AMIODARONE

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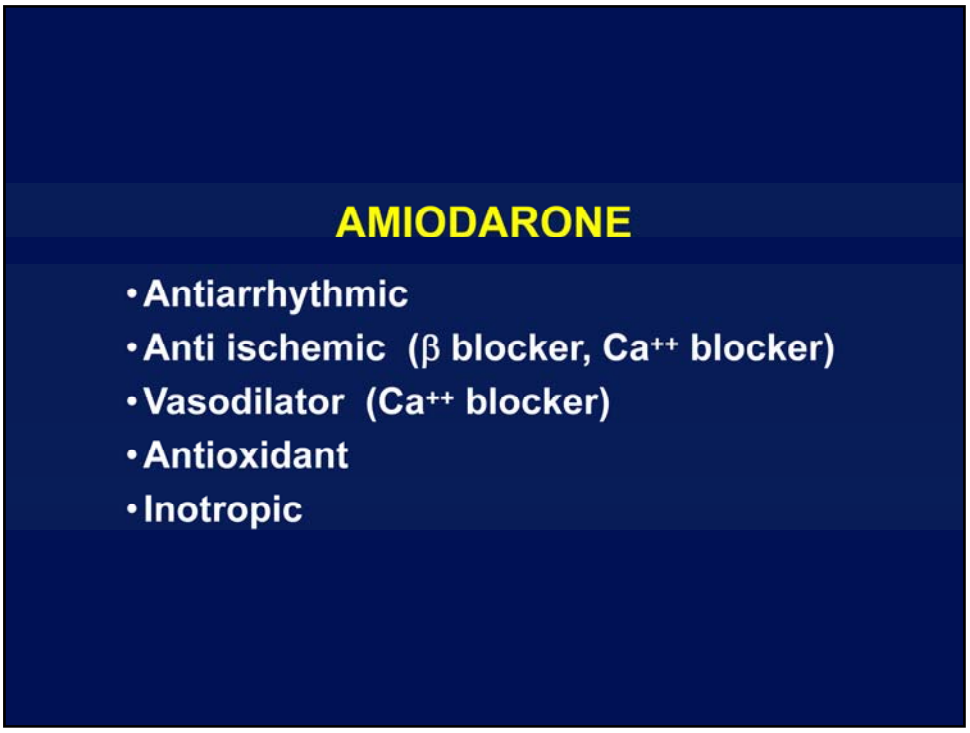
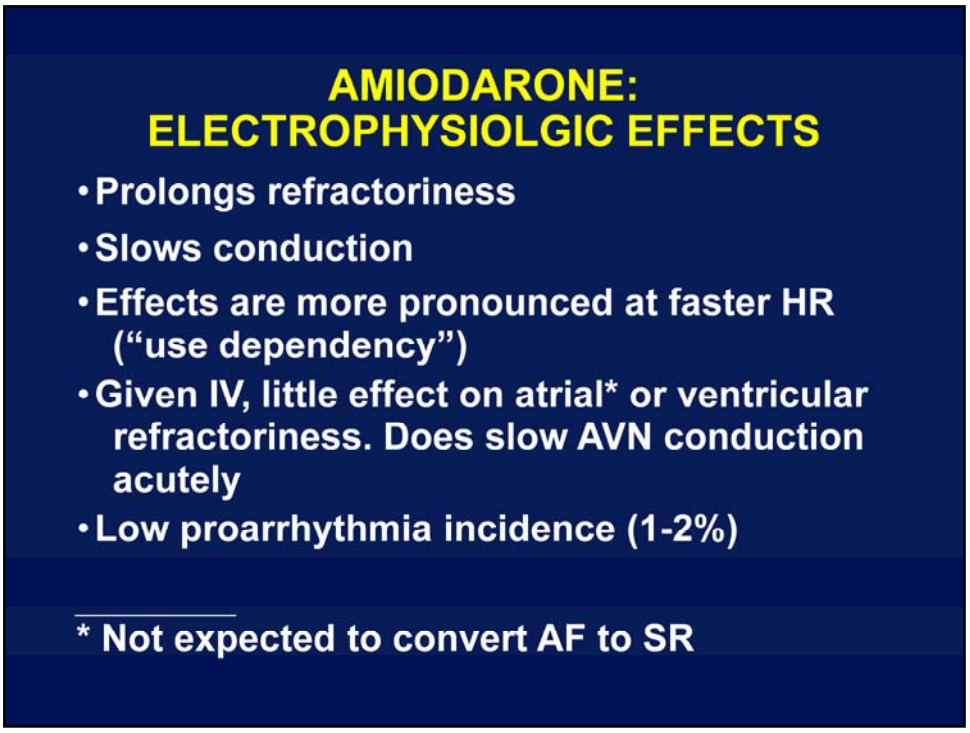
UCSF

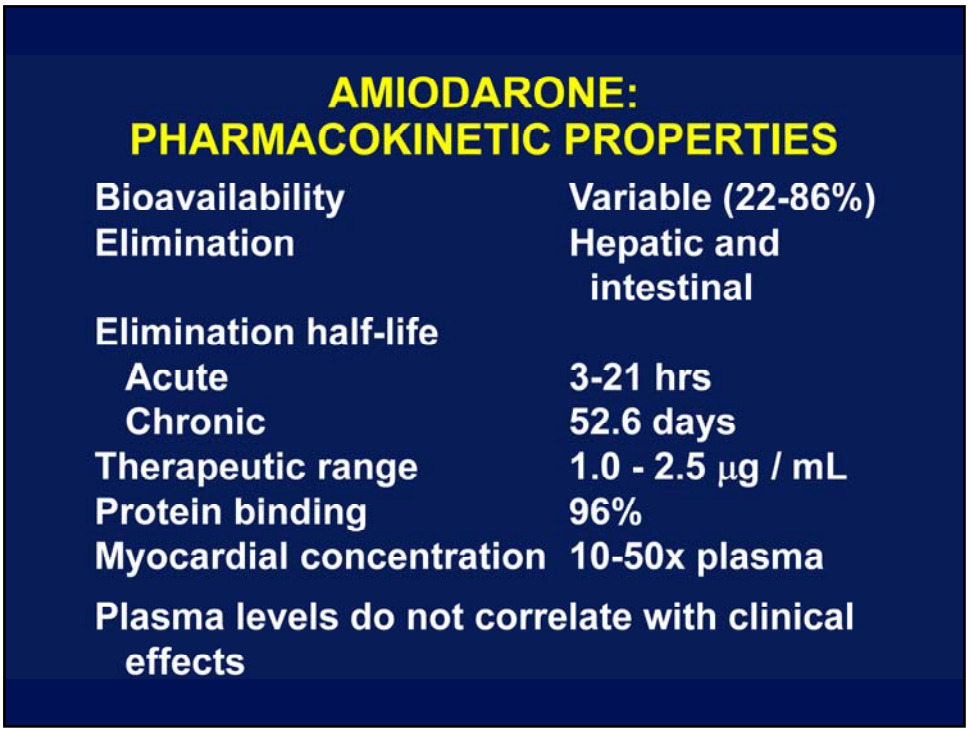
DISCLOSURES: NONE


AMIODARONE
•Antiarrhythmic
•Anti ischemic (β blocker, Ca++ blocker)
•Vasodilator (Ca++ blocker)
•Antioxidant
•Inotropic

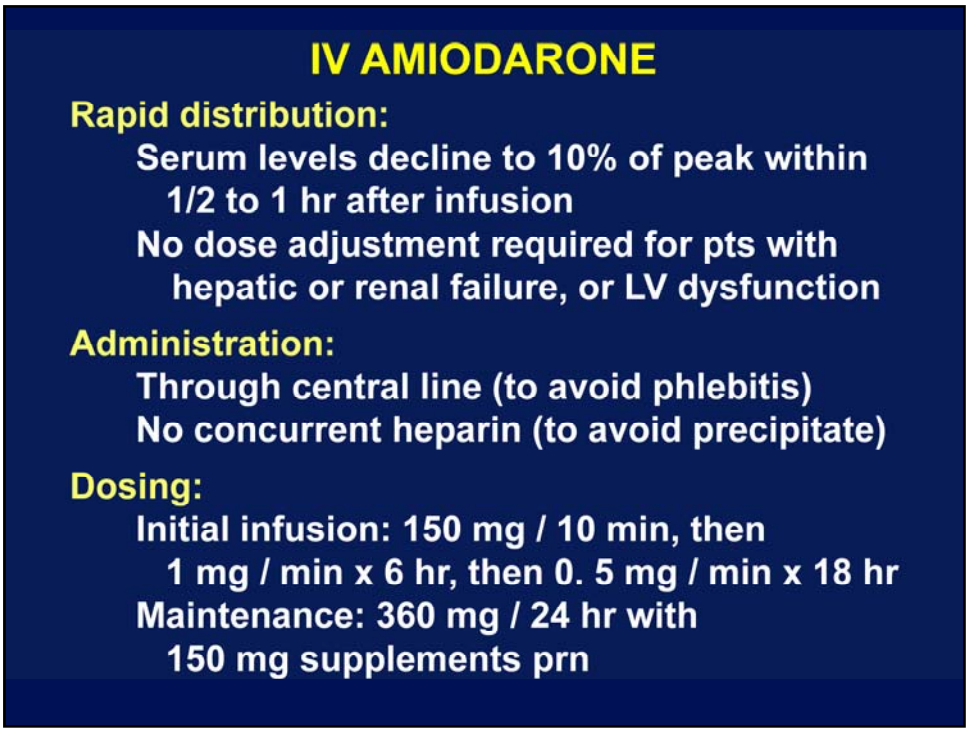
AMIODARONE



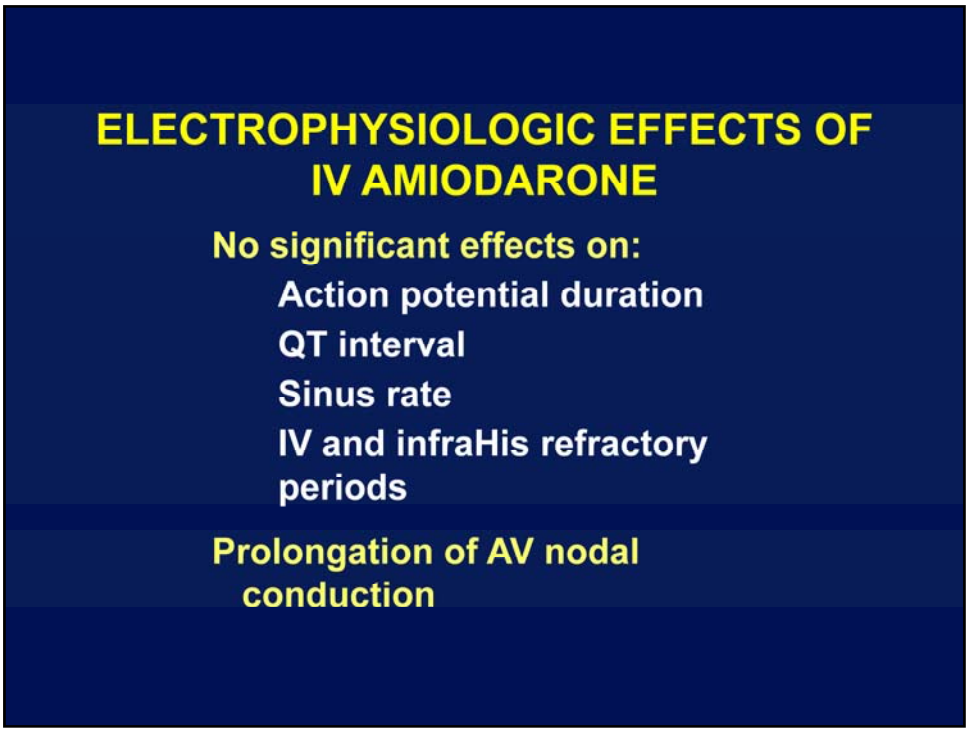
AMIODARONE: ELECTROPHYSIOLGIC EFFECT



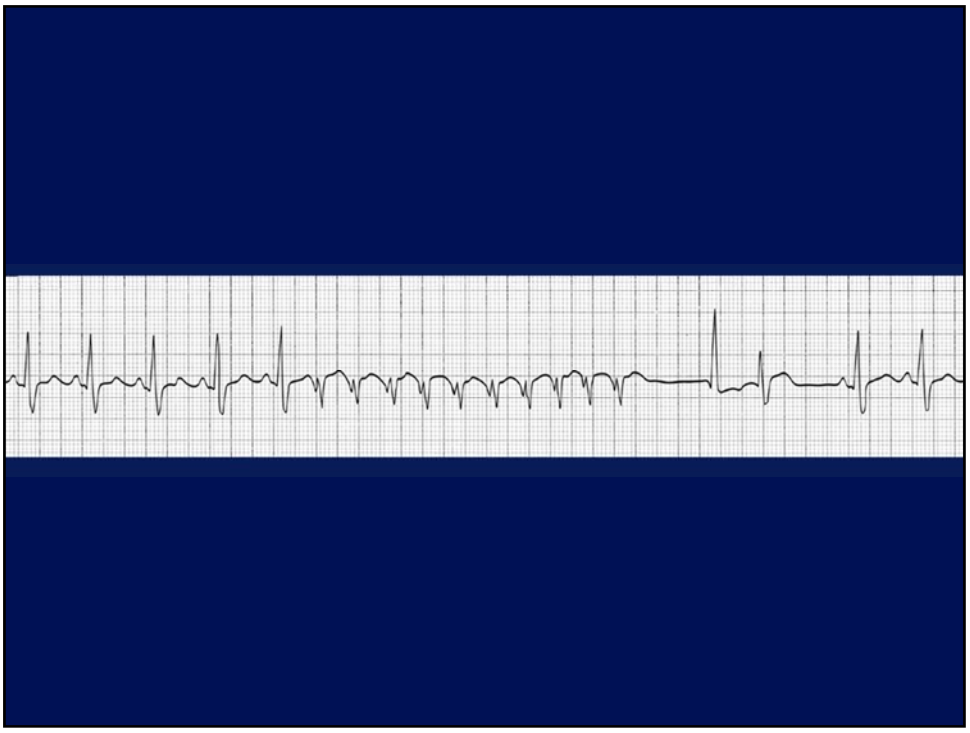
AMIODARONE: PHARMACOKINETIC PROPERTIES



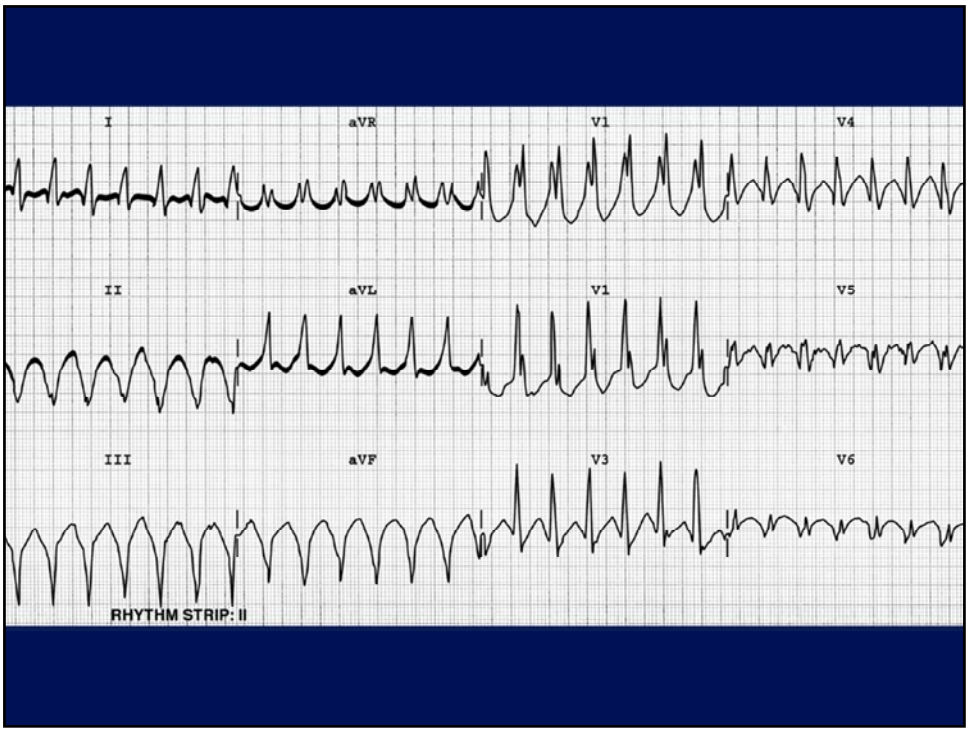
IV AMIODARONE



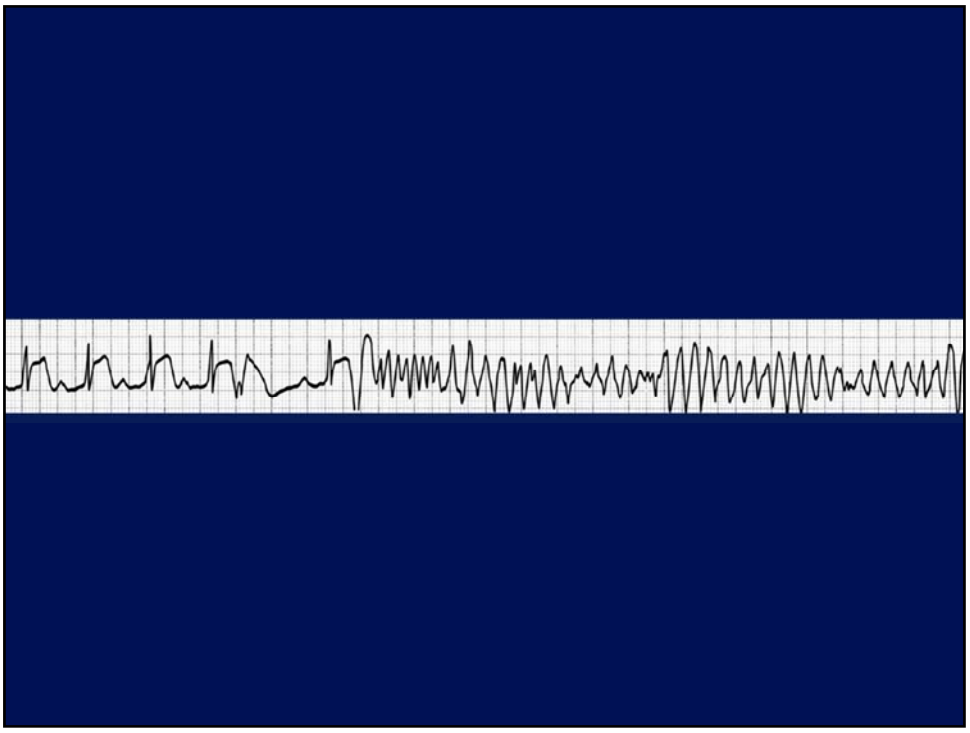
- **ELECTROPHYSIOLOGIC EFFECTS OF IV AMIODARONE**



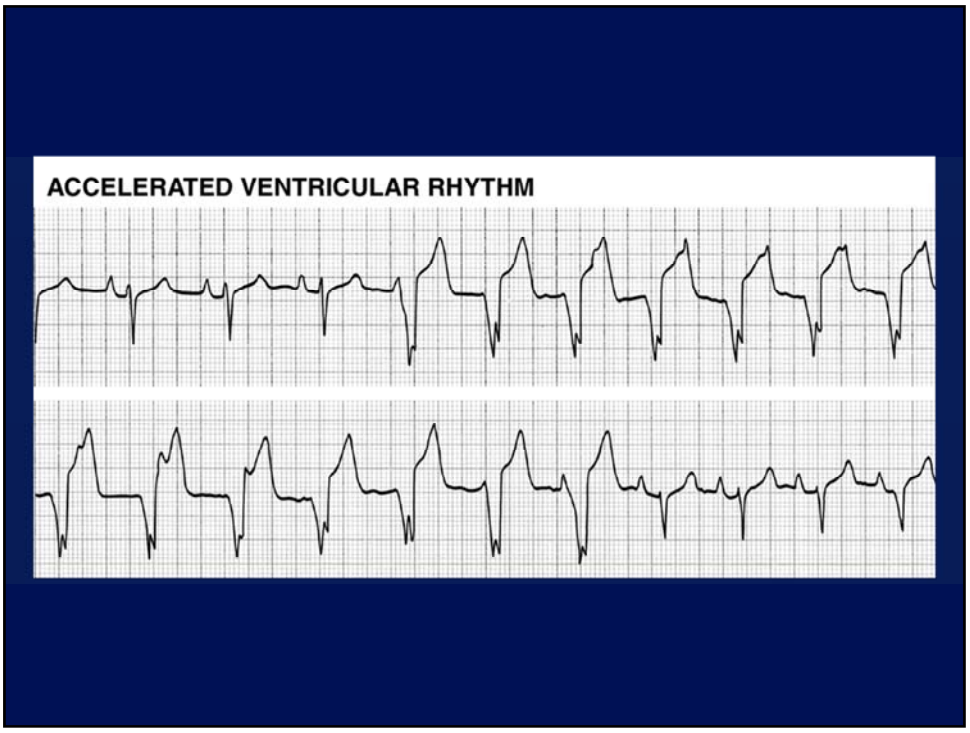
ecg



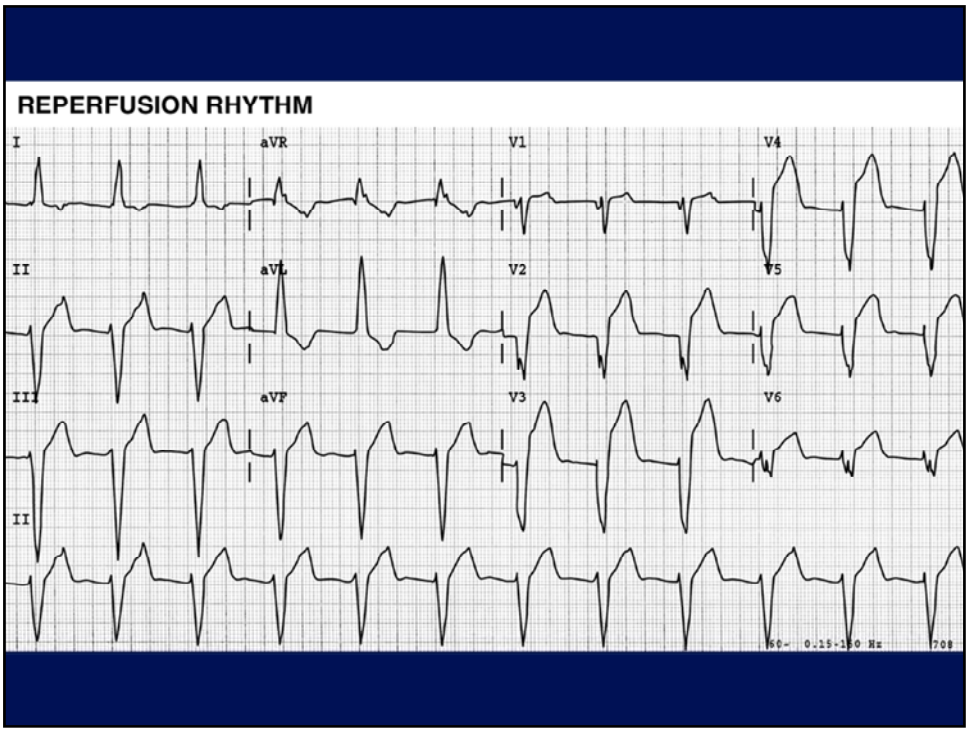
- VT Path 1



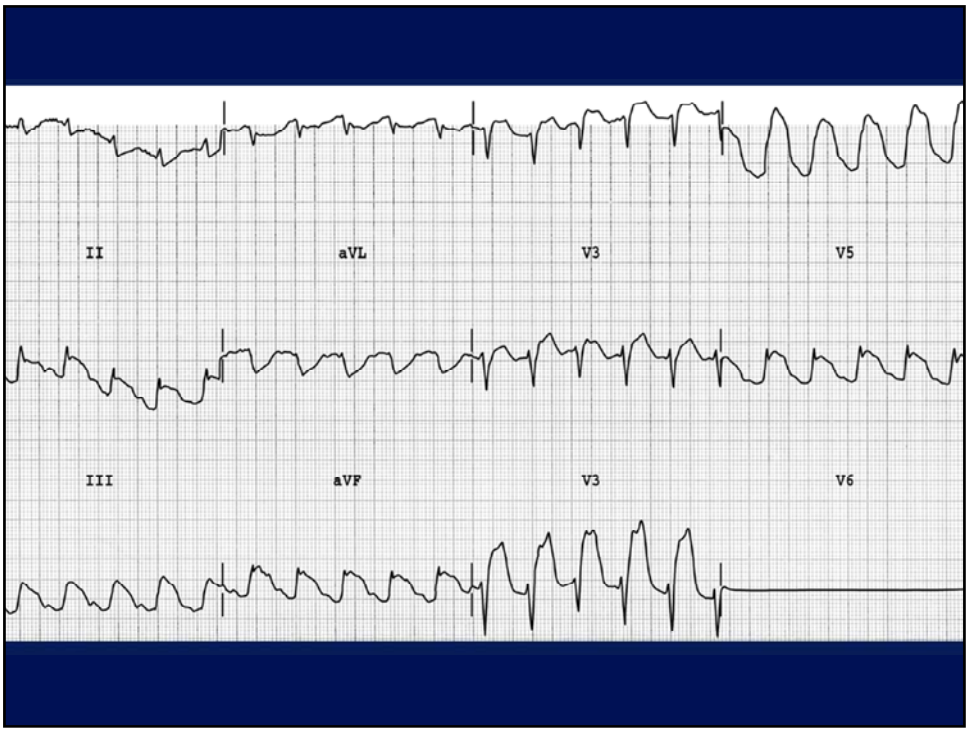
- Brady-dependant polymorphic VT



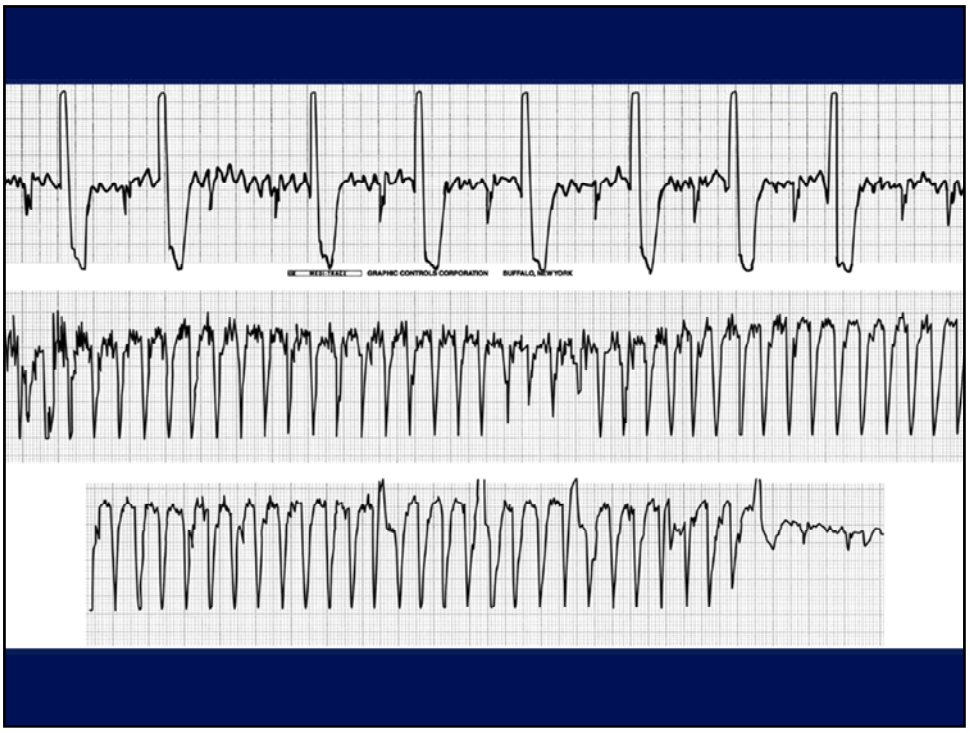
- Slow VT - Reperfusion



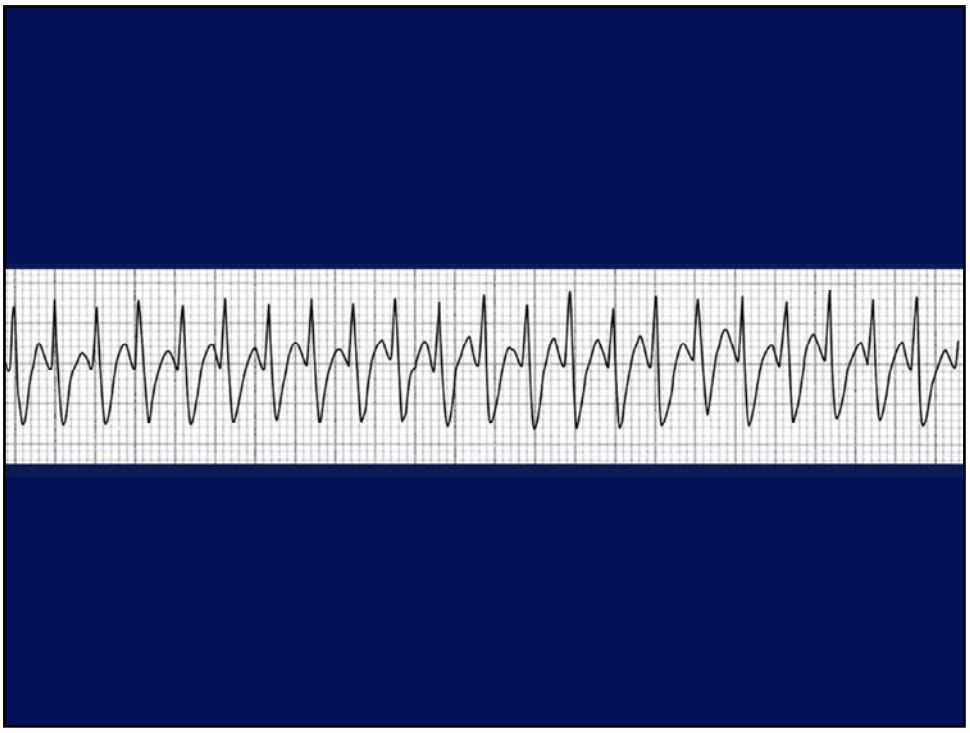
- Post PA AVR Ant. MI



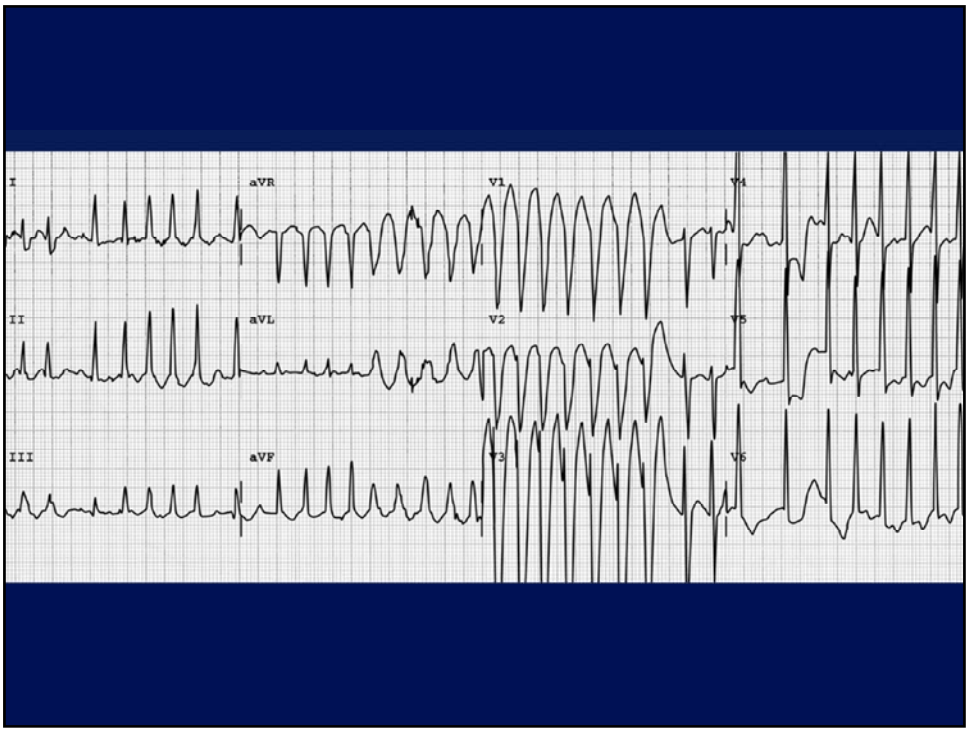
- ACUTE MI, NOT VT



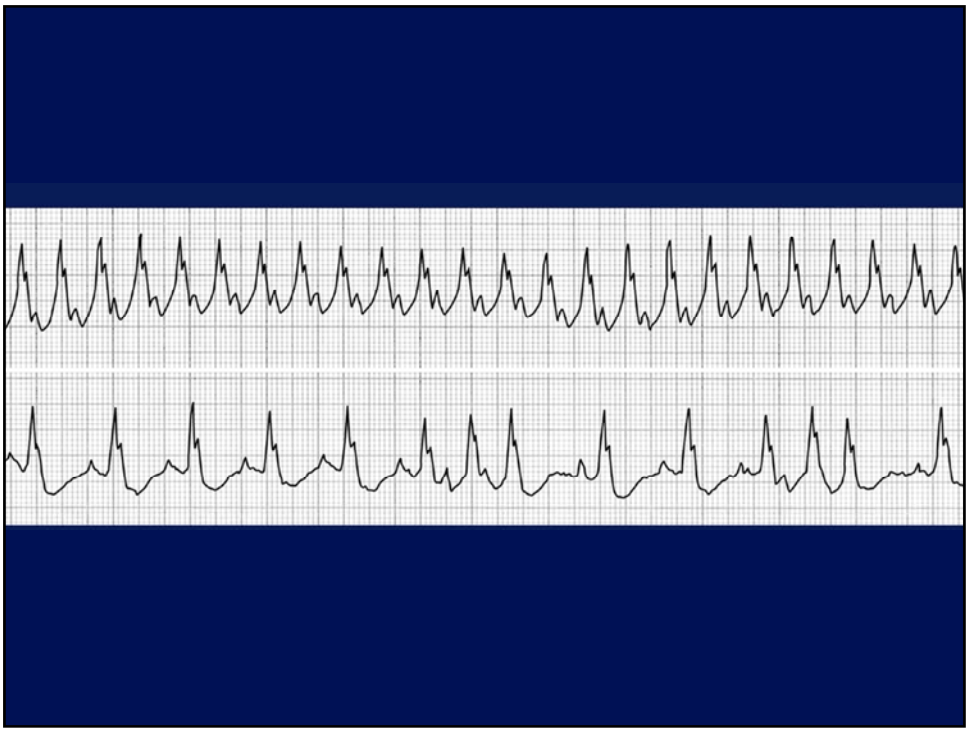
- CHEST PT, NOT VT



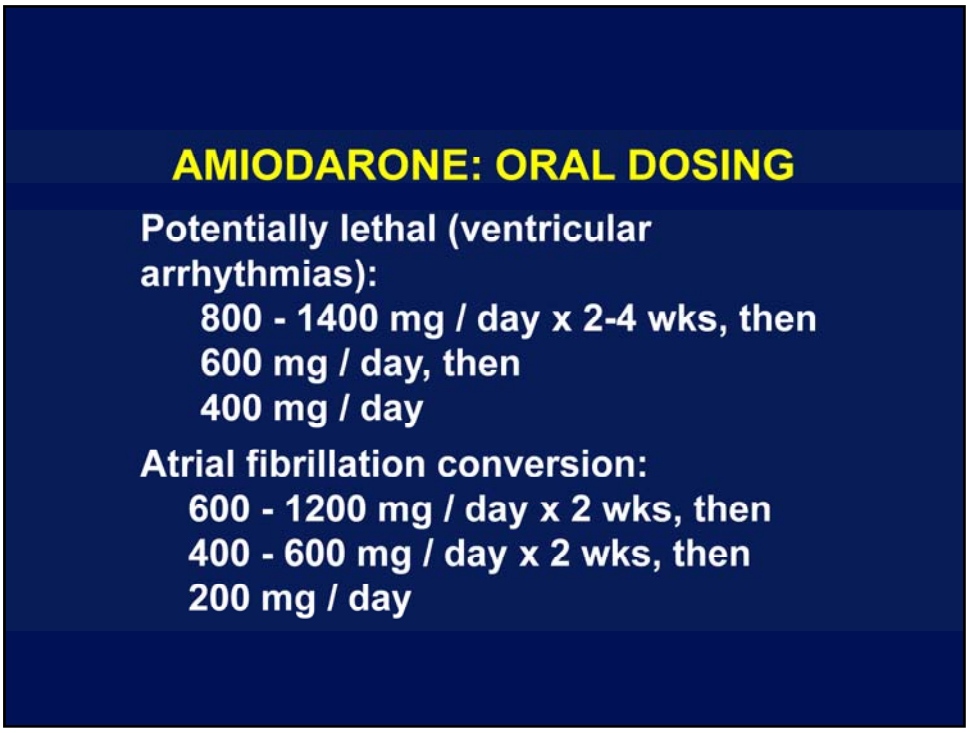
- FLUTTER 1:1



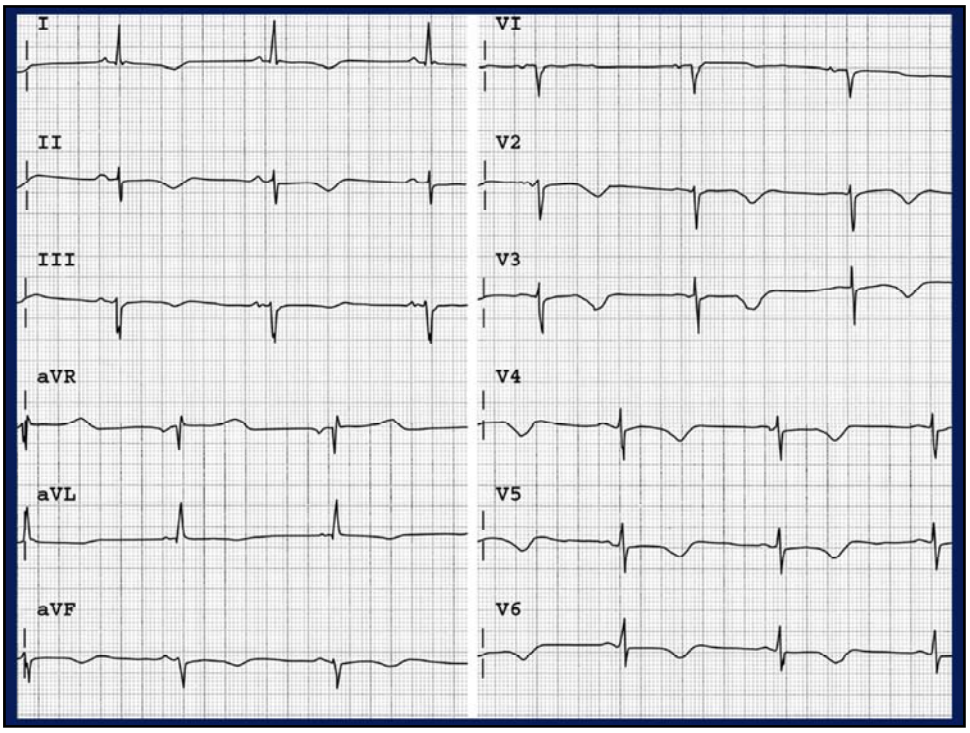
- AF, RATE=DEP, IV ABERRATION - NOT WPW

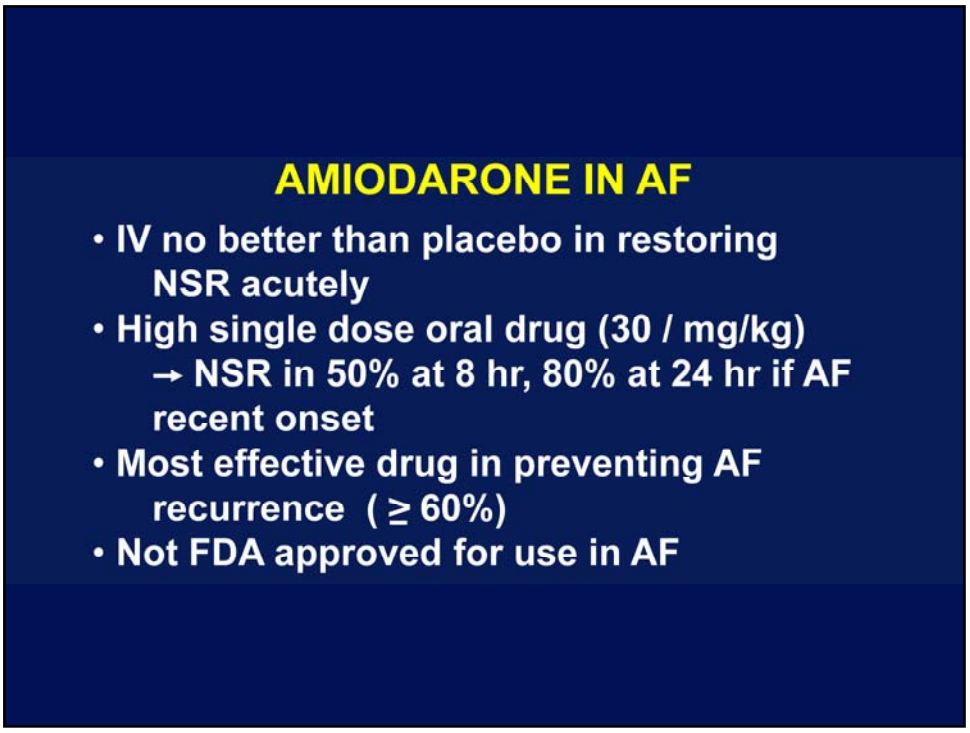


- AAT RESEMBLING VT



- AMIODARONE: ORAL DOSING


I
II
III
aVR
aVL
aVF
VI
V2
V3
V4
V5
V6

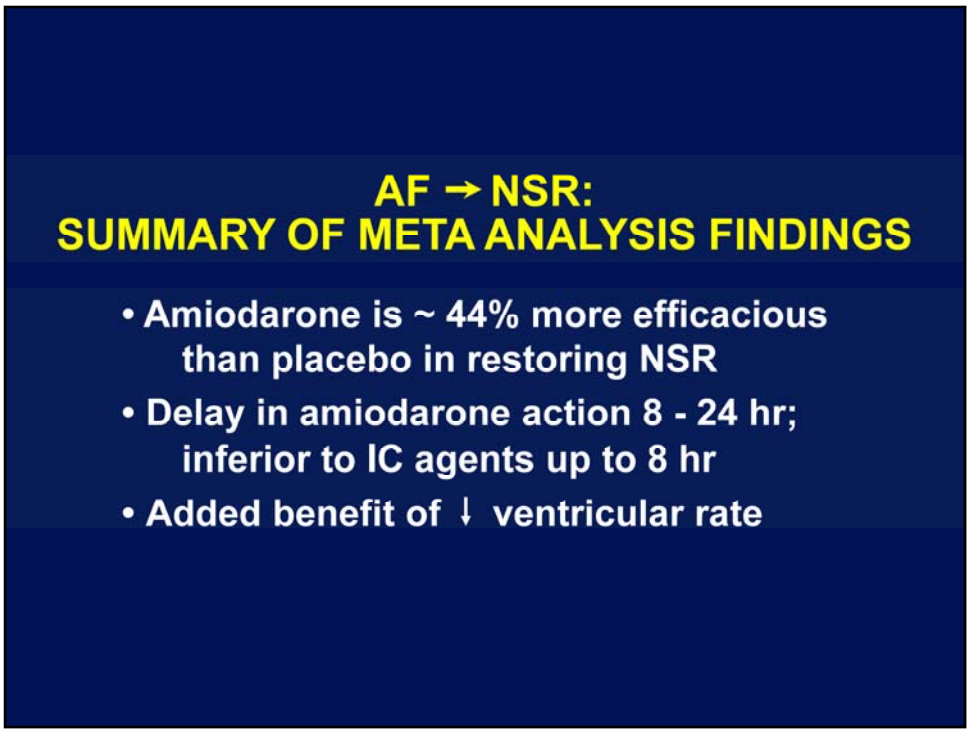


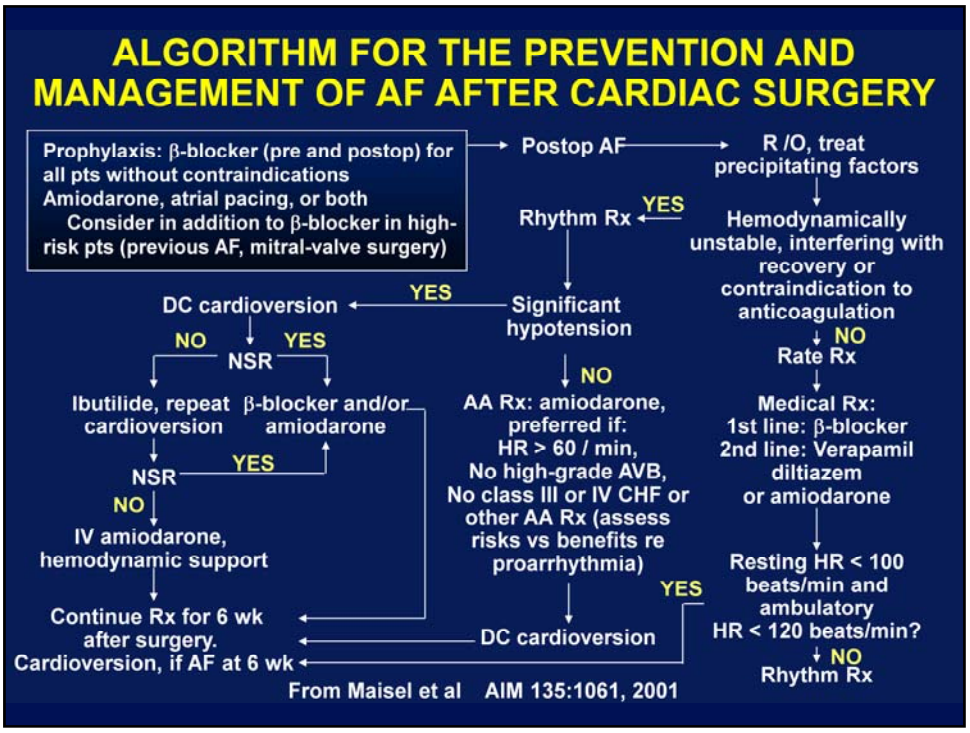
- AMIODARONE IN AF

META-ANALYSIS OF AMIODARONE vs PLACEBO AND IC AARx IN AF OF ≤ 7 DAYS' DURATION

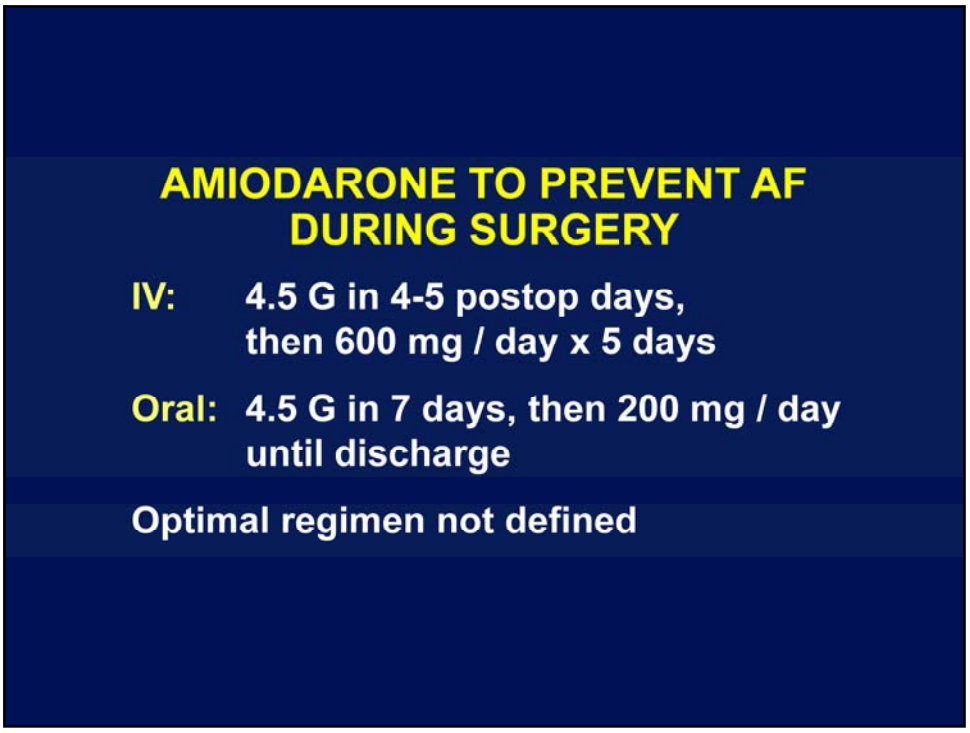
	NSR	1 - 2 h	6 - 8 h	24 h
Amio vs placebo		P = NS	< .02	< .001
IC vs Amio		P < .001	< .001	NS

Chevalier et al JACC 1.5.03
N = 595 RCT placebo
N = 579 RCT IC
Postop AF, excluded most drugs IV

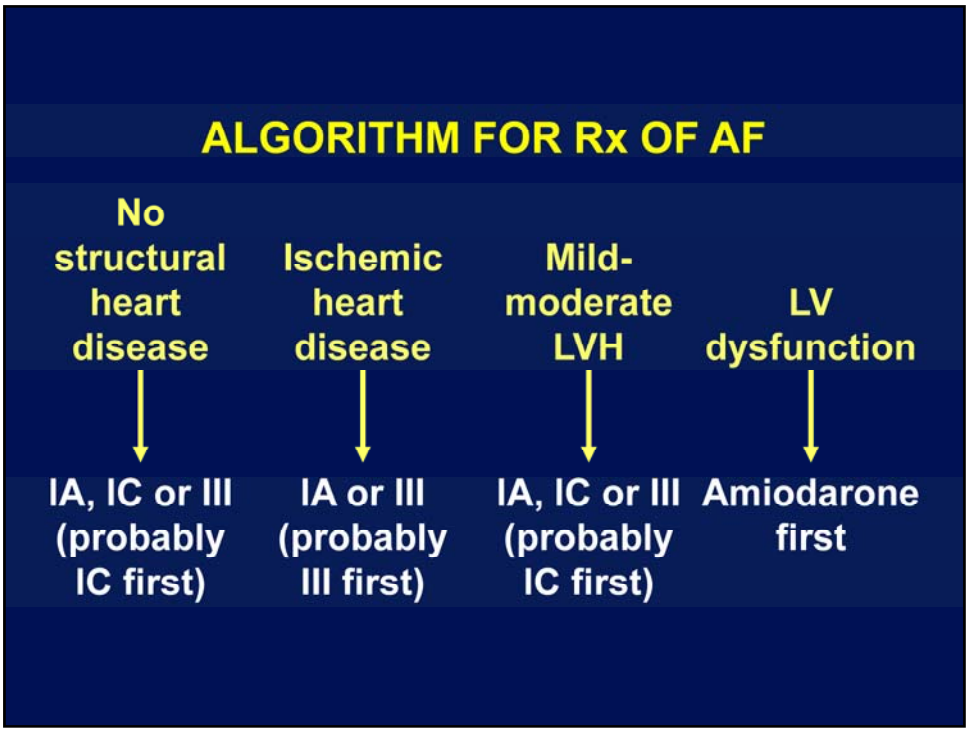

AF → NSR:
SUMMARY OF META ANALYSIS FINDINGS
• Amiodarone is ~ 44% more efficacious than placebo in restoring NSR
• Delay in amiodarone action 8 - 24 hr; inferior to IC agents up to 8 hr
• Added benefit of ↓ ventricular rate



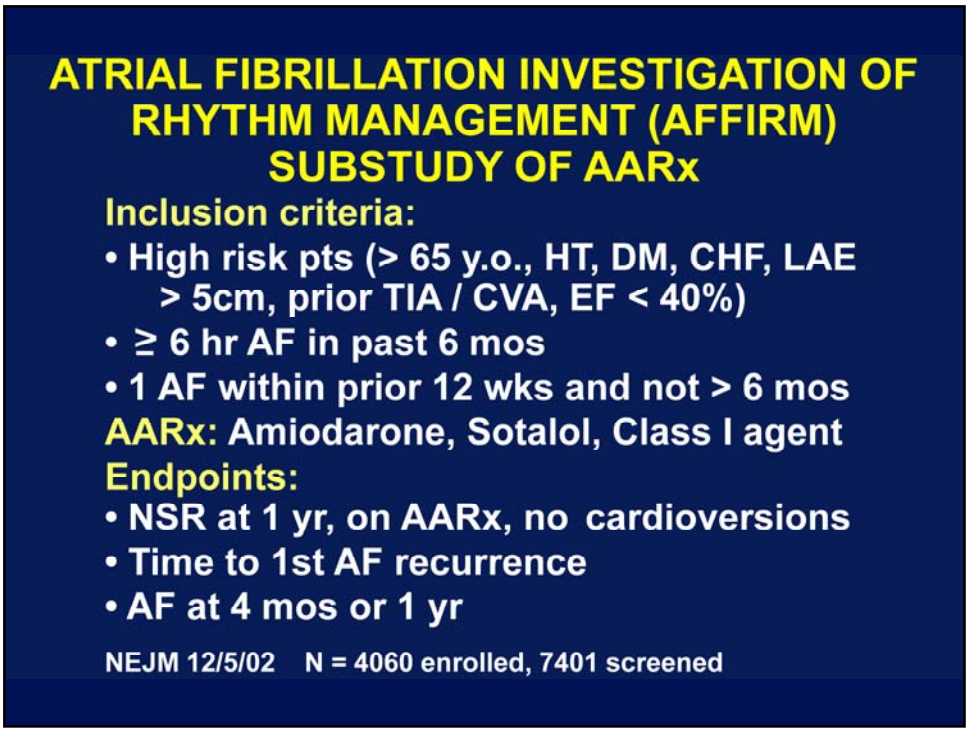
- ALGORITHM FOR THE PREVENTION AND MANAGEMENT OF AF AFTER CARDIAC SURGERY



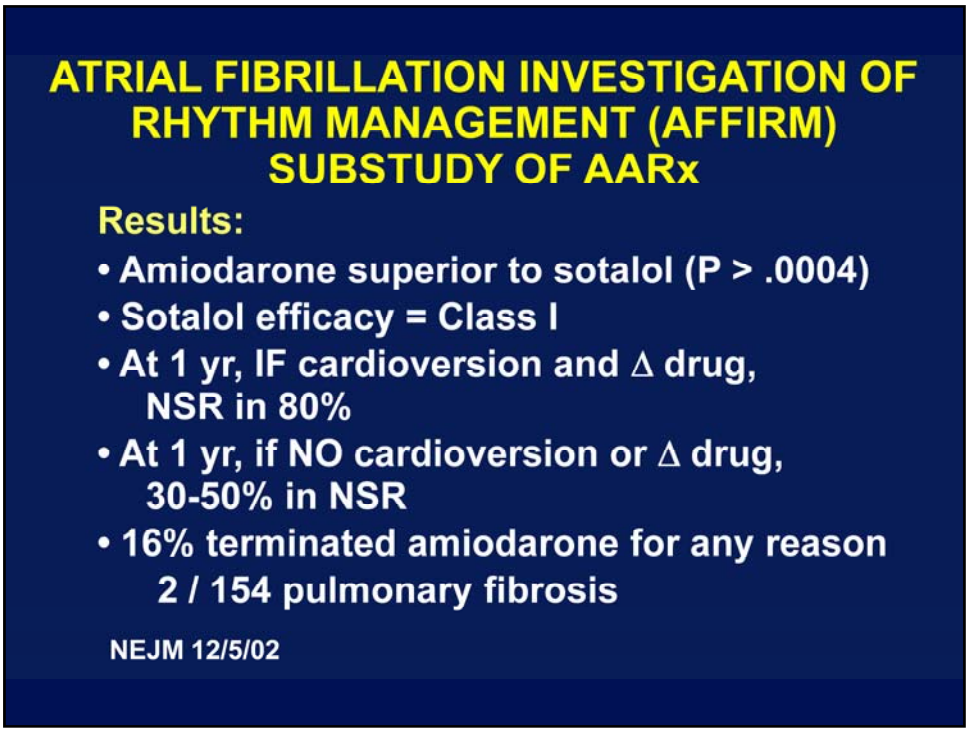
- AMIODARONE TO PREVENT AF DURING SURGERY



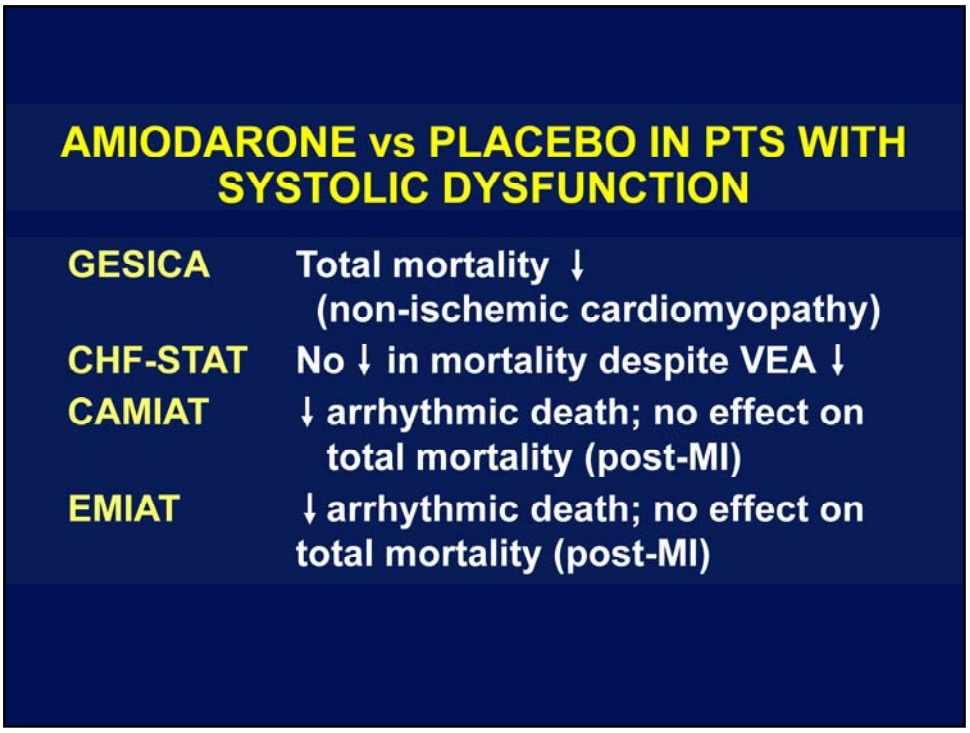
- ALGORITHM FOR Rx OF AF



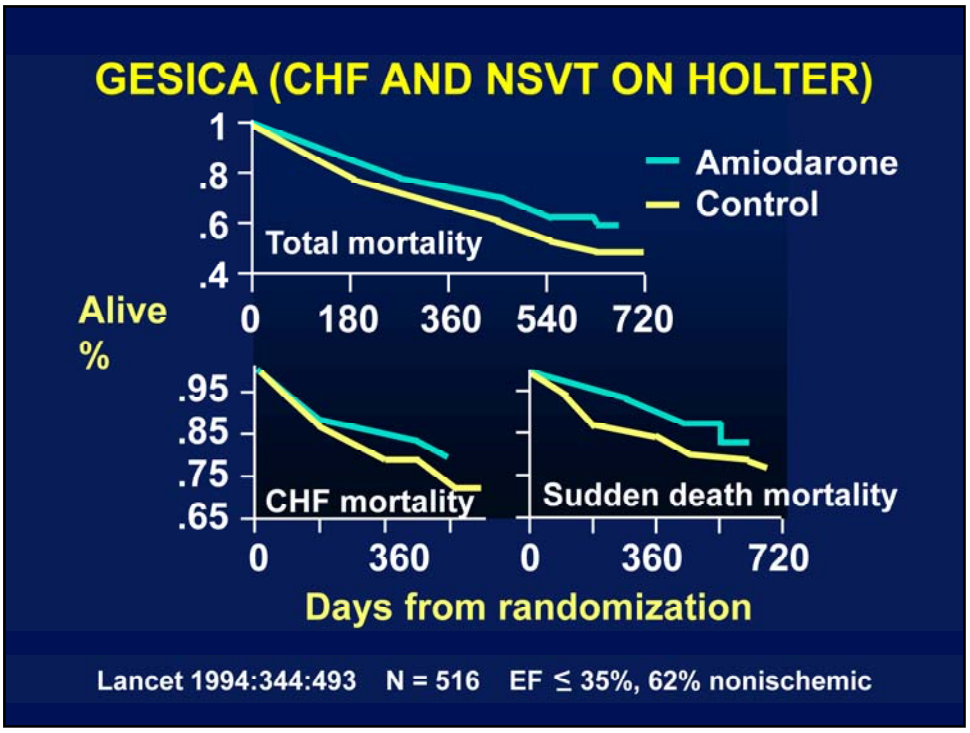
- ATRIAL FIBRILLATION INVESTIGATION OF RHYTHM MANAGEMENT (AFFIRM) SUBSTUDY OF AARx



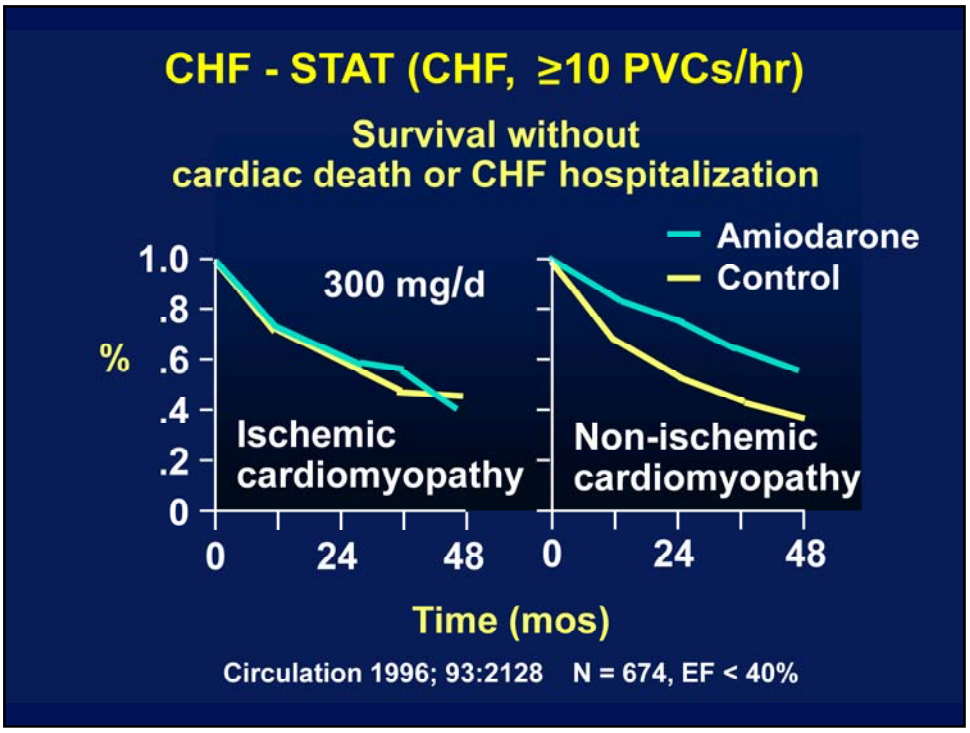
- ATRIAL FIBRILLATION INVESTIGATION OF RHYTHM MANAGEMENT (AFFIRM)SUBSTUDY OF AARx



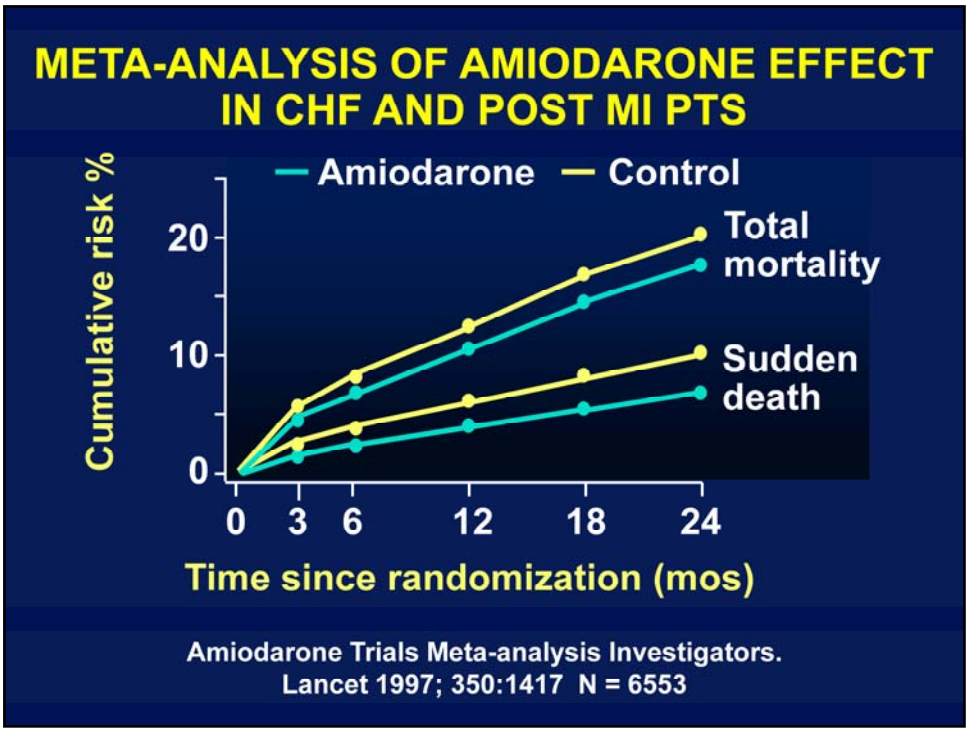
- AMIODARONE vs PLACEBO IN PTS WITH SYSTOLIC DYSFUNCTION



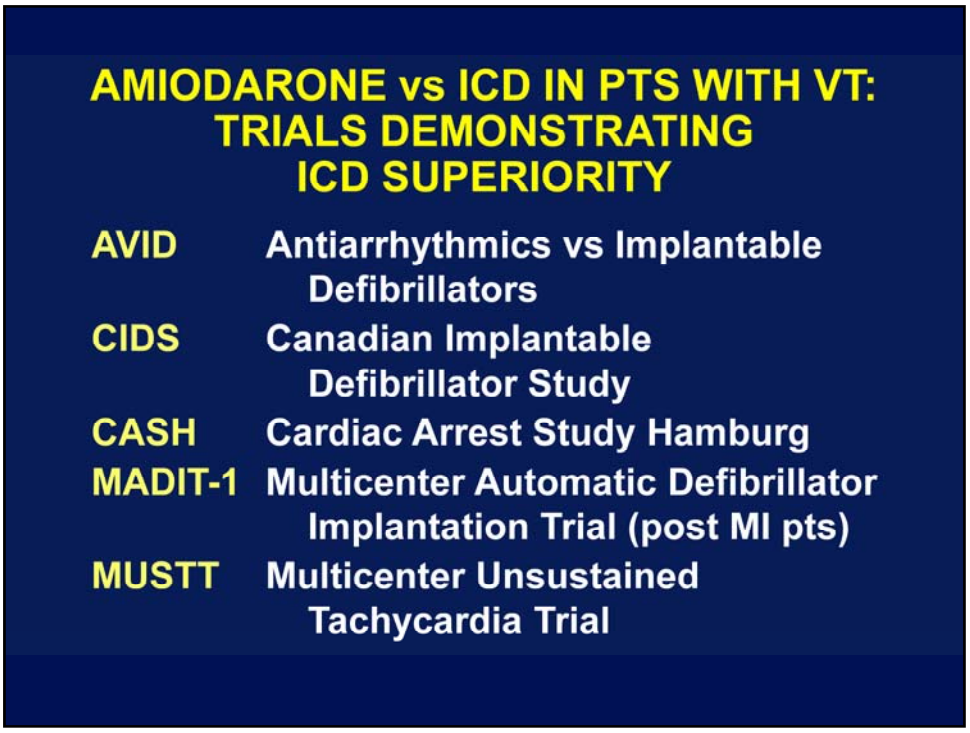
- GESICA (CHF AND NSVT ON HOLTER



- **CHF - STAT (CHF, > 10 PVCs/hr)**



- META-ANALYSIS OF AMIODARONE EFFECT IN CHF AND POST MI PTS



- AMIODARONE vs ICD IN PTS WITH VT:TRIALS DEMONSTRATING ICD SUPERIORITYs

AMIOVIRT TRIAL

ICD vs Amiodarone in NIDCM: 1° prevention trial

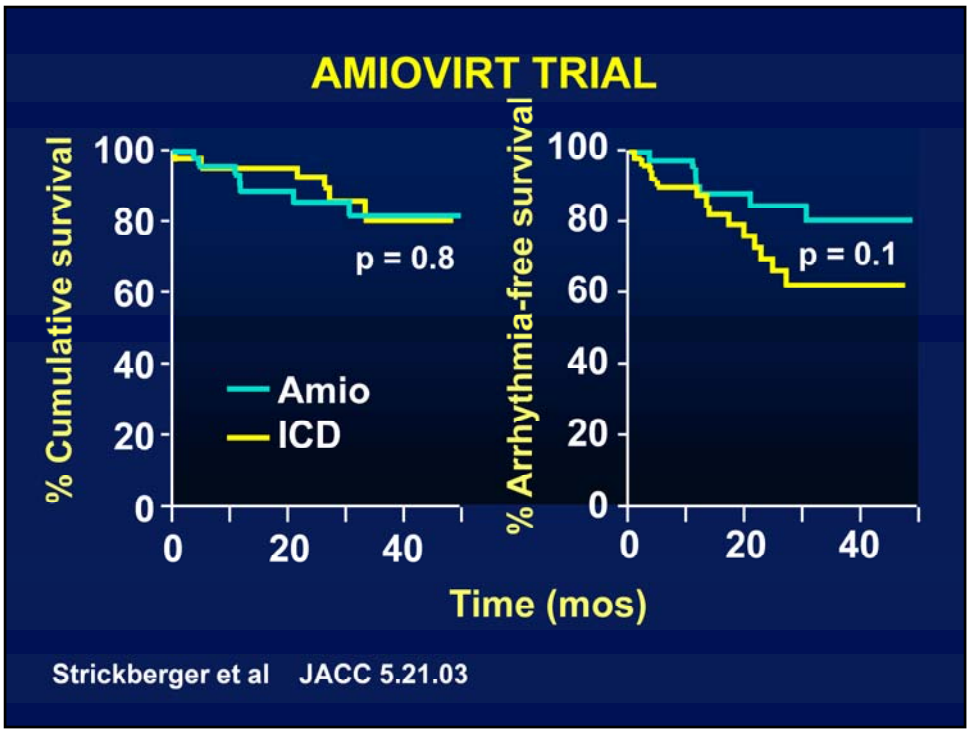
Inclusions: NIDCM
EF < 35%
NSVT (Asx)
NYHA I - III

Randomization: ICD vs amiodarone (n = 51,52)

Endpoints: 1° - Total mortality
2° - Sudden death, non-sudden death, syncope, arrhythmia-free survival, QOL

Study terminated early due to no effect

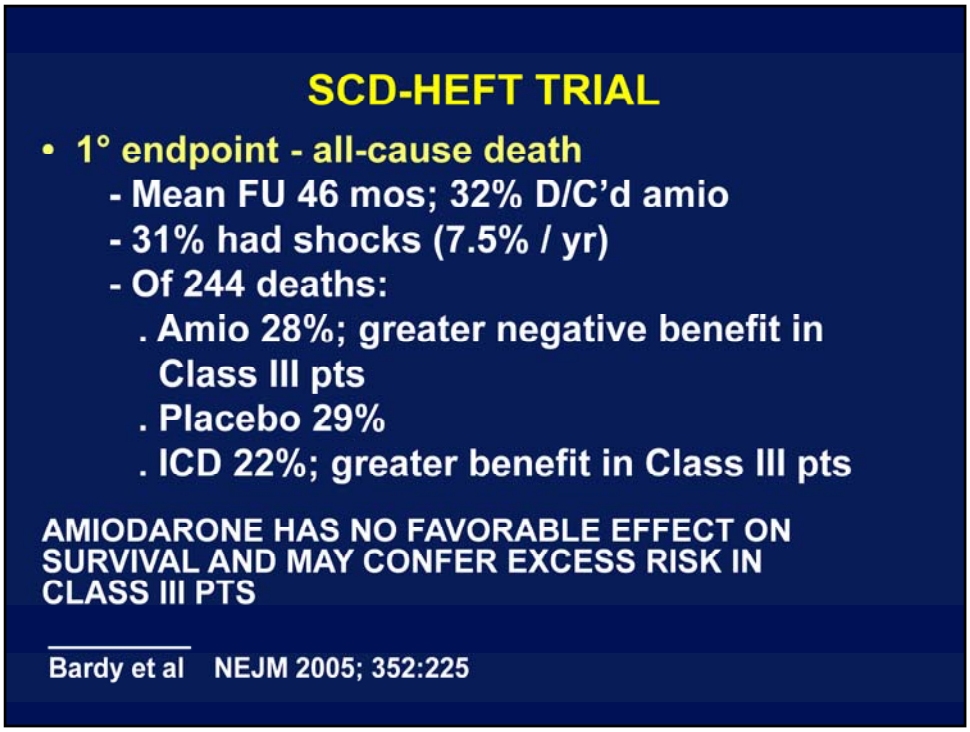
Strickberger et al JACC 5.21.03

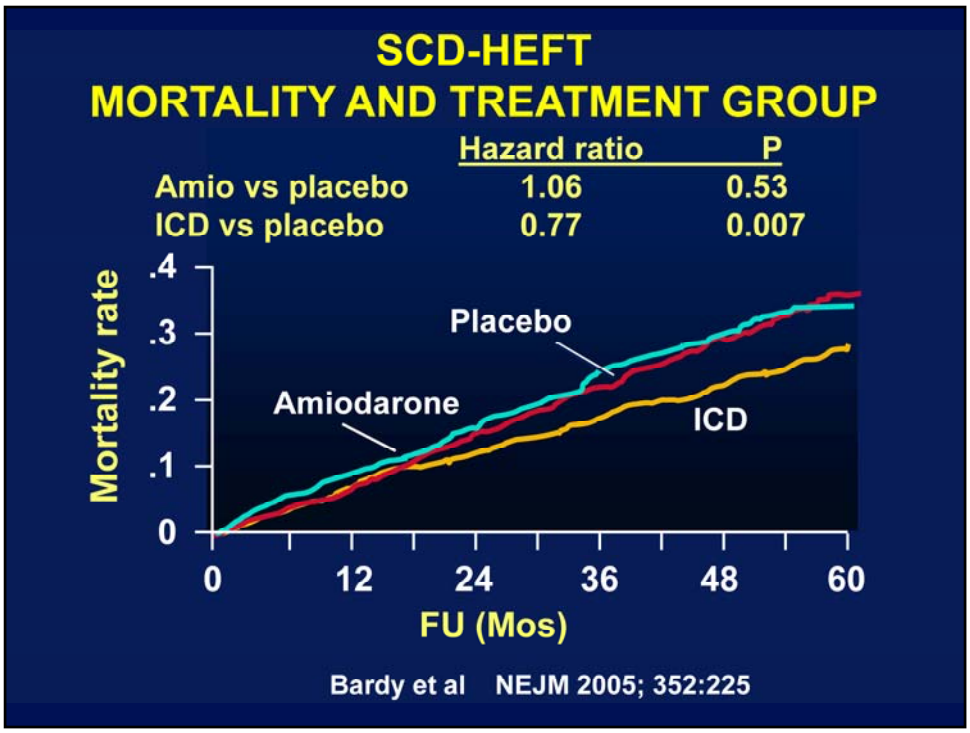

AMIOVIRT TRIAL
% Cumulative survival
100
80
60
40
20
0
0
20
40
p = 0.8
Amio
ICD
% Arrhythmia-free survival
100
80
60
40
20
0
0
20
40
p = 0.1
Time (mos)
Strickberger et al JACC 5.21.03

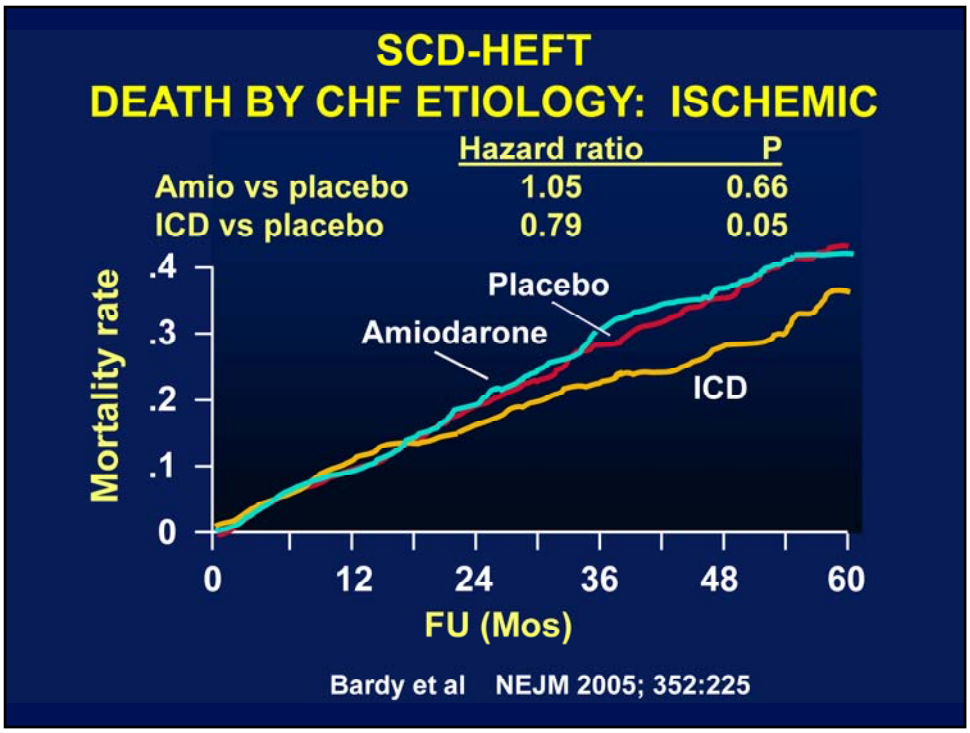
SCD-HEFT TRIAL

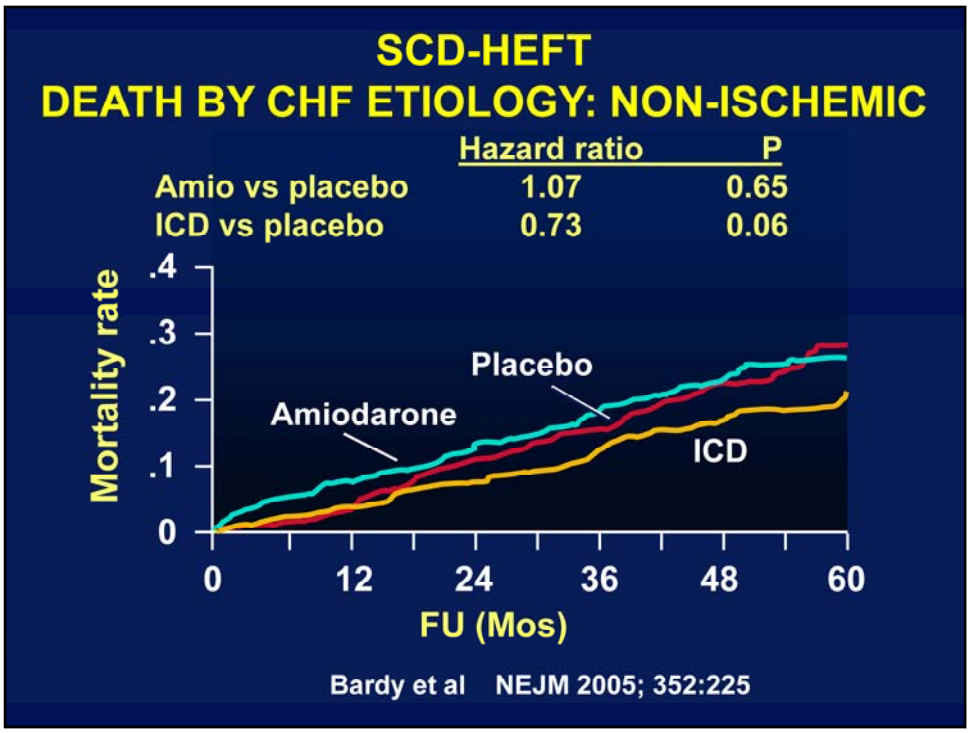
- N = 2521, NYHA II-III, EF ≤ 35%, ischemic (52%) + non-ischemic
  - Conventional Rx + placebo –N =847
  - Conventional Rx + amio –N =845
  - Conventional Rx + shock-only ICD–N =829

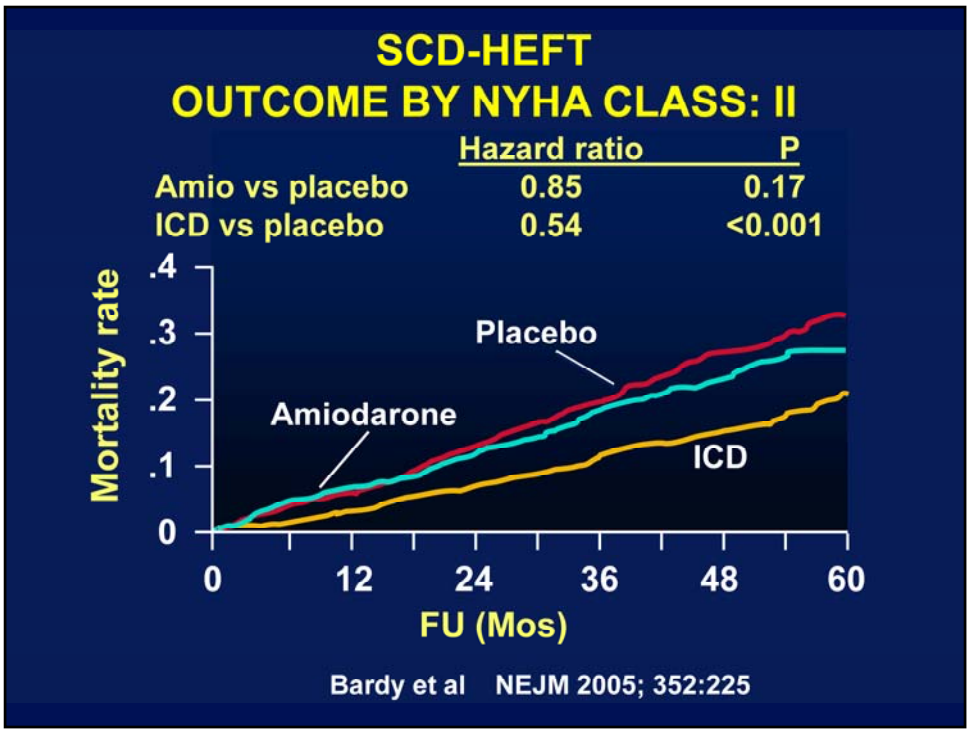
Bardy et al NEJM 2005; 352:225

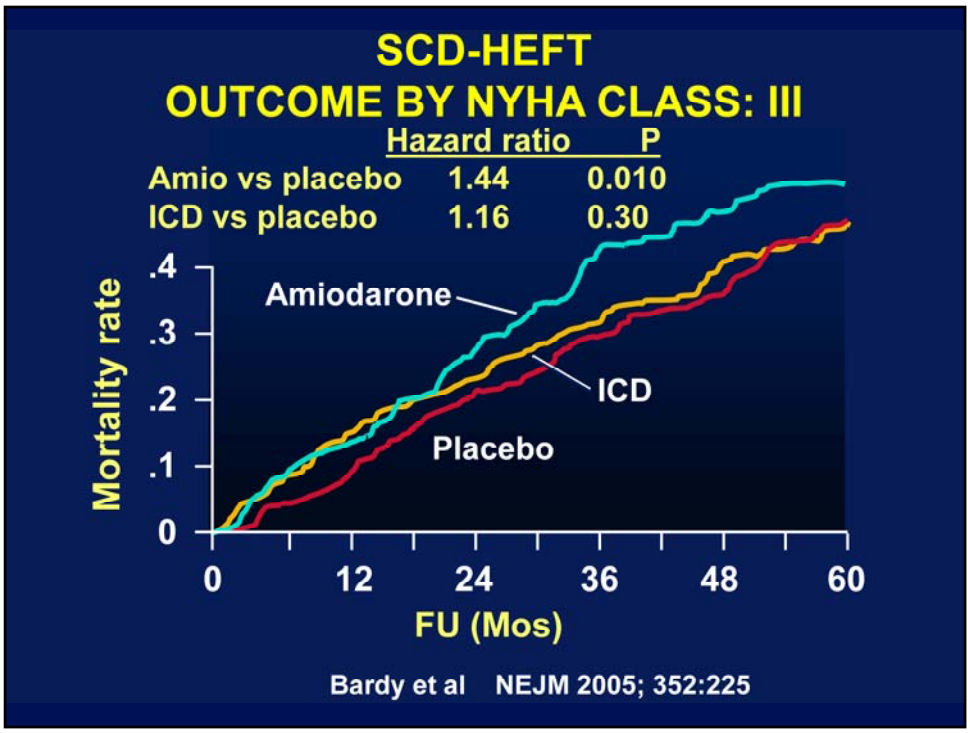

SCD-HEFT TRIAL
• 1° endpoint - all-cause death
- Mean FU 46 mos; 32% D/C'd amio
- 31% had shocks (7.5% / yr)
- Of 244 deaths:
. Amio 28%; greater negative benefit in Class III pts
. Placebo 29%
. ICD 22%; greater benefit in Class III pts
AMIODARONE HAS NO FAVORABLE EFFECT ON SURVIVAL AND MAY CONFER EXCESS RISK IN CLASS III PTS
Bardy et al NEJM 2005; 352:225

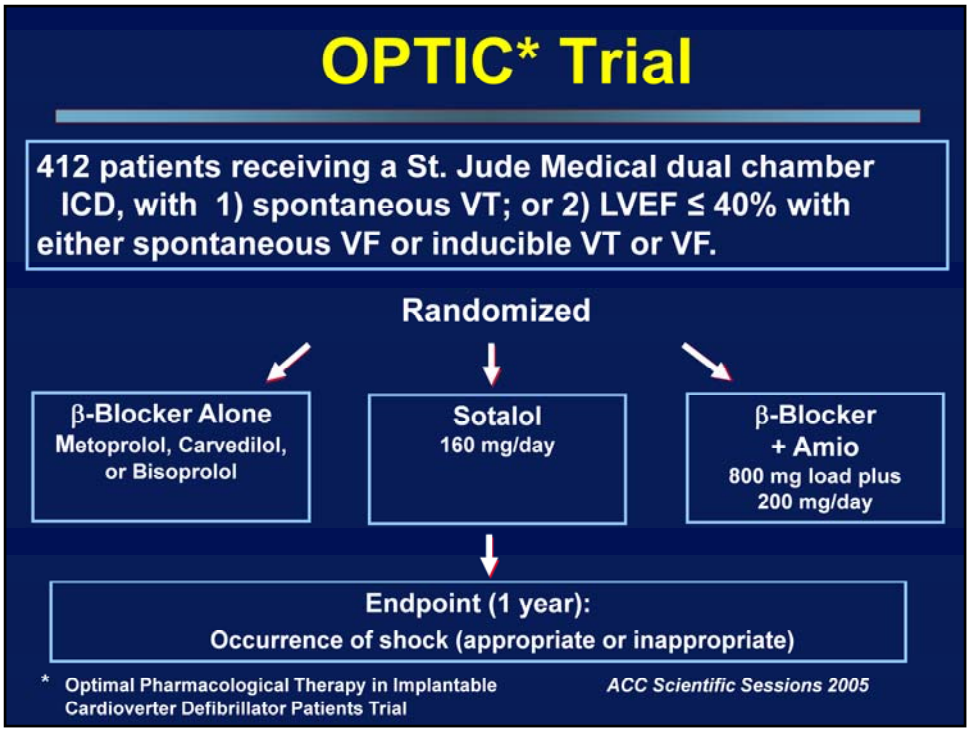

SCD-HEFT
MORTALITY AND TREATMENT GROUP
Hazard ratio P
Amio vs placebo 1.06 0.53
ICD vs placebo 0.77 0.007
Mortality rate
.4
.3
.2
.1
0
Placebo
Amiodarone
ICD
0
12
24
36
48
60
FU (Mos)
Bardy et al NEJM 2005; 352:225


SCD-HEFT
DEATH BY CHF ETIOLOGY: ISCHEMIC
Hazard ratio P
Amio vs placebo 1.05 0.66
ICD vs placebo 0.79 0.05
Mortality rate
.4
.3
.2
.1
0
Placebo
Amiodarone
ICD
0 12 24 36 48 60
FU (Mos)
Bardy et al NEJM 2005; 352:225

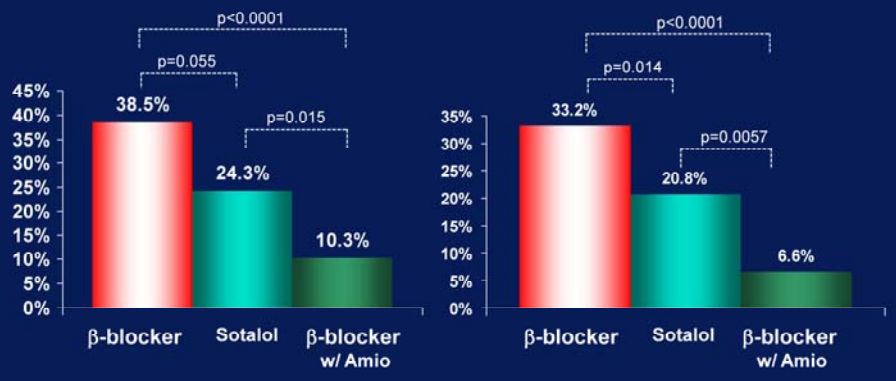

SCD-HEFT
DEATH BY CHF ETIOLOGY: NON-ISCHEMIC
Hazard ratio P
Amio vs placebo 1.07 0.65
ICD vs placebo 0.73 0.06
Mortality rate
.4
.3
.2
.1
0
Placebo
Amiodarone
ICD
0 12 24 36 48 60
FU (Mos)
Bardy et al NEJM 2005; 352:225


SCD-HEFT
OUTCOME BY NYHA CLASS: II
Hazard ratio
P
Amio vs placebo
0.85
0.17
ICD vs placebo
0.54
<0.001
Mortality rate
.4
.3
.2
.1
0
Placebo
Amiodarone
ICD
0
12
24
36
48
60
FU (Mos)
Bardy et al NEJM 2005; 352:225


SCD-HEFT
OUTCOME BY NYHA CLASS: III
Hazard ratio P
Amio vs placebo 1.44 0.010
ICD vs placebo 1.16 0.30
Mortality rate
.4
.3
.2
.1
0
Amiodarone
ICD
Placebo
0
12
24
36
48
60
FU (Mos)
Bardy et al NEJM 2005; 352:225


OPTIC* Trial
412 patients receiving a St. Jude Medical dual chamber ICD, with 1) spontaneous VT; or 2) LVEF ≤ 40% with either spontaneous VF or inducible VT or VF.
Randomized
β-Blocker Alone
Metoprolol, Carvedilol, or Bisoprolol
Sotalol
160 mg/day
β-Blocker + Amio
800 mg load plus 200 mg/day
Endpoint (1 year):
Occurrence of shock (appropriate or inappropriate)
* Optimal Pharmacological Therapy in Implantable Cardioverter Defibrillator Patients Trial
ACC Scientific Sessions 2005

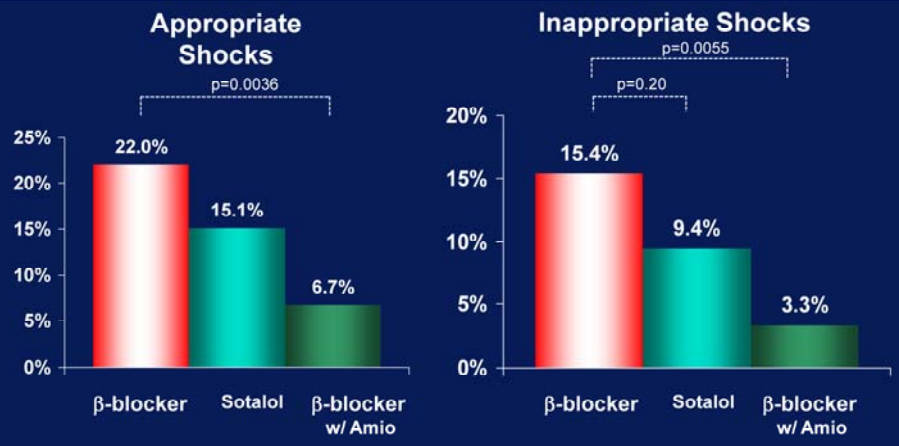
OPTIC Trial



- Baseline clinical characteristics were similar between the treatment groups: 80% had prior MI, 29% inducible VT or VF and 71% spontaneous VT or VF.

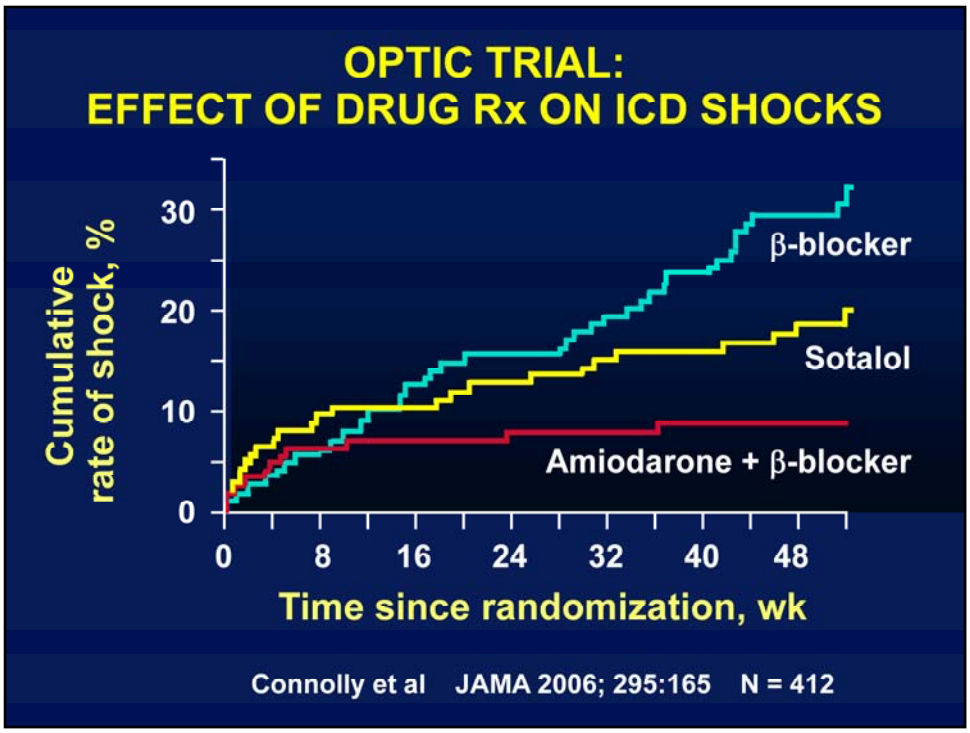
ACC Scientific Sessions 2005

OPTIC Trial



- Mean number of shocks per patient 4.32 in β-blocker alone group, 0.93 in sotalol group, and 0.51 of amio + β-blocker group.

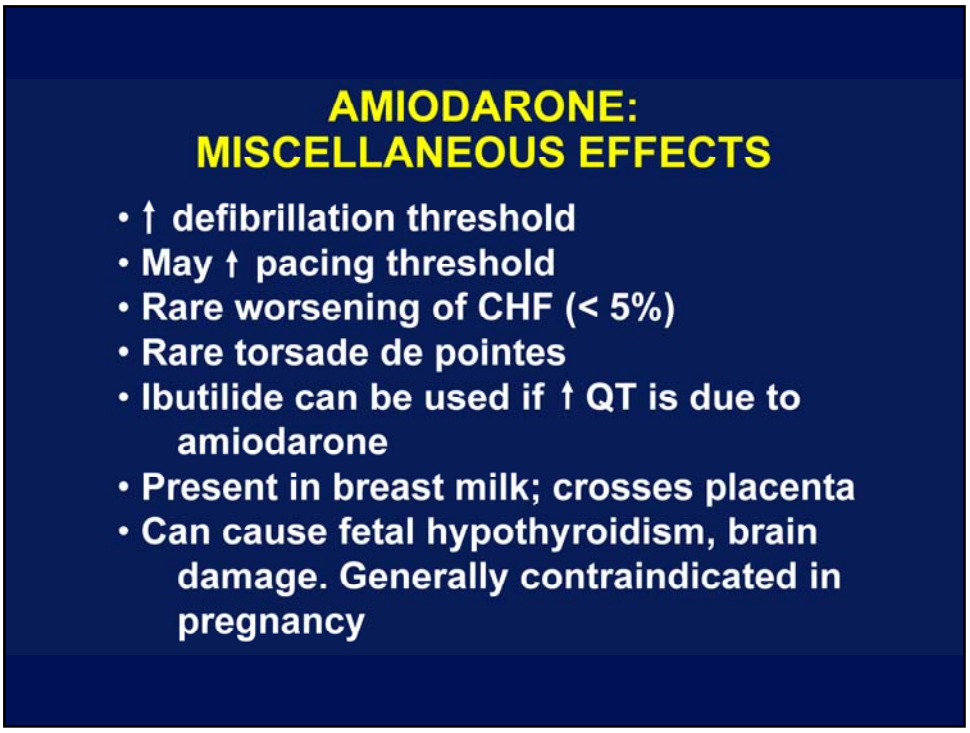
ACC Scientific Sessions 2005


OPTIC TRIAL:
EFFECT OF DRUG Rx ON ICD SHOCKS
Cumulative rate of shock, %
30
20
10
0
β-blocker
Sotalol
Amiodarone + β-blocker
0
8
16
24
32
40
48
Time since randomization, wk
Connolly et al JAMA 2006; 295:165 N = 412

OPTIC Trial: Summary

- Among patients receiving a dual chamber ICD for spontaneous or inducible VT or VF, sotalol and amiodarone + β-blocker were associated with ↓ in shocks at 1 year compared with β-blocker alone.
- The reductions in the amiodarone plus β-blocker group were greater than the sotalol group.
- The addition of amiodarone or sotalol was associated with ↓ in shock without an ↑ in adverse events, suggesting these therapies may improve quality of life in patients with an ICD.

ACC Scientific Sessions 2005

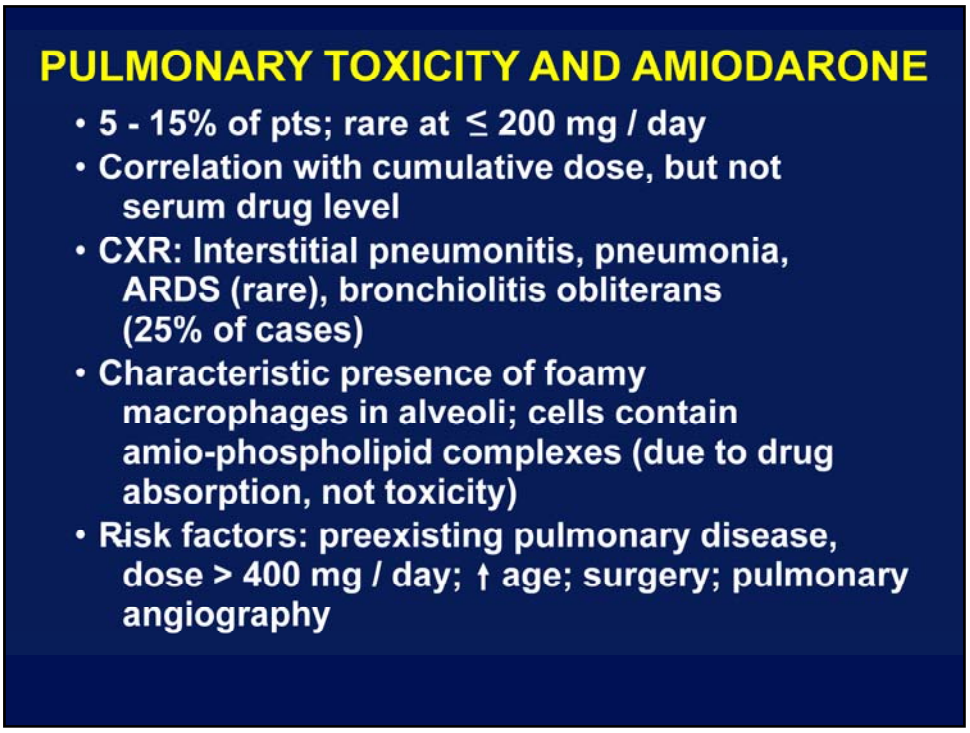


- AMIODARONE: MISCELLANEOUS EFFECTS

ADVERSE REACTIONS TO AMIODARONE

	Incidence (%)	Diagnosis	Management
Pulmonary	2	Cough and/or dyspnea, especially with local or high-resolution CT scan and decrease D_LCO from baseline	Usually discontinue drug; steroids may be considered in more severe cases; rarely, continue with steroid if no other option

Goldschlager et al, Heart Rhythm 2007



- PULMONARY TOXICITY AND AMIODARONE

ADVERSE REACTIONS TO AMIODARONE

	Incidence (%)	Diagnosis	Management
GI	30	Nausea, anorexia and constipation	Symptoms may decrease with decrease in dose
	15-30	AST or ALT level > 2 x normal	If hepatitis is considered, exclude other causes
	<3	Hepatitis and cirrhosis	Consider discontinuation, biopsy, or both to determine whether cirrhosis is present

Goldschlager et al, Heart Rhythm 2007

ADVERSE REACTIONS TO AMIODARONE

	Incidence (%)	Diagnosis	Management
Thyroid	4-22	Hypothyroidism	L-Thyroxine
	2-12	Hyperthyroidism	Steroids, propylthiouracil or methimazole; may need to discontinue drug; may need thyroidectomy.
Skin	<10	Blue	Reassurance; decrease in dose
	25—75	Photosensitivity	Avoidance of prolonged sun exposure; sunblock; decrease in dose

Goldschlager et al, Heart Rhythm 2007

ADVERSE REACTIONS TO AMIODARONE

	Incidence (%)	Diagnosis	Management
CNS	3-30	Ataxia, paresthesias peripheral polyneuropathy, sleep disturbance, impaired memory and tremor	Often dose dependent, may improve or resolve with dose adjustment

Goldschlager et al, Heart Rhythm 2007

ADVERSE REACTIONS TO AMIODARONE

	Incidence (%)	Diagnosis	Management
Ocular	<5	Halo vision, especially at night	Corneal deposits the norm; if optic neuropathy occurs, discontinue
	≤1	Optic neuropathy	Discontinue drug consult opthalmologist
	>90	Photophobia, blurring, and microdeposits	

Goldschlager et al, Heart Rhythm 2007

ADVERSE REACTIONS TO AMIODARONE

	Incidence (%)	Diagnosis	Management
Heart	5	Bradycardia and AV block	May need permanent cardiac pacing
	<1	Proarrhythmia	May need to discontinue drug
GU	<1	Epididymitis and and erectile dysfunction	Pain may resolve spontaneously

Goldschlager et al, Heart Rhythm 2007

RECOMMENDED LABORATORY TESTING IN PATIENTS RECEIVING AMIODARONE

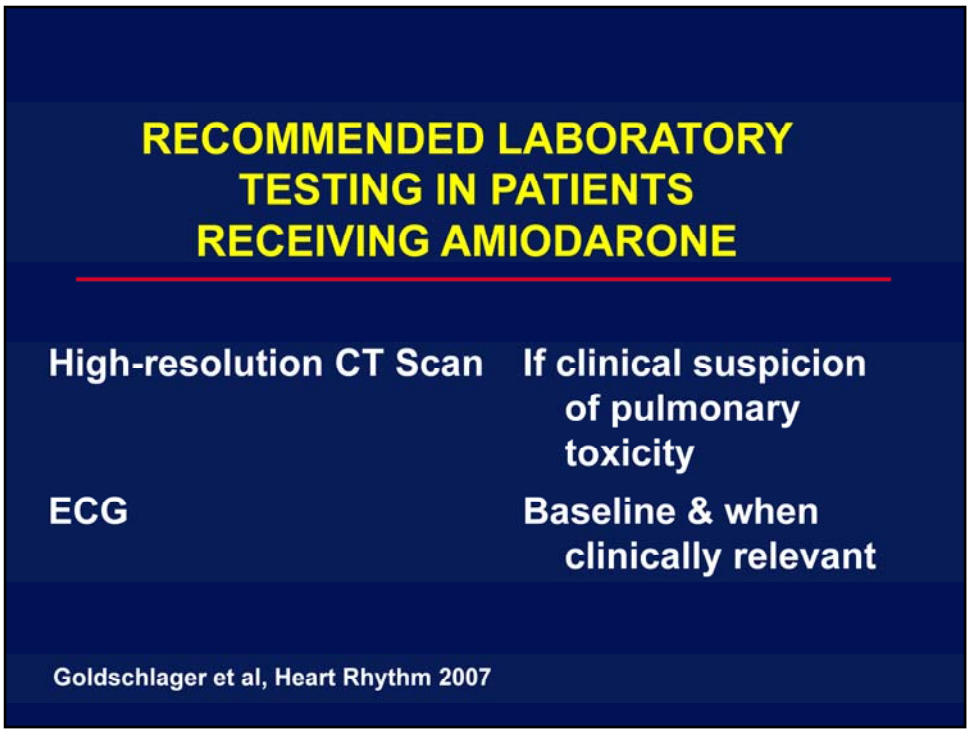
Liver function tests	Baseline & every 6 mo
Thyroid function tests	Baseline & every 6 mo
Chest x-ray	Baseline & yearly
Ophthalmologic evaluation	At baseline if visual impairment or for symptoms

Goldschlager et al, Heart Rhythm 2007

RECOMMENDED LABORATORY TESTING IN PATIENTS RECEIVING AMIODARONE

Pulmonary function tests (including D_LCO)	Baseline and for unexplained cough or dyspnea, especially if underlying lung disease, suggestive x-ray abnormalities, & if clinical suspicion of pulmonary toxicity

Goldschlager et al, Heart Rhythm 2007


RECOMMENDED LABORATORY TESTING IN PATIENTS RECEIVING AMIODARONE
High-resolution CT Scan
If clinical suspicion of pulmonary toxicity
ECG
Baseline & when clinically relevant
Goldschlager et al, Heart Rhythm 2007

MAJOR DRUG INTERACTIONS WITH AMIODARONE

Drug	Interaction
Digoxin	Increased concentration and effect with sinus and AV node depression and GI tract and CNS toxicity
Warfarin	Increased concentration and effect
Quinidine, procainamide, disopyramide	Increased concentration and effect, torsade de pointes VT
Diltiazem, verapamil	Bradycardia and AV block

Goldschlager et al, Heart Rhythm 2007

MAJOR DRUG INTERACTIONS WITH AMIODARONE

Drug	Interaction
β Blockers	Bradycardia and AV block
Flecainide	Increased concentration and effect
Phenytoin	Increased concentration and effect
Anesthetic drugs	Hypotension and bradycardia
Cyclosporine	Increased concentration and effect
Simvastatin, atorvastatin	Can promote liver function abnormalities

Goldschlager et al, Heart Rhythm 2007

WHEN TO REFER TO AN ELECTROPHYSIOLOGIST

- Worsening arrhythmia symptoms
- Evidence of amiodarone toxicity requiring changes in drug dosing or drug discontinuation. Until the arrhythmia problem stablizes the patient may require intensified monitoring, EPS, ablative therapy, or pacemaker or ICD implantation.
- Repeat defibrillation threshold testing recommended for patients with ICD due to drug effect of increasing this threshold.
- Assess amiodarone-induced slowing of VT rate in patients with an ICD such that VT would not be detected by the device and therapy not delivered.
- Pregnant patients
- Pediatric patients

Goldschlager et al, Heart Rhythm 2007

WHEN TO CONSULT A PULMONOLOGIST

- Abnormal chest radiography at baseline or follow-up.
- Abnormal pulmonary function tests (particularly forced vital capacity and (D_LCO)) at baseline or follow-up.
- New cough and/or dyspnea, especially if otherwise unexplained or unexpected.

Goldschlager et al, Heart Rhythm 2007

WHEN TO CONSULT AN ENDOCRINOLOGIST

- Any time hyperthyroidism is suspected (even if suppression of TSH is mild and subclinical disease is possible).
- An acutely ill patient where interpretation of TFTs will be complicated by euthyroid sick syndrome.
- When considering treating subclinical hypothyroidism.

Goldschlager et al, Heart Rhythm 2007