization
+ Initially excluded pts with AF duration > 12 months, subsequently rescinded
+ 10% screened patients enrolled

Canadian Trial

Canadian Trial

+ Amiodarone 10 mg/kg x 14 days → 300mg → 200mg

+ Sotalol 320 mg or 240 mg or 160 mg

+ Propafenone 600 mg or 450 mg

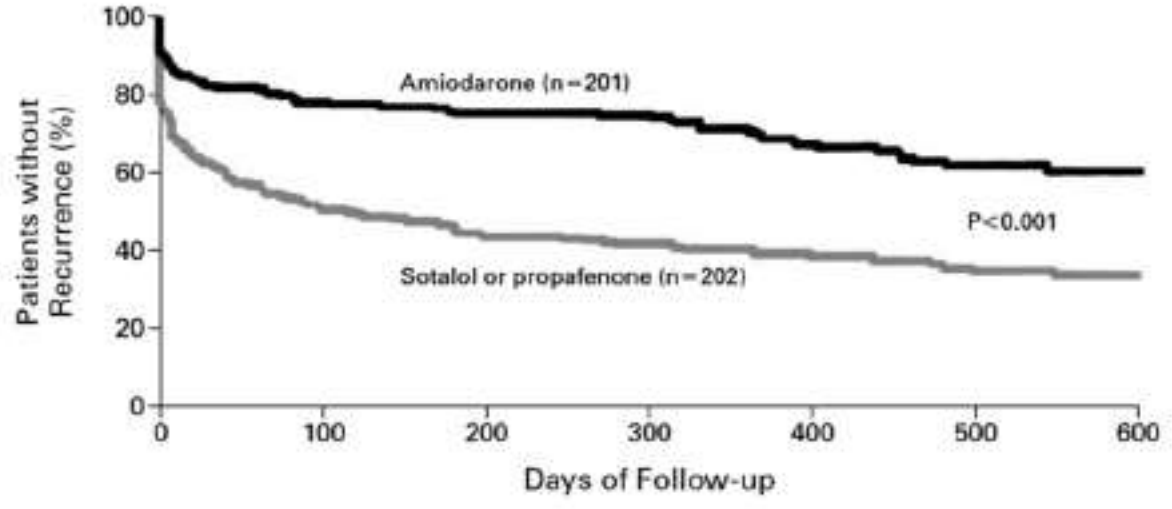
SAFE-T Trial

+ Amiodarone - 800mg x 14 days, 600mg x 14 days, 300mg 1 year ⟶ 200mg
+ Sotalol - 160mg x 7 days, then 320mg

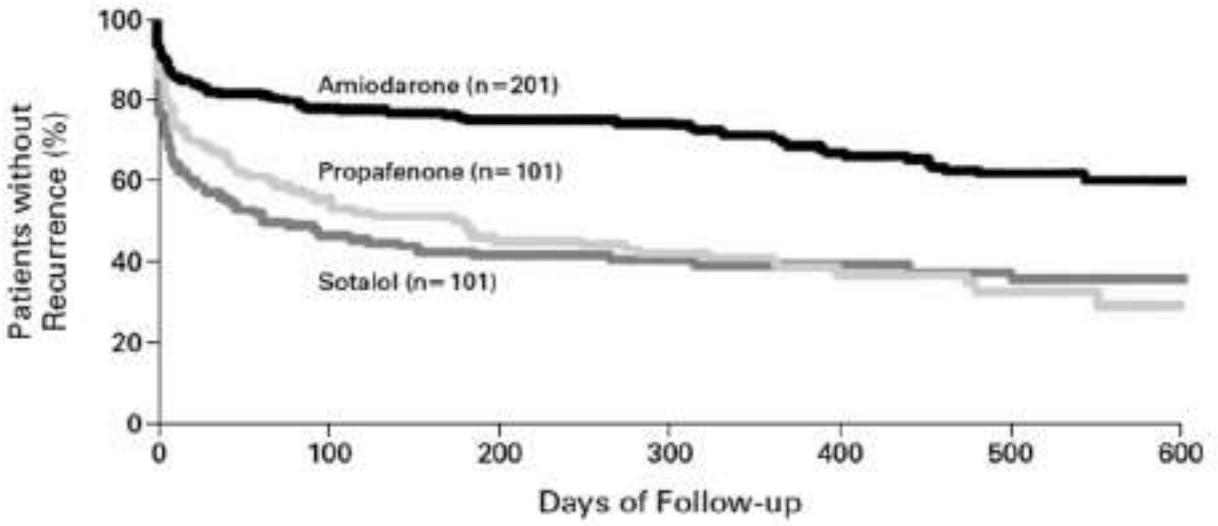
Trial	Mean daily dose (mg) at 12 months	Duration followup	Withdrew (%)	Mortality ratio
CANADIAN		468 ± 150 days		
Amiodarone	186 ± 48		34	9 deaths
Sotalol/Propafenone	224 ± 83		46	8 deaths
SAFE-T		1 - 4.5 years		
Amiodarone	(200)		(16)	2.0 (p=0.11)
Sotalol	(160)		(15)	1.8 (p=0.20)
Placebo			(20)	

Trial	Drug	Mean time to AF recurrence (days)	Probability of SR at 12 months
CANADIAN	Amiodarone Sotalol/Propafenone	>468 98	69% 39%
SAFE-T	Amiodarone Sotalol Placebo	487 74 6	52% 32% 13%

Canadian Trial



Canadian Trial



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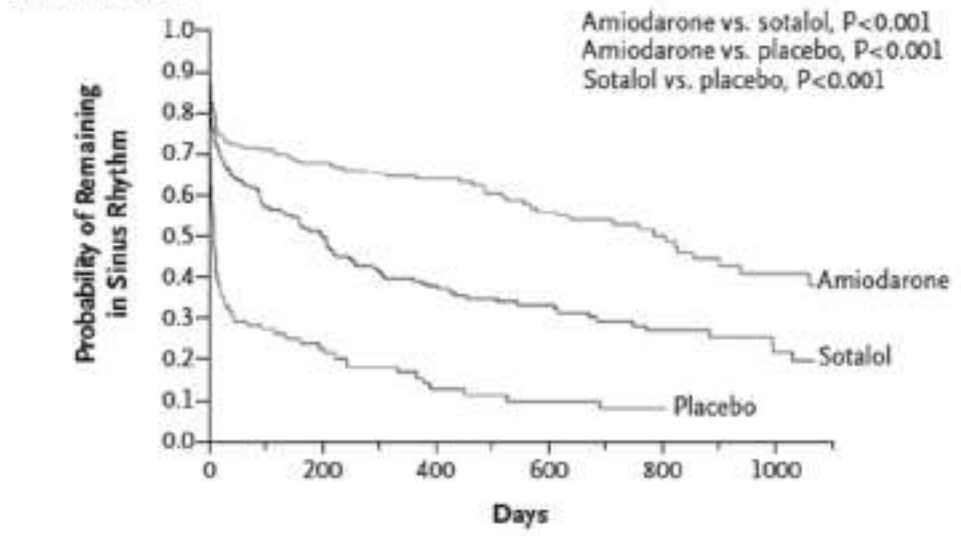
SAFE-T



No. at Risk						
Amiodarone	206	131	98	60	38	18
Sotalol	195	97	61	38	21	13
Placebo	90	21	11	8	5	2

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What can we conclude?

+ Amiodarone is the most effective drug for maintaing sinus rhythm – but we are reluctant to use it
+ There is some lingering concern about the safety of medical treatment
+ The comparative data for class IC drugs is inadequate

Treating for symptoms:

Rate-control strategy

+ AFFIRM
+ RACE II

Affirm

PRIMARY OBJECTIVE:

+ Antiarrhythmic drug therapy administered to maintain normal sinus rhythm has no effect on total mortality when compared with therapy that controls the heart rate.

N Eng J Med 2002; 347 : 1825-33

Target population ≥ 1 risk factors for stroke

+ Age ≥ 65 years
+ Hypertension
+ Diabetes
+ CHF
+ TIA

CVA
LA ≥ 50 mm
FS < 25%
EF < 0.40

What is 'Adequate' Rate control?

AFFIRM TARGET

+Resting rate <80 bpm and rate <110 bpm during a 6 min walk

OR

+Average heart rate <100 bpm on a 24 hr Holter monitor with no rate >110% age predicted heart rate

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N Engl J Med 2002;347:1834-50

Results

Rhythm Group

% Sinus at Follow-Up

1 Year	82
3 Years	73
5 Years	63

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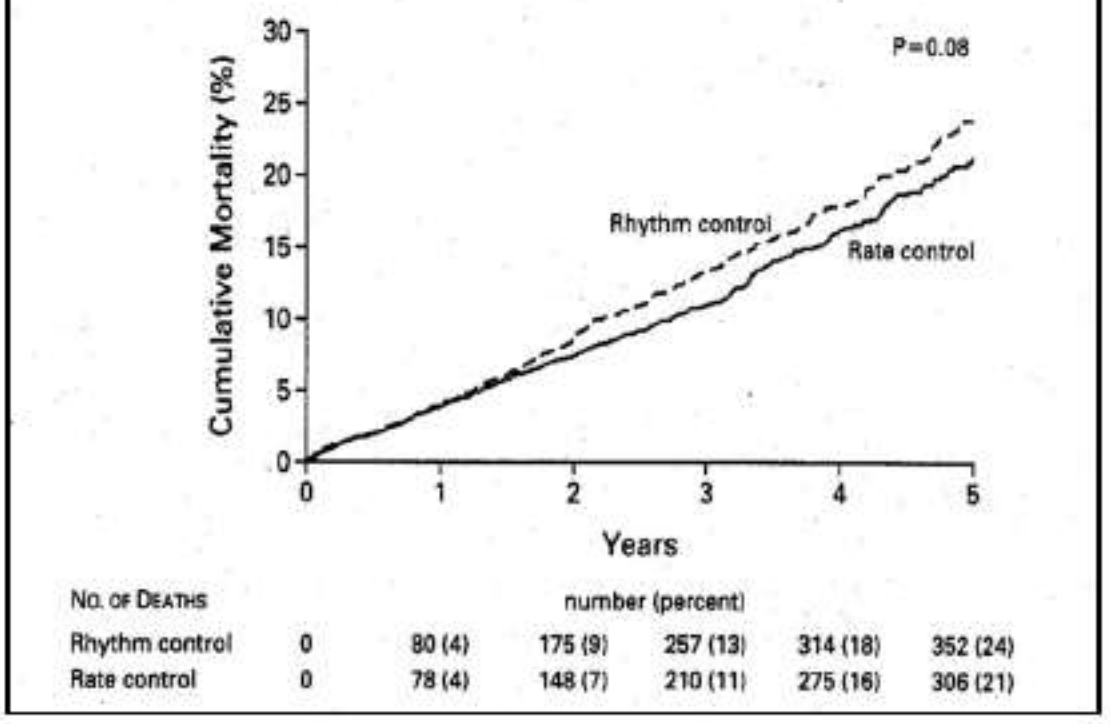

No. of Deaths		number (percent)				
Rhythm control	0	80 (4)	175 (9)	257 (13)	314 (18)	352 (24)
Rate control	0	78 (4)	148 (7)	210 (11)	275 (16)	306 (21)

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Conclusions

+ Rate control in older people is okay.

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RACE II

+ Prospective, multicentre (33)
+ Randomized
+ Open label
+ Recruiting January 2005 – June 2007

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Targets

+ Lenient Control Strategy
  + Resting HR < 110 bpm
+ Strict Control Strategy
  + Resting HR < 80 bpm
  + Exercise: HR < 110 bpm at 25% of maximal time bicycle exercise
  + Holter: after HR targets met

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Van Gelder, I.C. et al, NEJM 2010

Observations

+ Low-risk study population
+ < 20% pts had an EF ≤ 40%
+ 70% controlled ≤ 1 agent
+ Very little Amiodarone used

Results

	Lenient N=311	Strict N=303
Mean HR – resting	93	76
1 Year	86	75
2 Year	84	75
End	85	76
Met HR target	87%	53%

Results

	Lenient	Strict
Composite Endpoint %	12.9	14.9
All cause mortality %	5.6	6.6
Symptoms %	45.6	46

p = NS

Conclusions

+ The optimal target for a rate control strategy remains incompletely defined

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Protecting the left ventricle

Case Study

+ 62 yr old man - recent slight effort breathlessness
+ Physically fit, regular yoga, weight training, sailing
+ Moderate alcohol intake
+ In AF with uncontrolled heart rate - ↑ venous pressure
+ Echo - severe global systolic impairment, EF 23%
+ LA mildly enlarged (27 cm2), mod/severe functional MR
+ Mild RV impairment, moderate/severe tricuspid regurgitation

Case Study

+ Rate controlled with metoprolol CR 118.75 mg and digoxin 0.25 mg
+ Warfarinised and ACE inhibitor started
+ TOE guided cardioversion to sinus rhythm 6 wks after presentation
+ Normal LV systolic function, normal LA size and absent MR repeat echo 12 wks post cardioversion
+ Remains in sinus rhythm 6 mths later on no specific treatment

Conclusion

+ The true incidence of rate-related cardiomyopathy is uncertain and there is likely variable patient susceptibility

Final thoughts

+ Medical treatment for atrial fibrillation is unsatisfactory