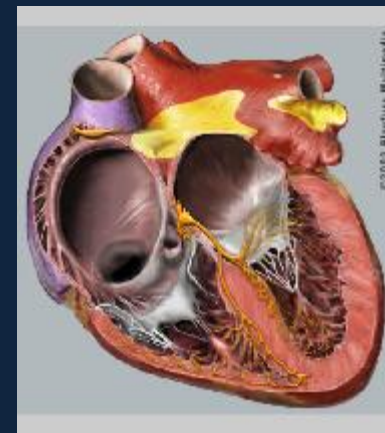


# The PALLAS Study Commentary

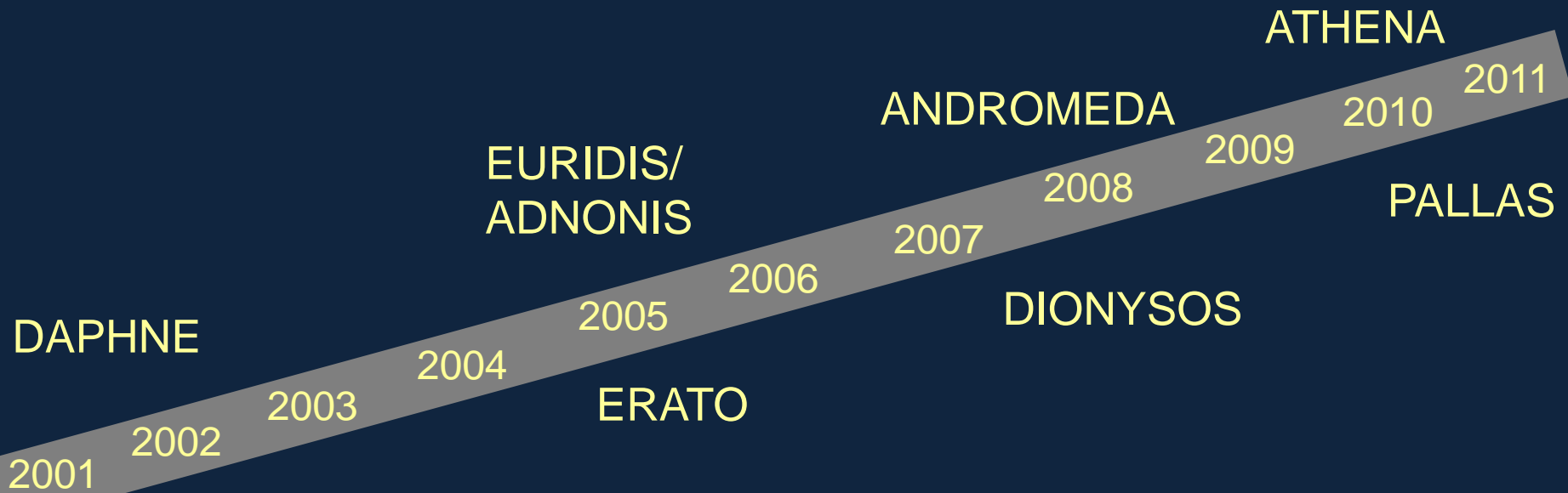


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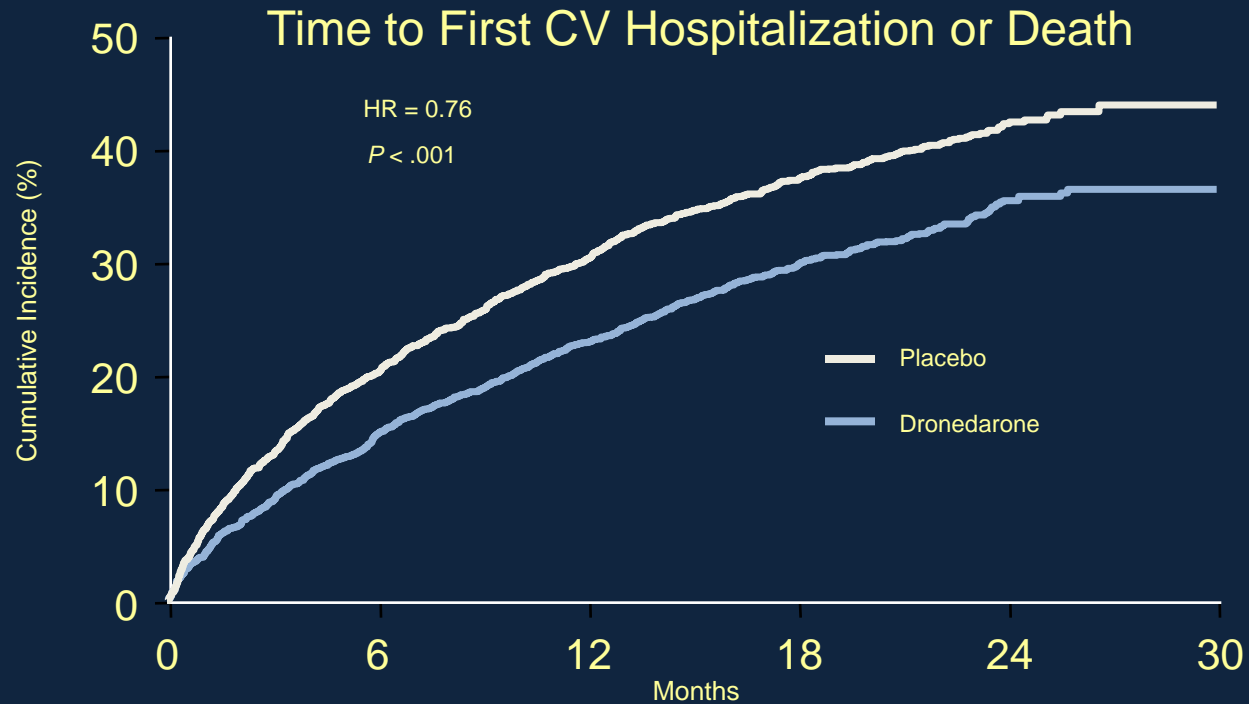
# Dronedarone Trials

- D was more effective than placebo in maintaining NSR and reducing ventricular rate during AF recurrence.
- D increased early mortality related to worsening of heart failure.
- D was less effective than amiodarone but had a better safety profile.



- D reduced hospitalization due to CV events or death.
- D increased the risk of stroke, MI, systemic embolism or CV death hospitalization or death largely due to increases in stroke and CV death.

# ATHENA: Primary Outcome

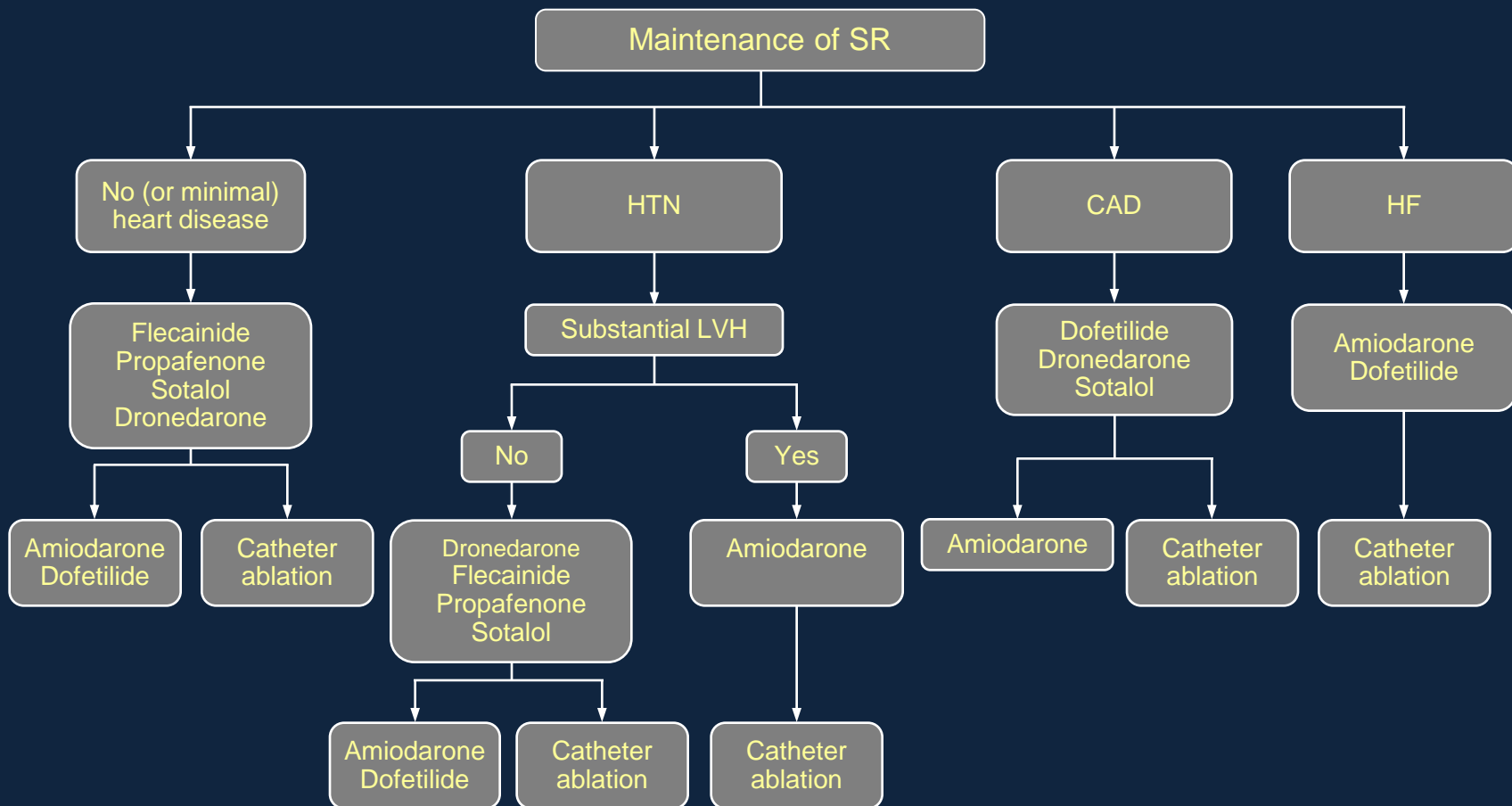


Patients at risk:	0 Months	6 Months	12 Months	18 Months	24 Months	30 Months
Placebo	2327	1858	1625	1072	385	3
Dronedaronne	2301	1963	1776	1177	403	2

Mean follow-up 21 ± 5 months

- Dronedarone- approved to reduce the risk of CV hospitalization in patients with paroxysmal or persistent AF with a recent episode of AF or AFL and associated CV risk factors (age >70, hypertension, DM, CVA, LA diameter  $\geq$ 50 mm or LVEF <40%) who are in NSR or who will be cardioverted.
- *The critical question:*  
*Do the unfavorable results of the PALLAS Study obtained in patients with permanent AF apply to patients who using dronaderone for the approved indication?*

# 2011 AHA/ACC Guidelines: Antiarrhythmic Approaches to Maintain SR in Patients with Recurrent PAF or Persistent AF Who Require SR\*



# ATHENA Trial

Outcome	Dronedaron (N= 2301)	Placebo (N= 2327)	Hazard Ratio for Dronedaron (95% CI)	P Value
Primary outcome — no. (%)	734 (31.9)	917 (39.4)	0.76 (0.69–0.84)	<0.001
First hospitalization due to cardiovascular events — no. (%)	675 (29.3)	859 (36.9)	0.74 (0.67–0.82)	<0.001
First hospitalization — no. (%)				
For atrial fibrillation	335 (14.6)	510 (21.9)	0.63 (0.55–0.72)	<0.001
For congestive heart failure	112 (4.9)	132 (5.7)	0.86 (0.67–1.10)	0.22
For acute coronary syndrome	62 (2.7)	89 (3.8)	0.70 (0.51–0.97)	0.03
For syncope	27 (1.2)	32 (1.4)	0.85 (0.51–1.42)	0.54
For ventricular arrhythmia or nonfatal cardiac arrest	13 (0.6)	12 (0.5)	1.09 (0.50–2.39)	0.83
Death from any cause — no. (%)	116 (5.0)	139 (6.0)	0.84 (0.66–1.08)	0.18
From noncardiovascular causes	53 (2.3)	49 (2.1)	1.10 (0.74–1.62)	0.65
From cardiovascular causes	63 (2.7)	90 (3.9)	0.71 (0.51–0.98)	0.03
From nonarrhythmic cardiac causes	17 (0.7)	18 (0.8)	0.95 (0.49–1.85)	0.89
From cardiac arrhythmia	26 (1.1)	48 (2.1)	0.55 (0.34–0.88)	0.01
From noncardiac vascular causes (including stroke)	20 (0.9)	24 (1.0)	0.84 (0.47–1.52)	0.57
Any hospitalization due to any cardiovascular event or death from any cause — no. (%) (no. of events per 100 patient-yr)	1253 (32.4)	1668 (42.6)	0.76 (0.68–0.84)	<0.001

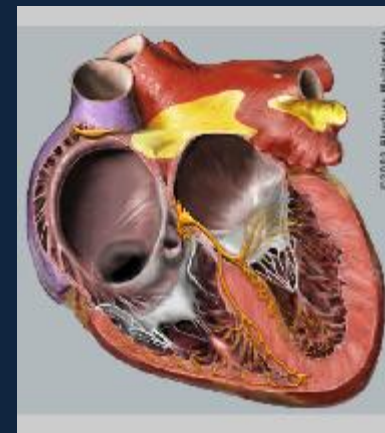
# Athena versus PALLAS

<u>Demographics</u>	<u>ATHENA</u>	<u>PALLAS</u>
Age (yrs)	71	75
Male (%)	51	65
Perm. AF > 2 yr	0	69
CAD (%)	30	41
History of HF	20	69
LVEF < .45 (%)	12	-
LVEF < .40 (%)	-	20

<u>Outcomes</u>	<u>ATHENA</u>	<u>PALLAS</u>
Follow-up (months)	22	4.2
Death	.84	1.94

- 
- Dronedarone should not be used in patients with heart failure or permanent AF.
  - Further data is needed to answer the critical question:
    - *Do the unfavorable results of the PALLAS Study apply to patients using dronedarone for the approved indication?*
  - Patients taking dronedarone should be monitored regularly (six months) to ensure that they remain within the approved indication and do not progress to permanent AF or new or worsening heart failure.
  - If clinicians elect to initiate or continue dronedarone they should ensure that patients have and maintain the clinical profile of the ATHENA patients.
-

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