UPDATE ON DRONEDARONE AND VERNAKALANT TWO YEARS AFTER ESC GUIDELINES

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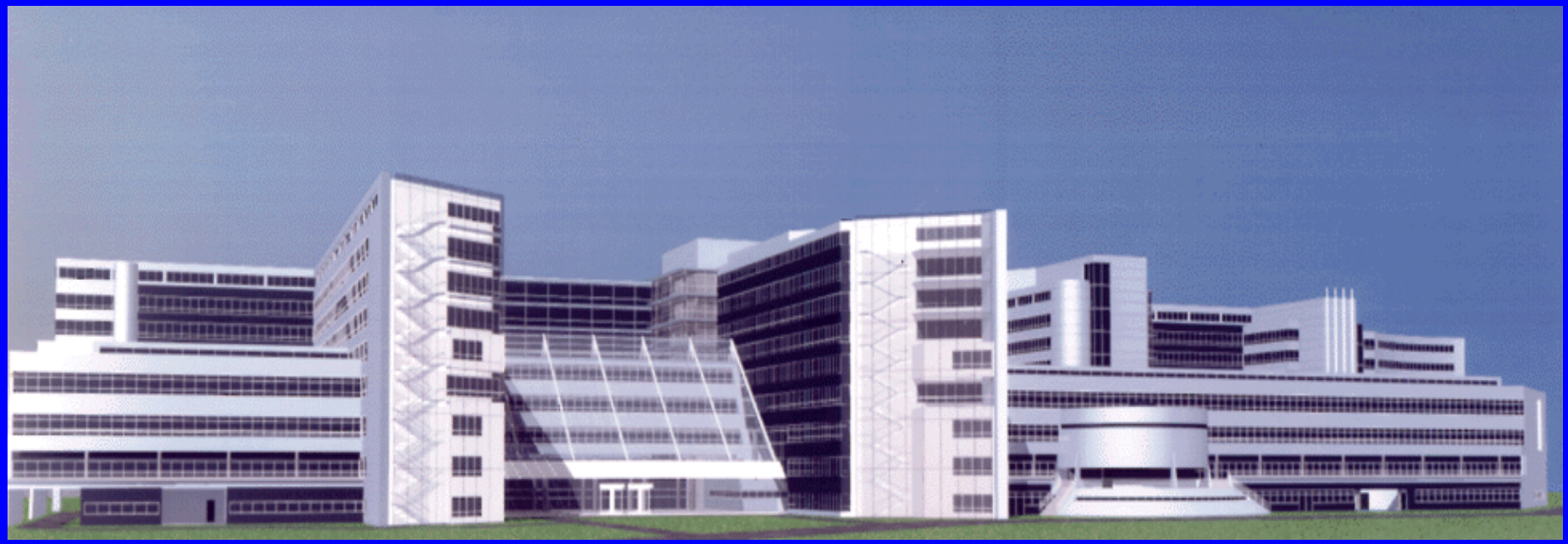

Turin, October 25, 2012

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ESC GUIDELINES

Guidelines for the management of atrial fibrillation

The Task Force for the Management of Atrial Fibrillation of the European Society of Cardiology (ESC)

Developed with the special contribution of the European Heart Rhythm Association (EHRA)†

Endorsed by the European Association for Cardio-Thoracic Surgery (EACTS)

European Heart Journal

http://eurheartj.oxfordjournals.org/

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The disclosure forms of the authors and reviewers are available on the ESC website www.escardio.org/guidelines

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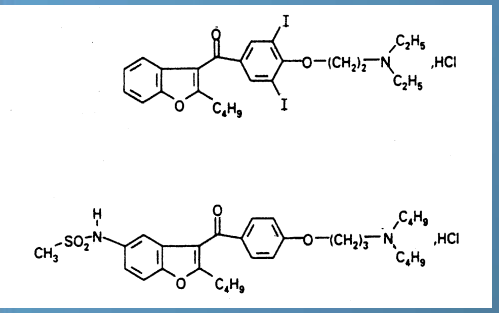
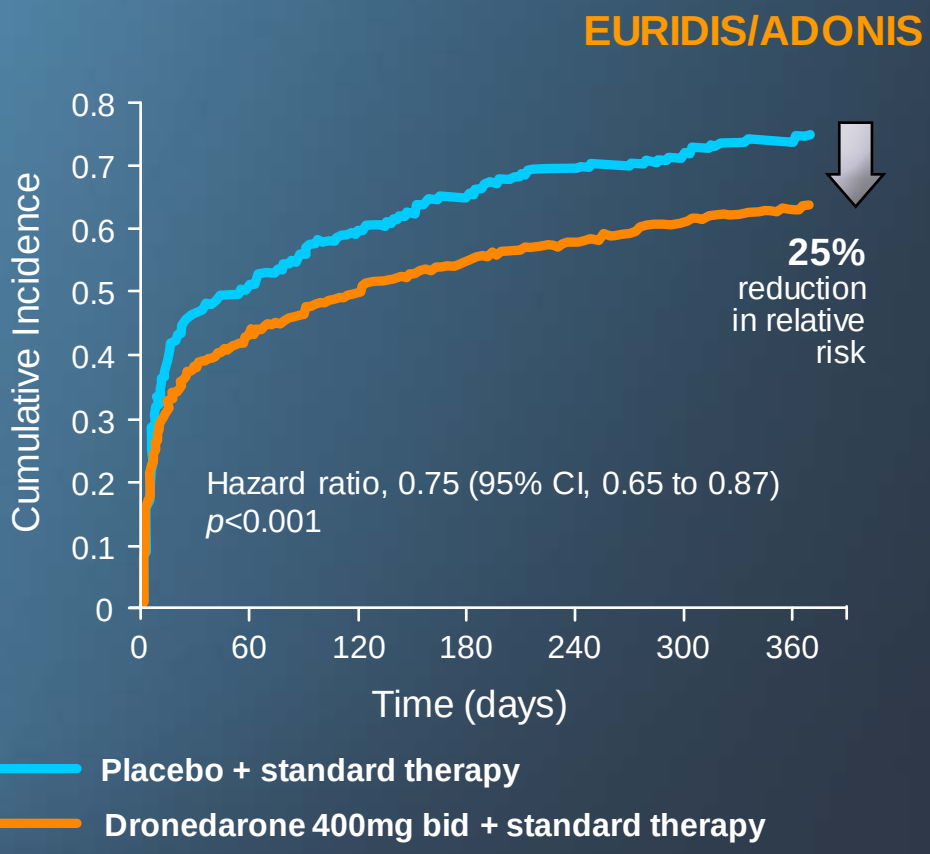
EURIDIS
ADONIS

Dronedarone Showed a Significant Reduction in First AF Recurrence in Combined Analysis

Amiodarone



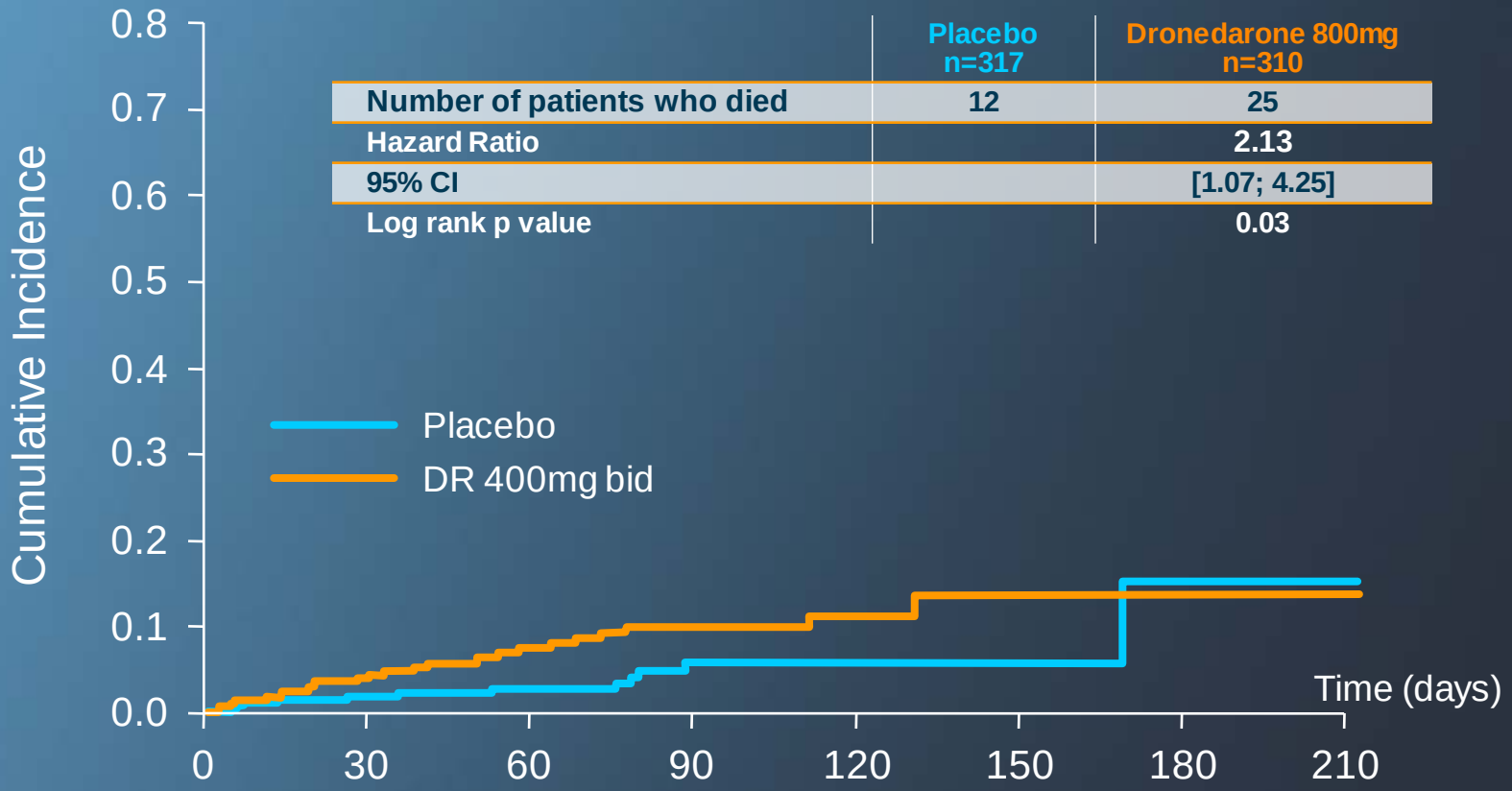
Dronedarone



Singh BN, *et al. N Engl J Med.* 2007;357:987-99.

Cumulative Incidence of All-cause Mortality

	Placebo n=317	Dronedarone 800mg n=310
Number of patients who died	12	25
Hazard Ratio		2.13
95% CI		[1.07; 4.25]
Log rank p value		0.03



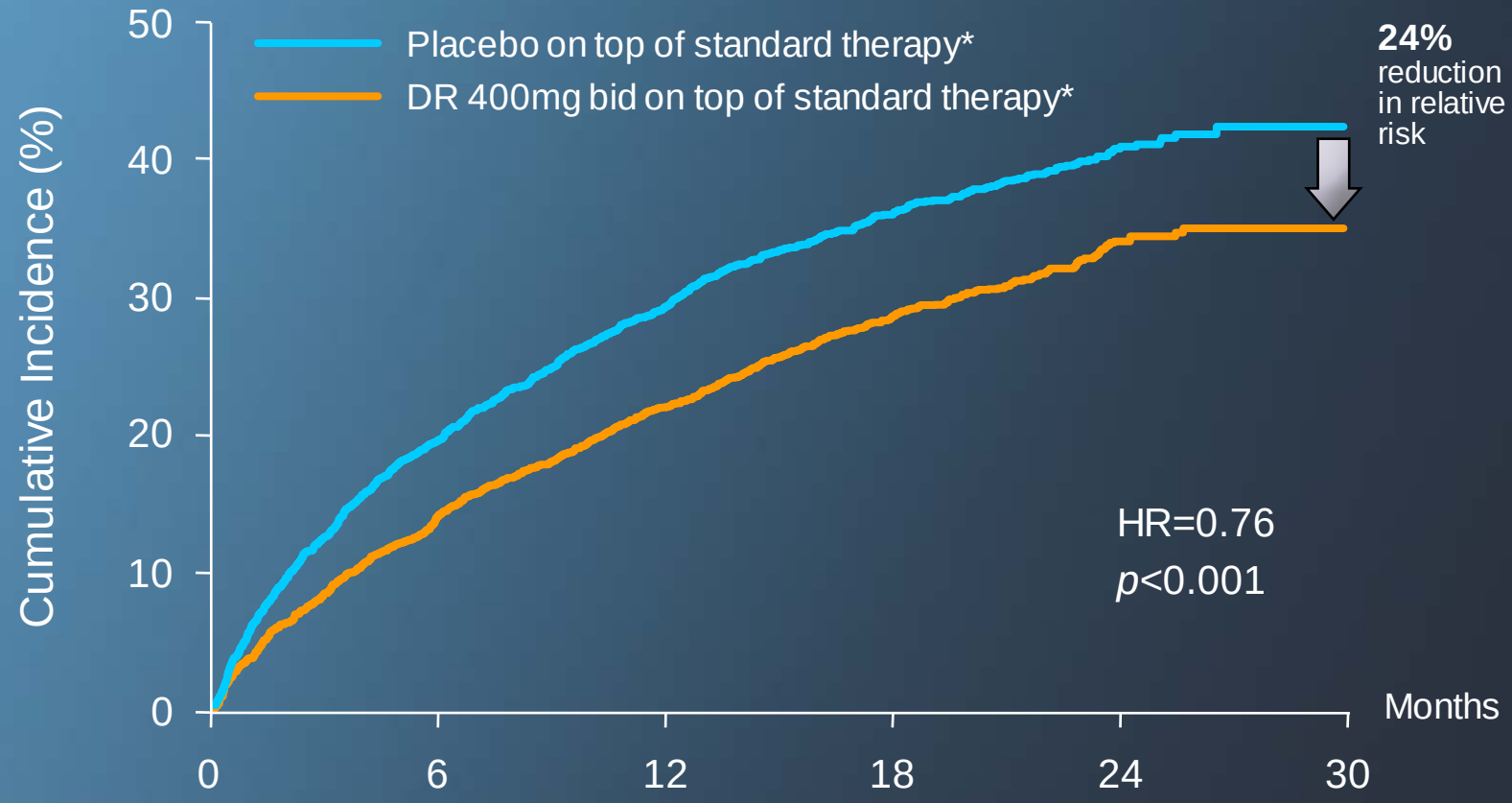
Patients at risk:

Placebo	317	256	181	103	50	18	6	1
DR 400mg bid	310	257	174	104	59	22	5	1

Køber L, *et al. N Engl J Med.* 2008;358:2678-87.

ATHENA

Dronedarone Significantly Decreased Risk of CV Hospitalisation or Death by 24%



Patients at risk:

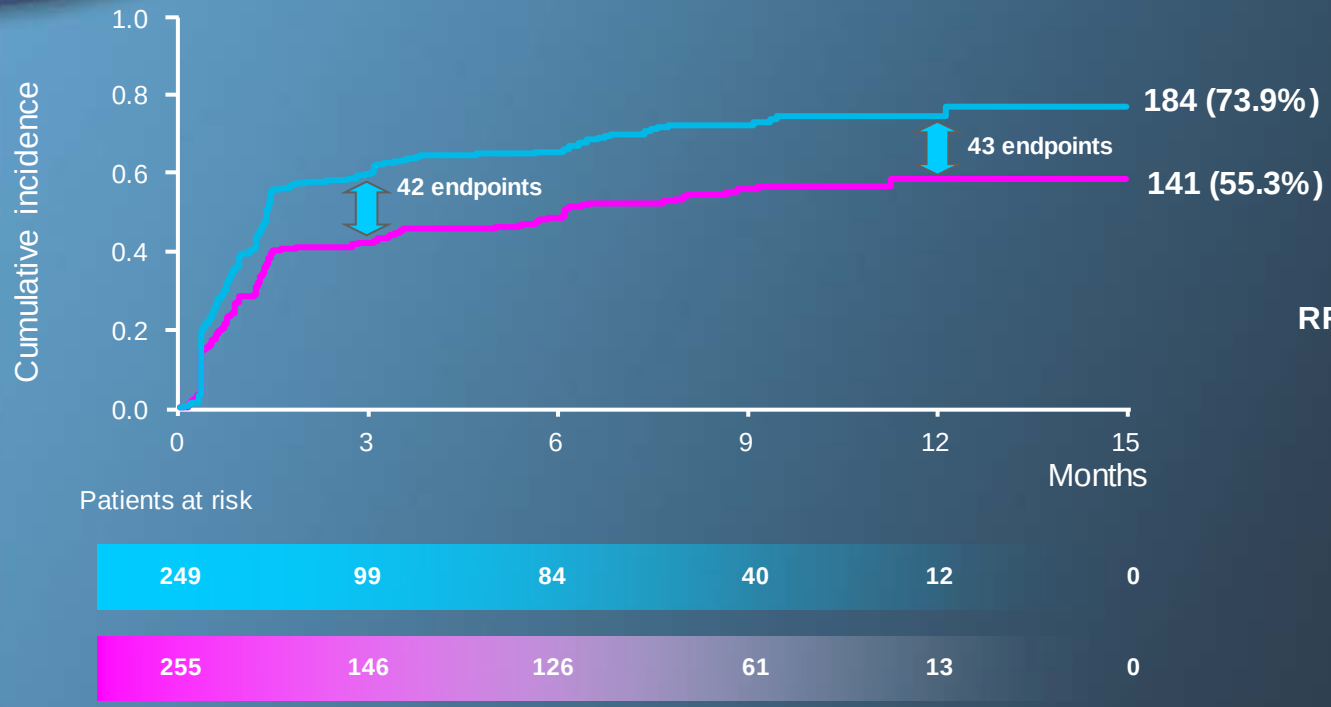
Placebo	2327	1858	1625	1072	385	3
DR 400mg bid	2301	1963	1776	1177	403	2

* Standard therapy may have included rate control agents (beta-blockers, and/or Ca-antagonist and/or digoxin) and/or anti-thrombotic therapy (Vit. K antagonists and /or aspirin and other antiplatelets therapy) and/or other cardiovascular agents such as ACEIs/ARBs and statins.

Mean follow-up 21 ±5 months.

Hohnloser SH *et al. N Engl J Med 2009;360:668-78.*

DIONYSOS Primary Endpoint: More AF Events But Less Early Discontinuation With Dronedarone



	Dronedarone (n=249)	Amiodarone (n=255)
Number of patients with endpoint	**184 (73.9%)**	**141 (55.3%)**
ECG documented AF endpoint	**158 (63.5%)**	**107 (42.0%)**
Documented AF after conversion	91 (36.5%)	62 (24.3%)
Unsucessful electrical cardioversion	29 (11.6%)	16 (6.3%)
No spontaneous conversion and no electrical cardioversion on day 10 to day 28	38 (15.3%)	29 (11.4%)
Premature study drug discontinuation	**26 (10.4%)**	**34 (13.3%)**
Lack of efficacy	1 (0.4%)	0
Intolerance	25 (10.0%)	34 (13.3%)

Le Heuzey J.Y. et al., J. Cardiovasc. Electrophysiol. 2010; 21 : 597 - 605

DRONEDARONE : 200,000 patients , two serious liver failure needing transplants

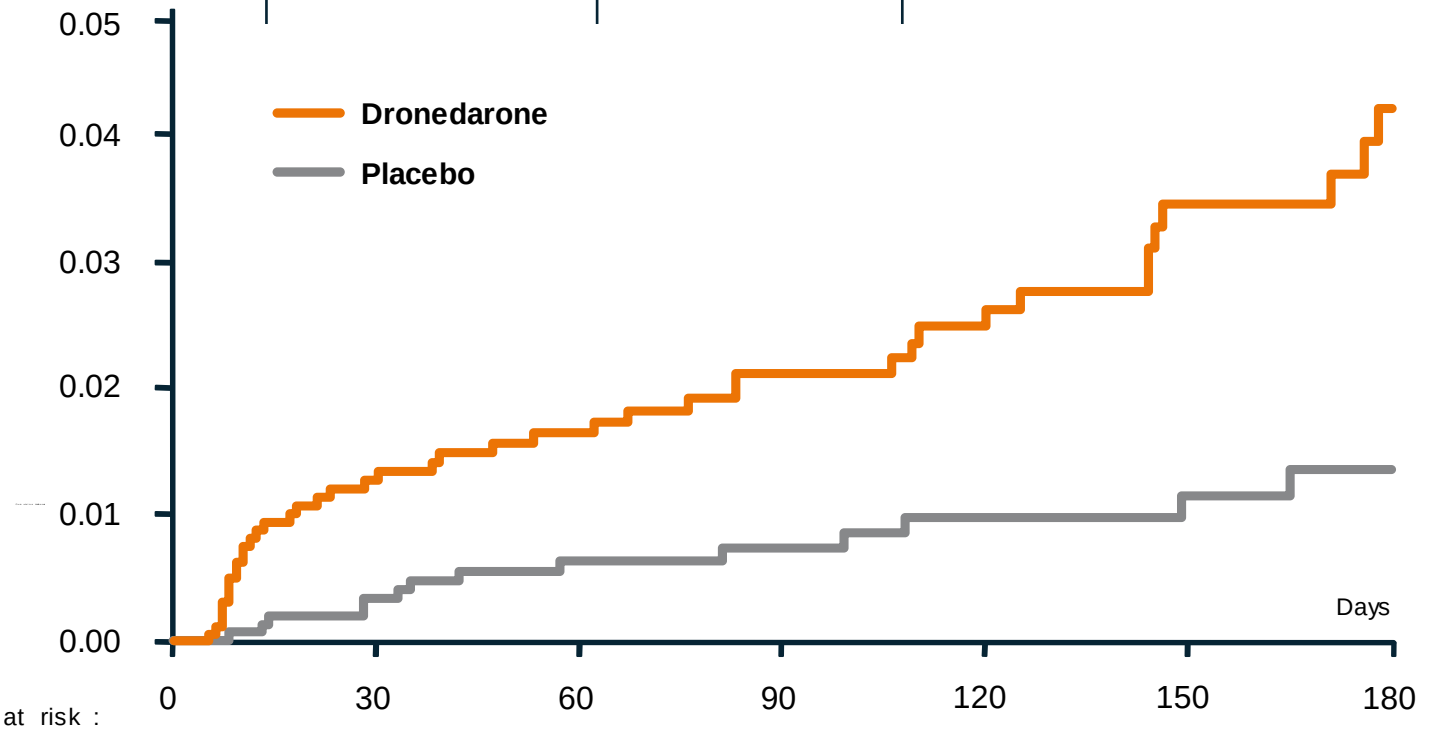
EMA recommandations, « Dear doctor letter » 21/01/11

- **Before starting treatment with Dronedarone, doctors should perform liver function tests. Tests should be repeated monthly for six months, at months 9 and 12, and periodically**

- **Doctors should stop treatment with Dronedarone in patients with raised levels of the liver enzyme ALAT (more than 3 times above the upper limit of normal). Appropriate investigation and close observation of patients should continue until the enzyme levels return to normal**

Stroke, systemic embolism, myocardial infarction or cardiovascular death

First Co-primary Outcome	Dronedarone	Placebo	Dronedarone vs placebo HR and 95% CI
	43 (2.7%)	19 (1.2%)	2.29 (1.34 – 3.94) p=0.002



Number at risk :

Dronedarone	1619	1421		930		353
Placebo	1617	1445		908		377

PALLAS
Permanent Atrial fibrILLAtion outcome Study using Dronedarone on top of standard therapy

Dronedarone Prescribing Information[1]

INDICATION

MULTAQ is indicated for the **maintenance of sinus rhythm after successful cardioversion*** in **adult clinically stable patients with paroxysmal or persistent atrial fibrillation (AF).**

Due to its safety profile (see sections 4.3 and 4.4), MULTAQ should only be prescribed after alternative treatment options have been considered.

MULTAQ should not be given to patients with left ventricular systolic dysfunction or to patients with current or previous episodes of heart failure.

CONTRAINDICATIONS†

- **Permanent AF with an AF duration ≥ 6 months**
- **Patients in unstable hemodynamic conditions**
- **History of, or current heart failure or left ventricular systolic dysfunction**
- **Patients with liver and lung toxicity related to the previous use of amiodarone**

1. Multaq (Dronedarone) SmPC Europe September 2011

†New contraindications (september 2011) listed, refer to Multaq SmPC for full list of contraindications and other prescribing information

Treatment with dronedarone should be initiated and monitored under specialist supervision

Patient selection	Patient monitoring
Paroxysmal or persistent AF (after successful cardioversion)	AF status: Serial ECGs and at least every 6 months
No CHF, no LVSD	Routine clinical assessment with special attention to heart failure and left ventricular systolic dysfunction (LVSD)
No previous liver or lung toxicity with amiodarone	LFTs and creatinine at 1 week, monthly LFTs 1–6 months, 9 and 12 months and regularly thereafter
Baseline LFTs and creatinine, appropriate anti-coagulation	

CHF: Congestive heart failure, LVSD: Left ventricular systolic dysfunction, LFTs: Liver function tests

Adapted from MULTAQ® SmPC Europe – September 2011. Refer to full MULTAQ® SmPC for full prescribing information.

~736,000 patients have received treatment with dronedarone worldwide since July 2009[1]

1. Cumulative number of patients. Estimated. IMS/MIDAS Worldwide Monthly Database, Standard Units Sold up until 31st March 2012

Dronedarone : Post-marketing Clinical Studies

Dronedarone Clinical Study	n	Population	Objective / Endpoint
ARTEMIS AF Loading*	170	Persistent AF randomised to 0, 2 or 4 week washout before dronedrone	Evaluate optimal washout for switch from amiodarone / time to first AF recurrence
ARTEMIS AF Long-term*	105	Paroxysmal or persistent AF and at least 6 months of amiodarone	Evaluate optimal washout for switch from amiodarone / PK profiles (dronedarone and its active metabolite) at 5 Time Points: “R” /3 hours / 1w / 2w / 4w)
HESTIA	112	Patients with persistent AF fitted with a pacemeker	Effect on AF burden / % time in AF
DROPPAF	39	Patients paroxysmal AF fitted with a pacemeker	Effect on AF burden

*Study stopped for operational reasons – results to be reported in 2012
www.clinicaltrials.gov

ARTEMIS - Rationale

- **Co-prescriptions of 2 antiarrhythmic drugs prolonging QT interval is usually not recommended (as well as two antiarrhythmic drugs of the same class)**

- **Prescribers need to be reassured about safety of Dronedarone in patients with amiodarone « still on board »**

- **They need a clear recommendation concerning the mode of switching, both after a loading dose or a after chronic amiodarone treatment**

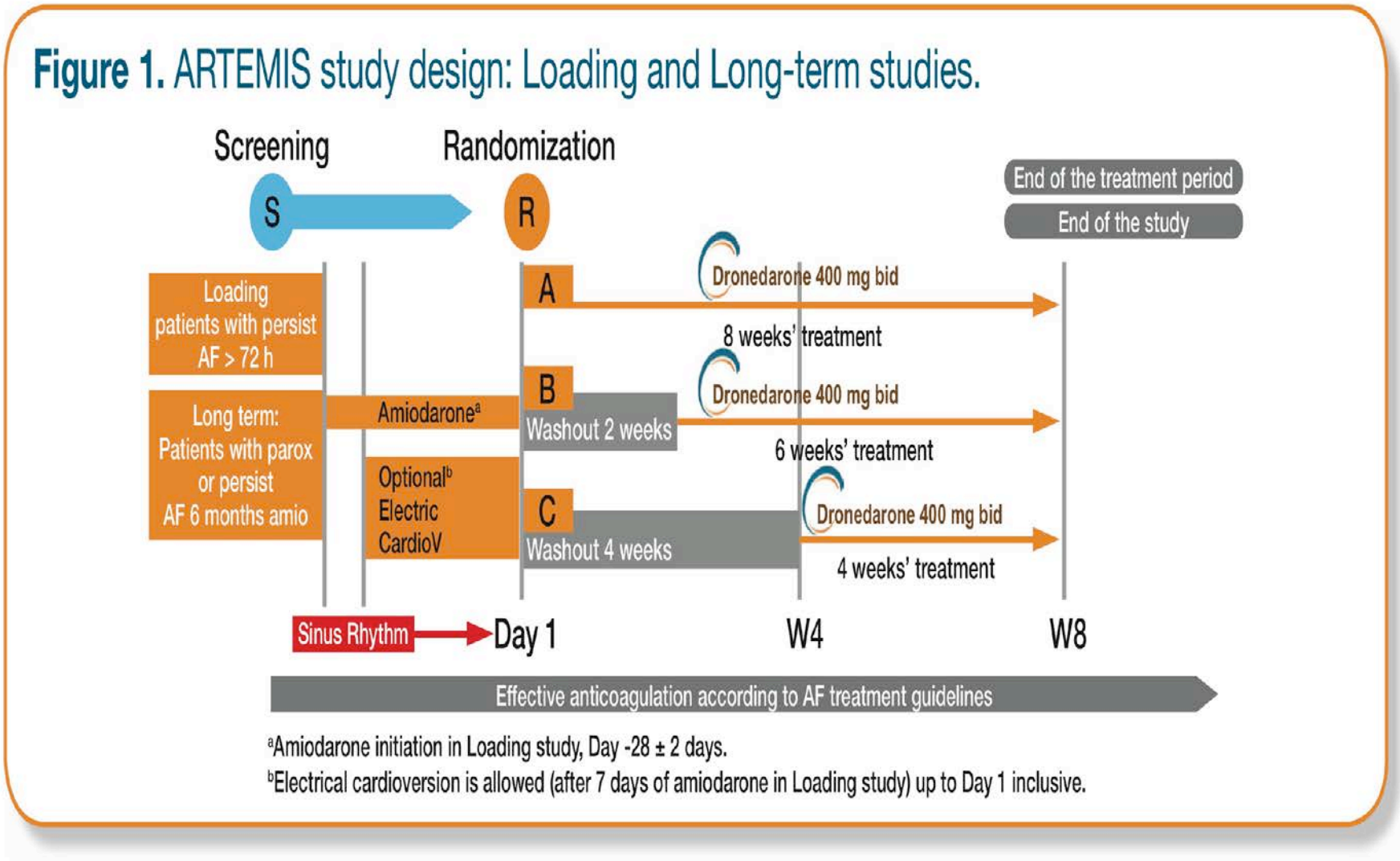
Retrospective Data from EURIDIS and ADONIS

- Suggest that a rapid switch (≤ 2 days) from amiodarone to dronedarone is feasible
- Evidence strongest in patients without low heart rates or prolonged QT intervals
- These data were exploratory and based on a small number of patients
- Further clinical investigation were needed in order to make more robust recommendations on how to optimally switch drugs

EURIDIS-ADONIS Data in Patients with Previous Amiodarone Treatment

Rate of events (%)	Amiodarone stopped within 2 days before randomization		No amiodarone before	
	Placebo n=56	Dronedarone n=98	Placebo n=334	Dronedarone n=680
Deaths	1.8	1.0	0.6	0.7
Serious adverse events	14.3	15.3	16.2	13.7
Bradyarrhythmia	0	1	0.9	1.3
Adverse events with drug discontinuation	3.6	8.2	6.3	9.1
Bradyarrhythmia	0	3.1	0	0.7
PR-interval ≥200 msec and increase ≥20 msec vs baseline	14.5	25.8	12.8	28.0
QTc-Fridericia ≥500 msec	3.6	7.9	0.3	4.4

ARTEMIS AF Loading and Long-Term : Study Design

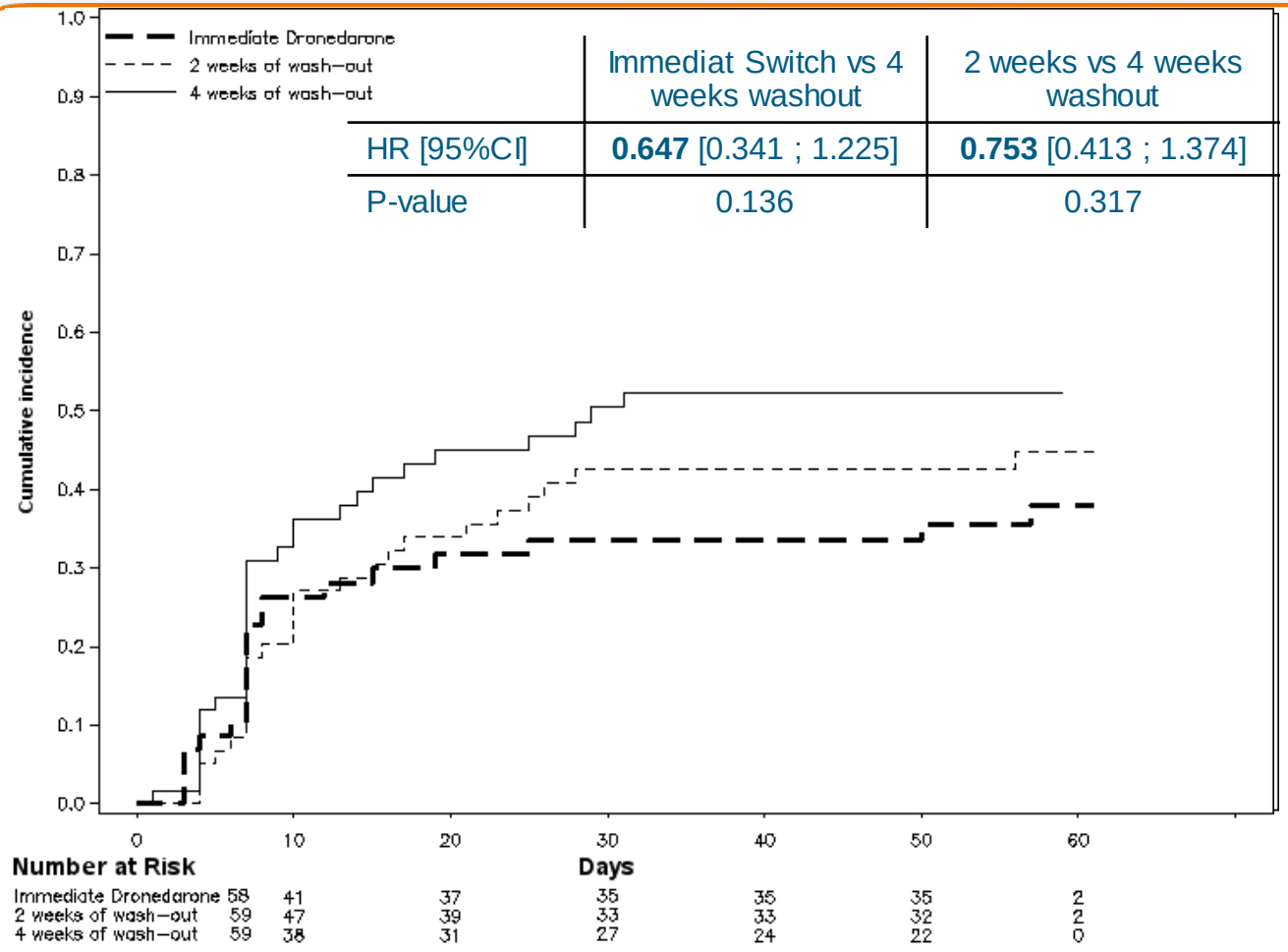


Study Follow-up

- **25th March 2010 – Initial protocol**
  - **Sample size:**
    - **860 screened patients planned**
    - **80% power to detect a decrease of AF recurrence between immediat switch and 4-weeks washout of 36.5%**
- **December 2010 – Amendment**
  - **Following 2 hepatic failures leading to liver transplantation, addition of hepatic laboratory measurements (ALT, AST and bilirubine)**
- **July 2011 – Amendment**
  - **Following the premature stop of the PALLAS study, addition of exclusion criterion at screening and randomization of LVEF < 35%**
- **October 2011 – Decision to stop the inclusions in the study**

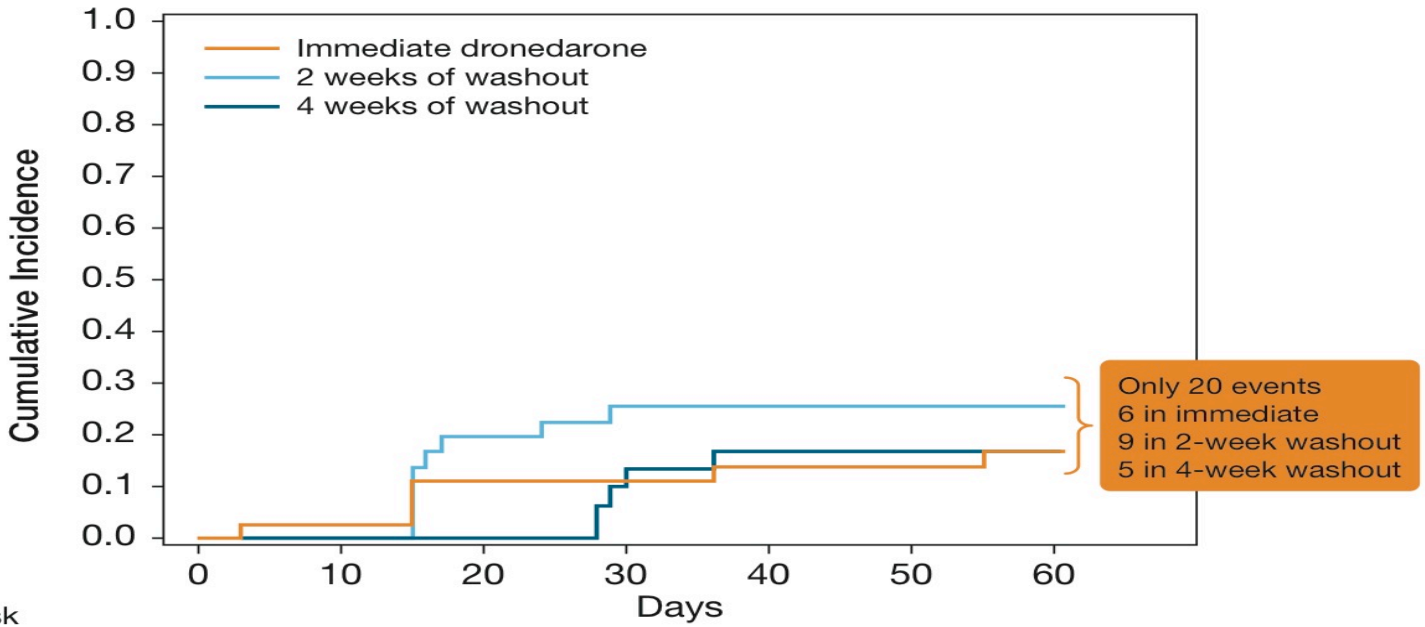
ARTEMIS AF Loading
Recurrences of Atrial Fibrillation

	Immediat Switch vs 4 weeks washout	2 weeks vs 4 weeks washout
HR [95%CI]	**0.647** [0.341 ; 1.225]	**0.753** [0.413 ; 1.374]
P-value	0.136	0.317



ARTEMIS AF Long term Recurrences of Atrial Fibrillation

Figure 3. First recurrence of AF 60 days after randomization (Long-term study)



Number at risk							
Immediate dronedarone	37	35	31	31	30	30	2
2 weeks of washout	38	36	27	23	23	22	3
4 weeks of washout	33	31	31	27	25	24	1

Cumulative incidence function with Kaplan-Meier estimates, based on adjudicated data.

ARTEMIS

SUMMARY OF CONCLUSIONS

Loading Study

- Recurrence of AF was lower in the immediate-treatment than in the 4-week washout group
- The overall safety profile was good in all groups with no increase of adverse events seen in the absence of a washout period
- Although in this small cohort of patients the tolerability of a rapid switch was acceptable, the decision of when to start dronedarone after the discontinuation of amiodarone should be taken on an individual basis, taking into account each patient's characteristics

Long-term Study

- While the overall safety profile appeared to be good in this study, few AF events were observed, and thus no firm conclusions can be drawn on the optimal time for initiation of dronedarone in patients with more than 6 months of exposure to amiodarone; further PK analysis will be required

ATHENA Baseline Patient Characteristics

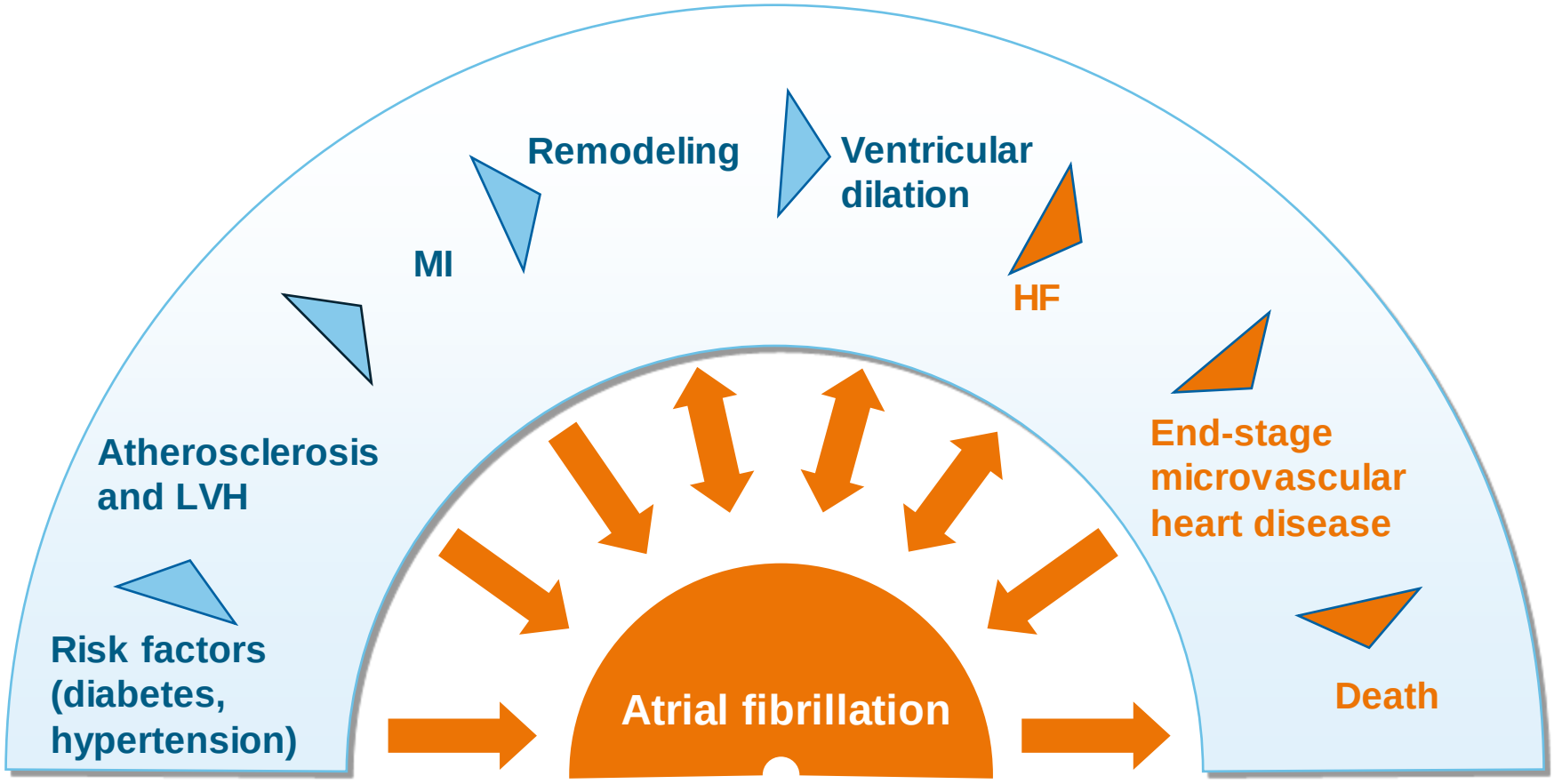
	Placebo n=2327	Dronedarone n=2301	All patients n=4628
Age (mean ±SD, years)	71.7 ±9.0	71.6 ±8.9	72 ±9.0
<65yr	442 (19.0%)	431 (18.7%)	873 (18.9%)
65 to 75yr	907 (39.0%)	923 (40.1%)	1830 (39.5%)
≥75yr	978 (42.0%)	947 (41.2%)	1925 (41.6%)
Female gender	1038 (44.6%)	1131 (49.2%)	2169 (46.9%)
AF/AFL at baseline	586 (25.2%)	569 (24.7%)	1155 (25.0%)
Structural heart disease	1402 (60.9%)	1330 (58.3%)	2732 (59.6%)
Hypertension	1996 (85.8%)	1999 (86.9%)	3995 (86.3%)
Coronary heart disease	737 (31.7%)	668 (29.0%)	1405 (30.4%)
Valvular heart disease	380 (16.3%)	379 (16.5%)	759 (16.4%)
Non-ischemic cardiomyopathy	131 (5.6%)	123 (5.3%)	254 (5.5%)
History of CHF NYHA II/III	515 (22.1%)	464 (20.2%)	979 (21.2%)
LVEF <0.45	285/2281 (12.5%)	255/2263 (11.3%)	540/4544 (11.9%)
LVEF <0.35	87/2281 (3.8%)	92/2263 (4.1%)	179/4544 (3.9%)
Lone atrial fibrillation	139 (6.0%)	140 (6.1%)	279 (6.0%)
Pacemaker	243 (10.4%)	214 (9.3%)	457 (9.9%)

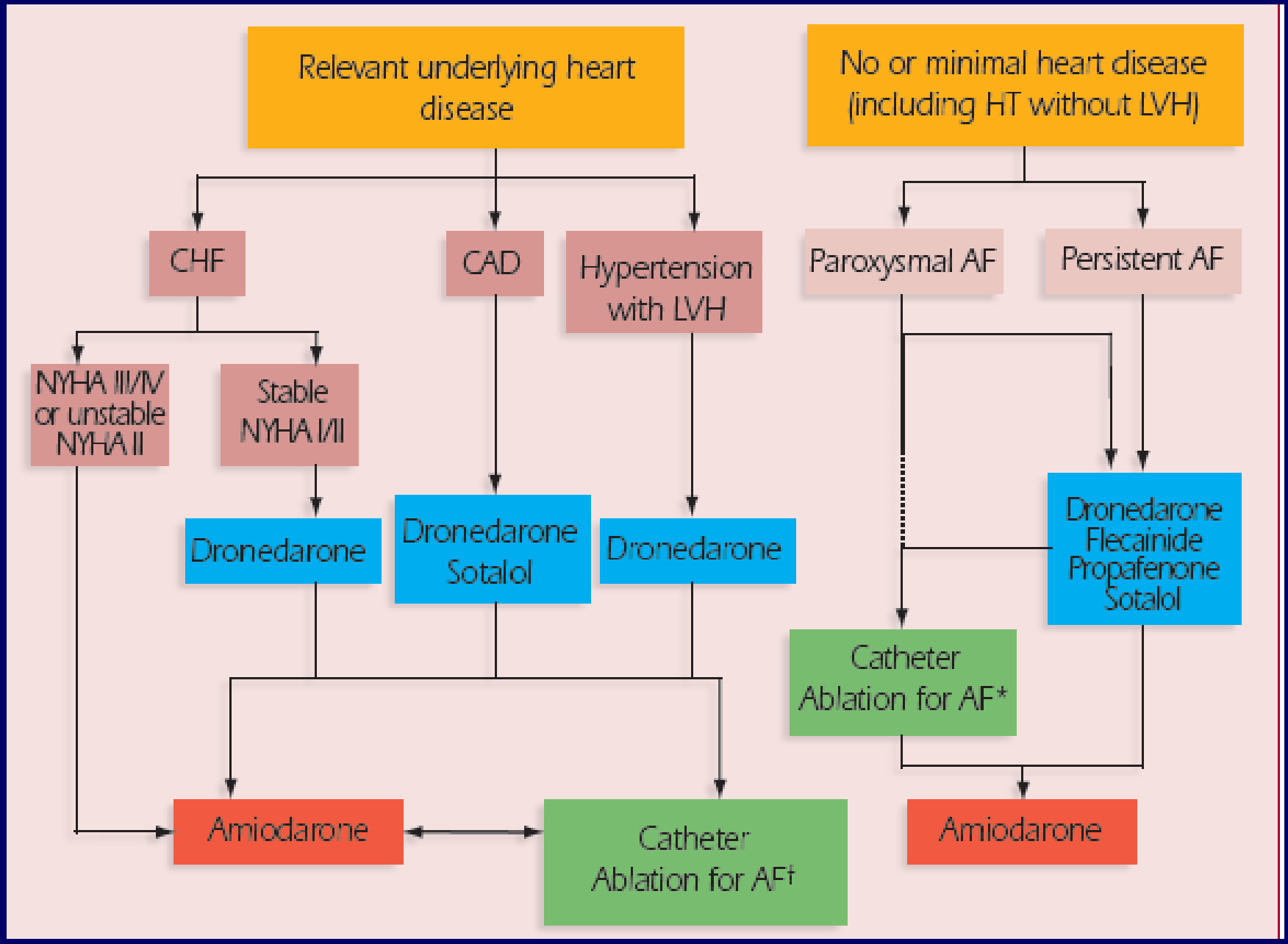
Hohnloser SH, *et al. J Cardiovasc Electrophysiol* 2008;19:69-73.

Baseline Characteristics

	Dronedarone N=1619	Placebo N=1617
Age years mean (SD)	75.0 (5.9)	75.0 (5.9)
Duration of permanent AF > 2 years	1119 (69.1%)	1124 (69.5%)
Coronary artery disease	661 (40.8%)	666 (41.2%)
Peripheral arterial disease	187 (11.6%)	213 (13.2%)
Prior Stroke or TIA	436 (26.9%)	458 (28.3%)
History of heart failure	1139 (70.4%)	1117 (69.1%)
Left ventricular ejection fraction ≤ 40%	345 (21.3%)	335 (20.7%)
Baseline use of a Beta-blocker	1201 (74%)	1201 (74%)
Baseline use of Vitamin K antagonist	1359 (84%)	1363 (84%)

Dronedarone : do not cross the red line !

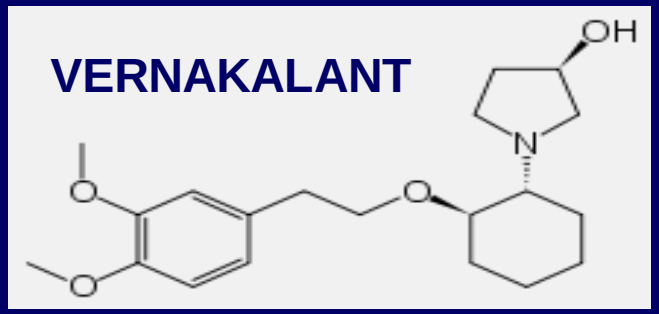


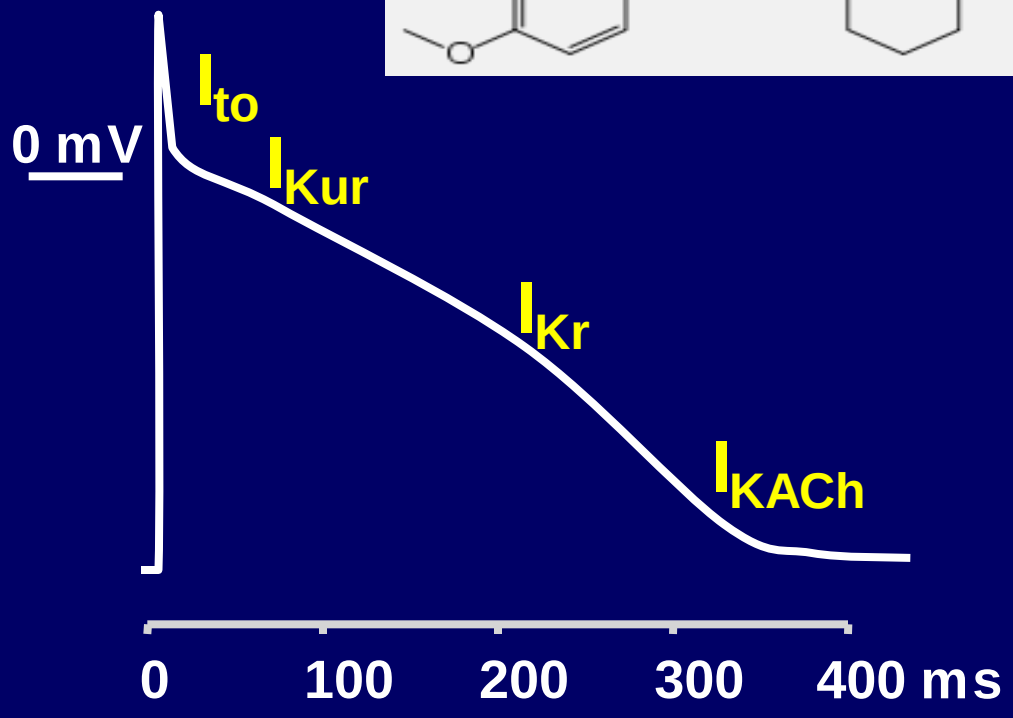


ESC GUIDELINES 2010

Figure 4 Choice of antiarrhythmic drug according to underlying pathology.

Potassium currents blocked by vernakalant, and potency



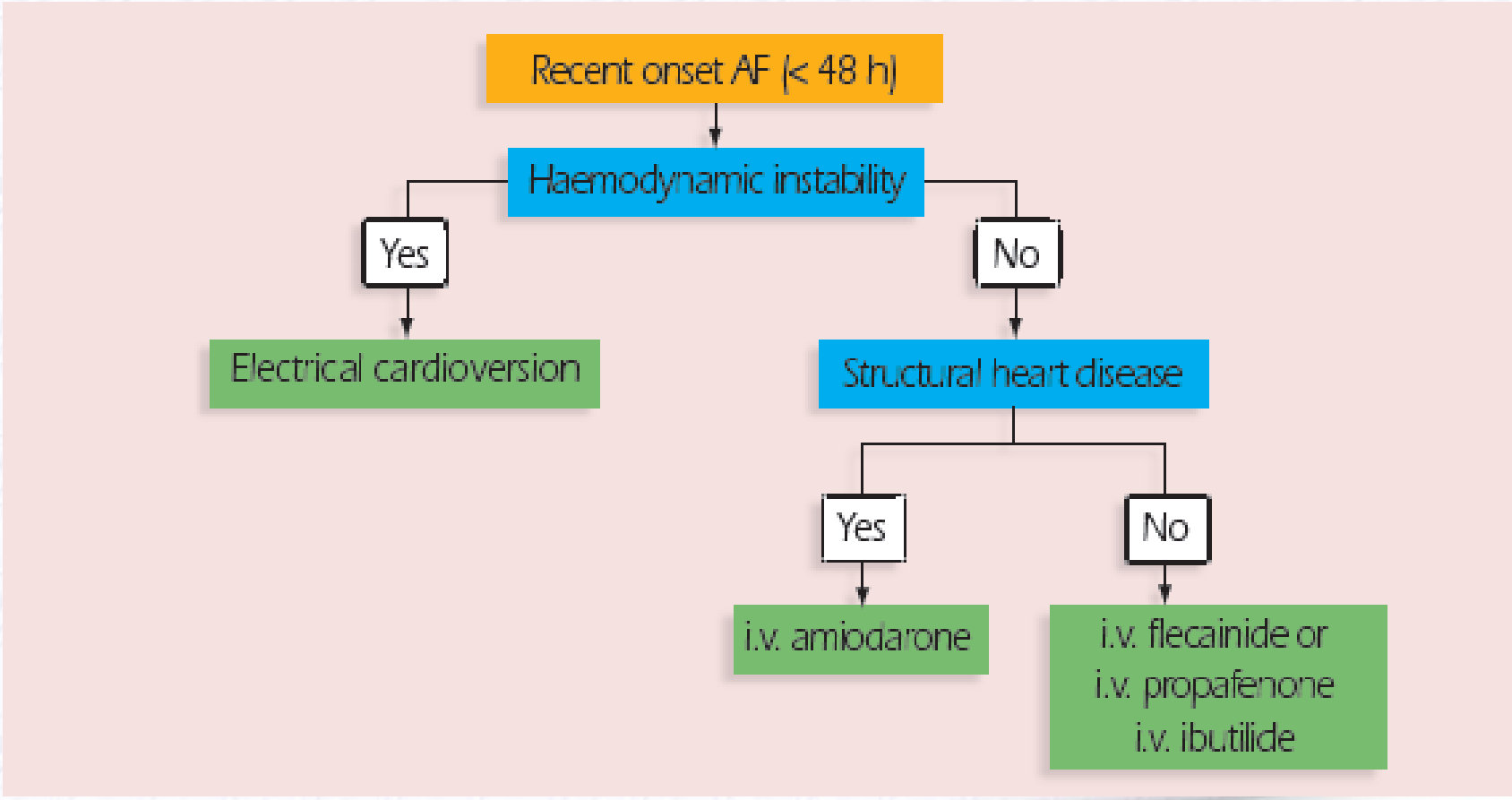


Current	IC_{50} (µM)
I_{to}	5-30
I_{Kur}	3-13
I_{KACh}	10
I_{Kr}	7-21
I_{Ks}	> 100
I_{K1}	> 100

AAD: Anti-arrhythmic drug
IC: Inhibitory concentration

Fedida et al. *J Card Electrophysiol* 2005, p1227-1238

DCC and pharmacological conversion recent-onset AF



Drugs and doses for pharmacological conversion of (recent-onset) AF

Drug	Dose	Follow-up dose	Risks
Amiodarone	5 mg/kg i.v. over 1 h	50 mg/h	Phlebitis, hypotenstion. Will slow the ventricular rate. Delayed AF conversion to sinus rhythm.
Flecainide	2 mg/kg i.v. over 10 min, or 200-300 mg p.o.	N/A	Not suitable for patients with marked structural heart disease; may prolong QRS duration, and hence the QT interval; and may inadvertently increase the ventricular rate due to conversion to atrial flutter and 1:1 conduction to the ventricles.
Ibutilide	1 mg i.v. over 10 min	1 mg i.v. over 10 min after waiting for 10 min	Can cause prolongation of the QT interval and torsades de pointes; watch for abnormal T-U waves or QT prolongation. Will slow the ventricular rate.
Propafenone	2 mg/kg i.v. over 10 min, or 450-600 mg p.o.		Not suitable for patients with marked structural heart disease; may prolong QRS duration; will slightly slow the ventricular rate, but may inadvertently increase the ventricular rate due to conversion to atrial flutter and 1:1 conduction to the ventricles.
Vernakalant	3 mg/kg i.v. over 10 min	Second infusion of 2 mg/kg i.v. over 10 min after15 min rest	So far only evaluated in clinical trials; recently approved*.

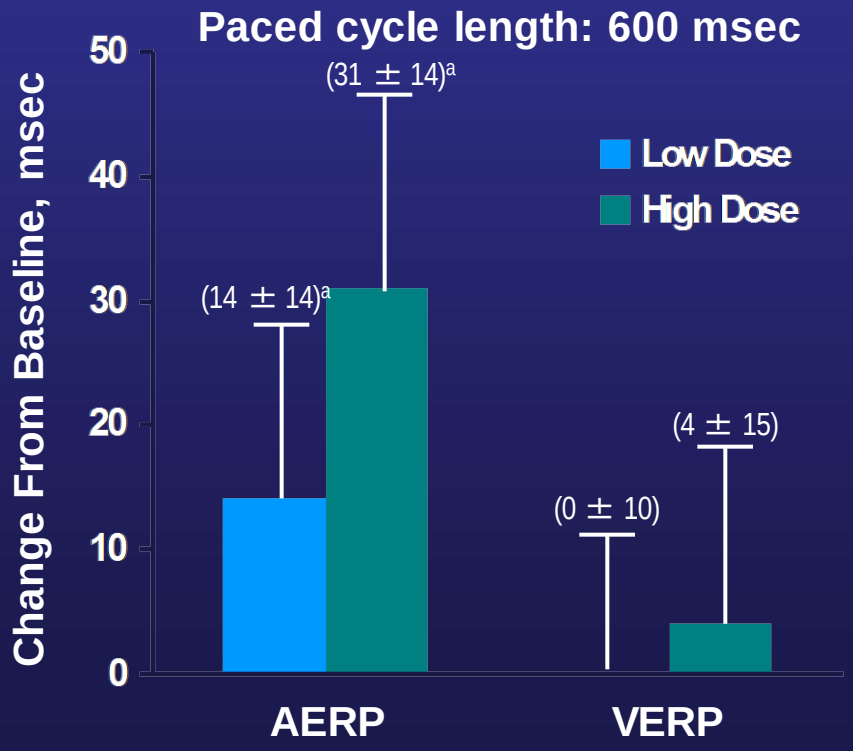
Mechanism of action: substantial antiarrhythmic effect predominant in the atria

- Vernakalant blocks important potassium currents that affect repolarization at all phases of the atrial action potential (I_{to}, I_{Kur}, I_{KACh}, I_{Kr})
- Vernakalant, at clinically relevant doses, does not inhibit I_{Ks} and I_{K1}, which are important for ventricular repolarization
- Vernakalant blocks sodium channels in a frequency- and voltage-dependent manner
- Vernakalant blocks the late component of sodium current.

Fedida D. *Expert Opin Investig Drugs* 2007;16:519-532; Fedida D et al. *J Cardiovasc Electrophysiol*. 2005;16:1227-1238.

Effect on AERP vs VERP

- In an open-label electrophysiologic study in 19 patients, vernakalant significantly prolonged atrial, but not ventricular, effective refractory period
  - Low-dose vernakalant: 2 mg/kg over 10 min + 0.5 mg/kg/h for 35 min (total dose, ~2.25 mg/kg)
  - High-dose vernakalant: 4 mg/kg over 10 min + 1 mg/kg/h for 35 min (total dose, ~4.5 mg/kg)



[a]*P*<0.05 vs baseline.
AERP=atrial effective refractory period; VERP=ventricular effective refractory period.

Dorian P et al. *J Cardiovasc Pharmacol.* 2007;50:35–40. Adapted with permission from Dorian P et al. *J Cardiovasc Pharmacol.* 2007.

Phase 3 Clinical Program Overview

	Study Population (AF/AFL Duration)	Design	Number of Patients	
			Vernakalant	Placebo/Control
ACT I Pivotal[1]	AF (3 hours-45 days)	Randomized, double-blind, placebo-controlled	221	115
ACT III Pivotal[2]	AF or AFL (3 hours-45 days)	Randomized, double-blind, placebo-controlled	134 (AFL: N=14)	131 (AFL: N=9)
ACT II Pivotal[3]	Post-cardiac surgery AF or AFL(3 hours-72 hours)	Randomized, double-blind, placebo-controlled	107 (AFL: N=7)	54 (AFL: N=4)
ACT IV[4]	AF (3 hours-45 days)	Open-label	236	NA
AVRO Pivotal[5]	AF (3 hours-48 hours)	Randomized, double-blind, active-controlled with amiodarone	116	116 (amiodarone)

AF = atrial fibrillation; AFL = atrial flutter; NA = not applicable.

1 Roy D et al. *Circulation*. 2008;117:1518–1525; 2. Pratt CM et al. *Am J Cardiol*. In press; 3. Kowey PR et al. *Circ Arrhythmia Electrophysiol*. 2009;2:652–659; 4. Stiell IG et al. *Am Heart J*. 2010;159:1095–1101; 5. EU Summary of Product Characteristics, BRINAVESS, MSD, 2010.

ACT Studies (Phase III)
Key Inclusion and Exclusion Criteria

Inclusion criteria

- ACT-I, ACT-III and ACT-IV studies
  - Age ≥ 18 years
  - Sustained (> 3 hrs up to 45 days) AF
    - ACT-III included patients with AF or atrial flutter
  - Hemodynamically stable (systolic BP >90 to <160; diastolic BP <95 mm Hg)
  - Adequate anticoagulant therapy
  - Weight 45 to 136 kg
  - Patients stratified in
    - Short-duration AF (3 hours to 7 days) (primary endpoint)
    - Long-duration AF (7-45 days)
- ACT-II study
  - Sustained AF or atrial flutter for 3 to 72 hours occurring between 24 hours and 7 days after a cardiac surgery

Exclusion criteria

- Female patients pregnant or nursing
- ECG findings:
  - Uncorrected QT interval >0.440 seconds or QRS >0.140 seconds
  - Bradycardia (<50 beats/min) or sick sinus syndrome, unless controlled by a pacemaker
- Cardiovascular disease: NYHA class IV heart failure, acute coronary syndrome, myocardial infarction, or cardiac surgery within 30 days before enrolment
- Other:
  - Failed direct-current cardioversion
  - IV antiarrhythmic therapy within 24 hrs
  - Reversible cause of AF
  - Previously failed electric conversion
  - Digoxin toxicity
  - End-stage disease, serious hepatic or renal disease
  - Uncorrected electrolyte imbalance
  - History of Torsade de Pointes (ACT II)

Roy D et al. Circulation. 2008;117:1518-25; Kowey PR et al. Circ Arrhythmia Electrophysiol 2009;2:652-9.

PROFILE OF THE PATIENTS

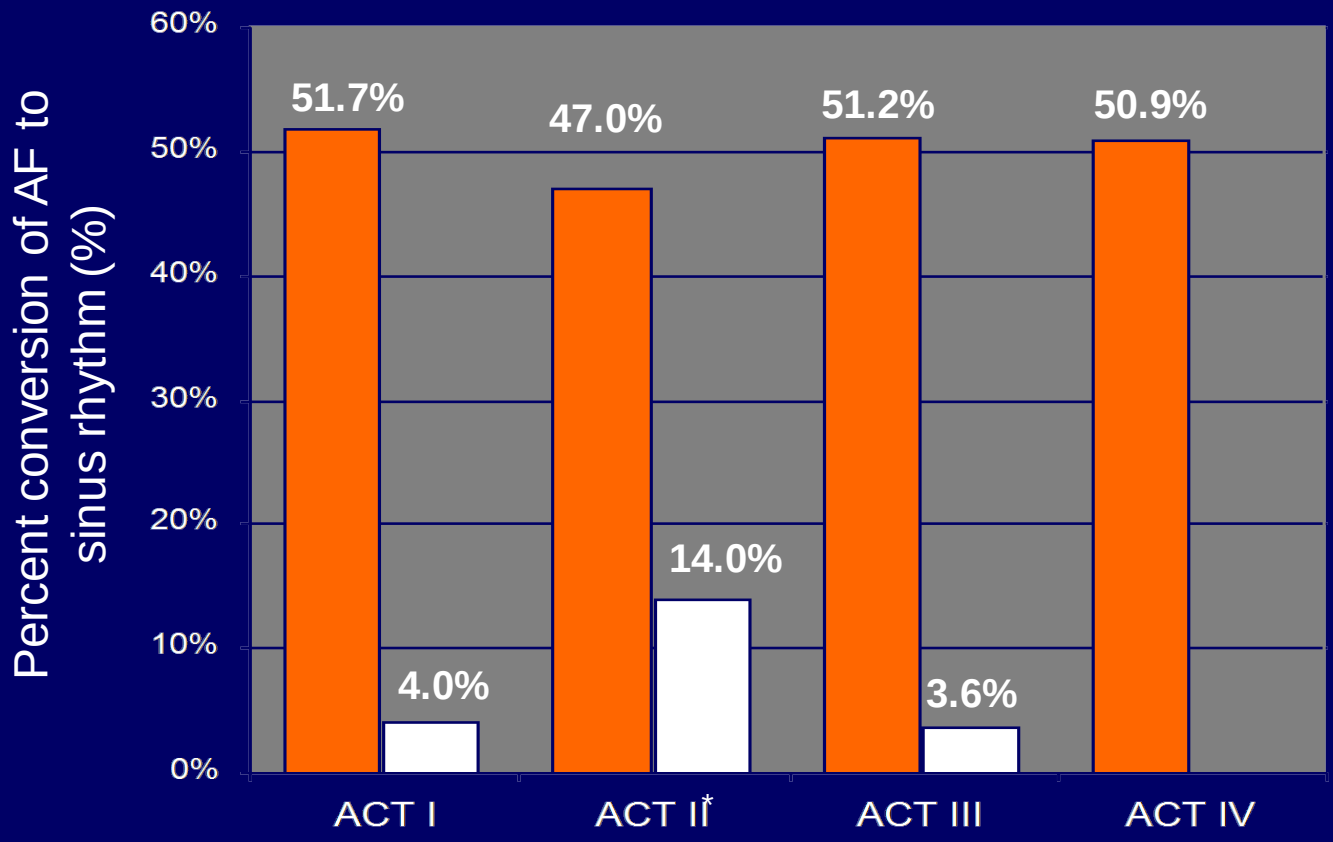
ACT I : MI 11%, CAD 20%, HT 41%, HF 14%

ACT II : CAD (bypass) 66%, valvular 26%

ACT III : MI 6%, CAD 6%, HT 48%, HF 14%

ACT IV : CAD 7%, HT 66%, HF 8%

ACT Studies (Phase III) Primary Efficacy Endpoint



p<0.001 compared to placebo in ACT I, ACT II, and ACT III

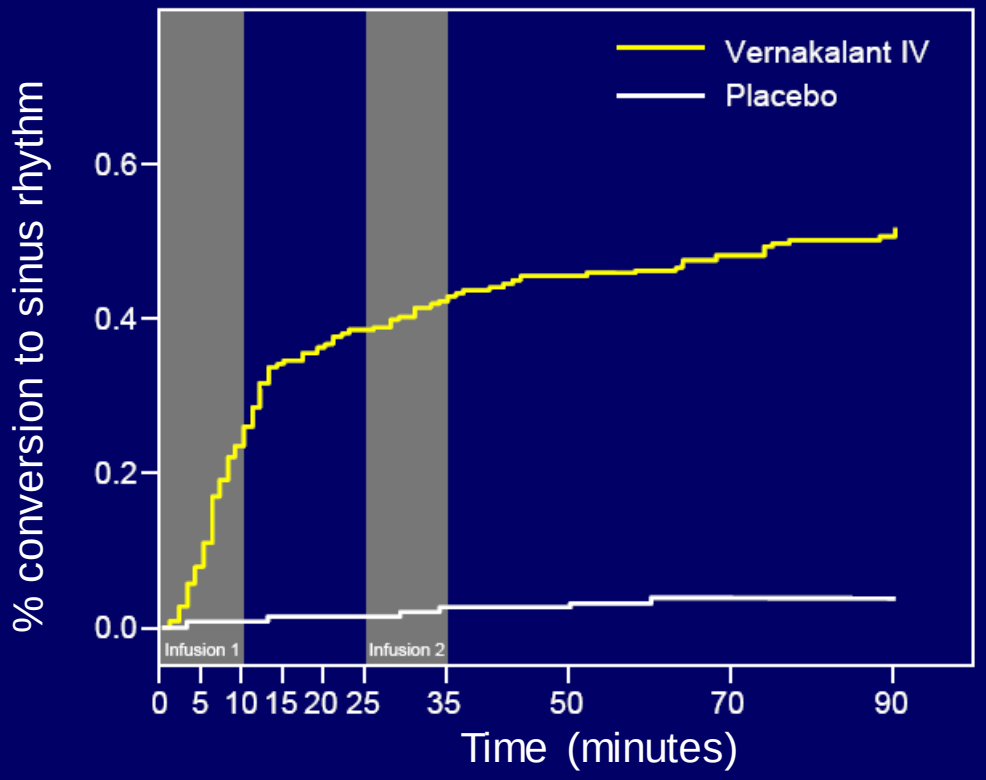
*ACT II enrolled patients with AF duration 3-72 hours.

Roy D et al. *Circulation*. 2008;117:1518-25; Kowey PR et al. *Circ Arrhythmia Electrophysiol* 2009;2:652-9.

ACT Studies (Phase III)
Other Findings

- In those patients who converted to sinus rhythm:
  - Conversion was successful with the first dose in ~75%
  - 97.2% of patients remained in sinus rhythm at 24 hours (pooled analysis of ACT I and ACT III studies)

- The median time to conversion to sinus rhythm with vernakalant was 11 minutes (pooled analysis of ACT I and ACT III studies)
- Vernakalant was not successful in terminating primary atrial flutter



Overall Safety

- Adverse events experienced most frequently in the vernakalant group were dysgeusia (taste disturbance), sneezing, paresthesia, nausea, and hypotension
- These events were generally transient and peri-infusional
- The incidence of SAEs within the first 24 hours after treatment was similar between placebo and vernakalant

Safety
Electrocardiographic Changes in ACT I Study

- **QT Interval** was slightly increased from baseline

	Baseline	Minute 10
QT interval, msec (SD)	361.5 (38.9)	386.0 (38.3)
QTcB, msec (SD)	449.3 (31.3)	473.8 (39.9)
QTcF, msec (SD)	416.8 (24.8)	441.5 (29.6)
The placebo group (not represented) did not show changes; SD: Standard Deviation		

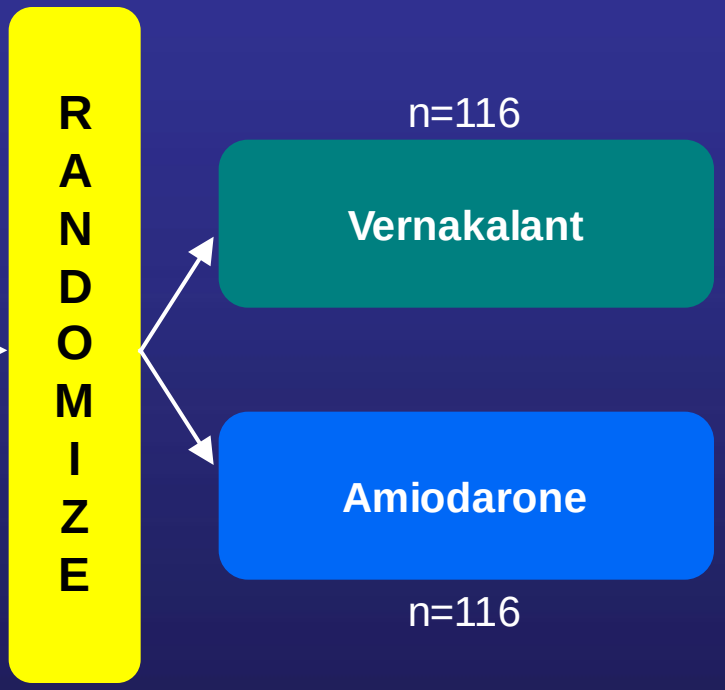
- In patients given vernakalant **who demonstrated conversion to sinus rhythm,** slight increases in QRS and QT were seen at the end of the first infusion

	Baseline	End of first infusion
QRS interval, msec (SD)	95.1 (11.9)	99.1 (12.3)
QTcF, msec (SD)	408.6 (24.1)	422.4 (22.1)
QRS and QTcF at baseline and at the end of the first infusion (Minute 10) of vernakalant in patients who converted to sinus rhythm. SD: Standard Deviation		

Roy D et al. *Circulation*. 2008;117:1518-25

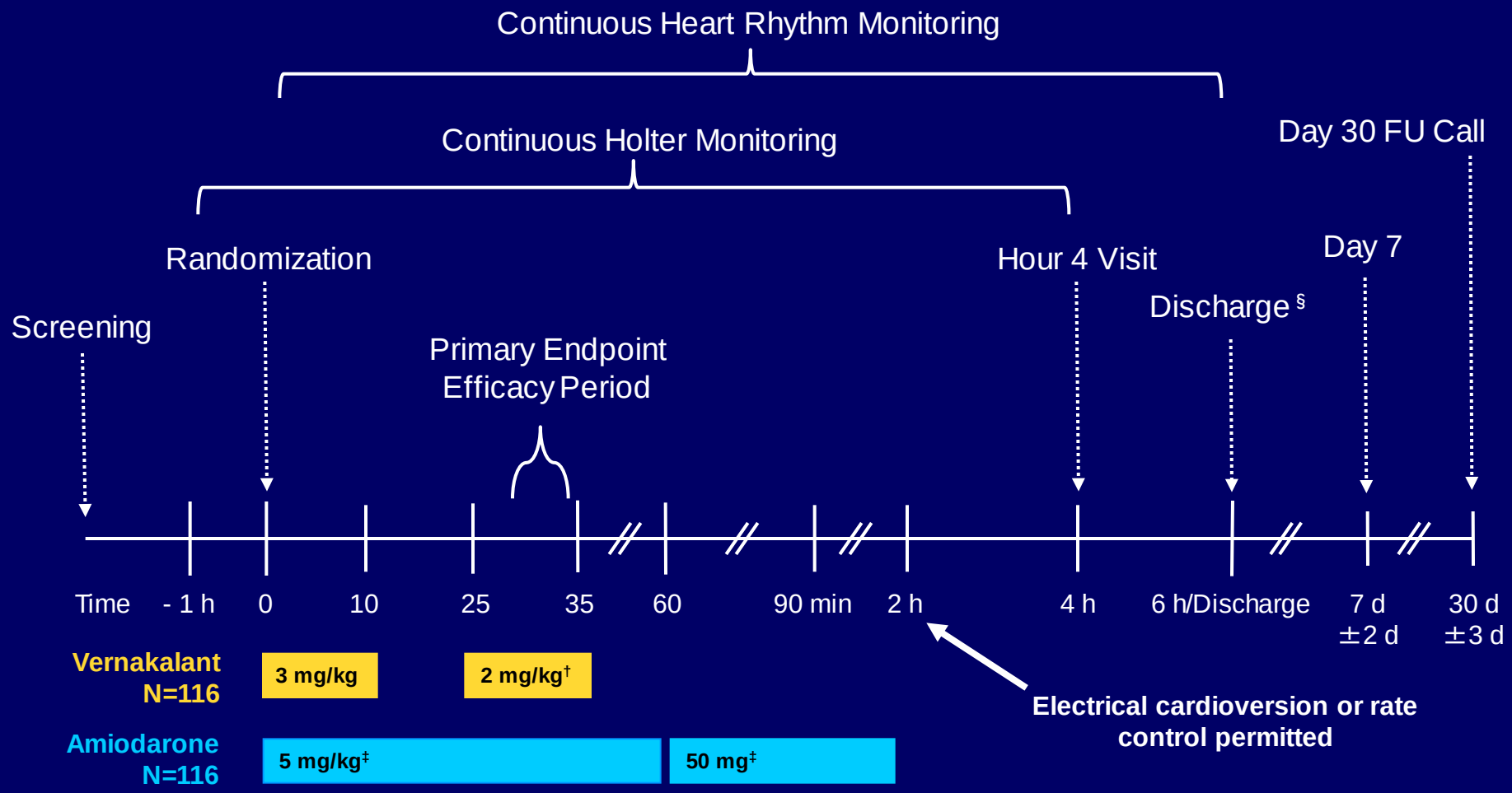
AVRO Study Design

- Phase 3, multicenter, randomized, double-blind, active-controlled trial
- Key inclusion criteria:
  - Age 18 to 85 years
  - Symptomatic AF of 3 to 48 hours duration
  - Eligible for cardioversion



- Primary endpoint: the proportion of patients in SR at 90 minutes after initiating therapy.

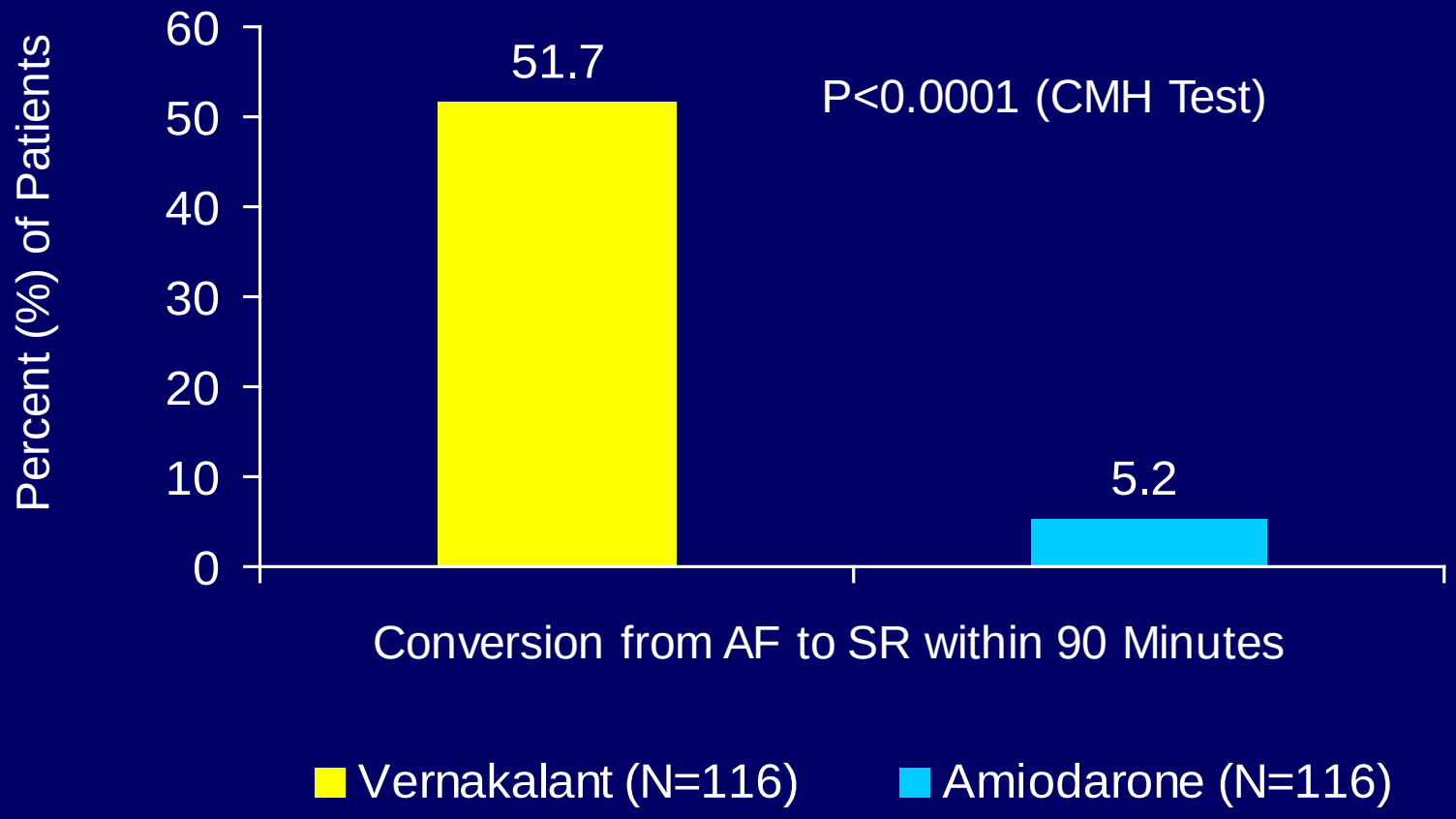
AVRO Study Design



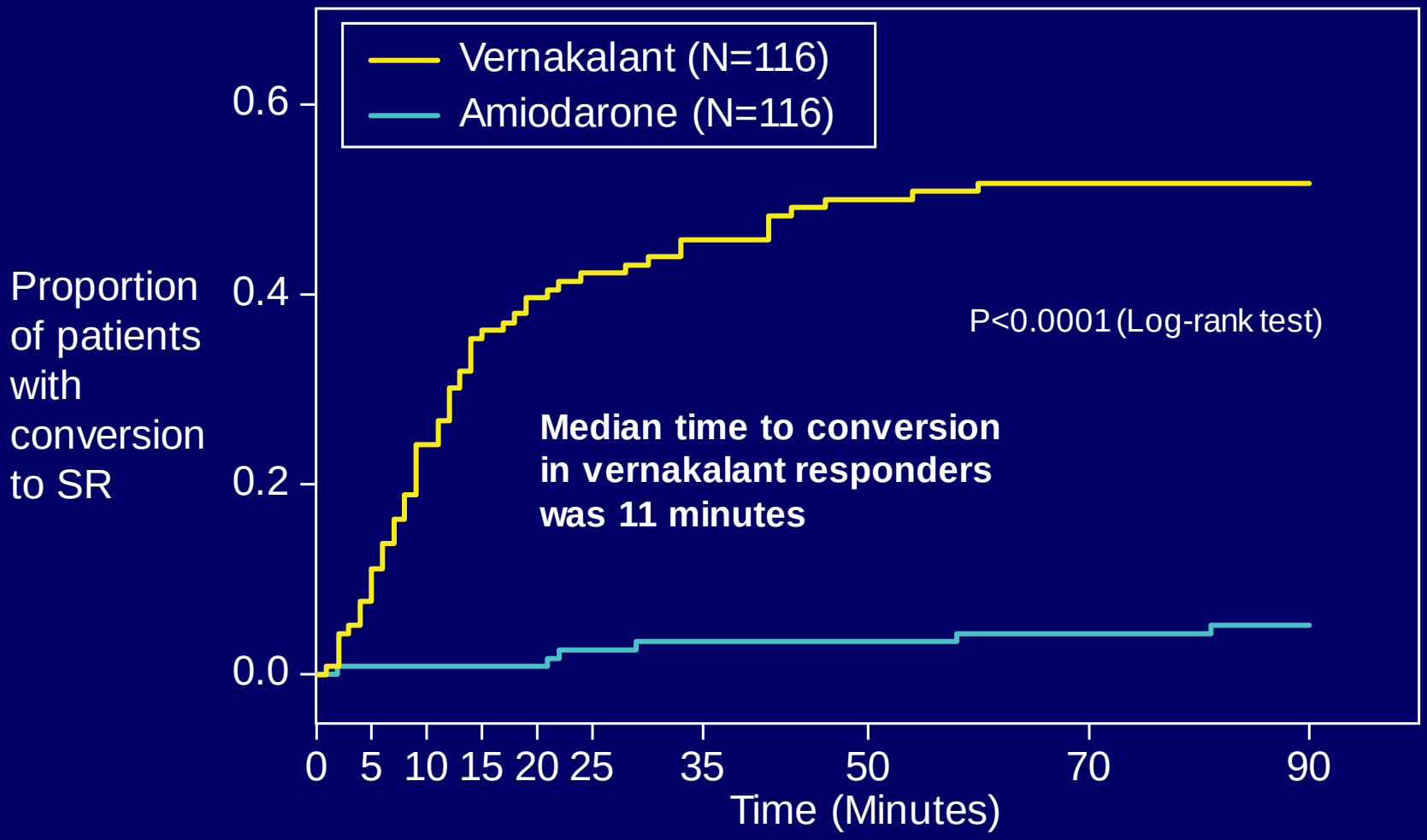
† Infusion only given if patient in AF.
‡ Infusion stopped upon conversion to SR.

§ Patient discharge was at the discretion of the investigator, but patients remained in the clinic at least 6 hours after randomization.

AVRO Primary Efficacy Endpoint: Conversion From AF to SR within 90 Minutes



AVRO Secondary Endpoint: Time to Conversion from AF to SR



AVRO Safety Summary

- There were more adverse events in the vernakalant group than the amiodarone group
- Most common side effects of vernakalant were dysgeusia (6.9%), sneezing (3.4%) and nausea (2.6%)
- One death (pulmonary embolism) in vernakalant group occurred on Day 24
- Cardiac arrest in amiodarone group occurred at 37 minutes after start of first infusion
- Ventricular arrhythmia, hypotension and bradycardia were rare and occurred at similar rates between vernakalant and amiodarone groups
- There were no cases of TdP or sustained VT
- More patients experienced AFL in the vernakalant group (8.6%) than the amiodarone group (0.9%)
- There was no 1:1 conduction of AFL

- EMEA labelling : rapid conversion of recent onset atrial fibrillation to sinus rhythm in adults
  - for non surgery patients : atrial fibrillation ≤ 7 days duration
  - for post cardiac surgery patients : atrial fibrillation ≤ 3 days duration.

- 3 mg/Kg over 10 minute period

- Caution +++ in patients with structural heart disease

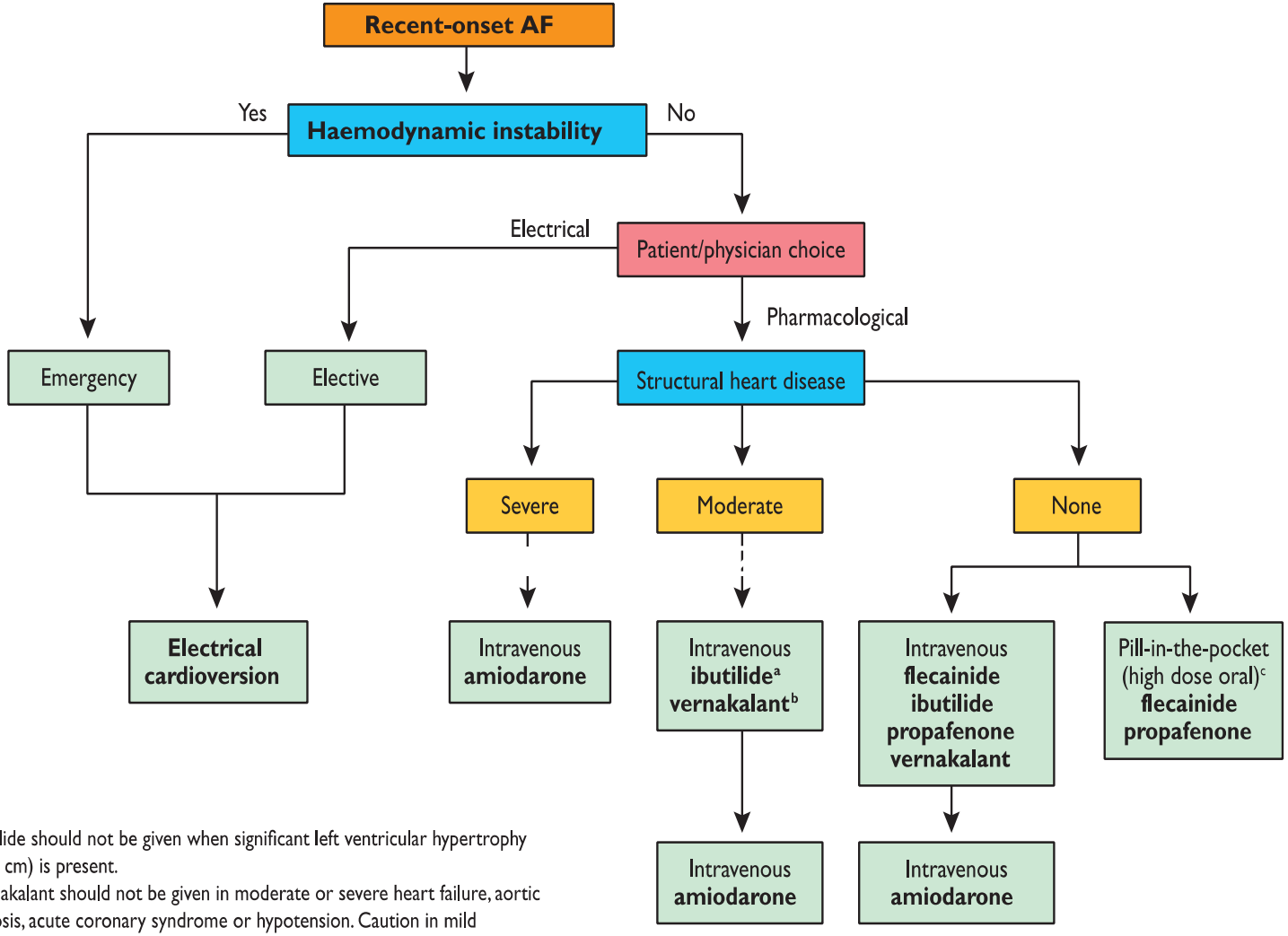
Recommendations for pharmacological cardioversion of recent-onset AF

Recommendations	Class[a]	Level[b]	Ref[c]
When pharmacological cardioversion is preferred and there is no or minimal structural heart disease, intravenous flecainide, propafenone, ibutilide, or vernakalant are recommended.	I	A	120, 121, 123, 124, 126, 127, 131–134
In patients with AF ≤7 days and moderate structural heart disease [but without hypotension <100 mm Hg, NYHA class III or IV heart failure, recent (<30 days) ACS, or severe aortic stenosis], intravenous vernakalant may be considered. Vernakalant should be used with caution in patients with NYHA class I–II heart failure.	IIb	B	120, 121, 124, 128
Intravenous vernakalant may be considered for cardioversion of postoperative AF ≤3 days in patients after cardiac surgery.	IIb	B	122

on; LoE = level of evidence;

NYHA = New York Heart Association.
[a]Class of recommendation.
[b]Level of evidence.
[c]References.

ESC GUIDELINES 2012 UPDATE



[a]Ibutilide should not be given when significant left ventricular hypertrophy (≥1.4 cm) is present.
[b]Vernakalant should not be given in moderate or severe heart failure, aortic stenosis, acute coronary syndrome or hypotension. Caution in mild heart failure.
[c]'Pill-in-the-pocket' technique – preliminary assessment in a medically safe environment and then used by the patient in the ambulatory setting.

ESC GUIDELINES 2012 UPDATE

hmic drugs for pharmacological cardioversion

in patients with recent-onset AF.

CONCUSIONS

In the update of ESC Guidelines published two months ago :

- Dronedarone is now contra-indicated in ALL patients with heart failure and / or left ventricular dysfunction (and history of) and in patients with permanent atrial fibrillation

- Vernakalant is recommended for intravenous pharmacological cardioversion of atrial fibrillation but must be used with caution in patients with structural heart disease

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